PEPTALK
THE PROTEIN SCIENCE WEEK

CHI-PepTalk.com

THE PREMIER GATHERING FOR PROTEIN SCIENCE RESEARCHERS

- Where research is shared, knowledge is gained, connections are made, and innovation shapes the future.

JANUARY 8-12, 2018 | SAN DIEGO, CA
HILTON SAN DIEGO BAYFRONT

FINAL WEEKS TO REGISTER

Cambridge Healthtech Institute's 17th Annual

PEPTALK
THE PROTEIN SCIENCE WEEK

CHI-PepTalk.com

1,300+	300+	22	6	9	100	150+	25+
International Participants	Influential Speakers	Conference Tracks	Short Courses	Training Seminars	Exhibitors	Research Posters	BuzZ Session Roundtables

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EVENT AT-A-GLANCE

JANUARY 8-12, 2018 | SAN DIEGO, CA

PART A		PART B		PART C	
JANUARY 8-9		JANUARY 9-10		JANUARY 11-12	
MONDAY	TUESDAY AM	TUESDAY PM	WEDNESDAY	THURSDAY	FRIDAY
Recombinant Protein Therapeutics		Enhancing Antibody Binding and Specificity		Emerging Technologies for Antibody Discovery	
Engineering Next-Generation Cancer Immunotherapies		Antibody-Drug Conjugates		Bispecific Antibody Therapeutics	
Advancing CNS Biotherapeutics and Crossing the Blood-Brain Barrier		Next-Generation Approaches to Antibody Screening and Discovery		Emerging Technologies for Antibody Discovery	
Optimizing Biologics Formulation Development		Lyophilization and Emerging Drying Technologies		Protein Aggregation and Emerging Analytical Tools	
Characterization of Biotherapeutics		Detection and Characterization of Particulates and Impurities		Bioprocess Analytics	
Single-Use Technologies and Continuous Processing		Protein Purification and Recovery		Higher-Throughput Protein Production and Characterization	
Engineering Genes and Hosts		Recombinant Protein Expression and Production		Optimizing Expression Platforms	
			CHO Cell Lines		
Engineering Genes and Hosts		Biocatalysis and Bio-Based Chemical Production		Microbial Production	
Introduction to Bioprocessing		Next-Generation Approaches to Antibody Screening and Discovery			
Introduction to Antibody Engineering		Introduction to Biologics Formulation Development			
Introduction to Cell Culture		Introduction to Biologics Analytical Development and Characterization			
		Dinner Short Courses*			

** Separate registration required for Short Courses*

Welcome to San Diego!

PepTalk: The Protein Science Week is one of the largest annual gatherings of protein science researchers in the world. In its 17th 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.

Training Seminars (1.5 days) populate more of the event, combining the depth of a short course and length of a conference track across an even broader range of topics, allowing you to enhance your knowledge and gain insight and perspective even more fruitfully than before.

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

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

PLAN YOUR WEEK AT PEPTALK | ADDITIONAL SCHEDULE TIMES

Monday, January 8
Exhibit hall open from 6:00 - 7:15 pm

BuzZ Sessions 3:15 - 4:30 pm

Tuesday, January 9
Exhibit hall open from 9:50 am - 4:30 pm

Wednesday, January 10
Exhibit hall open from 10:05 am - 6:45 pm

Thursday, January 11
Exhibit hall open from 10:00 am - 4:15 pm

Friday, January 12
BuzZ Sessions 8:00 - 9:00 am

Student Fellowship Poster Pavilion 10:35 - 11:15 am

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PEPTALK THE PROTEIN SCIENCE WEEK

FINAL WEEKS TO REGISTER

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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.

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 10, 2017.

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.

POSTER PAVILION

FRIDAY, JANUARY 12, 10:35 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.

2018 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 13, 2017.

- Interested students must complete the online application for the 2018 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 if they are accepted.
- Accepted Student Fellows will receive a discounted conference registration rate of $295*, which must be paid in full by November 10, 2017. (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 provides access to all conferences (January 8-12, 2018). Excludes Short Courses and Training Seminars.
- Accepted Fellows will be asked to help promote the event onsite, at their college, and throughout their social media networks.
- Students not accepted for the 2018 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! POSTER PAVILION** - 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 Training Seminars. It also does not include hotel, travel or meals.*

TUESDAY, JANUARY 9

DINNER SHORT COURSES*

■ TUESDAY, JANUARY 9 | 5:45 - 8:45 pm

SC1: Introduction to CAR-T Engineering for Protein Scientists

This course presents advances in CAR design with an eye toward clinical development. Topics include 1) screening and selection of active binding domains, 2) additional design steps needed to confer activity, 3) roles of linker and structural domain in CAR activity, 4) role of tumor-expressed cellular targets in regulating activity, 5) combining binding domains to create multi-targeting CARs that may prevent disease escape, and 6) novel structural domains that regulate association of binding to signaling domains to confer therapeutic control of CAR activity.

Instructor: Rimas J. Orentas, Ph.D., Scientific Director, Lentigen Technology, Inc.

SC2: Selection, Screening and Engineering for Affinity Reagents

Biologics such as recombinant antibodies and alternative binding scaffolds are routinely used in various applications. This success has led to the development of numerous selection, screening and engineering technologies for these molecules. This course gives a comprehensive overview on different display technologies and screening approaches for the selection of specific binders, engineering strategies including affinity maturation, and how to implement these strategies. Classical antibodies and antibody fragments and alternative binding scaffolds such as DARPins will be covered.

Instructors: Julia Neugebauer, Ph.D., Associate Director, Lead Discovery Programs R&D, MorphoSys AG

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

SC3: Protein Aggregation: Mechanism, Characterization and Consequences

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

Instructors: Thomas Laue, Ph.D., Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

Kevin Mattison, Principal Scientist, Bioscience, Malvern PANalytical

SC5: Optimizing Cell Line Development and Engineering

Recent achievements driven by the application of novel approaches and tools have caused significant savings in time and money for cell line selection and development. This course outlines the latest developments in cell and molecular biology, cell line development technologies, applications of automated tools, “-omics” technologies, CRISPR/Cas9, and engineering strategies to help you understand and improve the stability, quality, and workability of your cell lines to optimize upstream processing.

