PROTEIN ENGINEERING & DEVELOPMENT

- Recombinant Protein Therapeutics
- Enhancing Antibody Binding and Specificity
- Emerging Technologies for Antibody Discovery

ANTIBODY THERAPEUTICS

- Engineering Next-Generation Cancer Immunotherapies
- Antibody-Drug Conjugates
- Bispecific Antibody Therapeutics

FORMULATION & STABILITY

- Optimizing Biologics Formulation Development
- Lyophilization and Emerging Drying Technologies
- Protein Aggregation and Emerging Analytical Tools

BIOTHERAPEUTIC EXPRESSION & PRODUCTION

- Engineering Genes and Hosts
- Recombinant Protein Expression and Production
- CHO Cell Lines
- Optimizing Expression Platforms

ANALYTICS & IMPURITIES

- Characterization of Biotherapeutics
- Detection and Characterization of Particulates and Impurities
- Extractables and Leachables
- Bioprocess Analytics

PROCESS TECHNOLOGIES & PURIFICATION

- Single-Use Technologies and Continuous Processing
- Protein Purification and Recovery
- Higher-Throughput Protein Production and Characterization

ALTERNATIVE EXPRESSION & PRODUCTION

- Biocatalysis and Bio-Based Chemical Production
- Plant-Based Expression and Synthetic Biology
- Microbial Production

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16th Annual

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THE PROTEIN SCIENCE WEEK

January 9-13, 2017

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PepTalk: The Protein Science Week is one of the largest annual gatherings of protein science researchers in the world. In its 16th year, PepTalk attracts over 1,300 experts from academia, biotech and pharma who come together for one week of intensive learning and networking to discover new opportunities and promising partnerships.

This event covers a wide spectrum, from upstream protein R&D science to downstream biologics. And, whether you're a world-renowned researcher or a current graduate student, PepTalk has something to offer:

Conference Programs feature keynote presentations, case studies and new unpublished data from top influential leaders in academia and industry.

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 particular discipline or a helpful refresher for those who want to brush up on their knowledge or expand their horizons.

Training Seminars (1.5 days) offer an even deeper exploration of a specific topic and allow you to enhance your knowledge and gain insight and perspective.

Student Fellowships grant those entering the industry an opportunity to present their latest research and receive critical feedback for development and collaboration.

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

CONFERENCE AT-A-GLANCE

	SUNDAY	PART A: MONDAY	PART A: TUESDAY AM	PART B: TUESDAY PM	PART B: WEDNESDAY	PART C: THURSDAY	PART C: FRIDAY
Protein Engineering & Development	PRE-CONFERENCE DINNER SHORT COURSES*	Recombinant Protein Therapeutics		Enhancing Antibody Binding and Specificity		Emerging Technologies for Antibody Discovery	
Antibody Therapeutics		Engineering Next-Generation Cancer Immunotherapies		Antibody-Drug Conjugates		Bispecific Antibody Therapeutics	
Formulation & Stability		Optimizing Biologics Formulation Development		Lyophilization and Emerging Drying Technologies		Protein Aggregation and Emerging Analytical Tools	
Biotherapeutic Expression & Production		Engineering Genes and Hosts		Recombinant Protein Expression and Production		Optimizing Expression Platforms	
Analytics & Impurities		Characterization of Biotherapeutics		Detection and Characterization of Particulates and Impurities		Bioprocess Analytics	
Process Technologies & Purification		Single-Use Technologies and Continuous Processing		Protein Purification and Recovery		Higher-Throughput Protein Production and Characterization	
Alternative Expression & Production		Biocatalysis and Bio-Based Chemical Production		Plant-Based Expression and Synthetic Biology		Microbial Production	
Cambridge Healthtech Training SEMINARS		Introduction to Bioprocessing		Introduction to Biologics Formulation and Delivery			
		Introduction to Antibody Engineering		Immunology for Drug Discovery Scientists			
		Regulatory Requirements					
Short Courses*				Dinner Short Courses*			

CHO Cell Lines

* *Separate Registration Required for Short Courses*

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PRESENT YOUR RESEARCH POSTER AT PEPTALK!

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions.

POSTER PAVILION

FRIDAY, JANUARY 13, 10:05 AM

PepTalk is proud to support and recognize the protein scientists of tomorrow during the Poster Pavilion. This time has been set aside to view the Student Fellowship posters and interact with presenters one on one.

This opportunity gives job seekers the chance to share their expertise with future/potential employers or develop contacts to further their research.

Reasons you should present your research poster at this conference:

- 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 into our poster competition

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 18, 2016.

Register online, or by phone, fax or mail. Please indicate that you would like to present a poster. Once your registration has been fully processed, we will send an email with a unique link and instructions for submitting your abstract using our online abstract submission tool.

2017 STUDENT FELLOWSHIP PROGRAM

Full-time graduate students and Ph.D. candidates are encouraged to apply for the PepTalk: The Protein Science Week Student Fellowship. Applications are due by October 14, 2016.

- Interested students must complete the application for the 2017 Student Fellowship.
- Fellows are required to present a scientific poster. A poster title and abstract are due at the time of the application.
- All applications will be reviewed by the scientific review committee and the accepted students will be notified by October 28, 2016 if they were accepted for the 2017 Student Fellowship.
- Accepted 2017 Student Fellows will receive a discounted conference registration rate of $295*, which must be paid in full by November 18, 2016. (Payment is requested at the time of the application but will not be charged until the application is approved.)
- This fellowship is limited to 20 students and is for the Premium Conference Package only (January 9-13, 2017). Excludes Short Courses.
- All accepted 2017 Student Fellows will be asked to help promote the conference onsite, at their college, and throughout their social media networks.
- Students not accepted for the 2017 Student Fellowship can register at a discounted rate of $595*, and will not be required to present a poster.
- Student Fellows will be entered into the Conference's Poster Competition featuring cash prizes. All poster presenters are eligible to win.
- **ADDED BONUS!** In addition to the main poster viewing times, there will be a special FELLOW ONLY POSTER VIEWING on Friday morning.

** This discounted Fellow rate cannot be combined with any other discounts for this event. Your discounted registration does not grant access to any of the short courses or pre-conference events. It also does not include hotel, travel or meals.*

IT'S A WRAP:

PEPTALK 2017 CLOSING PLENARY PANEL DISCUSSION

FRIDAY, JANUARY 13, 12:00 PM Protein therapeutics is one of the fastest-growing global markets, driven by increasing adoption of protein over non-protein drugs, growing funding for protein engineering and reduced drug discovery timelines and costs. As the science improves, so does the complexity of the R&D organization: it really does "take a village" to bring next-generation therapies to market and patients who need them. Ensuring product quality plus speed to market requires collective insights from experts working across the stages of protein science R&D – as embodied by panelists representing each PepTalk Pipeline topic.

Join peers and colleagues for an interactive panel discussion and a recap of the week. Our industry experts share presentation highlights, key findings, perspective and future trends.

They discuss:
- Highlights from the week's presentations
- What's next for protein therapeutics?
- How to prepare for and solve these challenges

Moderator:

George O. Badescu, Ph.D.,
Senior Director, Scientific Affairs, Abzena

Panelists:

Tilman Schlothauer, Ph.D.,
Principal Scientist, Biochemical and Analytical Research, Large Molecule Research, Roche Pharma Research and Early Development (pRED), Roche Innovation Center Penzberg

Julie Q. Hang, Ph.D.,
Senior Scientist, Protein Chemistry, Genentech

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

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

Diane Paskiet, MS,
Senior Director, Global Scientific Affairs, West Pharmaceuticals

Andrew Fosberry, Ph.D.,
Manager, Expression and Fermentation Sciences, GlaxoSmithKline

Julio A. Camarero, Ph.D.,
Associate Professor, Department of Pharmacology and Pharmaceutical Sciences, School of Pharmacy, University of Southern California

ALL PARTICIPANTS ARE WELCOME!

DINNER SHORT COURSES*

■ SUNDAY, JANUARY 8 | 5:00 - 8:00 pm

SC1: Production Challenges for Complex Biologics: Antibody-Drug Conjugates and Fusion Proteins

This course addresses the typical production issues encountered with complex biologics, namely fusion proteins, antibody-drug conjugates and bispecific antibodies. Experts elucidate the structure and nature of these biologics in order to understand and master their properties. Along with exploring manufacturing challenges, the course also reveals how to overcome these challenges with practical insights and advice.

Instructor:
Stefan R. Schmidt, Ph.D., MBA, Vice President, Rentschler Biotechnology
Gang Gary Chen, Ph.D., Head, ADC Technology, Levena BioPharma
Laurent Ducry, Ph.D., Head, Bioconjugates R&D, Lonza Biologics, Inc.

SC2: A Modern Approach to Biologics Formulation Development

This course offers a forum on how to develop sound formulations for biologic drugs. Case studies will be presented to demonstrate how to incorporate QbD concepts to do risk assessment, design multivariate experiments, and assess critical quality attributes including subvisible particle characterization in order to develop robust formulation for bulk drug substance or final drug product in the context of designated container closure systems. This course utilizes real-world examples and interactive discussion.

Instructors:
Kevin Zen, Ph.D., Senior Director, Biologics Development, Allgenesis Biotherapeutics
Danny K. Chou, Pharm.D., Ph.D., President and Founder, Compassion BioSolution; Former Senior Research Scientist, Biologics Development, Gilead Sciences

SC3: A Lean Approach to Lab Management

Most directors of biotherapeutics labs find themselves thrust into these positions with little or no management training. We explore basics of Lean management in a lab setting and focus on a practical, straightforward approach to implementing some Lean techniques. These broad approaches to lab-level project management, optimizing inventory and ordering, and ensuring proper care of equipment apply to various laboratory or administrative settings. Attendees will walk away with tools to begin implementation in their own working environment.

Instructor:
Tracy Cooper, MAcc, Lab Manager, Vanderbilt Antibody and Protein Resource, Vanderbilt Institute for Chemical Biology, Vanderbilt University
Panelists:
Dominic Esposito, Ph.D., Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research, Leidos Biomedical Research, Inc.
Richard Altman, MS, Scientist, Protein Technologies, Amgen

SC4: Transfection Technologies

Transfection is a nonviral method to introduce foreign nucleic acid (DNA or RNA) to living eukaryotic cells and is commonly accomplished by chemical or electrical techniques. Transfection can be used to generate stable cell lines or to produce recombinant material transiently. This course explores the different transfection technologies currently in use. Learn from providers and users as they share what technique to use when to produce the desired product.

Instructor:
Elizabeth Greene, MS, Scientist, Immune Modulation and Biotherapeutics Discovery (IMBD), Boehringer Ingelheim
Additional Instructors to be Announced

SC5: Creating a Next-Generation Vaccine Facility: Merging High-Productivity Technologies for Robust and Cost-Effective Manufacturing

This course will focus on a new holistic approach that integrates tested strategies for cost-efficient manufacturing of vaccines, linking innovations in cell line development, bioreactor design, membrane chromatography and flexible facility design for a 500-fold increase in overall productivity. This next-generation facility merging high-productivity technologies to achieve simplified process architecture, increased robustness and augmented yield can be replicated anywhere to make production in developing countries in need of vaccines a reality.

Instructor:
Renaud Jacquemart, Ph.D., Author, BioProcess International
Additional Instructors to be Announced

SC6: Enzyme Screening, Design and Discovery

The design of catalysts to more efficiently prepare molecules of interest is a defining feature of modern organic chemistry. Despite tremendous advances, there are still challenges that classical approaches have difficulty addressing. This course provides a greater understanding of the latest tools, technologies, strategies driving the screening, discovery, design and development of new chemistries and enzymes in both academia and industry.

Instructors:
David Rozzell, Ph.D., Senior Vice President, Biocatalysis, Provivi, Inc.
Stephane Corgie, Ph.D., CEO and CTO, Zymtronix
Todd K. Hyster, Professor, Department of Chemistry, Princeton University

■ TUESDAY, JANUARY 10 | 5:45 - 8:45 pm

SC7: Ensuring Accelerated and Successful Drug Product Development of Biologics: Integrated Formulation Development, Process and Packaging Design

Suitable biotech drug product design is key to the success of patient treatment. The formulation, manufacturing process and primary packaging are integral components of the drug product. In addition, a focus on management of the interface of drug substance to drug product is essential for efficient and successful development. This short course is designed to discuss strategies on how to approach an appropriate design for a target product profile, formulation, primary packaging and manufacturing process.

Instructor:
Hanns-Christian Mahler, Ph.D., Head, Drug Product Services, Lonza AG

** Separate registration required*

DINNER SHORT COURSES*

SC8: Next-Generation Sequencing of Antibody Libraries: Details on Experimental and Bioinformatic Methods

Next-generation sequencing (NGS) of antibody repertoires provides a quantitative approach to measuring the diversity and distribution of antibody libraries. This course enables researchers on how to design, analyze, and perform antibody NGS studies, which have applications in antibody discovery and engineering. We go over the practical details of antibody NGS (using the Illumina platform) including library construction and quality control, data processing and analysis, and advanced methods for improving accuracy by molecular barcoding and error correction.

Instructor:

Sai Reddy, Ph.D., Assistant Professor, Biosystems Science and Engineering, ETH Zurich

SC9: Troubleshooting and Engineering of Antibody Constructs

Recombinant antibodies vary widely in their biophysical characteristics, from stable monomers to metastable aggregation-prone oligomers. In particular, antibody variable domains differ in their intrinsic thermodynamic stability and may require labor-intensive engineering. It is therefore essential to implement antibody engineering strategies in screening and initial characterization project phases in order to avoid time- and cost-consuming optimization strategies in later development.

Instructors:

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

Christian Kunz, Ph.D., Associate Director, Discovery Alliances & Technologies, MorphoSys AG

SC10: 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, Ph.D., Professor, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire

SC11: Transient Protein Production in Mammalian Cells

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

Instructors:

Richard Altman, MS, Scientist, Protein Technologies, Amgen

Henry C. Chiou, Ph.D., Associate Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific

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

SC12: Post-Translational Modification: Moving Plant-Made Biosimilars to Plant-Made Biobetters

For plant-made biosimilars to succeed, they must be safer, more affordable and more effective than competing and conventional products. This course examines the concepts and technologies needed to increase the PK and PD properties of plant-made pharmaceuticals (PMPs), such as reduced antigenicity/immunogenicity, increasing a PMP's mean residence time (MRT) in human blood, and increased cytotoxicity for monoclonal antibodies. Other topics include gene knockouts and knock-ins as well as genome editing to reduce potential antigenicity/immunogenicity in plant hosts.

Instructor:

Ray Rodriguez, Ph.D., Professor, Molecular & Cellular Biology, University of California, Davis

** Separate registration required*

Cambridge Healthtech Training SEMINARS

Please visit CHI-PepTalk.com to view detailed agendas for each training seminar

MONDAY, JANUARY 9 - TUESDAY, JANUARY 10, 2017

DAY 1 9:00 AM - 5:30 PM | DAY 2 8:30 AM - 12:30 PM

TS1: 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. The class is directed to attendees working in any aspect of industry, including scientific, technical, business, marketing or support functions, who would benefit from a detailed overview of this field.

Instructors:

Sheila G. Magil, Ph.D., Senior Consultant, BioProcess Technology Consultants, Inc.

Frank J. Riske, Ph.D., Senior Consultant, BioProcess Technology Consultants, Inc.

TS2: 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 ample opportunities to discuss technology with instructors.

Instructors:

Andrew M. Bradbury, Ph.D., MB, BS, Staff Scientist, Biosciences, Los Alamos National Laboratory

James D. Marks, M.D., Ph.D., Chief of Staff, Chief of Anesthesia, San Francisco General Hospital; Professor & Vice Chairman of Anesthesia, University of California, San Francisco

TS3: Regulatory Requirements across the Product Development Lifecycle

The successful development of a pharmaceutical product requires not only good science, but also compliance with FDA regulatory expectations. This seminar will include a comprehensive review of the Chemistry, Manufacturing and Controls (CMC) section of regulatory filings, with a focus on phase appropriate requirements. The level of detail that must be included in the filing will be discussed as well as systems and controls that must be in place in the manufacturing setting. This seminar is intended to provide participants from all facets of the pharmaceutical and biotech industry with a broad understanding of regulatory requirements across the product development lifecycle.

Instructor:
Christina Vessely, Ph.D., Senior Consultant, Biologics Consulting Group

TUESDAY, JANUARY 10 - WEDNESDAY, JANUARY 11, 2017

DAY 1 2:00 PM - 5:30 PM | DAY 2 8:30 AM - 5:30 PM

TS4: Introduction to Biologics Formulation and Delivery

CHI's Introduction to Biologics Formulation and Delivery training seminar focuses on strategies to plan and execute preformulation and formulation development studies for biologics. The seminar begins with an overview of biophysical and biochemical properties of proteins and protein structure, setting the stage for the concepts and goals at the core of protein formulation. The seminar 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, Ph.D., Associate Director, Biopharmaceutical Development, KBI Biopharma, Inc.

TS5: Immunology for Drug Discovery Scientists

To detect the presence of potential pathogens, the immune system must interact with every body system and circulate through every tissue. These unique skills and systemic reach mean that the immune system touches almost every human disease, either causally or as an avenue for therapy. In this seminar, we will explore therapeutic approaches that harness our knowledge of the immune system to treat human disease. From vaccines to cancer (not to mention cancer vaccines!) and diabetes to IBD, we will explore how the immune system can be shaped, engineered, and harnessed by exploring specific examples of current and future therapeutics, and the immunology behind them.

Instructor:
Kevin Bonham, Ph.D., Lecturer, Microbiology and Immunobiology, Harvard Medical School

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.

By combining modular building blocks that can reach targets not accessible to antibodies, Fusion Protein Therapeutics possess advantages over antibody-based therapies. Fusion Proteins' customizable functionality translates into lower patient dosing, reduced production costs, and improved product homogeneity. The Recombinant Protein Therapeutics conference explores the varying constructs and "designs" of fusion protein molecules, and will disclose how these proteins are being engineered to form more efficacious therapeutics that offer specificity with enhanced stability and longer half-life. Experts will present case studies from R&D through clinical data, and will share the results they've achieved.

SUNDAY, JANUARY 8

4:00 - 5:30 pm Registration

5:00 - 8:00 Dinner Short Courses *See pages 6-7 for details*

MONDAY, JANUARY 9

7:30 am Conference Registration and Morning Coffee

INNOVATING PROTEIN THERAPEUTICS

9:00 Welcome by Conference Organizer

Mary Ruberry, Senior Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks

Jennifer R. Cochran, Ph.D., Associate Professor, Bioengineering, Stanford University

KEYNOTE PRESENTATION

9:10 Fusion Protein Strategies for Generation of Biobetters

William R. Strohl, Ph.D., Vice President and Head, BioTherapeutics, Janssen R&D, Pharmaceutical Companies of Johnson & Johnson

The concept of making a "biobetter" biologic is to improve on the salient characteristics of a known biologic having clinical proof-of-concept or marketed product data. There already are several examples of biobetter biologics such as Neulasta®, a PEGylated, longer half-life version of Neupogen®, and Aranesp®, a longer half-life version of Epogen®. This presentation describes the use of protein fusion technologies to make biobetter drugs with more desirable pharmacokinetic profiles.

9:50 Therapeutic Strategies Combining Specificities on the Outside and Inside of Cells

Stefan Dübel, Ph.D., Professor and Head, Biotechnology, Technische Universität Braunschweig

We designed novel fusion proteins providing a cell-specific delivery of an intracellular regulator of immune activation. The E-selectin–specific "Sneaking Ligand" fusion protein inhibited NF- κB by interfering with endothelial IκB kinase 2 activity inside the cells *in vitro* and *in vivo*. The treatment drastically reduced the extravasation of inflammatory cells murine experimental peritonitis and significantly ameliorated the disease course in murine models of rheumatoid arthritis.

10:20 Coffee Break

RECOMBINANT PROTEINS TO HEAL AND FIGHT DISEASE

10:45 IgG Fusion Protein Therapeutics for CNS Treatment of Rare Disorders: Rett Syndrome and Lysosomal Storage Disorders

Ruben J. Boado, Ph.D., Vice President and Co-Founder, ArmaGen, Inc.

Protein therapeutics can be re-engineered as brain-penetrating IgG-fusion proteins for the CNS treatment of rare disorders, like Rett Syndrome and Lysosomal Storage Disorders (LSD). The protein therapeutic domain of the fusion protein exerts the pharmacological effect in the brain once across the BBB. Several brain penetrating enzyme fusion proteins have been engineered for LSD, and potentially for the treatment of Rett Syndrome. First-in-human clinical LSD trials are in progress.

11:15 Blocking IL-17A with Unparalleled Affinity Using an Engineered Affibody-Based Ligand Trap

Joachim Feldwisch, Ph.D., Director, Preclincal Development, Research, Affibody AB

Psoriasis is an IL-17-driven disease. An Affibody®-based ligand trap engineered to block IL-17A with femtomolar affinity will be described. The ligand trap has dual binding specificities and consists of two small Affibody® domains for IL-17A inhibition and an albumin binding domain for half-life extension. Clinical data confirm the expected half-life extension effect of the albumin binding domain and data from the ongoing first-in-human clinical trial will be provided.

11:45 Development of the Pharmacologically Highly Active Endogenous Protein Stathmin-1 to Treat Chronic Wounds

Manfred Schuster, Ph.D., CEO, RMB-Research GmbH

Stathmin-1 is a small, highly conserved protein, which was identified as an intracellular modulator of the eukaryotic cytoskeleton. We overtook development of this pharmacologically potent biologic and have started to investigate its therapeutic potential in a topical formulation to eventually treat chronic, not healing wounds. This presentation highlights our troubleshooting program, which identified and overcame several mistakes from previous development activities, and describes how we will address further clinical issues.

12:15 pm Extending Drug Half-Life to Achieve Monthly Dosing? The Potential of Veltis® Engineered Albumins for Optimized Dosing

Sponsored by Albumedix

Karen Bunting, Ph.D., Science Director, Molecular Biology & Fermentation, Albumedix Ltd.

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

12:45 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

FIGHTING CANCER

2:00 Chairperson's Remarks
Yanzhang Wei, Ph.D., Professor, Biological Sciences, Clemson University

2:05 Bifunctional Major Histocompatibility Class I Antibody Fusions Redirect CD8+ T Cells to Eliminate Tumor Cells *In Vivo*
Hendrik Knoetgen, Ph.D., Program Leader, Targeted Therapeutics, Roche Pharma Research and Early Development, F. Hoffmann-La Roche, Ltd.
Peptide-Major Histocompatibility Class I complexes (MHCI) flag infected cells for their elimination by CD8 T effector cells. Antibody-mediated delivery of recombinant viral peptide-MHCI complexes can mimic a viral infection of target cells and induce cell lysis after recruitment of specific cytotoxic CD8 T cells. Peptide-MHCI-IgG fusion proteins could successfully recruit pre-existing virus-specific CD8 T cells from human donor-derived lymphocytes and effectively trigger eradication of the targeted tumor cells *in vitro* (Schmittnaegel et al., Cancer Immunol Res, 2015). Here, we describe syngeneic surrogate *in vivo* models to address potency of antibody-targeted peptide-MHC class I cancer treatment.

2:35 Bispecific TNFR-Superfamily Agonists for Tumor Localized Immune Modulation
Shane Olwill, Ph.D., Vice President, Development and Head, Immuno-Oncology, Pieris Pharmaceuticals, Inc.
While multiple lines of evidence show that TNFR superfamily members are highly promising therapeutic targets in cancer, mAb-based approaches are not designed to achieve a tumor-target-driven activation of these pathways and may display a limited therapeutic window due to peripheral T cell and / or NK cell activation. To overcome this limitation, Pieris has generated bispecific TNFR-Superfamily Agonists that are only activated when they bind to a specific receptor on a tumor cell.

3:05 Sponsored Presentation *(Opportunity Available)*

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Engineered Ligand and Receptor Based Fusion Proteins as Next-Generation Cancer Therapeutics
Jennifer R. Cochran, Ph.D., Associate Professor, Bioengineering, Stanford University
We use natural ligands and receptors as scaffolds for protein engineering to leverage their inherent biophysical and biochemical properties. I will present our recent data on therapeutic candidates engineered to possess high affinity and unique specificities for applications in oncology.

4:30 Strategies for Improving Current Enzyme-Based Therapy of Acute Lymphoblastic Leukemia: Molecular Engineering and Directed Evolution of Human L-Asparaginases
Manfred Konrad, Ph.D., Research Director, Enzyme Biochemistry, Max Planck Institute for Biophysical Chemistry
The therapeutic effect of the enzyme drug L-asparaginase (L-ASNase) relies on the fact that in cancerous cells of acute lymphoblastic leukemia (ALL) the metabolic enzyme asparagine synthetase is downregulated. We designed *in vitro* evolved human enzymes displaying ASNase activity to identify catalytically improved variants. Furthermore, to increase the serum half-life of the proteins, we loaded L-ASNases into biocompatible microcapsules, thus enhancing serum stability and preventing exposure of the enzyme to the immune system.

5:00 Reshaping the Immunosuppressive Tumor Microenvironment: The Fusion Protein Strategy
Yanzhang Wei, Ph.D., Professor, Biological Sciences, Clemson University
Advanced tumor cells often create immunosuppressive microenvironment. The conversion of the environment from immunosuppressive to immunoactive holds hopes for effective cancer immunotherapy. Fusion proteins coupled with appropriate delivery approaches represent a promising strategy for this conversion. In the last decade, we created various fusion cytokine proteins (GPI-anchored IL-2/IL-12, MULT1E/FasTI, MULT1E/IL-12, IL-12/FasTI) and demonstrated their anticancer activities. We are in the process of developing effective methods to deliver the fusion proteins specifically into tumors.

5:35 BuzZ Session A
Join your peers and colleagues for interactive roundtable discussions.
Please see page 74 for additional information.

6:20-7:30 Welcome Reception in the Exhibit Hall with Poster Viewing

7:30 Close of Day

TUESDAY, JANUARY 10

8:00 am Conference Registration and Morning Coffee

ALBUMIN FUSION PROTEINS

8:30 Chairperson's Remarks
Manfred Konrad, Ph.D., Research Director, Enzyme Biochemistry, Max Planck Institute for Biophysical Chemistry

8:35 FcRn Mediated Intracellular Trafficking and Recycling of Albumin Fusion Protein Therapeutics
Anne Verhagen, Ph.D., Group Leader, Cellular Biochemistry, CSL Limited
Albumin and IgG are abundant plasma proteins with long half-lives owing to an efficient recycling system mediated by the neonatal Fc receptor (FcRn). Fusion to Fc or albumin provides a mechanism for otherwise short-lived proteins to engage with the FcRn recycling system and avoid lysosomal degradation. We have developed novel cellular assays to track the movement of FcRn therapeutic ligands through the early, lysosomal and recycling endosomes.

9:05 Human Serum Albumin Fusion Proteins Function as Therapeutics as Well as Drug Carriers for Synergistic Cancer Treatment

Zhiyu Li, Ph.D., Associate Professor, Pharmaceutical Sciences, Philadelphia College of Pharmacy

HSA and p53-derived peptide fusion protein (rHSA-p53i) induces cytotoxicity irrespective of p53 status in cancer cells. Fatty acid-modified 5-flurouracil and paclitaxel form stable non-covalent complexes with rHSA-p53i. This new formulation co-delivers two or more therapeutics together to one target. Chemotherapeutics cause DNA damage and induce apoptosis, while rHSA-p53i enhances apoptotic responses of cancer cells. The synergistic therapeutic efficacies of this approach have been well demonstrated in SJSA-1 and MDA-MB-231 xenograft mouse models.

9:35 Sponsored Presentation *(Opportunity Available)*

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

EFFICACIOUS ENGINEERING

11:00 Effects of Protein Aggregates on Fc Receptor Binding of Fusion Proteins and Antibody Therapeutics

Marina Feschenko, Ph.D., Senior Scientist, Analytical Development, Biogen

Aggregates of antibodies and Fc-fusions are known to affect protein–protein binding. The magnitude of these effects varies for different products and assays. We demonstrated that presence of aggregates in samples significantly increased binding potency values in AlphaScreen-based FcRn and Fcγ receptor binding assays, sometimes masking the loss of potency in stressed samples. Biolayer interferometry technology was found to be less sensitive to aggregates and presented fast and reliable method for measuring Fc receptor binding.

11:30 Antibody Glycosylation and Its Impact on the Pharmacokinetics and Pharmacodynamics of Monoclonal Antibodies and Fc-Fusion Proteins

Liming Liu, D.Phil., Principal Scientist, Pharmacokinetics, Pharmacodynamics and Drug Metabolism (PPDM), Merck Research Laboratory

Understanding the impact of glycosylation and keeping a close control on glycosylation of product candidates are required for both novel and biosimilar monoclonal antibodies (mAbs) and Fc-fusion protein development to ensure proper safety and efficacy profiles. This presentation will review and discuss the impacts of major glycans on the pharmacokinetics (PK) and pharmacodynamics (PD) of mAb and Fc-fusion proteins.

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

12:30 Session Break

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

1:15 Close of Conference

Enhancing Antibody Binding and Specificity

Scientific Strategies for Engineering Biotherapeutic Binding and Specificity for Next-Generation Antibody Therapeutics

CHI-PepTalk.com

As the industry expands its repertoire of antibody drug products into new therapeutic areas, product formats and protein constructs, the control of antibody/antigen targeting, binding and specificity will take on a new level of importance for researchers in this field. The second meeting in the Peptalk Protein Engineering & Development pipeline, Enhancing Antibody Binding and Specificity, presents innovative approaches to the modulation of binding activity, mechanism of action and difficult target challenges such as transmembrane proteins and intracellular targeting.

TUESDAY, JANUARY 10

1:00 pm Conference Registration

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

2:00 Chairperson's Opening Remarks
Javier Chaparro-Riggers, Ph.D., Director, Antibody Technology, Pfizer

KEYNOTE PRESENTATION

2:05 Antibody Generation and Selection: A Very Different Fetal Life
Eric R.F. Meffre, Ph.D., Associate Professor, Immunobiology, Yale University School of Medicine
By studying the B cell selection in human fetuses, we found that central B cell tolerance is already active in both fetal liver and fetal bone marrow. But peripheral B cell tolerance checkpoint was not yet functional in 3-4 month old fetuses that virtually lacked T cells. Fetal restricted V(D)J recombination may play an important role in restraining autoimmunity in the absence of a peripheral B cell tolerance checkpoint.

ANALYTICAL METHODS

2:45 Toward an Integrated Biosensor Platform to Support Biotherapeutic Discovery
Kerry Kelleher, MS, MSCIS, Senior Principal Scientist, Biomedicines Design, Pfizer
We have established an integrated, complementary set of biosensor platforms to enable the efficient selection of lead antibody candidates. This presentation will highlight examples using parallel processing of the OctetRED384 to expedite epitope binning and off-rate ranking; high throughput Biacore 4000 to facilitate screening hundreds of antibody candidates; Biacore T200 to provide flexibility, sensitivity, and accuracy; and KinExA to determine solution equilibrium KDs of ultra-high affinity leads.

