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THE PROTEIN SCIENCE WEEK

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18th Annual

PEPTALK 2019

THE PROTEIN SCIENCE WEEK

January 14-18, 2019
Hilton San Diego Bayfront
San Diego, CA

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ONE OF THE LARGEST ANNUAL GATHERINGS OF PROTEIN SCIENCE RESEARCHERS IN THE WORLD!

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WELCOME TO SAN DIEGO!

PepTalk: The Protein Science Week is one of the largest annual gatherings of protein science researchers in the world. Now, in its 18th year, PepTalk features renowned speakers from academia, biotech and pharma who bring global expertise and perspective to the forefront. An international delegation of over 1,300 participants will convene for intensive learning and networking to discover new opportunities, apply alternative solutions, and develop promising partnerships.

Conference Programs feature keynote presentations, case studies and new unpublished data from top influential leaders in academia and industry.

Training Seminars (1.5 days) offer focused instruction in topics related to your field using a mix of lecture and interactive discussion formats and are led by experienced instructors. These may be combined with conferences to customize your week at PepTalk.

Dinner Short Courses (3 hours) offer a unique, intimate setting to delve into a particular topic. Each course provides a great introduction for those who are new to a discipline or a helpful refresher for those who want to brush up on their knowledge or expand their horizons.

Exhibit Hall provides face-to-face networking with Technology & Service Providers ready to share their latest products and services.

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EVENT AT-A-GLANCE

PART A Mon. - Tue. AM | Jan. 14-15	PART B Tue. PM - Wed. | Jan. 15-16	PART C Thu. - Fri. | Jan. 17-18
Recombinant Protein Therapeutics	Computational and Analytical Tools for Protein Engineering	Deep Sequencing and Single Cell Analysis for Antibody Discovery
Advancing CNS Biotherapeutics and Crossing the Blood-Brain Barrier	Next-Generation Approaches to Antibody Screening and Discovery	Deep Sequencing and Single Cell Analysis for Antibody Discovery
Engineering Next-Generation Cancer Immunotherapies	Antibody-Drug Conjugates	Bispecific Antibody Therapeutics
Optimizing Biologics Formulation Development	Lyophilization and Emerging Drying Technologies	Protein Aggregation and Emerging Analytical Tools
Characterization of Biotherapeutics	Detection and Characterization of Particulates and Impurities	Protein Aggregation and Emerging Analytical Tools
Bioprocess Data Management	Protein Purification and Recovery	Higher-Throughput Protein Production and Characterization
Engineering Genes, Vectors, Constructs, and Clones	Recombinant Protein Expression and Production CHO Cell Lines	Optimizing Expression Platforms
Engineering Genes, Vectors, Constructs, and Clones	Advances in Vector Production and Scale-Up for Cell and Gene Therapy	Microbial Production
> Introduction to Bioprocessing > Introduction to Antibody Engineering > Fundamentals of Proteins and Protein Solutions	> Next-Generation Approaches to Antibody Screening and Discovery > Introduction to Biologics Formulation Development > GMP and Validation Requirements for Biologics Processes – Phase I through to Commercial Manufacturing	

Tue. PM Dinner Short Courses

WEDNESDAY, JANUARY 16 | 2:00 - 3:05 PM

PLENARY KEYNOTE PANEL

PepTalk Perspectives:
Point-Counterpoint Discussions

POINT:
"Change is inevitable. Progress is a choice."
Dean Lindsey

COUNTERPOINT:
"Permanence, perseverance, and persistence in spite of all obstacles, discouragements, and impossibilities: It is this, that in all things distinguishes the strong soul from the weak."
Thomas Carlyle

IT IS HUMAN NATURE to resist change, especially in the ultraconservative biopharmaceutical industry. Despite this, there is a corresponding desire to make things better whenever possible. However, do advances in technology always result in progress? By design, PepTalk's eight Pipelines cover a range of topics from R&D discovery to product development where exciting new developments are presented, each with the potential to have significant impact on the discovery and product development lifecycle. Are these changes universally positive? The positive-negative viewpoint may differ depending on a company's or individual's perspective.

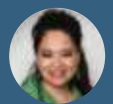
In thought-provoking point-counterpoint discussions, panelists address the impact and implications of new technology and other advances on accelerating biopharma product development, with topics including:

- Dealing with Regulatory Reform
- Pros and Cons of Accelerating Time to Market
- Impact of Implementing New Technologies
- Impact of Adopting New Therapies and Targets
- What, Where, and When Impact of Big Data

Moderator:

Howard Levine, PhD, *President and CEO, BioProcess Technology Consultants*

Panelists:



Zhimei Du, PhD, *Director Bioprocess & Clinical Manufacturing, Merck*

Lorenz Mayr, PhD, *CTO, GE Healthcare Life Sciences*

Additional Panelists to be Announced

Present Your Research Poster at PepTalk!

Gain exposure by presenting your work in the PepTalk poster sessions!

- Your poster will be seen by our international delegation, representing leaders from top pharmaceutical, biotech, academic and government institutions.
- Receive $50 off your registration.
- Your poster abstract will be published in our conference materials.
- You will automatically be entered in the poster competition.
- STUDENT FELLOWSHIPS
  Students are encouraged to present a research poster and qualify as a student fellow of the event.

Students must present a valid/current student ID to qualify for the student rate.

To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by November 16, 2018.

Training SEMINARS

By Cambridge Healthtech Institute

Please visit CHI-PepTalk.com to view detailed agendas for each Training Seminar

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

SUNDAY, JANUARY 13 | PRE-CONFERENCE REGISTRATION 4:00 - 6:00 PM

MONDAY, JANUARY 14 - TUESDAY, JANUARY 15

DAY 1: MONDAY

9:00 am - 6:00 pm ..... **Seminar Sessions**

12:30 - 2:00 pm ..... **Lunch Provided**

3:15 - 4:30 pm ..... **BuzZ Sessions**

6:00 - 7:15 pm ..... **Welcome Reception**

DAY 2: TUESDAY

8:30 am - 12:30 pm ..... **Seminar Sessions**

Exhibit Hall Refreshment Breaks also provided.

TS8A: Introduction to Bioprocessing
CHI's Introduction to Bioprocessing training seminar offers a comprehensive survey of the steps needed to produce today's complex biopharmaceuticals, from early development through commercial. The seminar steps through the stages of bioprocessing, beginning with cell line development and ending at scaling up for commercial production. The seminar also explores emerging process technologies, facility design considerations and the regulatory and quality standards that govern our industry throughout development. The important roles of analytical methods and formulation development are also examined.
Instructors:

Sheila G. Magil, PhD, Senior Consultant, BioProcess Technology Consultants, Inc.

Frank J. Riske, PhD, Senior Consultant, BioProcess Technology Consultants, Inc.

TS9A: Introduction to Antibody Engineering
In this training seminar, students will learn about antibody basics, including structure, genetics and the generation of diversity, as well as the generation of potential therapeutic antibodies. This latter part will include antibody humanization, affinity and specificity maturation, display technologies, creation of naïve libraries and antibody characterization. The seminar will be fully interactive with students provided with ample opportunities to discuss technology with instructors.
Instructors:

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

James D. Marks, MD, PhD, Chief of Staff, Chief of Performance Excellence, Zuckerberg San Francisco General Hospital and Trauma Center; Professor of Anesthesia, UCSF Department of Anesthesia and Perioperative Care

TS10A: Fundamentals of Proteins and Protein Solutions
A simple energy framework is presented that allows a fundamental, but very practical, understanding of protein structure, folding, stability, interactions and solution behavior. The seminar focuses on the practical understanding and application of the energy framework. Building on a review of basic biochemistry and central energy concepts, the framework is used to build up a deeper understanding of how protein folding and structure arise from the properties of its constituent atoms and amino acids. This same energy framework is used to understand protein interactions with small molecules, surfaces, other proteins, and other macromolecules. The importance of cooperativity to biological processes is discussed.
Instructor:

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

TUESDAY, JANUARY 15 - WEDNESDAY, JANUARY 16

DAY 1: TUESDAY

2:00 - 5:30 pm ..... **Seminar Sessions**

DAY 2: WEDNESDAY

8:15 am - 6:05 pm ..... **Seminar Sessions**

12:15 - 1:30 pm ..... **Lunch Provided**

6:05 - 7:00 pm ..... **Networking Reception**

Exhibit Hall Refreshment Breaks also provided.

TS2B: Next-Generation Approaches to Antibody Screening and Discovery
Over the space of a few years, DNA sequencing and data analysis, DNA synthesis, single-cell isolation, and genome engineering using CRISPR/Cas9 have improved greatly in both capability and affordability and have now been adapted to enhance the discovery and development of antibodies and other immunotherapies. This training seminar will evaluate these new developments and their applications in antibody and immunotherapy discovery and development.
Instructor:

David Bramhill, PhD, Founder, Bramhill Biological Consulting, LLC

TS10B: Introduction to Biologics Formulation Development
In this training, you will learn strategies to plan and execute preformulation and formulation development studies for biologics. The seminar offers an overview of biophysical and biochemical properties of proteins and protein structure, then continues with an exploration into the theory and application of the relevant analytical and biophysical techniques that support preformulation and formulation development studies. The seminar provides an in-depth discussion of typical formulation development workflows, including statistical analysis and use of DoE, and an examination of real-world case studies.
Instructor:

Donald E. Kerkow, PhD, Director, Biopharmaceutical Development, KBI Biopharma, Inc.

TS11B: GMP and Validation Requirements for Biologics Processes – Phase I through to Commercial Manufacturing
This seminar looks at the current requirements and expectations for GMP manufacturing and testing at all stages of the product lifecycle, from Phase I through all clinical phases to commercial manufacturing and maintaining validated status. It will cover phase-appropriate GMP and the evolution of the pharmaceutical quality system to address the requirements at different phases of development and of the commercial product lifecycle. It will also look at how the challenges can vary for different types of biological products. Topics covered will include the regulatory background, process and analytical development, process knowledge, and the impact of single-use systems, process qualification, continuous process verification, and specific considerations for challenging and/or unusual processes, including live vaccines and cell therapy products.
Instructor:

Trevor Deeks, PhD, QA/QC and GMP Consultant, Deeks Pharmaceutical Consulting Services, LLC

TRAINING SEMINAR INFORMATION

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

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

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

TUESDAY, JANUARY 15 | 5:45 - 8:45 PM

DINNER SHORT COURSES*

SC1: Introduction to CAR-T Engineering for Protein Scientists
While great strides have been made in CAR functionality, much remains to be done in expanding the reach of CARs beyond hematologic malignancies, addressing tumor escape by engineering multiple CAR targets, and building regulatory capacities into CAR cells to avoid toxicity issues. This course explores the past, present, and future of CAR design with an eye toward making CARs a "plug and play" system and circumventing the empirical and expensive CAR optimization previously required for clinical relevance.
Instructor:
Brian Webster, PhD, R&D Scientist, Lentigen Technology

SC2: Structure-Based Optimization of Antibodies
CHI's "Structure-Based Optimization of Antibodies" is a 3-hour lecture offering a quick overview to the concepts, strategies and tools of structure-based optimization of antibodies. This lecture will cover structure-based techniques to modulate affinity, create novel constructs (such as Fc-fusions, bispecifics, etc.) along with increasing the manufacturability of a biologic. The class is directed at scientists new to the industry, academic scientists, and career protein engineers wanting a quick overview about how structure can aid in guiding experimental design.
Instructor:
Christopher Corbeil, PhD, Research Officer, Human Health Therapeutics, National Research Council Canada

SC3: Protein Aggregation: Mechanism, Characterization and Consequences
Protein aggregation is recognized by regulatory agencies and the biopharmaceutical industry as a key quality attribute of biotherapeutics. Various aggregates hold the potential for adversely impacting production and patients in a variety of ways. This in-depth course reviews the origins and consequences of aggregation in biotherapeutics, and then examines strategies for predicting and quantifying aggregation in biopharmaceuticals. It benefits scientists engaged in development, production, analytical characterization and approval of biotherapeutics, and who require a good working knowledge of protein aggregation.
Instructor:
Thomas Laue, PhD, Professor Emeritus, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire

SC4: Immunogenicity for Biologics
All protein drugs generate an immunogenic response. This short course provides a practical, comprehensive overview of immunogenicity – the causes, how to assess, predictive tools and what to do if you observe immunogenicity during preclinical, clinical and post-market approval. Focus will also be given to immunogenicity for immuno-oncology therapies.
Instructor:
Sofie Pattijn, CTO, ImmunXpert

SC5: Transient Protein Production in Mammalian Cells
A variety of mature protein production systems exist that can be used to create an expression toolbox to address protein production challenges. This short course focuses on transient protein production in mammalian cells including the concepts, technologies, and optimization strategies needed for the rapid generation 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 directed towards intermediate-level scientists, but is still appropriate for expression scientists of all experience levels.
Instructors:
Richard Altman, MS, Scientist, Protein Technologies, Amgen
Henry C. Chiou, PhD, Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific
Additional Instructors to be Announced

PROTEIN ENGINEERING & DEVELOPMENT

As biologics gain greater prominence, protein engineers are adapting to new indications, new advances in targeting science, new product formats, and products that are truly differentiated in the marketplace. The Protein Engineering & Development pipeline offers a weeklong exploration of state-of-the-art approaches for developing safe and effective protein and antibody-based therapeutics, including improving product qualities, emerging computational and analytical technologies, and the application of deep sequencing and single cell analysis.

JANUARY 14-15

AGENDA Recombinant Protein Therapeutics

JANUARY 15-16

AGENDA Computational and Analytical Tools for Protein Engineering

JANUARY 17-18

AGENDA Deep Sequencing and Single Cell Analysis for Antibody Discovery

Also part of **INNOVATIONS IN DISCOVERY & DEVELOPMENT**

MONDAY-TUESDAY, JANUARY 14-15 | 15TH ANNUAL

RECOMBINANT PROTEIN THERAPEUTICS

Fusion Proteins and Beyond

CAMBRIDGE HEALTHTECH INSTITUTE'S 15th Annual Recombinant Protein Therapeutics conference presents the latest developments in non-antibody therapeutics from international leaders. The conference focuses on the varying designs of fusion protein-based therapeutics and the latest data from R&D to post-approval, including case studies. By combining modular building blocks that can reach targets not accessible to antibodies, Fusion Protein Therapies possess advantages over antibody-based therapies; their customizable functionality translates into lower patient dosing, reduced production costs, and improved product homogeneity. This conference will demonstrate how these molecules are being engineered to form more efficacious therapeutics that offer specificity with enhanced stability and longer half-life.

SUNDAY, JANUARY 13

4:00 - 6:00 pm Pre-Conference Registration

MONDAY, JANUARY 14

7:00 am Registration and Morning Coffee

ANALYZING & CHARACTERIZING THERAPEUTIC FUSION PROTEINS

9:00 Welcome by Conference Organizer
Mary Ruberry, Senior Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks
Uli Binder, MSc, CTO, XL-protein GmbH

KEYNOTE PRESENTATION

9:10 The Evolving Science and Long-Term Outcomes of Fc Fusion Factors
Jennifer Dumont, PhD, Executive Director, Medical Affairs, Bioverativ, Inc.

9:50 Selection of the Recommended Phase II Dose for M7824, a Bifunctional Fusion Protein Targeting TGF-β and PD-L1
Yulia Vugmeyster, PhD, Associate Director, Clinical Pharmacology, EMD Serono R&D Institute, Inc.
M7824 (MSB0011359C) is an innovative, first-in-class, bifunctional fusion protein composed of a human IgG1 mAb against PDL1 fused with two extracellular domains of TGF-β receptor II to function as a TGF-β "trap." The selection of the recommended Phase II dose (RP2D) for M7824 will be presented. The current RP2D dose selection is informed by preclinical and clinical data, such as tolerability/safety, efficacy, pharmacokinetic and pharmacodynamic profiles, and is supported by the population PK and exposure-response modeling.

10:20 Networking Coffee Break

FIGHTING DISEASE WITH THERAPEUTIC FUSION PROTEINS

10:45 Proinsulin-Transferrin Fusion Protein to Overcome Insulin Resistance
Wei-Chiang Shen, PhD, John A. Biles Professor, Pharmacology and Pharmaceutical Sciences, University of Southern California School of Pharmacy
We have previously shown that proinsulin-transferrin fusion protein (ProINS-Tf) is a highly liver-targeted and long-lasting insulin analog for the treatment of diabetes in mouse models. Recently, we have found that the liver-activated ProINS-Tf, due to simultaneous binding to both transferrin and insulin receptor, can overcome insulin-resistance in cell cultures and in NOD mice. ProINS-Tf can serve as a model of insulin analogs for treating insulin-resistance in diabetes and other diseases.

11:15 IL-DR2 Fc Is a Novel Regulator of Immune Homeostasis and Inducer of Antigen-Specific Tolerance
Stephen D. Miller, PhD, Judy Gugenheim Research Professor, Director, Interdepartmental Immunobiology Center, Microbiology-Immunology, Northwestern University Medical School
ILDR2 is a member of the Ig superfamily and has a putative role in pancreatic islet health and survival. We recently found a novel role for ILDR2 in delivering inhibitory signals to T cells. ILDR2-Fc displays a unique mode of action, combining immunomodulation, regulation of immune homeostasis, and re-establishment of Ag-specific immune tolerance via induction of regulatory T cells. These findings support the potential of ILDR-Fc as a promising therapeutic approach for the treatment of autoimmune diseases.

11:45 xB^3 Platform Delivers a Protein-Based Interleukin 1 Receptor Antagonist across the BBB and Ameliorates Neuropathic Pain in a Preclinical Model
Mei Mei Tian, PhD, Vice President and Head, External Research, Bioasis Technologies, Inc.
Utilizing a 12 amino-acid peptide, xB^3, we have shown improved brain delivery of antibody payload. xB^3-antibody fusion demonstrated similar plasma kinetics to control antibody, however, with significantly increased brain exposure for the duration of the study. In a neuropathic pain model, fusion to interleukin-1receptor antagonist is able to induce significant and durable analgesia following peripheral administration. These data demonstrate the utility of xB^3 in delivering therapeutic levels of drug to the brain.

12:15 pm Sponsored Presentation
(Opportunity Available)

12:45 Session Break

12:55 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

THERAPEUTIC FUSION PROTEINS TO FIGHT CANCER

2:00 Chairperson's Remarks
Vladimir Muzykantov, MD, PhD, Professor, Pharmacology, The Center for Translational Targeted Therapeutics and Nanomedicine (CT3N) and Systems Pharmacology, Perelman School of Medicine, University of Pennsylvania

2:05 Antibody-Cytokine Fusion Proteins Targeting Tumor Associated Antigens for the Treatment of Malignancy
Sherie Morrison, PhD, Distinguished Research Professor, Microbiology, Immunology and Molecular Genetics, University of California, Los Angeles
Many cytokines have anti-tumor efficacy, however, their utility for treating malignancy is often limited by toxicities that are dose limiting. To address this problem, we have genetically fused cytokines to antibodies that recognize tumor-associated-antigens. Among other things, we have used this strategy to target interferons to tumor cells using anti-CD20 and anti-CD138 specific antibodies. We have found these antibody fusion proteins effective in the treatment of both lymphoma and myeloma.

2:35 Optimization of a Bispecific Anti-CD3 Antibody-Folate Conjugate for the Treatment of Ovarian Cancer
Harun Rashid, PhD, Senior Principal Scientist, Molecular Technology, Ambrx, Inc.
Here, we report the optimization of an anti-CD3 Fab-folate conjugate that targets cytotoxic T cells to folate receptor positive (FR+) tumor cells for optimal efficacy, reduced toxicity and optimal pharmacokinetic (PK). The optimized conjugates showed potent and selective *in vitro* activity, good serum half-life, and potent *in vivo* activity in xenograft mouse models. This semi-synthetic approach shows promise for the generation of additional anti-CD3 bispecific agents using small molecule ligands selective for other TAAs.

3:05 Find Your Table and Meet Your BuzZ Session Moderator

3:15 BuzZ Sessions with Refreshments
Join your peers and colleagues for interactive roundtable discussions.
See page 11 for details.

THERAPEUTIC FUSION PROTEINS TO FIGHT CANCER *(Cont.)*

4:30 Advancing Targeted Protein Therapeutics (TPTs) in Clinical Drug Development
Jeannick Cizeau, PhD, Director, Research, Sesen Bio, Inc.
The design and differential mechanism of action of Sesen's TPTs comprising an antibody fragment genetically fused to a protein toxin versus traditional small molecule drugs used for ADCs will be discussed. Data from an ongoing pivotal Phase III trial in non-muscle invasive bladder cancer will be presented to illustrate the rationale design approach of TPTs for use in clinical oncology.

5:00 Hexavalent Agonists Targeting Co-Stimulatory Receptors of the TNFR-Superfamily for Cancer Immunotherapy
Christian Gieffers, PhD, Vice President, Analytics/Protein Chemistry, Apogenix AG
Apogenix's novel hexavalent TNFR-SF agonists (HERA) are developed for the immunologic treatment of cancer. The construction principle is based on trivalent molecular mimics of the TNF-SF Receptor binding domains fused to a dimerization scaffold. The resulting hexavalent fusion proteins are potent TNFR-SF agonists that activate distinct immune cell populations. HERA compounds show single-agent anti-tumor activity and provide exciting opportunities for combinatorial treatment.

WHAT'S THE BUZZ ABOUT?

BuzZ sessions

PepTalk BuzZ Sessions are focused, stimulating discussions in which delegates discuss important and interesting topics related to upstream protein expression and production through downstream scale-up and manufacturing. This is a moderated discussion with brainstorming and interactive problem-solving between scientists from diverse areas who share a common interest in the discussion topic.

Continue to check the event website for detailed discussion topics and moderators.

5:30 **Prospects of PASylation for the Design of Protein Therapeutics and Tumor Imaging Reagents**
Uli Binder, MSc, CTO, XL-protein GmbH
PASylation®, the genetic fusion or chemical coupling of proteins or peptides with conformationally disordered polypeptides comprising the L-amino acids Pro, Ala, and/or Ser (PAS), is a superior way to enlarge the hydrodynamic volume and to extend plasma half-life. Further to illustrating the fundamental concepts of PASylation technology, this presentation will highlight a first proof-of-concept tumor imaging study in a human patient.

6:00 - 7:15 **Welcome Reception in the Exhibit Hall with Poster Viewing**

Sponsored by proteinsimple

7:15 **Close of Day**

TUESDAY, JANUARY 15

8:00 am **Registration and Morning Coffee**

IMPROVING PROPERTIES

8:30 **Chairperson's Remarks**
Yulia Vugmeyster, PhD, Associate Director, Clinical Pharmacology, EMD Serono R&D Institute, Inc.

8:35 **Engineered FcRn Binding Fusion Peptides for Half-Life Extension**
Jeffrey Boyles, MSc, Research Scientist, Biotechnology Discovery Research, Eli Lilly and Company
The therapeutic potential of small proteins, peptides, and mAb derived domains can be significantly limited by their rapid peripheral clearance *in vivo*. We show that small FcRn binding peptides (FcRnBPs) fused to the N- and/or C-termini of a Fab can significantly improve the pharmacokinetics of the protein in cynomolgus monkeys. The extent of this benefit can be modulated by number, structure, and post-translational modifications of the FcRnBP.

9:05 **Developing a Conjugation-Based Multivalent Ab Format**
Diego Ellerman, PhD, Principal Scientific Researcher, Protein Chemistry, Genentech, Inc.
A multivalent Ab format based on protein conjugation was developed (TRAC) to enable a plug and play system for the rapid screening of new multispecific/multivalent Abs. The building blocks used are mAbs and Fabs with good expression yields and stability. A conjugation site was identified that supports high conjugation rates, an efficient process and a stable molecule. We provide examples of different TRACS that require concurrent binding of all Fabs for their biological activity.

9:35 **Sponsored Presentation** *(Opportunity Available)*

9:50 **Coffee Break in the Exhibit Hall with Poster Viewing**

11:00 **Therapeutic Fusion Proteins Targeted to Blood and Vascular Cells**
Vladimir Muzykantov, MD, PhD, Professor, Pharmacology, The Center for Translational Targeted Therapeutics and Nanomedicine (CT3N) and Systems Pharmacology, Perelman School of Medicine, University of Pennsylvania
Conjugating biotherapeutics including thrombomodulin with scFv to blood cells boosts bioavailability, while conjugating with scFv binding to endothelial determinants provides endothelial targeting. Selecting determinants that permit fusion cooperation with cofactors boosts the effect. Further, dual targeting of two fusions delivering collaborative cargoes to adjacent epitopes maximizes binding and effect. Vascular targeting of anti-thrombotic and anti-inflammatory fusions affords beneficial effects unrivaled by untargeted counterparts in animal models of acute lung injury, ischemia-reperfusion and sepsis.

11:30 **Enabling and Expanding Therapeutic Development of Microbial-Derived Biologics through the Use of Tolerogenic Nanoparticles**
Kei Kishimoto, PhD, CSO, Selecta Biosciences
We have developed tolerogenic nanoparticles to induce antigen-specific immune tolerance to biologic drugs and prevent the formation of anti-drug antibodies. I will present three case studies: 1) Phase II clinical data for a fungal-derived uricase enzyme for the treatment of severe gout; 2) Phase I clinical program of a bacterial-derived recombinant immunotoxin for the treatment of mesothelioma; and 3) enabling repeat dosing of an AAV viral vector for gene therapy.

12:00 pm **Sponsored Presentation**
(Opportunity Available)

12:30 **Session Break**

12:40 **Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 **Close of Recombinant Protein Therapeutics Conference**

TUESDAY-WEDNESDAY, JANUARY 15-16 | INAUGURAL

COMPUTATIONAL AND ANALYTICAL TOOLS FOR PROTEIN ENGINEERING

Next-Generation Modeling and Informatics Tools for Biotherapeutic Engineering and Development

IMPROVEMENTS IN COMPUTING power, instruments, modeling software and imaging technology are driving a new wave of interest in the application of these tools in antibody discovery and protein engineering. Structural biology and computational modeling are now routinely applied in identifying unique epitopes and binding activity, and it is becoming standard practice to run a suite of assays and structural studies to evaluate the developability and manufacturability before advancing leads into development. PepTalk's new Computational and Analytical Tools for Protein Engineering conference gives researchers a comprehensive exchange in which to consider best practices and new technologies used to support the work of protein engineers on new constructs and the discovery of unique new biotherapeutics.

TUESDAY, JANUARY 15

1:00 pm Registration

1:30 Refreshment Break in the Exhibit Hall with Poster Viewing

2:00 Chairperson's Opening Remarks
Johan Fransson, PhD, Director, Antibody Discovery and Development, Northern Biologics

KEYNOTE PRESENTATION

2:05 A New Source of Tumor Neoantigens and Platform for Their Identification
Stephen Albert Johnston, PhD, CEO, Calviri, Inc.; Director and Professor, Biodesign Center for Innovations in Medicine, Arizona State University
We have discovered that frameshift neoantigens from RNA mis-processing are a rich source of components for cancer vaccines. All tumors produce many of these neoantigens. We have developed a peptide array that allows simple identification of the neoantigens in each tumor from a drop of blood.

PREDICTING PROTEIN BEHAVIOR

2:45 Improved Computational Modeling of Antibody-Antigen Complexes by Integration of Deep Mutational Scanning Data
Andrew Wollacott, PhD, Principal Scientist, Visterra, Inc.
Accurate computational prediction of the structure of antibody-antigen complexes remains challenging due, in part, to the difficulty in identifying near-native models from incorrect poses. We have developed a workflow which integrates experimental deep mutational scanning data with antibody-antigen docking for robust model generation. The presentation will describe an application of this workflow to a panel of antibodies, which enabled rational selection and engineering of one antibody for cross-species antigen binding.

3:15 Advanced Analytics and Visualization for Biologics Drug Discovery
Sponsored by dotmatics
Andrew LeBeau, PhD, Senior Manager, Biologics Marketing, Dotmatics, Inc.
Biologics drug discovery places significant demands on software to handle the volumes of data and advanced computational routines necessary to uncover promising candidates. The software should also be accessible to the wide range of scientists involved in the process. This presentation will highlight such capabilities within Dotmatics Vortex.

3:30 Antibody Protein Sequencing with Mass Spectrometry
Sponsored by RAPID NOVOR
Mingjie Xie, CEO, Co-Founder, 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.

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

4:30 Overcoming Challenges of High-Resolution Epitope Mapping by Use of NMR Spectroscopy: Case Studies and Practical Solutions
Feng Ni, PhD, Project Lead and Laboratory Supervisor, Human Health Therapeutics, National Research Council Canada
Practical epitope mapping is still limited by: (1) the ability to prepare soluble antigen-antibody complexes with lasting stability; (2) efficient collection of multi-dimensional NMR data; (3) the intrinsic dynamics of the binding interactions. We will present three case studies of (i) an intrinsically-unfolded domain of carbonic anhydrase IX; (ii) the well-folded Ig1 domain of human Axl with high affinity binding and (iii) the Ig2 domain of Axl with dynamic interactions.

5:00 Cellular and Analytical Assays for PK Engineering
Runyi Adeline Lam, PhD, Researcher, Chugai Pharmabody Research, Japan
During antibody optimization, antibodies with different properties are generated and these are evaluated using various cell-based or analytical assays. This presentation focuses on development of novel cell-based assays to aid in the screening process. Examples from different projects would be shown to illustrate how this can improve the screening workflow.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

5:45 - 8:45 Dinner Short Courses*
See page 8 for details.
**Separate registration required*

WEDNESDAY, JANUARY 16

7:45 am Registration and Morning Coffee

EXPERIMENTAL VALIDATION OF COMPUTATIONAL RESULTS

8:15 Chairperson's Remarks
Marissa Mock, PhD, Principal Scientist, Therapeutic Discovery, Biologics, Amgen

8:20 Using Interface Expansion to Manipulate the Affinity and Specificity of Protein-Protein Interactions
Brian Kuhlman, PhD, Professor, Biochemistry and Biophysics, University of North Carolina at Chapel Hill
Protein binding affinity and specificity can be manipulated by redesigning contacts that already exist at an interface or by expanding the interface to allow interactions with residues adjacent to the original binding site. Two alternative methods for interface expansion with the Rosetta molecular modeling program will be discussed. These approaches have been used to engineer tight binders for MAP kinases and the ubiquitin ligase KEAP1.

8:50 Computational Design of Protein Libraries
Chris Bailey-Kellogg, PhD, Professor, Computer Science, Dartmouth College
To increase the hit rate of discovering diverse, high-performance protein variants via library screening, we have developed computational library design methods that bias entire populations towards simultaneous improvements in multiple properties of interest. In application to biotherapeutic deimmunization, we have subjected optimized libraries to a single round of activity screening and successfully isolated highly mutated variants that are functionally equivalent to wild-type while also evading T cell recognition.

METHODS AND MODELS FOR DEVELOPABILITY ASSESSMENT

9:20 A Platform Approach to Manage Developability and Manufacturability Risks of Biologics Molecules
Maria Wendt, Head, Science, Biologics, Genedata
We present a workflow system that enables very systematic developability and manufacturability assessments from the very early stage to the later stages of the biologics R&D process, using both *in silico* methods and high throughput analytical confirmatory methods. We show use cases not only for mAbs but also for complex multi/bispecific formats, as well as engineered therapeutic cell lines (e.g., CAR T cells). We also discuss building predictive models for developability utilizing such a system.

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

10:35 How Large is the Sequence Space for Aggregation-Resistant Antibodies?
Christopher J. Roberts, PhD, Professor, Chemical & Biomolecular Engineering, University of Delaware
This presentation will focus on a multi-scale molecular modeling approach to providing design "rules" for down-selecting antibodies from a large number of sequence variants, without the need for expensive calculations or extensive expression screens, with a view towards creating antibodies that are aggregation resistant. The test systems are primarily monoclonal antibodies, but the approach can be extended to additional constructs.

11:05 Building Methods to Predict Large Molecule Developability for the Early Research Pipeline
Marissa Mock, PhD, Principal Scientist, Therapeutic Discovery, Biologics, Amgen
During the preclinical development of large molecule therapeutics, panels of engineered variants are designed, generated, and screened to optimize the developability of lead candidates. Since many standard assays for developability require large quantities of protein and are resource-intensive, we have developed and will present strategies and methods to predict complex biophysical behaviors from a combination of primary sequence and high throughput screening data.

11:35 *In silico* and Empirical Developability Assessment of Therapeutic Antibodies
Johan Fransson, PhD, Director, Antibody Discovery and Development, Northern Biologics
Antibody developability assessments are a key part of every discovery campaign. Typically, both *in silico* and empirical methods are used to rank candidates and assess risks impacting manufacturing, release and stability studies. An overview of current *in silico* and empirical methods employed in our lab will be provided. Case studies will also be presented, highlighting how molecular modeling can guide rational design and selection of better behaved lead candidate mAbs.

12:05 pm Session Break

12:15 Computational Design Coupled with Massively-Parallel Synthesis and Screens to Discover Interface Representative Peptides
Sponsored by RubrYc THERAPEUTICS
Matthew Greving, PhD, Co-Founder, Vice President, Technology, RubrYc Therapeutics

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

1:15 Session Break

2:00 PLENARY KEYNOTE PANEL
See page 5 for details.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

COMPUTATIONAL ANTIBODY DESIGN

4:00 Chairperson's Remarks
Philip M. Hemken, PhD, Principal Research Scientist, R&D, Abbott Laboratories

4:05 Structural Bioinformatics of Antibodies and Antibody Computational Design
Roland L. Dunbrack, Jr., PhD, Professor, Institute for Cancer Research, Fox Chase Cancer Center
We have performed extensive structural bioinformatics studies of the CDRs of antibodies as well as the 'de'

loop or CDR4. We have developed a computational antibody design algorithm in Rosetta that utilizes our CDR clusters to graft new CDRs and to perform sequence optimization according to sequence variation observed in clusters of similar CDR conformations. We have benchmarked this method with a novel metric and validated it experimentally.