Instructor: Osama O. Ibrahim, Ph.D., Consultant, Bio Innovation USA

** Separate registration required. Please visit our website for more details.*

Training SEMINARS

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

SUNDAY, JANUARY 7 PRE-REGISTRATION 4:00 - 6:00 PM

MONDAY, JANUARY 8 - TUESDAY, JANUARY 9

DAY 1 - 9:00 AM - 6:00 PM | DAY 2 - 8:30 AM - 12:30 PM

TS8A: Introduction to Bioprocessing

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

TS9A: Introduction to Antibody Engineering

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

Instructors:

Andrew M. Bradbury, Ph.D., MB, CSO, Specifica, Inc.

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

TS10A: Introduction to Cell Culture

The seminar will describe the basic requirements for establishing and maintaining mammalian cell cultures both in the laboratory and in large-scale operations. The objective of the seminar is to provide detailed information of the scientific principles behind the use of mammalian cell culture techniques at either a laboratory scale or at a large scale for the production of biopharmaceuticals, which include monoclonal antibodies, recombinant proteins, viral vaccines as well as cell-based therapies. Some attention will also be given to the quality of the increasing list of biopharmaceuticals that have been licensed and are in large-scale manufacture.

Instructor:

Michael Butler, Ph.D., CSO, National Institute of Bioprocessing Research & Training (NIBRT), Ireland

TUESDAY, JANUARY 9 - WEDNESDAY, JANUARY 10

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

TS3B: Next-Generation Approaches to Antibody Screening and Discovery

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

Instructor:

David Bramhill, Ph.D., Founder, Bramhill Biological Consulting, LLC

TS10B: Introduction to Biologics Formulation Development

CHI's Introduction to Biologics Formulation Development 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.

Training SEMINARS

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

TUESDAY, JANUARY 9 - WEDNESDAY, JANUARY 10

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

TS11B: Introduction to Biologics Analytical Development and Characterization

This training seminar will review analytical method development and validation in the context of IND regulatory filing of therapeutic proteins, including monoclonal antibodies and recombinant proteins. The curriculum will provide a broad overview of biologics analytical and characterization and is beneficial to individuals involved in biologics drug development, analytical development, quality control, quality assurance, regulatory affairs, project management, process development, formulation development or related functional areas. Attendees will learn the practical aspects of commonly used analytical panel not only for DS/DP release and stability but also for monitoring manufacturing process and facilitating formulation development: product purity and impurity analysis, product strength and potency, plus matrix verification of the most common process-related impurities. The characterization panel specifically emphasizes structure elucidation by mass spectroscopy, posttranslational modification, biophysical characterization of higher order structure (HOS), and protein aggregates. Real-world case studies and common pitfalls will be presented.

Instructor:

Kevin Zen, Ph.D., Senior Director, Analytical Development, CMC Biologics, AnaptysBio, Inc.

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.

PROTEIN ENGINEERING & DEVELOPMENT

JANUARY 8-9

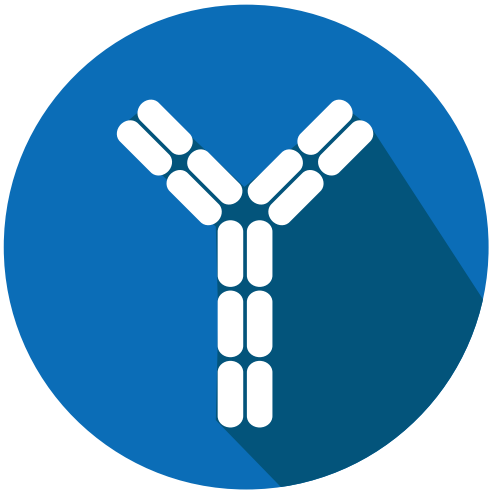
AGENDA Recombinant Protein Therapeutics

JANUARY 9-10

AGENDA Enhancing Antibody Binding and Specificity

JANUARY 11-12

AGENDA Emerging Technologies for Antibody Discovery



JANUARY 8-9 | 14TH ANNUAL

Recombinant Protein Therapeutics

Fusion Proteins & Beyond

Cambridge Healthtech Institute's Fourteenth Annual Recombinant Protein Therapeutics conference profiles the varying designs of therapeutic fusion proteins in differing stages of development, and investigates the challenges and benefits associated with these promising therapies. By combining modular building blocks that can reach targets not accessible to antibodies, fusion protein therapeutics possess advantages over antibody-based therapies; their customizable functionality translates into lower patient dosing, reduced production costs, and improved product homogeneity. This conference will disclose how these molecules are being engineered to form more efficacious therapeutics that offer specificity with enhanced stability and longer half-life.

SUNDAY, JANUARY 7

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

MONDAY, JANUARY 8

7:00 am Registration and Morning Coffee

CREATING EFFICACIOUS PROTEIN THERAPEUTICS

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

9:05 Chairperson's Opening Remarks
Stefan Schmidt, Ph.D., MBA, CSO, Development and Innovation, Rentschler Biotechnology

KEYNOTE PRESENTATION

9:10 Fusion Proteins: An Intro to the Field and Selected Case Studies from Roche's Research & Early Development Pipeline
Stefan Weigand, Ph.D., Head, Large Molecule Research, Roche Innovation Center, Roche Pharma Research & Early Development (pRED)

This talk will introduce the concept of fusion proteins, provide an overview on which fusion proteins are on the market, how they compare to classical antibodies in the same field, and look at general trends for fusion proteins from development pipelines of biotech and big pharma. In the second part, I will provide examples from Roche's pipeline how to discover, design, develop, and deliver differentiated, multi-functional therapeutics that allow for tailored solutions for the biological problem at hand.

9:50 Making Proteins "Druggable": Fc Fusion Proteins as a Therapeutic Class
Steven Chamow, Ph.D., Principal Consultant, Chamow & Associates, Inc.

Immunoglobulin G has substantial *in vivo* stability due to its binding to the neonatal Fc receptor (FcRn) which is responsible for IgG recycling. By creating an Fc fusion, a protein with a short *in vivo* half-life can be transformed into a stable therapeutic product. This technology has been applied broadly and there are now 6 FDA approved products from this therapeutic class. Their structures and properties will be reviewed.

10:20 Networking Coffee Break

NEXT-GEN ENGINEERING

10:45 Generating Ion Channel Blocking Antibodies by Fusing Cysteine-Knot Miniproteins into Peripheral CDR Loops
John McCafferty, Ph.D., CEO, Antibody Engineering, IONTAS, Ltd.