3:15 Sponsored Presentation *(Opportunity Available)*

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

4:30 Broad Epitope Coverage Obtained from a Human *In Vitro* Antibody Library
Yasmina Abdiche, Ph.D., Research Fellow; Head, Bioanalytics Group, Rinat-Pfizer

5:00 Epitope Binning and Characterization at the Early Stages of Therapeutic Antibody Discovery
Sam Wu, Ph.D., Principal Scientist, Biologics Research, Janssen BioTherapeutics
High-throughput epitope binning can be employed with functional activity screens, enabling the rapid identification of leads that exhibit functional epitopes. To characterize the initial panel of phage-derived antibodies, a label-free, array-based SPR imager was performed. The mapping results, together with relative affinity and functional activities, allowed the selection of lead candidates for testing *in vivo*. Data suggests that affinity and killing capacity are correlated, but epitope determines killing capacity.

5:30 Close of Day

5:30 - 5:45 Short Course Registration
5:45 - 8:45 Dinner Short Courses* ***See pages 6-7 for details***
**** Separate registration required***

WEDNESDAY, JANUARY 11

8:00 am Conference Registration and Morning Coffee

REGULATING TARGET SELECTIVITY IN BISPECIFIC ANTIBODIES

8:30 Chairperson's Remarks
David A. Scheinberg, M.D., Ph.D., Vincent Astor Chair and Chairman, Molecular Pharmacology Program, Sloan Kettering Institute

8:35 Optimizing T-Cell Engaging Full Length Bispecific Antibodies
Javier Chaparro-Riggers, Ph.D., Director, Antibody Technology, Pfizer
Pfizer developed a T-cell engaging antibody platform, which allows the formation of full length human IgG1 and IgG2 antibodies *in vitro* or *in vivo*. The effect of IgG isotype and affinities of the T-cell- and tumor antigen-targeting arm were explored and optimized.

9:05 Enhancing Tumor-Targeting Selectivity by Modulating Bispecific Antibody's Binding Affinity and Format Valence
Yariv Mazor, Ph.D., Senior Scientist, Antibody Discovery & Protein Engineering, MedImmune LLC
Dual targeting is believed to enhance biological efficacy, limit escape mechanisms, and increase target selectivity via a strong avidity effect mediated by concurrent binding of the bsAb to both antigens on the surface of the same cell. However, factors that regulate the extent of target selectivity are not well understood and are often overlooked. We show that dual targeting alone is not sufficient to promote efficient target selectivity and report the pivotal role played by the intrinsic affinity of the individual arms, overall avidity and format valence.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

Enhancing Antibody Binding and Specificity

Scientific Strategies for Engineering Biotherapeutic Binding and Specificity for Next-Generation Antibody Therapeutics

INTRACELLULAR TARGETS

10:50 Targeting Undruggable Proteins with Antibodies

David A. Scheinberg, M.D., Ph.D., Vincent Astor Chair and Chairman, Molecular Pharmacology Program, Sloan Kettering Institute

Many important mutated or oncogenic proteins are not expressed on the cell surface, nor are these proteins druggable by small molecules. TCR mimic mAb (TCRm) can bind to peptides from intracellular targets in the context of HLA on the cell surface, even at extremely low density. Such TCRm mAb are effective in preclinical models of cancer. Issues related to efficacy, pharmacology, toxicity, and resistance to these approaches will be discussed.

11:20 Intracellular Targets for Cancer Immunotherapy

Bryan Zimdahl, Ph.D., Research Scientist, Preclinical Development, Eureka Therapeutics, Inc.

Chimeric antigen receptor (CAR) T-cell therapies for solid tumors have made little progress. A key challenge facing CAR T therapies for solid tumors is that the majority of specific markers for solid tumors are intracellular/secreted proteins and therefore, inaccessible by conventional antibodies/CARs. We will discuss Eureka's unique approach to targeting intracellular proteins and demonstrate CAR T-cell therapy can be used to target these proteins for the treatment of solid tumors.

11:50 iTAbs for Therapeutic Regulation of Intracellular Targets

Heehyoung Lee, Ph.D., Director, Target Discovery and Validatiown, LA Cell, Inc.

Up to now, antibody-based therapies could only reach proteins on the cell surface. However, most disease-causing molecules are located within the cells. To address current unmet clinical needs, LA Cell developed iTAbs, intracellular targeting antibodies which efficiently cross the cell membrane. Using various approaches, the efficacy of iTAbs in binding to the intended targets and in blocking effector pathways was demonstrated, supporting the feasibility of using iTAbs for targeted therapies.

12:20 pm Sponsored Presentation *(Opportunity Available)*

12:50 Session Break

Sponsored by

integral molecular

1:00 Luncheon Presentation I: New Approaches for mAb Discovery against GPCRs, Ion Channels, and Transporters

Joseph Rucker, Ph.D., Vice President, Research & Development, Integral Molecular

To enable the discovery of mAbs against membrane proteins, Integral Molecular has developed the MPS Discovery Engine®. MPS harnesses 15 years of expertise in membrane protein expression and analysis, and proprietary technologies including Lipoparticles for high-concentration membrane protein presentation, Picodroplet technology for microfluidic B-cell screening, and Shotgun Mutagenesis for epitope mapping and mAb optimization. MPS has resulted in mAbs against previously intractable GPCR, ion channel, and transporter targets.

1:30 Luncheon Presentation II *(Sponsorship Opportunity Available)*

OPTIMIZATION AND CONTROL OF BINDING AND SPECIFICITY

2:00 Chairperson's Remarks

Tilman Schlothauer, Ph.D., Principal Scientist, Biochemical and Analytical Research, Large Molecule Research, Roche Pharma Research and Early Development (pRED), Roche Innovation Center Penzberg

2:05 *In vivo* Imaging of Probody™ Activation at the Tumor Site

Olga Vasiljeva, Ph.D., Associate Director, Head, Protease Biology, CytomX Therapeutics

Probody therapeutics are fully recombinant antibody prodrugs that are converted to active antibodies by tumor-associated proteases, thereby minimizing toxicity while maximizing anti-tumor activity. Using NIR optical imaging in combination with antigen or protease activity blocking approaches, activation of Probody therapeutics at the tumor site was demonstrated for multiple programs, supporting the concept of Probody therapeutics for the treatment of cancer.

2:35 Analyzing Specificity and Valency of Antibody Binding by Cell-Free Assays

Tilman Schlothauer, Ph.D., Principal Scientist, Biochemical and Analytical Research, Large Molecule Research, Roche Pharma Research and Early Development (pRED), Roche Innovation Center Penzberg

Protein-protein interactions can be difficult to evaluate by the classical 1:1 langmuir binding model. Next to the bivalency of wild type IgG scaffolds, the heterogeneity of antibody preparations prevents a meaningful evaluation of surface plasmon resonance data in many cases. An additional difficulty is hidden in the nature of surface-based protein-protein interaction determinations. Here we will show a case study on how to circumvent such problems.

3:05 Highly Efficient Sweeping Antibody Using Novel Engineering Technology

Atsuhiko Maeda, Ph.D., Research Scientist, Pharmaceutical Technology, Chugai Pharmaceutical Co., Ltd.

In this presentation, we will introduce novel sweeping antibody technology that enables highly efficient elimination of soluble antigens from plasma. The novel technology can be applied to various antigens, and these antibodies can efficiently eliminate the antigens from plasma in cynomolgus monkey by >1000-fold compared to conventional antibodies, and allow targeting antigens present in very high concentrations in plasma.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:30 Achieving Selectivity Using Dual Targeting Bispecific Antibodies

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

Cell surface receptors involved in diseases such as cancer are often also expressed on healthy cells, limiting the therapeutic window of drugs. We have

developed a series of bispecific antibodies enabling selective targeting on tumor cells of CD47, a ubiquitously expressed checkpoint molecule. The mode of action relies on co-engagement of two receptors at the cell surface, as well as on different affinities of the two arms of the bispecific antibody.

5:00 Computationally Driven Identification of Antibody Epitopes

Chris Bailey-Kellogg, Ph.D., Professor, Computer Science, Dartmouth College

We have developed an epitope mapping method that, given an antibody sequence, computationally designs and experimentally evaluates targeted mutations to the antigen in order to test predictions of possible antibody binding modes. Retrospective tests, along with prospective application to a tumor cell ligand and binding antibody of unknown binding mode, demonstrate that the method can in general successfully localize an epitope with only a small set of mutagenesis experiments.

5:35 BuzZ Session B

Join your peers and colleagues for interactive roundtable discussions.

Please see page 74 for additional information.

6:20-7:20 Reception in the Exhibit Hall with Poster Viewing

7:20 Close of Conference

Emerging Technologies for Antibody Discovery

Cutting-Edge Technologies to Enable the Discovery of Novel Biotherapeutic Targets for Antibodies and Emerging Constructs

As large pharma continues its integration of biologic drugs into its product portfolios and discovery operations, it is imperative that industry companies identify truly novel drug targets for unmet medical needs. The Emerging Technologies for Antibody Discovery meeting offers a forum for showcasing the current state of the art for research methodologies that will support the discovery of next-generation biotherapeutics. The meeting explores the evolution of traditional library and display approaches, along with emerging technologies with the potential to have significant near-term impacts on the ability of scientists to discover and develop unique, differentiated biologic drugs.

THURSDAY, JANUARY 12

7:45 am Conference Registration and Morning Coffee

8:15 Chairperson's Opening Remarks

Michael Hornsby, Ph.D., Researcher, UCSF Antibiome and Recombinant Antibody Network, Pharmaceutical Chemistry, University of California, San Francisco

KEYNOTE PRESENTATION

8:20 Increasing the Content of High-Content Assays: Targeting Diseases & Characterizing Compounds via Cell Painting

Anne Carpenter, Ph.D., Director, Imaging Platform, Broad Institute

Images contain rich information about the state of cells, tissues, and organisms. We work with biomedical researchers around the world to extract quantitative information from images, in high-content screening experiments involving physiologically relevant model systems. We extract more from images through profiling experiments, where thousands of morphological features are measured from each cell's image. We harvest similarities in these "profiles" for important applications including identifying drug targets and disease-associated phenotypes.

DISPLAY AND LIBRARY TECHNOLOGIES

9:00 Plug-and-(Dis)play Mammalian Cells for Protein Expression and Engineering

Sai Reddy, Ph.D., Assistant Professor, Biosystems Science and Engineering, ETH Zurich

Here I will present a platform for rapid reprogramming of hybridoma antibody specificity by immunogenomic engineering. We used CRISPR-Cas9 to generate targeted double-stranded breaks in immunoglobulin loci. Multiplexed-targeting enabled deletion of the native variable light chain and homology directed repair allowed replacement of the endogenous variable heavy chain with a fluorescent reporter protein, mRuby. New antibody genes were then introduced by using Cas9 to target mRuby and promote replacement.

9:30 Optimized Antigen Expression and Automated Antibody-Phage Display Pipeline for the Generation of Antibody Reagents to Cancer Related Surface Proteins

Michael Hornsby, Ph.D., Researcher, UCSF Antibiome and Recombinant Antibody Network, Pharmaceutical Chemistry, University of California, San Francisco

I will describe our target discovery pipeline for identifying surface proteome changes in oncogene transformed cell lines. Along with this, we have optimized an antigen expression and purification workflow that supports our robotic antibody development pipeline. Validated antibody reagents developed here have potential use as basic research tools and biotherapeutics.

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

11:00 WebPhage: An Informatics Platform to Facilitate Biotherapeutic Discovery and Engineering

Steve Comeau, Ph.D., Principal Scientist, Vaccinex

The discovery of protein-based drugs frequently hinges on the effective interrogation of libraries containing billions of members. Advances in automated liquid handling have simplified library screening, but tools to capture and process associated experimental data have not advanced at the same rate. To address this and support antibody discovery and protein engineering initiatives, Shire has developed a scalable workflow system, WebPhage, the design and future of which will be discussed.

Sponsored by ProImmune

11:30 Integrating Best-in-Class *in vitro* and *ex vivo* Assays to Manage Immunogenicity Risk in Biologics

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

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

Sponsored by Chemical Computing Group

12:00 pm Protein-Protein Docking with Sequential Coarse-Grained Minimization

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

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

12:30 Session Break

Sponsored by proteinsimple

12:45 Luncheon Presentation to be Announced

1:15 Ice Cream Break in the Exhibit Hall with Poster Viewing

SEQUENCING AND SCREENING TECHNOLOGIES FOR ANTIBODY AND CAR T DISCOVERY

2:00 Chairperson's Remarks
Gregory C. Ippolito, Ph.D., Research Assistant Professor, Molecular Biosciences, The University of Texas at Austin

2:05 T-Cell Antigen Profiling by Deep Sequencing
Robert Holt, Ph.D., Head, Sequencing, Michael Smith Genome Sciences Center, BC Cancer Agency
Deep sequencing can now reveal the mutational spectrum of evolving tumors and the clonal diversity of tumor associated T cells. However, linking the two remains difficult. A small minority of T cells in the tumor environment are tumor-reactive and they recognize only a small minority of potential tumor neoantigens. New approaches for direct and indirect neoantigen discovery and validation that are relevant to this problem will be discussed.

2:35 Natively Paired B- and T-Cell Immune Repertoires and the Discovery of Potent Antibody Therapeutics
Sean Carroll, Ph.D., Scientist, Atreca
Immune Repertoire Capture (IRC™) technology generates full-length sequences of natively paired variable regions from B and T-cells. Using IRC™, we have assembled repertoires from patients and models across multiple indications. Analyses of these repertoires has uncovered specific receptor clonal lineages, facilitated cross-subject/time-point comparisons, and identified sequences for further characterization. This is leading to new immunologic insights and identification of potent antibodies in immuno-oncology, infectious disease, and autoimmune disease.

Sponsored by HiFiBiO HIGH FIDELITY BIOLOGY

3:05 Functional Therapeutic Antibody Discovery for Challenging Targets by Single-B-Cell Screening in Nano-Droplets
Roshan Kumar, Group Leader, Cambridge Site, HiFiBiO, Inc.
CelliGO is a fully integrated and highly efficient antibody discovery process combining the power of droplet-based microfluidics and single-cell-specific next-generation sequencing. Our ability to interrogate millions of B-cells per experiment and deeply mine the immune response enables the discovery of valuable antibodies to diverse epitopes including rare functional epitopes.

Sponsored by TRIANNI

3:20 The Trianni Mouse: Best-In-Class Technology for Human Antibody Discovery
David Meininger, Ph.D., Chief Business Officer, Trianni, Inc.
The Trianni Mouse is the only human transgenic antibody discovery platform offering a complete heavy, kappa and lambda repertoire in a single organism. Sequences of the variable domain exons are human while genetic machinery including extensively optimized promoters and enhancers are of mouse origin.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Immunosequencing Enables Novel Therapeutics Discovery via Unprecedented High-Throughput TCR or BCR Chain Pairing
Catherine Sanders, Ph.D., Director, Scientific Liaisons, Adaptive Biotechnologies
Building on Adaptive Biotechnologies' TCR/BCR single chain sequencing technology, Adaptive has validated its pairSEQ approach that combines proprietary multiplex PCR methodology with high-throughput sequencing. By leveraging the diversity of the TCR repertoire, pairSEQ identifies native TCRα and TCRβ sequence pairs at an unprecedented throughput. Adaptive is further extending this approach to enable the identification of BCR heavy and light chain pairs for a broad spectrum of novel therapeutic applications.

4:45 Applying Sequencing Technology Combinations for Human Serum mAb Discovery
Gregory C. Ippolito, Ph.D., Research Assistant Professor, Molecular Biosciences, The University of Texas at Austin
The synergistic combination of IgG protein mass spectrometry and B-cell VH:VL NextGen sequencing enables the facile discovery and testing of antigen-specific recombinant monoclonal antibodies (mAbs) mined from human serum. We have documented the selective enrichment of serum mAbs for high-affinity binding, broad neutralizing activity, and potent *in vivo* protection in three case studies to date (poliovirus, influenza, HIV). These data plus extrapolation of the technique to immuno-oncology will be presented.

5:15 Simultaneous DNA Barcoding of Proteins, RNAs and Natively Paired Immune Receptors from Millions of Single Cells for Immunotherapy Discovery
Adrian Briggs, Head, Technology Development, Receptor Discovery, Juno Therapeutics, Inc.
TILs hold the key to understanding anti-cancer immune responses but remain challenging to study due to their vast ranges of phenotype, function and abundance. Our single cell sequencing-based method allows deep and unbiased TIL profiling directly from tumor tissue, providing insights into TIL diversity across a wide range of disease and sample types, with widespread potential for basic and applied research into the patient immune response to cancer and the dynamics of immunotherapy.

5:45 Close of Day

FRIDAY, JANUARY 13

8:00 am Conference Registration and Morning Coffee

COMPUTATIONAL, IMAGING, AND STRUCTURAL BIOLOGY TOOLS FOR ANTIBODY DISCOVERY

8:30 Chairperson's Remarks
John Wheeler, Principal Research Scientist, Janssen BioTherapeutics

Emerging Technologies for Antibody Discovery

Cutting-Edge Technologies to Enable the Discovery of Novel Biotherapeutic Targets for Antibodies and Emerging Constructs

8:35 EM by EM: High-Efficiency Epitope Mapping Using High-Throughput Electron Microscopy

Claudio Ciferri, Ph.D., Scientist, Structural Biology, Genentech

We have implemented a fast and robust platform to perform epitope mapping using high-throughput Electron Microscopy (EM) and single particle analysis. This technology serves as an important tool for antigen design, selection of therapeutic targets, and vaccine development. Future efforts will focus on streamlining the preparation of mAb-antigen complexes for Cryo-EM analysis to improve the resolution and obtain greater insights into antigen-antibody recognition.

9:05 Measuring Oncogene Signaling with ImmunoPET

Michael Evans, Ph.D., Assistant Professor, Radiology and Biomedical Imaging, University of California, San Francisco

We have pioneered a workflow in which we apply "omics" technologies to interrogate the biology downstream of an oncogene of interest to identify cell surface antigens that are compatible with PET imaging, and selectively regulated by the oncogene. We have developed the first translational imaging tools to measure the activity of oncogenes like the androgen receptor, MYC, mTORC1, and RAS with PET, and we have begun to validate these imaging biomarkers in man.

9:35 Using NGS to Enhance Cell-Based Antibody Phage Panning

John Wheeler, Principal Research Scientist, Janssen

Several receptor targets cannot be made as soluble proteins and others are problematic for discovery of antibodies that bind to native protein conformations. Cell-based phage panning can identify antibodies to such targets, but is inefficient, often producing low antibody diversity. We utilized next generation sequencing to improve the robustness of cell-based selections. We have thus identified large panels of diverse antibody sequences to several difficult receptor targets.

10:05 Coffee Break with a Poster Pavilion *See page 4 for details*

11:00 Ultra-High Throughput Screening of Soluble, Secreted mAbs against Intact Cancer Cells

Yongliang Fang, Researcher, Thayer School of Engineering, Dartmouth College

We have developed a high throughput screening platform for the discovery and engineering of secreted, soluble, full-length mAbs that bind membrane proteins on the surface of intact target cells. This technology couples fluorescence-activated cell sorting (FACS) with hydrogel microdroplet (GMD) encapsulation, thereby linking phenotype and genotype in ultra-high throughput library screens. This GMD-FACS platform makes a valuable tool for antibody discovery and optimization in both academic and industrial settings.

11:30 The HELM Editor: How to Fully Describe Even Complex Antibody Formats in Depth

Alexander Jarasch, Ph.D., Life Science Business Consultant, Quattro Research GmbH

The "HELM Antibody Editor" (HAbE) is a valuable tool for handling complex biotherapeutics. Based on the Pistoia Alliance's HELM project, HAbE was developed by Roche and quattro research. HAbE allows the registration of complex biomolecules in databases using the emerging standard HELM. Roche donated a public version of HAbE back to the HELM community. HELM, including the HAbE, is an open source project available on GitHub.

12:00 pm IT'S A WRAP: PEPTALK 2017 CLOSING PLENARY PANEL DISCUSSION *See page 5 for details*

1:15 Close of Conference

Engineering Next-Generation Cancer Immunotherapies

New Science and Technologies for Protein Engineers and Discovery Scientists to Support Development of Novel Immunotherapeutics and Treatment Combinations

A succession of strong clinical successes by antibody therapeutics against the mainstream checkpoint targets has spawned a surge of interest from across the industry in advancing novel immunotherapeutics and agents that perform well in treatment combinations. Cambridge Healthtech Institute's Third Annual Engineering Next-Generation Cancer Immunotherapies meeting offers important updates on scientific strategies and technologies that will be used by protein engineers and discovery scientists to support the development of the next wave of highly efficacious cancer immunotherapies.

SUNDAY, JANUARY 8

4:00 - 5:30 pm Registration

5:00 - 8:00 Dinner Short Courses *See pages 6-7 for details*

MONDAY, JANUARY 9

7:30 am Conference Registration and Morning Coffee

TARGET IDENTIFICATION FOR NOVEL IMMUNOTHERAPIES

9:00 Welcome by Conference Organizer

Kent Simmons, Senior Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks

Birgit Schoeberl, Ph.D., Head, Discovery, Vice President, Merrimack

KEYNOTE PRESENTATION

9:10 An NIH Perspective on Emerging Target Classes for Cancer Immunotherapy

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

Antibodies have a major role in cancer treatment. To increase their efficacy, we need to design them to inhibit signaling pathways responsible for the growth of cancer. This can be done by decreasing the size of the antibody so it can target cryptic or buried functional regions in receptors or signaling complexes. Another need is to identify new therapeutic targets in cancer and make antibodies that modulate their activity.

9:50 ADAPTIR™ Bispecifics, a Novel Platform for Development of Immuno-Oncology Therapeutics

Jane Gross, Ph.D., Vice President, Research and Non-Clinical Development, Emergent Biosolutions

Bispecific T-cell engagers, an emerging technology, have received attention from the approval of BLINCYTO™ (blinatumomab) targeting CD19/CD3 for treatment of ALL. The ADAPTIR™ platform is a novel technology with improved characteristics that address concerns around stability, manufacturability and half-life of bispecifics, while retaining potent and distinct preclinical activity. The ADAPTIR platform is being used to develop bispecifics that mediate T-cell engagement and bispecifics with new mechanisms of action in immune-oncology.

10:20 Coffee Break

10:45 Emerging Predictive Biomarkers for Cancer Immunotherapy

Sandip P. Patel, M.D., Assistant Professor, Cancer Immunotherapy Program, Experimental Therapeutics, Thoracic Oncology, Moores Cancer Center, University of California, San Diego

The advent of cancer immunotherapy has revolutionized oncology. With a growing pipeline of therapeutic targets, the need for predictive biomarkers to optimize immunotherapeutic regimens is of increasing importance. This presentation will review novel immunotherapeutic biomarker assays and their role in the clinic.

11:15 Hexavalent Single-Chain TNFSF-RBD-FC Fusion Proteins for Cancer Immunotherapy

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

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

11:45 New Pathways for T Cell Costimulation and Coinhibition

Xingxing Zang, MMed, Ph.D., Miriam Mandel Faculty Scholar in Cancer Research Associate Professor, Microbiology & Immunology, Albert Einstein College of Medicine

CTLA-4 and the PD-1/PD-L1 pathway are current focuses in cancer immunotherapy. This presentation will discuss other new immune checkpoints for future human cancer immunotherapy.

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

12:45 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

MULTISPECIFICS AND IMMUNOTHERAPY COMBINATIONS

2:00 Chairperson's Remarks

John Desjarlais, Ph.D., CSO, Xencor

2:05 Mechanisms of Action for the Application of BiTE Antibodies in Immunotherapy Combinations

Tara Arvedson, Ph.D., Director, Oncology Research, Amgen

Recent clinical data have demonstrated the potency and significance of T-cells in anti-tumor activity. For example, the CD19/CD3 bispecific T-cell engager (BiTE®) blinatumomab is now a proven means of harnessing T-cells for the treatment of cancer, and a CD33/CD3 BiTE is currently in clinical development. This presentation will cover mechanisms of action for BiTE® molecules and the potential for immunotherapy combinations.

2:35 Bispecific Antibodies for T-Cell Redirection and Dual Checkpoint Blockade

John Desjarlais, Ph.D., CSO, Xencor

We have optimized a plug-and-play, Fc-containing bispecific antibody platform with high stability, efficient production, and antibody-like pharmacokinetics. This

Engineering Next-Generation Cancer Immunotherapies

New Science and Technologies for Protein Engineers and Discovery Scientists to Support Development of Novel Immunotherapeutics and Treatment Combinations

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optimized bispecific format resembles a standard monoclonal antibody, with one of the Fab arms replaced by a stability-optimized single-chain Fv (scFv) (scFv-Fab-Fc). We will present application of the platform to create a pipeline of CD3 bispecifics for T-cell redirection, and dual checkpoint blockade bispecifics for T-cell activation.

3:05 Sponsored Presentation *(Opportunity Available)*

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Design and Engineering of Targeted TNFR Superfamily Ligand Fusion Proteins

Birgit Schoeberl, Ph.D., Head, Discovery, Senior Vice President, Merrimack

TNF ligands and receptors are involved in diverse biological processes ranging from the selective induction of cell death in potentially dangerous and superfluous cells to providing costimulatory signals that help mount an effective immune response. This regulatory role in immunity has sparked great interest in the development of TNFL/TNFR-targeted cancer immunotherapeutics. We will show examples of how we use Systems Biology insights to design bispecific targeted TNFR superfamily ligand fusion proteins.

4:30 Chemically Programmed Bispecific Antibodies

Christoph Rader, Ph.D., Associate Professor, Cancer Biology and Molecular Therapeutics, The Scripps Research Institute

Chemically programmed bispecific antibodies (cp-biAbs) endow tumor-targeting small molecules with the ability to recruit and activate T cells for selective and potent killing of tumor cells. We merged two different clinically translated antibody technologies to generate a novel cp-biAb platform and demonstrated its utility for cancer therapy *in vitro* and *in vivo*. Thus, our technology provides tumor-targeting compounds access to the power of cancer immunotherapy.

5:00 Combination Therapy of CAR T-Cells and Checkpoint Blockade

Prasad S. Adusumilli, M.D., FACS, Deputy Chief, Thoracic Service, Memorial Sloan Kettering Cancer Center

Adaptive resistance developed by the solid tumors following immune attack poses a hurdle for achieving durable responses by both CAR T-cell therapy and checkpoint blockade. We have shown that the effector function of CAR T-cells was restored through PD-1 antibody checkpoint blockade or with cell-intrinsic PD-1 blockade mediated by shRNAs or a dominant negative receptor. These findings provide a translatable strategy for combining CAR therapy and PD-1/PD-L1 blockade.

5:35 BuzZ Session A
Join your peers and colleagues for interactive roundtable discussions.
Please see page 74 for additional information.

6:20-7:30 Welcome Reception in the Exhibit Hall with Poster Viewing

7:30 Close of Day

TUESDAY, JANUARY 10

8:00 am Conference Registration and Morning Coffee

MECHANISMS OF ACTION FOR IMMUNOTHERAPEUTICS

8:30 Chairperson's Remarks

Dimiter S. Dimitrov, Ph.D., Senior Investigator, Protein Interactions Section, Cancer and Inflammation Program, National Cancer Institute, NIH

8:35 The 2.3 Angstrom Structure of Pembrolizumab, a Full-Length Anti-PD1 Therapeutic IgG4 Antibody

Giovanna Scapin, Ph.D., Principal Scientist, Structural Chemistry, Merck & Co., Inc.

The structure of Pembrolizumab shows that it is a compact molecule, with one of the Fc CH2 domains rotated about 120 degrees with respect to the position observed in other structures. This novel conformation is possibly driven by the shorter and more constrained IgG4 hinge. The structure suggests a role for the S228P mutation in preventing arm exchange, and may explain some specific characteristics of the IgG4 subclass.

9:05 Affinity and Epitope Interplay in Antibody Efficacy

Dimiter S. Dimitrov, Ph.D., Senior Investigator, Protein Interactions Section, Cancer and Inflammation Program, National Cancer Institute, NIH

The antibody affinity could correlate with efficacy, but in many cases, its epitope is critical. The dependence of efficacy on affinity/avidity and epitope is complex and affected by the antibody format and target properties including surface concentration. Several examples of the important role of the antibody epitope for efficacy will be discussed including our antibodies against CD22 and folate receptor beta.

9:35 Sponsored Presentation *(Opportunity Available)*

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

11:00 Functionalization of Monoclonal Antibodies Using Mechanical Bonds

John Williams, Ph.D., Professor, Molecular Medicine, Director, X-Ray Core Facility, Beckman Institute, City of Hope

Through diffraction studies and rational design efforts, we have significantly improved the affinity of the meditope interaction, enabling us to thread an azide through the Fab hole and use click chemistry to create a mechanical bond. Offering an efficient and rapid means to functionalize meditope-enabled mAbs, we will present recent data using mechanical bonds including imaging and novel BiTE approaches for immunotherapy

11:30 Improving Immunotherapy with the HexaBody Platform

Paul W.H.I. Parren, Ph.D., Senior Vice President & Scientific Director, Genmab

Monomeric IgG antibodies organize into ordered hexamers after binding their cognate antigen expressed on a cell-surface. This process is dependent on specific Fc:Fc interactions located in the interface between neighboring IgG molecules in the hexamer. Based on this concept, we developed the HexaBody technology to generate potentiated antibody therapeutics. Their ability to induce improved cell killing when used alone or in combination will be discussed.

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

12:30 Session Break

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

1:15 Close of Conference

Antibody-Drug Conjugates

Engineering for Clinical Success

CHI-PepTalk.com

With more than 30 ADCs in clinical trials, and more on the way, antibody-drug conjugates have reached an exciting point in development, particularly with the current next-generation strategies. Cambridge Healthtech Institute's Antibody-Drug Conjugates conference reveals the engineering that has brought about today's revolution, and examines how to design safe and effective ADCs. In addition, strategies for advancing ADCs to the clinic will be discussed along with considerations for clinical trial design. Analyzing ADCs to explore conjugation, stability, payloads and tumor penetration will also be addressed in this leading ADC event.