4:35 Exploration of Small Protein Folds and Their Defining Features
Eva-Maria Strauch, PhD, Assistant Professor, Pharmaceutical and Biomedical Sciences, University of Georgia
Nature only samples a small fraction in sequence space, yet many more amino acid combinations can fold into stable proteins. We developed a computational platform that enables us to efficiently sample and design any given topologies with high structural diversity to serve as new scaffolding proteins, guide future design efforts and help our general understanding of stability. Using a high-throughput stability screen, we evaluated 45,000 of 9 topologies designed with our new pipeline and derived stability prediction models using machine learning algorithm.

APPLICATIONS IN BIOPHARMACEUTICAL DEVELOPMENT

5:05 Development of Automated Companion Diagnostic Immunoassays in Collaboration with Therapeutic Partners
Philip M. Hemken, PhD, Principal Research Scientist, R&D, Abbott Laboratories
Abbott partnered to develop two automated diagnostic immunoassays as potential future companion diagnostic tests to identify patients with severe asthma who would most likely benefit from an investigational anti-IL-13 immunotherapy. Abbott developed tests to measure the serum levels of the proteins periostin and DPP4 (dipeptidyl peptidase-4), which have potential to be predictive biomarkers for up-regulated IL-13 in patients with severe asthma.

5:35 Assessment of Orthogonal Techniques for Epitope Mapping of Therapeutic Antibodies
Sam Wu, PhD, Principal Scientist, Janssen BioTherapeutics
Epitope mapping provides crucial information for selecting therapeutic antibodies. A progressive approach to mapping is applied to help identify new function, support antibody engineering, define a mechanism of action, and enable intellectual property. Specifically, DEPC-labelling and hydroxyl radical footprinting (HRF) results with epitopes of therapeutic antibodies identified by solution HDX-MS will be presented. Examples of the impact of binding site mapping on progression of antibody discovery will be described.

6:05 - 7:00 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Computational and Analytical Tools for Protein Engineering Conference

THURSDAY-FRIDAY, JANUARY 17-18 | INAUGURAL

DEEP SEQUENCING AND SINGLE CELL ANALYSIS FOR ANTIBODY DISCOVERY

Technologies and Best Practices for Applying Repertoire Analysis in the Discovery of Therapeutic Proteins

Also part of **INNOVATIONS IN DISCOVERY & DEVELOPMENT**

THE RAPID ADOPTION of deep sequencing and single B cell analysis offers discovery scientists an extraordinary view into human and animal immune repertoires that is now informing all aspects of biopharmaceutical R&D. This dynamic field is bringing together the disciplines of immunology, structural and computational biology, informatics and microfluidics to offer previously unimaginable perspectives that will drive discovery of the next generation of biologics. PepTalk's Inaugural Deep Sequencing and Single Cell Analysis for Antibody Discovery conference explores the vast range of new science and technology in this field and how these new capabilities are being integrated with traditional discovery methods.

THURSDAY, JANUARY 17

7:45 am Registration and Morning Coffee

INTEGRATING DEEP SEQUENCING WITH TRADITIONAL ANTIBODY DISCOVERY METHODS

8:10 Organizer's Welcome Remarks
Kent Simmons, Senior Conference Director, Cambridge Healthtech Institute

8:15 Chairperson's Opening Remarks
Gabriel W.C. Cheung, PhD, Senior Director, BioMedicine Design, Medicinal Sciences, Worldwide Research and Development, Pfizer, Inc.

KEYNOTE PRESENTATION

8:20 Leveraging Immune Repertoire Deep Sequencing to Extend Traditional Antibody Discovery Methods
Isidro Hotzel, PhD, Senior Scientist, Genentech
Hybridoma and B cell cloning remain the main technologies for antibody discovery in the industry. Although significantly improved over the years, these technologies still have a relatively limited repertoire sampling capacity which often results in relatively limited panel sizes and antibody leads that require further optimization. Deep sequencing technologies have been integrated in the antibody discovery workflow to enhance the sampling of immune repertoires for rapid discovery of optimized antibody leads.

9:00 Ultra-Deep Sequencing of the Baseline Human Antibody Repertoire
Bryan Briney, PhD, Assistant Professor, Immunology and Microbiology, The Scripps Research Institute
In principle, humans can make an antibody response to any non-self-antigen molecule. We have examined the circulating B cell populations of ten healthy human subjects and present the largest single collection of human adaptive immune receptor sequences described to date, comprising almost 3 billion nearly full-length antibody heavy chain sequences. This repertoire-scale dataset reveals a surprising degree of repertoire uniqueness, a subpopulation of public antibody clonotypes and exceptional repertoire diversity.

9:30 Presentation to be Announced
Speaker to be Announced, AbCellera Biologics Inc.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 Sequence-Based Prediction of Antibody Specificities
Sai Reddy, PhD, Associate Professor, Biosystems Science and Engineering, ETH Zurich, Switzerland
In this presentation, I will describe how we are decrypting antibody repertoires by identifying convergent antigen-associated molecular patterns. Molecular convergence is specifically identified by bioinformatic recoding of high-throughput sequencing data of antibody repertoires into constituent biochemical sequence space. By combining this approach with a statistical learning framework, we are able to accurately predict antigen exposure and antigen specificity based on antibody sequences alone.

11:30 Rapid Functional Interrogation of Immune Repertoire
Gabriel W.C. Cheung, PhD, Senior Director, BioMedicine Design, Medicinal Sciences, Worldwide Research and Development, Pfizer, Inc.
Numerous disruptive technologies, from NGS of BCRs to bottom-up serum Ig proteomic, have been developed to study B cell repertoires in the past decade. At Pfizer, we are further pushing the boundary of technologies to enable fast and comprehensive interrogation of functionally relevant, antigen-specific B cells from both peripheral and bone marrow compartments through the use of proprietary high-throughput automation, novel single cell technology and deep sequencing.

12:00 pm Session Break

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

MINING HUMAN ANTIBODY REPERTOIRES

2:15 Chairperson's Remarks
Gregory C. Ippolito, PhD, Research Assistant Professor, Molecular Biosciences, Georgiou Lab, The University of Texas at Austin

2:20 Predicting Personal Immune Scenarios
Enkelejda Miho, PhD, Professor, Digital Life Sciences, FHNW University of Applied Sciences and Arts Northwestern Switzerland, Switzerland
Antibodies protect against pathogens and are important diagnostics and therapeutics. Sequence

diversity of antibody repertoires has been recently recorded from the advancement of high-throughput sequencing technologies. Antibody repertoires can now be represented as large-scale networks where antibodies are sequence-nodes connected by similarity-edges. We show how this network model can serve as the base to track entire personalized antibody repertoires in the theoretical antibody sequence space, thus predicting immune status scenarios.

2:50 High-Throughput Discovery of Patient-Specific, Immune-Selected, Anti-Tumor B Cells and Immunoglobulins in Breast Cancer
Gregory C. Ippolito, PhD, Research Assistant Professor, Molecular Biosciences, Georgiou Lab, The University of Texas at Austin
The synergistic combination of Ig protein mass spectrometry (Ig-Seq) and a DNA sequencing method that preserves the natural pairing of heavy (VH) and light (VL) chain variable regions (VH:VL BCR-Seq) can prospectively identify tumor-reactive B cells and also confirm the presence of functional, high-affinity, circulating anti-tumor Ig in cancer patients. This strategy capitalizes on the *in vivo* immune response and may provide an unbiased screening of antibody specificities that have been immune-selected by cognate tumor antigens.

3:20 Sponsored Presentation *(Opportunity Available)*

3:35 Networking Refreshment Break

SINGLE CELL CLONING AND SCREENING PLATFORMS

4:00 Linked Experimental and Computational Analysis to Accelerate Antibody Discovery from Natively Paired VH:VL Antibody Libraries
Brandon DeKosky, PhD, Assistant Professor, Pharmaceutical Chemistry and Chemical Engineering, University of Kansas
Next-generation technologies have amplified the power of antibody screening technologies. Recent advances in paired heavy:light sequencing and native antibody library display offer new possibilities for discovering and annotating antibody functional performance on a repertoire scale. We will discuss the application of these new technologies in combination with next-generation computational data analysis and precise screening methods to understand immune function and to discover and identify new antibody molecules with desired functional properties.

4:30 Functional Antitumor Antibodies from Immunoglobulin Repertoires of Cancer Patients
Daniel Emerling, PhD, Senior Vice President, Research, Atreca, Inc.
We sequenced natively-paired, immunoglobulin (IgG) heavy and light chains from activated B cells of over 100 cancer patients and used sequence repertoire analyses to select specific IgGs for recombinant expression and characterization. Screened antibodies bound non-autologous human-derived tumor tissues at a high rate, consistent with recognition of public tumor antigens. Some antibodies caused tumor regression in mouse cancer models. Starting from patient anti-tumor responses, we've established a discovery strategy for novel cancer therapies.

5:00 Isolation of Single Antigen Specific T Cells for Rapid TCR Sequencing and Cloning
Paul Armistead, MD, PhD, Associate Professor, Medicine, Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill
Cloning cancer-antigen specific T cells is important for immunotherapeutic development. Because of the inefficiencies of limiting dilution and tetramer-FACS based T cell cloning, we have developed a cellular microarray-based platform that can identify, isolate and clonally expand individual T cells from a large population based upon their antigen specific cytotoxicity. Ongoing studies will further develop this platform to select and isolate antigen specific T cells based upon clonal, antigen-specific proliferation.

5:30 Close of Day

FRIDAY, JANUARY 18

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast
Protein therapeutics is a fast-growing global market. As the science improves, so does the complexity of the R&D organization. Ensuring product quality plus speed to market requires insights from stakeholders working across the stages of protein science R&D. Join experts representing this PepTalk pipeline, peers, and colleagues for an interactive roundtable discussion. Topics include highlights from the week's presentations, new technologies and strategies, challenges, and future trends.
Moderator: Vu Truong, PhD, CSO & CEO, R&D, Aridis Pharmaceuticals, Inc.
Moderator: Sam Wu, PhD, Principal Scientist, Janssen BioTherapeutics

APPLICATION CASE STUDIES

9:00 Chairperson's Remarks
Marcin Paduch, PhD, Senior Staff Scientist, Product Development, GRAIL, Inc.

9:05 Recombinant Human B Cell Repertoires Enable Screening for Rare, Specific and Natively-Paired Antibodies
Sarav Rajan, PhD, Scientist, Antibody Discovery & Protein Engineering, MedImmune
We present an approach to encapsulate millions of 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 and rapidly drove selection towards cross-reactive antibodies targeting influenza hemagglutinin. Most antibodies 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.

9:35 Engineered Virus-Like-Particles for GPCR-Specific Therapeutic Antibody Discovery
Mart Ustav, Jr., PhD, Postdoctoral Fellow, Sidhu Lab, University of Toronto
We have established a robust method for the expression of GPCRs on HIV-1 gag Virus-Like-Particles (VLPs). We engineered the gag protein of HIV-1 to enable tight interaction with a short peptide fused to the C-terminal tail of therapeutically relevant GPCRs. We used these engineered VLPs for the isolation of mAbs from large phage- libraries and through Next-

Generation-Sequencing (NGS) were able to identify mAbs binding therapeutically relevant GPCRs.

10:05 Sequencing Cancer Genome Data for Diagnostic Discovery and Development
Marcin Paduch, PhD, Senior Staff Scientist, Product Development, GRAIL, Inc.
Large-scale cancer genome sequencing efforts are rapidly increasing our power to identify tumor genetic and epigenetic biomarkers with unprecedented precision. Expanded knowledge of tumor biology, genetics, cfNAs and other types of cancer-related molecules open up uncharted paths to discovery of new diagnostic and therapeutic markers. I will discuss the development of approaches that capture complexity of disease states such as cancer and take advantage of extensive data sets being generated.

10:35 Networking Coffee Break

11:00 Identification of Therapeutic Antibodies and Orphan TCR Targets by Microfluidics Based Single Cell Analysis
George Wu, PhD, CEO, Amberstone
It remains to be a major bottleneck to efficiently discover a functional antibody lead for a therapeutic target. Here we present a case study to show the power of a cutting-edge microfluidic based single cell platform technology in the discovery of a functional antibody against immunotherapeutic targets. We also show the platform's usefulness in the antigen discovery for an orphan T cell receptor (TCR) with therapeutic applications.

11:30 Comprehensive B Cell Repertoire Screening and Stabilization of Selected B Cell Using Novel Cell Fusion Technology
Vu Truong, PhD, CSO & CEO, R&D, Aridis Pharmaceuticals, Inc.
Development of monoclonal antibody therapeutics derived from B cell repertoire screening of infected hosts has been limited by two barriers: 1) how to comprehensively screen the entire repertoire which typically comprises over 1 million of unique B cells generated against the pathogen and 2) how to rapidly manufacture mAbs without employing traditional recombinant DNA and cell line process development steps. We will present a novel approach to addressing these two barriers.

12:00 pm Conference Wrap-Up
Sam Wu, PhD, Principal Scientist, Janssen BioTherapeutics

12:30 Close of Conference

INNOVATIONS IN DISCOVERY & DEVELOPMENT

The PepTalk Innovations in Discovery & Development pipeline offers an in-depth examination of cutting-edge science and technology to support the discovery and development of novel and differentiated drug products. Full-length programs will consider strategies for delivering therapies across the blood-brain barrier and developing highly efficacious agents against CNS disorders and emerging sequencing and single cell analysis technologies for antibody discovery.

JANUARY 14-15

AGENDA Advancing CNS Biotherapeutics and Crossing the Blood-Brain Barrier

JANUARY 15-16

AGENDA Next-Generation Approaches to Antibody Screening and Discovery | Training SEMINARS By Cambridge Healthtech Institute

JANUARY 17-18

AGENDA Deep Sequencing and Single Cell Analysis for Antibody Discovery | Also part of PROTEIN ENGINEERING & DEVELOPMENT

MONDAY-TUESDAY, JANUARY 14-15 | 2ND ANNUAL

ADVANCING CNS BIOTHERAPEUTICS AND CROSSING THE BLOOD-BRAIN BARRIER

Opportunities, New Targets, Models and Tools, and Delivery

CAMBRIDGE HEALTHTECH INSTITUTE'S 2nd Annual Advancing CNS Biotherapeutics and Crossing the Blood-Brain Barrier conference will provide a platform to brainstorm ideas and share new research on topics such as the biologics for CNS targets and biomarkers, brain cancer, neurodegeneration, neuroinflamation, neuroimmunology, alteration of CNS/BBB barriers due to injury or disease, preclinical models, neuroimaging, tools for prediction of brain penetration, and updates from the industry on topics such as antibody delivery and vector-mediated transport across BBB. This conference will feature stimulating discussions and a friendly place to network with peers.

SUNDAY, JANUARY 13

4:00 - 6:00 pm Pre-Conference Registration

MONDAY, JANUARY 14

7:00 am Registration and Morning Coffee

NEW TARGETS, OPPORTUNITIES AND DRUG DELIVERY FOR BIOLOGICS

9:00 Welcome by Conference Organizer
Nandini Kashyap, Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks
Miroslaw Janowski, MD, PhD, Associate Professor, Radiology, Johns Hopkins University

KEYNOTE PRESENTATION

9:10 Nanoparticles, Cells and Exosomes for CNS Therapeutics
Alexander (Sasha) Kabanov, PhD, DrSci, Distinguished Professor, Eshelman School of Pharmacy, University of North Carolina and Chapel Hill
Polyion complexes, cell drug carriers and exosomes are engineered for treatments of neurodevelopmental and neurodegenerative diseases. Polyion complexes entrap antioxidant enzymes, stoichiometric and catalytic scavengers of organophosphorus toxins (OP) and neurotrophins to treat obesity, stroke, Parkinson's disease (PD), OP poisoning, and lysosomal storage diseases (LSD). Genetically modified macrophages and exosomes are natural delivery vectors for proteins and nucleic acids as exemplified in experimental models of PD and LSD.

9:50 Differentiation of Human Pluripotent Stem Cells into High Resistance Barrier-Endothelial Cells Using Genome Editing, Genomics and Chemogenomic Library Screening Approaches
Filip Roudnicky, PhD, Senior Scientist, Disease Relevant Cellular Assays, F. Hoffmann-La Roche Ltd.
We will present a method to generate high-resistance barrier endothelial cells from human pluripotent stem cells (hPSCs). We have generated using genome editing a claudin 5 (CLDN5) transcriptional reporter in hPSCs to serve as a surrogate marker for high-resistance endothelial barrier. Finally, using evidence-based chemical-probe library, designed to span a large number of molecular targets, we have screened for chemical-probes that induce CLDN5 expression in differentiated endothelial cells.

10:20 Networking Coffee Break

10:45 Intra-Arterial Delivery of Antibodies to the Central Nervous System
Miroslaw Janowski, MD, PhD, Associate Professor, Radiology, Johns Hopkins University
Antibodies are increasingly used as therapeutic agents, though blood-brain barrier (BBB) hampers their penetration to the central nervous system (CNS). We are witnessing tremendous advances in development of endovascular tools with an excellent safety profile. Intra-arterial route increases delivery of antibody to the CNS and preceding it with hyperosmolar BBB opening further increases efficiency of this process. However, hyperosmolar BBB opening does not improve BBB penetration of intravenously administered antibody.

11:15 Boosting Brain Uptake of a Therapeutic Antibody through Conjugation to an Aptamer against Transferrin Receptor
Dongping He, MS, Senior Scientific Researcher, Biochemical & Cellular Pharmacology, Genentech/Roche
A nuclease stabilized RNA aptamer against human Transferrin receptor (huTfR) was conjugated to a bivalent therapeutic antibody. The antibody-aptamer conjugate increased brain uptake in huTfR transgenic mice compared to the control, and without the toxicity observed for the TfR bispecific antibody. Taking advantage of the small size of aptamers, this study opens up possibilities of increasing brain uptake capacities using novel multi-specific therapeutic modalities.

CNS AND BBB AT SITES OF PATHOLOGY DURING DISEASE AND INJURY

11:45 An Emerging Role for Glial Cells and Guidance Molecules in Neurodegeneration
Elizabeth Evans, PhD, Vice President, Preclinical Research, Vaccinex, Inc.
Glial cell structural and inflammatory changes may have a significant impact on neurodegeneration. Reactive gliosis, BBB integrity, and survival of glial precursor cells that repair brain lesions can be regulated by semaphorin guidance molecules. Translational mechanistic studies and preliminary brain imaging data from an ongoing Phase I/II trial with pepinemab (VX15/2503) support the hypothesis that SEMA4D antibody blockade preserves brain volume and restores metabolic activity in early Huntington's disease.

12:15 pm Sponsored Presentation
(Opportunity Available)

12:45 Session Break

12:55 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

PRECLINICAL TOOLS, BIOMARKERS, ANIMAL AND CELL BASED MODELS

2:00 Chairperson's Remarks
Alexander (Sasha) Kabanov, PhD, DrSci, Distinguished Professor, Eshelman School of Pharmacy, University of North Carolina and Chapel Hill

2:05 3D Models to Understand Complex Neural Networks and Neurotoxicity
Monica Moya, PhD, Research Engineer, Materials Engineering Division, Lawrence Livermore National Laboratory
With growing interest in developing selective and potent inhibitors for the treatment of CNS diseases, there is a need to understand the challenging aspect of crossing the BBB and relevant physiological models of the BBB are germane to the success of those studies. We have developed a versatile 3D human BBB platform to more accurately investigate compound permeability from the bloodstream to the CNS (a second on-chip platform) at increasing degrees of complexity.

2:35 Modeling Vascular Dysfunction in Neurological Disease
Georgette Suidan, PhD, Scientist II, Alzheimer's Disease and Dementia Research Unit, Biogen
Apart from the classical pathological characteristics of AD, studies have shown that the majority of AD patients present with vascular abnormalities including cerebral amyloid angiopathy, reduced cerebral blood flow (hypoperfusion) and blood brain barrier breakdown. I will give an overview of the reported literature and discuss approaches to identify and validate targets for improving vascular dysfunction in neurological disease.

3:05 Find Your Table and Meet Your BuzZ Session Moderator

3:15 BuzZ Sessions with Refreshments
Join your peers and colleagues for interactive roundtable discussions.
See page 11 for details.

4:30 Development of a Translatable Biomarker Assay for Proteopathic Amyloid Seeds
Kimberly McDowell, PhD, Research Scientist, Preclinical Research, Proclara Biosciences, Inc.
Many diseases are characterized by protein(s) misfolding into a common cross beta-sheet amyloid structure. In Alzheimer's disease, pathology spreads throughout the brain via a prion-like process where amyloid seeds nucleate new sites of aggregation. Current biomarker assays do not specifically measure proteopathic seeds. We developed a versatile and translatable RT-QuIC assay that quantifies the seeding potential of soluble misfolded tau species to study disease progression and preclinical efficacy.

5:00 BBB Organoids as Next-Generation *in vitro* Model
Choi-Fong Cho, PhD, Instructor, Neurosurgery, Brigham and Women's Hospital, Harvard Medical School
In vitro BBB models are indispensable in facilitating drug analysis and discovery. Here, we describe the utility of 3D multicellular BBB organoids made of human brain endothelial cells (ECs), brain pericytes and astrocytes as a next-generation screening model for brain-penetrating molecules. This high-throughput model can lead to better design of brain therapeutics and improve prediction of drug delivery in a living model, paving the way for breakthrough discoveries in neuroscience.

5:30 Cell Based Models of the Human Blood-Brain Barrier
Birgit Obermeier, Scientist II, Translational Cellular Sciences, Biogen
Recent developments in microfluidics engineering have resulted in promising *in vitro* BBB models, with improved throughput and physiological relevance. Leveraging Mimetas and Nortis technology, we established two novel models of the human BBB, employing co-culture of multiple cell types in a 3D vessel microenvironment. Together with traditional Transwell systems, our BBB toolkit enables high-throughput screening and characterization of BBB penetration, supporting drug discovery and fundamental research of neurological disorders.

6:00 - 7:15 Welcome Reception in the Exhibit Hall with Poster Viewing
Sponsored by proteinsimple

7:15 Close of Day

TUESDAY, JANUARY 15

8:00 am Registration and Morning Coffee

PRECLINICAL AND CLINICAL UPDATES

8:30 Chairperson's Remarks
Choi-Fong Cho, PhD, Instructor, Neurosurgery, Brigham and Women's Hospital, Harvard Medical School

8:35 Platform Technology for Treatment of the Brain in Lysosomal Storage Disorders with Igg-Fusion Proteins: Preclinical and Clinical Update
Ruben Boado, PhD, Vice President, Research & Development/Co-Founder, ArmaGen, Inc.
Lysosomal enzymes, such as iduronase (IDUA) and sulfatases, are large molecule drugs that do not cross the blood-brain barrier (BBB). The BBB-penetration of enzyme therapeutics is enabled by re-engineering the recombinant enzyme as bi-functional IgG fusion proteins, wherein the IgG domain targets a specific endogenous receptor-mediated transporter system within the BBB, such as the human insulin receptor (HIR). The enzyme therapeutic domain of the fusion protein exerts the pharmacological effect in brain once across the BBB. Several brain penetrating IgG-LSD fusion proteins have been engineered and validated. First in human proof-of-concept Phase II clinical trial in LSD will be discussed.

9:05 Engineering, Biomanufacturing and Preclinical Development of a Blood-Brain Barrier-Crossing, Amyloid-ß Targeting Fusion Protein
Balu Chakravarthy, PhD, Senior Research Officer, Human Health Therapeutics, National Research Council
We are developing a polypeptide (ABP) that targets aggregated amyloid-ß implicated in Alzheimer's disease pathogenesis. To enable brain-delivery of ABP, we have engineered and produced a bi-functional fusion protein, KAL-ABP-BBB, consisting of a novel blood-brain barrier-crossing domain antibody. PK/PD studies demonstrated brain-delivery and target engagement in mouse, rat and dog models. Humanized KAL-ABP-BBB has been biomanufactured in CHOBRI and characterized in support of clinical studies led by KalGene Pharmaceuticals.

9:35 Sponsored Presentation *(Opportunity Available)*

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 Using Single-Domain Antibodies to Shuttle Biotherapeutics through the Blood-Brain Barrier
Krzysztof B. Wicher, PhD, Principal Scientist and Group Leader, Ossianix, Inc.
Combination of *in vivo* and *in vitro* phage selections allowed for identification of efficient, cross-species reactive, and safe CNS shuttles specific to TfR1 receptor. The shuttle mediates uptake of small peptides, antibodies and enzymes to the brain parenchyma, where these cargos can exert their physiologic/therapeutic action. Affinity/activity maturation of the lead molecule yielded the shuttle with the enhanced properties.

11:30 Blood-Brain Barrier Penetrating Biologics for Treating CNS Diseases
Denise Karaoglu Hanzatian, PhD, Principal Research Scientist, Biologics Discovery, AbbVie

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Session Break

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Close of Advancing CNS Biotherapeutics and Crossing the Blood-Brain Barrier Conference

TUESDAY-WEDNESDAY, JANUARY 15-16

NEXT-GENERATION APPROACHES TO ANTIBODY SCREENING AND DISCOVERY

Also part of Training SEMINARS By Cambridge Healthtech Institute

TUESDAY, JANUARY 15 - WEDNESDAY, JANUARY 16

DAY 1: TUESDAY

2:00 - 5:30 pm ..... **Seminar Sessions**

DAY 2: WEDNESDAY

8:15 am - 6:05 pm ..... **Seminar Sessions**

12:15 - 1:30 pm ..... **Lunch Provided**

6:05 - 7:00 pm ..... **Networking Reception**

Exhibit Hall Refreshment Breaks also provided.

Instructor: David Bramhill, PhD,
Founder, Bramhill Biological Consulting, LLC

Over the space of a few years, a series of technologies have improved greatly in both capability and affordability and these have been adapted to enhance the discovery and development of antibodies and other immunotherapies. Among these technologies, DNA sequencing and data analysis, DNA synthesis, single cell isolation, and genome engineering using CRISPR/Cas9 combine to drive significant advances in how we can engineer antibodies and cell lines. This seminar will evaluate these new developments their applications to antibodies and immunotherapy discovery and development.

Attendees will learn about:

- "Next-Generation Sequencing" of DNA – new capabilities: light, torrents and pores
- DNA sequencing applied to single cells and entire immune responses
- Data analysis of whole population responses to immunogen/vaccine
- Cell sorting and other direct isolation-selection of B cells
- Protein-level antibody sequencing capabilities
- Application of new insights to humanization and engineering of IgG
- CRISPR/Cas9 applied to engineer libraries and cell lines
- CAR-T cells, armored CARs and engineered NK cells

Instructor Biography:

Dr. Bramhill has over 20 years' experience in biologics, both in large biopharma and startup biotech companies. He has experience in isolating and improving antibodies using phage display and is an inventor on library design techniques for small scaffolds. He also has experience in diverse expression systems for producing antibodies, antibody fragments and different scaffolds. He has taught numerous technical courses for over 10 years at international conferences.

THURSDAY-FRIDAY, JANUARY 17-18 | INAUGURAL

DEEP SEQUENCING AND SINGLE CELL ANALYSIS FOR ANTIBODY DISCOVERY

Technologies and Best Practices for Applying Repertoire Analysis in the Discovery of Therapeutic Proteins

Also part of **PROTEIN ENGINEERING & DEVELOPMENT**

THE RAPID ADOPTION of deep sequencing and single B cell analysis offers discovery scientists an extraordinary view into human and animal immune repertoires that is now informing all aspects of biopharmaceutical R&D. This dynamic field is bringing together the disciplines of immunology, structural and computational biology, informatics and microfluidics to offer previously unimaginable perspectives that will drive discovery of the next generation of biologics. PepTalk's Inaugural Deep Sequencing and Single Cell Analysis for Antibody Discovery conference explores the vast range of new science and technology in this field and how these new capabilities are being integrated with traditional discovery methods.

THURSDAY, JANUARY 17

7:45 am Registration and Morning Coffee

INTEGRATING DEEP SEQUENCING WITH TRADITIONAL ANTIBODY DISCOVERY METHODS

8:10 Organizer's Welcome Remarks
Kent Simmons, Senior Conference Director, Cambridge Healthtech Institute

8:15 Chairperson's Opening Remarks
Gabriel W.C. Cheung, PhD, Senior Director, BioMedicine Design, Medicinal Sciences, Worldwide Research and Development, Pfizer, Inc.

KEYNOTE PRESENTATION

8:20 Leveraging Immune Repertoire Deep Sequencing to Extend Traditional Antibody Discovery Methods
Isidro Hotzel, PhD, Senior Scientist, Genentech
Hybridoma and B cell cloning remain the main technologies for antibody discovery in the industry. Although significantly improved over the years, these technologies still have a relatively limited repertoire sampling capacity which often results in relatively limited panel sizes and antibody leads that require further optimization. Deep sequencing technologies have been integrated in the antibody discovery workflow to enhance the sampling of immune repertoires for rapid discovery of optimized antibody leads.

9:00 Ultra-Deep Sequencing of the Baseline Human Antibody Repertoire
Bryan Briney, PhD, Assistant Professor, Immunology and Microbiology, The Scripps Research Institute
In principle, humans can make an antibody response to any non-self-antigen molecule. We have examined the circulating B cell populations of ten healthy human subjects and present the largest single collection of human adaptive immune receptor sequences described to date, comprising almost 3 billion nearly full-length antibody heavy chain sequences. This repertoire-scale dataset reveals a surprising degree of repertoire uniqueness, a subpopulation of public antibody clonotypes and exceptional repertoire diversity.

9:30 Presentation to be Announced
Speaker to be Announced, AbCellera Biologics Inc.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 Sequence-Based Prediction of Antibody Specificities
Sai Reddy, PhD, Associate Professor, Biosystems Science and Engineering, ETH Zurich, Switzerland
In this presentation, I will describe how we are decrypting antibody repertoires by identifying convergent antigen-associated molecular patterns. Molecular convergence is specifically identified by bioinformatic recoding of high-throughput sequencing data of antibody repertoires into constituent biochemical sequence space. By combining this approach with a statistical learning framework, we are able to accurately predict antigen exposure and antigen specificity based on antibody sequences alone.

11:30 Rapid Functional Interrogation of Immune Repertoire
Gabriel W.C. Cheung, PhD, Senior Director, BioMedicine Design, Medicinal Sciences, Worldwide Research and Development, Pfizer, Inc.
Numerous disruptive technologies, from NGS of BCRs to bottom-up serum Ig proteomic, have been developed to study B cell repertoires in the past decade. At Pfizer, we are further pushing the boundary of technologies to enable fast and comprehensive interrogation of functionally relevant, antigen-specific B cells from both peripheral and bone marrow compartments through the use of proprietary high-throughput automation, novel single cell technology and deep sequencing.

12:00 pm Session Break

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

MINING HUMAN ANTIBODY REPERTOIRES

2:15 Chairperson's Remarks
Gregory C. Ippolito, PhD, Research Assistant Professor, Molecular Biosciences, Georgiou Lab, The University of Texas at Austin

2:20 Predicting Personal Immune Scenarios
Enkelejda Miho, PhD, Professor, Digital Life Sciences, FHNW University of Applied Sciences and Arts Northwestern Switzerland, Switzerland
Antibodies protect against pathogens and are important diagnostics and therapeutics. Sequence

diversity of antibody repertoires has been recently recorded from the advancement of high-throughput sequencing technologies. Antibody repertoires can now be represented as large-scale networks where antibodies are sequence-nodes connected by similarity-edges. We show how this network model can serve as the base to track entire personalized antibody repertoires in the theoretical antibody sequence space, thus predicting immune status scenarios.

2:50 High-Throughput Discovery of Patient-Specific, Immune-Selected, Anti-Tumor B Cells and Immunoglobulins in Breast Cancer
Gregory C. Ippolito, PhD, Research Assistant Professor, Molecular Biosciences, Georgiou Lab, The University of Texas at Austin
The synergistic combination of Ig protein mass spectrometry (Ig-Seq) and a DNA sequencing method that preserves the natural pairing of heavy (VH) and light (VL) chain variable regions (VH:VL BCR-Seq) can prospectively identify tumor-reactive B cells and also confirm the presence of functional, high-affinity, circulating anti-tumor Ig in cancer patients. This strategy capitalizes on the *in vivo* immune response and may provide an unbiased screening of antibody specificities that have been immune-selected by cognate tumor antigens.

3:20 Sponsored Presentation *(Opportunity Available)*

3:35 Networking Refreshment Break

SINGLE CELL CLONING AND SCREENING PLATFORMS

4:00 Linked Experimental and Computational Analysis to Accelerate Antibody Discovery from Natively Paired VH:VL Antibody Libraries
Brandon DeKosky, PhD, Assistant Professor, Pharmaceutical Chemistry and Chemical Engineering, University of Kansas
Next-generation technologies have amplified the power of antibody screening technologies. Recent advances in paired heavy:light sequencing and native antibody library display offer new possibilities for discovering and annotating antibody functional performance on a repertoire scale. We will discuss the application of these new technologies in combination with next-generation computational data analysis and precise screening methods to understand immune function and to discover and identify new antibody molecules with desired functional properties.

4:30 Functional Antitumor Antibodies from Immunoglobulin Repertoires of Cancer Patients
Daniel Emerling, PhD, Senior Vice President, Research, Atreca, Inc.
We sequenced natively-paired, immunoglobulin (IgG) heavy and light chains from activated B cells of over 100 cancer patients and used sequence repertoire analyses to select specific IgGs for recombinant expression and characterization. Screened antibodies bound non-autologous human-derived tumor tissues at a high rate, consistent with recognition of public tumor antigens. Some antibodies caused tumor regression in mouse cancer models. Starting from patient anti-tumor responses, we've established a discovery strategy for novel cancer therapies.

5:00 Isolation of Single Antigen Specific T Cells for Rapid TCR Sequencing and Cloning
Paul Armistead, MD, PhD, Associate Professor, Medicine, Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill
Cloning cancer-antigen specific T cells is important for immunotherapeutic development. Because of the inefficiencies of limiting dilution and tetramer-FACS based T cell cloning, we have developed a cellular microarray-based platform that can identify, isolate and clonally expand individual T cells from a large population based upon their antigen specific cytotoxicity. Ongoing studies will further develop this platform to select and isolate antigen specific T cells based upon clonal, antigen-specific proliferation.