Cysteine-knot miniproteins (knottins) have potential as therapeutic agents to block proteases and ion channels involved in cancer, autoimmunity and pain, but suffer from manufacturing difficulties, short half-lives, and a lack of specificity. Using X-ray crystallography and biochemical assays, we have demonstrated that functional knottins can be inserted into peripheral antibody CDRs via short linkers. Thus, the resulting "KnotbodyTM" retains the advantage of blocking activity from the knottin while enjoying the extended half-life and additional specificity conferred by the antibody molecule.

11:15 High-Resolution Mass Spectrometry Confirms the Presence of a Hydroxyproline (Hyp) Post-Translational Modification in the GGGGP Linker of an Fc-Fusion Protein
Chris Spahr, Senior Scientist, Therapeutic Discovery, Discovery Attribute Sciences, Amgen, Inc.

(G4P)n protein linkers were proposed to replace the commonly used (G4S)n linkers recently found to carry heterogeneous xylose-containing O-glycosylation. Using high-resolution mass spectrometry (HR-MS) and MSn, we demonstrated the presence of an unexpected hydroxylation of a prolyl residue (Hyp) in a (G4P) linker. Further efforts in determining whether the modification is 3-hydroxyproline (3-Hyp) or 4-hydroxyproline (4-Hyp) will be discussed.

11:45 Turning Affibody Molecules into Efficient Peptide Binders by Dimerization
John Löfblom, Ph.D., Associate Professor, Protein Technology, Biotechnology, KTH Royal Institute of Technology

Affibody molecules are small three-helical affinity proteins. Generating binders for the amyloid ß peptide yielded variants with 300-pM affinity, and with unique mode of binding, sequestering the peptide in a tunnel-like cavity. Similar binders for other peptides have been engineered, involving structural rearrangements of both affibody and peptide upon binding, indicating that it is well suited for such molecular recognitions. This presentation will include unpublished preclinical data for the Aß binder.

12:15 pm Veltis® Engineered Albumins and Their Potential for Improved Therapeutic Performance *Sponsored by* Albumedix
Helen Rawsthorne, Ph.D., Senior Research Scientist, Molecular Biology and Fermentation, Albumedix

The natural properties of albumin have ensured its use for decades in enhancing the pharmacokinetic and pharmacodynamic properties of drug candidates. We have designed rationally engineered albumins to enhance these properties. A half-life of more than double that seen for native sequence albumin is obtainable for therapeutic candidates associated with Veltis® albumins engineered for increased FcRn binding affinity. Newly developed thio-engineered albumins with additional free thiol groups allow further options for multi-valent site-specific drug loading.

12:45 **Session Break**

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

IMPROVING THERAPEUTIC PROPERTIES AND MANUFACTURING

2:00 **Chairperson's Remarks**

John McCafferty, Ph.D., CEO, Antibody Engineering, IONTAS, Ltd.

2:05 **Design, Structure and Manufacturability: Lessons Learned from Fusion Proteins**

Stefan Schmidt, Ph.D., MBA, CSO, Development and Innovation, Rentschler Biotechnology

Next-generation therapeutic proteins are typically human designed molecules with no counterpart in living organisms. As they have not been selected in a natural evolution process, they can suffer from low expression, mis-assembly and mis-folding, disulfide scrambling, a tendency to aggregate, and sensitivity to protease degradation. In this presentation, I will show examples from our portfolio and the literature demonstrating how to avoid these product-related impurities by smart fusion protein design and strategies to eliminate these impurities in efficient bioprocesses.

2:35 **Advanced Bi- and Multi-Specific Antibody Derivatives and Fusion Proteins for Targeted Therapy: From Molecular Design to Therapeutic Application**

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

'Success needs Diversity - Diversity breeds Success': Roche develops bi & multifunctional antibody derivatives in diverse compositions and formats (as opposed to 'one-size/format-fits-all' approaches). The presentation will highlight examples of the variety of multifunctional antibody formats, covering examples of diverse molecules in clinical development as well as novel approaches in preclinical evaluation.

3:05 **Transition to BuzZ Sessions**

3:15 **BuzZ Sessions with Refreshments**

BuzZ sessions

Join your peers and colleagues for interactive roundtable discussions.

Please see page 78 for additional information.

FIGHTING DISEASE WITH FUSION PROTEIN THERAPEUTICS

4:30 **SELECTED POSTER PRESENTATION: Computational Driven Protein Engineering Platform Enables the Discovery and Development of Next-Gen Antibacterial Therapeutics**

Yongliang Fang, Ph.D., Scientist, Thayer School of Engineering, Dartmouth College

Conventional small-molecule antibiotics only inhibit the growth of MRSA and are known to rapidly induce new resistance once they are applied in the clinic. Therefore, there is a critical need for an alternative approach to combat this threat to public health. Lysostaphin is an antibacterial enzyme which has drawn the attention of researchers, pharmaceutical companies, and the medical community because of its extraordinary potency against MRSA both *in vitro* and *in vivo*. The success of our methods for deimmunization of lysostaphin demonstrates the potential impact of computationally-driven engineering throughout the biotherapeutic pipeline. In addition, the computational algorithms will also allow us to develop various types of therapeutic proteins with lower immunogenicities and may ultimately aid the rising tide of biologics that are currently entering the R&D pipeline.

5:00 **Protein Engineering to Further Improve Clotting Factor-Fc Fusions and Create Novel FVIIIa Mimetic Bispecific Antibodies**

Robert Peters, Ph.D., Senior Vice President, Research, Bioverativ, Inc.

Further protein engineering was performed on clotting factor-Fc fusions with a goal to further improve protection from bleeds provided by a prophylaxis regimen, and to potentially enable subcutaneous administration, while preserving the biology of the coagulation system. Considerations and the path to creation of rFVIIIFc-VWF-XTEN and rFIX(R338L) Fc-XTEN fusion proteins will be presented, as well as antibody screening methods used to generate a true FVIIIa mimetic bispecific (FIXa/FX) antibody.