TUESDAY, JANUARY 10

1:00 pm Conference Registration

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

ADCs TO FIGHT CANCER

2:00 Chairperson's Opening Remarks
Vaughn Smider, Ph.D., Assistant Professor, Molecular Biology, Scripps Research Institute; CSO, Sevion Therapeutics

KEYNOTE PRESENTATION

2:05 Antibody-Drug Conjugate Therapeutics and Their Evolving Role in Oncology
Arvind Rajpal, Ph.D., Vice President, Protein Therapeutics, Bristol-Myers Squibb Co.
ADCs are a maturing therapeutic class with more than 50 candidates in clinical development and two approved molecules on the market. The emergent role of immunotherapy in oncology presents several challenges and opportunities for ADCs. Successful positioning of current and future ADC candidates, in light of these changes, will require strategic imperatives that enhance the complementary role of ADCs to immunotherapy.

2:45 The Multifacets and Potentials of ADC in the Era of Immune-Oncology
David Miao, Ph.D., CSO, Concortis Biotherapeutics

3:15 Sponsored Presentation *(Opportunity Available)*

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

4:30 Leveraging Ultra-Potent Toxins in Novel ADCs for Highly Effective Anti-Tumor Therapy
Ulf Grawunder, Ph.D., CEO & Founder, NBE-Therapeutics, Ltd.
The development of antibody-drug conjugates (ADCs) is associated with the challenge of selective delivery of highly potent toxins to tumors. ADC stability, homogeneity, binding specificity and the engagement of immune-mediated cell death (ICD) mechanisms are critical factors to achieve an optimal therapeutic index of ADCs, especially if ultra-potent toxic payloads are engaged. Data on the anti-tumor activity of novel, next-generation ADCs with ultra-potent toxins will be presented.

5:00 Antigen-Targeted Amanitin-Conjugates (ATACs) – Expanding the ADC Landscape with a New Payload Targeting RNA Polymerase II
Andreas Pahl, Ph.D., CSO, Heidelberg Pharma
Antigen-Targeted Amanitin-Conjugates (ATACs) represent a new class of ADCs using the payload Amanitin. This payload introduces a novel mode of action into oncology therapy, the inhibition of RNA polymerase II. The technology platform around ATACs includes Amanitin supply, site-specific conjugation, a demonstrated safety profile and a biomarker. A BCMA-ATAC has been selected based on favorable preclinical data to start the clinical development of the first ATAC.

5:30 Close of Day

5:30 - 5:45 Short Course Registration
5:45 - 8:45 Dinner Short Courses* ***See pages 6-7 for details***
**** Separate registration required***

WEDNESDAY, JANUARY 11

8:00 am Conference Registration and Morning Coffee

MOVING ADCs INTO THE CLINIC

8:30 Chairperson's Remarks
Dorin Toader, Ph.D., Senior Scientist, Antibody Discovery and Protein Engineering, MedImmune LLC

8:35 Clinical Pharmacology of vc-MMAE Antibody-Drug Conjugates: Platform Approach to Characterize Pharmacokinetics and Peripheral Neuropathy
Chunze Li, Ph.D., Senior Scientist, Therapeutic Area Lead for ADCs, Clinical Pharmacology, Genentech
This presentation will provide clinical pharmacology learnings and challenges for vc-MMAE antibody-drug conjugates (ADCs), and describe the innovative platform approach to integrate clinical pharmacology data across vc-MMAE ADCs to inform clinical strategy. I will also discuss the clinical pharmacokinetic characteristics across several vc-MMAE ADCs, and the exposure response relationship and risk factors for peripheral neuropathy associated with the use of vc-MMAE ADCs in clinical testing.

9:05 Peripheral Neuropathy with Microtubule Inhibitor Containing Antibody-Drug Conjugates: Challenges and Perspectives in Translatability from Nonclinical Toxicology Studies to the Clinic
Nicola Stagg, Ph.D., Scientist/Toxicologist, Safety Assessment, Genentech
The valine citriline monomethyl auristatin E (vcMMAE) ADC platform has shown promising clinical activity in a variety of cancers, but peripheral neuropathy (PN) has been observed in the clinic that was not observed in nonclinical toxicology studies. We evaluated four possible hypotheses for the lack of translatability of PN. The ultimate goal is to be able to have a model to screen the next generation MTI ADCs for reduced incidence and severity of peripheral neuropathy.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

ANALYTICAL STRATEGIES

10:50 How *in vivo* & *in vitro* ADC Stability Data Is Used to Advance Projects at Pfizer

Anokha Ratnayake, Ph.D., Principal Scientist, Medicine Design - ADC Oncology, Pfizer

The design and development of a successful ADC require identification and implementation of reliable analytical techniques and assays (such as LBA and DAR-based PK, plasma stability) at an early stage, to help drive decisions about project advancements. A fundamental understanding of ADC metabolism enables problem solving that may "rescue" payloads that were previously deprioritized. Site of conjugation can play a major role in ADC metabolism, hydrophobicity and PK.

11:20 An Integrated Multiplatform Bioanalytical Strategy for Antibody–Drug Conjugates: A Novel Case Study

Vangipuram S. Rangan, Ph.D., Senior Director, Protein Chemistry, Bristol-Myers Squibb Co.

This talk describes the utilization of reagents specifically tailored to an ADC with a microtubule polymerization inhibitor payload and cathepsin B cleavable linker. The PK strategy includes the evaluation of physiological levels of total antibody, active ADC, total ADC, antibody-conjugated payload and unconjugated payload. These data are evaluated in the context of target and antidrug antibody levels to elucidate bioactive ADC.

11:50 Neutropenia Translation of ADC: Perspective from Mechanistic Modeling

Shangchiung Chen, Ph.D., Scientist, Clinical Pharmacology, Genentech

A quantitative preclinical/clinical translational model for neutropenia was developed using PK and PD data from multiple vc-MMAE ADCs. The translational PK/PD model can be used to predict potential risk of neutropenia based on preclinical observation in monkeys and facilitate dose/regimen selection.

12:20 pm Sponsored Presentation *(Opportunity Available)*

12:50 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

ADC PROMISE AND INNOVATION

2:00 Chairperson's Remarks

Andreas Pahl, Ph.D., CSO, Heidelberg Pharma

FEATURED PRESENTATION

2:05 Challenges and Opportunities in Design and Development of Antibody-Drug Conjugates

John M. Lambert, Ph.D., Executive Vice President & Distinguished Research Fellow, ImmunoGen, Inc.

ADCs with potent tubulin-acting and DNA-acting agents can be effective anti-cancer agents with good TI. However, not all cell-surface targets have proven susceptible to the development of effective ADCs utilizing first generation ADC chemistries. Lessons from the past 15 years of ADC preclinical and clinical experience have created new opportunities in design and development of ADCs to meet the challenges in creating successful ADCs, as illustrated with the progress of ImmunoGen's advancing ADC.

2:35 MMETA – A Tubulysin Analog for Antibody-Drug Conjugates

Dorin Toader, Ph.D., Senior Scientist, Antibody Discovery and Protein Engineering, MedImmune LLC

Tubulysins are a class of naturally occurring highly cytotoxic peptides of fungal origin. The observed picomolar activity of tubulysins against a range of cancer cell lines makes them excellent candidates for targeted delivery as conjugates with monoclonal antibodies. This presentation describes the discovery and development of a fully synthetic tubulysin analog MMETA and its application to antibody-drug conjugates for oncology.

3:05 Multiparatopic and Multispecific Nanobody-Based Drug Conjugates

Carlo Boutton, Ph.D., Director, Technology & Information Management, Ablynx nv

The modularity of the Nanobody platform allows an easy generation of multivalent, multiparatopic and multispecific constructs. By combining several Nanobodies with similar or different functionalities, the properties of the proposed drug can be tuned. This is an extremely powerful platform to direct Nanobody-based drug conjugates to diseased cells.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

SITE-SPECIFIC CONJUGATION

4:30 Selecting the Optimal Cysteine Site for THIOMAB-Drug Conjugates

Hans Erickson, Ph.D., Associate Director, Protein Chemistry, Genentech

Antibodies with cysteine mutations for conjugation are widely used for the preparation of homogeneous ADCs with defined molar ratios of the payload to the antibody (site-specific). The factors that drive stability are not well understood. I propose to describe how we have optimized our cysteine engineering (THIOMAB™) technology to build better ADCs and also share some of the research conducted to understand the factors that drive stability of protein conjugates using maleimide and disulfide-based attachment chemistries.

5:00 Pcl and PPTase – Two Innovative Methods for the Preparation of Homogenous ADCs

Bernhard H. Geierstanger, Ph.D., Director, Protein Engineering, Genomics Institute of the Novartis Research Foundation

Pyrroline-carboxy-lysine (Pcl) is readily incorporated by the unmodified pyrrolysyl-tRNA/tRNA synthetase pair into proteins at TAG codons and reacts specifically with 2-amino-benzaldehyde reagents. Similarly, post-translational modification catalyzed by phosphopantetheinyl transferases (PPTases) can be used to site-specifically label proteins with structurally diverse molecules. Both methods can be used to efficiently prepare homogenous, site-specifically conjugated ADCs with excellent biophysical and PK characteristics, and high *in vitro* and *in vivo* potency.

5:35 BuzZ Session B

Join your peers and colleagues for interactive roundtable discussions.

Please see page 74 for additional information.

6:20-7:20 Reception in the Exhibit Hall with Poster Viewing

7:20 Close of Conference

Bispecific Antibody Therapeutics

Engineering Multispecificity

Cambridge Healthtech Institute's Bispecific Antibody Therapeutics conference explores the challenges of engineering multispecificity in order to achieve more effective therapies that bind to at least two molecular targets simultaneously. Next-generation antibody formats are proving fruitful in the efforts to conquer cancer and other diseases. Case studies highlight novel engineering approaches that address safety, stability, enhanced targeting, and manufacturability, as the conference examines current developments and also future directions of these promising molecules.

THURSDAY, JANUARY 12

7:45 am Conference Registration and Morning Coffee

BISPECIFICS TO FIGHT CANCER

8:15 Chairperson's Opening Remarks
Christoph Spiess, Ph.D., Senior Scientist, Antibody Engineering, Genentech

FEATURED PRESENTATION

8:20 T-Cell Vaccination Using Bispecific Antibody Armed T-Cells (BATs)
Lawrence G. Lum, M.D., D.Sc., Professor, Medicine, Director, Cellular Therapy, and Scientific Director, BMT, University of Virginia
Specific cytotoxicity mediated by anti-CD3 activated T-cells (ATC) armed with anti-CD3 x anti-Her2 BiAb in breast, prostate, and ovarian cancer, anti-CD3 x anti-EGFR for lung, brain, and pancreatic cancer, anti-CD3 x anti-CD20 BiAb for non-Hodgkin's lymphoma and multiple myeloma, and anti-CD3 x anti-GD2 for neuroblastoma. BATs exhibit clinical activity and immune activity in both solid and liquid tumors.

9:00 The Use of Bispecific Antibodies to Modulate Anti-Tumor Immune Responses
Neil D. Brewis, Ph.D., CSO, F-star Biotechnology, Ltd.
An attractive alternative to combining two antibodies is the development of bispecific antibodies that not only bring two biologies together but may result in novel biological mechanisms that are impossible to attain with combinations. A murine-specific anti-LAG-3 and PD-L1 bispecific antibody was engineered that binds both antigens simultaneously and with nanomolar affinities. This potency translates into *in vivo* efficacy, where the anti-LAG-3/PD-L1 bispecific antibody decreased tumor burden in the MC38 colon carcinoma model.

9:30 Development of MCLA-128 - A Bispecific Antibody Targeting HER2 and HER3
Mark Throsby, Ph.D., Executive Vice President & CSO, Merus B.V.
A proprietary platform technology was applied to generate the Biclonics® MCLA-128, a human common light chain bispecific antibody targeting HER2 and HER3. MCLA-128 specifically and potently inhibits ligand dependent HER2:HER3 signaling resulting in suppression of tumor growth *in vitro* and *in vivo*. This novel full-length bispecific antibody, that features ADCC enhancement, is undergoing clinical evaluation in a Phase I/II study of patients with HER2+ tumors.

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

11:00 Improving on Cancer Therapy: The Duobody Technology
Paul W.H.I. Parren, Ph.D., Senior Vice President & Scientific Director, Genmab A/S
The Duobody technology provides unsurpassed opportunities for the generation and development of bispecific antibodies (bsAb) as biopharmaceuticals. This presentation will highlight recent examples of Duobody molecules directed against a number of relevant tumor targets.

11:30 Engineering Next-Generation Biotherapeutics: Developability & Manufacturability
Christopher Smith, Ph.D., Senior Scientific Consultant, Biologics, Genedata
Next-generation biotherapeutics, specifically bi- and multispecifics, alternative scaffolds, and ADCs, provide significant advantages over traditional IgG-based molecules. As highly engineered molecules, they pose new design, cloning, expression, purification, and analytics challenges. Our workflow platform automates the engineering, production, and testing of large panels of these candidate therapeutic molecules. We demonstrate the platform's capability to explore the huge combinatorial space of novel molecule-specific designs, its high-throughput capability, and its built-in tools for developability and manufacturability assessments.

12:00 pm Session Break

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

1:15 Ice Cream Break in the Exhibit Hall with Poster Viewing

ENGINEERING INNOVATIONS

2:00 Chairperson's Remarks
Neil D. Brewis, Ph.D., CSO, F-star Biotechnology, Ltd.

2:05 Engineered Fab Domains Promote Efficient Production of Bispecific Antibodies in a Single Cell
Christoph Spiess, Ph.D., Senior Scientist, Antibody Engineering, Genentech
Bispecific antibodies have gained increased relevance in research and therapeutic settings despite the complexities in their production and challenges in finding the right combination. The presentation will discuss strategies and consideration to screen for the best bispecific antibody pair. In addition, a novel approach to produce a bispecific antibody with natural architecture in a single cell will be discussed. The technology now simplifies bispecific production for research and development.

2:35 Design Principles for Bispecific IgGs – Opportunities and Pitfalls of Artificial Disulfide Bonds
Itai Benhar, Ph.D., Professor, Biotechnology, Tel Aviv University
We present a solution for correct pairing of heavy and light chains of bispecific IgGs; an engineered disulfide bond between the antibodies' variable domains that asymmetrically replaces the natural disulfide bond between CH1 and CL. A novel approach for precise evaluation of correct chain pairing by LC-MC-MS combined with chemical crosslinking is presented. Examples will be provided for some of these bsAbs and future directions of the study will be discussed.

3:05 A Stable Episomal Expression System to Streamline Antibody Production *Sponsored by* ICOSAGEN

Meelis Kadaja, Ph.D., MBA, Director, Business Development, Icosagen Technologies Inc.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Engineering Multivalent and Bispecific Death Receptor Agonists for Cancer Therapy

Eric Tam, Ph.D., Principal Scientist, Antibody Engineering, Merrimack Pharmaceuticals, Inc.

4:45 Creating Multivalent Bispecific Antibody Forms through Bio-Conjugation

Julie Q. Hang, Ph.D., Senior Scientist, Protein Chemistry, Genentech

Bio-conjugation of multivalent bispecific Fab arms is achieved with branched PEGs carrying maleimides generated Fab multimers with variable valencies such as tetramers and octamers. The multivalent formats provide unique biological activities from high avidity and dosing options of two bispecific arms at variable ratios. The branched PEG had no interference on the activities of the multivalent bispecific Fabs. Case examples of multivalent bispecific generation and activity assessment are explored.

5:15 Antibody Based Nucleic Acid Delivery Vehicles

Ulrich Brinkmann, Ph.D., Expert Scientist, Pharma Research & Early Development, Roche Innovation Center Munich

Bispecific antibody derivatives can be applied for specific targeting of nucleic acids to and delivery into cells. Targeting of nucleic acids to desired cells can be achieved by 'standard' engineering approaches. Uptake into cells and escape from vesicular compartments is a bottleneck that needs to be overcome to achieve intracellular activity.

5:45 Close of Day

FRIDAY, JANUARY 13

8:00 am Conference Registration and Morning Coffee

PLATFORM INNOVATIONS

8:30 Chairperson's Remarks

Mark Throsby, Ph.D., Executive Vice President & CSO, Merus B.V.

8:35 Novel Bispecific Antibody Constructs for Targeting Tumor-Specific Carbohydrate Antigens

Steffen Goletz, Ph.D., CEO and CSO, Glycotope GmbH

Carbohydrate targeting antibodies have great potential for the generation of bispecific antibodies. As shown for novel glyco-epitope targeting antibodies, carbohydrates on the surface of cancer cells represent promising targets for different approaches like dual-antigen targeting or effector cell recruitment. Tumor specificity and effector functions were shown by immunohistochemistry and antibody-dependent cellular cytotoxicity, respectively. Moreover, several constructs were generated to demonstrate the feasibility of carbohydrates as valuable targets for different bispecific approaches. The antibody constructs were glycooptimized for improvement of effector functions.

9:05 From DART to Trident: Tailoring Bi- or Multispecific Formats and Specificities for Different Therapeutic Modalities

Syd Johnson, Ph.D., Vice President, Antibody Engineering, MacroGenics, Inc.

This presentation will focus on the optimization of bi- and tri-specific formats for research and clinical use. Factors such as affinity, avidity or the valency of the binding domains and how they can influence and be optimized for specific indications will be discussed. Examples will highlight several molecules in the DART or Trident formats to demonstrate the power and flexibility of the platform.

9:35 Utilizing the CrossMAb Engineering Platform to Suit Biological Needs

Jörg Thomas Regula, Ph.D., Head, Functional Characterization, pRED Large Molecule Research, Roche Diagnostics GmbH

The CrossMAb technology (Schäfer, et al., 2011) can be used to generate a bispecific antibody from two independent parental antibodies by immunoglobulin domain exchange. Besides the initial CH1-CL domain exchange, the Vl-Vh domain exchange can be enabled by the exchange of charged amino acids. This CrossMAb engineering toolbox can be used to design bispecific molecules to suit their biological need.

10:05 Coffee Break with a Poster Pavilion *See page 4 for details*

ADVANCING BISPECIFICS INTO THE CLINIC

KEYNOTE PRESENTATION

10:50 BiTE Antibody Constructs for Cancer Therapy

Benno Rattel, Ph.D., Executive Director, Nonclinical Development ARM, AMGEN Research (Munich) Gmbh

Bispecific T-cell engagers, commonly referred to as BiTE® antibody constructs, can transiently link tumor cells with resting polyclonal T-cells for induction of a surface target antigen-dependent re-directed lysis of tumor cells. Blinatumomab (BLINCYTO®) is directed against CD19 and is the first approved T-cell engaging antibody. The nonclinical characterizations of blinatumomab as well as of various BiTE® antibody constructs and their translation into the clinic will be presented.

11:30 Using Multivalent and Multispecific Nanobodies to Create Differentiated Drugs

Antonin De Fougerolles, Ph.D., CSO, Ablynx NV

This presentation will provide an outline of our Nanobody® platform, and how the flexibility of Nanobody formatting can be used to create differentiated drugs. My talk will include examples of multi-specific Nanobody drugs that are in preclinical development and in the clinic.

12:00 pm IT'S A WRAP: PEPTALK 2017 CLOSING PLENARY PANEL DISCUSSION *See page 5 for details*

1:15 Close of Conference

Optimizing Biologics Formulation Development

Formulation Strategies in an Era of Accelerated Timelines, New Product Formats and Novel Delivery Systems

Each year, the PepTalk Optimizing Biologics Formulation Development meeting brings together an international audience of analytical and formulation scientists from leading industry companies to hear solutions to the most significant challenges in their field. For 2017, the conference focuses on the science and strategies of formulation development in an era of compressed timelines, novel molecular and product formats and products based on novel device and packaging systems.

SUNDAY, JANUARY 8

4:00 - 5:30 pm Registration

5:00 - 8:00 Dinner Short Courses *See pages 6-7 for details*

MONDAY, JANUARY 9

7:30 am Conference Registration and Morning Coffee

9:00 Welcome by Conference Organizer

Kent Simmons, Senior Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks

Murali Bilikallahalli, Ph.D., Associate Director, Vaccines & Biologics, MedImmune LLC

KEYNOTE PRESENTATION

9:10 Formulation Development in the Rapidly Evolving Biotechnology Environment

Nicholas Warne, Ph.D., Senior Director, Pharmaceutical R&D, BioTherapeutics Pharmaceutical Sciences, Pfizer

Formulation development of biologics is evolving rapidly. While teams seek efficient approaches to screening compounds to assess developability, the increased complexity of biologics is demanding innovative approaches to formulation and dosage form development. It is critical to make 'simple things simple' and streamline efforts on monoclonal antibodies amenable to platform approaches. This efficiency creates capacity for challenging multi-antigenic vaccines, enzymes, and novel modalities such as gene and cell based therapies.

EARLY STAGE MOLECULAR ASSESSMENT

9:50 Techniques and Strategies for Evaluating Developability of Novel Modalities

Francis Kinderman, Ph.D., Senior Scientist, Drug Product and Formulation Technologies, Amgen

Novel therapeutic modalities present new challenges for drug development. New techniques and additional characterization are required for such products due to unique product quality attributes and poor platform fits. Early characterization of attributes and exploration of formulation space are crucial to improve the understanding of newly engineered molecules and to screen for candidates with the best potential to fulfill the intended target product profile.

10:20 Coffee Break

FORMULATION IMPACTS OF PRODUCT AND DOSAGE FORM DESIGN

10:45 Patient Centricity and System Integration as New Drivers of Biologic Drug Product Design Strategy

Didier Pertuy, Vice President, Global Drug Device Integrated Development, Sanofi

Health ecosystem evolution and the rise of chronic treatments are shifting customer decision power from physicians to patients and payers. In parallel, the technology demand for self-administrated injectable Drug Device Combinations, which are complex integrated systems, is increasing significantly with emerging penetration of the digital ecosystem into the drug delivery world. These trends make patient-centricity and system integration two key drivers of Biologic Drug Product design.

11:15 Early Device and Container Closure System Evaluation

Adam McCullough, Principal Engineer, Advanced Device Technologies, Amgen

Early identification of risks enables focused evaluation of 'devicibility' and 'show-stoppers' early in the assessment process. Factors such as user needs, drug product compatibility, container closure integrity, particulate risks, development status, and fit to manufacturing network are important to consider before committing significant resources to new biologics delivery platforms. Some underlying principles around design space consideration and case studies will be included in this presentation.

11:45 Overcoming the Challenges in Developing Multi-Dose Formulations of Aggregation-Prone Peptides

Jingtao Zhang, Ph.D., Principal Scientist, Pharmaceutical Sciences, Merck Research Laboratories

Preservatives needed in multi-dose peptide formulations can greatly increase stability risks and can frequently cause compatibility concerns. This talk will discuss these challenges, present state-of-the-art understandings in peptide formulation, and highlight several strategies in overcoming the challenges. The unique aspect of formulation development experiences in the talk could be highly applicable to other biologicals that may require preservatives or stabilizers.

Sponsored by UNCHAINED LABS

12:15 pm Meet Our UNcle: The All-in-One Biologics Stability Platform

Speaker to be Announced

Characterizing biologic stability is a wrestling match with disjointed data from sub-optimized tools. Not anymore. UNcle combines fluorescence, SLS, and DLS reads in one instrument. This allows you to quickly and efficiently characterize all the size, aggregation, thermal ramp, isothermal and viscosity information you want.

12:45 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

Optimizing Biologics Formulation Development

Formulation Strategies in an Era of Accelerated Timelines, New Product Formats and Novel Delivery Systems

FORMULATION DEVELOPMENT FOR NOVEL MODALITIES

2:00 Chairperson's Remarks
Krishnan Sampath, Ph.D., Senior Director, Drug Product Sciences, MacroGenics, Inc.

2:05 Pushing Formulation Development into Discovery through Antibody Design and High-Throughput Screening
Bruce Kerwin, Ph.D., Vice President, Drug Product Design, Just Biotherapeutics
The stability of the protein is considered in the context of drug development as a whole from inception of the biopharmaceutical to understanding the needs of the patient and commercialization which then defines strategies for stabilization, concentration and delivery. This talk will focus on an integrated approach to drug product design encompassing *in silico* tools, high throughput screening and development of predictive tools that can integrate with the commercialization process.

2:35 Formulation Development for Dual Affinity Antibody-Based Molecules
Krishnan Sampath, Ph.D., Senior Director, Drug Product Sciences, MacroGenics, Inc.
Dual-Affinity Re-Targeting (DART) are antibody-based molecules designed to simultaneously bind to two or more targets. These versatile molecules have the potential for improved safety profile through enhanced selectivity and recruitment of specialized effector cells. Some of these DARTs pose formulation and process challenges related to self-association properties of the molecules. The presentation will discuss the formulation and process development strategy using this novel class of molecules as a case study.

3:05 Presentation to be Announced
Sponsored by FUJIFILM Diosynth biotechnologies

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Development of Coformulated Protein Biologics
Murali Bilikallahalli, Ph.D., Associate Director, Vaccines & Biologics, MedImmune LLC
Having a two or more therapeutic proteins in a single drug product has several advantages for oncology and infectious diseases therapeutics area. Advantages may include patient compliance, cost reductions, market capture and differentiation. This talk will highlight the challenges involved in developing such combination drug products.

4:30 Development of Formulations Containing Monoclonal Antibodies and Recombinant Hyaluronidase (rHuPH20)
Claudia Mueller, Ph.D., Senior Scientist, Late-Stage Pharmaceutical and Processing Development, Pharmaceutical Development & Supplies, F. Hoffmann-La Roche Ltd.
Subcutaneous application faces limitations regarding the drug volume to be administered. Potential strategies to enable delivery of the necessary doses are increase in drug concentration and/or temporary enlargement of the interstitial space at the injection site, e.g. by using rHuPH20. The presentation focuses on challenges for product development arising from combination of two proteins, rHuPH20 and a mAb, in order to maintain both stability and activity in a single formulation.

5:00 Formulation Development for Novel Antibody Drug Conjugates
Mike Fleming, Scientist, Analytical and Pharmaceutical Sciences, ImmunoGen, Inc.
Antibody-drug conjugate (ADC) formulation development can be particularly challenging, not only due to the complexity and heterogeneity of the product, but also due to potential changes in higher order structure of the monoclonal antibody (mAb) component that can occur during the conjugation process. Conjugation of hydrophobic compounds to mAbs also adds to these challenges. This presentation will address several case studies where these formulation challenges have been addressed.

5:35 BuzZ Session A
Join your peers and colleagues for interactive roundtable discussions.
Please see page 74 for additional information.

6:20-7:30 Welcome Reception in the Exhibit Hall with Poster Viewing

7:30 Close of Day

TUESDAY, JANUARY 10

8:00 am Conference Registration and Morning Coffee

INNOVATION

8:30 Chairperson's Remarks
John Wang, Ph.D., FAAPS, Principal Scientist, Genentech

8:35 Evaluation of Emerging Analytical Method and Instrument Combinations
Steve LaBrenz, Ph.D., Scientific Director, Janssen R&D LLC
Multi-sample/multi-assay devices may introduce bias into experimental results that are not analyzed in an orthogonal manner, on a different instrument. Complications with each sample may affect the results on one detector, but are either overlooked or unaccounted for in a separate detector leading to potential errant results? Incorporation of results between multiple instruments may alleviate single instrument bias and provide necessary data that demonstrates where to avoid errant results, improving experimental outcomes.

9:05 New Grade of Polysorbate to Overcome Particle Formation
John Wang, Ph.D., FAAPS, Principal Scientist, Genentech
It has been shown that residual enzymes, present in drug substance in minute quantity, are capable of degrading polysorbate 20 and 80 in drug products and subsequently generate subvisible and visible particles. A new grade of polysorbate 20 that is composed of >98% lauric ester was evaluated and found to generate no particle upon enzyme hydrolysis. We proposed to USP to include this material in polysorbate monograph.

Optimizing Biologics Formulation Development

Formulation Strategies in an Era of Accelerated Timelines, New Product Formats and Novel Delivery Systems

CHI-PepTalk.com

Sponsored by BEND RESEARCH

9:35 Spray Dried Biologics: Formulation Considerations

Michael Burke, Senior Research Chemist, Bend Research

Spray drying is a method for the continuous collection of dry powder. The process is tunable and scalable, which allows for rapid small-scale formulation screening and cGMP manufacture. Key aspects include mild temperature exposures, rapid drying kinetics, and ability to vary particle size, bulk densities, and reconstitution quality. Functional excipients can be added and include high Tg sugars, polymers, amino acids, buffer salts and/or surfactants to enhance selected properties.

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

FORMULATION CHALLENGES DURING CLINICAL DEVELOPMENT

11:00 Clinical Stage Evaluation of a Biologic Formulation Using Novel Robustness Diagrams

Radhakrishna Maroju, Ph.D., Senior Scientist, Drug Product Development and Operations, Teva Biopharmaceuticals

Formulation robustness is critical to ensure product quality and is required to be demonstrated in a marketing application. An effective QbD approach associated with a novel method of displaying robustness will be presented. Termed in context as 'robustness diagrams,' they allow comprehending the acceptable limits of all formulation variables simultaneously at one glance across multiple quality attributes. Such diagrams are handier and would potentially help accelerate the review process.

11:30 In-Use Stability Evaluations for Enabling Low Dose Intravenous Administration

Xiaofeng Lu, Ph.D., Principal Research Scientist, AbbVie Biotherapeutics, Inc.

In-use stability evaluations are performed to assess the effect of dose preparation, handling and administration on product quality attributes. In this presentation, technical and practical challenges encountered in enabling low dose intravenous administration for a bispecific protein will be discussed. A testing approach for robust in-use stability assessment will be recommended.

Sponsored by Albumedix

12:00 pm When Standard Formulation Strategies Fail - Recombinant Albumin for Stabilization of Hard-to-Formulate Biotherapeutics

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

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

12:30 Session Break

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

1:15 Close of Conference

Lyophilization and Emerging Drying Technologies

Formulation and Process Optimization, QbD, Process and Scale-Up Challenges

The popular Tenth Annual Lyophilization and Emerging Drying Technologies conference covers latest trends and challenges in lyophilization and emerging drying technologies. This conference features in-depth case studies, new and unpublished data and discussions on developing scientifically sound formulation, process optimization for biologics and vaccines. It also presents cutting-edge research and case studies on freeze/thaw and formulation challenges, storage stability, particulates issues, QbD and PAT approaches and strategies for scale-up from R&D scale to full production level, and selection of container closure systems.

TUESDAY, JANUARY 10

1:00 pm Conference Registration

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

QbD, PAT, PROCESS SCALE-UP AND TECH TRANSFER

2:00 Chairperson's Opening Remarks

Serguei Tchessalov, Ph.D., Associate Research Fellow, Bio Therapeutics R&D, Pfizer

KEYNOTE PRESENTATIONS

2:05 Resolving Scale-Up Problems in Freeze Drying: Differences in Dry Layer Resistance and in Effective Vial Heat Transfer Coefficients

Michael Pikal, Ph.D., Distinguished Endowed Chair in Pharmaceutical Technology & Professor, Department of Pharmaceutics, University of Connecticut

The two major scale-up problems associated with primary drying originate because of differences in ice nucleation temperature, thereby causing differences in mass transfer through the dry layer, and in vial heat transfer coefficients, causing differences in heat input. Here we present theoretical results and both laboratory and manufacturing data that address these differences and also outline procedures by which one can make adjustments to laboratory results for application to production.