5:30 Close of Day

FRIDAY, JANUARY 18

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast
Protein therapeutics is a fast-growing global market. As the science improves, so does the complexity of the R&D organization. Ensuring product quality plus speed to market requires insights from stakeholders working across the stages of protein science R&D. Join experts representing this PepTalk pipeline, peers, and colleagues for an interactive roundtable discussion. Topics include highlights from the week's presentations, new technologies and strategies, challenges, and future trends.
Moderator: Vu Truong, PhD, CSO & CEO, R&D, Aridis Pharmaceuticals, Inc.
Moderator: Sam Wu, PhD, Principal Scientist, Janssen BioTherapeutics

APPLICATION CASE STUDIES

9:00 Chairperson's Remarks
Marcin Paduch, PhD, Senior Staff Scientist, Product Development, GRAIL, Inc.

9:05 Recombinant Human B Cell Repertoires Enable Screening for Rare, Specific and Natively-Paired Antibodies
Sarav Rajan, PhD, Scientist, Antibody Discovery & Protein Engineering, MedImmune
We present an approach to encapsulate millions of 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 and rapidly drove selection towards cross-reactive antibodies targeting influenza hemagglutinin. Most antibodies 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.

9:35 Engineered Virus-Like-Particles for GPCR-Specific Therapeutic Antibody Discovery
Mart Ustav, Jr., PhD, Postdoctoral Fellow, Sidhu Lab, University of Toronto
We have established a robust method for the expression of GPCRs on HIV-1 gag Virus-Like-Particles (VLPs). We engineered the gag protein of HIV-1 to enable tight interaction with a short peptide fused to the C-terminal tail of therapeutically relevant GPCRs. We used these engineered VLPs for the isolation of mAbs from large phage- libraries and through Next-

Generation-Sequencing (NGS) were able to identify mAbs binding therapeutically relevant GPCRs.

10:05 Sequencing Cancer Genome Data for Diagnostic Discovery and Development
Marcin Paduch, PhD, Senior Staff Scientist, Product Development, GRAIL, Inc.
Large-scale cancer genome sequencing efforts are rapidly increasing our power to identify tumor genetic and epigenetic biomarkers with unprecedented precision. Expanded knowledge of tumor biology, genetics, cfNAs and other types of cancer-related molecules open up uncharted paths to discovery of new diagnostic and therapeutic markers. I will discuss the development of approaches that capture complexity of disease states such as cancer and take advantage of extensive data sets being generated.

10:35 Networking Coffee Break

11:00 Identification of Therapeutic Antibodies and Orphan TCR Targets by Microfluidics Based Single Cell Analysis
George Wu, PhD, CEO, Amberstone
It remains to be a major bottleneck to efficiently discover a functional antibody lead for a therapeutic target. Here we present a case study to show the power of a cutting-edge microfluidic based single cell platform technology in the discovery of a functional antibody against immunotherapeutic targets. We also show the platform's usefulness in the antigen discovery for an orphan T cell receptor (TCR) with therapeutic applications.

11:30 Comprehensive B Cell Repertoire Screening and Stabilization of Selected B Cell Using Novel Cell Fusion Technology
Vu Truong, PhD, CSO & CEO, R&D, Aridis Pharmaceuticals, Inc.
Development of monoclonal antibody therapeutics derived from B cell repertoire screening of infected hosts has been limited by two barriers: 1) how to comprehensively screen the entire repertoire which typically comprises over 1 million of unique B cells generated against the pathogen and 2) how to rapidly manufacture mAbs without employing traditional recombinant DNA and cell line process development steps. We will present a novel approach to addressing these two barriers.

12:00 pm Conference Wrap-Up
Sam Wu, PhD, Principal Scientist, Janssen BioTherapeutics

12:30 Close of Conference

ANTIBODY THERAPEUTICS

The weeklong Antibody Therapeutics pipeline reveals the exciting developments in next-generation antibody therapeutics, including Antibody-Drug Conjugates, Bispecific Antibody Therapeutics, and Cancer Immunotherapies. Along with engineering breakthroughs, this pipeline also explores successful R&D strategies, translational case studies, clinical results, and efficacy data for these promising molecules as they seek to conquer cancer and other diseases, and promote human health.

JANUARY 14-15

AGENDA Engineering Next-Generation Cancer Immunotherapies

JANUARY 15-16

AGENDA Antibody-Drug Conjugates

JANUARY 17-18

AGENDA Bispecific Antibody Therapeutics

MONDAY-TUESDAY, JANUARY 14-15 | 5TH ANNUAL

ENGINEERING NEXT-GENERATION CANCER IMMUNOTHERAPIES

New Protein Engineering Science and Technology to Support the Development of Novel Immunotherapeutics and Treatment Combinations

IT HAS NOW been seven years since the first approval of ipilimumab, and there are now six mainstream checkpoint inhibitors approved for a range of cancers. Based on these clinical successes, the industry is now directing its attention to combination treatments, single agent therapeutics with multiple modes of action, confronting resistance mechanisms, reducing toxicity and the persistent challenge of solid tumors. Cambridge Healthtech Institute's 5th Annual Engineering Next-Generation Cancer Immunotherapies conference provides a forum in which research scientists can discuss the contributions of protein engineering to the discovery and development of novel biotherapeutics in the oncology space.

SUNDAY, JANUARY 13

4:00 - 6:00 pm Pre-Conference Registration

MONDAY, JANUARY 14

7:00 am Registration and Morning Coffee

RESEARCH TOOLS FOR ENGINEERING NEXT-GENERATION IMMUNOTHERAPIES

9:00 Welcome by Conference Organizer
Kent Simmons, Senior Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks
John Williams, PhD, Professor, Department of Molecular Medicine, Beckman Research Institute; Member, Cancer Immunotherapeutics Program, City of Hope Comprehensive Cancer Center

KEYNOTE PRESENTATION

9:10 Integrative Pharmacology: Advancing Development of Effective Immunotherapies
Mohammad Tabrizi, PhD, Director, Biologics PPDM, Merck Research Laboratories Palo Alto
With the recent advances in cancer immunotherapy, it is now evident that the antigen-specific activation of the patients' immune responses can be utilized for achieving significant therapeutic benefits. Due to the nature of immunotherapy, i.e., harnessing the patient's immune system, it becomes critical to evaluate the important variables that can guide development and effective clinical dosing paradigms following single and combination therapies. Critical topics related to preclinical, translational and clinical development of IO agents are discussed.

9:50 T Cell Engaging Bispecific Antibodies: Comparing Pfizer's Platforms
Javier Chaparro-Riggers, PhD, Senior Director, Protein Engineering, Pfizer
T cell engaging bispecific antibodies are a promising therapeutic approach for the treatment of multiple cancer types. A variety of formats are currently being tested in the clinic. Pfizer has developed several Fc-containing T cell engaging bispecific antibody platforms that increase the half-life and allow for conventional dosing. These platforms are currently evaluated in the clinic. Here, we will compare these platforms and the challenges and opportunities of each platform will be highlighted.

10:20 Networking Coffee Break

10:45 Development and Validation of Imaging Biomarkers for IO Applications
Michael Evans, PhD, Assistant Professor, Radiology and Biomedical Imaging, University of California, San Francisco
This presentation will outline recent efforts at UCSF to apply omics technologies and phage display to identify and target with recombinant human antibodies cell surface antigens that are upregulated by important oncogenic drivers. Recent screening efforts have identified new antibodies against cell surface proteins upregulated by mutant KRAS, c-MYC, and mTORC1, and the antibodies have been further matured for nuclear medicine applications like PET imaging and radioimmunotherapy.

11:15 Development of a New Patient Derived Xenograft Humanized Mouse Model to Study Human Specific Tumor Microenvironment and Immunotherapy
*Qingfeng Chen, PhD, Principal Investigator, Institute of Molecular and Cell Biology, A*STAR, Singapore*
Recently, we transplanted patient-derived xenograft tumors with type I human leukocyte antigen-matched human immune system in NOD-scid Il2rg-/- mice. Similar to patients, the human immune system in our model is educated by tumor and exhibits exhaustion phenotypes. Our model also demonstrates both therapeutic and side effects of immune checkpoint inhibitors. Thus, we provide a model for immune-oncology study and a useful parallel-to-human platform for anti-HCC drug testing, especially immunotherapy.

11:45 Pritumumab, the Journey from the Bench to the Bedside
Mark C. Glassy, PhD, CSO, Nascent Biotech
Pritumumab, a natural human IgG1 kappa antibody recognizes an altered form of vimentin called ecto-domain vimentin (EDV) expressed on the surface of cancer cells. In a Phase II clinical trial with Japanese brain cancer patients, pritumumab showed an overall response rate of 25-30%. A recombinant version of pritumumab was made from CHO cells and is currently being prepared for additional FDA-approved clinical trials.

12:15 pm Sponsored Presentation *(Opportunity Available)*

12:45 Session Break

12:55 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

ENGINEERING THE NEXT GENERATION OF CHECKPOINT INHIBITORS

2:00 Chairperson's Remarks
Yariv Mazor, PhD, Senior Scientist, Antibody Discovery & Protein Engineering, MedImmune, LLC

2:05 Checkpoint Inversion by INBRX-105: A Bispecific Multivalent PD-L1 x 41BB Single Domain Antibody Therapeutic Delivering Checkpoint Blockade and Conditional Immune Activation within the Tumor
John Timmer, PhD, Vice President, Research, InhibRx
InhibRx has developed a bispecific multivalent antibody with conditional 41BB agonist activity and potent PDL1 checkpoint blockade. This checkpoint inversion converts T cell suppressive PDL1 within the tumor into 41BB agonism driving anti-tumor T cell co-stimulation while avoiding toxicity from systemic 41BB activation. INBRX-105 is built from InhibRx's proprietary single domain antibody platform and innovative therapeutic format. Potent preclinical efficacy combined with a clear safety profile have propelled INBRX-105 toward the clinic.

2:35 Development of the First Enzyme-Based Immune Checkpoint Inhibitor for Cancer Therapy
Christos Karamitros, PhD, Director, Protein Engineering, Aeglea Biotherapeutics
It is well established that kynurenine, a key intermediate metabolite of the tryptophan catabolic pathway, has very potent immunosuppressive properties. Current clinical approaches focus on the development of IDO1 and TDO inhibitors to impair kynurenine synthesis. However, our novel approach degrades kynurenine into non-toxic and immunologically inactive metabolites in order to relieve immune suppression in cancer. This work showcases the first enzyme-based immune checkpoint inhibitor.

3:05 Find Your Table and Meet Your BuzZ Session Moderator

3:15 BuzZ Sessions with Refreshments
Join your peers and colleagues for interactive roundtable discussions.
See page 11 for details.

BISPECIFICS AND SINGLE AGENTS WITH COMBINATION EFFECTS

4:30 Design Meets Biology – Engineering a PD-1/CTLA-4 Bispecific Antibody to Improve Both Safety and Efficacy
Yariv Mazor, PhD, Senior Scientist, Antibody Discovery & Protein Engineering, MedImmune, LLC
MEDI5752 is a monovalent bispecific IgG1 antibody (DuetMab), targeting the two clinically validated receptors; PD-1 and CTLA-4. The bispecific antibody introduces novel MOAs that may provide an improved therapeutic index when compared to the two monotherapies and mAb combinations. MEDI5752 is currently being clinically evaluated for safety and efficacy.

5:00 Functionalization of mAbs Using Natural Amino Acids
John Williams, PhD, Professor, Department of Molecular Medicine, Beckman Research Institute; Member, Cancer Immunotherapeutics Program, City of Hope Comprehensive Cancer Center
Many disparate genetic and chemical approaches have been developed to leverage the exquisite specificity of antibodies for therapeutic and diagnostic intent. Here, we use the site-specific meditope interaction to catalyze the efficient formation of a disulfide bond without the need for incorporating non-natural amino acids or post-translational, enzymatic modifications. This 'swappable' platform permits the stable modification of antibodies through the exchange of meditopes functionalized to include imaging agents, cytotoxins and biologics.

5:30 Tumor Antigen-Dependent T Cell Activation and Tumor Localization Induced by a Novel 4-1BB x 5T4 ADAPTIR™ Bispecific Antibody
Peter Ellmark, PhD, Vice President, Discovery, Alligator Bioscience AB, Sweden
ALG.APV-527 is designed to induce potent tumor specific CD8 T cell activation by activating 4-1BB on T cells only when simultaneously engaging 5T4 on tumor cells. Pre-clinical *in vitro* and *in vivo* data demonstrates that ALG.APV-527 stimulates increased T cell activation in the presence of 5T4-expressing cells, localizes to 5T4 positive tumors and inhibits tumor growth. This data supports its potential to provide effective tumor-directed immune activation with reduced systemic side effects.

6:00 - 7:15 Welcome Reception in the Exhibit Hall with Poster Viewing
Sponsored by proteinsimple

7:15 Close of Day

TUESDAY, JANUARY 15

8:00 am Registration and Morning Coffee

ENGINEERING CHALLENGES FOR CAR-TS

8:30 Chairperson's Remarks
Peter Ellmark, PhD, Vice President, Discovery, Alligator Bioscience AB, Sweden

8:35 Application of Single Domain Antibody Technology in CAR-T Cells for Treating Solid Tumors
Mitchell Ho, PhD, Senior Investigator, National Cancer Institute, NIH
Single domain antibodies represent a very different class of molecules: small, easy to express, stable and capable of revealing buried epitopes unreachable by conventional antibodies. We have generated single domain antibodies that target tumor antigens (e.g. mesothelin, GPC3 and GPC2) and developed CAR T cells based on these antibodies. Construction and next-generation sequencing analysis of our new phage-displayed shark and camel single domain antibody libraries will also be described.

9:05 CAR-Ts and Combination Therapy with Checkpoint Blockade
Prasad S. Adusumilli, MD, Head, Solid Tumors Cell Therapy, Cellular Therapeutics Center (CTC), Memorial Sloan-Kettering Cancer Center
In solid tumor immunotherapy, we have shown that regional administration of CAR T cells will have increased potency and decreased toxicity, and that exhausted PD-1 expressing CAR T cells can be functionally rescued by use of checkpoint blockade agents. We now have translated both concepts to clinical trials. The specifics of patient stratification for combination immunotherapy, evaluation parameters

and outcomes interpretation are ongoing areas of clinical and translational investigation.

9:35 **Sponsored Presentation** *(Opportunity Available)*

9:50 **Coffee Break in the Exhibit Hall with Poster Viewing**

11:00 **Rewiring T Cell Responses to Soluble Factors with Chimeric Antigen Receptors**
Yvonne Chen, PhD, Assistant Professor, Chemical & Biomolecular Engineering, UCLA
Immunosuppression in the tumor microenvironment presents a critical barrier to chimeric antigen receptor (CAR)-T cell therapy for solid tumors. Here, we discuss the development of CARs that respond to soluble antigens in general and the immunosuppressive cytokine TGF-β in particular. The development of CAR-T cells that can convert soluble immunosuppressive factors into potent T cell stimulants offers a new approach to engineering effective CAR-T cell therapies for solid tumors.

11:30 **Development of a Universal CAR-T Cell Targeting System**
Mauro Castellarin, PhD, Postdoctoral Researcher, Center for Cellular Immunotherapies, University of Pennsylvania School of Medicine
CAR T cell (CART) targeting of solid tumors is hindered by heterogeneous tumor clones with diverse antigen profiles. To counter this, we developed a universal CAR that can attach to different antigen recognition molecules and enables CARTs to kill a diverse set of tumor cells. This is a promising new advancement as it allows CART treatment to adapt to changes in the tumor landscape throughout the course of the disease.

12:00 pm **Sponsored Presentation**
(Opportunity Available)

12:30 **Session Break**

12:40 **Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 **Close of Engineering Next-Generation Cancer Immunotherapies Conference**

TUESDAY-WEDNESDAY, JANUARY 15-16 | 6TH ANNUAL

ANTIBODY-DRUG CONJUGATES

Next-Gen Engineering

AS MORE ANTIBODY-DRUG conjugates head to market, the next generation of ADCs looms on the horizon. Next-gen engineering requires designing an optimal antibody, payload, linker and conjugation method while ensuring stability, targeted delivery, and limited off-target effects. Cambridge Healthtech Institute's Antibody-Drug Conjugates conference will explore the engineering finesse required to achieve the crucial balance between efficacy and safety, thus leading the way to more potent and targeted molecules. Case studies and data will be shared that exemplify the ongoing efforts to engineer ADCs, move them into the clinic, and fight cancer along with potentially non-oncological indications.

TUESDAY, JANUARY 15

1:00 pm Registration

1:30 Refreshment Break in the Exhibit Hall with Poster Viewing

FIGHTING CANCER WITH ANTIBODY-DRUG CONJUGATES

2:00 Chairperson's Opening Remarks
Marc Damelin, PhD, Senior Director, Biology, Mersana Therapeutics, Inc.

KEYNOTE PRESENTATION

2:05 Advances in Next-Generation ADCs, Immunotherapies and Combinations in the War against Cancer
Rakesh Dixit, PhD, Vice President and Global Head, Translational Sciences-Biologics Safety Assessment, MedImmune, LLC
In my talk, I will discuss advances in next-generation ADCs that are meeting the challenges; some new, some old. One persistent challenge is mitigating dose-limiting toxicities of ADCs and improving therapeutic index. I will also address next-generation immunotherapies and their combinations, and synergies between ADCs and immunotherapies.

2:45 ADCs with IGN Payload in Hematologic Malignancies
Yelena Kovtun, PhD, Associate Director, Pipeline Research and Development, ImmunoGen, Inc.
Several ADCs with mono-imine containing Indolinobenzodiazepine (IGN) payload entered the clinic recently, including IMGN779 and IMGN632, conjugates targeting CD33 and CD123 respectively. The strategy to select targets in hematologic malignancies, as well as to design optimal antibody, payload and conjugation method for IMGN779 and IMGN632 will be covered in the presentation.

3:15 Simple and Efficient Production of Homogeneous, Site-Specific ADCs with Transglutaminase & RESPECT™
Sponsored by morphotek
Jared Spidel, PhD, Senior Principal Scientist, Antibody Development, Morphotek, Inc

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

FIGHTING CANCER WITH ANTIBODY-DRUG CONJUGATES *(Cont.)*

4:30 Transvascular Pumping of ADC into Solid Tumors Boosts Drug Potency and Safety
Jan E. Schnitzer, MD, Director and Professor, Cellular & Molecular Biology, Proteogenomics Research Institute for Systems Medicine (PRISM)
Current ADCs can't deliver drugs inside solid tumors specifically, rapidly or robustly. Near MTD doses required to drive ADCs passively across endothelial cell barriers are inadequate to unleash drug potency inside tumors. We circumvent this passive transvascular delivery paradigm by generating the first antibody to actively penetrate solid tumors. This enables precision tumor targeting and imaging within one hour, boosts therapeutic indices >100-fold and even eradicates multi-drug resistant tumors at doses well below MTD.

5:00 Antibody-Drug Conjugates Targeting Tumor Stromal Cells
Dimiter Dimitrov, PhD, Director, Center for Antibody Therapeutics, University of Pittsburgh Medical School
Targeting the tumor stromal cells in addition to tumor cells with ADCs is a promising anti-cancer strategy. CD276 and TEM8 are variably expressed in a variety of cancers and to different extents on tumor stromal cells and tumor cells. Both CD276-ADC-PBD and TEM8-ADC-MMAE eradicated large established tumors and metastases and improved long-term overall survival in several different mouse models of cancer. Data for ADCs targeting other cancer-related molecules will also be discussed.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

5:45 - 8:45 Dinner Short Courses*
See page 8 for details.
**Separate registration required*

WEDNESDAY, JANUARY 16

7:45 am Registration and Morning Coffee

NEXT-GEN ENGINEERING STRATEGIES FOR ADCs

8:15 Chairperson's Remarks
Shalom Goldberg, PhD, Principal Scientist, Discovery Sciences, Janssen Research & Development/Johnson & Johnson

FEATURED PRESENTATION
8:20 Next-Generation ADCs: Considerations and Examples
Marc Damelin, PhD, Senior Director, Biology, Mersana Therapeutics, Inc.
In this case study, I will discuss key opportunities for the discovery and development of next-generation ADCs as informed by learnings from our collective experience. Topics will include molecular design, preclinical studies and development strategy. In this context, I will highlight the rationale and early data from selected technologies and clinical molecules.

8:50 Conjugated or Engineered Antibodies -- Benefits and Limits of Different Therapeutic Modalities
Stefan R. Schmidt, PhD, MBA, Head, Operations (COO), Bioatrium, AG
During the last decade, we could observe disruptive developments in antibody technologies. On the one hand, a broader understanding of drug conjugates and their optimization could be gained. On the other hand, protein engineering was massively applied to improve critical features of antibodies in general. In this talk, the different strategies will be discussed, comparing their benefits and limits and highlighting recent success stories of both therapeutic modalities in the context of functionality and manufacturing.

9:20 Presentation to be Announced

Sponsored by MabFlex

9:35 Sponsored Presentation
(Opportunity Available)

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

HONING IN ON ADC TARGETS

10:35 Targeting of Tumor-Initiating Cell-Associated Antigens with Antibody-Drug Conjugates
Alex Bankovich, PhD, Senior Director, Late Stage Research, Abbvie Stemcentrx, LLC
Tumor-initiating cells (TICs) will remain controversial until findings in the lab translate into drugs providing significant clinical benefit to patients. Antibody drug conjugates (ADCs) are a promising class of drugs able to target and reduce the frequency of TICs in patient-derived xenografts. My company has worked to discover TIC phenotypes and to utilize methods well-suited to specifically identify cell surface proteins targetable by specific ADCs. My talk expands on the drug development path we followed and provides some new insights.

11:05 Using Multi-Omics Data and Functional Screens to Select Antibody-Drug Conjugate Targets
Jennifer Hill, PhD, Team Lead, MS & NMR Analytics, National Research Council Canada (NRC)
Antibody drug conjugates (ADCs) are a promising therapeutic class for cancer therapy. We describe our approach to identify new ADC targets, incorporating gene expression data mining and glycoproteomic profiling, followed by *in vitro* screening through a surrogate ADC assay. Based on these target selection methods, we are producing thousands of monoclonal and single-domain antibodies generated against a variety of cancer-associated targets and screening them for ADC activity, *in vitro* and *in vivo*.

11:35 SILAC-Based Proteomics Screen to Select Potential ADC Targets
Julian Andreev, PhD, Senior Staff Scientist, Oncology and Angiogenesis, Regeneron Pharmaceuticals
Rapid constitutive lysosomal internalization of Prolactin Receptor (PRLR) is the mechanism behind PRLR ADC efficacy. By bridging PRLR, or another high turnover protein, Amyloid Precursor-like Protein 2 (APLP2), with surface tumor target HER2 using bispecific antibodies, HER2 lysosomal degradation can be triggered, and HER2 ADC efficacy can be significantly improved. Our study opens up a possibility to exploit high turnover proteins such as PRLR and APLP2 in combination with bispecific antibodies to enhance efficacy of ADCs.

12:05 pm Session Break

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

1:15 Session Break

2:00 PLENARY KEYNOTE PANEL
See page 5 for details.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

IMPROVING SITE-SPECIFIC CONJUGATION, PAYLOADS & SCAFFOLD ENGINEERING

4:00 Chairperson's Remarks
Yelena Kovtun, PhD, Associate Director, Pipeline Research and Development, ImmunoGen, Inc.

4:05 Development of a Site-Specific Peptide-Antibody Conjugation Platform
Yuan Cheng, PhD, Principal Scientist, Medicinal Chemistry, Amgen, Inc.
We developed a site-specific conjugation platform using cysteine-mutant antibody or protein. In this presentation, we describe the optimization of this platform by changing the disulfide caps to cysteamine, using a mild reducing agent, and monitoring individual reaction steps. The conjugation sites and linkers had a significant effect on conjugation efficiency, biological activity, and pharmacokinetic profiles. The platform allowed efficient SAR studies in a variety of research projects and demonstrated feasibility in multi-gram conjugation.

4:35 Highly Homogeneous Antibody-Drug Conjugates Based on Dual Variable Domains
Christoph Rader, PhD, Associate Professor, Immunology and Microbiology, The Scripps Research Institute
Homogeneous antibody-drug conjugates (ADCs) that use a highly reactive buried lysine residue embedded in a dual variable domain (DVD) format can be assembled with high precision and efficiency under mild conditions and reveal potent and specific tumor cell killing *in vitro* and *in vivo*. Building on this DVD-ADC platform, we have developed orthogonal conjugation strategies that enable the loading of two different payloads in a one-pot reaction.

5:05 Antibody PBD Conjugates
Philip Howard, PhD, Senior Fellow, MedImmune, Inc.; CSO, Spirogen, Ltd.
Pyrrolobenzodiazepines (PBDs) have found extensive use in the field of antibody drug conjugates. PBD payloads have been studied in more than 20 clinical trials; currently these trials are dominated by tesirine and talirine payloads. This presentation will focus on the learnings from the clinical studies and development of the next generation of PBD payloads.

5:35 Design, Characterization, and LC/MS/MS Bioanalysis of Protein-Drug Conjugates
Shalom Goldberg, PhD, Principal Scientist, Discovery Sciences, Janssen Research & Development/Johnson & Johnson
Antibody- and other protein-drug conjugates have multiple parameters that can be tailored to increase the therapeutic window. Here we describe the design and characterization of a drug conjugate using the Centyrin alternative scaffold, as well as the development of broadly-applicable methods for *in vivo* characterization using LC/MS/MS.

6:05 - 7:00 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Antibody-Drug Conjugates Conference

THURSDAY-FRIDAY, JANUARY 17-18 | 8TH ANNUAL

BISPECIFIC ANTIBODY THERAPEUTICS

Engineering Multi-Specificity

CHI'S BISPECIFIC ANTIBODY Therapeutics conference explores the challenges of engineering multi-specificity to achieve more effective therapies that bind to at least two molecular targets simultaneously. These next-generation antibody formats are showing efficacy in the efforts to conquer cancer and other diseases by employing breakthrough technologies and engineering brilliance. Case studies will highlight novel engineering approaches that address safety, stability, enhanced targeting, and manufacturability, as the conference examines current developments and future directions for these promising molecules.

THURSDAY, JANUARY 17

7:45 am Registration and Morning Coffee

T CELL ENGAGING BISPECIFIC ANTIBODIES

8:10 Organizer's Welcome Remarks
Mary Ruberry, Senior Conference Director, Cambridge Healthtech Institute

8:15 Chairperson's Opening Remarks
James Ernst, PhD, Senior Scientist, Protein Chemistry, Genentech, Inc.

KEYNOTE PRESENTATION

8:20 T Cell Therapeutics in Hematological Malignancies and Solid Tumors
Tara Arvedson, PhD, Director, Oncology Research, Amgen, Inc.
T cell therapeutics have demonstrated a clinical benefit in hematological malignancies and there is early evidence of activity in solid tumors. Analysis of data derived from T cell therapeutics in hematological malignancies will increase the chances of success for similar therapeutics in solid tumors. This presentation will describe key findings from recent trials of T cell therapeutics in hematological malignancies and will relate these findings to approaches for treating solid tumors.

9:00 Expanding Bispecific Antibody Technology to Enable Multiple Avenues of T Cell Activation
Matthew Bernett, PhD, Associate Director, Protein Engineering, Xencor, Inc.
Xencor has applied its XmAb® bispecific technology platform to create multiple novel modalities for T cell derepression and activation. These include dual checkpoint inhibitors such as PD1 x CTLA4 and CTLA4 x LAG3 bispecific antibodies, as well as a PD1 x ICOS bispecific antibody that combines checkpoint blockade and costimulation into a single molecule. Finally, we have utilized our heterodimeric Fc domain to create a novel long-acting IL15/IL15Rα-Fc for immunotherapy.

Sponsored by PROIMMUNE www.proimmune.com

9:30 An Integrated Approach to Managing Immunogenicity Risk and Optimum Protein Design
Jeremy Fry, Director, Sales, ProImmune, Ltd.
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 and undiluted whole blood cytokine storm assays.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

T CELL ENGAGING BISPECIFIC ANTIBODIES *(Cont.)*

11:00 A Novel Multi-Specific Antibody Targeting PD-L1-Overexpressing Cancers that Stimulates Antigen-Committed CD8+ T Cells through Concomitant Engagement the Costimulatory Receptor 4-1BB
Sebastian Meyer, PhD, COO, Numab Innovation AG
Targeting PD-L1 and 4-1BB with a multi-specific antibody format holds the promise of increased potency while improving safety. Numab develops a molecule that potently blocks PD-L1/PD-1 signaling and elicits further T cell activation through its costimulatory domain solely in the close proximity of cells that overexpress PD-L1. Preclinical data show efficacy on tumor growth in combination with an enhanced intratumoral CD8+ T cell activation when compared to the combination of the PD-L1 and 4-1BB modalities.

11:30 Leveraging Anti-Tumor Immunity through Bispecific DART Molecules
Paul Moore, PhD, Vice President, Immunology & Cell Biology, MacroGenics, Inc.
Boosting host immune responses through antibody-based blockade of checkpoint pathways has provided unprecedented response rates in select cancer types. Bispecific antibody targeting provides opportunity to optimize and expand benefit. Examples of such strategies utilizing the DART®/TRIDENT™ platforms will be presented, including simultaneous targeting of multiple checkpoints, redirected T-cell killing of tumor cells and tumor-anchored immune co-stimulation. Topics covered will span structural design, preclinical development and clinical proof-of-concept.

12:00 pm Session Break

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

BIPARATOPIC ANTIBODIES TO TARGET TUMORS AND HER2

2:15 Chairperson's Remarks
G. Jonah Rainey, PhD, CEO, Oriole Biotech, Inc.

2:20 Redefinition of RTK Tumor Targeting: How to Design Truly Potent Anti-HER2/3 Bispecific and Biparatopic Agents
Rastislav Tamaskovic, PhD, Head, TC Facility, Biochemistry, University of Zurich
Due to adaptiveness of oncogenic networks, tumors readily develop resistance against targeted therapies. Recently, we developed a new class of bispecific and biparatopic anti-HER2/3 targeting agents to overcome the adaptive resistance. These targeting vehicles achieve their superior tumoricidal activity by trapping tumor-driving receptor tyrosine kinases in inactive conformations and/or supramolecular assemblies. Analogously, we built a new platform for tumor RTK fingerprinting to identify prospective therapeutic leads and combination therapies.

2:50 ZW25/ZW49, Development of a HER2-Targeted Biparatopic Antibody and Biparatopic Antibody-Drug Conjugate
David Poon, PhD, Executive Director, External R&D and Alliances, Zymeworks, Inc.
ZW25 is a bispecific antibody directed against two distinct epitopes (biparatopic) on HER2 that has been successfully engineered using the Azymetric™ IgG1 antibody scaffold. ZW25 is well tolerated and has demonstrated promising single-agent anti-tumor activity in heavily pretreated HER2-expressing breast, gastric, and other cancers. Preclinical development of ZW49, a biparatopic antibody-drug conjugate based on the unique design of ZW25 and armed with our proprietary ZymeLink™ cytotoxic payload, will also be discussed.

3:20 Sponsored Presentation *(Opportunity Available)*

3:35 Networking Refreshment Break

FIGHTING CANCER WITH BISPECIFIC ANTIBODIES

4:00 SMITE Bispecifics: A Novel Combination Strategy to Combat Cancer
Ashok D. Bandaranayake, PhD, Director, Bioprocess Development and Automation, Protein Therapeutics Program, Fred Hutchinson Cancer Research Center
We propose a new way of gaining a high level of specificity for cancer by employing two bispecific molecules simultaneously. Importantly, each of these molecules is designed to have little or no activity on their own, so that healthy tissue bearing either one of the targets is not affected. However, when both targets are expressed (in cancer) the two bispecific molecules act in synergy, stimulating and co-stimulating T cells for maximum efficacy.

4:30 ATOR-1015, a Bispecific CTLA-4 x OX40 Antibody, Induces Anti-Tumor Effects through Tumor-Directed Immune Activation
Peter Ellmark, PhD, Vice President, Discovery, Alligator Bioscience AB
ATOR-1015, a next-generation CTLA-4 antibody designed to deplete Tregs and activate effector T cells. ATOR-1015 is tumor-directed, which is expected to result in a favorable benefit/risk profile. A clinical Phase I trial is planned to start in H2 of 2018.

5:00 Activating the Immune System with Bispecific Antibodies
Mihriban Tuna, DPhil, Vice President, Drug Discovery, F-star Biotechnology, Ltd.
Cancer proliferates through numerous evasion strategies and re-engaging the immune system is key in the control of tumor growth. In recent years, checkpoint immunotherapies and their combinations have rapidly progressed from being a promising therapeutic opportunity to a robust clinical reality. In this presentation, we will discuss how checkpoint-binding bispecific antibodies have the potential to go beyond combinations by reversing down-regulation of the immune system and promoting tumor elimination.

5:30 Close of Day

FRIDAY, JANUARY 18

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast
Protein therapeutics is a fast-growing global market. As the science improves, so does the complexity of the R&D organization. Ensuring product quality plus speed to market requires insights from stakeholders working across the stages of protein science R&D. Join experts representing this PepTalk pipeline, peers, and colleagues for an interactive roundtable discussion. Topics include highlights from the week's presentations, new technologies and strategies, challenges, and future trends.
Moderator: Rakesh Dixit, PhD, DABT, Vice President, Medimmune-AstraZeneca

ENGINEERING MULTI-VALENCY

9:00 Chairperson's Remarks
Peter Ellmark, PhD, Vice President, Discovery, Alligator Bioscience AB

9:05 Fully Human, Heavy-Chain Antibodies Facilitate Rapid Development of Multi-Specific Antibodies
Wim van Schooten, PhD, CSO, TeneoBio, Inc.
TeneoBio's discovery platform utilizes VH domains of fully human heavy chain antibodies (UniAbs) to develop bi-, tri-, and tetravalent antibodies. Binding domains of UniAbs are stable structures that can be easily put together into multi-specific antibodies. Clinical trials of TeneoBio's first trivalent antibody will be initiated in 2018.