5:30 **Designed Ankyrin Repeat Protein as Inhibitors of *Clostridium Difficile* Toxin B**

Zhilei Chen, Ph.D., Associate Professor, Microbial Pathogenesis and Immunology, Texas A&M College of Medicine

Using phage-panning combined with high-throughput *in vitro* functional screening, we recently engineered several designed ankyrin repeat protein (DARPin) with picomolar neutralization potency against *C. difficile* TcdB, which is 100-1000-fold more potent than bezlotoxumab. These anti-toxin DARPins were found to effectively protect mice against TcdB-associated mortality. Cryo-electromicroscopy studies revealed that binding of one of these DARPins induced significant conformational change of TcdB, likely rendering it unable to associate with the target receptor.

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

Sponsored by TEMPER

7:15 **Close of Day**

TUESDAY, JANUARY 9

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

FIGHTING CANCER

8:30 **Chairperson's Remarks**

Robert Peters, Ph.D., Senior Vice President, Research, Bioverativ, Inc.

8:35 **Combinatorial Protein Engineering of Proteolytically Resistant Mesotrypsin Inhibitors as Candidates for Cancer Therapy**

Niv Papo, Ph.D., Group Leader and Assistant Professor, Biotechnology Engineering, Ben-Gurion University

Our study describes a rapid methodology for identifying mutations that convert the human amyloid precursor protein Kunitz protease inhibitor domain (APPI), a natural substrate of the oncogenic protease mesotrypsin, into a proteolytically

stable high affinity inhibitor of mesotrypsin. We demonstrated that APPIM17G/I18F/F34V acts as a functional inhibitor in cell-based models of mesotrypsin-dependent prostate cancer cellular invasiveness. Additionally, by solving the crystal structure of the complex, we uncovered new insights into the structural and mechanistic basis for improved binding and proteolytic resistance.

9:05 **Redefinition of ErbB2/3 Tumor Targeting: Novel Platform for Development of Truly Efficient Anti-ErbB Bispecific and Biparatopic Agents**

Rastislav Tamaskovic, Ph.D., Senior Scientist, Biochemistry, University of Zurich

We built a new platform for RTK fingerprinting of tumors under therapy, for identification of points of fragility in oncogene-addicted tumors with the developed acquired resistance, and for the design of prospective therapeutic leads in a variety of bispecific formats. This novel approach heralds the next generation of ErbB targeting vehicles with beneficial properties owing to maximization of drug potency and minimization of the risk of side and off-target effects associated with the current drug formats.

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

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

11:00 **HERA: Engineering Next Generation TNFR-SF Agonists for Cancer Immunotherapy**

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

The HERA technology platform developed by Apogenix is based on trivalent but single-chain molecular mimics of the TNF-SF receptor binding domains (scTNFSF-RBDs) fused to a dimerization scaffold. These hexavalent fusion proteins are true agonists and their biological activity is, in contrast to agonistic anti-TNFR-SF antibodies, independent of secondary Fc-receptor based crosslinking events. We will present the molecular engineering concept and report on *in vitro* and *in vivo* activities of HERA-CD40L, HERA-CD27L, HERA-GITRL and HERA-CD137L.

11:30 **Improving Enzyme-Based Therapy of Acute Lymphoblastic Leukemia: Molecular Design of Human L-Asparaginases**

Manfred Konrad, Ph.D., Research Director, Enzyme Biochemistry, Max Planck Institute for Biophysical Chemistry

Acute lymphoblastic leukemia (ALL), the most common cancer in children, is a genetically heterogenous disease. We designed and engineered human enzyme homologues displaying the clinically established enzyme drug L-asparaginase (L-ASNase) activity with the aim of identifying catalytically efficient variants to substitute for the bacterial enzymes. Furthermore, to increase the serum half-life of the enzymes, we generated biocompatible microcapsules as carriers, thus enhancing serum stability and preventing exposure of the protein to the immune 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 Recombinant Protein Therapeutics Conference**

JANUARY 9-10 | 5TH ANNUAL

Enhancing Antibody Binding and Specificity

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

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, Cambridge Healthtech Institute's Fifth Annual Enhancing Antibody Binding and Specificity conference, presents innovative approaches to the modulation of binding activity for traditional antibodies, new product formats and difficult targets such as transmembrane proteins.

TUESDAY, JANUARY 9

1:00 pm Registration

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

ADVANCES IN TARGETING AND SIGNALING

2:00 Chairperson's Opening Remarks

Madhu Natarajan, Ph.D., Preclinical Therapeutic Area Head, Ophthalmology & Complement Biology, Shire

KEYNOTE PRESENTATION

2:05 Integrated Computational Design and Experimental Selection Leads to Custom Targeted Biologics

Philip M. Kim, Ph.D., Associate Professor, Computational and Integrative Biology, University of Toronto, Canada

I will present our technology platform on integrating a number of different computational protein strategies (including classic protein design, thermodynamic integration and machine learning) with high-throughput selection strategies (including phage display, yeast-2-hybrid and phenotypic selections in mammalian cell culture) to obtain custom targeted biologics.

2:45 Affinity-Tuned CARs Can Reduce On-Target Off-Tumor CAR T Cell Cytotoxicity

Mauro Castellarin, Ph.D., Postdoctoral Researcher, Center for Cellular Immunotherapies, University of Pennsylvania School of Medicine

CAR T cells can effectively kill malignant cells but autoimmune toxicity can occur when normal cells express the same targets. This type of on-target off-tumor toxicity can be lessened using affinity-tuned CARs. We developed an *in vivo* mouse model that expresses human tumor antigens in normal mouse tissue and showed that a low affinity Her2 CAR had a higher therapeutic index compared to its high affinity counterpart.

3:15 Featured Poster Presentation: An Integrated Nanofluidic and Optoelectronic Platform to Screen Engineered Antibody Panels

Fen-Fen Lin, Senior Scientist, Amgen

We explored an innovative nanofluidic cell culture platform from Berkeley Lights, the BeaconTM, to screen engineered antibody panels for the early stages of therapeutic antibody selection. We developed on-chip assays for both IgG secretion from mammalian cells and antigen binding and demonstrated correlation with standard assays. The Beacon™ platform could potentially compress timelines, increase capacity, and reduce resources required for our workflow.

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

4:30 Engineering a Therapeutic Antibody for Long-Acting Delivery to the Eye

Devin Tesar, Ph.D., Scientist, Drug Delivery, Genentech

Ocular delivery of protein therapeutics often requires favorable viscosity properties to support high-concentration formulations. Using structure-based design we generated high-affinity mutants of a backup Fab which exhibited superior viscosity properties but inferior target binding and inhibition as compared to the lead candidate. Two of these mutants, FM1 and FM2, exhibit binding and target inhibition equal or superior to that of the lead molecule, while retaining the superior viscosity profile.