2:35 An Industry Prospective on Application of Modeling to Lyophilization Process Scale-Up and Transfer

Serguei Tchessalov, Ph.D., Associate Research Fellow, Bio Therapeutics R&D, Pfizer

For many years, lyophilization process transfer and scale-up was a *trial-and-error* exercise. This talk will focus on an assessment of the current state of lyophilization process modeling and its role in efficient cycle transfer and scale-up. The assessment is based on combined experience of a few pharmaceutical companies that are collaborating on developing a harmonized approach to scale-up and tech transfer. The talk will also share the industry outlook on future strategies towards efficient and cost-effective implementation of commercial processes.

3:00 Influence of Process Conditions on Spatial Distribution of Individual Vial Heat Transfer Coefficients

Lindsay Wegiel, Ph.D., Research Scientist I, Pharmaceutical Development, Baxter

Kv is typically determined as an average value for a whole shelf of vials. This study has determined that there is a large range of Kv values depending on the vials placement on the shelf. The spatial distribution of Kv was influenced by the process conditions (chamber pressure and shelf temperature). In some cases the range of Kv values was minimal; however, other instances led to a wide range of Kv values.

Sponsored by MILLROCK TECHNOLOGY

3:15 New Methods and Simple Approaches for Cycle Optimization & Transfer

T.N. Thompson, President, Millrock Technology, Inc.

The use of the unique product temperature control system, AutoDry, and its importance for cycle optimization through maximum heat input will be discussed. The use of LyoPAT II and the direct measurement of Kv for cycle transfer is illustrated along with LyoSim, a freeze dryer simulator.

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

4:30 New Case Studies and Strategies for Manufacturing, Scale-Up and Tech Transfer

Alexander P. Herbert, Senior Process Engineer, Process Engineering and Pilot Plant, West-Ward Pharmaceuticals

Scaling and transfer is the most challenging step of process development, and success is firmly reliant both on strong experimental design principles and thorough understanding of equipment capabilities. This presentation will cover many important facets of scaling and transfer of lyophilization processes through case studies of two peptide product formulations.

5:00 Innovative Approaches for Lyophilization Process, Equipment and Drug Product Characterization

Ahmad M. Abdul-Fattah, Ph.D., Senior Scientist, Lyophilization Unit, Coriolis Pharma

Heat flux sensors are non-invasive alternatives to thermocouples and represent a promising PAT tool for lyophilization process monitoring, characterization and process control. We will shed light on some applications of this new tool for process characterization during and primary drying. On a different note, we will present some applications of headspace moisture analysis as a non-invasive high-throughput method for product, process and equipment characterization.

5:30 Close of Day

5:30 - 5:45 Short Course Registration
5:45 - 8:45 Dinner Short Courses* ***See pages 6-7 for details***
**** Separate registration required***

Lyophilization and Emerging Drying Technologies

Formulation and Process Optimization, QbD, Process and Scale-Up Challenges

WEDNESDAY, JANUARY 11

8:00 am Conference Registration and Morning Coffee

ROLE OF WATER AND ICE

8:30 Chairperson's Remarks

Bradley D. Anderson, Ph.D., Professor, Pharmaceutical Sciences, University of Kentucky

8:35 Role of Water in Chemical Instability of Freeze-Dried Proteins: Plasticization vs. Water Catalysis

Evgenyi Shalaev, Ph.D., Research Investigator, Pharmaceutical Development, Allergan

Water is a major factor which influences stability of lyophilized proteins. In this presentation, water's role in chemical instability of freeze-dried formulations is reconsidered, based on the analysis of specific chemical processes, i.e., amide hydrolysis and deamidation reactions. Water catalysis probably plays a major role in these reactions, whereas contribution from plasticization and molecular mobility enhancement is minor.

9:05 Mobility and Water Dependent Chemical Reaction Pathways in Lyophilized Formulations of Peptides and Proteins

Bradley D. Anderson, Ph.D., Professor, Pharmaceutical Sciences, University of Kentucky

This presentation focuses on chemical reactions of lyophilized peptides and proteins at particular "hot spots" (e.g., asparagine and cysteine residues). Molecular mobility/heterogeneous relaxation and the distribution of the drug, water, and excipients play a critical role in amorphous solid-state reactions. The multi-step nature of most peptide/protein reactions requires that one identify the rate-determining step and reactive intermediates in order to predict the rate of degradation and reaction products. Shifts in the dominant pathway often occur in response to differences in water content, reactant mobility, and proximity of reactant molecules.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

10:50 Optimization of a Low-Volume Resuscitation Fluid Formulation to Treat Hemorrhagic Shock

Raj Suryanarayanan, Ph.D., Professor, Peters Endowed Chair, Department of Pharmaceutics, University of Minnesota

A combination of melatonin (M) and D-ß-hydroxybutyrate (BHB) increases survival in animal hemorrhagic shock models. To achieve adequate melatonin solubility, the current BHB/M formulation contains 20% v/v dimethylsulfoxide (DMSO). Our objectives were to: 1) formulate a novel BHB/M, solid dosage form which can be readily and rapidly reconstituted into an aqueous solution, and 2) evaluate the efficacy of the formulation in a rat hemorrhagic shock model. Lyophilized BHB/M formulation showed adequate drug solubility and the cycle was optimized to generate an elegant, readily reconstitutable formulation.

MODELS AND TOOLS

11:15 Benchtop Methods for Predicting Stability of Freeze-Dried Proteins

Marcus T. Cicerone, Ph.D., Biomaterials Group, National Institute of Standards and Technology

The basic physics governing stabilization in the dry state is only now beginning to be understood, but reliable and accessible methods for measuring these processes have not been developed. As a consequence, engineering of the dried sugar formulations is currently based on a combination of weakly predictive metrics and long-term stabilization studies, leading to a situation in which there is much time and effort expended in finding optimal formulations. I will present bench-top methods for measuring the picosecond and nanosecond timescale dynamic processes that facilitate degradation of proteins in solid form.

11:40 Modeling the Secondary Drying Stage of Freeze Drying: Development and Validation of an Excel-Based Model

Ekneet Sahni, Ph.D., Senior Process Development Engineer, Manufacturing Science and Technology (MSAT), Pfizer

The purpose of this work is to develop and validate a simplified Excel-based secondary drying model that could aid in optimization of lyophilization processes minimizing the cycle development time. Comparisons were made between the Excel calculations and the experiments conducted using sucrose at different processing conditions. Agreement was satisfactory, being quantitative in most cases. Future studies will involve model validation for representative amorphous as well as partial-crystalline protein based formulations.

12:00 Lyophilizer Sublimation and Heat Transfer Modelling – Building Comparability and Scalability Models for Bioproducts – An Industrial Case Study

Timothy R. McCoy, MSc, Principal Scientist, Technical Development, Sanofi Ireland

12:20 pm Sponsored Presentation *(Opportunity Available)*

12:50 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

CRITICAL CONSIDERATIONS IN PRODUCT DEVELOPMENT: FORMULATION, STABILITY, PARTICLES AND PACKAGING

2:00 Chairperson's Remarks

Wendy Saffell-Clemmer, MS, Director, Research, Pharmaceutical Development, Baxter Healthcare

Lyophilization and Emerging Drying Technologies

Formulation and Process Optimization, QbD, Process and Scale-Up Challenges

2:05 Selection of Pre-Filled Syringe for Biologic Products on Particulate Matter and Product Stability – A Case Study

Wendy Saffell-Clemmer, MS, Director, Research, Pharmaceutical Development, Baxter Healthcare

Pre-filled syringes provide significant advantages to the clinician and the patient. However, the pre-filled syringe and syringe filling process can have a significant impact on particulate formation and product stability. Methodical laboratory studies on the formulation are needed to understand potential causes of particle formation. A case study describing development of a liquid monoclonal antibody pre-filled syringe product will be presented along with a discussion of manufacturing scale-up challenges.

2:35 Developing a Multi-Pronged Approach to the Identification of PS20 Degradation Mechanism

Anthony Tomlinson, Senior Research Associate, Late Stage Pharmaceutical Development, Genentech

Polysorbates are commonly used non-ionic surfactants in protein pharmaceuticals. In recent years, there has been increasing concern in the degradation of these materials on long-term stability and the subsequent increase of insoluble degradation products. In this talk, we will discuss the detection of PS20 degradation products and the identification of the mechanism of degradation for root cause analysis.

3:05 Subvisible Particles: Rapid and High-Throughput Tools for Prediction, Detection and Characterization of Subvisible Particles and Other Aggregates

Andrea Hawe, Ph.D., CSO, Coriolis Pharma

Aggregates and subvisible particles (SVP) are considered cQA for biologics, and it is crucial to include a comprehensive characterization early during drug product development. Especially, for early development a reduction of required time, material and resources is essential. Within the talk, an overview of methods and strategies for SVP and aggregate analysis is given, with special focus on minimization of material requirements, increase in throughput and possibilities for prediction of stability.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:30 Prediction of Antibody Stability in Lyophilized Solids by Hydrogen Deuterium Exchange with Mass Spectrometric Analysis (HX-MS)

Kathleen Abadie, Engineer I, Late Stage Pharmaceutical Development, Genentech

We explore HX-MS to study protein structure in lyophilized solids for deeper understanding of solid state stability and to save time and resources in pharmaceutical development. HX probes structure by measuring the frequency of stabilizing amide H-bonds. Indeed, we show that reduced stability as indicated by increased deuterium uptake versus time correlates with increased aggregation propensity. Stability effects of lyoprotectant concentration and processing conditions are assessed by HX-MS.

5:00 Scaled Down Containers for Protein Stability Studies

Eric Meinke, Ph.D., Senior Scientist, AstraZeneca Supply Biologics

Real-time, real-condition stability study is essential to establish the expiry of biological therapeutics. For drug substances, stability study is typically performed in small scale containers that mimic the actual storage container/condition at scale. A case study will be presented to highlight the criticality of understanding and controlling of the scaled down container for stability studies.

5:35 BuzZ Session B

Join your peers and colleagues for interactive roundtable discussions.

Please see page 74 for additional information.

6:20-7:20 Reception in the Exhibit Hall with Poster Viewing

7:20 Close of Conference

Protein Aggregation and Emerging Analytical Tools

Mechanism, Prediction, Screening, Immunogenicity and Formulation Challenges

The popular Protein Aggregation and Emerging Analytical Tools conference covers latest trends, challenges and solutions in understanding, characterization and mitigation of problems generated by protein aggregation. It features in-depth case studies, new and unpublished data and interactive discussions on mechanisms of aggregation, new tools for detection and quantitation of aggregates, and how the data are used in regulatory filings. It also discusses mechanistic understanding of protein aggregation and presents case studies on prevention of particle formation by engineering and formulation approaches, impact of aggregation on production, aggregates as a factor for immunogenicity, and approaches for improvement of biophysical properties of protein solutions.

THURSDAY, JANUARY 12

7:45 am Conference Registration and Morning Coffee

UNDERSTANDING AND CONTROLLING PROTEIN AGGREGATION DURING PATIENT HANDLING AND USE

8:15 Chairperson's Opening Remarks

Peter Tessier, Ph.D., Department of Chemical & Biological Engineering, Center for Biotechnology and Interdisciplinary Studies, Rensselaer Polytechnic Institute

KEYNOTE PRESENTATION

8:20 Mishandling of Therapeutic Protein Products by End Users: Particle Formation and Potential Roles in Adverse Immunogenicity

John F. Carpenter, Ph.D., Professor, Pharmaceutical Sciences; Co-Director, Center for Pharmaceutical Biotechnology, University of Colorado Anschutz Medical Center

Subvisible particles can cause adverse immunogenicity, resulting in loss of efficacy of therapeutic proteins in patients. Companies work diligently to control particle levels in products. However, patients can receive high levels of particles due to product mishandling by end users. Mishandling includes exposure of prefilled syringes to temperature extremes, transport of IV bags through pneumatic tube systems in hospitals and repackaging of vialed Avastin into syringes for off-label intraocular use.

9:00 Towards Particle and Silicon-Free Protein Drug Products

Gerhard Winter, Ph.D., Professor, Chair, Pharmaceutical Technology and Biopharmaceutics, LMU Munchen

A more wide-spread bedside filtration and the use of silicon oil free polymer syringes could reduce the amount of particles and silicon oil droplets eventually injected into patients with protein drug products. A critical view on the performance and on open questions associated with the use of the two measures is presented. The quality of filters and the resolution of the oxygen permeability of plastic material are studied in detail.

PREVENTION AND CONTROL OF PROTEIN AGGREGATION

9:30 Understanding and Overcoming Tradeoffs between Antibody Affinity, Specificity and Stability

Peter Tessier, Ph.D., Department of Chemical & Biological Engineering, Center for Biotechnology and Interdisciplinary Studies, Rensselaer Polytechnic Institute

There are many challenges associated with the discovery and development of potent and stable antibody therapeutics. Our lab is addressing some of these challenges, including the design and evolution of antibodies with high affinity, specificity, stability and solubility. We will discuss our findings related to common tradeoffs between these antibody properties as well as directed evolution methods for overcoming these tradeoffs.

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

11:00 Applications of Fluorescence-Detected Analytical Ultracentrifugation (AU-FDS) to High-Concentration Antibody Interactions

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

AU-FDS may be used to characterize the size distributions of antibody complexes. Results will be shown for several systems such as participation of a "foreign" antibody in the self-association complexes of mAb, weak interaction of poly-IgG with mAbs, presence of non-reactive antigen in a poly-IgG binding assay, existence of species cross-reaction in a poly-IgG prep and characterization of Ab:Ag lattice formation 'overshoot' kinetics. Also, it can be used to study that the size distribution of Ab:Ag complexes differ in buffer and serum and how AU-FDS uniquely detects large complexes in patient serum.

11:30 Sponsored Presentation *(Opportunity Available)*

12:00 pm Session Break

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

1:15 Ice Cream Break in the Exhibit Hall with Poster Viewing

PREVENTION AND CONTROL OF PROTEIN AGGREGATION (CONT.)

2:00 Chairperson's Remarks

Jan Jezek, Ph.D., CSO, Research & Development, Arecor, Ltd.

2:05 Control of Protein Aggregation by Unconventional Formulation Parameters

Jan Jezek, Ph.D., CSO, Research & Development, Arecor, Ltd.

A number of formulation parameters, such as pH, ionic strength or surfactant, are traditionally optimized to minimize protein aggregation. The talk will show how unconventional parameters of formulation excipients can be exploited to control aggregation and enable products to be used outside the cold chain. This will be demonstrated on several data driven case studies using relevant therapeutic proteins, describing the specific formulation features employed to achieve superior stability.

Protein Aggregation and Emerging Analytical Tools

Mechanism, Prediction, Screening, Immunogenicity and Formulation Challenges

2:35 Optimizing Protein Stability through Integration of Cutting-Edge Analytical Tools with Rational, Molecule-Specific Approach to Process and Formulation Development

Danny K. Chou, Pharm.D., Ph.D., President and Founder, Compassion BioSolution; Former Senior Research Scientist, Biologics Development, Gilead Sciences

We are at the dawn of a new era with the emergence of new analytical tools that can enable both prediction and real-time monitoring of protein stability. The author will use real case studies to illustrate how to properly combine some of these new tools with tried and true strategies that incorporate the key factors/forces that impact physical stability (with focus on protein aggregation) of proteins in solution. Emphasis will be placed on high throughput, low sample volume strategies that are useful for industrial application.

3:05 Sponsored Presentation *(Opportunity Available)*

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Impact of Interfacial Interactions on the Formation of Particles, Aggregation of Proteins, and Their Prevention: Role of Surface Energetics and Their Application to Container Compatibility and Protein Purification

Jinjiang Li, Ph.D., Senior Principal Scientist, Drug Product Science & Technology, Bristol-Myers Squibb Co.

This talk will discuss the effect of surface energetics on protein adsorption, formation of aggregates, and particle formation, with/without surfactants. Common surfaces encountered in protein purification and storage will be used as examples. Surface energetics were characterized through measuring contact angles. Adsorption of proteins like lyozyme was measured using QCM-D. Particles formed were determined using MFI. For all cases, the protection role of PS 80 and Poloxamer was examined.

4:45 BREAKOUT DISCUSSIONS:

Topic 1: Innovation in Formulation – Novel Approaches versus Established Platforms

Moderator: Jan Jezek, Ph.D., CSO, Research & Development, Arecor, Ltd.

Topic 2: *In silico* Tools for Predicting Biotherapeutic Aggregation

Moderator: Russ Lehrman, Ph.D., President/Founder, R&D Consultation, BioSuperior Technology

Topic 3: Applications of AU-FDS to High-Concentration Antibody Interactions

Moderator: Thomas Laue, Ph.D., Professor, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire

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5:15 End of Breakout Discussions and Discussion Report Out

5:45 Close of Day

FRIDAY, JANUARY 13

8:00 am Conference Registration and Morning Coffee

RAPID TOOLS FOR PREDICTION, MEASUREMENT OF AGGREGATION, VISCOSITY AND STABILITY

8:30 Chairperson's Remarks

Danny K. Chou, Pharm.D., Ph.D., President and Founder, Compassion BioSolution; Former Senior Research Scientist, Biologics Development, Gilead Sciences

8:35 Application of *in silico* Predictions to the Mitigation of Biotherapeutic Aggregation

Russ Lehrman, Ph.D., President/Founder, R&D Consultation, BioSuperior Technology

Aggregation of biotherapeutic candidates affects drug safety, efficacy, and manufacturability. This degradation pathway occurs largely due to the presence of aggregation prone regions (APRs). Computer tools that identify APRs are available, but since each program is based on different properties, they often detect distinct protein regions. Effective use of these tools depends on an understanding of protein structure and aggregation mechanisms. Case studies that help demonstrate how to effectively use these programs for the identification of APRs will be presented.

9:05 A Rapid Real-Time Biosensor to Detect Preaggregates and Screen Formulations of Therapeutic Proteins

Subhashchandra Naik, Ph.D., Postdoctoral Researcher, Chemical and Biomolecular Engineering, University of Delaware

A biosensor for monitoring the structural integrity and physical stability of therapeutic proteins was developed by combining a bacterial protein GroEL with real-time biolayer interferometry. This biosensor detects structurally altered pre-aggregates within a minute in real-time, is sample sparing and is non-destructive. The data was supported and validated by orthogonal biophysical techniques. The biosensor can also be used to screen for formulations/excipients that stabilize proteins and suppress aggregate formation.

9:35 Integrating Novel Tools into Development Workflow of Biologics: nanoDSF and MST for Discovery, Development and QC

Alexey Rak, Ph.D., Director, Bio Structure & Biophysics, Sanofi R&D

Biophysical approaches are routinely used to assess biologics activities, stability and quality. Modern drug discovery operations require characterization of biomolecular interactions to be both time- and cost-effective as well as to be highly precise and reproducible. Here we report applications of two novel methods, nano-Differential Scanning Fluorimetry (nanoDSF) and MicroScale Thermophoresis (MST), that we are applying in our biologics discovery and characterization operations. The examples of the demonstrated effectiveness of the nanoDSF and MST will be presented and discussed.

10:05 Coffee Break with a Poster Pavilion *See page 4 for details*

Protein Aggregation and Emerging Analytical Tools

Mechanism, Prediction, Screening, Immunogenicity and Formulation Challenges

11:00 Advancements and Comparability Assessments of Amgen Automated Visual Inspection System for Therapeutic Molecules

David Le, MSc, Scientist, Drug Product Technologies, Amgen

Administration of therapeutic monoclonal antibodies through intravenous route involves dilution of drug product using intravenous infusion solutions such as saline or 5% dextrose. As a result, the original drug product is diluted, which will potentially change physical and chemical stability of the API. This presentation will discuss structural characterization, protein-protein interaction, concentration dependent aggregation, and methods to monitor time-dependent self-association in intravenous infusion solutions containing therapeutic antibodies.

11:30 Detection and Mitigation of Antibody Aggregation in Intravenous Infusion Solutions

Yin Lai, Ph.D., Senior Scientist, Formulation Development, Eli Lilly and Company

Administration of therapeutic monoclonal antibodies through intravenous route involves dilution of drug product using intravenous infusion solutions such as saline or 5% dextrose. As a result, the original drug product is diluted, which will potentially change physical and chemical stability of the API. This presentation will discuss structural characterization, protein-protein interaction, concentration dependent aggregation, and methods to monitor time-dependent self-association in intravenous infusion solutions containing therapeutic antibodies.

12:00 pm IT'S A WRAP: PEPTALK 2017 CLOSING PLENARY PANEL DISCUSSION *See page 5 for details*

1:15 Close of Conference

Engineering Genes and Hosts

Strategies in Systems and Synthetic Biology

Engineering therapeutic protein expression platforms is not for the faint of heart. Many variables 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. When challenges arise, protein expression engineers must design new cloning schemes by altering the DNA or amino acid sequence, moving a gene from one vector to another, transfecting the vector to an alternative host, re-selecting the clone, re-characterizing the expressed protein or any of the above – a laborious, time-consuming and expensive process.

Cambridge Healthtech Institute's Ninth Annual Engineering Genes and Hosts 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 8

4:00 - 5:30 pm Registration

5:00 - 8:00 Dinner Short Courses *See pages 6-7 for details*

MONDAY, JANUARY 9

7:30 am Conference Registration and Morning Coffee

SYSTEMS AND SYNTHETIC BIOLOGY

9:00 Welcome by Conference Organizer

Mary Ann Brown, Executive Director, Conferences & Team Lead, PepTalk, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks

Henry C. Chiou, Ph.D., Associate Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific

KEYNOTE PRESENTATION

9:10 Systems Engineering as a Strategy for Developing New Therapeutics against Infectious Diseases and Cancers

Nitin S. Baliga, MSc, Ph.D., Professor, Senior Vice President & Director, Institute for Systems Biology

Disease is manifestation of dysfunction in complex cellular and molecular networks. A systems approach is necessary to elucidate causal and mechanistic underpinnings of dysfunctional biological networks. I discuss how we use a systems approach to elucidate dysfunctional networks in human and microbial systems, and how that understanding is being used to discover new personalized therapies in brain cancer and fight drug tolerance in TB.

9:50 High-Throughput Multiplexed Genome Editing: Forgecraft

Eileen Spindler, Ph.D., Director, R&D Innovation, MUSE Biotechnology, Inc.

Advances in DNA synthesis and sequencing have motivated increasing efforts to program cells on laboratory timescales. While CRISPR-based methods for genome editing are extremely efficient, strategies for parallel editing throughout a genome have been limited. Here we describe CRISPR EnAbled Trackable genome Engineering (CREATE), a strategy that couples the high efficiency of CRISPR editing with massively parallel oligomer synthesis to perform precise, trackable editing on a genome-wide scale.

10:20 Coffee Break

10:45 Cell-Free Protein Synthesis: A Versatile Enabling Technology for Synthetic Biology

Rui Gan, Ph.D., Research Associate, Michael C. Jewett Laboratory, Chemical and Biological Engineering, Northwestern University

Cell-free protein synthesis (CFPS) has been widely applied to express various proteins due to its high yield and easy manipulation. In synthetic biology, this technology is found to be extremely powerful in directed evolution, metabolism network analysis, genetic circuit construction, and assembly of complex macromolecules. Combined with a microfluidics system, CFPS can be encapsulated into emulsion droplets to perform automatic analysis and evolution of enzymes.

11:15 Reinforcing Synthetic Biology against Evolutionary Failure Modes

Jeffrey E. Barrick, Ph.D., Assistant Professor, Molecular Biosciences, The University of Texas at Austin

Unwanted evolution makes genetic engineering less predictable and reliable. In particular, takeover of cultures by "cheater" cells with mutations that disrupt an engineered function can be a major problem in scaling up processes. I discuss high-throughput methods for profiling these evolutionary failure modes, how computational design can avoid inherently unstable DNA sequences, and the results of using directed evolution to isolate host cells that have lower-than-natural mutation rates.

FEATURED PRESENTATION

11:45 A Semi-Synthetic Organism with an Expanded Genetic Alphabet

Floyd Romesberg, Ph.D., Professor, Chemistry, The Scripps Research Institute

We have developed an unnatural base pair and recently reported its use in *E. coli* to create the first semi-synthetic organism that stores increased genetic information. Recent progress will be discussed that has resulted in a healthy semi-synthetic organism capable of the indefinite storage of multiple unnatural base pair. Progress toward the retrieval of that information via transcription and translation will also be discussed.

Sponsored by SELEXIS

12:15 pm Presentation to be Announced

12:45 Session Break

1:00 Luncheon Presentation: Engineering Biology on DNA, Protein and Genome Level

Sponsored by DNA 2.0

Claes Gustafsson, Co-Founder, CCO, DNA2.0

Modern machine learning combined with efficient gene synthesis allow for unprecedented ability to engineer biological systems at the protein, gene, vector, and genome levels with absolute precision. Transient and stable CHO/HEK protein expression yield is controlled over orders of magnitude by the systematic incorporation of validated sequence elements. The presentation will review how DNA2.0 engineering tools are leveraged for the rapid and efficient production and optimization of biotherapeutics.

GENOME EDITING USING CRISPR/CAS9 TECHNOLOGY

2:00 Chairperson's Remarks

Mark Welch, Ph.D., Vice President, Research and Development, DNA2.0

2:05 Targeted Isolation and Cloning of 100-kb Microbial Genomic Sequences by Cas9-Assisted Targeting of Chromosome Segments

Ting Zhu, Ph.D., Investigator & Associate Professor, School of Life Sciences, Tsinghua University

The cloning of long DNA segments, especially those containing large gene clusters, is of particular importance to synthetic and chemical biology efforts for engineering organisms. We have developed a technique (CATCH) that allows the targeted cloning of near-arbitrary, long bacterial genomic sequences of up to 100 kb to be accomplished in a single step. This technique can be an effective molecular tool for the targeted cloning of large gene clusters.

2:35 CRISPR/Cas9-Mediated Multiplex Genome Editing for Efficient CHO Cell Engineering

Byung-Kwan Cho, Ph.D., Associate Professor, Biological Sciences, Korea Advanced Institute of Science and Technology (KAIST)

Efficient and rational CHO cell engineering methods have been in high demand to improve quality and productivity. Here, we provide a novel genome-engineering platform for increasing desirable phenotypes of CHO cells based upon the integrative protocol of high-throughput RNA sequencing and DNA-free RNA-guided Cas9 (CRISPR-associated protein 9) nuclease-based genome editing.

3:05 Sponsored Presentation *(Opportunity Available)*

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Versatile Genome Engineering via CRISPR-Cas Systems

Ana Moreno, Research Scientist, Bioengineering, University of California, San Diego

Technologies to directly and precisely perturb genomic elements and combinations will be a critical toolset towards obtaining the complete functional annotation of genomic elements and genetic variants at the cellular and whole organism levels, and also to program the genome for medicinal or technological purposes. This talk provides an overview of the rapidly developing CRISPR-Cas genome engineering toolset, with a specific focus on therapeutic applications.

4:30 A High-Throughput Method for Parsing Complex DNA Libraries and Engineering Yeast

Robert St. Onge, Ph.D., Senior Research Scientist, Stanford Genome Technology Center, Stanford University

We have developed an inexpensive, high-throughput method for parsing and sequence-verification of array-synthesized oligonucleotide libraries, and are using it to produce DNA probes for molecular detection, guide RNAs for CRISPR/Cas9-based genome editing and programmable transcription, and building blocks for gene synthesis. The method allowed rapid creation of ~9,000 individually accessible CRISPR interference strains for the essential yeast genome. Applications for host and genome engineering will be presented.

5:00 CRISPR-Cas9 Tools for the Baculovirus-Insect Cell System

Hideaki Mabashi-Asazuma, Ph.D., Research Scientist, Molecular Biology, University of Wyoming

This study examines the utility of previously and newly identified insect U6 promoters for CRISPR-Cas editing of insect cell lines used as hosts for baculovirus vectors. We discovered surprisingly tight cross-species restrictions, which dictated the utility of different insect U6 promoters for CRISPR-Cas editing in different insect species. Ultimately, we identified efficacious U6 promoters for each host and a novel lepidopteran insect-specific sequence element required for optimal U6 promoter function.

5:35 BuzZ Session A

Join your peers and colleagues for interactive roundtable discussions.

Please see page 74 for additional information.

6:20-7:30 Welcome Reception in the Exhibit Hall with Poster Viewing

7:30 Close of Day

TUESDAY, JANUARY 10

8:00 am Conference Registration and Morning Coffee

CASE STUDIES: CELL LINE ENGINEERING

8:30 Chairperson's Remarks

James Brady, Ph.D., Director, Technical Applications, MaxCyte, Inc.

8:35 Engineering Mammalian Cells for Desired Bioprocess and Protein Quality Attributes

Nathan E. Lewis, Ph.D., Assistant Professor, Pediatrics, University of California, San Diego

In mammalian bioprocessing, product quality can vary widely, given the diverse nature of cells, even in seemingly clonal populations. Genomic and computational tools now allow us to understand mammalian host cells, and powerful genome editing systems allow us to engineer desired traits. I discuss efforts in which we have used systems biology techniques to design host cells to control glycosylation, protein yields and improved bioprocess traits.

9:05 Engineering Recombinant mRNAs for Increased Protein Expression, Better Secretion, and Improved Cell Physiology
Vincent P. Mauro, Ph.D., CSO & Senior Vice President, Promosome, LLC
Expression of a recombinant mRNA, e.g., in cell culture for bioproduction or *in vivo* for nucleic acid therapeutics and vaccines, is often limited by specific features of the mRNA that can decrease translation efficiency and negatively affect cell physiology. We have developed a method termed RESCUE™ to eliminate these negative features. RESCUE™-based modifications increase protein expression and secretion while minimizing conformational changes that can alter biological activity or cause immunogenicity.

9:35 Sponsored Presentation *(Opportunity Available)*

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

11:00 The IR/MAR Gene Amplification Technology and Recombinant Production
Noriaki Shimizu, Ph.D., Professor, Graduate School of Biosphere Science, Hiroshima University
We found that a plasmid bearing both a mammalian replication initiation region (IR) and a matrix attachment region (MAR) is spontaneously amplified in transfected mammalian cells to thousands of copies per cell in one step. We clarified the amplification mechanism and the amplified structure. We also found several ways that enhance the expression from the amplified genes. Consequently, the technology provides a rapid, easy and efficient platform for recombinant production.

FEATURED PRESENTATION

11:30 Improvements to the Baculovirus-Based Insect Cell Expression System to Enhance Protein Yield and Quality
Dominic Esposito, Ph.D., Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research, Leidos Biomedical Research, Inc.
In our lab, insect cell systems have been vital for production of post-translationally modified RAS proteins essential for cancer drug discovery. We have developed process and technology improvements which permit increased protein yield, protein quality, and virus stability. We discuss system enhancements and how they can be applied to high-level production of other clinically relevant proteins, and examine ways in which synthetic biology and genome engineering can further enhance the utility of this system.