9:35 Format and Isotype Selection for Optimal Bispecific Activity
G. Jonah Rainey, PhD, CEO, Oriole Biotech, Inc.
Bispecific antibodies are versatile molecules that allow diverse and potent mechanisms of action. As we move from the first-approved bispecifics that retarget killing of T cells to tumor cells, strategies that take into account the ability to interact with non-adaptive immune and non-immune components need to be exploited to achieve optimal efficacy and safety. Design considerations including valency, effector function, and half-life will be discussed.

10:05 A Toolbox for the Generation, Purification, and Customized Functional Adaptation of Bispecific ADCs
Harald Kolmar, PhD, Professor, Applied Biochemistry, Technical University Darmstadt
A platform was developed for the facile generation of common light chain antibodies using yeast display. pH-dependent binding can be introduced by

common light chain engineering. Bispecific ADCs are generated using SEED technology followed by enzyme-mediated coupling of a polymer-drug conjugate with high payload (DextraMab). We also established a route for the purification of bispecifics via affinity chromatography using tailor-made anti-idiotype binders.

10:35 Networking Coffee Break

CONQUERING DISEASE WITH BISPECIFIC ANTIBODIES

11:00 Development of Bispecific Antibodies at Novartis
John W. Blankenship, PhD, Senior Investigator, Antibody Discovery, Novartis Institutes for BioMedical Research, Inc.

11:30 A Bispecific Antibody Mimetic of FGF21 for the Metabolic Disease and NASH
James Ernst, PhD, Senior Scientist, Protein Chemistry, Genentech, Inc.
Activation of the FGF21 pathway has been shown to improve multiple features of metabolic disease in animals. Here we describe a novel bispecific antibody that mimics the function and metabolic effects of FGF21. Treatment with this antibody improves glycemic and lipid profiles in mouse disease models and reduces body weight in mice and non-human primates. These effects mimic the activity of FGF21 on both mice and non-human primates, suggesting that antibody-mediated activation of FGF21 pathway would be an effective treatment for type 2 diabetes.

12:00 pm Conference Wrap-Up
Rakesh Dixit, PhD, DABT, Vice President, Medimmune-AstraZeneca

12:30 Close of Conference

FORMULATION & STABILITY

As the industry advances biotherapeutic development, the formulation and process development functions play important roles, supporting the selection and optimization of molecules with better developability, manufacturability, stability, safety and efficacy. The popular Formulation & Stability pipeline presents case studies of the latest tools, technologies and cutting-edge approaches related to the progression of biologics, from R&D into the development of high-quality biotherapeutic products.

JANUARY 14-15

AGENDA Optimizing Biologics Formulation Development

JANUARY 15-16

AGENDA Lyophilization and Emerging Drying Technologies

JANUARY 17-18

AGENDA Protein Aggregation and Emerging Analytical Tools

Also part of **ANALYTICS & IMPURITIES**

MONDAY-TUESDAY, JANUARY 14-15 | 11TH ANNUAL

OPTIMIZING BIOLOGICS FORMULATION DEVELOPMENT

Exploring the Future of Tools and Techniques for Formulating Novel Biologic Drug Products

CAMBRIDGE HEALTHTECH INSTITUTE'S 11th Annual Optimizing Biologics Formulation Development conference is an essential international gathering of analytical and formulation scientists from leading industry companies, providing an exchange of scientific developments and emerging technologies in an environment that encourages discussion with colleagues. For 2019, the conference offers perspectives on the future of biotherapeutics formulation development. Presenters will address the formulation challenges of new modalities and delivery systems, consider strategies for accelerating and streamlining this stage of development and examine best practices for applying new technologies and analytical platforms.

SUNDAY, JANUARY 13

4:00 - 6:00 pm Pre-Conference Registration

MONDAY, JANUARY 14

7:00 am Registration and Morning Coffee

THE NEXT GENERATION OF PROTEIN DELIVERY

9:00 Welcome by Conference Organizer
Kent Simmons, Senior Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks
Zhenyu Gu, PhD, Development Scientist, Global Analytical and Pharmaceutical Development, Alexion Pharmaceuticals

KEYNOTE PRESENTATION

9:10 How Next-Generation Biotherapeutics Will Influence Formulation and Device Development
Kerstin Walke, PhD, Head, Pharmaceutical Development Biologicals, Boehringer Ingelheim
Patient self-administration is now expanding and the threshold limits for high concentrated formulations are driving development of high-volume delivery devices. Co-formulations of multiple monoclonal antibodies into a single drug product also offer patient convenience but drives the need for new analytical methods. There is also a trend toward advanced therapy medicinal products (ATMPs), a challenging new area for pharmaceutical development. This presentation will explore the impact of these trends on the formulation function.

9:50 Progress and Remaining Challenges in Formulating High Concentration Proteins for Patient Administration
Zhenyu Gu, PhD, Development Scientist, Global Analytical and Pharmaceutical Development, Alexion Pharmaceuticals
High-concentration protein formulation poses considerable challenges to the formulation and assay development. Manufacturing aspects including concentratability, viscosity and stability need to be considered in the early development. In this presentation, practical challenges and solutions to the molecule selection, formulation and analysis will be discussed for the formulation development of high protein concentrations.

10:20 Networking Coffee Break

MIXTURES AND CO-FORMULATIONS

10:45 Quality by Design and Design Control for Combination Product Development: Crossroads of Design Control and Manufacturing Risk Assessment
Leigh Bohack, PhD, Formulation Scientist, Pfizer
By developing an assembly, labeling and packaging (ALP) process Failure Mode and Effect Analysis (pFMEA), the fulfillment of user, product and regulatory requirements can be traced through the ALP process and identified risks can be mitigated. Utilizing engineering, PQ and PV manufacturing data is essential for building an understanding of this process and the impact to the combination product. This process generates a well-controlled process and quality product.

11:15 Analytical Strategies for Co-Formulated Products
George Svitel, PhD, Principal Scientist, Merck
Co-formulating multiple mAbs into a single drug product brings benefits including combined therapeutic effect, streamlined manufacturing/distribution and elevated patient convenience. But co-formulated products also bring additional product characterization challenges. Analytical methods originally developed for individual products need to be further developed for co-formulated products. There are also questions regarding mechanisms of degradation, aggregation pathways and possibility of creation of mixed aggregated species in co-formulated products.

11:45 Peptide Mixtures: Biophysical Characterization of Self-Association and Hetero-Oligomers
Marie Østergaard Pedersen, PhD, Specialist, Protein & Peptide Biophysics, Novo Nordisk, Denmark
Many peptides are prone to form oligomers with size and distribution depending on sequence, chemical modifications and formulation conditions. For mixtures of two different peptides, hetero-oligomer formation has the potential to alter stability properties and/or change pharmacokinetic profiles. Thus, a

thorough biophysical understanding of each individual component, and their interactions, is required. This talk will present an overview of biophysical techniques relevant to the study of peptide mixtures.

12:15 pm **Sponsored Presentation**
(Opportunity Available)

12:45 **Session Break**

12:55 **Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

NEXT-GENERATION VISCOSITY PREDICTION

2:00 **Chairperson's Remarks**
Brian Lobo, PhD, Associate Director, Formulation Development, MedImmune

2:05 **Exploring the Determinants of Viscosity and Self-Association in Highly Concentrated Antibody Solutions Using Molecular Dynamics**
Benjamin Walters, PhD, Scientist, Technology, Genentech
Using a novel physics-based multi-scale coarse-grained approach, we explore how high viscosity can emerge from weak self-interactions. Key developments that enabled this work are discussed, including our novel strategies to preserve electrostatic fields and hydrophobicity features. Our method improves on currently available approaches, evidenced by comparison against a large dataset, and facilitates formulation development activities, such as considering the effects of salt, without consumption of material.

2:35 **Protein-Protein Interactions and Relevance to Viscosity**
William Callahan, MSc, Senior Scientist, Process Development, Amgen
Protein viscosity is known to be correlated with protein-protein interactions. Using a solubility parameter approach, we show that common properties of water miscible solvents are involved in the degree to which protein-protein interactions occur as measured by differences in viscosity. These short-range interactions are related to the dispersion energy, polar energy and hydrogen bonding energy of test solvents. It can also be shown that the viscosity can be reasonably predicted through correlation with surface tension measurements of these solvents.

3:05 **Find Your Table and Meet Your BuzZ Session Moderator**

3:15 **BuzZ Sessions with Refreshments**
Join your peers and colleagues for interactive roundtable discussions.
See page 11 for details.

FORMULATION DEVELOPMENT FOR NOVEL MODALITIES

4:30 **Miniaturized High Throughput Screening for Formulation Development**
David Smithson, PhD, Scientist, Genentech
For the last four years our group has worked to develop miniaturized model systems suitable for formulation development efforts of biologics across our portfolio. These efforts have been focused in two distinct areas – physical miniaturization of our stability workflow and evaluation of improved high throughput amenable biophysical techniques for characterization of formulation candidates. We will present the current status of these efforts and discuss applicability of these techniques at various project stages.

5:00 **Formulation Development Challenges of Antibody Drug Conjugates**
Brian Lobo, PhD, Associate Director, Formulation Development, MedImmune
Antibody drug conjugates (ADCs) combine the physical-chemical stabilities and functions of monoclonal antibodies with the chemical and structural attributes of small molecule cytotoxics. Case studies are presented that demonstrate the challenges to assure stability and container compatibility of the mAb intermediate, frozen and liquid stability of ADC drug substance, stability of the ADC to lyophilization, and clinical compatibility of the ADC at very low doses for i.v. administration.

5:30 **Formulation and Delivery Challenges for AAV Gene Therapy Products**
Roberto DePaz, PhD, Associate Director, Formulation & Drug Product Development, RegenxBio
There is a growing pipeline of investigational gene therapy products using adeno-associated virus (AAV) vectors, boosted by encouraging clinical results and recent commercial approvals. A successful gene therapy product formulation must be stable during production, storage, and distribution, while meeting the dosage needs for the intended route of administration. This presentation will highlight some of the challenges encountered during the formulation development of these complex macromolecules.

6:00 - 7:15 **Welcome Reception in the Exhibit Hall with Poster Viewing**
Sponsored by proteinsimple

7:15 **Close of Day**

TUESDAY, JANUARY 15

8:00 am **Registration and Morning Coffee**

COMPUTATIONAL AND STRUCTURAL TOOLS FOR FORMULATION DEVELOPMENT

8:30 **Chairperson's Remarks**
Jun Zhang, PhD, Senior Scientist, Preformulation, AbbVie

8:35 **Antibody Design to Improve Physical Stability**
Christopher J. Roberts, PhD, Professor, Chemical & Biomolecular Engineering, University of Delaware
This presentation will focus on a series of coarse-grained molecular models and comparison to experimental data for predicting how changes in surface-charge distributions and formulation conditions can be used to predict protein-protein interactions and how these influence the physical stability of antibodies at low to high concentrations. Pros and cons of different modeling scales will be highlighted.

9:05 **Matching pH Values for Antibody Stabilization and Crystallization Suggest Rationale for Accelerated Development of Biological Drugs**
Hanno Sjuts, PhD, Postdoctoral Researcher, Protein Crystallization, Pharmaceutical Development Biologics, Sanofi, Germany
It is well known that the pH has critical influences on both a protein's colloidal stability and it's crystallization behavior. Here, differential scanning fluorimetry was used to determine pH values that exert highest thermal stabilities for three mAbs. Interestingly, the same pH values are required for successful crystallization of the respective mAbs. The results suggest strategies for how crystallography could be integrated into the development of novel biotherapeutic drugs for accelerated approval times.

9:35 Sponsored Presentation *(Opportunity Available)*

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

PREFORMULATION AND DEVELOPABILITY SCREENING

11:00 Toward Improved Candidate Selection and Formulation Development: Understanding Tangential Flow Filtration Instability of Proteins
Yuan Cheng, PhD, Senior Research Investigator, Discovery Pharmaceutics & Analytical Sciences, Bristol-Myers Squibb
Tangential flow filtration (TFF) is one of the common unit operations in biologics manufacturing. Some proteins are found to be sensitive to the stresses imposed during TFF process, leading to aggregate and particulate formation, which can cause significant delay in the development timeline. This talk focuses on introducing our efforts on building mechanistic understanding of TFF instability of proteins and developing predictive assays to help risk assessment in candidate selection and formulation development.

11:30 Biophysical Characterization of Therapeutic Antibody Non-Specific Binding for Drug Candidate Selection and Developability Screening
Jun Zhang, PhD, Senior Scientist, Preformulation, AbbVie
Understanding mAb properties that affect non-specific binding *in vivo* are important for sequence engineering and pharmacokinetic optimization. Both hydrophobicity and electrostatic mAb properties play important roles in non-specific binding *in vivo*. We show that heparin binding and FcRn affinity chromatography complement hydrophobicity assessment by HIC and that incorporating these methods into molecular profiling regimens provides insight into biodistribution in addition to stability during candidate developability screening.

12:00 pm Presentation to be Announced

Sponsored by UNCHAINED LABS

12:30 Session Break

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Close of Optimizing Biologics Formulation Development Conference

TUESDAY-WEDNESDAY, JANUARY 15-16 | 12TH ANNUAL

LYOPHILIZATION AND EMERGING DRYING TECHNOLOGIES

Formulation and Process Optimization, Models, PAT, and Drying Approaches for Biologics and Sensitive Products

THE POPULAR 12TH Annual Lyophilization and Emerging Drying Technologies conference covers latest trends, advances and challenges in lyophilization and emerging drying technologies. This conference will feature in-depth case studies, new and unpublished data, and discussions on developing freeze-dried formulation and process optimization for biologics and vaccines. It will also present cutting-edge research and case studies on drying in cartridges, storage stability, cell, gene and tissue-based products, QbD and PAT approaches for R&D scale to full production level and continuous manufacturing.

TUESDAY, JANUARY 15

1:00 pm Registration

1:30 Refreshment Break in the Exhibit Hall with Poster Viewing

2:00 Chairperson's Opening Remarks
Robin Bogner, PhD, Professor, Department of Pharmaceutical Sciences, School of Pharmacy, University of Connecticut

KEYNOTE PRESENTATION

2:05 Overcoming Implementation Challenges of Novel Drying Technologies and Continuous Manufacture
Satoshi Ohtake, PhD, Senior Director, Pharmaceutical Research and Development, Biotherapeutic Pharmaceutical Sciences, Pfizer, Inc.
While the pharmaceutical industry continues to demonstrate its creativity associated with novel compounds in development, the processing technologies utilized for their manufacture have not kept their pace. This is not a reflection of the paucity of innovation associated with processing technology. The barrier can broadly be classified as economic, logistical, technical and psychological, and all elements need to be overcome for successful implementation of a new technology.

QBD, PROCESS ANALYTICAL TECHNOLOGY, MODELING, AND CONTROL

2:45 Predictive Models of Lyophilization Process for Development, Scale-Up/Tech Transfer and Manufacturing
Ehab Moussa, PhD, Senior Scientist, Drug Product Development, AbbVie, Inc.
Scale-up and technology transfer of lyophilization processes remains a challenge that requires thorough characterization of the laboratory and larger scale lyophilizers. In this study, computational fluid dynamics and steady state heat and mass transfer modeling of the vial were utilized for scale-up and technology transfer. The models were verified experimentally for lyophilizers of different scales and were then applied to create and evaluate a design space for a drug product.

3:15 Sponsored Presentation *(Opportunity Available)*

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

4:30 Wireless Multipoint Temperature Sensors for Monitoring Pharmaceutical Lyophilization
Dimitrios Peroulis, PhD, Associate Dean for External Affairs, College of Engineering, Purdue University
In this talk, we discuss the design and evaluation of a fully wireless, multi-point temperature sensor system as a Process Analytical Technology (PAT) for lyophilization. Each sensor contains seven sensing elements which measure the product temperature at various positions of the contents of a glass vial. The sensor performance has been validated through a variety of freeze-drying experiments.

PREDICTION AND OPTIMIZATION OF STABILITY IN FREEZE-DRIED FORMULATIONS

5:00 CO-PRESENTATION: Detection of Protein Tertiary Conformational Changes in Lyophilized Protein in the Solid State
Robin Bogner, PhD, Professor, Department of Pharmaceutical Sciences, School of Pharmacy, University of Connecticut
Lauren Fontana, PhD Candidate, Department of Pharmaceutical Sciences, School of Pharmacy, University of Connecticut
A simple analysis of the lyophilized protein solid immediately after processing (requiring no reconstitution) that predicts stability would be ideal. FTIR is used to monitor secondary structural changes, but with limited prediction ability. Raman spectroscopy has more recently been suggested to characterize both secondary and tertiary protein structure in the solid state. Principal component analysis of Raman spectra can detect some of the subtler structural changes.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

5:45 - 8:45 Dinner Short Courses*
See page 8 for details.
**Separate registration required*

WEDNESDAY, JANUARY 16

7:45 am Registration and Morning Coffee

PREDICTION AND OPTIMIZATION OF STABILITY IN FREEZE-DRIED FORMULATIONS *(Cont.)*

8:15 Chairperson's Remarks
Satoshi Ohtake, PhD, Senior Director, Pharmaceutical Research and Development, Biotherapeutic Pharmaceutical Sciences, Pfizer, Inc.

8:20 Developing Low-Frequency Raman Methods to Predict Lyophilized Protein Stability
Marcus T. Cicerone, PhD, Project Leader, Biomaterials Group, National Institute of Standards and Technology
Lyophilized protein stability strongly correlates with fundamental steps of transport found at the picosecond timescale. In the past, these dynamic events have been measured by neutron scattering. We are developing benchtop optical approaches, particularly low-frequency Raman scattering, to be used as a rapid predictor of lyophilized protein stability.

8:40 Novel Methods to Study Effects of Moisture and Formulation on the Stability of Lyophilized Proteins
Anna Millqvist Fureby, PhD, Centre Director, NextBioForm; Senior Scientist, Surface, Process and Formulation, RISE Research Institutes of Sweden
Lyophilized protein formulations are influenced by composition processing and moisture. The distribution of protein and excipients is non-uniform, as studied by confocal Raman spectroscopy and other spectroscopic techniques. Moisture influences both the material properties and the stability of the protein, as studied by sorption calorimetry, DSC and high-resolution scattering techniques. A combination of analytical techniques enables a more comprehensive mechanistic understanding of protein stability in lyophilized formulations.

ADVANCES IN DRYING TECHNOLOGIES FOR COMPLEX DELIVERY SYSTEMS AND SENSITIVE BIOLOGICS

9:00 Back to Basics: Lyophilization Cycle Development for Stabilizing Complex Glycoproteins
Wendy Sunderland, BS, MBA, Director, Drug Product Development, Technical Operations, Amicus Therapeutics
The tendency when developing a lyophilized biologic is to be conservative, resulting in a product with necessary critical attributes, but an excessively long cycle. Lyophilizers are then greatly stressed, employing low shelf temperatures and chamber pressures, for a longer time, increasing risk for product failure. A case study will be presented for the lyophilization cycle development of a complex glycoprotein, thus reducing cycle time by half and increasing potential for success.

9:20 Sponsored Presentation *(Opportunity Available)*

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

10:35 Development of Vacuum-Foam Drying for Preservation of Human T Cells
Bryan Balthazor, MA, Scientist, Pharmaceutical Research and Development, Pfizer, Inc.
Vacuum-foam drying (VFD) is a novel pharmaceutical drying technology that uses evaporation to rapidly remove water, forming a solid foam structure. VFD has unique benefits, such as processing at near-ambient conditions, which can enable the drying of sensitive biologics. A case study is presented here using human T cells to demonstrate formulation, processing, and VFD optimization in order to minimize drying stresses and enable refrigerated storage of human T cells.

11:05 Atmospheric Spray Freeze Drying: The ASFD Future Is Dawning
Thomas D. Robinson, MD, Managing Director, DNA, Aerosol Therapeutics, LLC
Atmospheric Spray Freeze Drying (ASFD) is an innovative, "next-generation" process with broad utility. The process yields a fine, uniform powder. Specifically, the patented ASFD process promises an efficient, cost effective alternative to standard manufacturing processes. Although ideal for heat sensitive products and especially the more expensive, easily degraded proteins, the ASFD process can dry any solution, even the more concentrated solutions, to a target level moisture content.

11:35 Challenges in Stabilization of the Next Generation of Medicines: Cells and Tissue-Based Products
Rajiv Nayar, PhD, President, HTD Biosystems, Inc.

12:05 pm Session Break

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

1:15 Session Break

2:00 PLENARY KEYNOTE PANEL
See page 5 for details.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

EXCIPIENTS AND IMPURITIES IN PRE-FILLED SYRINGES AND FREEZE-DRIED FORMULATIONS

4:00 Chairperson's Remarks
Gregory A. Sacha, PhD, Senior Research Scientist, Baxter Healthcare Corporation

4:05 Impact of Silicone Oil on Fatty Acid Solubility and Polysorbate Related Particle Formation
Raphael Fish, Engineer I, Process Development, Genentech
Silicone oil coating on the interior of pre-filled syringes may act as a sink for fatty acids that are released upon hydrolytic degradation of polysorbates, potentially reducing risk of particle formation. Free fatty acids were shown to partition from an aqueous to a silicone oil phase in a glass vial model. However, the partitioning effect was not large enough to translate to significant reduction in particle formation risk at representative conditions. It was concluded that silicone oil levels in a PFS are too low to have any meaningful impact on polysorbate-related particle formation.

4:35 Protein Crowding in Solution, Frozen and Freeze-Dried States Studied by Small-Angle Neutron Scattering

Susan Krueger, PhD, NIST Center for Neutron Research, National Institute of Standards and Technology

Small-angle neutron scattering is uniquely qualified to study the structure of proteins in liquid and solid phases that are biotechnologically relevant. We have studied a model protein, lysozyme, in the liquid, water, ice and powder phases to determine its gross-structure, interparticle interactions and other properties. We also tested the effects of stabilizing excipients such as trehalose, glucose and sorbitol. Our results were compared to those from similar studies on antibodies.

5:05 Phase Behavior of an Alternative Surfactant, Poloxamer, during Freeze-Drying

Evgenyi Shalaev, PhD, Executive Director, Pharmaceutical Development, Allergan, Inc.

Poloxamers (e.g., P188) have been recently considered as alternative surfactants to polysorbates (tween20 and 80), as the latter are easily oxidized and can also undergo hydrolysis. In this study, complex phase behavior of aqueous solutions of a poloxamer is investigated using DSC, small-angle neutron scattering, and small- and wide-angle X-ray scattering.

5:35 The Effect of Co-Solvent Systems on the Drying Behavior of Common Excipients

Gregory A. Sacha, PhD, Senior Research Scientist, Baxter Healthcare Corporation

Many small molecules are poorly soluble in water and are often prepared in a co-solvent system prior to lyophilization. The co-solvent system may contain water and an organic solvent. This study examined the removal of the organic solvent from common excipients during primary drying using a residual gas analyzer. The drying behavior of amorphous and semi-crystalline formulations were examined as a function of organic solvent concentration.

6:05 - 7:00 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Lyophilization and Emerging Drying Technologies Conference

THURSDAY-FRIDAY, JANUARY 17-18 | 10TH ANNUAL

PROTEIN AGGREGATION AND EMERGING ANALYTICAL TOOLS

Immunogenicity, Prediction, Screening, Case Studies and New Research Highlights

Also part of **ANALYTICS & IMPURITIES**

THE POPULAR 10TH Annual Protein Aggregation and Emerging Analytical Tools conference covers latest trends, challenges and solutions in understanding, characterization and mitigation of problems generated by protein aggregation in biopharmaceuticals. This conference will feature in-depth case studies, new and unpublished data and interactive discussions on immunogenicity of aggregates, mechanisms of aggregation, new tools for detection and quantitation of aggregates, and how the data is used in regulatory filings. It will also discuss mechanistic understanding of protein aggregation and present case studies on prevention of particle formation by engineering and formulation approaches, aggregation in ADCs, bipecifics, impact of aggregation on production, aggregates as a factor for immunogenicity, and approaches for improvement of biophysical properties of protein solutions.

THURSDAY, JANUARY 17

7:45 am Registration and Morning Coffee

CHEMICAL MODIFICATIONS, PROTEIN POLYMORPHISM AND IMMUNOGENICITY

8:10 Organizer's Welcome Remarks
Nandini Kashyap, Conference Director, Cambridge Healthtech Institute

8:15 Chairperson's Opening Remarks
Thomas Laue, PhD, Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

KEYNOTE PRESENTATION

8:20 Chemical Protein Modifications and Immunogenicity Risks
Christian Schöneich, PhD, Takeru Higuchi Distinguished Professor and Chair, Department of Pharmaceutical Chemistry, The University of Kansas
Chemical modifications can play an important role in the immunogenicity of proteins. We have designed experiments to test whether specific chemical protein modifications induced by light are immunogenic. Peptides derived from a light-exposed humanized monoclonal antibody were fractionated, and these fractions injected into transgenic mice designed to tolerate native human IgG. Specific peptide fractions showed immunogenic responses, and chemical modifications present in these fractions were characterized by HPLC-MS/MS analysis.

FEATURED PRESENTATION

9:00 Protein Polymorphism, Heterogeneity and the Immunogenicity of Biotherapeutics
Roy Jefferis, PhD, MRCP, FRCPath, DSc, Emeritus Professor, Institute of Immunology & Immunotherapy, University of Birmingham
Administration of biotherapeutic drug may be considered: 1) to introduce/supplement a deficit in a natural (self) protein/glycoprotein (P/GP); 2) to manipulate/eliminate the activity of a self-molecule/cell. Clinical experience shows that a proportion of patients produce an anti-therapeutic antibody drug (ATA) immune response. This may be due to: 1) absence of the natural molecule or exposure to an unmatched polymorphic variant; 2) exposure to a molecule lacking structural fidelity with a self P/GP.

9:30 Next Steps in Biophysical Characterization and Screening: RPC/IEX-MALS and HT-SLS
Sponsored by WYATT TECHNOLOGY
Jeff Ahlgren, PhD, Senior Application Scientist, Wyatt Technology
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.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

MECHANISTIC UNDERSTANDING, PREDICTION AND CHARACTERIZATION OF PROTEIN AGGREGATION

11:00 IgG Charge
Thomas Laue, PhD, Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire
Charge is a fundamental property of practical and biological importance. ZDHH has been measured in formulation (pH 5) and physiological (PBS) solvent for three different IL-13-specific mAbs. For each mAb, ZDHH has been measured for four IgG subclasses, as well as their Fc and F(ab')2 fragments. Also, the distribution of ZDHH has been determined for human poly-IgG in PBS. The results illustrate how little is known about protein charge.

11:30 PANEL DISCUSSION: Protein Modifications and Immunogenicity Risks

- Chemical modification and relationship to immunogenicity
- *In vitro* and *in vivo* detection and analysis
- Clinical consequences

Moderator:
Thomas Laue, PhD, Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire
Panelists:
Christian Schöneich, PhD, Takeru Higuchi Distinguished Professor and Chair, Department of Pharmaceutical Chemistry, The University of Kansas
Wei Wang, PhD, Senior Scientist, Biologics Development, Bayer U.S. LLC
Peter M. Ihnat, PhD, Principal Scientist, Biologics Preformulation and Drug Delivery, Abbvie Bioresearch Center

12:00 pm Session Break

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

MECHANISTIC UNDERSTANDING, PREDICTION AND CHARACTERIZATION OF PROTEIN AGGREGATION *(Cont.)*

2:15 Chairperson's Remarks
Christian Schöneich, PhD, Takeru Higuchi Distinguished Professor and Chair, Department of Pharmaceutical Chemistry, The University of Kansas

2:20 Investigating the Mechanism of Protein Aggregation and Subvisible Particle Formation Mediated by Solid-Liquid Interfaces
Cavan Kalonia, PhD, Scientist, Late Stage Formulation Sciences, MedImmune
Physical degradation and aggregation of proteins at solid-liquid interfaces can negatively impact the manufacturability, shelf-life stability, and administration of protein therapeutics. Despite the critical impact of solid-liquid interfaces on protein stability, the mechanisms of interfacial degradations remain poorly understood and highly speculative in the pharmaceutical literature. In this work, we implement and develop state of the art metrology and modeling tools to investigate protein interfacial degradation at pharmaceutically relevant surfaces.

2:50 Mechanism, Consequence and Control of Protein Opalescence
Wei Wang, PhD, Senior Scientist, Biologics Development, Bayer U.S. LLC
Protein opalescence is a commonly-observed phenomenon. It is often accompanied by phase separation, especially at high protein concentrations. Both protein opalescence and phase separation are undesirable physical properties in the development of a successful protein pharmaceutical product. This presentation discusses the mechanism of protein opalescence, its potential consequences, and various means of controlling protein opalescence.

3:20 Sponsored Presentation *(Opportunity Available)*

3:35 Networking Refreshment Break

FORMULATION, PROCESS AND MANUFACTURING STRATEGIES TO OVERCOME AGGREGATION

4:00 Formulation and Container Closure System Strategies for Biopharmaceuticals with Higher Stability
Susumu Uchiyama, PhD, Professor, Department of Biotechnology, Graduate School of Engineering, Osaka University
We have identified causes of protein aggregation in biopharmaceuticals and attempted to optimize formulation and container closure system to reduce the protein aggregates. Secondary virial coefficient can be effective parameter for the prediction of aggregation tendency. Meanwhile, appropriate selection of barrel material is necessary for biopharmaceuticals with better quality. Silicon oil free polymer-based syringe is most suitable for biopharmaceuticals. All together formulation and container closure system strategies will be introduced.

4:30 Aggregation Mechanisms and Molecular Profiling of Therapeutic Antibodies
Peter M. Ihnat, PhD, Principal Scientist, Biologics Preformulation and Drug Delivery, Abbvie Bioresearch Center
Isothermal chemical denaturation was used to calculate the free energies of unfolding as a function of concentration and determine the mechanisms of oligomerization for a series of IgG1 antibodies. Most of the IgG1s favored the native state mechanism of association which was sensitive to pH. The mechanisms were correlated with thermal analysis, aggregation kinetics and structural attributes to illustrate screening and risk assessment of IgG1 candidates.

5:00 Novel Biopharmaceutical Compositions to Reduce the Rate of Aggregation
Jan Jezek, PhD, CSO, Research & Development, Arecor, Ltd.
Despite considerable progress in candidate screening and formulation approaches, protein aggregation during manufacturing, storage and use remains one of the key challenges of biopharmaceutical development, particularly for a number of new modalities such as bispecific antibodies. This talk will show on several case studies how novel and unconventional formulations can significantly decrease the rate of aggregation alongside other degradation pathways and enable development of competitive patient-friendly products.

5:30 Close of Day

FRIDAY, JANUARY 18

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast
Protein therapeutics is a fast-growing global market. As the science improves, so does the complexity of the R&D organization. Ensuring product quality plus speed to market requires insights from stakeholders working across the stages of protein science R&D. Join experts representing this PepTalk pipeline, peers, and colleagues for an interactive roundtable discussion. Topics include highlights from the week's presentations, new technologies and strategies, challenges, and future trends.
Moderator: Thomas Laue, PhD, Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

EMERGING ANALYTICAL TOOLS FOR DETECTION OF PROTEIN AGGREGATION

9:00 Chairperson's Remarks
Jan Jezek, PhD, CSO, Research & Development, Arecor, Ltd.

9:05 Novel Analytical Approaches for Mechanistic Understanding of Protein Aggregation
Ulla Elofsson, PhD, Associate Professor, Senior Scientist, RISE Research Institutes of Sweden
The use of scattering techniques (electrons, neutrons) to investigate aggregation mechanisms at high resolution in space and time will be explored. Predictive methods are built on this knowledge in combination with stability data generated by traditional (long term stability studies) and other techniques such as DLS and AF4. As an example, we will present methods to study surface induced protein aggregation.

9:35 Water Proton NMR for *in situ* Detection of Protein Aggregation
Yihua Bruce Yu, PhD, Professor, Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy
The water proton (1H2O) NMR signal is sensitive to protein aggregation. Compared with conventional analytical techniques, 1H2O NMR can be performed on protein solutions inside sealed containers and thereby is applicable to both drug substance and drug products. 1H2O NMR can detect both small (nanometer sized) and large (micrometer) aggregates. 1H2O NMR can be implemented using benchtop NMR spectrometers; data collection and analysis takes 1-2 min per sample.

10:05 Development Strategy of Fibril-Prone Peptide Therapeutics: Aggregation Kinetics, Predictive Methods, and Detection Methods
Jingtao Zhang, PhD, Principal Scientist, Pharmaceutical Sciences, Merck Research Laboratories
Peptide aggregation such as fibrillation presents significant challenges for DS and DP development of peptide therapeutics. Different development criteria and control strategy are required for fibril development in contrast to protein aggregation. The unique nature of fibril also presents significant challenges in the analytical development, especially in aggregation measurement. 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.

10:35 Networking Coffee Break

11:00 Stress-Induced Aggregation of Mouse IgG2c Depends on Antibody Nature and Sub-Micron Aggregates are Detectable by Cell-Surface Low Affinity Mouse Fcγ Receptors
Joshua R. Laber, Ph.D, Postdoctoral Fellow, Drug Product Development/Preformulation, AbbVie, Inc.
Proteinaceous aggregates have been linked to the incidence of immunogenic responses but specific factors responsible haven't been identified because the physiological mechanisms are not well understood. Where biophysical characterization of stressed IgG solutions showed little to no differences, using FACS we show significantly more binding to Fcγ receptors expressed on the surface of CHO cells compared to unstressed IgG solutions with solutions containing higher amounts of sub-micron sized aggregates.