5:00 Cytosol-Penetrating Antibody Technology for Targeting Oncogenic Ras Mutants

Yong-Sung Kim, Ph.D., Professor, Molecular Science and Technology, Ajou University, Korea

Oncogenic Ras mutants are high-priority anticancer drug targets. However, direct inhibition of Ras mutants with small molecules has been extremely challenging. In this talk, I will introduce the development of cytosol-penetrating antibody that internalizes into the cytosol of living cells and selectively binds to the activated form of oncogenic Ras mutants to block the interactions with effector proteins, thereby exerting *in vivo* anti-tumor activity in mouse models after systemic administration.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

5:45 - 8:45 Dinner Short Courses*

See page 5 for details

** Separate registration required*

WEDNESDAY, JANUARY 10

8:00 am Registration and Morning Coffee

ANALYTICAL METHODS

8:30 Chairperson's Remarks

Tilman Schlothauer, Ph.D., Principal Scientist, Biochemical and Analytical Research, Large Molecule Research, Roche Innovation Center Munich

8:35 Germline Reversion of Broadly Neutralizing Antibodies for Vaccine Development

Fernando Aleman, PhD, Research Associate, The Scripps Research Institute

A leading strategy for vaccine development aims at triggering broadly neutralizing antibodies, but how to achieve this goal is not yet clear. I will present an immunogenetic analysis of a panel of mouse monoclonal antibodies against Hepatitis C virus and highlight the two germline precursors that should be triggered for cross neutralization. The structure of the mature antibodies along with the germline precursors provide key templates for the needed antigen redesign.

JANUARY 9-10 | 5TH ANNUAL

Enhancing Antibody Binding and Specificity

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

9:05 Modeling Protein-Protein Complexes. The Good, the Bad and the Ugly

Enrico Purisima, Ph.D., Team Leader, Molecular Modeling, National Research Council Canada

The talk will examine the challenges of protein-protein docking with a particular emphasis on antibody-antigen complexes. A major complication is accounting for the conformational changes that can occur between the bound and free states of the docking partners. We will highlight recent progress in the field and describe specific efforts in our own lab. An assessment of what we can realistically expect from current methods will be given.

9:35 Featured Poster Presentation: Discovering Antibody Binding Signatures in Age-Related Macular Degeneration for Diagnostic Development

Joel Bozekowski, Ph.D. Candidate, Chemical Engineering, University of California, Santa Barbara

Signatures in the antibody repertoire can indicate the onset and presence of various diseases. Here, we utilized random peptide library screening to analyze the collection of peptides that bind serum antibodies from subjects at various stages of age-related macular degeneration (AMD). Bioinformatics analysis of the peptide sequences enabled the characterization of binding specificities present in AMD samples and absent from controls which could be utilized for early diagnostic development.

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

ENGINEERING BINDING AFFINITY

10:50 Conditional Fc Receptor Interactions – What Effector Cells Are Interested In

Tilman Schlothauer, Ph.D., Principal Scientist, Biochemical and Analytical Research, Large Molecule Research, Roche Innovation Center Munich

An assay platform has been established to assess antibody-Fc-receptor interaction. This platform, comprised of a broad panel of reagent tools and assay formats, is utilized for mechanistic studies towards the deeper understanding of Fc functionality. Besides the comparison of wildtype IgG1 antibodies, antibody variants with reduced or enhanced Fc-functionality can also be investigated by this comprehensive set of cell-free and cell-based *in vitro* functional assays.

11:20 Utilities of Biosensor Platforms in Antibody Discovery

Danlin Yang, Ph.D., Scientist, Biophysics, Biotherapeutics Discovery, Boehringer Ingelheim Pharmaceuticals

Label-free optical biosensors are powerful tools in drug discovery for the characterization of biomolecular interactions. Here, we compare the strengths and weaknesses of four routinely used biosensor platforms by assessing their ability to provide quality kinetic data on high affinity antibody-antigen interactions. Applications including the classification of antibody binding epitopes via epitope binning studies and the profiling of the quality of antigen-induced polyclonal immune responses in immune sera are demonstrated.

11:50 Human IgG Subtype Cross-Species Reactivity to Mouse and Cynomolgus Monkey FcɣReceptors

Mehabaw G. Derebe, Ph.D., Scientist, Biologics Engineering, Janssen BioTherapeutics

Animal models are routinely used to assess pharmacodynamics, toxicity, efficacy and other properties of candidate therapeutic antibodies. The interaction of human IgG molecules to endogenous Fcɣ receptors of animal models can be different from their interaction to human Fcɣ receptors. This study confirms the binding characteristics of human IgG subtypes IgG1, IgG2 & IgG4 as well as their silent versions to human, mouse and cynomolgus monkey Fcɣ receptors. To control interactions between Fab and Fc domains, the test articles all have the same variable regions.

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

12:50 Session Break

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

OPTIMIZING ANTIGEN SPECIFICITY

2:00 Chairperson's Remarks

Robert Pejchal, Ph.D., Scientist, Antibody Engineering, Adimab LLC

2:05 Engineering Antibodies to Modulate Their Spatiotemporal Behavior

E. Sally Ward, Ph.D., Professor, Molecular and Cellular Medicine, Texas A&M Health Science Center

The role of FcRn as a global regulator of antibody and albumin levels and transport in the body is well established. Recent studies using a combination of antibody engineering, microscopy and *in vivo* studies have led to strategies to modulate antibody levels for use in diagnostic imaging and therapy. Developments in these and other FcRn-related areas will be presented.

2:35 Altering Antibody Specificities for Better Clearance

Madhu Natarajan, Ph.D., Preclinical Therapeutic Area Head, Ophthalmology & Complement Biology, Shire

In recent years, the clearance of antibodies through antigen-mediated processes has re-emerged as a topic of interest, with the implication that engineering the affinities of therapeutic antibodies for antigens in a context-dependent manner can yield dramatic improvements in both pharmacokinetic and pharmacodynamic effects. We have systematically explored the biology and interdependencies of these mechanisms to understand and inform the rational engineering of novel therapeutic antibodies for improved pharmacodynamic and pharmacokinetic properties.