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

12:30 Session Break

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

1:15 Close of Conference

Recombinant Protein Expression and Production

Achieving Quality and Quantity

Biopharmaceuticals currently represent the fastest-growing sector of the pharmaceutical industry, driven by a rapid expansion in the manufacture of recombinant protein-based drugs. Consequently, the efficient expression and production of these valuable biomolecules face challenges in improving their quantity and quality while minimizing time and cost. To meet these demands, an increasing variety of recombinant production platforms are being developed. 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. To meet the demand, it is crucial to increase the throughput of expression, production and purification processes and systems.

Cambridge Healthtech Institute's 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 10

1:00 pm Conference Registration

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

BIOTHERAPEUTIC EXPRESSION AND PRODUCTION

2:00 Chairperson's Opening Remarks

Donald L. Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming; President, GlycoBac, LLC

KEYNOTE PRESENTATION

2:05 High-Throughput Screening and Selection of Mammalian Cells for Enhanced Protein Production

Michael Betenbaugh, Ph.D., Professor, Chemical & Biomolecular Engineering, Johns Hopkins University

VACCINES

2:45 The Beginning of the End: HIV-1 Vaccine Design and Production

Jiang Zhu, Ph.D., Assistant Professor, Department of Immunology and Microbial Science, Department of Integrative Structural and Computational Biology, Scripps Research Institute

Sponsored by ThermoFisher SCIENTIFIC

3:15 ExpiCHO: Latest Developments in High-Titer Transient Protein Expression in CHO Cells

Jonathan Zmuda, Director, Cell Biology, Thermo Fisher Scientific

The ExpiCHO™ transient expression system offers a turnkey solution for generating high-titer recombinant proteins for therapeutic drug development, reagent generation and hard-to-express proteins and has become an integral part of the transient expression workflow in companies around the world. Here, we share the latest data on the ExpiCHO expression system, tips for obtaining maximal performance and applications data supporting protein purification and characterization as well as protein production up to the multi-liter scale.

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

MEMBRANE PROTEINS

4:30 Strategies for Optimizing GPCR Expression and Production: Multi-Milligram Quantities of Functional Cannabinoid Receptor Isolated by Tandem Affinity Chromatography

Alexei Yeliseev, Ph.D., Staff Scientist, Laboratory of Membrane Biochemistry and Biophysics, NIAAA, NIH

Human cannabinoid receptor CB2, a GPCR, is an important target for pharmaceutical drug development. We expressed the functional CB2 receptor and optimized its purification using novel affinity resins StrepTactin XT and EF2 Ca-calbindin-based resins. Applications of the CDFast chromatographic technique and the results of the SPR binding analysis will be presented as well as examples of selectively stable isotope-labeled CB2 and NMR studies on the agonist- and inverse agonist-bound receptor.

5:00 Production of Chemokine/Chemokine Receptor Complexes for Structural Studies

Martin Gustavsson, Ph.D., Staff Scientist, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego

Chemokine receptors are seven-transmembrane proteins that interact with chemokine ligands to drive cell migration. Despite the development of new methods for expression and purification of seven-transmembrane receptors, production of stable complexes between chemokine receptors and chemokines remains a challenging task. We present methods for producing purified complexes by co-expression in Sf9 cells. These methods have been successfully used for crystallization and biophysical experiments of CC as well as CXC receptor/chemokine complexes.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

5:45 - 8:45 Dinner Short Courses* ***See pages 6-7 for details***

**** Separate registration required***

WEDNESDAY, JANUARY 11

8:00 am Conference Registration and Morning Coffee

BIOTHERAPEUTIC EXPRESSION AND PRODUCTION (CONT.)

ANTIBODIES

8:30 Chairperson's Remarks
Ashok D. Bandaranayake, Ph.D., Director, Bioprocess Development, Peptide Drug Discovery Initiative, Fred Hutchinson Cancer Research Center

8:35 Optimizing Antibody Expression by Using Natural Framework Diversity and Host Engineering in a Live Bacterial Antibody Display System
Noelle Lombana, Ph.D., Senior Scientific Researcher, Antibody Engineering, Genentech
We present insights into a novel bacterial display system using full-length formats for antibody and antigen in a live cell setting. We discuss ways to improve expression and stability of antibodies *in vitro* by mimicking the natural antibody selection process, which translates to a mammalian host, as well as ways to improve antibody expression in host expression strains. We also cover novel use of high-throughput screening to study translocation, stability and protein folding in *E. coli*.

9:05 Rapid Production of Biologics with *Pichia pastoris*
Kerry Routenberg Love, Ph.D., Research Associate & Technical Program Manager, InSCyT Program, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology
Pichia pastoris has demonstrated utility as a host organism, yet relatively little strain engineering has been performed. Here, we present recent results using our genomic and transcriptomic insights to improve cultivation conditions and strain performance during heterologous protein expression. These upstream process developments have enabled the deployment of *Pichia* as the production host in a portable and distributed platform for real-time manufacturing of biologic drugs.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

PEPTIDE AND PROTEIN THERAPEUTICS

10:50 Characteristics and Utility of an Sf-Rhabdovirus-Negative Insect Cell Line for Baculovirus-Mediated Recombinant Protein Production
Donald L. Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming; President, GlycoBac, LLC
Recent work suggests all *Spodoptera frugiperda*-derived insect cell lines are contaminated with an adventitious viral agent, now known as Sf-rhabdovirus. This talk focuses on the characteristics of a novel, Sf-rhabdovirus-negative Sf cell line and its utility as an improved host for recombinant protein production in the baculovirus system.

11:20 A Cell-Free Expression and Purification Platform for Rapid and Flexible Production of Protein Biologics
John Dresios, Ph.D., Chief Scientist and Technical Fellow, Leidos, Inc.
We report on the development of a fluidic process for rapid end-to-end production of recombinant proteins. This process incorporates a bioreactor hosting a cell-free system programmed for transcription/translation of engineered DNA integrated with a series of configurable downstream purification/formulation modules for process-specific isolation of protein targets. Using this approach, we demonstrate production of two bioactive protein therapeutics, each within 24 hours. This process is flexible, scalable and amenable to automation.

11:50 Optides: A Novel Mid-Size Medicine Drug Discovery Platform Based on Knotted Proteins
Ashok D. Bandaranayake, Ph.D., Director, Bioprocess Development, Peptide Drug Discovery Initiative, Fred Hutchinson Cancer Research Center
Knottins are highly disulfide crosslinked peptides associated with the venoms of insects. They inhabit a unique space between antibodies and small molecules but are difficult to make synthetically. We have developed a fully automated mammalian expression platform to generate these molecules as therapeutic leads. We call these optimized peptides Optides, and our first dye-peptide conjugate, Tumor Paint (Blaze Biosciences), is now in multiple clinical trials as a surgical aid for resecting tumors.

12:20 pm Presentation to be Announced

Sponsored by SELEXIS

12:50 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

ENGINEERING AND SELECTING HIGH(ER) PRODUCERS

2:00 Chairperson's Remarks
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

2:05 A Predictable, Plug-and-Play Cell Culture Platform Process
James Lambropoulos, MS, Engineer III, Cell Culture Development, Biogen
We have implemented a defined workflow for early stage clinical cell line development. A meta-analysis of several monoclonal antibody products, in multiple host cell lines, demonstrates predictable trends and correlations amongst growth, metabolite, productivity, and quality attributes. This analysis confirms that our development platform is a robust and reliable workflow for generating representative, high-quality protein material for clinical use, and offers interesting avenues for further refinement of the process.

Recombinant Protein Expression and Production

Achieving Quality and Quantity

2:35 In the Pursuit of High Producers: Use of the Sony SH800 Cell Sorter for the Selection of Cell Lines with Superior Productivity Characteristics

Nadia Amharref, Ph.D., Scientist, Cell Line Development, Vaccine Research Center, National Institute of Allergy and Infectious Diseases, NIH

We are developing a simple method using Fluorescence-Activated Cell Sorting (FACS) for screening high-producing recombinant CHO cell lines. Flow cytometry was partnered with a reporter protein for rapid, early stage identification of clones producing high levels of a therapeutic protein. A cell surface protein is co-expressed, as a reporter, with the therapeutic protein and detected using a fluorescently labeled antibody. The reporter protein's expression level accurately predicts relative expression level of the therapeutic protein for each clone.

3:05 Fast Cell Line Development for CHO Clones with High-Yield Protein Production Using Euchromatin-Containing BAC Expression Vectors

Anton Bauer, Ph.D., COO, The Antibody Lab GmbH

Upon stable cell line generation, chromosomal integration site of the vector DNA has a major impact on transgene expression. By using chromosomal loci in BACs and random integration into host cell chromosomes, we developed stable high-yield production cell lines at an unprecedented speed. We performed several case studies for CHO production clones, and we established for antibodies and even difficult-to-express proteins generation of production clones within three weeks from transfection.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:30 A Method for Specifically Targeting Two Independent Genomic Integration Sites for Co-Expression of Genes in CHO Cells

Joop van den Heuvel, Ph.D., Research Group Leader, Recombinant Protein Expression, Helmholtz Centre for Infection Research

5:00 Engineering Protein Production Hosts

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

We are using the combined competencies of scientific groups working within the areas of metabolic modelling, glycobiology, cell line engineering, high-throughput methodology and genome editing tool development to design and engineer the next generation of recombinant protein production hosts. The most recent results from high-throughput targeted genomic manipulations to engineer cells for tailored and homogenous glycosylation, increased productivity, improved product quality and more robust bioprocesses will be presented.

5:35 BuzZ Session B

Join your peers and colleagues for interactive roundtable discussions.

Please see page 74 for additional information.

6:20-7:20 Reception in the Exhibit Hall with Poster Viewing

7:20 Close of Conference

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. The 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 11

1:00 pm Conference Registration

CELL LINE DEVELOPMENT AND SELECTION

2:00 Chairperson's Remarks

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

2:05 A Predictable, Plug-and-Play Cell Culture Platform Process

James Lambropoulos, MS, Engineer III, Cell Culture Development, Biogen

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3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

CELL LINE ENGINEERING

4:30 A Method for Specifically Targeting Two Independent Genomic Integration Sites for Co-Expression of Genes in CHO Cells

Joop van den Heuvel, Ph.D., Research Group Leader, Recombinant Protein Expression, Helmholtz Centre for Infection Research

5:00 Engineering Protein Production Hosts

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

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5:35 BuzZ Session B

Join your peers and colleagues for interactive roundtable discussions.

Please see page 74 for additional information.

6:20-7:20 Reception in the Exhibit Hall with Poster Viewing

7:20 Close of Day

THURSDAY, JANUARY 12

7:45 am Morning Coffee

ENGINEERING FROM *IN VIVO* TO *IN SILICO*

8:15 Chairperson's Opening Remarks

Sohye Kang, Ph.D., Senior Scientist, Process Development, Amgen

KEYNOTE PRESENTATION

8:20 Strategies to Enable High-Throughput Recombinant Protein Production in Mammalian Cells for Preclinical Studies

Athena Wong, Ph.D., Senior Scientist & Senior Group Leader, Early Stage Cell Culture, Genentech

Transient transfections in HEK293 and CHO cells are used to rapidly generate proteins for discovery research and early development studies. Here we present our approaches to express microgram to multigram amounts of protein in automated 96 deep well plates and bioreactors. To increase transfection productivity, we performed host cell engineering followed by process optimization. Results showed that modifying media components provides significant benefits towards increasing yield and/or modulating product quality.

9:00 Upgrading CHO Clone Selection and Bioprocess Development by Metabolic Modeling Approaches

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

In-depth characterization of high producer cell lines and bioprocesses is essential to ensure robust and consistent production of recombinant therapeutic proteins in high quantity and quality for clinical applications. Millions of data points are captured during the development of Roche's innovative therapeutic proteins in DAMAS: the industry-leading solution to cope with the heterogeneity, variability and dynamics of data and information derived from very flexible bioprocesses.

9:30 Engineering Process Performance by Predictive Insilico Solutions

Dirk Müller, Ph.D., Head, R&D Services, Insilico Biotechnology AG

The biotech industry currently witnesses increasing use of modeling and simulation solutions, but is still far behind fields like electronics or automotive where each new product is designed employing computer simulations. Aiming in this direction, we present a technology platform enabling efficient setup of genome-based network models, OMICS data integration, and derivation of predictive dynamic models. We illustrate application of the platform to cell culture media design and strain engineering.

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

FEATURED PRESENTATION

11:00 Genome-Scale Big Data and Modeling Approaches to Optimizing Protein Production in CHO Cells

Bernhard Palsson, Ph.D., Galletti Professor, Bioengineering; Principal Investigator, Systems Biology Research Group, Bioengineering; Professor, Pediatrics, University of California, San Diego

Three technological drivers that advanced the development of microbial production strains are in place for CHO cells: whole-genome sequences, genome editing tools, and genome-scale models. The last item relies on big data analysis against a structured network reconstruction for metabolism and protein secretion. Network reconstructions are knowledge bases (BiGG k-bases) that formalize our knowledge of biochemistry, genetics, and genomics in CHO. We review the field's history, development and status, and consider the future.

11:30 Sponsored Presentation *(Opportunity Available)*

12:00 pm Session Break

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

1:15 Ice Cream Break in the Exhibit Hall with Poster Viewing

IMPROVING PRODUCTIVITY AND PRODUCT QUALITY

2:00 Chairperson's Remarks

Richard Altman, MS, Scientist, Protein Technologies, Amgen

2:05 Chromatin Function Modifying Elements in an Industrial Antibody Production Platform

Mark Ellis, Principal Scientist, Protein Expression and Purification, UCB Pharma

The isolation of stably transfected cell lines for the manufacture of biotherapeutic protein products can be an arduous process. This frequently involves transgene amplification and maintenance over many generations. We assessed four chromatin function modifying elements for their ability to negate chromatin insertion site position effects and their ability to maintain antibody expression. Stability analysis demonstrated that the reduction in expression was mitigated in the clones containing A2UCOE-augmented transgenes.

2:35 Cell Line Profiling to Improve Productivity and Product Quality

Sohye Kang, Ph.D., Senior Scientist, Process Development, Amgen

Despite the same host cell origin, recombinant production cell lines often display phenotypic variability in regard to growth rate, cell size and metabolic profiles. These intrinsic, cell line-specific variations can affect productivity and product quality. Technological advances in -omics and bioinformatics tools are providing unprecedented opportunity to probe the molecular systems that underlie various cellular phenotypes influencing quantity and quality of therapeutic protein production. Findings from these investigations allow opportunities for process improvement.

Sponsored by MaxCyte

3:05 Accelerating Biotherapeutic Development through Simultaneous High-Titer, CHO Transient Expression & Generation of High-Yield Stable Cell Lines Using Scalable Transfection

James Brady, Ph.D., Director, Technical Applications, MaxCyte, Inc.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Product Quality and Protein Expression in CHO Cells

Pauline Smidt, Process Development Scientist, Just Biotherapeutics

I discuss the evaluation of growth, titer and product quality in production CHO cell lines under various process conditions.

4:45 Rapid Production of Recombinant Proteins in CHO Cells Using Large-Scale Transfection or Stable Pools

Yves Durocher, Ph.D., Section Head, Mammalian Cell Expression - NRC Human Health Therapeutics Portfolio, National Research Council Canada

We describe our CHO transient expression platform for rapid production of recombinant proteins. For more difficult-to-express proteins or proteins needed in large quantities, we also developed an inducible CHO pool platform that allows generation of stable and scalable pools expressing high levels of monoclonal antibodies in two weeks post-transfection. Fc glycans present on monoclonal antibodies produced by transient transfection or stable pools are compared. The pools can also be used to derive stable and high-expressing CHO clones for manufacturing therapeutic candidates.

5:15 Toolbox for Cell Line Development – Next-Generation Cell Line Development Technologies

Holger Laux, Ph.D., Fellow, Integrated Biologics Profiling, Technical Development NBE, Novartis

CHO cells are the most widely used host for large-scale production of recombinant therapeutic proteins. A novel toolbox of vector elements, selection marker and novel engineered CHO cell lines were developed, which results in combination in significant increase of titer and improved product quality. Furthermore, we have identified a key protein severely affecting the quality of non-antibody format therapeutic proteins. Elimination of this protein via novel targeted gene disruption tools resulted in significant increased improved product quality.

5:45 Close of Conference

Optimizing Expression Platforms

Engineering Higher-Throughput Processes from Cells to Screens

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. In conjunction, rapidly screening and characterizing the protein product is necessary to speed the selection process. The rapidly increasing need for recombinant proteins necessitates further improvements in both technologies.

Cambridge Healthtech Institute's Fourth Annual Optimizing Expression Platforms conference convenes protein expression specialists who share their experiences of the differences, tradeoffs, and improvements in producing and screening recombinant proteins in transient or stable production systems.

THURSDAY, JANUARY 12

7:45 am Conference Registration and Morning Coffee

TRANSIENT PRODUCTION

8:15 Chairperson's Opening Remarks

Yves Durocher, Ph.D., Section Head, Mammalian Cell Expression - NRC Human Health Therapeutics Portfolio, National Research Council Canada

KEYNOTE PRESENTATION

8:20 Strategies to Enable High-Throughput Recombinant Protein Production in Mammalian Cells for Preclinical Studies

Athena Wong, Ph.D., Senior Scientist & Senior Group Leader, Early Stage Cell Culture, Genentech

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9:00 Transient Protein Production: Harmonizing the Process from Construct Generation through Protein Characterization

Richard Altman, MS, Scientist, Protein Technologies, Amgen

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

9:30 Development and Optimization of AAV hFIX Particles by Transient Transfection in an iCELLis Fixed Bed Bioreactor

Michael Meagher, Ph.D., Vice President, Therapeutics Production & Quality, St. Jude Children's Research Hospital

The clinical demand for AAV requires a scalable high-capacity technology. The presentation describes the production of AAV8-hFIX using a 2 plasmid transient transfection of HEK293T/17 cells using a disposable fixed bed bioreactor, the iCELLis® Nano. The iCELLis® can support as many as 2.5×10^8 cells/mL of fixed bed (1.9×10^6 cells/cm^2). Optimizing culture and transfection parameters resulted in 9.0×10^{14} AAV8 viral particles per square meter of fixed bed.

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

11:00 Sequential Injection Capillary Electrophoresis for Bioprocess Monitoring

Rosanne Guijt, Ph.D., Alexander von Humboldt Fellow and Senior Lecturer, Australian Centre for Research on Separation Science (ACROSS), University of Tasmania

Biological processes are naturally susceptible to variability because living cells consume substrates and produce metabolites and products in a dynamic way with variations in metabolic rate across short time intervals. This presentation explores the potential of capillary electrophoresis (CE) for bioprocess monitoring. Using a novel injection strategy, this fully automated system offers high sample throughput, good temporal resolution and low sample consumption combined with robustness, sensitivity and flexibility which provides a promising new platform for pharmacological and biotechnological studies.

Sponsored by

11:30 Strep-Tactin XT - A Superior Next-Generation System for Purification of Proteins & Assay Development

Dennis Niermeier, MSc, Scientist, IBA GmbH - Solutions for Life Sciences

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

11:45 Sponsored Presentation *(Opportunity Available)*

12:00 pm Session Break

Sponsored by

12:15 Luncheon Presentation: CHO & HEK293 New Screening Solutions, Tips and Tricks for Transient Transfection, and Stable Cell Lines

Sam Ellis, Vice President & Biochemist, Thomson Instrument Company

Evaluation of different transfection tools, product quality, and titer for both CHO and HEK293. CHO transient systems, reagents. Which system is best, and scalable? Titer vs. quality and repeatability for results? Data will be presented on techniques and technology that allow for mimicking large-scale fermentation with non-controlled devices from 15mL-3L. All of these techniques will be given with existing case studies for technologies involving protein or antibody production, and can lead to successful transfer from different protein groups.

1:15 Ice Cream Break in the Exhibit Hall with Poster Viewing

CHO CELL LINES: IMPROVING PRODUCTIVITY

2:00 Chairperson's Remarks
Richard Altman, MS, Scientist, Protein Technologies, Amgen

2:05 Chromatin Function Modifying Elements in an Industrial Antibody Production Platform
Mark Ellis, Principal Scientist, Protein Expression and Purification, UCB Pharma
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2:35 Cell Line Profiling to Improve Productivity and Product Quality
Sohye Kang, Ph.D., Senior Scientist, Process Development, Amgen
Despite the same host cell origin, recombinant production cell lines often display phenotypic variability in regard to growth rate, cell size and metabolic profiles. These intrinsic, cell line-specific variations can affect productivity and product quality. Technological advances in -omics and bioinformatics tools are providing unprecedented opportunity to probe the molecular systems that underlie various cellular phenotypes influencing quantity and quality of therapeutic protein production. Findings from these investigations allow opportunities for process improvement.

3:05 Accelerating Biotherapeutic Development through Simultaneous High-Titer, CHO Transient Expression & Generation of High-Yield Stable Cell Lines Using Scalable Transfection
Sponsored by MaxCyte
James Brady, Ph.D., Director, Technical Applications, MaxCyte, Inc.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Product Quality and Protein Expression in CHO Cells
Pauline Smidt, Process Development Scientist, Just Biotherapeutics
I discuss the evaluation of growth, titer and product quality in production CHO cell lines under various process conditions.

4:45 Rapid Production of Recombinant Proteins in CHO Cells Using Large-Scale Transfection or Stable Pools
Yves Durocher, Ph.D., Section Head, Mammalian Cell Expression - NRC Human Health Therapeutics Portfolio, National Research Council Canada
We describe our CHO transient expression platform for rapid production of recombinant proteins. For more difficult-to-express proteins or proteins needed in large quantities, we also developed an inducible CHO pool platform that allows generation of stable and scalable pools expressing high levels of monoclonal antibodies in two weeks post-transfection. Fc glycans present on monoclonal antibodies produced by transient transfection or stable pools are compared. The pools can also be used to derive stable and high-expressing CHO clones for manufacturing therapeutic candidates.

5:15 Toolbox for Cell Line Development – Next-Generation Cell Line Development Technologies
Holger Laux, Ph.D., Fellow, Integrated Biologics Profiling, Technical Development NBE, Novartis
CHO cells are the most widely used host for large-scale production of recombinant therapeutic proteins. A novel toolbox of vector elements, selection marker and novel engineered CHO cell lines were developed, which results in combination in significant increase of titer and improved product quality. Furthermore, we have identified a key protein severely affecting the quality of non-antibody format therapeutic proteins. Elimination of this protein via novel targeted gene disruption tools resulted in significant increased improved product quality.

5:45 Close of Day

FRIDAY, JANUARY 13

8:00 am Conference Registration and Morning Coffee

TECHNOLOGIES TO MANAGE A HIGHER-THROUGHPUT EXPRESSION AND PRODUCTION LAB

8:30 Chairperson's Remarks
Jonas V. Schaefer, Ph.D., Head, High-Throughput Binder Selection Facility, Biochemistry, University of Zurich

8:35 High-Throughput Methods for the Characterization of Relevant Protein Features
Jonas V. Schaefer, Ph.D., Head, High-Throughput Binder Selection Facility, Biochemistry, University of Zurich
To optimize the efficiency of the laborious process of generating specific affinity reagents, we established a streamlined pipeline consisting of simultaneous selections against 94 targets and subsequent high-throughput screenings and validations. This fast and efficient platform, allowing the reliable discovery of recombinant binders, requires the improvement of existing and the development of novel high-throughput methods which will be presented.

9:05 High-Throughput Biophysical and Biochemical Stability Screening for Early Stage Antibody Discovery
Yingda Xu, Ph.D., Associate Director, Protein Analytics, Adimab LLC
Problems in the development of antibodies can often be traced back to their intrinsic poor biophysical and biochemical stabilities. High-throughput screening assays are developed or adapted to fit in the scope of early discovery stage to filter out candidates with poor properties.

9:35 High-Throughput Manufacturability Assessment of Complex Biologics

Zhenyu Gu, Ph.D., Development Scientist III, Early Assay Development, Alexion Pharmaceuticals

Bispecific/biparatopic antibodies, modified enzymes and fusion proteins have gained increasing popularity due to their unique therapeutic profiles. However, these molecules often pose significant challenges to manufacture as a result of their complex designs. In this study, high-throughput mechanical/chemical stress relevant to manufacture process was coupled with high-throughput orthogonal characterization methods to screen these early stage molecules for their manufacturability, focusing on solubility, aggregation, colloidal and thermal stability.

10:05 Coffee Break with a Poster Pavilion *See page 4 for details*

11:00 Capillary Electrophoresis for Automated On-Line Monitoring of Suspension Cultures: Correlating Cell Density, Nutrients and Metabolites in Near Real-Time

Rosanne Guijt, Ph.D., Senior Lecturer, Pharmacy, School of Medicine, University of Tasmania; Von Humboldt Fellow, KIST Europe

11:30 High-Throughput Protein Analysis and Engineering Using Microcapillary Arrays

Spencer Alford, Ph.D., Protein Engineer, xCella Biosciences, Inc.

We developed a high-throughput screening platform that allows researchers to assay the functional activity of millions of protein variants, displayed on or secreted from cells. This talk describes several protein analysis and engineering applications performed with this new technology platform.

12:00 pm IT'S A WRAP: PEPTALK 2017 CLOSING PLENARY PANEL DISCUSSION *See page 5 for details*

1:15 Close of Conference

Characterization of Biotherapeutics

Improving Prediction, Screening and Characterization of New Biologics

New biotherapeutics formats are flooding the discovery and development pipelines and with this comes an increasing need for better and faster characterization tools and strategies, and improved biomolecular and biophysical assays for the new biotherapeutics. The Third Annual Characterization of Biotherapeutics conference presents new tools, strategies and case studies on analytical development and characterization of mAbs, ADCs, bispecifics, and other novel protein formats along with case studies on development of biosimilars.

SUNDAY, JANUARY 8

4:00 - 5:30 pm Registration
5:00 - 8:00 Dinner Short Courses *See pages 6-7 for details*

MONDAY, JANUARY 9

7:30 am Conference Registration and Morning Coffee

SCREENING, CHARACTERIZATION AND DEVELOPMENT OF NEW BIOTHERAPEUTICS

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

9:05 Chairperson's Opening Remarks
Shrikant Deshpande, Ph.D., Senior Director, Protein Chemistry, Biologics Discovery California, Bristol-Myers Squibb Co.

KEYNOTE PRESENTATION

9:10 Understanding Chemical Liabilities in Antibody Lead Selection
Shrikant Deshpande, Ph.D., Senior Director, Protein Chemistry, Biologics Discovery California, Bristol-Myers Squibb Co.
Chemical liabilities such as deamidation, and oxidation in an antibody sequence can alter the structure and activity of the lead molecule. So, it is important and necessary to assess and understand the risks they pose in the CMC as well as therapeutic setting. This presentation explores chemical liability risks in lead selection process and provides case studies that provide risk mitigation strategies.

9:50 Biophysical Characterization to Enable the Formulation Development of Multi-Dose Aggregation-Prone Peptide Conjugates
Jingtao Zhang, Ph.D., Principal Scientist, Pharmaceutical Sciences, Merck Research Laboratories
The presentation will focus on the characterization of reversible and irreversible fibril aggregates in peptide formulations, biophysical assays that that guide AME study design, and high resolution biophysical study to enable insights in formulation stabilization mechanism. Overall considerations on the development of multi-dose peptide formulations as well as strategies in overcoming the challenges will also be highlighted.

10:20 Coffee Break

BIOSIMILARITY AND COMPARABILITY

10:45 Biosimilars – The Analytical Challenge
Gerard Powell, Ph.D., Senior Principal Specialist, Product Characterisation, Analytical Sciences, Allergan Biologics Ltd.
An overview of biosimilars and biosimilar development with an emphasis on the unique analytical challenges they present. I will discuss strategies for establishment of analytical similarity and illustrate these with case study data generated on real biosimilar projects.

11:15 Bleeding-Edge Characterization of Biosimilars
Edward R. Zartler, Ph.D., Senior Group Leader, Biophysics, Analytical R&D, Pfizer
The robust structural characterization of biosimilars, complex therapeutic proteins, is crucial to demonstrating biosimilarity. NMR and X-ray are the two most powerful methods to address the structure of biosimilars.

11:45 Analytical Comparability and Characterization of a Non-Covalent Heterodimer Biotherapeutic
Justin Prien, Ph.D., Associate Director, Analytical Development, Shire
This presentation discusses the analytical comparability for a non-covalent heterodimer biotherapeutic performed to facilitate product developmental continuity. The analytical comparability strategy was designed to assess the similarity of the potential critical quality attributes and mitigate false negative results. At the development stage comparability can be challenging due to analytical method immaturity, the extent of process and product knowledge, and a limited number of manufacturing batches from the different processes.

12:15 pm Development of a High-Throughput Formulation Screening Platform for Therapeutic Monoclonal Antibodies
Yunsong (Frank) Li, Principal Scientist, Analytical and Formulation Development, Cook Pharmica

12:30 Sponsored Presentation *(Opportunity Available)*

12:45 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

ANALYTICAL DEVELOPMENT: CASE STUDIES AND

Characterization of Biotherapeutics

Improving Prediction, Screening and Characterization of New Biologics

CHI-PepTalk.com

TOOLS

2:00 Chairperson's Remarks
Edward R. Zartler, Ph.D., Senior Group Leader, Biophysics, Analytical R&D, Pfizer

2:05 Characterization of Protein Products
Sambit Kar, Ph.D., Principal Scientist; Head, Biophysics Center of Excellence, Molecular & Analytical Development, Bristol-Myers Squibb Co.

2:35 Role and Relationship between Biophysical and Analytical Data in Formulation Development and Comparability Assessments
Haripada Maity, Ph.D., Research Advisor, Formulation Development, CMC Development, Eli Lilly and Company

Biophysical and analytical measurements are often performed for formulation development and during comparability assessment of protein therapeutics. The roles and relationship of these data and how they relate to method sensitivity, analysis, and interpretation is an im-portant avenue of discussion. This presentation will discuss the utility of these multidimen-sional approaches and the connectivity of these data in terms of thermodynam-ic/conformational stability and kinetic stability of protein.