11:30 Investigation of Oxidation Potential of Protein Formulation Excipients and Processes Using Dansyl-Methionine
Lin M. Luis, Senior Research Associate, Late Stage Pharmaceutical Development, Genentech
Proteins and excipients are continually exposed to internal and external oxidants. The external factors and processes that give rise to these oxidants include light, metals, cavitation, etc. We have results showing dansyl-methionine is a good protein surrogate that is capable of picking up, irreversibly, very low amount of oxidation due to peroxides from formulation excipients and processes.

12:00 pm Conference Wrap-Up
Thomas Laue, PhD, Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

12:30 Close of Conference

ANALYTICS & IMPURITIES

Traditional biologics, new biotherapeutics modalities and biosimilars are flooding discovery and development pipelines. Thus, analytical function is rapidly evolving, demanding high-throughput and high-resolution tools, focused biomolecular and biophysical assays, and rapid analytical and impurity profiling strategies. The Analytics & Impurities pipeline features in-depth perspectives on the latest developments and most critical steps in characterization of biologics, stability issues arising from particles, impurities, immunogenicity, protein aggregates and their impact on stability and safety of biopharmaceuticals.

JANUARY 14-15

AGENDA Characterization of Biotherapeutics

JANUARY 15-16

AGENDA Detection and Characterization of Particulates and Impurities

JANUARY 17-18

AGENDA Protein Aggregation and Emerging Analytical Tools

Also part of **FORMULATION & STABILITY**

MONDAY-TUESDAY, JANUARY 14-15 | 5TH ANNUAL

CHARACTERIZATION OF BIOTHERAPEUTICS

Prediction, Screening and Characterization of New Biologics

THE POPULAR 5TH Annual Characterization of Biotherapeutics conference will bring together leading scientists from biopharmaceutical industry, academia and government to discuss case studies, new technologies, assays on analytical development and characterization of mAbs, ADCs, bispecifics, and other novel protein formats, biosimilar. Some of the hot topics for discussion this year will include regulatory expectations and developability of new product formats, cell and gene therapy products, biosimilars, high-throughput analytics, multi-attribute methods, glycosylation/post-translational modifications, biophysical assays and more.

SUNDAY, JANUARY 13

4:00 - 6:00 pm Pre-Conference Registration

MONDAY, JANUARY 14

7:00 am Registration and Morning Coffee

STRUCTURE, FUNCTION AND STABILITY RELATIONSHIP

9:00 Welcome by Conference Organizer
Nandini Kashyap, Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks
Kelly Loyet, PhD, Senior Scientist, Biochemical and Cellular Pharmacology, Genentech

KEYNOTE PRESENTATION

9:10 Antibody Therapy: From Substitution to Immunomodulation and Monoclonal Immunotherapy
Paul Imbach, MD, Professor, Ped. Oncology/Hematology, University of Basel, Switzerland
Polyvalent antibody concentrate substitutes patients with immune deficiency and severe infection and synergistically immunomodulates the disturbed immune system with no or mild adverse effects in patients with autoimmune disease. While monoclonal immunotherapy may evoke severe adverse effects such as immune deficiency, infection, autoimmune or oncologic diseases and others, the question arises whether to combine monoclonal with polyvalent antibody therapy for avoidance of severe adverse effects and for treatment of the loss of tolerance – the common cause of autoimmunity and cancer.

9:50 Structure and Function Relationships: Link Control Strategy to CQAs
Jane (Xiaoyao) Xiao, PhD, Senior Director, Biologics Characterization, Axcel BioPartners
Structure and function relationships are essential to a risk assessment for ranking and prioritizing quality attributes. The development of a robust control strategy in manufacturing process can be challenging due to the structural and functional complexity of therapeutic proteins. The presentation will focus on the approaches in establishing structure-function relationships to manage CQAs and to develop a control strategy, including aggregation, oxidation and glycan structures relationship with FcRn binding potency, proliferation potency and cytotoxicity bioactivity.

10:20 Networking Coffee Break

10:45 Approaches to Understanding the Manufacturability of Monoclonal Antibodies
Michael Anyadiegwu, PhD, Senior Scientist, Downstream Processing, Centre for Process Innovation Ltd., National Biologics Manufacturing Centre
A short list of 50 monoclonal antibody sequences was selected based on experimental data from 200 monoclonal antibodies sequences. These 50 molecules covered a range of titres and quality attributes. Using a standard CHO USP and DSP platforms, the 50 molecules were manufactured and purified to provide material for measurement of biochemical, biophysical and immunological information. This presentation provides an update on the project outputs and progress to linking biochemical and quality data to sequence and structural liabilities.

11:15 Sponsored Presentation *(Opportunity Available)*

11:45 Glycan Characterization Strategies to Guide Early Biotherapeutic Development
Nathan Brown, PhD, Senior Scientist III, Global Biologics, AbbVie, Inc.
Post translation modifications (PTMs) can significantly alter protein function and disposition and, therefore, necessitate detailed analytical characterization of protein therapeutics as well as the targeted proteins. One category of PTMs of interest, importance and complexity is protein glycosylation. Here, we present strategies utilizing multiple, orthogonal approaches, to characterize glycan micro- and macro-heterogeneity, guiding early development and providing increased understanding of novel biologics and their protein targets.

12:15 pm Cutting-Edge Capillary Electrophoresis Technology for Characterizing Biotherapeutic Protein
Sponsored by proteinsimple
Xin Jiang, Product Manager, iCE Marketing, ProteinSimple
Capillary electrophoresis (CE) is a standard method for analyzing complex biotherapeutic proteins. Maurice® system innovates the traditional CE technology by combining both cIEF and CE-SDS detection schemes into one fully automated instrument, enabling easy protein profiling by size or charge. This presentation discusses the application of Maurice for biotherapeutic characterization.

12:45 Session Break

12:55 Luncheon Presentation: N-Glycan Sample Preparation and Analysis Workflows for Screening and Characterization of Biotherapeutics

Sponsored by ProZyme, A part of Agilent

Aled Jones, PhD, Senior Product & Applications Manager, Marketing, ProZyme

The structure of N-glycans on biotherapeutics can potentially affect immunogenicity, pharmacokinetics and pharmacodynamics, making the characterization of N-glycans an essential part of the development process. We present N-glycan sample preparation and analysis workflows for biotherapeutics, including labeling of released glycans for characterization by liquid chromatography and mass spectrometry, and Gly-Q for rapid screening using an integrated system with capillary electrophoresis.

1:25 Luncheon Presentation II *(Sponsorship Opportunity Available)*

ASSAYS, ANALYTICAL CHARACTERIZATION AND DEVELOPABILITY OF NEW DRUG FORMATS

2:00 Chairperson's Remarks

Alexey Rak, PhD, Head of Bio-Structure and Biophysics, Integrated Drug Discovery, Sanofi R&D

2:05 Deamidation and Isomerization Liability Analysis of 131 Clinical Stage Antibodies

R. Paul Nobrega, PhD, Scientist, Protein Analytics, Adimab, LLC

The deamidation and isomerization liabilities of 131 mAbs were evaluated under high and low pH accelerated stress conditions. Tryptic peptide mapping was used to identify the modified residues and quantitate the modifications. Comparison across all of the mAbs in our dataset reveals that specific positions within the CDRs have elevated frequencies of modifications under our stress conditions.

2:35 Novel Concert of Biophysical Methods for Multi-Specific Biologics Characterization

Alexey Rak, PhD, Head of Bio-Structure and Biophysics, Integrated Drug Discovery, Sanofi R&D

Modern drug discovery requires characterization of biomolecular interactions to be time- and cost-effective, highly precise and reproducible. New multispecific biologics formats require new approaches to assess their developability. Here we report applications of novel biophysical methods Second Harmonics Generation, nano-Differential Scanning Fluorimetry, MicroScale Thermophoresis and thermal stability kinetics experiments that we are applying in our biologics discovery for multi-specific drugs as well as for mAbs and ADCs. The effectiveness of the novel integrated biophysical methods will be presented and discussed.

3:05 Find Your Table and Meet Your BuzZ Session Moderator

3:15 BuzZ Sessions with Refreshments

Join your peers and colleagues for interactive roundtable discussions.

See page 11 for details.

4:30 Bioanalytical Challenges for Ocular Therapeutics

Kelly Loyet, PhD, Senior Scientist, Biochemical and Cellular Pharmacology, Genentech

There is a need for long-acting delivery (LAD) modalities for back of the eye ocular biologics to reduce the injection burden and achieve better outcomes. Many proposed LAD modalities that rely on half-life extension pose challenges for bioanalysis due to molecular complexity, immunogenicity, and *in vitro* to *in vivo* translation. Here we present new strategies for overcoming bioanalytical challenges in order to better understand and evaluate potential LAD modalities.

5:00 Particle Size Characterization of an mRNA-Containing Lipid Nanoparticle Formulations

Jessica Banks, PhD, Scientist, Drug Product Analytical Development, Moderna Therapeutics

Understanding and controlling the size distribution of therapeutic lipid nanoparticles is essential to the development of a well-defined and stable drug product. Both sub-micron and micron-sized subvisible particles are relevant, highlighting the need for selective and orthogonal techniques applicable to a broad particle size range. This presentation will describe studies on a panel of biophysical techniques to characterize particle size attributes of an mRNA lipid nanoparticle drug product.

5:30 Early Stage Evaluation of Excipient Effects on the Stability of ADCs

Brittney J. Mills, PhD, Senior Scientist II, Drug Product Development, AbbVie, Inc.

Traditional excipients used in standard biologic formulations may affect ADCs differently due to the unique nature of the molecule. The distinct properties of the toxins used in the preparation of novel ADCs require extensive excipient screening to determine the formulation most suitable for the entire molecule. Performing this type of screening is difficult due to the limited material available at this stage in the development process. This presentation will focus on our miniaturized approach for evaluating the effects of excipients on the stability of ADCs.

6:00 - 7:15 Welcome Reception in the Exhibit Hall with Poster Viewing

Sponsored by proteinsimple

7:15 Close of Day

TUESDAY, JANUARY 15

8:00 am Registration and Morning Coffee

SCREENING AND CHARACTERIZATION OF BIOTHERAPEUTICS

8:30 Chairperson's Remarks

Jichao (Jay) Kang, PhD, RAC, Director, Analytical Development, Amicus

8:35 Setting Specification for Biologics

Jichao (Jay) Kang, PhD, RAC, Director, Analytical Development, Amicus

Setting appropriate specification is a key control strategy for consistently manufacturing quality biologics product. However, due to the complexity and heterogeneity nature of the biologic molecules, it is challenging to set appropriate specification that can effectively control process variation. The presentation will review the key considerations in setting specification for biologics product in different stages of product development life cycles with case studies presented.

9:05 Automated Carbohydrate Sequencing of Recombinant Protein Therapeutics
Andras Guttman, PhD, DSc, Professor, Horvath Csaba Laboratory for Bioseparation Sciences, Research Centre for Molecular Medicine, University of Debrecen
In this talk, we describe an automated carbohydrate sequencing approach using the appropriate exoglycosidase enzymes in conjunction with the utilization of some of the features of a capillary electrophoresis (CE) instrument to speed up the process. The enzymatic reactions were accomplished within the temperature-controlled sample storage compartment of a capillary electrophoresis unit and the separation capillary was also utilized for accurate delivery of the exoglycosidase enzymes. CE analysis was conducted after each digestion step obtaining in this way the sequence information of N-glycans in 60 and 128 minutes using the semi- and the fully-automated methods respectively.

9:35 Sponsored Presentation *(Opportunity Available)*

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 Understanding the Charge Requirements for Hyaluronic Acid Binding for Drug Delivery
Shrenik Mehta, Postdoctoral Fellow, Genentech
In this work a Microscale Thermophoresis (MST) based hyaluronic acid (HA) binding assay was developed that enabled the measurement of peptide - HA binding interactions. This assay was used to interrogate the charge requirements for HA binding. This work provides clues towards engineering peptides for drug delivery with different affinities for HA.

11:30 A Robust and Sensitive Workflow to Assess the *ex vivo* Stability of Antibody Variants Using CE-LIF
Cong Wu, PhD, Scientist, Biochemical and Cellular Pharmacology, Genentech
We report a highly sensitive and robust workflow to quantify the degraded products of multivalent antibodies using capillary electrophoresis-laser induced fluorescence (CE-LIF) after affinity capture of stressed samples and fluorescent labeling. The improved sensitivity and the simplified quantitative workflow of CE-LIF provide complementary information to LC-MS intact analysis and enables a faster and more reliable data turnaround to trigger in-depth investigation and to gate or rank drug candidates.

12:00 pm Improving Biotherapeutic PK Assays Using Highly Specific Anti-Idiotypic Affimers
Sponsored by Avacta LIFE SCIENCES
Matt Johnson, PhD, CTO, Avacta Life Sciences
The Affimer® scaffold is a versatile next-generation non-antibody platform that offers great potential for both novel biotherapeutics as well as research and diagnostics tools. We have successfully developed anti-idiotypic binders to a range of therapeutic antibody targets to facilitate and improve assays to better facilitate the drug development pipeline. This approach uses only a single target-specific reagent allowing for simpler, more robust and standardizable assay design.

12:30 Session Break

12:40 Luncheon Presentation: Better Protein Characterization Using Tycho to Reveal Protein Quality
Sponsored by NANOTEMPER
Peter Fung, Senior Manager, Product Marketing, NanoTemper Technologies Inc.
Starting with samples of questionable quality only leads to irreproducible results. Yet, researchers continue to use unvalidated material assuming it's fine or because they lack an easy test of sample quality. For the first time ever, quickly and precisely determine protein quality in just 3 minutes by using TychoTM NT.6. Tycho fits into any step of a purification or characterization workflow to easily monitor protein quality and enabling researchers to get more consistent results.

1:10 Close of Characterization of Biotherapeutics Conference

DETECTION AND CHARACTERIZATION OF PARTICULATES AND IMPURITIES

Hot Topics, Case Studies, New Tools and Strategies for Control of Impurities from Products, Excipients, Processes and Packaging

CAMBRIDGE HEALTHTECH INSTITUTE'S 5th Annual Detection and Characterization of Particulates and Impurities conference discusses hot topics, case studies, new technologies, and strategies to carry out risk assessment and mitigation for impurities arising from products, excipients, processes and packaging. Some of the hot topics for this year will be novel technologies for contaminant detection, host cell proteins, lipases and enzymatic degradation, excipient, particles and aggregates, leachable, chemistry and manufacturing controls (CMC) strategy for regulatory filings.

TUESDAY, JANUARY 15

1:00 pm Registration

1:30 Refreshment Break in the Exhibit Hall with Poster Viewing

RISK OF IMMUNOGENICITY POSED BY AGGREGATES AND IMPURITIES

2:00 Chairperson's Opening Remarks
Joël Richard, PhD, Vice President, Peptides, CMC & Engineering, Ipsen

KEYNOTE PRESENTATION

2:05 Aggregates and Particulates in Protein Formulation: Orthogonal Characterization Methods for a Data-Based Immunogenicity Risk Assessment
Joël Richard, PhD, Vice President, Peptides, CMC & Engineering, Ipsen
Aggregation remains a considerable challenge in the manufacturing, stability behavior and delivery of liquid protein formulations. Orthogonal biophysical techniques make it possible to characterize protein structure alteration and the subsequent mechanism of formation of sub visible aggregates and particulates, which are among the most striking issues suspected to trigger immunogenic reactions upon repeated subcutaneous administration. Clinical impact regarding potential safety issues will also be discussed, as identified by regulatory agencies.

PARTICLE CHARACTERIZATION AND ANALYTICAL METHODS DEVELOPMENT

2:45 Qualification and Validation Methods for New Particle Counting Instruments
Dean Ripple, PhD, Leader, Bioprocess Measurements Group, National Institute of Standards and Technology
The increased use of new types of particle counting instruments, such as flow imaging, has raised questions on how these instruments may be qualified and measurement methods validated. I will discuss the use of standards and a variety of independent measurements and data analysis methods that can address these needs, over a size range from 100 nm to visible.

3:15 Analysis of Various Process-Related Impurities by HPLC with Detection by ELSD, CAD or Fluorescence
Sponsored by charles river
Mario Dipaola, PhD, Senior Scientific Director, Biologics, Charles River Laboratory
During this presentation, several HPLC methods with varying detection methods will be discussed along with performance of these methods with respect to critical parameters such as LOD/LOQ/linearity range, etc. At least one case study will be presented, as well, to highlight some of the common challenges one is likely to face when developing a method for process residual testing.

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

CHARACTERIZATION OF SUBVISIBLE PARTICLES IN PROTEIN AND VIRAL VACCINES

4:30 Marina Kirkitadze, PhD, Deputy Director, Head of Biophysics and Conformation Unit, Analytical R&D Biochemistry, Sanofi Pasteur, Canada
The topic of this presentation is characterization of visible and subvisible particles in protein and viral vaccine formulations. Visible and subvisible particles were found to be inherent to the product, and were analyzed by several methods including MFI, DLS, and MS.

5:00 New Tools and Strategies for Characterization of Particles in Biologics
Andrea Hawe, PhD, CSO, Coriolis Pharma Research GmbH
Particles in the nanometer and micrometer size range need to be characterized as part of drug product development, both as impurities (e.g. protein aggregates, polysorbate degradation) and as active (e.g. virus, cells). An overview on innovative methods for micrometer particles (backgrounded membrane imaging, imaging flow cytometry, etc.) and nanometer particles (resistive pulse sensing, novel flow imaging set-ups, etc.) will be given, including a critical comparison to existing methods.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

5:45 - 8:45 Dinner Short Courses*
See page 8 for details.
**Separate registration required*

WEDNESDAY, JANUARY 16

7:45 am Registration and Morning Coffee

DETECTION, CHARACTERIZATION AND CONTROL OF PROCESS- AND PRODUCT-RELATED IMPURITIES

8:15 Chairperson's Remarks
Reza Nejadnik, PhD, Laboratory Head Formulation Development Biologics, Global Pharmaceutical Development Biologics, Sanofi

8:20 USP Standards for Monitoring Impurities in Biotherapeutics
Diane McCarthy, PhD, Senior Scientific Liaison, Global Biologics, US Pharmacopeia
The complexity of biotherapeutic products and manufacturing processes can yield a variety of impurities, including process-related impurities, such as host cell protein, host cell DNA and particulates, and product-related impurities, such as precursors, aggregates and degradation products. These impurities must be monitored and controlled to minimize safety concerns and ensure product quality. This presentation will provide an overview of approaches for monitoring impurities, including specific examples that leverage USP standards

8:50 Handling of Biologic Drug Products and Stability Challenges
Reza Nejadnik, PhD, Laboratory Head Formulation Development Biologics, Global Pharmaceutical Development Biologics, Sanofi
Although the pharmaceutical biotech industry has made great progress in improving bulk and drug product manufacturing as well as company-controlled storage and transportation conditions to minimize the level of product degradation, there is little control over the many factors that may affect product quality after the protein pharmaceuticals are released and shipped by the manufacturer. Routine handling or unintentional mishandling of therapeutic protein products may cause degradation that can potentially compromise the clinical safety and efficacy of the product.

9:20 Sponsored Presentation *(Opportunity Available)*

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

10:35 The Benefits and Risks of Using Croda Super Refined™ Polysorbate 20 over Tween™ 20 HP
Nidhi Doshi, MSc, Senior Research Associate, Late Stage Pharmaceutical Development, Genentech
Super Refined Polysorbate 20 (SR PS20) and Tween 20 HP (HP PS20) are two grades of Polysorbate 20 from Croda. Detailed side-by-side evaluation of the two grades revealed some benefit of using SR PS20 over HP PS20 for particle formation risk upon surfactant degradation. However, SR PS20 formulations showed faster protein oxidation and PS20 degradation (by oxidative mechanism) compared to HP. This talk will weigh the benefits and risks of using SR PS20 over HP PS20 and provide recommendations on when to use one versus the other.

11:05 Comparison of Automated Methods for Quantitation of Host Cell Proteins
Jamie Rusconi, PhD, Staff Scientist, Bioanalytical Method Development, Regeneron Pharmaceuticals, Inc.

11:35 Strategy on Raw Material Impurities
Jinshu Qiu, Principal Scientist, Amgen
Large numbers of raw materials are used for manufacturing biopharmaceuticals. Appropriate control strategies are needed to mitigate the risks of these raw materials. The toxicity of the raw materials, the quantities used, point of introduction in the process, the product's stage of development, the dose, and route of administration are important considerations. In this talk, tools for assessing the risks and developing the appropriate control strategies will be discussed.

12:05 pm Session Break

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

1:15 Session Break

2:00 PLENARY KEYNOTE PANEL
See page 5 for details.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

EXCIPIENTS AND IMPURITIES IN PRE-FILLED SYRINGES AND FREEZE-DRIED FORMULATIONS

4:00 Chairperson's Remarks
Gregory A. Sacha, PhD, Senior Research Scientist, Baxter Healthcare Corporation

4:05 Impact of Silicone Oil on Fatty Acid Solubility and Polysorbate Related Particle Formation
Raphael Fish, Engineer I, Process Development, Genentech
Silicone oil coating on the interior of pre-filled syringes may act as a sink for fatty acids that are released upon hydrolytic degradation of polysorbates, potentially reducing risk of particle formation. Free fatty acids were shown to partition from an aqueous to a silicone oil phase in a glass vial model. However, the partitioning effect was not large enough to translate to significant reduction in particle formation risk at representative conditions. It was concluded that silicone oil levels in a PFS are too low to have any meaningful impact on polysorbate related particle formation.

4:35 Protein Crowding in Solution, Frozen and Freeze-Dried States Studied by Small-Angle Neutron Scattering
Susan Krueger, PhD, NIST Center for Neutron Research, National Institute of Standards and Technology
Small-angle neutron scattering is uniquely qualified to study the structure of proteins in liquid and solid phases that are biotechnologically relevant. We have studied a model protein, lysozyme, in the liquid, water ice and powder phases to determine its gross-structure, interparticle interactions and other properties. We also tested the effects of stabilizing excipients such as trehalose, glucose and sorbitol. Our results were compared to those from similar studies on antibodies.

5:05 Phase Behavior of an Alternative Surfactant, Poloxamer, during Freeze-Drying
Evgenyi Shalaev, PhD, Executive Director, Pharmaceutical Development, Allergan, Inc.
Poloxamers (e.g., P188) have been recently considered as alternative surfactants to polysorbates (tween20 and 80), as the latter are easily oxidized and can also undergo hydrolysis. In this study, complex phase behavior of aqueous solutions of a poloxamer is investigated using DSC, small-angle neutron scattering, and small- and wide-angle X-ray scattering.

5:35 **The Effect of Co-Solvent Systems on the Drying Behavior of Common Excipients**
Gregory A. Sacha, PhD, Senior Research Scientist, Baxter Healthcare Corporation
Many small molecules are poorly soluble in water and are often prepared in a co-solvent system prior to lyophilization. The co-solvent system may contain water and an organic solvent. This study examined the removal of the organic solvent from common excipients during primary drying using a residual gas analyzer. The drying behavior of amorphous and semi-crystalline formulations were examined as a function of organic solvent concentration.

6:05 - 7:00 **Networking Reception in the Exhibit Hall with Poster Viewing**

7:00 **Close of Detection and Characterization of Particulates and Impurities Conference**

THURSDAY-FRIDAY, JANUARY 17-18 | 10TH ANNUAL

PROTEIN AGGREGATION AND EMERGING ANALYTICAL TOOLS

Immunogenicity, Prediction, Screening, Case Studies and New Research Highlights

Also part of **FORMULATION & STABILITY**

THE POPULAR 10TH Annual Protein Aggregation and Emerging Analytical Tools conference covers latest trends, challenges and solutions in understanding, characterization and mitigation of problems generated by protein aggregation in biopharmaceuticals. This conference will feature in-depth case studies, new and unpublished data and interactive discussions on immunogenicity of aggregates, mechanisms of aggregation, new tools for detection and quantitation of aggregates, and how the data is used in regulatory filings. It will also discuss mechanistic understanding of protein aggregation and present case studies on prevention of particle formation by engineering and formulation approaches, aggregation in ADCs, bipecifics, impact of aggregation on production, aggregates as a factor for immunogenicity, and approaches for improvement of biophysical properties of protein solutions.

THURSDAY, JANUARY 17

7:45 am Registration and Morning Coffee

CHEMICAL MODIFICATIONS, PROTEIN POLYMORPHISM AND IMMUNOGENICITY

8:10 Organizer's Welcome Remarks
Nandini Kashyap, Conference Director, Cambridge Healthtech Institute

8:15 Chairperson's Opening Remarks
Thomas Laue, PhD, Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

KEYNOTE PRESENTATION

8:20 Chemical Protein Modifications and Immunogenicity Risks
Christian Schöneich, PhD, Takeru Higuchi Distinguished Professor and Chair, Department of Pharmaceutical Chemistry, The University of Kansas
Chemical modifications can play an important role in the immunogenicity of proteins. We have designed experiments to test whether specific chemical protein modifications induced by light are immunogenic. Peptides derived from a light-exposed humanized monoclonal antibody were fractionated, and these fractions injected into transgenic mice designed to tolerate native human IgG. Specific peptide fractions showed immunogenic responses, and chemical modifications present in these fractions were characterized by HPLC-MS/MS analysis.

FEATURED PRESENTATION

9:00 Protein Polymorphism, Heterogeneity and the Immunogenicity of Biotherapeutics
Roy Jefferis, PhD, MRCP, FRCPath, DSc, Emeritus Professor, Institute of Immunology & Immunotherapy, University of Birmingham
Administration of biotherapeutic drug may be considered: 1) to introduce/supplement a deficit in a natural (self) protein/glycoprotein (P/GP); 2) to manipulate/eliminate the activity of a self-molecule/cell. Clinical experience shows that a proportion of patients produce an anti-therapeutic antibody drug (ATA) immune response. This may be due to: 1) absence of the natural molecule or exposure to an unmatched polymorphic variant; 2) exposure to a molecule lacking structural fidelity with a self P/GP.

9:30 Next Steps in Biophysical Characterization and Screening: RPC/IEX-MALS and HT-SLS
Sponsored by WYATT TECHNOLOGY
Jeff Ahlgren, PhD, Senior Application Scientist, Wyatt Technology
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.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

MECHANISTIC UNDERSTANDING, PREDICTION AND CHARACTERIZATION OF PROTEIN AGGREGATION

11:00 IgG Charge
Thomas Laue, PhD, Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire
Charge is a fundamental property of practical and biological importance. ZDHH has been measured in formulation (pH 5) and physiological (PBS) solvent for three different IL-13-specific mAbs. For each mAb, ZDHH has been measured for four IgG subclasses, as well as their Fc and F(ab')2 fragments. Also, the distribution of ZDHH has been determined for human poly-IgG in PBS. The results illustrate how little is known about protein charge.

11:30 PANEL DISCUSSION: Protein Modifications and Immunogenicity Risks

- Chemical modification and relationship to immunogenicity
- *In vitro* and *in vivo* detection and analysis
- Clinical consequences

Moderator:
Thomas Laue, PhD, Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire
Panelists:
Christian Schöneich, PhD, Takeru Higuchi Distinguished Professor and Chair, Department of Pharmaceutical Chemistry, The University of Kansas
Wei Wang, PhD, Senior Scientist, Biologics Development, Bayer U.S. LLC
Peter M. Ihnat, PhD, Principal Scientist, Biologics Preformulation and Drug Delivery, Abbvie Bioresearch Center

12:00 pm Session Break

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

MECHANISTIC UNDERSTANDING, PREDICTION AND CHARACTERIZATION OF PROTEIN AGGREGATION *(Cont.)*

2:15 Chairperson's Remarks
Christian Schöneich, PhD, Takeru Higuchi Distinguished Professor and Chair, Department of Pharmaceutical Chemistry, The University of Kansas

2:20 Investigating the Mechanism of Protein Aggregation and Subvisible Particle Formation Mediated by Solid-Liquid Interfaces
Cavan Kalonia, PhD, Scientist, Late Stage Formulation Sciences, MedImmune
Physical degradation and aggregation of proteins at solid-liquid interfaces can negatively impact the manufacturability, shelf-life stability, and administration of protein therapeutics. Despite the critical impact of solid-liquid interfaces on protein stability, the mechanisms of interfacial degradations remain poorly understood and highly speculative in the pharmaceutical literature. In this work, we implement and develop state of the art metrology and modeling tools to investigate protein interfacial degradation at pharmaceutically relevant surfaces.

2:50 Mechanism, Consequence and Control of Protein Opalescence
Wei Wang, PhD, Senior Scientist, Biologics Development, Bayer U.S. LLC
Protein opalescence is a commonly-observed phenomenon. It is often accompanied by phase separation, especially at high protein concentrations. Both protein opalescence and phase separation are undesirable physical properties in the development of a successful protein pharmaceutical product. This presentation discusses the mechanism of protein opalescence, its potential consequences, and various means of controlling protein opalescence.

3:20 Sponsored Presentation *(Opportunity Available)*

3:35 Networking Refreshment Break

FORMULATION, PROCESS AND MANUFACTURING STRATEGIES TO OVERCOME AGGREGATION

4:00 Formulation and Container Closure System Strategies for Biopharmaceuticals with Higher Stability
Susumu Uchiyama, PhD, Professor, Department of Biotechnology, Graduate School of Engineering, Osaka University
We have identified causes of protein aggregation in biopharmaceuticals and attempted to optimize formulation and container closure system to reduce the protein aggregates. Secondary virial coefficient can be effective parameter for the prediction of aggregation tendency. Meanwhile, appropriate selection of barrel material is necessary for biopharmaceuticals with better quality. Silicon oil free polymer-based syringe is most suitable for biopharmaceuticals. All together formulation and container closure system strategies will be introduced.

4:30 Aggregation Mechanisms and Molecular Profiling of Therapeutic Antibodies
Peter M. Ihnat, PhD, Principal Scientist, Biologics Preformulation and Drug Delivery, Abbvie Bioresearch Center
Isothermal chemical denaturation was used to calculate the free energies of unfolding as a function of concentration and determine the mechanisms of oligomerization for a series of IgG1 antibodies. Most of the IgG1s favored the native state mechanism of association which was sensitive to pH. The mechanisms were correlated with thermal analysis, aggregation kinetics and structural attributes to illustrate screening and risk assessment of IgG1 candidates.

5:00 Novel Biopharmaceutical Compositions to Reduce the Rate of Aggregation
Jan Jezek, PhD, CSO, Research & Development, Arecor, Ltd.
Despite considerable progress in candidate screening and formulation approaches, protein aggregation during manufacturing, storage and use remains one of the key challenges of biopharmaceutical development, particularly for a number of new modalities such as bispecific antibodies. This talk will show on several case studies how novel and unconventional formulations can significantly decrease the rate of aggregation alongside other degradation pathways and enable development of competitive patient-friendly products.

5:30 Close of Day

FRIDAY, JANUARY 18

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast
Protein therapeutics is a fast-growing global market. As the science improves, so does the complexity of the R&D organization. Ensuring product quality plus speed to market requires insights from stakeholders working across the stages of protein science R&D. Join experts representing this PepTalk pipeline, peers, and colleagues for an interactive roundtable discussion. Topics include highlights from the week's presentations, new technologies and strategies, challenges, and future trends.
Moderator: Thomas Laue, PhD, Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

EMERGING ANALYTICAL TOOLS FOR DETECTION OF PROTEIN AGGREGATION

9:00 Chairperson's Remarks
Jan Jezek, PhD, CSO, Research & Development, Arecor, Ltd.

9:05 Novel Analytical Approaches for Mechanistic Understanding of Protein Aggregation
Ulla Elofsson, PhD, Associate Professor, Senior Scientist, RISE Research Institutes of Sweden
The use of scattering techniques (electrons, neutrons) to investigate aggregation mechanisms at high resolution in space and time will be explored. Predictive methods are built on this knowledge in combination with stability data generated by traditional (long term stability studies) and other techniques such as DLS and AF4. As an example, we will present methods to study surface induced protein aggregation.

9:35 Water Proton NMR for *in situ* Detection of Protein Aggregation
Yihua Bruce Yu, PhD, Professor, Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy
The water proton (1H2O) NMR signal is sensitive to protein aggregation. Compared with conventional analytical techniques, 1H2O NMR can be performed on protein solutions inside sealed containers and thereby is applicable to both drug substance and drug products. 1H2O NMR can detect both small (nanometer sized) and large (micrometer) aggregates. 1H2O NMR can be implemented using benchtop NMR spectrometers; data collection and analysis takes 1-2 min per sample.

10:05 Development Strategy of Fibril-Prone Peptide Therapeutics: Aggregation Kinetics, Predictive Methods, and Detection Methods
Jingtao Zhang, PhD, Principal Scientist, Pharmaceutical Sciences, Merck Research Laboratories
Peptide aggregation such as fibrillation presents significant challenges for DS and DP development of peptide therapeutics. Different development criteria and control strategy are required for fibril development in contrast to protein aggregation. The unique nature of fibril also presents significant challenges in the analytical development, especially in aggregation measurement. 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.

10:35 Networking Coffee Break

11:00 Stress-Induced Aggregation of Mouse IgG2c Depends on Antibody Nature and Sub-Micron Aggregates are Detectable by Cell-Surface Low Affinity Mouse Fcγ Receptors
Joshua R. Laber, Ph.D, Postdoctoral Fellow, Drug Product Development/Preformulation, AbbVie, Inc.
Proteinaceous aggregates have been linked to the incidence of immunogenic responses but specific factors responsible haven't been identified because the physiological mechanisms are not well understood. Where biophysical characterization of stressed IgG solutions showed little to no differences, using FACS we show significantly more binding to Fcγ receptors expressed on the surface of CHO cells compared to unstressed IgG solutions with solutions containing higher amounts of sub-micron sized aggregates.

11:30 Investigation of Oxidation Potential of Protein Formulation Excipients and Processes Using Dansyl-Methionine
Lin M. Luis, Senior Research Associate, Late Stage Pharmaceutical Development, Genentech
Proteins and excipients are continually exposed to internal and external oxidants. The external factors and processes that give rise to these oxidants include light, metals, cavitation, etc. We have results showing dansyl-methionine is a good protein surrogate that is capable of picking up, irreversibly, very low amount of oxidation due to peroxides from formulation excipients and processes.