3:05 Refreshment 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

4:00 Highly Efficient Recovery of GPCR-Specific Antibodies Coupling Yeast Library Selection and Next-Generation Sequencing

Robert Pejchal, Ph.D., Scientist, Antibody Engineering, Adimab LLC

Discovery of antibodies specific to GPCRs, and other challenging multi-spanning membrane protein targets, has been a long-standing challenge for drug development. Adimab's platform utilizes whole mammalian cells over-expressing the target membrane protein for selection and couples next generation sequencing (NGS) to identify antibodies with desired specificities. Methodologies and outcomes for discovery and optimization efforts on GPCR and tetra-spanning targets will be reviewed.

4:30 ProTIA – Bispecific T Cell Engagers Designed for Local Activation in the Tumor Environment

Ulrich Ernst, PhD, COO/SVP Technical Operations, Amunix Inc.

Amunix is developing ProTIA (Protease Triggered Immune Activator) therapeutics based on our proprietary XTEN™ protein polymer platform. ProTIAs are administered as inactive prodrugs that are activated in the tumor environment by release of their blocking XTEN polymer. AMX-168 is a ProTIA molecule targeting EpCAM, which is overexpressed in the majority of solid malignancies. AMX-168 has shown excellent efficacy and selectivity in a range of *in vivo* models.

5:00 Presentation Title to be Announced

5:30 - 6:45 Networking Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Enhancing Antibody Binding and Specificity Conference

JANUARY 11-12 | 3RD ANNUAL

Emerging Technologies for Antibody Discovery

Exploring the Intersection of Display Technologies, Next-Generation Sequencing and Informatics for the Discovery of Next-Generation Biotherapeutics

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 – and that the biotherapeutics against these are selected and engineered to minimize development risk. For 2018, Cambridge Healthtech Institute's Third Annual Emerging Technologies for Antibody Discovery conference considers the intersection of traditional display based screening and selection approaches with next-generation tools such as immune repertoire sequencing, *in silico* modeling and high-resolution imaging.

THURSDAY, JANUARY 11

7:45 am Registration and Morning Coffee

8:15 Chairperson's Opening Remarks
Andrew Bradbury, Ph.D., CSCO, Specifica, Inc.

KEYNOTE PRESENTATION

8:20 Remodeling of Cell Surfaceomes in Cancer
James A. Wells, Ph.D., Professor, Pharmaceutical Chemistry, University of California, San Francisco
The cell surface proteome (surfaceome) is the primary hub for cells to communicate with the outside world. My lab studies how the surfaceome is remodeled in cancer. We find the new set of proteins promote enhanced cell growth and detachment from native tissues allowing metastasis. Our primary goal is to systematically understand how cancer cells remodel their membrane proteomes (surfaceomes) during cancer transformation and develop antibodies to detect and attack them.

FUNCTIONAL SCREENING

9:00 Combining Screening with Phenotypic Selection in Antibody Phage Display
Marcin Paduch, Ph.D., Pipeline Director, Recombinant Antibody Network, University of Chicago
State-of-the-art methods for generating recombinant antibodies do not necessarily allow for targeting the particular cellular phenotype posing a fundamental challenge. A set of next generation high-throughput technologies that allow for phenotypic selection has to be developed. Intimate knowledge of conformation states and biochemistry of antigens can be exploited to mimic native-like environments and create the possibility of trapping physiologically-relevant states otherwise not accessible by current methods.

9:30 Phage-Displayed Ubiquitin Variant (UbV) LibraPhage-Displayed Ubiquitin Variant (UbV) Libraries to Rapidly Identify Potent and Highly Selective Protein-Based Inhibitors
Joan Teyra, Ph.D., Research Associate, University of Toronto, Canada
E3 ligases and deubiquitinases regulate diverse cellular processes and are implicated in numerous human diseases. However, targeting these enzymes potently and specifically remains a big challenge. We thus devised a screening platform to develop protein-based modulators for ubiquitin-proteasome system components

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

11:00 Efficient B Cell Cloning and Antibody Engineering Platform for Rare Ab Generation
Feng Shu, Ph.D., Senior Researcher, Chugai Pharmabody Research, Singapore
Here we describe a high throughput antibody identification system by single B cell cloning, which can generate and evaluate a large number of antibodies with high diversity to identify the rare antibodies with required properties such as pH dependency. A robust antibody engineering system is also introduced, where thousands of antibodies with designed mutations can be generated and evaluated in 2 weeks' time to further accelerate the antibody discovery process.

11:30 Antibody Protein Sequencing with Mass Spectrometry
Sponsored by RAPID NOVOR
Mingjie Xie, MSc, MBA, CEO, Rapid Novor Inc
Many applications in antibody engineering require the direct sequencing of antibody proteins. At Rapid Novor (rapidnovor.com) we have developed a robust workflow and routinely sequenced antibody proteins. Here we share the success experiences, examine common mistakes novices make, and present our practices to ensure the correctness of every amino acid.

12:00 pm Session Break

12:15 Luncheon Presentation I: Next-Generation Capillary Electrophoresis Technology for Protein Analysis
Sponsored by proteinsimple
Wei-Chiang Chen, Ph.D., Scientist, Analytical Development, Biogen
Recombinant adeno-associated virus (AAV) is a promising platform in human gene therapy. AAV vectors contain a protein outer shell called capsid, which is comprised of 60 subunits containing three viral proteins. To confirm the purity of the AAV capsids, we developed a CE-SDS method on the Maurice platform, which automates analysis of 96 samples in one batch. This assay demonstrates good separation of viral proteins (LOQ at 5e11 vg/ml), and comparable results with SDS-PAGE gels.

12:45 Presentationto be Announced

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

ADVANCES IN DISPLAY TECHNOLOGIES AND LIBRARY DESIGN

2:00 Chairperson's Remarks
Nicolas Fischer, Ph.D., Head, Research, Novimmune SA, Switzerland

2:05 Enhancing the Chemical Versatility of Yeast Display
James Van Deventer, Ph.D., Assistant Professor, Chemical and Biological Engineering, Tufts University
We have established a version of yeast display that supports the integration of chemical groups into displayed proteins using noncanonical amino acid incorporation. We are currently investigating strategies for positioning chemical groups within antibodies in order to enhance and change the molecular recognition capabilities of these proteins. This talk will highlight our recent progress in constructing, evaluating, and

Emerging Technologies for Antibody Discovery

Exploring the Intersection of Display Technologies, Next-Generation Sequencing and Informatics for the Discovery of Next-Generation Biotherapeutics

screening "hybrid" structures with potential applications in the tumor microenvironment.