3:05 Get the Full Picture and Predict Biotherapeutics Stability with nanoDSF

Sponsored by NanoTemper Technologies

Stefan Duhr, Ph.D., CEO, NanoTemper Technologies

To support scientists on their cumbersome way to the perfect biotherapeutics product in terms of developability and long-term stability, we designed the Prometheus instruments for rapid and precise high-throughput stability screenings using nanoDSF. Get introduced to case studies with major biopharmaceutical companies and learn how they revolutionized development of biotherapeutics.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Comprehensive Characterization of Product Variants and Higher-Order Structure of Monoclonal Antibodies with Case Studies
Renata Varga, Ph.D., Characterization Scientist, Analytical Sciences, Global Biological CMC, Teva Pharmaceuticals

Characterization of monoclonal antibodies under development is a key step to better understand the properties and behavior of that new mAb, especially for product variants. After a critical quality attribute assessment, the anticipated variants can be thoroughly characterized based on a well-designed plan. Characterization data on mAb size variants, aglycosylated species, and isoforms (charge, disulfide) by several analytical methodologies will be presented.

4:30 Therapeutic Protein Characterization for Process Development – a Case Study
Quanzhou Luo, Ph.D., Senior Scientist, Process Development, Amgen

Although therapeutic proteins are relatively stable, they can undergo a variety of degradations during manufacturing, formulation and storage. It is, therefore, very important to characterize the biophysical and biochemical properties of the degradations to better assess their safety and efficacy. With the implementation of the quality by design (QbD) concept to drug devel-opment, monitoring product quality attributes (PQAs) during process development has be-come increasingly critical.

5:00 Characterization of Aluminum Adjuvant and Adsorbed Proteins
Marina Kirkitadze, Ph.D., MBA, Deputy Director, Analytical R&D Biochemistry, Sanofi Pasteur

This presentation summarizes the characterization of the physicochemical and compositional properties of vaccine components: aluminum-based adjuvant and adsorbed protein antigens. Particle size distribution was measured by Laser Diffraction, whereas Raman and Fourier Transform Infrared spectroscopies were used to analyze the compositional properties of aluminum-based adjuvant and adsorbed protein antigens.

5:35 BuzZ Session A
Join your peers and colleagues for interactive roundtable discussions.
Please see page 74 for additional information.

6:20-7:30 Welcome Reception in the Exhibit Hall with Poster Viewing

7:30 Close of Day

TUESDAY, JANUARY 10

8:00 am Conference Registration and Morning Coffee

APPLICATION OF MASS SPECTROSCOPY AND OTHER ANALYTICAL TECHNIQUES

8:30 Chairperson's Remarks
Allison Derenne, Ph.D., Researcher, Structure and Function of Biological Membranes, Université libre de Bruxelles

8:35 Assessing the Higher-Order Structure of Therapeutic Monoclonal Antibodies by NMR Spectroscopy
Yves Aubin, Ph.D., Research Scientist, Regulatory Research Division, Health Canada

Monoclonal antibodies (mAbs) are the fastest growing class of therapeutic protein. In addition, a number of mAb products have lost or will lose patent protection. Here we will present our latest efforts in applying NMR spectroscopy to obtain high-resolution structural information to facilitate the assessment of this critical quality attribute. The approach is applicable in the context of a comparability exercise, whether it is for innovator or biosimilar products alike.

9:05 Use of Steady-State and Time-Resolved Fluorescence Spectroscopy for Higher-Order Structure Characterization
Michael Ignatov, Ph.D., Senior Scientist, Biologics Development Analytical Sciences, Allergan, Plc

Intrinsic tryptophan fluorescence serves as a highly sensitive indicator of the higher-order structure of proteins. Tryptophan fluorescence properties are extremely sensitive to the local environment around tryptophan and solvent accessibility. Differences in the fluorescence properties of proteins are measured

to monitor the changes in the higher-order structure. Effect of chemical modifications, chemical unfolding, thermal unfolding, etc. on the spectral properties and fluorescence lifetimes is assessed using several model proteins.

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

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

11:00 **FTIR Spectroscopy as a Multi-Parameter Analytical Tool for Comparability Testing and Stability Studies of Therapeutic Proteins**

Allison Derenne, Ph.D., Researcher, Structure and Function of Biological Membranes, Université libre de Bruxelles

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

11:30 **Use of Fast LC/MS Techniques to Identify, Characterize and Evaluate Therapeutic Antibodies**

Amy Hilderbrand, Ph.D., Technical Development Scientist, Protein Analytical Chemistry, Genentech

12:00 pm **Presentation to be Announced**

Sponsored by Lonza

12:30 **Session Break**

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

1:15 **Close of Conference**

Detection and Characterization of Particulates and Impurities

Rapid Tools and Strategies for Risk Assessment, Prediction and Characterization of Particles and Impurities from Products, Excipients and Processes

Particles and impurities can come from the products, any stage of bioprocessing, or the delivery devices and primary packaging, and they have potential to impact stability, safety, and efficacy of the biomolecules and biologic products. Therefore, early understanding, detection and characterization of the impurities are critical to ensure safety and efficacy of the drug product for its intended duration of use. The Third Annual Detection and Characterization of Particulates and Impurities conference provides a platform to explore novel tools and strategies to detect, characterize and carry out risk assessment of particles and impurities.

TUESDAY, JANUARY 10

1:00 pm Conference Registration

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

REGULATORY GUIDANCE, REFERENCE STANDARDS AND CONTROL

2:00 Chairperson's Opening Remarks
Mehrshid Alai, Ph.D., Head, Global RA CMC (interim), Regulatory Affairs, Shire

KEYNOTE PRESENTATION

2:05 Regulatory Requirements and Guidance on Particles and Impurities for Late Stage Submissions
Mehrshid Alai, Ph.D., Head, Global RA CMC (interim), Regulatory Affairs, Shire
The regulatory concern on particles and impurities is an evolving topic. The expectations from regulatory agencies are increasing and it is important to ensure they are adequately addressed for a successful submission. In this presentation, we will examine some key regulatory guidance documents, as well as compare and contrast expectations from some key regulatory agencies. Some strategies around dealing with regulatory requirements in late stages of development will be discussed.

2:45 Detection of Impurities: Use of Pharmacopeia Reference Standards
Fouad Atouf, Ph.D., Director, Global Biologics, United States Pharmacopeia (USP)
This presentation will provide an overview of the type of reference standards (RSs) provided by the United States Pharmacopeia, specifically the RSs used to detect and measure impurities. Information on characterization of these materials as well as data to support their suitability for use will be presented. Cases studies from simple peptide molecules to complex biological preparations will be discussed.

3:15 Sponsored Presentation *(Opportunity Available)*

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

DETECTION AND CHARACTERIZATION OF PROCESS-RELATED IMPURITIES

4:30 LCMS Detection of the Residual Peptides from Yeast Extract and Hypep in In-Process Samples of Biotherapeutical Drug Substance
Guifeng Jiang, Ph.D., Senior Manager, Analytical Science, Boehringer Ingelheim
Some peptides from yeast and soy proteins may be immunogenic, raising safety concerns. Health authorities expect data showing clearance of the components of yeast/Hypep hydrolysates during the downstream purification process to be included in the BLA. A reverse phase liquid chromatography with high resolution mass spectrometry method was developed to separate and detect components of the Yeast extract/Hypep and to demonstrate the clearance of the components during the purification process.

5:00 Sources, Detections and Control Strategies of Beta-Glucan Impurity in Biopharmaceutical Manufacturing Processes
Jinshu Qiu, Ph.D., Principal Scientist, Process Development, Amgen
(1→3)-β-D-glucans (beta-glucans) are a process-related impurity arising from raw materials used in biopharmaceutical manufacturing processes. Beta-glucans can be an indicator of invasive fungal infection or modulate an innate immune response, therefore their presence in drug products may pose a potential safety concern unless controlled below safety limits. Hence, it is critical to ensure their clearance during manufacturing. Beta-glucan sources, detections, and control strategies will be discussed in the presentation.

5:30 Close of Day

5:30 - 5:45 Short Course Registration
5:45 - 8:45 Dinner Short Courses* ***See pages 6-7 for details***
**** Separate registration required***

WEDNESDAY, JANUARY 11

8:00 am Conference Registration and Morning Coffee

ANALYZING AND MANAGING HOST CELL PROTEIN IMPURITIES

8:30 Chairperson's Remarks
Qingchun Zhang, Ph.D., Senior Scientist, Attribute Sciences, Amgen

FEATURED PRESENTATIONS

8:35 What We Learned from MS-Based HCP Analysis
Qingchun Zhang, Ph.D., Senior Scientist, Attribute Sciences, Amgen
Host cell proteins are important process-related impurities for biologics. A mass spectroscopy based HCP analysis approach and its applications will be discussed.

9:05 Host Cell Protein (HCP) Control Strategy Reassessment for a CHO-Derived Protein Therapeutic
John Rolf, Ph.D., Director, Corporate Quality, Product Quality Leader, Amgen
Immunoassay tests are standard to establish HCP impurity specifications

Detection and Characterization of Particulates and Impurities

Rapid Tools and Strategies for Risk Assessment, Prediction and Characterization of Particles and Impurities from Products, Excipients and Processes

and monitor protein therapeutic lot-to-lot consistency. However, multi-analyte Immunoassay tests may over- or under-quantify. xhsngln this case study, Mass Spectroscopy (MS) identified and quantified individual HCPs from protein product drug substance, comparing results to the Immunoassay. The case study demonstrates how MS testing (and supplemental characterization data) was used to redefine the HCP control strategy – without impacting product or patient safety.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

10:50 Specific Immune Response to a Host Cell Protein Impurity

Sally Fischer, Ph.D., Principal Scientist, BioAnalytical Sciences, Assay Development and Technology, Department of Development Sciences, Genentech

A product related impurity was identified in the material used in clinical study. To assess the potential ability of patients to develop an immune response to the impurity and impact on immunogenicity of the therapeutic two bridging ELISA were developed and validated. Samples from treated subjects were evaluated in both assays. This presentation will discuss the results of the immunogenicity assessment to the impurity and observed immunogenicity rate of the therapeutic.

11:20 Assessing Immunogenicity Risk in Biotherapeutic Product and Process Development

Valerie Quarmby, Ph.D., Staff Scientist and Director, BioAnalytical Sciences, Genentech

Every biotherapeutic has the potential to elicit unwanted immune responses, and these may compromise safety and efficacy. Several approaches can be used during lead selection and optimization to assess the likelihood that a biotherapeutic may be immunogenic. Some of these may also be used to assess immunogenicity risk from product variants or process related impurities. This talk will review immunogenicity risk assessment systems in the context of process development.

11:50 PANEL DISCUSSION: Establishing Relationship of Impurity to Potency and Activity and How They Affect Patients, Storage and Shelf Life

Moderator:

Sally Fischer, Ph.D., Principal Scientist, BioAnalytical Sciences, Assay Development and Technology, Department of Development Sciences, Genentech

Panelists:

Valerie Quarmby, Ph.D., Staff Scientist and Director, BioAnalytical Sciences, Genentech

Qingchun Zhang, Ph.D., Senior Scientist, Attribute Sciences, Amgen

John Rolf, Ph.D., Director, Corporate Quality, Product Quality Leader, Amgen

12:20 pm Sponsored Presentation *(Opportunity Available)*

12:50 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

CRITICAL CONSIDERATIONS IN PRODUCT DEVELOPMENT: FORMULATION, STABILITY, PARTICLES AND PACKAGING

2:00 Chairperson's Remarks

Wendy Saffell-Clemmer, MS, Director, Research, Pharmaceutical Development, Baxter Healthcare

2:05 Selection of Pre-Filled Syringe for Biologic Products on Particulate Matter and Product Stability – A Case Study

Wendy Saffell-Clemmer, MS, Director, Research, Pharmaceutical Development, Baxter Healthcare

Pre-filled syringes provide significant advantages to the clinician and the patient. However, the pre-filled syringe and syringe filling process can have a significant impact on particulate formation and product stability. Methodical laboratory studies on the formulation are needed to understand potential causes of particle formation. A case study describing development of a liquid monoclonal antibody pre-filled syringe product will be presented along with a discussion of manufacturing scale-up challenges.

2:35 Developing a Multi-Pronged Approach to the Identification of PS20 Degradation Mechanism

Anthony Tomlinson, Senior Research Associate, Late Stage Pharmaceutical Development, Genentech

Polysorbates are commonly used non-ionic surfactants in protein pharmaceuticals. In recent years, there has been increasing concern in the degradation of these materials on long-term stability and the subsequent increase of insoluble degradation products. In this talk, we will discuss the detection of PS20 degradation products and the identification the mechanism of degradation for root cause analysis.

3:05 Subvisible Particles: Rapid and High-Throughput Tools for Prediction, Detection and Characterization of Subvisible Particles and Other Aggregates

Andrea Hawe, Ph.D., CSO, Coriolis Pharma

Aggregates and subvisible particles (SVP) are considered cQA for biologics, and it is crucial to include a comprehensive characterization early during drug product development. Especially, for early development a reduction of required time, material and resources is essential. Within the talk an overview of methods and strategies for SVP and aggregate analysis is given, with special focus on minimization of material requirements, increase in throughput and possibilities for prediction of stability.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:30 Prediction of Antibody Stability in Lyophilized Solids by Hydrogen Deuterium Exchange with Mass Spectrometric Analysis (HX-MS)

Kathleen Abadie, Engineer I, Late Stage Pharmaceutical Development, Genentech

We explore HX-MS to study protein structure in lyophilized solids for deeper understanding of solid state stability and to save time and resources in pharmaceutical development. HX probes structure by measuring the frequency of stabilizing amide H-bonds. Indeed, we show that reduced stability as

indicated by increased deuterium uptake versus time correlates with increased aggregation propensity. Stability effects of lyoprotectant concentration and processing conditions are assessed by HX-MS.

5:00 Scaled Down Containers for Protein Stability Studies

Eric Meinke, Ph.D., Senior Scientist, AstraZeneca Supply Biologics

Real-time, real-condition stability study is essential to establish the expiry of biological therapeutics. For drug substance, stability study is typically performed in small scale containers that mimic the actual storage container/condition at scale. A case study will be presented to highlight the criticality of understanding and controlling of the scaled down container for stability studies.

5:35 BuzZ Session B

Join your peers and colleagues for interactive roundtable discussions.

Please see page 74 for additional information.

6:20 - 7:20 Reception in the Exhibit Hall with Poster Viewing

7:20 Close of Conference

Extractables and Leachables

Protecting Quality of Biologics by Ensuring Safety and Compatibility

In biopharmaceutical development and manufacturing, containers, drug combination products, and even disposable equipment may leach chemicals into the product that can pose significant risks to product quality and potentially compromise the stability, safety and efficacy of the biotherapeutics. The Fifth Annual Extractables and Leachables (E&L) conference brings together industry experts and thought leaders to share their insights on the latest updates and guidelines, how to design analytical testing strategies for E&L, case studies on identification and risk assessment of E&L in single-use systems, container closure systems and delivery devices, and the impact of leachables on biocompatibility.

TUESDAY, JANUARY 10

1:00 pm Conference Registration

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

UPDATES FROM INDUSTRY AND WORKING GROUPS

2:00 Chairperson's Opening Remarks

Kim Li, Ph.D., DABT, MPH, Senior Manager, Environment, Health, Safety and Sustainability Product Stewardship Toxicology, Amgen

KEYNOTE PRESENTATION

2:05 Extractables & Leachables Safety Information Exchange (ELSIE) Consortium – Update

Kim Li, Ph.D., DABT, MPH, Senior Manager, Environment, Health, Safety and Sustainability Product Stewardship Toxicology, Amgen

The ELSIE consortium, consisting of members from the pharmaceutical, biotechnology and medical device companies, advances the knowledge of chemical and toxicology assessment of extractables and leachables (E&L) through scientific and regulatory outreach. In October 2015, the consortium conducted a workshop in Basel Switzerland to understand the current practices of E&L risk assessment. This presentation will highlight the findings from the workshop and describe our collaborative efforts toward best practices.

2:45 USP GENERAL CHAPTER <661.3>: Plastic Components and Systems Used to Manufacture Pharmaceutical Drug Products

Desmond G. Hunt, Ph.D., Senior Scientific Liaison, Standards Development, United States Pharmacopeia (USP)

USP General Chapter <661.3> contains tests, test methods and specifications for characterizing materials used to construct manufacturing components and for components used in manufacturing systems. The philosophy behind the development and contents of <661.3> will be discussed, specifically focusing on similarities and differences between packaging (addressed in <661.1> and <661.2>) and manufacturing. The essential aspects of <661.3>, including the Initial Assessment, the Risk Evaluation Matrix, and the Standard Extraction Protocol will be introduced.

3:15 Sponsored Presentation *(Opportunity Available)*

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

4:30 USP GENERAL CHAPTER <661.3>: Rationale for the Standard Extraction Protocol (SEP) Used in <661.3>

Dennis Jenke, Ph.D., Baxter Distinguished Scientist, Research & Development, Baxter Healthcare Corp.

The Standard Extraction Protocol (SEP) is applied in those high risk circumstances where extractables profiling of components is necessary. In this presentation the rationale behind the SEP is explained and the major features of the Protocol (extraction solvents, times and durations) are justified. Additionally, practical considerations in terms of generating extracts for different manufacturing components (e.g., bags, tubing, filters etc) are discussed. Lastly, the SEP will be compared to other proposed extraction protocols.

5:00 Redefine Extractable and Leachable (E&L) Terminologies for All Stakeholders

Ken Wong, Deputy Director, Process Technology, Sanofi Pasteur

The extractables and leachables terminologies have been used interchangeably by most stakeholders for over a decade. This has caused some confusion. In this talk, the speaker will propose a new definition for extractables and leachables which could help distinguish between the extractables and leachables regardless of who you are speaking to (suppliers, regulators, and drug manufacturers). Several examples will be examined from all stakeholder perspectives to demonstrate the confusion and clarity under the old and proposed definitions.

5:30 Close of Day

5:30 - 5:45 Short Course Registration
5:45 - 8:45 Dinner Short Courses* *See pages 6-7 for details*
**** Separate registration required***

WEDNESDAY, JANUARY 11

8:00 am Conference Registration and Morning Coffee

ESTABLISHING DEVICES AND CONTAINER CLOSURE SAFETY: NEW TOOLS AND CASE STUDIES

8:30 Chairperson's Remarks

Ping Wang, Ph.D., Principal Scientist, Material Sciences, Janssen R&D

Extractables and Leachables

Protecting Quality of Biologics by Ensuring Safety and Compatibility

8:35 Strategies for Managing the Impact of a Material Change in Components of Container Closure Systems

Michael A. Ruberto, Ph.D., President, Material Needs Consulting, LLC

The characterization and control of extractables and leachables from the plastic and elastomers used in container closure systems is a formidable task for the pharmaceutical industry. This presentation will provide a comprehensive review of the polymer supply chain for pharmaceutical packaging components as well as potential areas of concern. Case studies that illustrate the types of changes that can occur, both announced and unexpected, their chemical and regulatory impact, and strategies for managing the change will be discussed.

9:05 Updates on Guidelines on Establishing Delivery Device and Container Closure Safety

Diane Paskiet, MS, Senior Director, Global Scientific Affairs, West Pharmaceuticals

This presentation will discuss PQRI safety and compatibility guidance based on chemistry of components used in delivery systems. It will also discuss regulatory expectations for chemical data on container closure systems, combination products and delivery devices. Lastly, it will also discuss how to use USP elemental impurity data for elastomers and correlating baseline data to finished systems for indented use.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

10:50 Generic Approaches of Extractable Assessment of Ancillary Devices for Parenteral Dosing

Ping Wang, Ph.D., Principal Scientist, Material Sciences, Janssen R&D

Ancillary devices are usually needed for the delivery of biologics to patients. Those devices include iv bags, iv admin sets and/or extension sets, etc. The extractable/leachable risks of those devices are not widely studied comparing to manufacturing materials and container closure systems, even though the ancillary devices are closer to patient and therefore have higher safety risks. A generic approach has been developed to assess the E&L risks of the commonly used iv bags (8), iv sets (9) and extension sets (8). Results will be reported.

11:20 Forensic Features and Mitigations of Glass-Related Particles in Parenteral Glass Vials

"Gary" Guiyang Li, Ph.D., Senior Scientist, Attribute Science, Amgen

Proper classification and investigation of the glass-related particles (GRP) occurring in product will help to understand GRP formation mechanism, improve process control, reduce GRP occurrence rate, and deliver safer parenteral drugs to patients. In this talk, we introduce a classification scheme and characterization tools for GRP. We propose to classify GRP as glass chip, glass lamella/flake, and silica gel particles. This study summarized their forensic differentiations based on SEM and FTIR and mitigation methods for each type of particles.

11:50 PANEL DISCUSSION: Interaction between E&L and Proteins and Its Impact on Stability, Potency and Immunogenicity of Drug Substance and Drug Product

Moderator:
Diane Paskiet, MS, Senior Director, Global Scientific Affairs, West Pharmaceuticals
Panelists:
Michael A. Ruberto, Ph.D., President, Material Needs Consulting, LLC
Ping Wang, Ph.D., Principal Scientist, Material Sciences, Janssen R&D
Gary Li, Ph.D., Senior Scientist, Forensic Lab, Systems Analytics, Amgen

12:20 pm Sponsored Presentation *(Opportunity Available)*

12:50 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

E&L CHALLENGES IN SINGLE-USE SYSTEMS AND PROCESSES

2:00 Chairperson's Remarks

Diane Paskiet, MS, Senior Director, Global Scientific Affairs, West Pharmaceuticals

2:05 New Studies on Leachables in Protein Production Lines

Gerhard Winter, Ph.D., Professor, Chair, Pharmaceutical Technology and Biopharmaceutics, LMU Munchen

Leachable studies on production lines under commercial scale conditions using four marketed protein drug products are presented. The lines combine disposable container systems, steel vessels, silicone tubings, filters and gaskets. GC –MS was used as the main analytical method. The use of fluor-polymer coated extraction twisters followed by heat desorption allowed excellent leachable detection and quantification in the presence of the protein drugs. Leachables were found in extremely low concentrations.

2:35 Creating a Holistic Extractables and Leachables Program for Biotechnology Products

Yasser Nashed-Samuel, Ph.D., Principal Scientist, Process and Product Development, Amgen

The risk mitigation of extractables and leachables (E&L) presents significant challenges to regulators and drug manufacturers with respect to the development, as well as the lifecycle management of drug products. A holistic program should include a science- and risk-based strategy for testing E&L for primary containers, drug delivery devices and single-use systems for the manufacture of biotechnology products. The strategy should be designed to ensure patient safety and product quality.

3:05 Impact of Single-Use Systems on the Risk for Product Quality During Pharmaceutical Processing

Nina Xiao, Senior Research Associate, Late Stage Pharmaceutical Development, Genentech

Application of single-use systems for the manufacturing of biologics has increased significantly over the years and poses challenges for pharmaceutical

processing in terms of leachables and their potential impact on product quality. There is a potential risk for protein particle formation with prolonged liquid storage in bioprocess containers and from silicone tubing originating from gamma irradiated single-use assemblies. Extractable analysis on localized silicone tubing discoloration will be examined and discussed.

3:35 **Refreshment Break in the Exhibit Hall with Poster Viewing**

4:30 **SUS Leachables Testing: Leachables Study Design for Single-Use Components**

Kathryn A. McGohan, MS, Associate Scientist II, Manufacturing Sciences and Technology: Materials Science, Bristol-Myers Squibb Co.

5:00 **E&L Requirements for Infusion Systems, Dialysis and Self-Administration Devices, Implantable Devices, Pre-Filled Syringes and Process Components**

Shawn Cao, Ph.D., Principal Scientist, Process and Product Development, Amgen

5:35 **BuzZ Session B**

Join your peers and colleagues for interactive roundtable discussions.

Please see page 74 for additional information.

6:20 - 7:20 **Reception in the Exhibit Hall with Poster Viewing**

7:20 **Close of Conference**

Bioprocess Analytics

Data Measurement, Monitoring and Modeling Allow Informed Control of Bioprocesses

The biopharmaceutical industry is meeting increasing demands and costs for biotherapeutics through process optimization. Advanced instrumentation with sampling techniques, new sensor technologies and analyzers have emerged to monitor both upstream and downstream processes. These analytical tools, however, result in large, complex datasets with multivariate interactions. The inherently complex nature of these datasets makes extraction of meaningful and relevant information a difficult task.

Cambridge Healthtech Institute's Inaugural Bioprocess Analytics conference addresses statistical analysis strategies including multivariate data analysis (MVDA), quality by design (QbD), and process analytical technology (PAT), allowing for optimized and informed control of bioprocessing.

THURSDAY, JANUARY 12

7:45 am Conference Registration and Morning Coffee

OPTIMIZING CELL LINE DEVELOPMENT

8:15 Chairperson's Opening Remarks
Sohye Kang, Ph.D., Senior Scientist, Process Development, Amgen

KEYNOTE PRESENTATION

8:20 Today a Caterpillar, Tomorrow a Butterfly: The Transformation of Bioprocess Analytics
Beth Junker, Ph.D., Principal Consultant, BioProcess Advantage LLC
The volume and complexity of bioprocess data are increasing dramatically, requiring a transformation of bioprocess analytics to effectively extract meaningful information. Whether in clinical development or commercial manufacturing, tomorrow's focus is moving away from Big Data towards Smart Data approaches. Available tools such as Multivariate data analysis as well as other statistical methods overlay the necessary structure. This permits purposeful analytics which ultimately reveal valuable insights into process and analytical understanding.

9:00 Upgrading CHO Clone Selection and Bioprocess Development by Metabolic Modeling Approaches
Oliver Popp, Dr. rer. nat., Senior Scientist, Pharma Research and Early Development, Large Molecule Research, Roche Innovation Center Munich, Roche Diagnostics GmbH
In-depth characterization of high producer cell lines and bioprocesses is essential to ensure robust and consistent production of recombinant therapeutic proteins in high quantity and quality for clinical applications. Millions of data points are captured during the development of Roche's innovative therapeutic proteins in DAMAS: the industry-leading solution to cope with the heterogeneity, variability and dynamics of data and information derived from very flexible bioprocesses.

9:30 Engineering Process Performance by Predictive Insilico Solutions
Dirk Müller, Ph.D., Head, R&D Services, Insilico Biotechnology AG
The biotech industry currently witnesses increasing use of modeling and simulation solutions, but is still far behind fields like electronics or automotive where each new product is designed employing computer simulations. Aiming in this direction, we present a technology platform enabling efficient setup of genome-based network models, OMICS data integration, and derivation of predictive dynamic models. We illustrate application of the platform to cell culture media design and strain engineering.

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

FEATURED PRESENTATION

11:00 Genome-Scale Big Data and Modeling Approaches to Optimizing Protein Production in CHO Cells
Bernhard Palsson, Ph.D., Galletti Professor, Bioengineering; Principal Investigator, Systems Biology Research Group, Bioengineering; Professor, Pediatrics, University of California, San Diego
Three technological drivers that advanced the development of microbial production strains are in place for CHO cells: whole-genome sequences, genome editing tools, and genome-scale models. The last item relies on big data analysis against a structured network reconstruction for metabolism and protein secretion. Network reconstructions are knowledge bases (BiGG k-bases) that formalize our knowledge of biochemistry, genetics, and genomics in CHO. We review the field's history, development and status, and consider the future.

11:30 Sponsored Presentation *(Opportunity Available)*

12:00 pm Session Break

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

1:15 Ice Cream Break in the Exhibit Hall with Poster Viewing

ENHANCING CELL CULTURE PROCESSES

2:00 Chairperson's Remarks
Rainer Stahn, Ph.D., Director, Process Development, Glycotope GmbH

2:05 Statistical Analysis of Data from Limited Dilution Cloning to Assess Monoclonality in Generating Manufacturing Cell Lines
Jorge Quiroz, Ph.D., Principal Scientist, Research CMC Statistics, Merck
We propose the use of confidence intervals for assessing monoclonality for limiting dilution cloning in the generation of recombinant manufacturing cell lines based on a single round. The use of confidence intervals instead of point estimates allows practitioners to account for the uncertainty present in the data. When two consecutive subclonings are required, we improved the present methodology by reducing the infinite series proposed by Coller and Coller (Hybridoma1983;2:91–96) to a simpler series.

Bioprocess Analytics

Data Measurement, Monitoring and Modeling Allow Informed Control of Bioprocesses

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2:25 A Cost- and Time-Effective Approach for QbD and PAT in Upstream Bioprocess Development and Optimization: Combining Intensified Design of Experiments (iDoE) and Hybrid Modeling

Moritz von Stosch, Ph.D., Lecturer, School of Chemical Engineering and Advanced Materials, Newcastle University

iDoE compresses a classical DoE into a lower number of experiments by intra-experiment process condition changes. The process response is analyzed with hybrid models that combine fundamental knowledge with data-driven techniques, because their development is cost effective. The results of different processes (microbial and mammalian) show that it is possible to reduce the number of experiments compared to classical DoE by a factor of 2-3, while increasing process understanding beyond static endpoint correlations.

2:45 Optimizing a Novel Algae Platform for the Commercial Production of Heterologous Proteins

Robert McBride, Ph.D., Director, Triton Algae Innovations

Algae are increasingly being used for the production of valuable natural products, and many strains have been coopted for commercial production. Here we show how commercially relevant process was developed for the production of heterologous proteins in a new algal strain with no prior history of commercial use. We used Design of Experiment strategies to screen variables in an iterative process that enabled this process to move into the realm of commercially relevant performance targets.

3:05 Sponsored Presentation *(Opportunity Available)*

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Leveraging the MAM for Process Control with Real-Time Monitoring and Feedback to Bioreactors

Richard Rogers, Ph.D.,Scientist 4, Just Biotherapeutics

We have developed and implemented a mass spectrometry-based multi-attribute method (MAM) that monitors known CQAs but also has the ability to identify new CQAs on the biotherapeutics. New peak detection is an instrumental element of the MAM that ensures novel modifications on the biotherapeutics are not overlooked. We are able to detect unexpected events during manufacturing by comparing a test sample to a reference standard.

4:45 Scalability of Growth Characteristics and Product Quality: Efficient Downscale Perfusion Bioprocess Development Using DOE Studies

Rainer Stahn, Ph.D., Director, Process Development, Glycotope GmbH

The sedimentation-based down-scale perfusion system SAM (10mL reactor volume) has been developed to characterize the upstream process parameters and their influence on product quality. Using DoE studies we gain a highly efficient method for media development as well as process optimization to achieve higher cell densities and higher productivities. Scalability and reproducibility of perfusions bioreactors (10mL-1000L) will be highlighted with data of the fully human, high-yield production and glycol-optimization platform GlycoExpress (GEX).

5:15 Advanced Analytical Methods to Assess the Impact of Intracellular Reactive Oxygen Species (ROS) on Mammalian Cells Productivity and Product Quality

Weimin Lin, Ph.D., Senior Scientist, Process Development, Biogen

Reactive oxygen species (ROS), a phrase used to describe a number of reactive molecules and free radicals derived from molecular oxygen, can cause negative impact to cell growth, productivity and product quality. We developed an easy, quick, reliable, near-real-time, and inexpensive method to detect ROS level in production of mammalian cell lines. Fluorescent probes were used to establish an analytical method to measure ROS level in mammalian cells. The implementation of this method and other florescent tools could increase speed and quality of bioprocess development, improve cell productivity and product quality.