12:00 pm Conference Wrap-Up
Thomas Laue, PhD, Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

12:30 Close of Conference

PROCESS TECHNOLOGIES & PURIFICATION

The Process Technologies & Purification pipeline provides insights into new technologies and advanced strategies for protein processing, including high-throughput, continuous processing, and achieving optimized operations through cutting-edge data analytics and interpretation. Ensuring quality while streamlining process steps will also be addressed as well as developing methods that translate into scale-up. The weeklong pipeline explores practical methods that improve processes, trim costs, and lead to successful results.

JANUARY 14-15

AGENDA Bioprocess Data Management

JANUARY 15-16

AGENDA Protein Purification and Recovery

JANUARY 17-18

AGENDA Higher-Throughput Protein Production and Characterization

MONDAY-TUESDAY, JANUARY 14-15 | 3RD ANNUAL

BIOPROCESS DATA MANAGEMENT

Advancing Bioprocessing through Instrumentation, Characterization, Control, and Analytics

THE BIOPHARMACEUTICAL INDUSTRY is meeting increasing demands and costs for biotherapeutics through process optimization. Advanced instrumentation through sampling techniques, new sensor technologies, and analyzers have emerged to monitor both upstream and downstream processes. When well-prepared and analyzed, this data leads to process knowledge, process control, and continuous improvement resulting in greater speed, quality, and economy. Cambridge Healthtech Institute's 3rd Annual Bioprocess Data Management conference addresses statistical analysis strategies including multivariate data analysis (MVDA), quality by design (QbD), process analytical technology (PAT), and multi-attribute method (MAM), allowing for optimized and informed control of bioprocessing.

SUNDAY, JANUARY 13

4:00 - 6:00 pm Pre-Conference Registration

MONDAY, JANUARY 14

7:00 am Registration and Morning Coffee

KNOWLEDGE MANAGEMENT IN THE PROCESS PIPELINE

9:00 Welcome by Conference Organizer
Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks
Steven LaBrenz, PhD, Scientific Director, Cell and Developability Sciences, Janssen R&D, BioTherapeutic Development

FEATURED PRESENTATION
9:10 A Control Strategy Approach to Knowledge Management – Some Perspectives
Kumar Dhanasekharan, PhD, Senior Director and Head, Biologics Process and Analytical Development, Amicus Therapeutics
This talk discusses key elements of a process control strategy (PCS) using Quality by Design (QbD) principles by leveraging technical development history, manufacturing history and process characterization to ultimately become a knowledge management tool in the product and process lifecycle of a molecule.

FEATURED PRESENTATION
9:50 Beyond Purely Data-Driven Approaches for Efficient Knowledge Management in Process Development
Moritz von Stosch, PhD, Senior Manager, Technical R&D, GlaxoSmithKline Vaccines
Knowledge from first principles is freely available and generally valid, and when integrated along with Artificial Intelligence (data-driven) methods, it can greatly improve the understanding and applicability. The applications of such an approach, referred to as hybrid modeling, to a fermentation and controlled drug release case are presented and the learnings from the development of these models are shared.

10:20 Networking Coffee Break

HIGH-THROUGHPUT PLATFORMS: DATA MANAGEMENT AND MODELING

10:45 Automated Data Management and Assurance of Data Integrity during High-Throughput Characterization of Proteins
Michael Siedler, PhD, Head, NBE High-Throughput and Advanced Formulation Sciences, Development Sciences, AbbVie Deutschland GmbH & Co. KG
Lab automation and high-throughput analytics provide huge amounts of data. Standard tools for managing the data and assuring data integrity are insufficient and could become a major hurdle for efficiently converting data into knowledge. Big data tools allow for new solutions for efficient automated data management as demonstrated by a use case.

11:15 Platformization of Multi-Specific Protein Engineering: From Handling Complex Data to Bioinformatics Workflow Support for High-Throughput Screening
Norbert Furtmann, PhD, Lab Head, Bioinformatics, High Throughput Biologics, Sanofi-Aventis Deutschland GmbH
As the success rate to identify a multi-specific lead molecule with favorable drug-like properties increases with the number of variants tested, we established a novel, automated platform process for the fast generation of large panels of multi-specific variants (up to 10,000). Here we report on our integrated bioinformatics platform to support and steer our screening process as well as on our tools for analyzing and handling the generated datasets.

FEATURED PRESENTATION
11:45 High-Throughput Pre-Formulation Platform: Large Dataset Generation and Evaluation in the Pre-NME Space Using a DoE Technique
Steven LaBrenz, PhD, Scientific Director, Cell and Developability Sciences, Janssen R&D, BioTherapeutic Development
To accelerate development timelines and improve early development outcomes, we have developed a high-throughput screening platform that adapts to the needs of a molecule, not adaptation of a molecule to a set-piece process. The process utilizes Design of Experiment structure and adapts inputs to generate an HTS experiment, tailored to the molecule. Using 384-well plate-based experimentation, DoE datasets are collected and analyzed to generate statistically significant results.

12:15 pm Sponsored Presentation
(Opportunity Available)

12:45 Session Break

12:55 Luncheon Presentation to be Announced *Sponsored by* UNCHAINED LABS

1:25 Luncheon Presentation II
(Sponsorship Opportunity Available)

CONTINUED PROCESS VERIFICATION

2:00 Chairperson's Remarks
Moritz von Stosch, PhD, Senior Manager, Technical R&D, GlaxoSmithKline Vaccines

2:05 Strategy and Gap Analysis on Integrated Downstream Platform at Boehringer Ingelheim Fremont
Raquel Orozco, PhD, Senior Bioprocess Engineer, Bioprocess Engineering, Process Science, Boehringer Ingelheim Fremont, Inc.
BI Fremont, Inc. and Pfizer are investing in intensified (continuous/integrated) processing to provide early stage clinical material radically cheaper and with little development, while keeping in mind a path to commercialization. Our process is highly automated, reduces in-process pools, is fully disposable, and is GMP-capable. The downstream system is designed to be scalable-in-place by changing column sizes, and buffer volumes – enabling the ability to make up to 3kg of drug substance per day utilizing the same operational space. We have demonstrated the capability of making >1kg mAb of drug substance in ≤15 days using 100 L bioreactor and devised a strategy for a commercially available process. In order to implement the highly productive and automated process on site, stakeholders need a business case. This talk describes a thorough gap analysis on challenges around continuous viral inactivation, periodic viral filtration, periodic UFDF, buffer supply, and bioburden control.

2:35 Data at Your Fingertips: The Benefits of an Integrated Informatics System
Carly Cox, Process Informatics Manager, Global Engineering, Pfizer
With the advent of Continued Process Verification (CPV) and the data volumes and analysis frequencies, informatics systems that can help pull together data from disparate systems and organize it to be ready for analysis are more important than ever before. This talk covers some of the key elements to include in the design of an informatics system as well as the benefits that can be achieved.

3:05 Find Your Table and Meet Your BuzZ Session Moderator

3:15 BuzZ Sessions with Refreshments
Join your peers and colleagues for interactive roundtable discussions.
See page 11 for details.

PROCESS DEVELOPMENT AND VALIDATION

4:30 Strategic Integration of the Multi-Attribute Method to Inform Bioprocess Optimization
Keith A. Johnson, PhD, Senior Principal Scientist, Analytical Research and Development, Pfizer
The development of a stable, high-yielding, and scalable bioprocess requires accurate and timely analytical monitoring of product quality attributes to better understand and control parameters that affect the product profile. The Multi-Attribute Method is intended to replace various analytical methods by utilizing liquid chromatography-mass spectrometry peptide mapping methodology to identify and monitor multiple product quality attributes simultaneously in a single assay to support process optimization.

5:00 Implementation of an Integrated Bioprocess Development Workflow Platform
Matthew Schwartz, MSc, Senior Scientist, Upstream Process Development, Celgene
Celgene's strategy for implementation of a workflow platform for streamlining development activities will be presented. The new system acts as a cross-functional data backbone that integrates all bioprocess development workflows from post-discovery through transfer to manufacturing and will lead to a significant increase in Celgene's operational efficiency and throughput. It has the capability to capture output data automatically (online, at-line and offline) along the process from various laboratory equipment.

5:30 PANEL DISCUSSION: Measuring, Storing, Modeling, and Analyzing Data: How Can We Extract Understanding and What Is the Value?
- Can we link the information of various data sources via modeling techniques, achieving a more holistic view, and exploit redundancies for information consolidation?
- Can we exploit the data for cross-process unit modeling, extracting traces of information from the process unit chain that otherwise would not be apparent?
- From CQAs to CPPs and back: A need for one-stop historic-data-based solutions
- Models as a tool for knowledge transfer management, or why data does not scale
- Where do we get all the modeling and data scientists from?

Moderator:
Moritz von Stosch, PhD, Senior Manager, Technical R&D, GlaxoSmithKline Vaccines
Panelists to be Announced

6:00 - 7:15 Welcome Reception in the Exhibit Hall with Poster Viewing *Sponsored by* proteinsimple

7:15 Close of Day

TUESDAY, JANUARY 15

8:00 am Registration and Morning Coffee

CHO CELL LINE DEVELOPMENT AND ENGINEERING

8:30 Chairperson's Remarks
Alessandro Mora, PhD, Senior Scientist, CMC, Jounce Therapeutics

8:35 Integration of Process Analytical Technology in Upstream Bioprocessing of CHO Cells
Erica Fratz-Berilla, PhD, Staff Fellow, Office of Biotechnology Products, Division of Biotechnology Review and Research II, U.S. Food and Drug Administration
Monitoring and control of upstream bioprocesses are vital to obtain high protein yields and meet all quality specifications for a biotherapeutic. Process analytical technology (PAT) can be used in process development to optimize physical, chemical, and biological parameters that may result in changes in CHO cell growth, titer, and product quality attributes. Additionally, PAT can be used to detect deviations in CHO cell culture parameters that may have otherwise remained unnoticed.

9:05 Integration of Cell Culture High-Throughput Techniques and Multivariate Statistical Modeling to Simplify the Development of CHO Cell Lines
Alessandro Mora, PhD, Senior Scientist, CMC, Jounce Therapeutics
The establishment of a robust high-throughput screening platform directly impacts the selection of CHO production clones. Consistent data collection, dataset construction and statistical modeling further improve the identification of bottlenecks during the clones' transition into mature stages of upstream development. In this talk, we present the integration between 24-Deep Well Pates screening with Multivariate Data Analysis, and how their alignment simplifies upstream workflow, while elucidating CHO cells' biology under process conditions.

9:35 Sponsored Presentation *(Opportunity Available)*

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 Genetic Engineering Process Optimization in CHO Cells
Stephanie L. Sandefur, MSc, Consultant Biologist, Bioprocess Research & Development, Eli Lilly and Company
Over the past decade, considerable progress has been made in improving the effectiveness and efficiency of generating highly productive recombinant CHO cell lines. While these efforts have been primarily centered on driving cell culture productivity, more recently, focus has turned to approaches to impact product quality. This presentation describes potential approaches to maximizing the effectiveness of host cell engineering and reducing the time to successfully impact biotherapeutic product quality profiles.

11:30 A Multi-Landing Pad DNA Integration Platform for Mammalian Cell Engineering
Liliana Wroblewska, PhD, Principal Scientist, Biomedicine Design, Pfizer
Reliable, large-scale engineering of CHO cells through precise insertion of large amounts of heterologous DNA into well-characterized genomic loci would have broad applications for mammalian synthetic biology, recombinant protein production, and biomanufacturing. Using multi-gene payload vectors, cell lines with multiple landing pads, and recombinase technology, we demonstrated controlled integration of up to nine copies of a monoclonal antibody (about 100 kb of heterologous DNA), and a corresponding linear increase in antibody expression.

12:00 pm Talk Title to be Announced
Pierre-Alain Girod, PhD, CSO, Selexis SA
Sponsored by SELEXIS

12:30 Session Break

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Close of Bioprocess Data Management Conference

TUESDAY-WEDNESDAY, JANUARY 15-16 | 11TH ANNUAL

PROTEIN PURIFICATION AND RECOVERY

Streamlining and Innovating Processes

IN THE WORLD of biologics, purifying proteins remains a constant bottleneck and nagging headache. A process that works great for one protein, may not work at all for the next. Not only are the tasks challenging, but outcomes must be ensured to result in properly folded protein. CHI's Protein Purification and Recovery conference examines the strategies that efficiently lead to pure protein for research or therapeutic use. This leading conference illustrates how 'traditional' strategies (protein A, chromatography, affinity tags) are being innovated and improved, while also demonstrating the new technologies that are being introduced and integrated to help streamline purification while ensuring quality. This conference will also explore the finesse required when purifying complex molecules, such as membrane proteins and bispecific antibodies, in the ever-present quest for purity.

TUESDAY, JANUARY 15

1:00 pm Registration

1:30 Refreshment Break in the Exhibit Hall with Poster Viewing

PURIFYING ANTIBODIES

2:00 Chairperson's Opening Remarks
Peter Schmidt, PhD, Director, Recombinant Technologies Research, CSL Behring

KEYNOTE PRESENTATION

2:05 Evaluation of Recent Innovations for Capture of Antibodies and Antibody-Like Biotherapeutics
Alan K. Hunter, PhD, Director, Purification Process Sciences, MedImmune, LLC
As therapeutic use of monoclonal antibodies and related molecules continues to grow, affinity chromatography remains the primary capture modality due to high specificity, platformability, and strong regulatory track record. In this work, we provide a comprehensive evaluation of next-generation Protein A stationary phases for biotherapeutic manufacture. Lastly, we discuss purification strategies for bispecific antibodies with a mAb-like architecture using light chain affinity chromatography.

2:45 Replacing Protein A/G with Nucleotide Binding Site Ligands on Resins and Membranes for Chromatography and Spin Columns for Antibody Purification
Basar Bilgicer, PhD, Associate Professor, Chemical and Biomolecular Engineering, Mike and Josie Harper Cancer Research Institute, NDnano Center for Nano Science and Technology, University of Notre Dame
The traditional techniques of protein A/G affinity chromatography for antibody purification have well established limitations commonly overlooked due to convenience and absence of reliable options. We utilize the conserved nucleotide-binding site (NBS) of immunoglobulins to enable capturing of antibody on an affinity column. The results reveal >99% column efficiency with >99% purity for antibodies, suggesting that the NBS column is a universal, stable, reusable, and inexpensive alternative for purification of humanized and chimeric antibodies.

3:15 Sponsored Presentation *(Opportunity Available)*

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

PURIFYING ANTIBODIES *(Cont.)*

4:30 Purification of Common Light Chain IgG-Like Bispecific Antibodies Using Highly Linear pH Gradients
Beth Sharkey, Scientist I, High Throughput Expression, Adimab, LLC
A variety of bispecific constructs benefit from the use of a single variable light region pairing with multiple distinct variable heavy regions. This talk will demonstrate new techniques to purify these common light chain bispecific IgG molecules to homogeneity. Data will be shared on the production of a panel of bispecific antibodies that bind each target with high affinity and exhibit favorable biophysical properties, similar to traditional therapeutic antibodies.

5:00 MsbA Structural Studies Using Novel Amphiphiles
Qinghai Zhang, PhD, Associate Professor, Integrative Structural and Computational Biology, The Scripps Research Institute
MsbA is an inner membrane lipid A flippase and an essential ATP-binding cassette (ABC) transporter in gram-negative bacteria with homology to human multidrug resistance transporters. I will present our X-ray and EM structural studies of MsbA, which have been facilitated by the synthesis and characterization of novel stabilizing amphiphiles. The relevance of MsbA structures will be discussed in the context of a dynamic conformational pathway, thereby offering fresh insights into MsbA-mediated lipid A transport mechanism.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

5:45 - 8:45 Dinner Short Courses*
See page 8 for details.
**Separate registration required*

WEDNESDAY, JANUARY 16

7:45 am Registration and Morning Coffee

CONTINUOUS TECHNOLOGY FOR ANTIBODY PURIFICATION

8:15 Chairperson's Remarks
Yuyi Shen, PhD, Principal Scientist, Technical Department, Grifols, S.A.

FEATURED PRESENTATION
8:20 Continuous Downstream Processing of Monoclonal Antibodies
Andrew Zydney, PhD, Distinguished Professor, Chemical Engineering, The Pennsylvania State University
There is growing interest in the development of integrated continuous bioprocesses with enhanced productivity and greater flexibility. This talk will present several recent efforts from our group to develop continuous processes based on the concept of countercurrent staging. This includes the use of countercurrent staged diafiltration for continuous protein formulation and the use of continuous countercurrent tangential chromatography for continuous steady-state product capture and purification.

8:50 Optimization of High-Throughput Antibody Purification Using Continuous Chromatography Matrices
Peter Schmidt, PhD, Director, Recombinant Technologies Research, CSL Behring
Monoclonal antibodies are the fastest growing segment in the drug market. The development of mAbs requires purification of large numbers of variants with sufficient yield. However, established high-throughput purification strategies have been limited by the binding capacity of established affinity matrices. Our results show that matrices developed for continuous chromatography applications can help to overcome this limitation and increase the yield in high-throughput and lab-scale antibody purification.

9:20 Sponsored Presentation *(Opportunity Available)*

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

OVERCOMING PURIFICATION CHALLENGES

10:35 Development and Optimization of Challenging Unit Operations with Line of Sight to Manufacturing for a Shear Sensitive, Aggregation Prone, & Low pI Monoclonal Antibody
Sandra E. Rios, PhD, Principal Scientist, Downstream Process Development and Engineering, Merck & Co.

11:05 Detection and Assessment of Dilute Dosing Solutions of Potent Bispecific Molecules
Melissa Thomas, PhD, Principal Scientist, Biologics – Protein Technologies, Amgen, Inc.
To ensure accurate dosing for Amgen's BiTE therapeutic molecules, we need to assess drug product stability; however, detection and stability assessment of highly dilute protein solutions can be challenging. We have developed a sensitive HPLC-based method for detecting dilute solutions of proteins under simulated dosing conditions at concentrations of 100 ng/ml. This method has been used to evaluate and indicate potential liabilities of preclinical molecules, enabling selection and prioritization ahead of *in vivo* characterization.

11:35 Single-Step Purification of Intrinsic Protein Complexes for Functional Characterization in *Saccharomyces cerevisiae* Using Regenerable Calmodulin Resin: A Story of the ySet1C Enzyme-Substrate Network
Kyle Biggar, PhD, Assistant Professor & Director, Carleton Functional Proteomics Facility, Biochemistry, Carleton University
The tandem affinity purification (i.e., TAP) method has been extensively used to purify native protein complexes under near physiological conditions in *Saccharomyces cerevisiae*. Our modification of this method provides an inexpensive single-step purification alternative to the traditional two step affinity purification of TAP-tagged proteins using only the calmodulin-binding peptide affinity tag. To demonstrate the effectiveness of our approach, we successfully purified and characterized the *in vitro* substrate preferences of the ySet1c methyltransferase complex.

12:05 pm Session Break

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

1:15 Session Break

2:00 PLENARY KEYNOTE PANEL
See page 5 for details.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

INNOVATING & IMPROVING PURIFICATION PROCESSES

4:00 Chairperson's Remarks
Basar Bilgicer, PhD, Associate Professor, Chemical and Biomolecular Engineering, Mike and Josie Harper Cancer Research Institute, NDnano Center for Nano Science and Technology, University of Notre Dame

4:05 Application of a Small EF Affinity Tag for Expression, Purification and SPR Studies of G Protein-Coupled Membrane Receptors
Alexei Yeliseev, PhD, Staff Scientist, Group Leader, LMBB, NIH, NIAAA
We developed a novel calcium-dependent EF-based affinity system that allows capture and high recovery of GPCR from dilute solutions containing detergents, salts and glycerol. The binding of the EF1 tag to the resin at these conditions is very strong that allows efficient purification without any loss of the target protein. The elution of the captured receptor is achieved by addition of EDTA, at very mild conditions that do not hinder the activity of this labile protein.

4:35 A Virtual QC Platform for High-Throughput Protein Purification
Philip E. Hass, Senior Scientific Manager, Genentech, Inc.

5:05 Establishing Innovative and Efficient Tool Boxes for Optimal and Scalable Processes for Recombinant Proteins
Yuyi Shen, PhD, Principal Scientist, Technical Department, Grifols, S.A.
Innovative technologies evolve bioprocessing, and advance manufacturing in the pharmaceutical industry. The presenter will share case studies of successfully implementing innovative tools for process development and improvements for mAbs and complex recombinant proteins. The talk will discuss the major drive for innovative technologies and how to overcome key challenges of process integration and upgrades. The talk also provides

insight into risk mitigation by balancing needs for quality, cost and speed.

5:35 **A Universal Peptide-Tag System for Protein Purification and Analysis Based on Nanobody Technology**
Ulrich Rothbauer, PhD, Professor, Natural and Medical Sciences Institute, University of Tübingen, and Co-Founder, ChromoTek GmbH
Single-domain antibodies - referred to as nanobodies - have emerged as an attractive alternative to traditional antibodies and became highly valuable tools for numerous bioanalytical and biotechnical applications. Here we present a novel nanobody-derived capture/detection system that enables fast and efficient isolation of epitope-tagged proteins from prokaryotic and eukaryotic expression systems. The high-affinity-binding and modifiable peptide tag of this system renders it a versatile and robust tool to combine biochemical analysis with microscopic studies.

6:05 - 7:00 **Networking Reception in the Exhibit Hall with Poster Viewing**

7:00 **Close of Protein Purification and Recovery Conference**

HIGHER-THROUGHPUT PROTEIN PRODUCTION AND CHARACTERIZATION

Improving Processes

HIGH-THROUGHPUT PROCESSING HAS come of age by transforming the traditional protein-by-protein trial-and-error approach for testing criteria and scaling up. In CHI's Higher-Throughput Protein Production and Characterization conference, HTP is explored in the quest to develop methods that ensure quality and translate to large scale much more quickly and efficiently than in the past. Automation, robotics and liquid handlers will be discussed, along with developing small-scale models that shed light on bioproduction. Case studies will be presented that illustrate how leaders in the field are integrating HTP approaches to reduce the time and effort needed to successfully analyze proteins, fine tune processes, and achieve well-folded, pure protein.

THURSDAY, JANUARY 17

7:45 am Registration and Morning Coffee

HIGH-THROUGHPUT TO IMPROVE DOWNSTREAM PROCESSES

8:10 Organizer's Welcome Remarks
Mary Ruberry, Senior Conference Director, Cambridge Healthtech Institute

8:15 Chairperson's Opening Remarks
Kelcy Newell, PhD, Senior Scientist, Laboratory Automation & High-Throughput Process Development, MedImmune, LLC

KEYNOTE PRESENTATION

8:20 Downstream Processing in Biomanufacturing: Multimodal Chromatography, Affinity Precipitation and Integrated Bioprocessing
Steven Cramer, PhD, William Weightman Walker Professor, Isermann Department of Chemical and Biological Engineering, Rensselaer Polytechnic Institute
Targeted experiments and molecular simulations will be used to shed light on the importance of protein surface clusters and ligand properties for creating selective separations in multimodal chromatography. Affinity precipitation using smart biopolymers for the simultaneous recovery and purification of both mAb and non-mAb biologics will then be presented. Finally, results will be given on a novel approach for the rapid development of integrated downstream biomanufacturing processes for biological products.

9:00 Platformization of Multi-Specific Protein Engineering II: From Automated Transfection to High-Throughput Multi-Parametric Characterization of Large Variant Libraries
Joerg Birkenfeld, PhD, Section Head, High Throughput Biologics, R&D Biologics Research/Protein Therapeutics, Sanofi-Aventis Deutschland GmbH
The success rate to identify a multi-specific lead molecule with favorable drug-like properties increases with the number of engineered variants tested. We recently established a novel, fully automated platform process for the *in silico* design and fast generation of large panels of multi-specific variants. Here, we report on the integration of miniaturized lab unit operations with cutting-edge automation for transient transfection, expression, purification and characterization of up to 10,000 engineered variants in high-throughput.

9:30 Sponsored Presentation *(Opportunity Available)*

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

IMPROVING HIGH-THROUGHPUT PROCESSES

11:00 Applications of Modular Expression Toolboxes in High-Throughput Protein Expression
Ernst Weber, PhD, Laboratory Head, Biologics Lead Optimization, Project Leader, Ophthalmology, Bayer HealthCare
The presentation will focus on the setup of a modular expression toolbox, consisting of standardized elements influencing expression levels, which allow the rapid generation of multiple expression constructs and also the generation of complex expression optimization libraries. Advantages and implications of a modular cloning system including implementation into protein expression optimization workflows will be discussed and a number of successful case studies will be presented.

11:30 Self-Cleaving Tags Based on Split Inteins: Increased Reliability Enabling Higher-Throughput Applications
David Wood, PhD, Professor, Chemical & Biomolecular Engineering, The Ohio State University
An important limitation of intein-based self-cleaving tag systems is a lack of reliability for arbitrary target proteins. In some cases, the intein tags cleave too quickly, while in others the tags cleave too slowly or not at all. In our recent work, we have developed several systems to interrogate the sources of rate variations, and can now provide detailed guidance on design and operation of these methods in higher-throughput applications.

12:00 pm Session Break

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

NOVEL TOOLS TO STREAMLINE PROCESSES

2:15 Chairperson's Remarks
Edward Kraft, PhD, Senior Scientific Manager, BioMolecular Resources, Genentech, Inc.

2:20 Improving High-Throughput Characterization of Intact Proteoform Using Ion-Photon and Ion-Ion Reactions in the Gas-Phase
Luca Fornelli, PhD, Assistant Professor, Biology, University of Oklahoma
Top-down proteomics (TDP) allows the characterization of proteoforms, or proteins with specific sets of genetic and chemical modifications. Therefore, TDP provides a description of the proteome with high molecular specificity, finding mechanistic connections with phenotypes of interest. Here, we describe novel tools to improve TDP. Ultraviolet photodissociation (UVPD) uses 213 nm photons to fully characterize proteoforms <30 kDa, while ion-ion proton transfer facilitates the identification of large proteoforms (30-60 kDa).

2:50 Nanodelivery of a Functional Membrane Receptor to Manipulate Cellular Phenotype
Matthew Coleman, PhD, Senior Scientist, Physical Life Sciences, Lawrence Livermore National Laboratory (LLNL)
We have developed a platform that enables multiplex investigation of G-protein-coupled receptors (GPCRs) by coupling cell-free expressed GPCR in *E. coli* with functional profiling at the single-molecule level for delivery of the active GPCR into mammalian cells. Specifically, our work shows that we can assemble full-length, wild-type β2AR associated with nanolipoprotein particles (NLPs) in cell-free *E. coli* lysates in a single step process. We then functionally characterized the nanoassemblies by demonstrating ligand-induced confirmation activation.

3:20 Sponsored Presentation *(Opportunity Available)*

3:35 Networking Refreshment Break

HIGH-THROUGHPUT ANALYTICS

4:00 Bridging the Silos: Integration of HTPD Scale-Down Models and High Throughput Analytics Enables and Accelerates Process Development of Biopharmaceuticals
Kelcy Newell, PhD, Senior Scientist, Laboratory Automation & High-Throughput Process Development, MedImmune, LLC
As biopharmaceutical companies shift their pipeline to increasingly novel therapeutics, development is filled with new challenges including different novel product quality attributes, new product and process related impurities, and/or accelerated product degradation pathways. We have adopted a cross-functional approach to minimize disruption of development timelines and even enable acceleration to market when required. This talk will spotlight multiple cross-functional high-throughput process development strategies that have been successfully utilized for problematic biopharma molecules in development.

4:30 A Computational High-Throughput Method for the Study of Modified RNA Interactions with Proteins
Phanourios Tamamis, PhD, Assistant Professor, Chemical Engineering, Texas A&M University
Little is known about the abundance of protein-RNA modification interactions and how these interactions may regulate protein function. Here, we present the first, to our knowledge, computational protocol for the characterization of interactions between proteins and RNAs containing post-transcriptional modifications. As an initial test case, we implemented our CHARMM-based protocol to investigate interactions between *E. coli* polynucleotide phosphorylase protein with modified RNAs, demonstrating a reasonably high agreement between computational and experimental results.

5:00 Application of Native MS for the Characterization of Bispecific Antibodies during Drug Development
Markus Haberger, PhD, Senior Scientist, Pharma Technical Development Analytics Extended Characterization, Roche Diagnostics GmbH
High-molecular weight aggregates, such as antibody dimers and other side products derived from incorrect light or heavy chain association, typically represent critical product-related impurities for bispecific antibody formats. In this study, an approach employing ultra-pressure liquid chromatography size-exclusion separation combined with native electrospray ionization mass spectrometry for the simultaneous formation, identification and quantification of size variants in recombinant antibodies was developed. Samples exposed to storage and elevated temperature(s) enabled the identification of various bispecific antibody size variants.

5:30 Close of Day

FRIDAY, JANUARY 18

8:00 am Registration

BuzZ sessions

8:00 BuzZ Sessions with Continental Breakfast
Protein therapeutics is a fast-growing global market. As the science improves, so does the complexity of the R&D organization. Ensuring product quality plus speed to market requires insights from stakeholders working across the stages of protein science R&D. Join experts representing this PepTalk pipeline, peers, and colleagues for an interactive roundtable discussion. Topics include highlights from the week's presentations, new technologies and strategies, challenges, and future trends.
Moderator: David Wood, PhD, Professor, Chemical & Biomolecular Engineering, The Ohio State University

HIGH-THROUGHPUT PROTEIN PURIFICATION

9:00 Chairperson's Remarks
Markus Haberger, PhD, Senior Scientist, Pharma Technical Development Analytics Extended Characterization, Roche Diagnostics GmbH

FEATURED PRESENTATION
9:05 Medium Scale (0.25-10L) High-Throughput Paramagnetic Purification of Biologics
John Kawooya, PhD, Director, Biologics Optimization, Discovery Research, Amgen, Inc.
Here, we describe a transformative medium-scale rare earth magnetic (NdFeB) system which purifies biologics directly from crude cell culture with cells. The capture step on the beads starts 18-24 hours before the end of protein expression, thereby eliminating the cycle time traditionally spent during centrifugation, clarification and sample loading. The output of the system is amplified by formatting and magnetizing sixteen tanks each capable of purifying more than 2 grams of protein in less than two hours.

9:35 High-Throughput Purification of Synthetic Peptides
Mathias Schaffrath, PhD, Group Head, R&D IDD In vitro Biology & HT Chemistry Library, Chiral & Peptide Purification, Sanofi-Aventis Deutschland GmbH
The purification of synthetic peptides is still a challenge. Reversed phase chromatography is in many cases the method of choice. Sometimes orthogonal reversed phase methods with two chromatographic steps and two different column selectivities are needed to increase the purity to more than 95%. Chromatographic experience, a thorough method development and up scaling is needed for successful separations. Partial automation of the process leads to remarkable throughput, which is particularly important in the field of research.

10:05 Evolving the High-Throughput Protein Purification Pipeline
Edward Kraft, PhD, Senior Scientific Manager, BioMolecular Resources, Genentech, Inc.
The development of high-throughput protein expression and purification pipelines are an essential component for predicting construct design success and scalability for protein production. This process requires significant expertise spread across biochemistry, biology, automation and informatics to create a system that has the flexibility to impact all types of proteins. This talk will present our work to continually adapt our high throughput protein production workflows to support the diversity of non-antibody proteins in support of research across Genentech.

10:35 Networking Coffee Break

AUTOMATION IN HTP PROCESSES

11:00 Library-Based Glycan Identification by Mass Spectrometry in Combination with Fluorescence Quantification as a Biopharma Solution for Automated Glycan Characterization
Sven Bahrke, PhD, Senior Director, Research & Development, Glycotope GmbH
In the present study, proteins comprising different numbers of glycosylation sites were analyzed by release of N-glycans with N-glycanase F, fluorescence labeling of N-glycans, data recording by use of HILIC-UPLC-FLD-ESI-QTOF MS/MS (hydrophilic interaction ultra-performance chromatography with fluorescence detection coupled to electrospray ionization quadrupole time-of-flight tandem mass spectrometry). Subsequently, automatic data processing was performed, and final reporting of all data in a certificate of analysis.

11:30 Beyond Miniaturization and Parallelization: Standard and Tailor-Made Automated Workflows for Smart Microbial Phenotyping and Bioprocessing
Marco Oldiges, PhD, Professor and Head, Bioprocesses and Bioanalytics, Institute of Bio- and Geosciences, IBG-1, Biotechnology, Forschungszentrum Jülich GmbH
Microbial production of heterologous proteins demands increased cultivation throughput at well-defined bioprocess conditions. Making use of miniaturization, parallelization and automation, standard and tailor-made workflows need to be put in place, comprising the full experimental pipeline from upstream processing, cultivation, process analytics, data management and design-of-experiment. Case studies illustrate how developments in miniaturized cultivation combined with smart lab automation and data processing are amalgamated in workflows for more efficient microbial phenotyping and bioprocess development.

12:00 pm Conference Wrap-Up
David Wood, PhD, Professor, Chemical & Biomolecular Engineering, The Ohio State University

12:30 Close of Conference

BIOTHERAPEUTIC EXPRESSION & PRODUCTION

The demand for high-quality biotherapeutics has never been greater. Higher-throughput protein expression, production and purification as well as more flexible expression systems and techniques are necessary to meet the demands for both biotherapeutic research and manufacturing pipelines. Throughout the week, the Biotherapeutic Expression & Production pipeline explores the newest data, innovations and strategies to make the expression of therapeutic proteins more efficient, effective and trouble-free.