2:35 How Big Are Antibody Libraries Really? And Are We Accessing the Full Diversity?

Andrew Bradbury, Ph.D., CSO, Specifica, Inc.

In vitro antibody libraries have been used to generate antibodies against many different therapeutic lead targets. Analyses indicate that one would expect to select 1-3 antibodies from a 1e7 library. However, this does not appear to scale to larger libraries with diversities estimated to be >1 billion, suggesting that libraries are less diverse than thought or selection methods do not tap the full diversity. This talk discusses the use of NGS to explore these issues and the application of NGS to the creation of improved antibody libraries.

3:05 Featured Poster Presentation: Mapping the Antibody Response to Vaccines Directly from Patient Serum

Michael Szardenings, Ph.D., Vice Head Department of Immunology, Fraunhofer Institute for Cell Therapy and Immunology, Germany

A novel phage display-based platform provides a promising alternative technology to determine epitopes of vaccines. Antibody epitope variations were studied over 6 years in the serum of a single patient (influenza, Hepatitis B vaccines and traces of other infections). Information about the natural antibodies' epitopes may help to design vaccines and to clone or design antibodies for multiple therapeutic and diagnostic applications.

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

4:15 Dual Display Technology for "In Format" Selection and Screening of Bispecific Antibodies

Nicolas Fischer, Ph.D., Head, Research, Novimmune SA, Switzerland

The desired biological activity of bispecific antibodies is often dependent on the adequate geometry of the two antibody binding sites, thus requiring extensive combinatorial testing of isolated antibodies. Being able to evaluate candidates 'in format' as early as possible would greatly facilitate the development of bispecific antibodies. To achieve that goal, we have developed methodologies that allow 'in format' phage display selection and screening of candidates early in discovery.

4:45 Synthetic Human Antibody Fragment Libraries for CAR T Cell Therapy

Thomas J. Van Blarcom, Ph.D., Associate Research Fellow, Rinat Laboratories, Oncology Research and Development, Pfizer, Inc.

Unlike most therapeutic antibodies, CAR T cells are typically generated with single chain variable fragment (scFv) antibodies. In this study, we present a human synthetic scFv antibody library that we use to simplify the generation and testing of large panels of antibodies for use as CAR T cells. The CAR T cells generated from these antibodies had desirable phenotypes and demonstrated robust and specific cytotoxic activity *in vitro*.

5:15 Highly Multiplexed Cell Surfaceomics Using Genetically Barcoded Antibody-Phage

Samuel Pollock, Researcher, Pharmaceutical Chemistry, University of California, San Francisco

Cells express thousands of different surface proteins that can be used for their classification. We present a surface proteomic method using genetically barcoded antibodies called Phage-antibody Next Generation Sequencing. We use PhaNGS to reveal changes in surface protein abundance in the contexts of drug resistance, adaptation to oncogenes, and on the single-cell level. Linking selective, genetically encoded binders to NGS enables direct, multiplexed protein detection, comparable to RNAseq for mRNA.

5:45 Close of Day

FRIDAY, JANUARY 12

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast

BuzZ sessions

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

Table Moderator: James Van Deventer, Ph.D., Assistant Professor, Chemical and Biological Engineering, Tufts University

Table Moderator: Marcin Paduch, Ph.D., Pipeline Director, Recombinant Antibody Network, University of Chicago

INTEGRATED DISCOVERY PLATFORMS

9:00 Chairperson's Remarks

Sagar Kathuria, Ph.D., Senior Scientist, Protein Engineering, Sanofi Genzyme

9:05 Generation of Mono and Bispecific Antibodies from Immunized Transgenic Rodents and the Potential to Engineer Multi-Specific Entities Using Common Light Chain Paratopes

Simon Krah, Ph.D., Senior Scientist, Protein Engineering and Antibody Technologies, Merck KGaA, Germany

We demonstrate that by using Yeast Surface Display (YSD), a more effective coverage of the antibody diversity generated during the course of an immunization can be realized in comparison to classical hybridoma technology. Moreover, we show that bispecific antibodies can also be readily engineered via such YSD approaches in combination with the application of common light chains. In addition, we established a methodology which facilitates the tedious and time-consuming process of YSD library generation.

9:35 Discovery Platform for Antibody Generation and Screening for Different Applications

Anne Marcil, Team Lead, Monoclonal Antibodies, National Research Council, Canada

The National Research Council of Canada has a strong history in target discovery, antibody generation and characterization, resulting in the production of new antibodies against hundreds of targets. An overview of our antibody discovery pipeline which includes bioinformatics and MS analysis for target discovery, monoclonal, single-

Emerging Technologies for Antibody Discovery

Exploring the Intersection of Display Technologies, Next-Generation Sequencing and Informatics for the Discovery of Next-Generation Biotherapeutics

domain and antibody library screening, *in vitro* screening for function (ADCs, Blood-brain barrier crossers, electrophysiology, etc.) and *in vivo* screening will be presented.

10:05 A Patient-Centric Function F.I.R.S.T™ Approach to Cancer Immunotherapy Discovery

Björn Frendéus, Ph.D., CSO, Bioinvent, Sweden

We have developed a patient-centric phenotypic discovery approach (F.I.R.S.T) that utilizes primary cancer patients' cells from the initial steps of isolating antibodies from a naïve human antibody library through POC studies and subsequent identification of targeted receptors. A lead candidate which blocks FcgRIIB internalization and acts in synergy with rituximab to boost responses and help overcome resistance in the background of emerging targeted therapies as well as conventional chemotherapy *in vivo*, is now in clinical phase testing.

10:35 Coffee Break with a Poster Pavilion

See page 4 for details

11:15 Tool and Platform Development for Antibody Developability Assessment and Mitigation

Sagar Kathuria, Ph.D., Senior Scientist, Protein Engineering, Sanofi Genzyme

Antibodies have emerged as very successful biological drugs in the recent past. The growth of this industry has highlighted a need for a comprehensive set of non-redundant assays and corresponding threshold values to identify likely candidates early during research and prioritize their development. We make use of several high-throughput biophysical and biochemical tools for antibody characterization towards achieving this goal. Results from some test cases will be discussed.