5:45 Close of Day

FRIDAY, JANUARY 13

8:00 am Conference Registration and Morning Coffee

ENHANCING PRODUCT QUALITY

8:30 Chairperson's Remarks

Barthélemy Demeule, Ph.D., Senior Scientist & Senior Group Leader, Late Stage Pharmaceutical Development, Genentech

8:35 QbD Approaches to Design Leaner Formulation Robustness Studies

Barthélemy Demeule, Ph.D., Senior Scientist & Senior Group Leader, Late Stage Pharmaceutical Development, Genentech

QbD offers a formal framework for process and formulation design. Through case studies, we show how historical data and multivariate studies can be used to design lean, worst-case formulation robustness studies supporting formulation specifications.

9:05 Understanding Origins of Sequence Variants during Drug Development

Thomas Slaney, Ph.D., Scientist I, Molecular and Analytical Development, Global Manufacturing & Supply, Biologics Development & Operations, Bristol-Meyers Squibb Co.

Liquid chromatography-mass spectrometry analysis is an information-rich technique for the characterization of therapeutic proteins. This method can be employed to examine the primary sequence of expressed biotherapeutics to determine its integrity. The distribution of sequence variants observed can be utilized to discern the mechanism of their occurrence during process development.

9:35 QbD Applied to Analytical Method Optimization for Biotherapeutic Products

Alessandra Tieri, Ph.D., Researcher Scientist, Protein Chemistry, Analytical Development, Merck

Product quality should be measurable, thus accurately measuring CQAs is a must. Robust, capable analytical methods are strictly required to deliver a quality product to patients. A QbD approach is key for long-lasting analytical methods, successful troubleshooting and effective investigation closures. In the frame of analytical development and validation, tools like RA and DoE guarantee faster flows, robustness and results reliability. In the frame of the methods LCM, the DoE drive to their right adjustments.

Bioprocess Analytics

Data Measurement, Monitoring and Modeling Allow Informed Control of Bioprocesses

10:05 **Coffee Break with a Poster Pavilion** *See page 4 for details*

INNOVATIVE INSTRUMENTATION AND SAMPLING

11:00 **Sequential Injection Capillary Electrophoresis for Bioprocess Monitoring**

Rosanne Guijt, Ph.D., Alexander von Humboldt Fellow and Senior Lecturer, Australian Centre for Research on Separation Science (ACROSS), University of Tasmania

Biological processes are naturally susceptible to variability because living cells consume substrates and produce metabolites and products in a dynamic way with variations in metabolic rate across short time intervals. This presentation explores the potential of capillary electrophoresis (CE) for bioprocess monitoring. Using a novel injection strategy, this fully automated system offers high sample throughput, good temporal resolution and low sample consumption combined with robustness, sensitivity and flexibility which provides a promising new platform for pharmacological and biotechnological studies.

11:30 **High-Throughput Protein Analysis and Engineering Using Microcapillary Arrays**

Spencer Alford, Ph.D., Protein Engineer, xCella Biosciences, Inc.

We developed a high-throughput screening platform that allows researchers to assay the functional activity of millions of protein variants, displayed on or secreted from cells. This talk describes several protein analysis and engineering applications performed with this new technology platform.

12:00 pm **IT'S A WRAP: PEPTALK 2017 CLOSING PLENARY PANEL DISCUSSION** *See page 5 for details*

1:15 **Close of Conference**

Single-Use Technologies and Continuous Processing

Advancing Bioprocessing through Technological Innovation

CHI-PepTalk.com

The steady adoption of single-use technologies and subsequent move toward continuous processing for clinical and commercial manufacture have created a great need to evaluate the risks, challenges, opportunities and strategies for implementing these types of technologies into modern-day bioprocessing. Cambridge Healthtech Institute's Fourth Annual Single-Use Technologies and Continuous Processing conference once again gathers technology providers and end users to discuss approaches to current challenges, trends in technology, case studies on successful implementation, and ultimately identify how to derive as much value as possible from single-use technologies.

SUNDAY, JANUARY 8

4:00 - 5:30 pm Registration

5:00 - 8:00 Dinner Short Courses *See pages 6-7 for details*

MONDAY, JANUARY 9

7:30 am Conference Registration and Morning Coffee

CONTINUOUS PROCESSING: CONSIDERATIONS, IMPLEMENTATION AND ENABLING TECHNOLOGIES

9:00 Welcome by Conference Organizer
Kip Harry, Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks
Dennis Jenke, Ph.D., Baxter Distinguished Scientist, Technology Resources, Baxter Healthcare Corp.

FEATURED PRESENTATION

9:10 Challenges and Limitations of Continuous Processing and Use of Disposables
Berthold Boedeker, Ph.D., Chief Scientist, Global Biologics Development, Bayer Pharma AG

Continuous processing in combination with use of disposables has made significant advances in the past years. However, despite many advantages to standard processing, there are still many hurdles ahead of us, before these technologies will be suitable for routine production. This talk will summarize several aspects of necessary improvements as well as some risks associated with these technologies, which are often underestimated in their impact, such as process validation, process characterization and scale-down models.

9:50 Economics of Continuous Processing vs. Traditional Batch
Jeff Johnson, New Technology Lead, Merck & Co., Inc.

Opportunities for applying new technologies integrated with continuous processing and enabled by single use will be discussed for monoclonal antibody production. The combined efficiencies gained by continuous processing will be compared by economic criteria to current manufacturing methods. In addition, the impact of the new approaches to multi product manufacturing facilities will be described.

10:20 Coffee Break

10:45 A Single-Use Strategy to Enable Manufacturing of Affordable Biologics
Renaud Jacquemart, Ph.D., Author, BioProcess International

Single-use technologies and continuous upstream processes have proven to be cost-efficient options to increase biomass production. This case study summarizes how a single-use strategy including a holistic process approach, continuous operation, full utilization of media life (up-to 100 cycles per batch) and high throughput chromatography (residence time ≤6s and loads in kg/L media) can overcome scale limitations and enable cost-efficient manufacturing to support the growing demand for affordable biologics.

11:15 Scalability of Growth Characteristics and Product Quality: Efficient Downscale Perfusion Bioprocess Development Using DOE Studies
Steffen Kreye, Scientist, USP Development, Glycotope GmbH

The sedimentation-based down-scale perfusion system SAM (10mL reactor volume) has been developed to characterize the upstream process parameters and their influence on product quality. Using DoE studies, we gain a highly efficient method for media development as well as process optimization to achieve higher cell densities and higher productivities. Scalability and reproducibility of perfusions bioreactors (10mL-1000L) will be highlighted with data of the fully human, high-yield production and glycooptimization platform GlycoExpress (GEX).

11:45 Flexible Facility Designs Complementing Continuous Processing
Dennis Powers, Director, Sales Engineering, G-CON Manufacturing

In the future, traditional cleanroom environments and facilities will need to be more agile to adapt with manufacturers' product portfolio and throughput needs, and will require faster implementation in order to respond to new opportunities and demand around the world. The discussion will focus on advancements in single-use technologies and continuous manufacturing, future manufacturing and facility needs, and innovative cleanroom and facility designs being developed to address these needs.

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

12:45 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

STANDARDS AND RECOMMENDATIONS FOR SINGLE-USE EQUIPMENT AND PROCESS

2:00 Chairperson's Remarks
Jerold Martin, MSc, Chairman, BPSA BoD and Technology (E+L) Committee

2:05 Plastic Components and Systems Used on the Manufacturing of a Drug Product: Current Compendial Perspectives
Desmond G. Hunt, Ph.D., Senior Scientific Liaison, Standards Development, United States Pharmacopeia (USP)
USP General Chapter <661.3> contains tests, test methods and specifications for characterizing materials used to construct manufacturing components and for components used in manufacturing systems. In this presentation, the philosophy behind the form and contents of <661.3> is discussed, specifically focusing on similarities and differences between packaging (addressed in <661.1> and <661.2>) and manufacturing.

2:35 USP's Risk Evaluation Matrix
Dennis Jenke, Ph.D., Baxter Distinguished Scientist, Technology Resources, Baxter Healthcare Corp.
During this presentation, I will go into an essential aspect of <661.3>, the Risk Evaluation Matrix, in detail, thus providing the attedees with necessary clarifications and insights.

3:05 Sponsored Presentation *(Opportunity Available)*

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Wide-Scale Adoption of Single-Use Systems – What Are the Challenges ahead from the Regulators', Suppliers' and End Users' Perspectives?
Jerold Martin, MSc, Chairman, BPSA BoD and Technology (E+L) Committee
This presentation will focus on continuing developments in implementation and standardization of single use technologies and practices, especially the ongoing efforts to standardize extractables testing, but also other activites like change control and notification, GMP practices for particulate control, integrity testing, etc. I will also focus on BPSA activities along with the those of USP, ISO, ASME and ASTM.

4:30 Co-Presentation: Update on BPOG / BPSA Collaborative Efforts on Single-Use Systems
Eric Isberg, Member, Change Notification and User Specification Groups, The Bio-Process Systems Alliance (BPSA)
Ken Davis, Member, Biophorum Operations Group (BPOG)
Suppliers and end users from BioPhorum Operations Group (BPOG) and Bio-Process Systems Alliance (BPSA) were assembled to identify challenges in the Single-Use industry. Two areas that were first selected were the supplier change-control management process and the establishment of user requirements for single-use systems. This presentation will be an update on the progress that both teams have made in creating industry best practices for single-use system change notifications and user requirements.

5:00 Case Study: Efficiency Gains Using a Hybrid Disposables/ Stainless Steel Manufacturing Process
Tyler Gadoury, Chemical (Process) Engineer, Bristol-Myers Squibb Co.

5:35 BuzZ Session A
Join your peers and colleagues for interactive roundtable discussions.
Please see page 74 for additional information.

6:20-7:30 Welcome Reception in the Exhibit Hall with Poster Viewing

7:30 Close of Day

TUESDAY, JANUARY 10

8:00 am Conference Registration and Morning Coffee

RISK MITIGATION STRATEGIES FOR SINGLE-USE TECHNOLOGIES

8:30 Chairperson's Remarks
Adam Goldstein, MSc, Principal Scientist, Global Technology, Roche/Genentech

8:35 Implementation Strategies and Challenges for Single-Use at Clinical to Commercial Scale: Integrity Testing, Material Qualification, Handling Risks
Adam Goldstein, MSc, Principal Scientist, Global Technology, Roche/Genentech
This talk will focus on those challenges single-use applications currently have and may have in the future of biotech manufacturing processes. Areas of focus will be regulatory challenges for filings, leak testing and large-scale process limitations for SUTs. Strategies for on-boarding new technologies will be discussed as well.

9:05 BPOG's Five-Year Vision Plan for Disposables
Ken Wong, Deputy Director, Process Technology, Sanofi Pasteur
The uptake of disposables in GMP biomanufacturing has been gaining momentum for over the last five years. To fully incorporate such disruptive technology into commercial operation, it is necessary for biomanufacturers along with suppliers and regulators to develop and lay out a cohesive plan to realize the full benefit of disposables. During this talk, a five-year vision plan developed by BPOG members will be presented.

9:35 Sponsored Presentation *(Opportunity Available)*

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

11:00 Extractables from Single-Use Bioreactors and Impact on Cell Culture Performance
Yasser Nashed-Samuel, Ph.D., Principal Scientist, Attribute Sciences, Process Development, Amgen
Biopharmaceuticals are drugs manufactured by growing genetically engineered cells in bioreactors to produce a therapeutic protein. Plastic single-use bioreactors are of interest to biopharmaceutical drug manufacturers due their significant environmental and cost benefits and flexibility over stainless steel bioreactors. Effect of plastics on the bio-manufacturing process is not yet completely understood. A case study on extractables from single-use bioreactors and impact on cell culture performance will be presented.

11:30 Scalability of a Single-Use Bioreactor Platform for Biopharmaceutical Manufacturing

Niket Bubna, Senior Scientist, Process Development, KBI Biopharma

Here we provide an overview of the key differences between single-use and conventional stainless steel bioreactors, and highlight factors that are employed while scaling-up from small-scale glass bioreactors to 2000 L-scale single-use bioreactors. Several case studies focusing on process performance across scales into single-use bioreactors are provided. This analysis confirms that the 2000 L-scale single-use bioreactor system can be robustly employed for biopharmaceutical manufacturing.

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

12:30 Session Break

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

1:15 Close of Conference

Protein Purification and Recovery

Streamlining Processes with Innovative Technologies

Protein purification is the most costly and time-consuming process in the manufacture of proteins. Challenges are multiplied when purifying complex molecules, such as membrane proteins, bispecifics or antibody-drug conjugates. This leading purification meeting on Protein Purification and Recovery will explore how experts are optimizing processes to achieve pure protein while curtailing cost and time. Along with innovating "traditional" technologies such as Protein A and chromatography, leaders will also address alternatives and breakthroughs, such as continuous processing.

TUESDAY, JANUARY 10

1:00 pm Conference Registration

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

PURIFICATION STRATEGIES FOR CONQUERING DISEASE

2:00 Chairperson's Opening Remarks

William Gillette, Ph.D., Principal Scientist, RAS Protein Production, and Deputy Director, Protein Expression Laboratory, Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research (FNL)

KEYNOTE PRESENTATION

2:05 Advances in Purification Technologies Accelerate Vaccine Development

Yan-ping Yang, Ph.D., Senior Director and Head, Bioprocess R&D North America, Sanofi Pasteur

Over the last 25 years, significant breakthroughs in bioprocesses have been achieved. The advances in downstream technologies have benefited the vaccine industry enormously as purifying vaccine candidates to achieve consistent purity and quality in a timely manner is an integral part of the vaccine product development process. Case studies will be presented to illustrate how advances in purification technologies have facilitated vaccine process development and moved candidates faster to clinical evaluations.

2:45 Using Interaction Proteomics to Identify Novel Signaling Components Relevant for Cancer

Alexey Veraksa, Ph.D., Associate Professor, Biology, University of Massachusetts, Boston

We are interested in the structure and function of signaling networks that control cell proliferation and differentiation, and in the mechanisms that cause aberrant signaling through these networks in disease. We interrogate signaling pathways using interaction proteomics, in particular, affinity purification-mass spectrometry (AP-MS). When applied to cancer-relevant pathways, such as Notch, RTK/ERK, and Hippo, our approaches have identified novel interactions that control these signaling networks under normal and pathological conditions.

3:15 Presentation to be Announced

Sponsored by
FUJIFILM Diosynth biotechnologies

3:30 Sponsored Presentation *(Opportunity Available)*

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

PURIFYING MEMBRANE PROTEINS

4:30 New Chemical Tools for Stabilization of Membrane Proteins

Qinghai Zhang, Ph.D., Associate Professor, Integral Structural and Computational Biology, The Scripps Research Institute

Integral membrane proteins comprise about a third of proteins encoded in genomes and more than half FAD-approved drug targets. The hydrophobic nature of membrane proteins requires their solubilization as isolated stable and functional particles but also presents a challenge for many biochemical and biophysical studies. We will present new chemical tool development that enhances the stability of membrane proteins and enables successful structural determinations.

5:00 Solving the Challenges of Membrane Proteins through Nanotechnology

Stephen G. Sligar, Ph.D., Director, Swanlund Endowed Chair, Molecular and Cellular Biology, The University of Illinois

Membrane proteins are involved in numerous vital biological processes, including transport, signal transduction and the enzymes in a variety of metabolic pathways. Unfortunately, membrane proteins are inherently recalcitrant to study using the normal toolkit available to scientists. The Nanodisc platform circumvents these challenges by providing a self-assembled system that renders typically insoluble, yet biologically and pharmacologically significant, targets such as receptors, transporters, enzymes, and viral antigens soluble in aqueous media.

5:30 Close of Day

5:30 - 5:45 Short Course Registration
5:45 - 8:45 Dinner Short Courses* ***See pages 6-7 for details***
**** Separate registration required***

WEDNESDAY, JANUARY 11

8:00 am Conference Registration and Morning Coffee

BEAD-BASED PURIFICATION

8:30 Chairperson's Remarks

Christopher Gray, Ph.D., Structural Biology Team Leader, Drug Discovery Program, CRUK Beatson Institute

8:35 Magnetic Beads for Antibody Purification

Ray Low, Ph.D., Scientist, Biologics Optimization, Amgen

Current linear chromatography technologies take relatively long purification processing time from CM to purified protein. I will talk about how, using the magnetic beads with some basic tools, the processing time can be radically reduced. The product quality, processing speed and recovery parameters comparing to the traditional column based chromatography will also be discussed.

Protein Purification and Recovery

Streamlining Processes with Innovative Technologies

9:05 Core Bead Chromatography for Preparation of Highly Pure, Infectious Respiratory Syncytial Virus in the Negative Purification Mode

Sophia T. Mundle, Ph.D., Deputy Director, Protein Chemistry, Sanofi Pasteur

Respiratory syncytial virus (RSV) is an important human pathogen, and a frequent viral cause of respiratory disease in infants, the elderly and immunocompromised. The overall disease burden warrants the development of a safe and effective prophylactic vaccine. One approach to vaccination against viral pathogens is the live-attenuated virus. The data which will be presented describe a scalable, chromatography-based purification procedure for preparation of highly pure, infectious live-attenuated RSV.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

COMPUTATIONAL & MODULAR PROCESSES

10:50 Modular Approaches for Complex Therapeutic Molecules: Reinventing Smart Bioprocessing

Stefan R. Schmidt, Ph.D., MBA, Vice President, Rentschler Biotechnology

Our concept relies on the intelligent deconvolution of general purification issues in manageable chunks that are systematically rearranged to form a logical sequence of minimally required steps to achieve the intended quality and purity profile. Multiple modules are then assembled for each new molecule to redesign a quasi-platform downstream process. I will present the current status of our modular approach to transfer well-proven elements from platforms into downstream processes.

11:20 Case Study: Protease-Resistant Peptides for Protein Purification from Animal Plasma

Stefano Menegatti, Ph.D., Assistant Professor, Chemical and Biomolecular Engineering, North Carolina State University

Our goal is to develop synthetic peptide ligands with high biochemical stability and selectivity for protein purification from animal sera. To this end, we have devised a combined computational/experimental framework for generating variants of peptide ligands using non-natural amino acids. Initially, variants of antibody-binding sequences were designed and selected *in silico*. Our results strongly support the use of non-natural amino acids for designing peptide ligands with enhanced biorecognition and proteolytic stability.

11:50 Bespoke Bacterial Expression Vectors and Automated 3-Dimensional Lab Scale Purification Increases Throughput and Capacity in a Drug Discovery Protein Production Facility

Christopher Gray, Ph.D., Structural Biology Team Leader, Drug Discovery Program, CRUK Beatson Institute

The protein production section of the Beatson Drug Discovery Program supplies a considerable number of highly purified and active recombinant proteins for structural biology, biophysical and biochemistry applications. In order to minimize any bottleneck, we have devised a series of bespoke in-house bacterial expression vectors that allow the production of proteins with multiple, protease cleavable, affinity and/or solubilizing tags resulting in parallel purification of numerous proteins with minimal operator intervention.

12:20 pm Sponsored Presentation *(Opportunity Available)*

12:50 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

INNOVATING PURIFICATION PROCESSES

2:00 Chairperson's Remarks

Stefan R. Schmidt, Ph.D., MBA, Vice President, Rentschler Biotechnology

2:05 Overload vs. Bind and Elute Cation Exchange Chromatography: A Case Study

David Glover, Engineer II, Purification Development, Genentech

An alternative purification approach, overload cation-exchange chromatography, has been shown to have the potential to match the impurity removal capabilities of operating in bind and elute mode while expanding the window of operation. This talk will discuss the two operation cation-exchange chromatography modes and focus on a case study comparing and contrasting the benefits and drawbacks from both a process design and manufacturing perspective.

2:35 An Affinity Chromatography Method for Antibody Purification via Nucleotide Binding Site Targeting Ligand

Basar Bilgicer, Ph.D., Associate Professor, Chemical and Biomolecular Engineering, University of Notre Dame

This talk describes a novel affinity chromatography technique that utilizes a small ligand that targets the nucleotide-binding site (NBS) located on Fab domain for the purification of antibodies from complex protein mixtures such as cell culture media and ascites fluids. Results of this study established in two different solid support applications, provided high levels of antibody recovery (>98%) and purity (>98%), and yielded reproducible chromatograms maintaining column stability over multiple injections.

3:05 Purification of Viral Particles

Yingxia Wen, Ph.D., Director and Head, Protein Biochemistry, Research, Seqirus, a CSL Company

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:30 The RAS Initiative at the Frederick National Lab: Producing RAS and RAS-Binding Proteins for Structural Biology, Biochemistry, and Assay Development

William Gillette, Ph.D., Principal Scientist, RAS Protein Production, and Deputy Director, Protein Expression Laboratory, Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research (FNL)

Producing proteins for experiments in XRAY crystallography, NMR, SPR, assay development, CryoEM, biochemistry, tethered by layers, and neutron scattering platforms, the RAS Initiative is working closely with a large collection of internal and external groups to help advance knowledge on the structurally and biochemical properties of KRAS and its binding partners. My talk will review our progress and continuing challenges by presenting primary purification data and downstream application data.

Protein Purification and Recovery

Streamlining Processes with Innovative Technologies

5:00 Scaling-Up of a Downstream Purification Process for a New Recombinant Product (Nuwiq)

Martin Linhult, Ph.D., Head, Bio100 Line 1, Biopharmaceuticals, Octapharma

Octapharma has developed a new process for the production of a recombinant human FVIII product derived from a human cell line (HEK293F cells). Clinical trials are ongoing with positive results. During process development, several different approaches have been tested, old established techniques as well as new ones have been evaluated. In this presentation, I will discuss scale-up of a new downstream purification process and also different affinity ligands that could be applied.

5:35 BuzZ Session B

Join your peers and colleagues for interactive roundtable discussions.

Please see page 74 for additional information.

6:20 - 7:20 Reception in the Exhibit Hall with Poster Viewing

7:20 Close of Conference

Higher-Throughput Protein Production and Characterization

Innovating Processes

High-throughput processes have transformed the traditional protein-by-protein trial-and-error approach for testing criteria and scaling up. In this leading conference on Higher-Throughput Protein Production and Characterization, HTP will be explored in the quest to develop methods that ensure quality and translate to large scale. 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 in order to reduce the time and effort needed to successfully analyze proteins, fine tune processes, and achieve well-folded, pure protein.

THURSDAY, JANUARY 12

7:45 am Conference Registration and Morning Coffee

HIGH-THROUGHPUT PROTEIN PURIFICATION

8:15 Chairperson's Opening Remarks

William Clay Brown, Ph.D., Associate Research Scientist and Scientific Director, High-Throughput Protein Lab, Center for Structural Biology/Life Sciences Institute, University of Michigan

KEYNOTE PRESENTATION

8:20 Scale-Down Models for High-Throughput Chromatography of Proteins

Alois Jungbauer, Ph.D., Professor, Laboratory of Protein Technology and Downstream Processing, Austrian Center of Biotechnology, Department of Biotechnology, University of Natural Resources and Life Sciences (BOKU)

To get reliable data from high throughput methods used for development and optimization of protein chromatography the measured parameters must allow prediction to pilot and large-scale operation. Microtiter plates are used to estimate equilibrium data. Models to predict the power input and stirring efficiency will be shown, and for kinetic data, scale-down models using mini chromatography columns will be discussed and methodology, how to scale it will be shown.

9:00 Automation Solutions for Different Stages of Protein Purification Process Development

Jean Aucamp, Ph.D., Principal Scientist, Technology Development, Novel Biological Entities, Novartis Pharma AG

Advances in biotechnology significantly decreased timelines required for lead development while simultaneously increasing the number of leads of interest. These technology and cost drivers demand increased efficiencies in purification operations. Examples are presented demonstrating how automation supports protein purification and various stages of process development. Emphasis will be on approaches for combinatorial process synthesis, process robustness evaluation, scaled process confirmation and process characterization studies.

9:30 Enabling High Throughput Antibody Purification: Achieving mg Scale Antibody Production with Throughput and Quality

Jiyoung Hwang, MSc, Associate Scientist, Biology, Gilead Sciences

High-throughput antibody purification has become a growing area of focus. We have implemented a HTP purification platform that can process culture volumes ranging from 500uL up to 30mL, with elution products showing high purity. Coupling our HTP transient transfection of Expi293F and ExpiCHO cultures with our HTP purification platform has allowed us to produce milligram-scale titers of many antibodies, which has expanded our capability in supporting Gilead's large molecule programs.

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

11:00 Multistage Purification of Human Antibodies for Candidate Selection Using an Automated Liquid Handler Platform That Enables High Throughput and High Recovery

Louis Fabri, Director, Protein Technologies, Research, CSL Limited

The selection of lead antibodies in pharmaceutical drug development programs initially involves generating a diverse repertoire of proteins using optimized transient mammalian expression systems. This presentation will describe the rapid purification of proteins, through multiple stages of chromatography, that have been generated via commercially available high titre transient mammalian expression systems such as Expi293F™ or ExpiCHO™, using our recently described Janus platform system coupled to a robotic arm.

11:30 Sponsored Presentation *(Opportunity Available)*

12:00 pm Session Break

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

1:15 Ice Cream Break in the Exhibit Hall with Poster Viewing

INNOVATING PROCESSES WITH HTP STRATEGIES

2:00 Chairperson's Remarks

Louis Fabri, Director, Protein Technologies, Research, CSL Limited

2:05 Applying Synthetic Biochemistry and High-Throughput Processes to Enable Bugs to Make Drugs

Andrew Fosberry, Ph.D., Manager, Expression and Fermentation Sciences, GlaxoSmithKline

Chemical bio-transformations using enzymes and microbes to make small molecule drugs were a thing of the past, but not now! The realisation that bacteria make pretty good medicinal chemists and can actually do things that chemists cannot, along with other pressures such as cost of goods, and sustainability of our processes triggered a route change. I will give examples on how Synthetic Biochemistry is bringing chemistry and biology closer together to discover drugs.

2:35 Using High-Throughput Techniques to Produce Difficult Targets: Flavivirus NS1, an Updated Case Study

William Clay Brown, Ph.D., Associate Research Scientist and Scientific Director, High-Throughput Protein Lab, Center for Structural Biology/Life Sciences Institute, University of Michigan

Flavivirus, such as West Nile, Dengue and Zika, represent a serious global threat to human health. We applied high-throughput cloning and expression evaluation techniques and a matrix buffer screen to develop a robust production pipeline for NS1 protein, a multi-functional virulence factor, from several different Flavivirus, which resulted in the determination of crystal structures of full-length, glycosylated NS1.

3:05 Sponsored Presentation *(Opportunity Available)*

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

Higher-Throughput Protein Production and Characterization

Innovating Processes

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4:15 HTP Production of the Human PDZ Repertoire, Identification and Ranking of the PDZ Interacting with the Human Papillomavirus E6 Oncoprotein

Renaud Vincentelli, Ph.D., Head, Protein Production, Structural Biology Facility, CNRS Univ Aix Marseille I & II

Using our custom *E. coli* HTP protein production pipeline (Saez et al, JOVE 2014), we could produce the 266 human single PDZ domains. To characterize and quantify the HPV E6 - PDZome binding interactions, we automated the hold-up assay (Vincentelli et al, Nature Methods 2015), a quantitative and versatile *in vitro* protein-protein interaction assay. The protocol and some new results on this application will be exposed during the seminar.

4:45 A Fluorescent Protein Toolbox for Visualizing Protein Trafficking, Protein Interactions, and Membrane Protein Biogenesis

Geoffrey Waldo, Ph.D., Team Leader, Los Alamos National Laboratory

We describe the split fluorescent protein toolbox we have developed for studying protein trafficking and protein-protein interactions. The system differs from others by the use of small peptide tags rather than large protein fragments. We describe case studies of its application in our lab and elsewhere to host-pathogen protein-protein interactions, trafficking of effectors, and protein-RNA interactions. We also cover recent applications for experimental elucidation of membrane protein topology and compare capturing the split GFP tag on nascent protein with detection after the membrane protein has been folded into the membrane.

5:15 A Miniaturized Process Chain Representing the Entire Downstream Process for Inclusion Bodies

Cornelia Walther, Ph.D., Scientist, Biotechnology, University of Natural Resources and Life Sciences Vienna (BOKU)

We present a miniaturized high-throughput purification process representing the entire downstream purification for inclusion bodies from mechanical cell disruption to chromatographic purification. This downstream process chain connects extensive DoE setups in upstream development with the recovery of the active protein from inclusion bodies at a very early stage of process development. This fast and material saving platform method reduces the initial barrier for IB processes thus opening potential for new products.

5:45 Close of Day

FRIDAY, JANUARY 13

8:00 am Conference Registration and Morning Coffee

USING HTP TO EXTRACT DATA AND ASSESS MANUFACTURABILITY

8:30 Chairperson's Remarks

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

8:35 High-Throughput Methods for the Characterization of Relevant Protein Features

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

To optimize the efficiency of the laborious process of generating specific affinity reagents, we established a streamlined pipeline consisting of simultaneous selections against 94 targets and subsequent high-throughput screenings and validations. This fast and efficient platform allowing the reliable discovery of recombinant binders requires the improvement of existing and the development of novel high-throughput methods which will be presented.

9:05 High-Throughput Biophysical and Biochemical Stability Screening for Early Stage Antibody Discovery

Yingda Xu, Ph.D., Associate Director, Protein Analytics, Adimab LLC

Problems in the development of antibodies can often be traced back to their intrinsic poor biophysical and biochemical stabilities. High-throughput screening assays are developed or adapted to fit in the scope of early discovery stage to filter out candidates with poor properties.

9:35 High-Throughput Manufacturability Assessment of Complex Biologics

Zhenyu Gu, Ph.D., Development Scientist III, Early Assay Development, Alexion Pharmaceuticals

Bispecific/biparatopic antibodies, modified enzymes and fusion proteins have gained increasing popularity due to their unique therapeutic profiles. However, these molecules often pose significant challenges to manufacture as a result of their complex designs. In this study, high-throughput mechanical/chemical stress relevant to manufacture process was coupled with high-throughput orthogonal characterization methods to screen these early stage molecules for their manufacturability, focusing on solubility, aggregation, colloidal and thermal stability.

10:05 Coffee Break with a Poster Pavilion *See page 4 for details*

MANAGING A NIMBLE PRODUCTION LAB

11:00 Sequential Injection Capillary Electrophoresis for Bioprocess Monitoring

Rosanne Guijt, Ph.D., Alexander von Humboldt Fellow and Senior Lecturer, Australian Centre for Research on Separation Science (ACROSS), University of Tasmania

Biological processes are naturally susceptible to variability because living cells consume substrates and produce metabolites and products in a dynamic way with variations in metabolic rate across short time intervals. This presentation explores the potential of capillary electrophoresis (CE) for bioprocess monitoring. Using a novel injection strategy, this fully automated system offers high sample throughput, good temporal resolution and low sample consumption combined with robustness, sensitivity and flexibility which provides a promising new platform for pharmacological and biotechnological studies.