JANUARY 14-15

AGENDA Engineering Genes, Vectors, Constructs, and Clones

Also part of ALTERNATIVE EXPRESSION & PRODUCTS

JANUARY 15-16

AGENDA Recombinant Protein Expression and Production

JANUARY 16-17

AGENDA CHO Cell Lines

JANUARY 17-18

AGENDA Optimizing Expression Platforms

MONDAY-TUESDAY, JANUARY 14-15 | 11TH ANNUAL

ENGINEERING GENES, VECTORS, CONSTRUCTS, AND CLONES

Exploring Strategies in Systems Engineering and Synthetic Biology

Also part of
ALTERNATIVE EXPRESSION & PRODUCTS

THE DEMAND FOR high-quality biotherapeutic proteins has never been greater. Many variables still must be considered during the engineering process, including verification and sequence analysis of the gene or protein of interest, codon optimization, vector construction and clone/host selection – a time-consuming and expensive process. Additionally, protein expression scientists are now exploring new engineering tools including synthetic biology and systems engineering. Ultimately, these tools must be weighed against traditional expression and production strategies to achieve the desired quantity and quality. Cambridge Healthtech Institute's 11th Annual Engineering Genes, Vectors, Constructs, and Clones conference continues the tradition of applying effective engineering strategies for protein expression and production research leading to functional biotherapeutic products. Learn from seasoned, savvy researchers as they share their real-world experiences, applications and results.

SUNDAY, JANUARY 13

4:00 - 6:00 pm Pre-Conference Registration

MONDAY, JANUARY 14

7:00 am Registration and Morning Coffee

SYSTEMS BIOLOGY: ELUCIDATING THE CONNECTIONS

9:00 Welcome by Conference Organizer
Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks
Simpson Joseph, PhD, Professor, Department of Chemistry & Biochemistry, University of California, San Diego

KEYNOTE PRESENTATION

9:10 COBRAme: A Computational Framework for Genome-Scale Models of Metabolism and Gene Expression
Bernhard Palsson, PhD, Galletti Professor, Bioengineering; Principal Investigator, Systems Biology Research Group, Bioengineering; Professor, Pediatrics, University of California, San Diego

9:50 Using Systems Approaches to Improve Protein Production in Mammalian Cell with Targeted Engineering
Nathan E. Lewis, PhD, Assistant Professor, Department of Pediatrics, University of California, San Diego
Genomic resources have provided a comprehensive view of all the cell parts in mammalian cells, and systems biology is elucidating how they are all connected. We are now using systems biology modeling and omics data analysis to guide efforts to engineer mammalian cells for protein production.

10:20 Networking Coffee Break

CELL-FREE SYSTEMS

10:45 Integrating Cell-Free Protein Expression and Coarse-Grain Molecular Simulation for Rapid Design-Build-Test-Learn Cycles to Discover the Locational Impact of Site-Specific PEGylation
Bradley C. Bundy, PhD, Associate Professor, Department of Chemical Engineering, Brigham Young University
A cell-free approach to synthetic biology enables direct control of and access to the biological machinery for rapid Build-Test-Learn engineering cycles. The exponentially growing field is beginning to impact the biotherapeutics, biocatalysis, and biosensing industries. This presentation highlights recent advances combining course-grain molecular simulation with cell-free protein expression screening to rapidly determine the optimal location(s) for site-specific PEGylation.

11:15 Energy Consumption in a Cell-Free Expression System
Simpson Joseph, PhD, Professor, Department of Chemistry & Biochemistry, University of California, San Diego
Although much progress has been achieved in the design and synthesis of artificial cells, presently they are far inferior to living cells in robustness, stability and the production of biomaterials. One of the reasons for the poor performance of synthetic cells is due to inefficient energy regeneration in cell-free protein synthesis (CFPS) systems. I discuss methods to enhance energy regeneration in a cell-free expression system.

11:45 A Cell-Free Protein Synthesis Platform for Robust Epitope Screening and Novel Vaccine Development
John Dresios, PhD, Senior Biology Director, Chief Scientist and Leidos Technical Fellow, Advanced Solutions Group, Leidos
Expression of antigenic peptides for vaccine screening is challenging due to the poor and/or variable expression of predicted epitopes. In this respect, the value of a screen is minimized if only a small fraction of the epitopes is expressed, or if the expressed peptides are produced at dramatically different levels. Here we describe a cell-free platform for high-yield, balanced peptide expression that enables rapid epitope screening and multi-epitope vaccine development.

12:15 pm Productivity through Diversity - a Protein Production Toolbox to UNLOCK PICHIA *Sponsored by VTU technology*
Iskandar Dib, PhD, Principal Scientist, Process Development & Analytics, VTU Technology GmbH

12:45 Session Break

12:55 Luncheon Presentation to be Announced *Sponsored by ATUM*

1:25 Luncheon Presentation II *(Sponsorship Opportunity Available)*

TOOLS FOR ENHANCING EXPRESSION: CODONS, CONSTRUCTS, AND CLONES

2:00 Chairperson's Remarks
Chao-Guang Chen, PhD, Senior Scientist, Research Department, CSL Limited

2:05 Synonymous Codon Selection to Improve Protein Folding Yield
Patricia L. Clark, PhD, O'Hara Professor of Chemistry & Biochemistry; Concurrent Professor of Chemical & Biomolecular Engineering, University of Notre Dame
We have developed a sensitive system to detect effects of synonymous codon substitutions on the co-translational folding of proteins expressed in *E. coli*, coupling the success of folding to *E. coli* fitness. We find that position-specific synonymous codon changes can have dramatic effects on folding yield, particularly at those positions that correspond to sub-domain "motif" structures.

2:35 Translational Attenuation Strategies to Improve Soluble Yields in Bacterial Expression Systems
Christopher H. Gray, PhD, Staff Scientist & Team Leader (Structural Biology), Drug Discovery Program, CRUK Beatson Institute
High levels of protein expression in *Eschericha coli* frequently produce inclusion bodies. Alleviating strategies, modulating transcription or folding, are often modestly successful. We have enhanced soluble expression by manipulating translation, slowing the processing of target transcripts by regulating ribosome binding or by incorporating rare codons at strategic positions within the cDNA. This specific attenuation of translation results in greater soluble yields and offers a novel strategy to enhance production.

3:05 Find Your Table and Meet Your BuzZ Session Moderator

3:15 BuzZ Sessions with Refreshments
Join your peers and colleagues for interactive roundtable discussions.
See page 11 for details.

4:30 High-Throughput Antibody Construct Generation and Expression
Chao-Guang Chen, PhD, Senior Scientist, Research Department, CSL Limited
Antibody construct generation, also referred to as IgG reformatting, is a key step in antibody-display phage library screening. Following library screening, positive Fab expression constructs must be converted into IgG format before they can be expressed as soluble antibodies for further testing and characterization. An efficient strategy for high-throughput antibody construct generation and expression that solves many of the technical challenges associated with IgG reformatting will be presented.

5:00 Rapid Construction of Recombinant Plasmids by QuickStep-Cloning
Tuck Seng Wong, PhD, Senior Lecturer, Chemical and Biological Engineering, University of Sheffield
Molecular cloning is an essential step in biological engineering. Megaprimer-based PCR of a whole plasmid is a widely used method. However, linear amplification, use of self-annealing megaprimers and difficulty of performing point insertion of DNA are some of its limitations. QuickStep-Cloning overcomes these problems yet retains the simplicity of whole-plasmid amplification. It utilizes asymmetric PCRs to create a megaprimer pair with 3'-overhangs, and hence, facilitates the subsequent exponential whole-plasmid amplification.

5:30 Sponsored Presentation *(Opportunity Available)*

6:00 - 7:15 Welcome Reception in the Exhibit Hall with Poster Viewing *Sponsored by proteinsimple*

7:15 Close of Day

TUESDAY, JANUARY 15

8:00 am Registration and Morning Coffee

NOVEL TOOLS ARE ENHANCING PRODUCTION

8:30 Chairperson's Remarks
Mark Welch, PhD, Vice President, Research and Development, ATUM

8:35 Titer Estimation for Quality Control (TEQC) Method: A Practical Approach for Optimal Production of Protein Complexes Using the Baculovirus Expression Vector System
Yuichiro Takagi, PhD, Associate Professor, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine
The baculovirus expression vector system (BEVS) is becoming the method of choice for expression of many eukaryotic proteins and protein complexes. However, what influences the overall production of proteins or protein complexes remains largely unclear. We developed the Titer Estimation for Quality Control (TEQC) method, which enables researchers to quantitatively optimize protein expressions utilizing BEVS in a highly reproducible fashion.

9:05 *De novo* DNA Synthesis Using Enzymes
Sebastian Palluk, MSc, CTO, Ansa Biotechnologies
DNA synthesis, the ability to "write" DNA, is a foundational technology in life sciences research and engineering. Currently, all synthetic DNA is made using organic chemistry via a method that has remained unchanged for 35 years and has approached a plateau. This talk describes current efforts in the field of enzymatic DNA synthesis and presents a novel DNA synthesis technology that is based on polymerase-nucleotide conjugates.

9:35 Sponsored Presentation *(Opportunity Available)*

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 Genetic Engineering Process Optimization in CHO Cells
Stephanie L. Sandefur, MSc, Consultant Biologist, Bioprocess Research & Development, Eli Lilly and Company
Over the past decade, considerable progress has been made in improving the effectiveness and efficiency

of generating highly productive recombinant CHO cell lines. While these efforts have been primarily centered on driving cell culture productivity, more recently, focus has turned to approaches to impact product quality. This presentation describes potential approaches to maximizing the effectiveness of host cell engineering and reducing the time to successfully impact biotherapeutic product quality profiles.

11:30 A Multi-Landing Pad DNA Integration Platform for Mammalian Cell Engineering
Liliana Wroblewska, PhD, Principal Scientist, Biomedicine Design, Pfizer
Reliable, large-scale engineering of CHO cells through precise insertion of large amounts of heterologous DNA into well-characterized genomic loci would have broad applications for mammalian synthetic biology, recombinant protein production, and biomanufacturing. Using multi-gene payload vectors, cell lines with multiple landing pads, and recombinase technology, we demonstrated controlled integration of up to nine copies of a monoclonal antibody (about 100 kb of heterologous DNA), and a corresponding linear increase in antibody expression.

12:00 pm Talk Title to be Announced
Pierre-Alain Girod, PhD, CSO, Selexis SA
Sponsored by SELEXIS

12:30 Session Break

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Close of Engineering Genes, Vectors, Constructs, and Clones Conference

TUESDAY-WEDNESDAY, JANUARY 15-16 | 21ST ANNUAL

RECOMBINANT PROTEIN EXPRESSION AND PRODUCTION

Achieving Quality and Quantity

GREAT STRIDES HAVE been made in the expression, production, and purification of biotherapeutics. However, hurdles remain. The efficient expression and production of these valuable biomolecules face challenges in improving their quantity and quality while minimizing time and cost. Thus, higher-throughput expression and purification as well as more flexible expression platforms are in even greater demand. Unfortunately, there is no "universal" production system which can guarantee high yields of recombinant protein, particularly as every biomolecule itself causes its own issues in terms of expression. Cambridge Healthtech Institute's 21st Annual Recombinant Protein Expression and Production conference explores the newest data and innovations relating to the best choices in hosts/systems, as well as ways to "rescue" existing systems and make them work more effectively to produce the quality and quantity of the desired biotherapeutic.

TUESDAY, JANUARY 15

1:00 pm Registration

1:30 Refreshment Break in the Exhibit Hall with Poster Viewing

FROM PROTEIN EXPRESSION TO BIOTHERAPEUTIC PRODUCT

2:00 Chairperson's Opening Remarks
Henry C. Chiou, PhD, Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific

KEYNOTE PRESENTATION

2:05 Expression Systems for Various Biologics Modalities: Today and Tomorrow
Zhimei Du, PhD, Director, Bioprocess & Clinical Manufacturing, Merck
Developing a robust expression system is the most critical step during biologics development for all modalities, including mAb, non-mAb complex molecules, and CAR-T, etc. A robust expression system can impact the productivity, also product qualities and process controls. In this presentation, we discuss the details of the major factors that need to be considered when developing the new expression system, and how to apply Quality-by-Design strategy at this stage.

FEATURED PRESENTATION

2:45 Roadmap to Developing End-to-End Cell Line Development Automation to Increase Efficiency
David Shaw, PhD, Senior Scientist, Cell Culture, Pharma Technical Development, Genentech, Inc.
Lab automation can be leveraged to increase efficiency and free up resources to take on other value-added research. We discuss End-to-End Cell Line Development Automation implementation to increase efficiency and throughput while reducing required resources. We have been able to exploit our robust, targeted integration cell line development platform to develop automated workflows which increase efficiency, consistency and provide flexibility.

3:15 ExpiSf, ExpiCHO and Expi293: Latest Developments in High-Titer Transient Protein Expression
Sponsored by ThermoFisher SCIENTIFIC
Jonathan Zmuda, PhD, Director, Cell Biology, Thermo Fisher Scientific
The Expi Expression Systems comprise three different cell hosts to provide researchers with unprecedented access to high-titer recombinant proteins. Here, we highlight the latest data and recent additions to the Expi family of products, including the first ever chemically defined insect expression system, ExpiSf, a structural biology module for the Expi293 expression system, GMP-banked Expi293 and ExpiCHO-S cells and ExpiCHO Stable Production Media to support the transition from transient to stable protein expression.

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

EFFECTIVE EXPRESSION AND PRODUCTION OF:

VECTORS FOR GENE THERAPY

4:30 Optimizing Sf9-Based Stable Cell Lines for the Production of Highly Infectious rAAV Vectors
Sergei Zolotukhin, PhD, Professor, Department of Pediatrics, College of Medicine, University of Florida
We describe a new insect cell-based production platform utilizing attenuated Kozak sequence and a leaky ribosome scanning to achieve a serotype-specific modulation of AAV capsid proteins stoichiometry. By way of example, rAAV5 and rAAV9 were produced and comprehensively characterized side by side with HEK293-derived vectors. The data will be presented demonstrating a superior infectivity and higher genetic identity of OneBac-derived rAAV vectors providing a scalable platform for good manufacturing practice (GMP)-grade vector production.

5:00 LVV Production Process: Recent Advances and Opportunities for Innovation
Yogesh Waghmare, PhD, Associate Director, Vector Downstream Process Development, Bluebird Bio
LentiViral Vector (LVV)-based Cell and Gene Therapy products are steadily increasing in number. Industrial production of LVV poses significant challenges compared to AAV due to the large size, complexity, and labile nature of LVV. An overview of industrial LVV production process evolution, recent technological advances, and LVV specific challenges will be presented.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

5:45 - 8:45 Dinner Short Courses*
See page 8 for details.
**Separate registration required*

WEDNESDAY, JANUARY 16

7:45 am Registration and Morning Coffee

EFFECTIVE EXPRESSION AND PRODUCTION OF:

ANTIBODIES

8:15 Chairperson's Remarks
Jie Zhu, PhD, Associate Director, Cell Culture & Fermentation Sciences, MedImmune

FEATURED PRESENTATION
8:20 Controlling Protein Quality and Antibody Expression
Anne Skaja Robinson, PhD, Chair, Chemical and Biomolecular Engineering, Catherine and Henry Boh Professor of Engineering, Tulane Brain Institute Faculty Member, Tulane University
Monoclonal antibodies (mAbs) are a class of commercially valuable biopharmaceuticals that are used for treating diseases that are typically expressed in mammalian cell lines such as Chinese Hamster Ovary (CHO) cells to enable posttranslational modifications. One such posttranslational modification that results in structural and pharmacological changes in the protein is N-linked glycosylation. This talk addresses approaches to maintaining desired product quality of mAbs in the presence of process variations during manufacturing.

8:50 Therapeutic Antibody Fragments: Simplifying the Choice of the Expression Platform and Optimizing Protein L Capture
Philippe Billiald, PharmD, PhD, Professor, Biochemistry, University of Paris-Sud; Co-Founder, Acticor Biotech
Therapeutic antibody fragments are produced from various hosts, but no downstream process is well established. Here, we report a universal method to confer Protein L binding ability to any antibody fragment. In addition, based on a case study, we assess *E. coli*, *P. pastoris* and CHO expression systems in terms of cell line development, culture time, product quality and cost. We report differences to consider before pharmaceutical development and moving forward to the clinic.

9:20 Presentation to be Announced
Sponsored by FUJIFILM Diosynth Biotechnologies

9:35 Scaling Up and Scaling Out: Pushing the Boundaries of Transient Protein Production
Sponsored by absolute antibody
Ian Wilkinson, PhD, CSO, Research & Development, Absolute Antibody Ltd.
Whilst transient yields have improved drastically in the last decade, scalable systems are time-consuming and costly to implement. Absolute Antibody has developed systems which scale up and scale out protein expression and purification, enabling the rapid and cost-effective production of milligram-to-gram quantities of large panels of proteins.

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

10:35 Multi-Specificity of a Recombinant Monoclonal Antibody
Gary McLean, PhD, Reader in Molecular Immunology, Cellular and Molecular Immunology Research Centre, London Metropolitan University; Honorary Senior Research Fellow, National Heart and Lung Institute, Imperial College London
The concept of antibody multi-specificity is a phenomenon defined as multiple interactions of the antibody paratope with diverse structures. This presentation shows the multi-specific nature of one recombinant monoclonal antibody that was generated to a peptide sequence specific to the cellular molecular switch protein m-ras. The monoclonal antibody, despite being derived from antiserum that was m-ras specific, bound numerous peptide sequences that contained multiple positively charged amino acid residues.

11:05 Mammalian Display Platform for Facile, FACS-Based Engineering of Antibodies and Other Receptors
Jennifer Maynard, PhD, Associate Professor, Chemical Engineering, University of Texas at Austin
Mammalian cells are used for large-scale production because of the complex antibody structure. To circumvent problems associated with changing hosts, we developed a screening platform on CHO cells which allows for antibody selection in the same host used for manufacturing. We have used this approach to affinity mature an antibody Fab, a human T cell receptor and modulate binding of human IgG1 Fc to the FcgRIIIa receptor.

11:35 Understanding and Engineering Fc Glycans in CHO Cells for the Production of Therapeutic Proteins
Jie Zhu, PhD, Associate Director, Cell Culture & Fermentation Sciences, MedImmune
Glycosylation of monoclonal antibody and derivatives plays an important role for complement-dependent cytotoxicity (CDC) and antibody-dependent cell-mediated cytotoxicity (ADCC) functions. Case studies are presented here on the generation of stable CHO cells cell line to produce recombinant proteins with desirable and consistent glycosylation patterns in Fc domain using both vector and host engineering approaches.

12:05 pm Session Break

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

1:15 Session Break

2:00 PLENARY KEYNOTE PANEL
See page 5 for details.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

EFFECTIVE EXPRESSION AND PRODUCTION OF:

RECOMBINANT PROTEINS

4:00 Chairperson's Remarks
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

4:05 Implementing Next-Generation Sequencing for DNA-Based Sequence Variant Analysis of Recombinant Proteins
Ulrich Goepfert, PhD, Principal Scientist, Large Molecule Research, Roche Pharma Research & Early Development, Roche Innovation Center Munich
Sequence variants are unintended amino acid substitutions in biopharmaceuticals, which can either be due to the manufacturing process or mutations of the transgene. Transgene mutations are permanent

properties of affected cell lines and may give rise to critical quality attributes. Therefore, mutated cell lines need to be identified and excluded from development. We share our experience with Next-Generation Sequencing as an efficient and highly sensitive method to detect DNA-based sequence variants.

4:35 The BEST of Both Worlds – Targeted Integration and Multiple Copies: How Can These Go Together for Improved Cell Line Development?
Anton Bauer, PhD, MBA, COO, R&D, The Antibody Lab GmbH
Targeted Hot Spot integration and multiplication of independent expression units – can this go together and even speed up cell line development? By targeting the Rosa26 Hot Spot *in vitro* we generated BAC-based expression vectors, which integrated in multiple copies into the CHO host cell chromatin and acted as independent expression units. This allowed us to adapt the selection process and developed long-term stable high-yield production cell lines at an unprecedented speed.

5:05 Optimizing Productivity and Product Quality of Difficult-to-Express Biosimilars with a Novel NS0 Platform
Darryl Sampey, PhD, President & CEO, Research & Development, BioFactura, Inc.
Biosimilar cell lines that produce complex glycoproteins such as monoclonal antibodies must be both highly productive and express a product with critical quality attributes closely matching those of the innovator references. In this presentation, a novel biomanufacturing platform and case studies are described that harness the commercially established NS0 host cell in new ways to create stable, productive cell lines with product characteristics meeting biosimilar technical and regulatory demands.

5:35 Engineering CHO Cell Lines for the Production of Hard-to-Produce Proteins
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark
Using our high-throughput cell line engineering platform, we have engineered CHO cells able to produce a therapeutic protein that has previously not been possible to produce in CHO cells. This approach may result in improved therapeutic proteins, with better biological properties, such as increased half-life, improved activity, etc.

6:05 - 7:00 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Recombinant Protein Expression and Production Conference

WEDNESDAY-THURSDAY, JANUARY 16-17 | 5TH ANNUAL

CHO CELL LINES

Enhancing Expression, Performance, and Process

CHO CELLS' RAPID rise in production prominence is due to their adaptability to various culture conditions, gene plasticity, and ability in proper folding, posttranslational modifications, and glycosylation of desired proteins. Thus, advances in CHO cell lines and culture continue to significantly improve biotherapeutic production. This achievement is due to progress in engineering stable and transient cell lines, enhancing cell culture conditions and performance, as well as optimizing process development. When all are accomplished, higher-production titers and better product quality result. Cambridge Healthtech Institute's CHO Cell Lines conference gathers cell line engineers, cell culture specialists, and bioprocess development managers to explore the latest data, tools, and strategies for improving protein expression, production, and product quality.

WEDNESDAY, JANUARY 16

7:45 am Registration and Morning Coffee

PROCESS DEVELOPMENT RESULTS IN HIGHER CHO PRODUCTIVITY

8:15 Chairperson's Opening Remarks
Jie Zhu, PhD, Associate Director, Cell Culture & Fermentation Sciences, MedImmune

FEATURED PRESENTATION
8:20 Controlling Protein Quality and Antibody Expression
Anne Skaja Robinson, PhD, Chair, Chemical and Biomolecular Engineering, Catherine and Henry Boh Professor of Engineering, Tulane Brain Institute Faculty Member, Tulane University
Monoclonal antibodies (mAbs) are a class of commercially valuable biopharmaceuticals that are used for treating diseases that are typically expressed in mammalian cell lines such as Chinese Hamster Ovary (CHO) cells to enable posttranslational modifications. One such posttranslational modification that results in structural and pharmacological changes in the protein is N-linked glycosylation. This talk addresses approaches to maintaining desired product quality of mAbs in the presence of process variations during manufacturing.

8:50 Therapeutic Antibody Fragments: Simplifying the Choice of the Expression Platform and Optimizing Protein L Capture
Philippe Billiald, PharmD, PhD, Professor, Biochemistry, University of Paris-Sud; Co-Founder, Acticor Biotech
Therapeutic antibody fragments are produced from various hosts, but no downstream process is well established. Here, we report a universal method to confer Protein L binding ability to any antibody fragment. In addition, based on a case study, we assess *E. coli*, *P. pastoris* and CHO expression systems in terms of cell line development, culture time, product quality and cost. We report differences to consider before pharmaceutical development and moving forward to the clinic.

9:20 Presentation to be Announced

Sponsored by FUJIFILM Diosynth biotechnologies

9:35 Scaling Up and Scaling Out: Pushing the Boundaries of Transient Protein Production

Sponsored by absolute antibody

Ian Wilkinson, PhD, CSO, Research & Development, Absolute Antibody Ltd.
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2:00 PLENARY KEYNOTE PANEL
See page 5 for details.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

ENGINEERING CHO TO OPTIMIZE PRODUCTIVITY AND PRODUCT QUALITY

4:00 Chairperson's Remarks
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

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6:05 - 7:00 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

THURSDAY, JANUARY 17

7:45 am Registration and Morning Coffee

IMPROVING STABLE CHO CELL LINES

8:10 Organizer's Remarks
Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

8:15 Chairperson's Remarks
Howard R.G. Clarke, PhD, Principal Scientist, Cell Sciences, Seattle Genetics

KEYNOTE PRESENTATION

8:20 Chromosome Stability Approach: Lengthening of High-Yield Production Levels of IgG-Producing CHO Cells by Downregulation of Breast Cancer 1
Takeshi Omasa, PhD, Professor, Department of Material and Life Science, Graduate School of Engineering, Osaka University
The effects of breast cancer 1 (BRCA1) downregulation on gene amplification efficiency and long-term productivity were investigated in CHO cells. Our results suggest that high-producing cells, which maintain their productivity long term, were efficiently established by BRCA1 downregulation. In this presentation, I would like to introduce the chromosome stability and effect of BRCA1 downregulation.

9:00 Antibody Expression Stability in CHO Clonally Derived Cell Lines and Their Subclones
Howard R.G. Clarke, PhD, Principal Scientist, Cell Sciences, Seattle Genetics
Cell line development involves lengthy screening to identify a stable line having consistent growth, productivity and product quality. To investigate production stability in CHO cells, we analyzed primary clones and their respective subclones. Cell lines derived from single cell progenitors grow into populations of cells with phenotypic heterogeneity. Here I present the genetic and epigenetic characterization of these heterogeneous cell line populations.

9:30 Presentation to be Announced *Sponsored by* MaxCyte

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 Manufacturing and Characterization of Novel HIV-1 Vaccine Candidates – Success and Challenges
Antu K. Dey, MSc, PhD, Senior Director, R&D, Vaccine Product Development Center, International AIDS Vaccine Initiative (IAVI)
Recent success of new HIV-1 vaccine candidates in preclinical studies has prompted manufacturing efforts to support cGMP production of some of these HIV-1 recombinant protein vaccine candidates for evaluation in (proof-of-concept) Phase I clinical studies. Through expression in stable CHO cell lines and after extensive characterization for desired attributes, Phase I clinical trial material was generated.

11:30 Engineering a Stable CHO Cell Line for the Expression of a MERS-Coronavirus Vaccine Antigen
Mun Peak Nyon, PhD, Research Associate, Pediatrics, Pediatric Tropical Medicine, Baylor College of Medicine
Human vaccine against MERS-CoV is not available. We have developed a stably transfected adherent CHO cell line for the production of the MERS-CoV protein subunit, S377-588 (Fc tagged). The adjuvanted protein vaccine expressed in adherent CHO could protect transgenic animal model from infection with live MERS-CoV. We also have developed a suspension monoclonal CHO cell line able to express S377-588-Fc in serum-free media, which is ready for scaled-up production.

12:00 pm Session Break

12:10 Luncheon Presentation I: New Tools for Screening & Harvesting Solutions for CHO & HEK293 Cells, for Both Transient and Stable Cells *Sponsored by* THOMSON INSTRUMENT COMPANY
Samuel Ellis, Vice President, Thomson Instrument Company
Evaluation of different transfection tools, product quality, and titer for both CHO and HEK293 cell lines. Data will be presented on techniques and technology that mimic large-scale bioreactors in non-controlled devices from 1mL-3L. Technologies presented include well plates and culture tube systems with incorporated filtration methodology. A new direct harvesting technique will also be introduced that eliminates centrifugation while maintaining 0.2um sterile filtration. All of these tools will be presented with case studies from scientists.

12:40 Luncheon Presentation II *(Sponsored Opportunity Available)*

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

2:15 Close of CHO Cell Lines Conference

OPTIMIZING EXPRESSION PLATFORMS

Tools for Effective Expression, Production, and Purification

THE UTILIZATION OF engineered therapeutic proteins for basic research, clinical diagnostics, and therapy continues to expand. Consequently, protein expression laboratory managers and researchers face challenges for efficient expression, production, and purification even while improving quantity and quality and minimizing time and cost. Transient protein production (TPP) has the advantage of speed and limiting risk while stable transfection – the longer and more complex process – has the advantage of producing long-term expression of the biotherapeutic of interest. The rapidly increasing need for recombinant proteins necessitates further improvements in both technologies. Cambridge Healthtech Institute's 6th Annual Optimizing Expression Platforms conference convenes protein expression specialists who share their experiences with process and platform differences, tradeoffs, and improvements for producing recombinant proteins in their expression and production laboratories.

THURSDAY, JANUARY 17

7:45 am Registration and Morning Coffee

IMPROVING PRODUCTION WITH STABLE CELL LINES

8:10 Organizer's Welcome Remarks
Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

8:15 Chairperson's Opening Remarks
Howard R.G. Clarke, PhD, Principal Scientist, Cell Sciences, Seattle Genetics

KEYNOTE PRESENTATION

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12:00 pm Session Break

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Sponsored by THOMSON Solutions At Work INSTRUMENT COMPANY

Samuel Ellis, Vice President, Thomson Instrument Company
Evaluation of different transfection tools, product quality, and titer for both CHO and HEK293 cell lines. Data will be presented on techniques and technology that mimic large-scale bioreactors in non-controlled devices from 1mL-3L. Technologies presented include well plates and culture tube systems with incorporated filtration methodology. A new direct harvesting technique will also be introduced that eliminates centrifugation while maintaining 0.2um sterile filtration. All of these tools will be presented with case studies from scientists.

12:40 Luncheon Presentation II *(Sponsored Opportunity Available)*

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

TOOLS FOR TRANSIENT PROTEIN PRODUCTION (TPP)

2:15 Chairperson's Remarks
Masamichi Kamihira, PhD, Professor, Faculty of Engineering, Department of Chemical Engineering, Kyushu University

2:20 Scaling Up a High-Titer HEK293 Transient Transfection Process
Tia Arena, MSc, Engineer I, Department of Cell Culture, Genentech
HEK293 transient expression systems are often used to quickly generate protein for research and preclinical studies. Here we describe engineering a HEK293 cell line that is more resistant to apoptosis and shear stress. After process optimization for seed train (35 L) and transient transfections (up to 25 L), this robust cell line-enabled expression of antibodies and non-antibody proteins up to 800 mg/L in 7 days.

2:50 Recombinant Production of the Toxic Anti-Cancer Lectin Viscumin in Tobacco Plants and Microbial Cells: A Comparative Analysis of Yield, Process Costs and Toxicity
Johannes Buyel, Dr. rer. nat., Dr.-Ing., MSc, Head, Integrated Production Platforms, Fraunhofer Institute for Molecular Biology and Applied Ecology IME
Viscumin is a potential anti-cancer protein that cannot be produced in mammalian cells due to its inherent toxicity. Manufacturing in microbial systems is cumbersome due to the formation of inclusion bodies that require a complex process, which provides only low recoveries. Instead, plants can be used as a cost-effective alternative expression system that simplifies production and yields a more active product.

3:20 Sponsored Presentation *(Opportunity Available)*

3:35 Networking Refreshment Break

4:00 Manipulating Glycan Profile in a Transient Expression System and Application of a High-Throughput Capillary Western Method Using Lectins for Detection
Silvino Sousa, MSc, Senior Scientist, Global Protein Sciences, AbbVie Bioresearch Center, AbbVie
I discuss approaches for modulating N-linked glycosylation of recombinant therapeutic proteins by manipulating media, process and/or genetics of the host cell factory. What is also needed is a rapid, simple, yet protein- and titer-agnostic method for deriving detailed glycan signature directly and simultaneously from multiple samples of cell culture conditioned medium. I review methods that we have implemented for rapidly screening for glycan signatures directly from cell culture supernatants.

4:30 Accumulative Transgene Integration into a Predetermined Chromosomal Site of CHO Cells
Masamichi Kamihira, PhD, Professor, Faculty of Engineering, Department of Chemical Engineering, Kyushu University
An accumulative site-specific gene integration system (AGIS) based on the Cre-recombinase/loxP system, using mutated loxP sites (Kameyama et al., 2010, Biotechnol. Bioeng., 105, 1106–1114) has been applied for the generation of recombinant CHO cells for producing antibodies (Wang et al., 2016, J. Biosci. Bioeng., 124, 583–590). AGIS can provide an efficient tool for repeated integration of transgenes into a predetermined chromosomal locus.

5:00 PANEL DISCUSSION: Transient, Stable or Both?
Speed, limiting risk and protein quality are often cited as advantages of transient protein production (TPP), while stable transfection – the longer and more complex process – has the advantage of producing long-term expression of the biotherapeutic of interest. The rapidly increasing need for recombinant proteins necessitates further improvements in both technologies.
Moderator:
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Howard R.G. Clarke, PhD, Principal Scientist, Cell Sciences, Seattle Genetics
Silvino Sousa, MSc, Senior Scientist, Global Protein Sciences, AbbVie Bioresearch Center, AbbVie

5:30 Close of Day

FRIDAY, JANUARY 18

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast
Protein therapeutics is a fast-growing global market. As the science improves, so does the complexity of the R&D organization. Ensuring product quality plus speed to market requires insights from stakeholders working across the stages of protein science R&D. Join experts representing this PepTalk pipeline, peers, and colleagues for an interactive roundtable discussion. Topics include highlights from the week's presentations, new technologies and strategies, challenges, and future trends.
Moderator: Richard Altman, MS, Scientist, Protein Technologies, Amgen

MANAGING A PROTEIN PRODUCTION LAB: HOW TO MAKE THE MOST OF YOUR RESOURCES

9:00 Chairperson's Remarks
Richard Altman, MS, Scientist, Protein Technologies, Amgen

9:05 Managing a Collaborative Multidisciplinary Laboratory: Challenges, Strategies, and Benefits
Challise Sullivan, Life Scientist III, Advanced Solutions Group, Leidos
The advantages of a laboratory staffed with skilled, versatile personnel and equipped with systems applicable to numerous applications can be vast. Integrating scientific and engineering expertise, cutting-edge technology, and a collaborative team enables innovations spanning a wide range of disciplines and applications beyond those typically attained by conventional academic or industrial practices. This talk encompasses approaches to effectively manage multidisciplinary laboratory teams along with the challenges and benefits of doing so.