11:30 High-Throughput Protein Analysis and Engineering Using Microcapillary Arrays

Spencer Alford, Ph.D., Protein Engineer, xCella Biosciences, Inc.

We developed a high-throughput screening platform that allows researchers to assay the functional activity of millions of protein variants, displayed on or secreted from cells. This talk describes several protein analysis and engineering applications performed with this new technology platform.

12:00 pm IT'S A WRAP: PEPTALK 2017 CLOSING PLENARY PANEL DISCUSSION *See page 5 for details*

1:15 Close of Conference

Biocatalysis and Bio-Based Chemical Production

Where Biocatalysis Meets Synthetic Biology

New chemical pathways and custom-made biocatalysis are creating exciting opportunities for bio-based chemical production across a range of industries, from pharma to food, fine chemicals to agriculture. Coupled with advances in synthetic biology, the opportunities in industrial biotech have never been greater.

Cambridge Healthtech Institute's Biocatalysis and Bio-Based Chemical Production conference tackles the latest advances in biocatalysis and synthetic biology in enzyme engineering with dedicated sessions on novel applications, enzyme design, screening, development and new synthetic pathways.

SUNDAY, JANUARY 8

4:00 - 5:30 pm Registration

5:00 - 8:00 Dinner Short Courses *See pages 6-7 for details*

MONDAY, JANUARY 9

7:30 am Conference Registration and Morning Coffee

WHY THE TIME FOR BIOCATALYSIS IS NOW - OPPORTUNITIES AND INDUSTRIAL APPLICATIONS

9:00 Welcome by Conference Organizer
Daniel Barry, Senior Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks
John Grate, Ph.D. , Grate Consulting

KEYNOTE PRESENTATION

9:10 Innovation by Evolution: Expanding the Enzyme Universe
Frances Arnold, Ph.D., Dickinson Professor of Chemical Engineering, Bioengineering and Biochemistry, California Institute of Technology
Not satisfied with nature's vast catalytic repertoire, we want to create new enzymes and expand the range of chemical reactions that can be genetically encoded. I will describe how we can use the most powerful algorithm for biological design, evolution, to optimize existing enzymes and invent new ones. We have made enzymes that catalyze important reactions not (yet) known in nature, thereby adding new chemistry to the biological world.

9:50 Engineering Biocatalysts for Non-Natural Reactions
David Rozzell, Ph.D., Senior Vice President, Biocatalysis, Provivi, Inc.
The surprising discovery that heme enzymes can catalyze carbene and nitrene transfer reactions has provided chemists with a new biocatalytic alternative for cyclopropanation and other related chemistry. Key to the success is the engineering of enzymes to increase both the rate and the stereoselectivity of the reaction. We will describe recent progress in developing highly selective cyclopropanation biocatalysts for producing important chiral intermediates for the pharmaceutical and agricultural industries.

10:20 Coffee Break

10:45 Engineering Biocatalysts for the Selective Functionalization of Biomolecules
Keith A. Canada, Ph.D., Director, Chemical Biotechnology, Head of Protein Engineering, Merck Research Laboratories
Site-specific bioconjugation chemistry is a focus area of the pharmaceutical industry due to its ability to produce novel biomolecules, facilitate imaging studies, enhance drug delivery, and alter pharmacokinetics. Unfortunately, there is a limited tool box for site-selective modification of chemical entities on proteins. Our efforts to engineer biocatalysts to site-selectively functionalize insulin to aide in the synthesis of next generation diabetes therapies will be described.

11:15 Industrial Application of Biocatalysis - BASF Case Study
David Weiner, Ph.D., Vice President, Technology & Product Development, BASF Enzymes, LLC
Biocatalysis involves the use of one or more enzymes to catalyze chemical reactions. Using examples, this presentation will look at the end-to-end discovery, design and development of industrial applications of biocatalysis at BASF.

11:45 Development of Biocatalytic Routes to APIs - Evaluate; Design; Build; Test; Repeat!
Karen Holt-Tiffin, Ph.D., Head, Biocatalysis, Dr. Reddy's Laboratories Ltd.
Dr. Reddy's has more than 20 years' experience of using biocatalysis as an enabling technology for the development of efficient processes to chiral intermediates and APIs. This presentation will tell the story of the development of a novel and efficient route to a launched anti-hepatitis C API. We will frame the discussion using the design cycle concept of Evaluate; Design; Build; Test, a useful management and communication tool.

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

12:45 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

INDUSTRIAL APPLICATIONS OF BIOCATALYSIS - DISCOVERY, DESIGN AND DEVELOPMENT

2:00 Chairperson's Remarks
James Lalonde, Senior Vice President, R&D, Codexis

2:05 Bioconversion of Methane to Chemical and Protein Products
Lori Giver, Ph.D., Vice President, Biological Engineering, Calysta
Calysta, Inc. has developed a platform for host organisms (methanotrophs) capable of metabolizing this abundant domestic feedstock to a variety of products including higher value biochemicals and single cell protein. The genetic tools, together with innovative fermentation and bioprocess approaches, enable the rapid implementation of well-characterized pathways to utilize natural gas as a biological feedstock instead of sugar. Longer term, biomass-to-methane strategies may eventually enable a fully renewable carbon cycle.

Biocatalysis and Bio-Based Chemical Production

Where Biocatalysis Meets Synthetic Biology

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2:35 Cyanuric Acid Hydrolase: New Applications for an Ancient Enzyme
Lawrence P. Wackett, Ph.D., McKnight Professor, Biochemistry, Molecular Biology and Biophysics, University of Minnesota

Cyanuric acid is a prebiotic compound, produced industrially in the modern world, and metabolized by a microbial enzyme having a unique fold and a novel mechanism. Cyanuric acid occurs principly as a product of water disinfection. Particularly for recreational waters (pools and spas), an enzyme-based cyanuric acid removal filter has long been sought. The fundamental properties and application of an immoblized, thermophilic cyanuric acid hydrolase will be described.

3:05 Sponsored Presentation *(Opportunity Available)*

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Examining Crosstalk between Biocatalytic and Chemocatalytic Chemistry
David B. Berkowitz, Ph.D., Willa Cather Professor of Chemistry, Department of Chemistry, University of Nebraska

This talk will discuss several approaches to exploiting enzymes for asymmetric synthetic ends. On the one hand, enzymes are employed for asymmetric transformations directly, with particular attention to dynamic reductive kinetic resolution (DYRKR). Related to this, the use of enzymatic chemistry and novel sigmatropic rearrangement chemistry in sequence is used to forge more complicated synthons. Finally, the *in situ* Enzymatic Screening (ISES) technique for catalyst/reaction discovery will be described.

4:30 Smart Library Design as Enabler for Protein Engineering in Today's Industrial Biotechnology
Tim Hitchman, Ph.D., Director, Innovation, DSM Food Specialties

Protein engineering began in the 1970s with site-directed mutagenesis based on rational targeting of functional amino acids. The molecular biology revolution that followed allowed for broad, impartial interrogation of sequence space, facilitated by high-throughput screening technologies. The modern genomic and bioinformatics era provides a wealth of structural and sequence data that allows for a return to smart protein engineering. Examples from DSM's industrial biotechnology experience will be presented.

5:00 Quorum Quenching Lactonases: Towards a Specific Control of Complex Microbial Communities?
Mikael Elias, Ph.D., Assistant Professor, Biochemistry, Molecular Biology and Biophysics, University of Minnesota

Interfering with bacterial chemical signaling has emerged as a powerful mean to inhibit bacterial virulence and biofilms. We focus on the study and the molecular engineering of enzymes that can degrade signaling molecules. Specifically, we improve these enzymes for higher stability and activity as well as exquisite specificity. We highlight the ability of these molecules to control bacterial virulence *in vivo* and change complex microbial communities.

5:35 BuzZ Session A
Join your peers and colleagues for interactive roundtable discussions.
Please see page 74 for additional information.

6:20-7:30 Welcome Reception in the Exhibit Hall with Poster Viewing

7:30 Close of Day

TUESDAY, JANUARY 10

8:00 am Conference Registration and Morning Coffee

THE ROLE OF SYNTHETIC BIOLOGY IN BIOCATALYSIS

8:30 Chairperson's Remarks
Yoram Barak, Group Leader, Fine Chemicals and Biocatalysis Research, BASF

8:35 An Overview of Synthetic Biology in the Production of Biocatalysts
Rina Singh, Ph.D., Senior Director, Industrial and Environmental Section, Biotechnology Innovation Organization (BIO)

9:05 Synthetic Biology Approach to Natural Product Diversification
Gavin Williams, Ph.D., Associate Professor, Chemistry, North Carolina State University

We describe a comprehensive program of enzyme engineering, directed evolution, and synthetic biology aimed at constructing artificial bacterial strains capable of producing complex natural products that are modified with non-natural chemical functionality. Key to our synthetic biology approach is the development of genetically encoded biosensors for non-natural small molecules that enable ultra high-throughput methods to engineering biosynthetic pathways. This approach expands the synthetic capabilities of natural product diversification strategies.

9:35 Sponsored Presentation *(Opportunity Available)*

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

11:00 Rapid Enzyme Engineering Strategies for Synthetic Biology
Richard Fox, Ph.D., Executive Director, Data Sciences and Information Technologies, Intrexon

Numerous approaches seeking to accelerate the process of enzyme engineering have been proposed over the last several decades, however, few principles have been agreed upon by the community that would allow practitioners to ascertain the best strategy for their system. Using supporting examples to illustrate core principles, this presentation will offer a much needed framework to adjudicate competing claims of efficacy, cost, and speed for synthetic biology engineering.

11:30 The Development and Engineering of Enzymes for New Synthetic Pathways
Jason Micklefield, Ph.D., FRSC, Professor of Chemical Biology, University of Manchester

The presentation will focus on the engineering of enzymes from secondary metabolism to enable the structural diversification and optimization of natural product scaffolds of therapeutic and agrochemical applications. The deployment of enzymes in new synthetic pathways (cascades), both *in vivo* and *in vitro*, to create novel non-natural bioactive small molecules will also be described.

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

12:30 Session Break

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

1:15 Close of Conference

Plant-Based Expression and Synthetic Biology

Enabling the Power of Plants

Interest in plant-made pharmaceuticals is rising again following recent positive regulatory approvals, government support and improvements in production methods. Cambridge Healthtech Institute's Inaugural Plant-Based Expression and Synthetic Biology conference showcases the latest developments in plant-based product development, with in-depth case studies on protein engineering, expression, process development, scale-up, commercialization and synthetic biology for host improvement.

TUESDAY, JANUARY 10

1:00 pm Conference Registration

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

ADVANCES IN MOLECULAR PHARMING AND STRATEGIES FOR BRINGING PRODUCTS TO MARKET

2:00 Chairperson's Opening Remarks

Julian Ma, Ph.D., Hotung Chair of Molecular Immunology, Institute for Infection and Immunity, St. George's Hospital Medical School, University of London

KEYNOTE PRESENTATION

2:05 Understanding the Unique Selling Points of Plants for the Future of Molecular Pharming

Julian Ma, Ph.D., Hotung Chair of Molecular Immunology, Institute for Infection and Immunity, St. George's Hospital Medical School, University of London

After two decades, the first two commercial products of molecular pharming were recently licensed. In Europe, approval of a GMP-compliant manufacturing process for monoclonal antibody production in tobacco plants dispelled concerns around quality control of plant-derived biologics. Significant progress in transient expression technologies has been made with influenza vaccines and ZMapp antibodies entering clinical trials.

2:45 ZMapp: The Road to Regulatory Approval through an Epidemic

Michael Pauly, Ph.D., CSO, Mapp Biopharmaceuticals

ZMapp is a drug composed of three monoclonal antibodies that target the Ebola virus. Although there is limited infrastructure to manufacture plant-made pharmaceuticals, it was only because ZMapp was being produced at Kentucky BioProcessing that any ZMapp was available for compassionate use during the recent Ebola epidemic in West Africa. This talk will discuss how Mapp is using multiple manufacturing platforms to meet both the patient and regulatory requirements for ZMapp.

3:15 Sponsored Presentation *(Opportunity Available)*

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

4:30 Regulatory Perspectives in the Development of Plant-Made Recombinant Biologics

Daniel Tusé, Ph.D., Managing Director, DT/Consulting Group

Plant-manufactured products including biopharmaceuticals, food additives, industrial reagents and pesticides must satisfy quality criteria coincident with their end use. In the U.S. the development and approval of these products fall under the scrutiny of one or more regulatory agencies, including FDA, USDA and EPA, with analogous situations in other countries. Case studies will be presented to illustrate the regulatory landscape impacting various plant-made product classes and the options available for accelerated product approval.

5:00 Interberry alpha®: Development Process, Licensing Process and Necessary Approval

Akira Ito, Ph.D., Senior Researcher, Plant Molecular Technology Research Group, Bioproduction Research Institute, AIST Japan

Edible and oral administration of raw plant materials as medicine are some of the benefits of PMPs. However, it had been thought that it is impossible to comply with GMP regulations. Here, we introduce the development of Interberry alpha®, which is used for canine gingivitis, as an example of orally administered medicine composed of freeze-dried transgenic strawberry powder.

5:30 Close of Day

5:30 - 5:45 Short Course Registration
5:45 - 8:45 Dinner Short Courses* ***See pages 6-7 for details***
**** Separate registration required***

WEDNESDAY, JANUARY 11

8:00 am Conference Registration and Morning Coffee

PROCESS OPTIMIZATION IN MOLECULAR PHARMING

8:30 Chairperson's Remarks

Somen Nandi, Ph.D., Managing Director, Global HealthShare® Initiative, Department of Molecular & Cellular Biology, University of California

8:35 Critical Considerations for Recombinant Protein Process Development

Somen Nandi, Ph.D., Managing Director, Global HealthShare® Initiative, Department of Molecular & Cellular Biology, University of California

Currently most of the therapeutics are made of recombinant proteins. Plant-based platforms are becoming commercially acceptable as recombinant protein production for human therapeutics. Early analysis of any developing processes is pivotal in transforming an R&D process into a manufacturing one. It is important to develop and integrate the process that is linearly scalable. The critical considerations for process development particularly from plant-derived recombinant proteins for manufacturing will be discussed.

9:05 Transient Modulation of *Nicotiana benthamiana* Host Cell Physiology: Insights, Implications and Improvements

Frank Sainsbury, Ph.D., Associate Group Leader, Australian Institute for Bioengineering and Nanotechnology (AIBN), The University of Queensland

Transient expression enables non-sequential co-transformation of multiple genes, permitting the concurrent and rational modulation of host factors to

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Enabling the Power of Plants

improve recombinant protein stability. This approach has been used to modulate proteolytic activity and to modify organellar pH, increaseing yields of susceptible proteins. This talk will highlight proteomic approaches used to understand the impact of transient host modification in *Nicotiana benthamiana* leaves, providing insight into mechanisms and regulation of recombinant protein production.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

10:50 Scale-Up Production of IBIO-CFB03 Using the *Nicotiana benthamiana* Transient Expression Platform

Sylvain Marcel, Ph.D., Senior Scientist, Molecular Biology, iBio CMO

Transient expression in *Nicotiana benthamiana* employs a single plant as the bioreactor unit. The process scales linearly by simply growing more plants and is not dependent on exhaustive comparability studies as commonly observed in stirred tank bioreactor-based expression platforms. The case study for commercial cGMP scale-up manufacturing of IBIO-CFB03, a drug candidate for the treatment of fibrosis, will be presented. The scale-up study was supported by Quality-by-Design to allow direct process translation and creation of design space.

11:20 Plant Cell Cultures – A New Host for a New Era

Karen A. McDonald, Ph.D., Professor, Chemical Engineering, University of California, Davis

Plant cell bioreactor production of recombinant proteins offers a number of advantages over traditional microbial and/or mammalian host systems such as intrinsic safety, cost-effective bioprocessing, and capacity for protein post-translational modifications. Since plant cells grow as aggregates, they are well-suited to integrated continuous bioprocessing strategies. Semicontinuous bioreactor-based production of recombinant proteins from transgenic lines as well as transient production in plant cell suspension cultures will be presented.

11:50 Pre-Column Product Purification – Selecting Methods that Facilitate Clarification and HCP Removal

Johannes Felix Buyel, Ph.D., Head, Integrated Production Platforms; Fraunhofer Institute for Molecular Biology and Applied Ecology IME

Host cell proteins (HCPs) can account for a large share of total soluble protein (TSP) in plant extracts reducing the product specific capacity on a first chromatographic capture step and potentially putting the target protein at risk of proteolytic degradation. Here we present several heat and membrane-based methods that facilitate the removal of up to 95% of HCPs prior to chromatographic purification of three multi-domain malaria vaccine candidate proteins, thereby simplifying subsequent product purification and preventing proteolytic degradation.

12:20 pm Sponsored Presentation *(Opportunity Available)*

12:50 Session Break

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

PROCESS OPTIMIZATION IN MOLECULAR PHARMING

2:00 Chairperson's Remarks

Sylvain Marcel, Ph.D., Senior Scientist, Molecular Biology, iBio CMO

2:05 "4 P" Impurities that Impact Downstream Processing Efficiency and Cost

Zivko Nikolov. Ph.D., P.E., Dow Professor, Biological and Ag Engineering, National Center for Therapeutic Manufacturing, Texas A&M University

Phenolics, phytic acid, proteases and polysaccharides (4Ps) can cause unsolicited "pain" during process development. Often, their presence in plant extracts is not anticipated or considered important until the purification optimization stage is reached. These days, phenolics and proteases in leafy extracts are an expected nuisance, but the other two are less so. The impact of these impurities on purification efficiency is product dependent and possible to overcome by modifying extraction conditions and primary recovery.

2:35 Clinical Development of Moss-aGal for Treatment of Fabry Disease

Andreas Schaaf, Ph.D., CSO, Greenovation Biotech GmbH

BryoTechnology is a plant-based cGMP expression platform using the moss Physcomitrella. Highly amenable to genome engineering, this higher eukaryotic organism enables the design and manufacture of next generation therapeutics. Moss-aGal, a moss-made version of human alpha-galactosidase developed for enzyme replacement therapy (ERT) in Fabry patients exhibits an extraordinary homogenous N-glycosylation profile being relevant for cellular uptake into patients' cells. Advantages of moss-based production will be discussed along this case study.

3:05 Rapid Engineering and Production of Novel Biopharmaceuticals Using a Plant Viral Vector System

Nobuyuki Matoba, Ph.D., Associate Professor, Department of Pharmacology and Toxicology, James Graham Brown Cancer Center, University of Louisville School of Medicine

Plants provide an alternative manufacturing platform for recombinant proteins. The advent of transient overexpression vectors has opened a new avenue, enabling rapid design, screening and production of novel biopharmaceuticals. As an example, I will present the development of a "lectibody" using a plant viral vector system. The lectibody showed high binding specificity to oligomannose glycans and exhibited broad anti-viral and anti-cancer activity with a high therapeutic index.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:30 The Role of Molecular Pharming for Biosimilars

Don Stewart, Ph.D., CEO, PlantForm Corporation

5:00 Plant-Based Production of Industrial Proteins

Elizabeth E. Hood, Ph.D., CEO, Infinite Enzymes, LLC, Distinguished Professor of Agriculture, Arkansas State University

The plant production system is advantageous for industrial enzymes and proteins. Markets of choice are enzymes with large-scale applications that demand low-cost manufacturing. Plants are also advantageous for products that are harmful to single cell systems, for example oxidation/reduction enzymes.

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Enabling the Power of Plants

Four classes of enzymes will be discussed: peroxidase, amylase, cellulase and lipase/phospholipase. Advantages of plants, issues that have arisen, and potential for addressing markets will be demonstrated by these examples.

5:35 **BuzZ Session B**
Join your peers and colleagues for interactive roundtable discussions.
Please see page 74 for additional information.

6:20-7:20 **Reception in the Exhibit Hall with Poster Viewing**

7:20 **Close of Conference**

Microbial Production

Optimizing the Production of Microbial-Based Expression Systems

CHI-PepTalk.com

Microbial-based expression systems offer significant advantages over their mammalian counterpart by delivering faster development times, higher yields, improved product quality and lower production costs, particularly in *E. coli*.

Cambridge Healthtech Institute's Microbial Production conference covers the latest developments in microbial-based expression and production, helping you optimize your microbial R&D and clinical stage processes, from screening to strain development, expression to scale-up. The meeting also features sessions on optimizing microbial systems for industrial applications.

THURSDAY, JANUARY 12

7:45 am Conference Registration and Morning Coffee

OPTIMIZING PROTEIN EXPRESSION IN MICROBIAL SYSTEMS

8:15 Chairperson's Opening Remarks
T.K.S. Kumar, Ph.D., Professor, Chemistry & Biochemistry, University of Arkansas

KEYNOTE PRESENTATION

8:20 Bacterial Glycoengineering: From Cellular Enzymes and Pathways to Human Therapeutics and Vaccines
Matthew P. DeLisa, Ph.D., William L. Lewis Professor of Engineering, Chemical and Biomolecular Engineering, Cornell University

9:00 Development of a High-Titer *E. coli* Extracellular Expression System
Teri Aldrich, Ph.D., Principal Investigator, Bio-Process Development, ZymoGenetics, a Bristol-Myers Squibb Co.
This presentation will describe the development of a high titer *E. coli* expression system that combines the favorable characteristics of this organism with the benefits of extracellular protein production. This system can quickly generate a production strain capable of producing greater than 6 g/L recombinant protein in a 60 hour, fed-batch fermentation process.

9:30 *E. coli* Periplasmic Expression of Antibody Fab' Fragments
Mark Ellis, Principal Scientist, Protein Expression and Purification, UCB Pharma
Engineered variants of wild type *E. coli* strains have been developed which significantly improved periplasmic Fab expression yields. Furthermore, co-expression of *E. coli* host proteins, combined with engineered strains and fermentation process refinements have enabled Fab yields over 5g/L. These increases have been achieved without compromising cell viability or the quality of the Fab produced.

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

11:00 Altered *E. coli* Enables the Production of Challenging Proteins
Feras Hatahet, Ph.D., Scientist, Protein Technologies, Amgen

11:30 Unleash the Yeast - Enhancing Expression of Biotherapeutics in *Pichia*
Sponsored by VTU technology
Iskandar Dib, Ph.D., Principal R&D Manager, Process Development & Analytics, VTU Technology GmbH
A library of AOX promotor variants has been used to express therapeutic protein candidates in *Pichia pastoris* at unprecedented yields often exceeding 10 g/L by finding the ideal promotor variant for each target protein. The technology can further be used to enable cells to provide expression enhancing factors in a well-dosed manner and just in time during expression of a target protein. Both yield and quality of the target protein are thus maximized.

12:00 pm Session Break

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

1:15 Ice Cream Break in the Exhibit Hall with Poster Viewing

OPTIMIZING PROTEIN PRODUCTION IN MICROBIAL SYSTEMS

2:00 Chairperson's Remarks
T.K.S. Kumar, Ph.D., Professor, Chemistry & Biochemistry, University of Arkansas

2:05 Strain Engineering to Improve the *E. coli* Fermentation Platform
Karthik Veeravalli, Ph.D., Senior Engineer, Late Stage Cell Culture, Genentech
This talk will discuss two examples of how production strains were engineered for enhancing our fermentation platform. In the first example, an amino acid biosynthetic pathway was engineered to prevent a potential sequence variant. In the second example, metabolic pathways were engineered to reduce the formation of an undesirable metabolite thus improving process robustness and product titer.

2:35 PeriTune: Matching Expression Rate to Secretion Capacity
Neil Dixon, Ph.D., BBSRC Fellow, MIB, University of Manchester
Here we report the development and application of a clone optimization platform PeriTune, for the expression of clinically relevant recombinant proteins into the periplasmic space of *E. coli*. This platform is underpinned by a novel expression system that operates at the translational level. The RiboTite system permits tight basal control, high levels of expression upon induction, and tunable cellular level regulation permitting avoidance of host cell secretion capacity overload.

3:05 Sponsored Presentation *(Opportunity Available)*

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Expression of the Cytokine IL-7 in *E. coli* and *Pichia pastoris* for the Identification of IL-7 Mutants that Modulate T-Cell Signaling
Ralf Paul, Ph.D., Senior Scientist Protein Sciences, Biology Department, Medivir AB
To establish a robust protocol for IL-7 cytokine purification we compared recombinant expression in *E. coli* and *P. pastoris*. Refolding from *E. coli* inclusion bodies yielded monomeric protein for all of about two dozen IL-7 mutants designed for modified receptor binding. Mapping the IL-7/ common gamma chain (CD132) interaction surface and identification of IL-7 mutants deficient in T-cell signaling may serve as a starting point for small molecule inhibitor development.

Microbial Production

Optimizing the Production of Microbial-Based Expression Systems

4:45 Expression of XTEN, an Unstructured Polypeptide Which Enables Improved *in vivo* Half Life, and the Development of XTENylated Biotherapeutics

Jonathan Mott, MS, Process Development Engineer, Amunix Operating

XTEN is a class of non-repetitive protein polymers - composed of Ala, Pro, Glu, Gly, Ser, and Thr - designed to increase *in vivo* half-lives of therapeutic peptides and proteins. Through codon usage screening, as well as host and plasmid backbone engineering, the XTEN platform has been enhanced to also enable high titer soluble expression in *Escherichia coli*, even with fusions of difficult to express payloads such as hGH, Glucagon, and ScFvs.

5:15 Data Science for Microbial Manufacturing: Root Cause Analysis to Increase Downstream Processing Step Yields

Christoph Herwig, Ph.D., Professor, Head, Research Division, Biochemical Engineering, Vienna University of Technology

Manufacturing process variations in upstream, recovery and downstream unit operations frequently lead to non-acceptable downstream yields or even failed batches. Although process data is available, identifying the root cause(s) is challenging due to i) high number of potential impacting factors and interaction between parameters. Based on a case study, we demonstrate how analytical, process control system and batch record data to improve step yields based on a data science approach.

5:45 Close of Day

FRIDAY, JANUARY 13

8:00 am Conference Registration and Morning Coffee

THE POWER OF MICROBES TO PRODUCE NOVEL PROTEINS AND PRODUCTS

8:30 Chairperson's Remarks

Julio A. Camarero, Ph.D., Associate Professor, Department of Pharmacology and Pharmaceutical Sciences, School of Pharmacy, University of Southern California

8:35 Engineering High-Titer Heterologous Protein Secretion in Bacteria

Danielle Tullman-Ercek, Ph.D., Department of Chemical and Biological Engineering, Northwestern University

Biotherapeutic production in bacteria would benefit greatly from a high-titer secretion strategy. We engineered the type III secretion system in Salmonella enterica for this purpose because it is non-essential for bacterial metabolism and allows for target proteins to cross both bacterial membranes in one step. Our platform enables the high-titer production of a variety of biochemically challenging heterologous proteins at titers >100 mg/ml and >85% purity.

9:05 Expression of Recombinant Hc Fragment of Botulinum Neurotoxin as an Alternative Antigen for Botulinum Antitoxin Production

Ran Zichel, Ph.D., Department of Biotechnology, Head, Israel Institute for Biological Research

The Hc fragment of botulinum neurotoxins is a promising vaccine candidate. However, its expression in *E. coli* is considered challenging. In the current study, a thorough optimization process was used to improve expression yield by an order of magnitude, obtaining the gram-quantities required to immunize horses for antitoxin production. The process was scaled up to 4-L fermentation scale, and went through full validation. Preliminary immunogenicity results in horses are encouraging.

9:35 Microbial Production of Opiates and Related Isoquinoline Alkaloids

Fumihiko Sato, Ph.D., Professor, Division of Integrated Life Science, Graduate School of Biostudies, Kyoto University

Plants produce a variety of isoquinoline alkaloids with strong physiological activities, e.g., analgesic morphine, and antimicrobial berberine. However, the production of these compounds can suffer from a variety of serious problems due to the plant origins. Our group has successfully developed microbial platforms for the production of plant isoquinoline alkaloids including opiates. The present investigation should lead to new opportunities for the microbial production of plant secondary metabolites.

10:05 Coffee Break with a Poster Pavilion *See page 4 for details*

11:00 Recombinant Expression of Circular Cys-Knotted Microproteins. Application for In-Cell High-Throughtput Screening of Specific Protein-Protein Antagonists

Julio A. Camarero, Ph.D., Associate Professor, Department of Pharmacology and Pharmaceutical Sciences, School of Pharmacy, University of Southern California

We report the biosynthesis of natively-folded MCoTI-based cyclotides inside live *E. coli* cells using a split protein splicing units. Biosynthesis of genetically encoded cyclotide-based libraries opens the possibility of using single cells as microfactories where the biosynthesis and screening of particular inhibitor can take place in a single process within the same cellular cytoplasm. We will show an example, where a large cyclotide-based genetically-encoded library was used to screen for antagonists for the Hdm2-HmX RING-mediated interaction.

11:30 Synthetic Biology Approach to Hygiene Control of *E. coli* Continuous-Flow Bioreactor Systems

Ouwei Wang, Ph.D., John D. Coates Laboratory, Energy Biosciences, University of California, Berkeley

Phage and microbial contaminations in industrial fermentation processes constitute one of the most devastating threats to the productivity and operational costs of biotechnology facilities. Although bleach derivatives can be added to process waters to prevent infection, these disinfectants are also biocidal against the process organism. We focus on engineering a process *E. coli* strain to grow in high concentrations oxychlorine disinfectants allowing for chemostat culturing with low risk of contamination.

12:00 pm IT'S A WRAP: PEPTALK 2017 CLOSING PLENARY PANEL DISCUSSION *See page 5 for details*

1:15 Close of Conference

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Sunday, January 8 | 5:00-8:00 PM
SC1: Production Challenges for Complex Biologics: ADCs, Bispecifics and Fusion Proteins
SC2: A Modern Approach to Biologics Formulation Development
SC3: A Lean Approach to Lab Management
SC4: Transfection Technologies
SC5: Creating a Next-Generation Vaccine Facility: Merging High-Productivity Technologies for Robust and Cost-Effective Manufacturing
SC6: Enzyme Screening, Design and Discovery

Tuesday, January 10 | 5:45-8:45 PM
SC7: Ensuring Accelerated and Successful Drug Product Development of Biologics: Integrated Formulation Development, Process and Packaging Design
SC8: Next-Generation Sequencing of Antibody Libraries: Details on Experimental and Bioinformatic Methods
SC9: Troubleshooting and Engineering of Antibody Constructs
SC10: Protein Aggregation: Mechanism, Characterization and Consequences
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