9:35 High-Throughput Cloning for Biomarker Discovery and Functional Genomics
Vel Murugan, PhD, MBA, Research Scientist, Virginia G. Piper Center for Personalized Diagnostics, The Biodesign Institute, Arizona State University
We generate and distribute expression clones around the world. DNASU is a central repository for plasmid clones and collections (DNASU.org). Currently we store and distribute over 300,000 plasmids including 75,000 human and mouse plasmids, full genome collections, the protein expression plasmids from the Protein Structure Initiative as the PSI: Biology Material Repository (PSI : Biology-MR), and both small and large collections from individual researchers. We discuss HT cloning methods that we employ for generating expression clones and laboratory management.

10:05 Recombinant Protein Production: Harmonizing the Process from Construct Generation through Protein Characterization
Richard Altman, MS, Scientist, Protein Technologies, Amgen
A robust, flexible 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.

10:35 Networking Coffee Break

11:00 Making More Proteins: How to Get the Work Done and How to Avoid It
Peter Schmidt, PhD, Director, Recombinant Technologies Research, CSL Behring
The increasing number of projects in early R&D combined with the need to characterize and evaluate new approaches and ideas result in a continuously increasing number of requests to purify and QC proteins. In order to meet these demands, it is necessary to find a good balance between available resources and goals that can be realistically achieved.

11:30 CLOSING PANEL DISCUSSION: Protein Production Lab Challenges: Methodologies, Strategies, and the Art of Managing Multiple Projects
There are many challenges in operating protein production labs. This panel focuses on the following topics: initiating projects, basic expression and purification systems, pros and cons for each system, screening platforms, troubleshooting and how much time should be spent on each system before moving to the next option. On top of "hands on" tips, we touch upon strategies on how to manage multiple "top priority" projects.
Moderator:
Richard Altman, MS, Scientist, Protein Technologies, Amgen
Panelists:
Vel Murugan, PhD, MBA, Research Scientist, Virginia G. Piper Center for Personalized Diagnostics, The Biodesign Institute, Arizona State University
Peter Schmidt, PhD, Director, Recombinant Technologies Research, CSL Behring
Challise Sullivan, Life Scientist III, Advanced Solutions Group, Leidos
Silvino Sousa, MSc, Senior Scientist, Global Protein Sciences, AbbVie Bioresearch Center, AbbVie
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

12:30 pm Close of Conference

ALTERNATIVE EXPRESSION & PRODUCTS

The need to develop more complex biologics, whether they be proteins, cells, vectors or novel constructs, is forcing industry to investigate new production methods and pathways. The Alternative Expression & Products pipeline focuses on the engineering of existing and emerging hosts, strains, vectors and cells to synthesize, express and manufacture novel products with commercially relevant application. Special attention will be paid to enabling technologies such as systems and synthetic biology, microbial-based production, and, new for 2019, vector expression and production.

JANUARY 14-15

AGENDA Engineering Genes, Vectors, Constructs, and Clones

Also part of **BIOTHERAPEUTIC EXPRESSION & PRODUCTION**

JANUARY 15-16

AGENDA Advances in Vector Production and Scale-Up for Cell and Gene Therapy

JANUARY 17-18

AGENDA Microbial Production

MONDAY-TUESDAY, JANUARY 14-15 | 11TH ANNUAL

ENGINEERING GENES, VECTORS, CONSTRUCTS, AND CLONES

Exploring Strategies in Systems Engineering and Synthetic Biology

Also part of
BIOTHERAPEUTIC EXPRESSION & PRODUCTS

THE DEMAND FOR high-quality biotherapeutic proteins has never been greater. Many variables still must be considered during the engineering process, including verification and sequence analysis of the gene or protein of interest, codon optimization, vector construction and clone/host selection – a time-consuming and expensive process. Additionally, protein expression scientists are now exploring new engineering tools including synthetic biology and systems engineering. Ultimately, these tools must be weighed against traditional expression and production strategies to achieve the desired quantity and quality. Cambridge Healthtech Institute's 11th Annual Engineering Genes, Vectors, Constructs, and Clones conference continues the tradition of applying effective engineering strategies for protein expression and production research leading to functional biotherapeutic products. Learn from seasoned, savvy researchers as they share their real-world experiences, applications and results.

SUNDAY, JANUARY 13

4:00 - 6:00 pm Pre-Conference Registration

MONDAY, JANUARY 14

7:00 am Registration and Morning Coffee

SYSTEMS BIOLOGY: ELUCIDATING THE CONNECTIONS

9:00 Welcome by Conference Organizer
Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks
Simpson Joseph, PhD, Professor, Department of Chemistry & Biochemistry, University of California, San Diego

KEYNOTE PRESENTATION

9:10 COBRAme: A Computational Framework for Genome-Scale Models of Metabolism and Gene Expression
Bernhard Palsson, PhD, Galletti Professor, Bioengineering; Principal Investigator, Systems Biology Research Group, Bioengineering; Professor, Pediatrics, University of California, San Diego

9:50 Using Systems Approaches to Improve Protein Production in Mammalian Cell with Targeted Engineering
Nathan E. Lewis, PhD, Assistant Professor, Department of Pediatrics, University of California, San Diego
Genomic resources have provided a comprehensive view of all the cell parts in mammalian cells, and systems biology is elucidating how they are all connected. We are now using systems biology modeling and omics data analysis to guide efforts to engineer mammalian cells for protein production.

10:20 Networking Coffee Break

CELL-FREE SYSTEMS

10:45 Integrating Cell-Free Protein Expression and Coarse-Grain Molecular Simulation for Rapid Design-Build-Test-Learn Cycles to Discover the Locational Impact of Site-Specific PEGylation
Bradley C. Bundy, PhD, Associate Professor, Department of Chemical Engineering, Brigham Young University
A cell-free approach to synthetic biology enables direct control of and access to the biological machinery for rapid Build-Test-Learn engineering cycles. The exponentially growing field is beginning to impact the biotherapeutics, biocatalysis, and biosensing industries. This presentation highlights recent advances combining course-grain molecular simulation with cell-free protein expression screening to rapidly determine the optimal location(s) for site-specific PEGylation.

11:15 Energy Consumption in a Cell-Free Expression System
Simpson Joseph, PhD, Professor, Department of Chemistry & Biochemistry, University of California, San Diego
Although much progress has been achieved in the design and synthesis of artificial cells, presently they are far inferior to living cells in robustness, stability and the production of biomaterials. One of the reasons for the poor performance of synthetic cells is due to inefficient energy regeneration in cell-free protein synthesis (CFPS) systems. I discuss methods to enhance energy regeneration in a cell-free expression system.

11:45 A Cell-Free Protein Synthesis Platform for Robust Epitope Screening and Novel Vaccine Development
John Dresios, PhD, Senior Biology Director, Chief Scientist and Leidos Technical Fellow, Advanced Solutions Group, Leidos
Expression of antigenic peptides for vaccine screening is challenging due to the poor and/or variable expression of predicted epitopes. In this respect, the value of a screen is minimized if only a small fraction of the epitopes is expressed, or if the expressed peptides are produced at dramatically different levels. Here we describe a cell-free platform for high-yield, balanced peptide expression that enables rapid epitope screening and multi-epitope vaccine development.

12:15 pm Productivity through Diversity - a Protein Production Toolbox to UNLOCK PICHIA *Sponsored by VTU technology*
Iskandar Dib, PhD, Principal Scientist, Process Development & Analytics, VTU Technology GmbH

12:45 Session Break

12:55 Luncheon Presentation to be Announced *Sponsored by ATUM*

1:25 Luncheon Presentation II *(Sponsorship Opportunity Available)*

TOOLS FOR ENHANCING EXPRESSION: CODONS, CONSTRUCTS, AND CLONES

2:00 Chairperson's Remarks
Chao-Guang Chen, PhD, Senior Scientist, Research Department, CSL Limited

2:05 Synonymous Codon Selection to Improve Protein Folding Yield
Patricia L. Clark, PhD, O'Hara Professor of Chemistry & Biochemistry; Concurrent Professor of Chemical & Biomolecular Engineering, University of Notre Dame
We have developed a sensitive system to detect effects of synonymous codon substitutions on the co-translational folding of proteins expressed in *E. coli*, coupling the success of folding to *E. coli* fitness. We find that position-specific synonymous codon changes can have dramatic effects on folding yield, particularly at those positions that correspond to sub-domain "motif" structures.

2:35 Translational Attenuation Strategies to Improve Soluble Yields in Bacterial Expression Systems
Christopher H. Gray, PhD, Staff Scientist & Team Leader (Structural Biology), Drug Discovery Program, CRUK Beatson Institute
High levels of protein expression in *Eschericha coli* frequently produce inclusion bodies. Alleviating strategies, modulating transcription or folding, are often modestly successful. We have enhanced soluble expression by manipulating translation, slowing the processing of target transcripts by regulating ribosome binding or by incorporating rare codons at strategic positions within the cDNA. This specific attenuation of translation results in greater soluble yields and offers a novel strategy to enhance production.

3:05 Find Your Table and Meet Your BuzZ Session Moderator

3:15 BuzZ Sessions with Refreshments
Join your peers and colleagues for interactive roundtable discussions.
See page 11 for details.

4:30 High-Throughput Antibody Construct Generation and Expression
Chao-Guang Chen, PhD, Senior Scientist, Research Department, CSL Limited
Antibody construct generation, also referred to as IgG reformatting, is a key step in antibody-display phage library screening. Following library screening, positive Fab expression constructs must be converted into IgG format before they can be expressed as soluble antibodies for further testing and characterization. An efficient strategy for high-throughput antibody construct generation and expression that solves many of the technical challenges associated with IgG reformatting will be presented.

5:00 Rapid Construction of Recombinant Plasmids by QuickStep-Cloning
Tuck Seng Wong, PhD, Senior Lecturer, Chemical and Biological Engineering, University of Sheffield
Molecular cloning is an essential step in biological engineering. Megaprimer-based PCR of a whole plasmid is a widely used method. However, linear amplification, use of self-annealing megaprimers and difficulty of performing point insertion of DNA are some of its limitations. QuickStep-Cloning overcomes these problems yet retains the simplicity of whole-plasmid amplification. It utilizes asymmetric PCRs to create a megaprimer pair with 3'-overhangs, and hence, facilitates the subsequent exponential whole-plasmid amplification.

5:30 Sponsored Presentation *(Opportunity Available)*

6:00 - 7:15 Welcome Reception in the Exhibit Hall with Poster Viewing *Sponsored by proteinsimple*

7:15 Close of Day

TUESDAY, JANUARY 15

8:00 am Registration and Morning Coffee

NOVEL TOOLS ARE ENHANCING PRODUCTION

8:30 Chairperson's Remarks
Mark Welch, PhD, Vice President, Research and Development, ATUM

8:35 Titer Estimation for Quality Control (TEQC) Method: A Practical Approach for Optimal Production of Protein Complexes Using the Baculovirus Expression Vector System
Yuichiro Takagi, PhD, Associate Professor, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine
The baculovirus expression vector system (BEVS) is becoming the method of choice for expression of many eukaryotic proteins and protein complexes. However, what influences the overall production of proteins or protein complexes remains largely unclear. We developed the Titer Estimation for Quality Control (TEQC) method, which enables researchers to quantitatively optimize protein expressions utilizing BEVS in a highly reproducible fashion.

9:05 *De novo* DNA Synthesis Using Enzymes
Sebastian Palluk, MSc, CTO, Ansa Biotechnologies
DNA synthesis, the ability to "write" DNA, is a foundational technology in life sciences research and engineering. Currently, all synthetic DNA is made using organic chemistry via a method that has remained unchanged for 35 years and has approached a plateau. This talk describes current efforts in the field of enzymatic DNA synthesis and presents a novel DNA synthesis technology that is based on polymerase-nucleotide conjugates.

9:35 Sponsored Presentation *(Opportunity Available)*

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 Genetic Engineering Process Optimization in CHO Cells
Stephanie L. Sandefur, MSc, Consultant Biologist, Bioprocess Research & Development, Eli Lilly and Company
Over the past decade, considerable progress has been made in improving the effectiveness and efficiency

of generating highly productive recombinant CHO cell lines. While these efforts have been primarily centered on driving cell culture productivity, more recently, focus has turned to approaches to impact product quality. This presentation describes potential approaches to maximizing the effectiveness of host cell engineering and reducing the time to successfully impact biotherapeutic product quality profiles.

11:30 A Multi-Landing Pad DNA Integration Platform for Mammalian Cell Engineering
Liliana Wroblewska, PhD, Principal Scientist, Biomedicine Design, Pfizer
Reliable, large-scale engineering of CHO cells through precise insertion of large amounts of heterologous DNA into well-characterized genomic loci would have broad applications for mammalian synthetic biology, recombinant protein production, and biomanufacturing. Using multi-gene payload vectors, cell lines with multiple landing pads, and recombinase technology, we demonstrated controlled integration of up to nine copies of a monoclonal antibody (about 100 kb of heterologous DNA), and a corresponding linear increase in antibody expression.

12:00 pm Talk Title to be Announced
Pierre-Alain Girod, PhD, CSO, Selexis SA
Sponsored by SELEXIS

12:30 Session Break

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Close of Engineering Genes, Vectors, Constructs, and Clones Conference

TUESDAY-WEDNESDAY, JANUARY 15-16 | INAUGURAL

ADVANCES IN VECTOR PRODUCTION AND SCALE-UP FOR CELL AND GENE THERAPY

Enabling Vector Design, Expression, Development to Meet Commercial Scale Production Demands

TWO AUTOLOGOUS CAR T therapies are now on the market, but how will companies manufacture these product at the commercial scale? What technologies and production processes are needed to meet the commercial scale demand? Cambridge Healthtech Institute's Inaugural Advances in Vector Production and Scale-Up for Cell and Gene Therapy conference will bring together leading scientists from biopharmaceutical industry, academia and government to discuss and showcase innovation in design and engineering of vectors and strategies to overcome production challenges for cell and gene therapy products.

TUESDAY, JANUARY 15

1:00 pm Registration

1:30 Refreshment Break in the Exhibit Hall with Poster Viewing

TRENDS, CHALLENGES AND OPPORTUNITIES

2:00 Chairperson's Opening Remarks
Sandro Matosevic, PhD, Assistant Professor, Department of Industrial and Physical Pharmacy, Purdue University

KEYNOTE PRESENTATION

2:05 Current Trends, Opportunities and Challenges of Gene Therapy Development and Manufacturing
Palani Palaniappan, PhD, Head, Technical Operations & Andover Site, Sarepta Therapeutics
The keynote will review current status of gene therapy CMC and manufacturing with a view towards future and share Sarepta's vision in this area. Progress in manufacturing area to align with clinical progression of the pipeline will be highlighted.

2:45 Strategies and Advances in Lentiviral Vector Manufacturing and Scale-Up
Bo Kara, Head, Process Development, Cell & Gene Therapy Platform CMC, GSK
In this presentation, we will discuss strategies and advances in lentiviral vector manufacturing and scale-up such as transient vs. stable cell line approaches, development and optimization of upstream and downstream scalable unit operations, improving process robustness and cost of goods.

3:15 Sponsored Presentation *(Opportunity Available)*

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

OPPORTUNITIES FOR INNOVATION IN PRODUCTION PROCESSES

4:30 Optimizing Sf9-Based Stable Cell Lines for the Production of Highly Infectious rAAV Vectors
Sergei Zolotukhin, PhD, Professor, Department of Pediatrics, College of Medicine, University of Florida
We describe a new insect cell-based production platform utilizing attenuated Kozak sequence and a leaky ribosome scanning to achieve a serotype-specific modulation of AAV capsid proteins stoichiometry. By way of example, rAAV5 and rAAV9 were produced and comprehensively characterized side by side with HEK293-derived vectors. The data will be presented demonstrating a superior infectivity and higher genetic identity of OneBac-derived rAAV vectors providing a scalable platform for good manufacturing practice (GMP)-grade vector production.

5:00 LVV Production Process: Recent Advances and Opportunities for Innovation
Yogesh Waghmare, PhD, Associate Director, Vector Downstream Process Development, Bluebird Bio
LentiViral Vector (LVV)-based Cell and Gene Therapy products are steadily increasing in number. Industrial production of LVV poses significant challenges compared to AAV due to the large size, complexity, and labile nature of LVV. An overview of industrial LVV production process evolution, recent technological advances, and LVV specific challenges will be presented.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

5:45 - 8:45 Dinner Short Courses*
See page 8 for details.
**Separate registration required*

WEDNESDAY, JANUARY 16

7:45 am Registration and Morning Coffee

VECTOR DESIGN, DEVELOPMENT AND CHARACTERIZATION FOR LARGE-SCALE PRODUCTION

8:15 Chairperson's Remarks
Junghae Suh, PhD, Associate Professor, Bioengineering, Rice University

8:20 Synthetic Virology Approaches to Designing AAV Vectors
Junghae Suh, PhD, Associate Professor, Bioengineering, Rice University
Adeno-associated virus (AAV)-based gene delivery vectors are some of the most promising in the gene therapy field today. To make viral gene delivery a more predictable process, we must obtain control over the naturally encoded biomolecular programs already embedded in the AAV capsids. I will discuss my lab's work on rewriting the details of what cues can be accepted as input and what functional outputs can be produced by AAV.

8:50 Vector Development and Large-Scale Manufacturing
Jacek Lubelski, PhD, Vice President, Global Pharmaceutical Development, uniQure

9:20 Sponsored Presentation *(Opportunity Available)*

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

10:35 Scaling Adherent Manufacturing Systems for the Production of AAV Vectors
John Huynh, PhD, Senior Director, Manufacturing Science & Technology, Gene Therapy Program, University of Pennsylvania
Adherent cell culture is traditionally thought of as non-scalable; however, recent advances in fixed-bed bioreactor technology may address current challenges with scaling adherent production systems. Here, we describe the development of an AAV production process using the iCELLis bioreactor.

11:05 Analytical Development and Challenges to Characterize AAV Vector
Christine LeBec, PhD, Head of Analytical Development, Genethon

11:35 PANEL DISCUSSION: Challenges and Opportunities in Viral and Non- Viral Vector Development and Production
- New vectors
- Closing the production gap
- New production technologies
- Vector characterization

Moderator:
Sandro Matosevic, PhD, Assistant Professor, Department of Industrial and Physical Pharmacy, Purdue University
Panelists:
Bo Kara, Head Process Development, Cell & Gene Therapy Platform CMC, GSK
Palani Palaniappan, PhD, Head, Tech Ops & Andover Site, Sarepta Therapeutics
Jacek Lubelski, PhD, Vice President, Global Pharmaceutical Development, uniQure
John Huynh, PhD, Senior Director, Manufacturing Science & Technology, Gene Therapy Program, University of Pennsylvania

12:05 pm Session Break

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

1:15 Session Break

2:00 PLENARY KEYNOTE PANEL
See page 5 for details.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

DELIVERY AND THERAPY SPECIFIC CHALLENGES

4:00 Chairperson's Remarks
Yogesh Waghmare, PhD, Associate Director, Vector Downstream Process Development, Bluebird Bio

4:05 Non-Viral Immunometabolic Reprogramming of Natural Killer Cells for Immunotherapies of Solid Tumors
Sandro Matosevic, PhD, Assistant Professor, Department of Industrial and Physical Pharmacy, Purdue University
The anti-tumor immunity of natural killer (NK) cells is highly impaired due to immunometabolic suppression in the microenvironment of solid tumors. For that reason, reprogramming these cells is a therapeutic necessity to enhance their effector function. Here, we discuss the genetic reprogramming of NK cells using non-viral approaches, including recent work focused on imparting new functionality upon NK cells targeting immunometabolism and immune evasion by cancer cells.

4:35 Strategies to Optimize Lentiviral and Retroviral Transduction of NK and T Cells for Adoptive Immunotherapy
Evren Alici, MD, PhD, Assistant Professor of Hematology, Karolinska Institutet, Department of Medicine, Stockholm, Sweden
In order to manufacture more efficient NK cell therapy products, it is essential to develop novel strategies such as genetic modification of NK cells. The introduction of either activating or chimeric antigen receptors customized for NK cells presents an attractive prospect for further clinical applications. Although NK cells are inherently resistant to retroviral and lentiviral transductions, recently, our group has significantly enhanced retroviral and lentiviral gene delivery to NK cells through enhanced proliferation and targeting intracellular viral defense mechanism by small molecule inhibitors.

5:05 Scalable Production of rAAV Vector for Gene Therapy Applications
Pranav Joshi, M. Tech, PhD Candidate, Bioengineering, McGill University
Adeno-Associated Virus (AAV)-based recombinant vectors are conclusively the most successful class of vectors for *in vivo* somatic cell gene delivery. Despite numerous advancements in production protocols, production of AAV to meet exceptionally high demand (1016-1017 VGs) in late clinical stages and eventually systemic delivery poses critical challenges. The insect-cell baculovirus system, a well-established platform for scalable production of vaccines and recombinant protein, is emerging for scalable manufacturing of clinical grade rAAVs.

5:35 Breakout Discussions
Join the moderated discussions to share ideas, gain insights, establish collaborations, or commiserate about persistent challenges. Then continue the discussion as you head into the lively Exhibit Hall.

6:05 - 7:00 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Advances in Vector Production and Scale-Up for Cell and Gene Therapy Conference

THURSDAY-FRIDAY, JANUARY 17-18 | 3RD ANNUAL

MICROBIAL PRODUCTION

Optimizing the Expression and Production of Microbial Expressed Proteins

MICROBIAL-BASED EXPRESSION SYSTEMS offer significant advantages over other hosts by offering faster development times, greater yields, and lower production costs, particularly in *E. coli*. However, limitations around expression, glycosylation and central metabolic pathways poses significant challenges. Cambridge Healthtech Institute's 3rd Annual Microbial Production conference examines the latest developments in microbial-based production – from strain development to metabolic engineering, assembly to scale-up, process development to analytics. Particular focus is with particular focus on the role of *E. coli* for biotherapeutics, novel products and other industrial applications.

THURSDAY, JANUARY 17

7:45 am Registration and Morning Coffee

MICROBIAL EXPRESSION OF BIOTHERAPEUTICS

8:10 Organizer's Welcome Remarks
Daniel Barry, Senior Conference Director, Cambridge Healthtech Institute

8:15 Chairperson's Opening Remarks
Danielle Tullman-Ercek, PhD, Associate Professor, Department of Chemical and Biological Engineering, Northwestern University

KEYNOTE PRESENTATION

8:20 Bacterial Cell-Based and Cell-Free Systems for Biosynthesis of Complex Glycans and Glycoconjugates
Matthew P. DeLisa, PhD, William L. Lewis Professor, Chemical & Biomolecular Engineering, Cornell University
Our group has harnessed natural biological pathways and engineered synthetic designer pathways in bacteria for making complex glycans and conjugating these to lipids and proteins. In this talk, I will discuss how these efforts have resulted in the transformation of bacteria and their cell-free extracts into robust platforms for scalable, bottom-up production of complex glycoconjugates by design.

9:00 Shaping *Escherichia coli* for Recombinant Protein Production
Jan-Willem de Gier, PhD, Associate Professor, Department of Biochemistry and Biophysics, Stockholm University
My laboratory has been using both evolutionary and engineering approaches to shape *E. coli* for the production of recombinant proteins. In my talk, I will focus on how we have been engineering *E. coli* for the production of recombinant proteins in the periplasm as well as the development of vaccines.

9:30 Presentation to be Announced
Sponsored by WACKER

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

HOST ENGINEERING AND STRAIN DEVELOPMENT IN *E. COLI*

11:00 Parallel Approach to Membrane Protein Production
Jonas Lee, PhD, Scientist, Amgen
Membrane proteins are vital therapeutic targets. Despite this, production of these critical reagents relies mostly on reproducing published results in painstaking ways. We developed an efficient systematic approach to screen multiple expression systems and different protein formulation to efficiently produce membrane protein reagents.

11:30 Optimizing Expression of an Antibody Fab Fragment in *Escherichia coli* with Non-Native Amino Acid (NNAA) Incorporated by Plasmid and Strain Engineering
Harun Rashid, PhD, Senior Principal Scientist, Molecular Technology, Ambrx
In this study, expression of a 'difficult-to-express' antibody Fab fragment with a NNAA inserted was systematically optimized by expression vector & strain engineering. Among the various genetic elements on expression vector tested, only the DNA coding sequence, periplasmic chaperone, Fab heavy chain (HC) carboxy-terminal extension and the presence of partition locus parB were beneficial. These four components were then put together into a single expression vector that resulted in significant improvement in Fab titer over the starting strain.

12:00 pm Session Break

12:10 Luncheon Presentation: Leveraging Platform Approaches and High-Throughput Tools to Expedite Process Development in a Multi-Product Microbial Manufacturing Environment
Sponsored by FUJIFILM Diosynth Biotechnologies
Nigel Shipston, PhD, Director, Program Design, FUJIFILM Diosynth Biotechnologies

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

2:15 Chairperson's Remarks
Nigel Shipston, PhD, Director of Program Design, FUJIFILM Diosynth Biotechnologies

2:20 Robust Protein Production and Secretion in Bacteria via the Type III Secretion System
Danielle Tullman-Ercek, PhD, Associate Professor, Department of Chemical and Biological Engineering, Northwestern University
Bacteria are receiving renewed interest as protein production hosts because of their fast growth and tractability. The Salmonella enterica Type III Secretion System secretes non-native proteins at product titers of up to 400 mg/L in rich media, but is highly sensitive to environmental and growth conditions and therefore not robust. To make this system commercially relevant, we optimized media components and bioreactor conditions and engineered the strain.

2:50 Development of a Scalable Platform for Protease Triggered Immuno-Oncologic Activators
Ulrich Ernst, PhD, COO and Senior Vice President, Technical Operations at Amunix
The design of ProTIA molecules represents a technical enhancement of bispecific scFv therapeutic formats, with the benefits of significantly improved circulatory half-life, enhanced tumor-targeting and safety profiles. To enable clinical application of its pipeline of ProTIA therapeutics, Amunix has applied its extensive experience with XTENylation of proteins, thus, yielding a scalable, platform process for efficient production of these new therapeutic compounds.

3:20 Sponsored Presentation *(Opportunity Available)*

3:35 Networking Refreshment Break

4:00 *E. coli* Glycosylation Platform for Producing Bioconjugate Vaccines
Christian Lizak, PhD, Group Leader Biochemistry, Research Department, LimmaTech Biologics AG
The discovery of an N-linked protein glycosylation system in Campylobacter jejuni allowed its reconstitution in *Escherichia coli*. LimmaTech Biologics exploits this system to generate bioconjugate vaccines containing surface glycan structures of pathogenic bacteria. This innovative approach simplifies the production of conjugate vaccines substantially and has been used to generate multivalent bioconjugates against pathogens like Shigella, Streptococcus, *E. coli* and Staphylococcus, some of which have been successfully tested in clinical studies.

4:30 Glycoengineering Next Generation Conjugate Vaccines with Novel Oligosaccharyltransferases
Christian Harding, PhD, CSO, VaxNewMo
Glyco-conjugate vaccines, consisting of a polysaccharide attached to a carrier protein, are excellent immunogens manufactured using labor-intensive chemical crosslinking steps. As an innovative alternative, VaxNewMo utilizes a glycoengineering strategy to generate "bioconjugates" in *Escherichia coli*. Key to this process is a conjugating enzyme, which attaches a polysaccharide to a protein.

5:00 Bryotechnology: High Quality Complex Proteins from Moss-Based Expression
Andreas Schaaf, PhD, CSO, Greenovation
BryoTechnology, i.e., moss-based production of biopharmaceuticals, has evolved into a GMP manufacturing technology with products already in clinical development. Whilst leveraging the mosses advantages, comparability to mammalian cell-based technologies was a priority in process development. Today's moss process relies on latest single use technologies and follows the established routines of mammalian cell-based production. Thus, moss-based production fits easily into existing cleanroom environments and offers rapid changeover and flexible configuration.

5:30 Close of Day

FRIDAY, JANUARY 18

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast
Protein therapeutics is a fast-growing global market. As the science improves, so does the complexity of the R&D organization. Ensuring product quality plus speed to market requires insights from stakeholders working across the stages of protein science R&D. Join experts representing this PepTalk pipeline, peers, and colleagues for an interactive roundtable discussion. Topics include highlights from the week's presentations, new technologies and strategies, challenges, and future trends.
Moderator: Suresh Kumar Thallapuranam, PhD, Professor, Department of Chemistry & Biochemistry, University of Arkansas

BIOPROCESSING OF MICROBIAL-BASED PRODUCTS

9:00 Chairperson's Remarks
Suresh Kumar Thallapuranam, PhD, Professor, Department of Chemistry & Biochemistry, University of Arkansas

9:05 Integrated Process Development: Overcoming Developability Challenges
Georg Klima, Dipl. Ing., Executive Director, Process Science, Boehringer Ingelheim RCV GmbH & Co. KG
Novel biotherapeutic formats pose unique development challenges. Strategies for successful development need to holistically consider all aspects of biopharmaceutical processes such as expression strategies, novel unit operations, automated high-throughput process development, as well as scale-up and transfer from bench to large-scale manufacturing. We present our holistic approach based on a HTPD toolbox to lever the complexity of manufacturing development for non-platform biotherapeutics. Integration of the whole process is also discussed.

9:35 Novel Affinity Tags for Large Scale Production and Purification of Recombinant Proteins
Suresh Kumar Thallapuranam, PhD, Professor, Department of Chemistry & Biochemistry, University of Arkansas

SYNTHETIC BIOLOGY AND CELL-FREE SYSTEMS

10:05 A Semi-Synthetic Organism That Stores and Retrieves Increased Genetic Information
Floyd Romesberg, PhD, Professor, Chemistry, The Scripps Research Institute
We have examined a large number of different unnatural nucleotides bearing mainly hydrophobic nucleobase analogs that pair based on packing and hydrophobic interactions rather than H-bonding. More recently, we have engineered *E. coli* to import the requisite unnatural triphosphates and shown that DNA containing the unnatural base pair is efficiently replicated, transcribed, and translated within the cell, resulting in the first semi-synthetic organism that stores and retreives increased information.

10:35 Networking Coffee Break

11:00 Building a Cell-Free RNA Production Platform
Himanshu Dhamankar, PhD, Senior Scientist, Pathway & Process Development, GreenLight Biosciences Inc.
Availability of low-cost RNA products can unlock numerous applications spanning the agricultural and biopharmaceutical spaces. GreenLight Biosciences has developed a scalable and cost-effective RNA production platform that employs a proprietary one-pot cell-free reaction to synthesize nucleotide triphosphates from an inexpensive nucleotide source, that are then polymerized into desired RNA products via transcription from an engineered DNA template. The presentation will feature building of the platform and on-going efforts towards improvements.

11:30 Rapid and Scalable Characterization of CRISPR Technologies Using an *E. coli* Cell-Free Transcription-Translation System
Vincent Noireaux, PhD, Associate Professor, Synthetic Biology, Biological Physics, University of Minnesota
CRISPR-Cas systems offer versatile technologies for genome engineering, yet their implementation has been outpaced by ongoing discoveries of new Cas nucleases and anti-CRISPR proteins. Here, we present the use of *E. coli* cell-free transcription-translation (TXTL) systems to vastly improve the speed and scalability of CRISPR characterization and validation. TXTL can express active CRISPR machinery from added plasmids and linear DNA, and TXTL can output quantitative dynamics of DNA cleavage and gene repression – all without protein purification or live cells.

12:00 pm Conference Wrap-Up
Suresh Kumar Thallapuranam, PhD, Professor, Department of Chemistry & Biochemistry, University of Arkansas

12:30 Close of Conference

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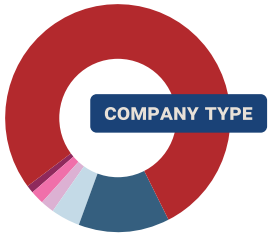

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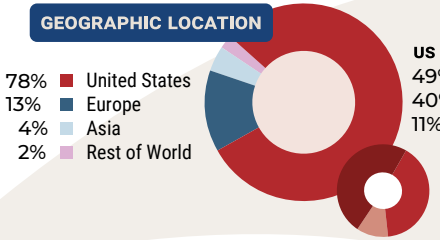

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Early Registration until October 19	$2,599	$1,299
Advance Registration until November 16	$2,799	$1,399
Registration after November 16	$3,049	$1,499

BASIC PACKAGE *(Includes access to 1 conference and/or Training Seminar. Excludes Short Courses.)*

Early Bird Registration until September 7	$1,549	$799
Early Registration until October 19	$1,749	$899
Advance Registration until November 16	$1,899	$949
Registration after November 16	$2,099	$1,099

CONFERENCE DISCOUNTS

Poster Submission - Discount ($50 Off): Poster abstracts are due by November 16. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact jring@healthtech.com. *CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

Sponsoring Organization Discounts: CHI is pleased to offer our partnering organization members a 20% discount to attend. Please see the online registration page for details and offers.

REGISTER 3 - 4th IS FREE: Individuals must register for the same conference or conference combination and submit completed registration form together for discount to apply.

Alumni Discount: SAVE 20%: CHI appreciates your participation at our events. As a result of the great loyalty you have shown us, we are pleased to extend to you the exclusive opportunity to save an additional 20% off the registration rate.

Group Discounts: Discounts are available for multiple attendees from the same organization. For more information on group rates contact David Cunningham at +1-781-972-5472.

**Alumni, Antibody Society, Twitter, LinkedIN, Facebook or any other promotional discounts cannot be combined. Discounts not applicable on event Short Courses.*

If you are unable to attend but would like to purchase the PepTalk CD for $750 (plus shipping), please visit CHI-PepTalk.com. Massachusetts delivery will include sales tax.

ADDITIONAL REGISTRATION DETAILS
Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link.
Handicapped Equal Access: In accordance with the ADA, Cambridge Healthtech Institute is pleased to arrange special accommodations for attendees with special needs. All requests for such assistance must be submitted in writing to CHI at least 30 days prior to the start of the meeting.
To view our Substitutions/Cancellations Policy, go to healthtech.com/regdetails
Video and or audio recording of any kind is prohibited onsite at all CHI events.

How to Register: **CHI-PepTalk.com**
reg@healthtech.com • P: 781.972.5400 or Toll-free in the U.S. 888.999.6288

Please use keycode **PTK EF** when registering!