11:45 High Content Confocal for Antibody Selection and Potency Screening

Tianyi Wang, Ph.D., Scientist, R&D, Sorrento Therapeutics

This talk outlines applications of high content confocal and cell-by-cell metrics for selection and potency of antibodies with applications toward intracellular targets. 3D spheroids and high content confocal *in vitro* system are used to screen the phenotypic effects of selected intracellular-targeting antibodies. 3D spheroids, by mimicking tumor microenvironment, are a better predictor of clinical potential of antibody therapeutics. Our method proposes multiparametric analyses of spheroids to elucidate mechanism of action.

12:15 pm Conference Wrap-Up

Tilman Schlothauer, Ph.D., Principal Scientist, Biochemical and Analytical Research, Large Molecule Research, Roche Innovation Center Munich

12:45 Close of Conference

ANTIBODY THERAPEUTICS

JANUARY 8-9

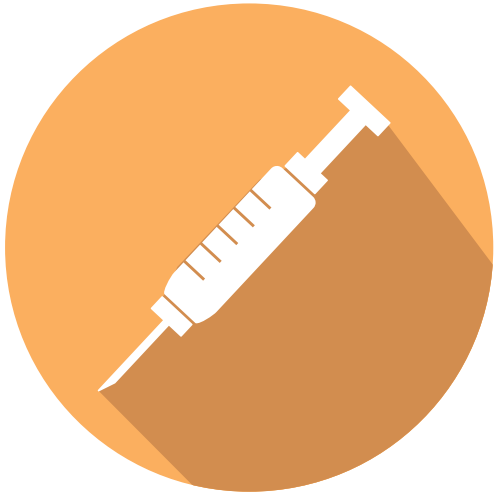
AGENDA Engineering Next-Generation Cancer Immunotherapies

JANUARY 9-10

AGENDA Antibody-Drug Conjugates

JANUARY 11-12

AGENDA Bispecific Antibody Therapeutics



JANUARY 8-9 | 4TH ANNUAL

Engineering Next-Generation Cancer Immunotherapies

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

A succession of strong clinical successes with antibodies against checkpoint targets has spawned a surge of interest from across the industry in the development of antibody immunotherapeutics and treatment combinations. The major challenges facing those now entering the field include establishing clinical proof of concept, product and target differentiation, selection of patient responders and the rational design of effective immunotherapy combinations. CHI's Fourth Annual Engineering Next-Generation Cancer Immunotherapies conference offers protein engineering strategies to improve the efficacy of immunotherapeutics and drive the progress of more personalized treatments in this space.

SUNDAY, JANUARY 7

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

MONDAY, JANUARY 8

7:00 am Registration and Morning Coffee

ANTIBODY ENGINEERING CHALLENGES FOR IMMUNOTHERAPEUTICS

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

9:05 Chairperson's Opening Remarks
Dimiter S. Dimitrov, Ph.D., Senior Investigator, Protein Interactions Section, Cancer and Inflammation Program, National Cancer Institute, NIH

KEYNOTE PRESENTATION

9:10 Evolution and Advancements in Cancer Immunotherapy
Partha Chowdhury, Ph.D., Senior Director and Head, Antibody Discovery, Sanofi Genzyme
Cancer is an immunological disease characterized by hijacking and evasion of the natural immune response of the host. Although the idea to exploit the host's immune response to fight against cancer is decades old, clinical success of immunotherapy is a relatively new achievement. This talk will focus on the various strategies used to manipulate a multitude of factors that underlies the phenomenon of immunotherapy, including recent advancements on new targets and approaches to enhance the therapeutic efficacy of novel biological drugs.

9:50 Tumor-Activated Checkpoint Inhibitors
John C. Williams, PhD, Professor, Molecular Medicine, Beckman Research Institute at City of Hope
Targeting immune checkpoints is rapidly changing the clinical management of a growing list of tumor entities. However, checkpoint therapy is encumbered by immune-related adverse events (irAEs), which can be severe. We present our engineering efforts to reduce irAEs, demonstrating the localized activity of murine checkpoint surrogates effectively eliminates *in vivo* tumor growth while markedly reducing activation of regulatory T cells in healthy tissue.

10:20 Networking Coffee Break

10:45 The Impact of mAb Format in Targeting the Tumor Microenvironment
Stephen Beers, Ph.D., Associate Professor, Cancer Immunology and Immunotherapy, University of Southampton, United Kingdom
Monoclonal antibodies (mAb) are transforming cancer therapy. Although the number of mAb reaching the clinic continues to rise rapidly, successful targets are scarce and new ones frequently fail. Understanding why promising pre-clinical candidates do not translate to humans is a critical question. Here we show how mAb format can be key to efficacy and that this could be particularly relevant when seeking new mAb to target the tumor microenvironment.

11:15 Novel Therapeutic Antibodies for Cancer Isolated from Single Human B Cells
Edward F. Patz, Jr., M.D., Professor, Radiology, Pharmacology and Cancer Biology Duke University Medical Center
In an effort to develop novel therapeutic antibodies, we took cues from the native immune response in "exceptional outcomes" patients. We identified relevant tumor antigens by exploring the humoral response against the tumor, and then isolated and expressed DNA sequences from the relevant single B cells. A recombinant antibody was produced, and showed anti-tumor activity. This strategy represents an alternative paradigm in anti-cancer drug discovery.

11:45 Manipulation of Affinity Maturation and B Cell Subsets *in vivo*
Ali Zarrin, Ph.D., Senior Scientist, Immunology and Antibody Engineering, Genentech
B cells diversify their immunoglobulin genes to produce high affinity antibodies. Antigen specific B cells are selectively differentiated in the germinal centers to seed short- or long- lived plasma cells, a process known as affinity maturation. It is not clear how B cells commit to short or long-lived plasma cell fate. Our study provides insights on how this decision might be made during immune response and autoimmunity.

12:15 pm Antigen Epitope Analysis and De-Immunogenicity of Antibody/Protein Drugs *Sponsored by* ABMAX
Le Sun, Ph.D., CEO, AbMax Biotechnology
The presentation will describe the prediction of immunogenicity based on a.a. sequence using B-cell epitope analysis and explore the strong correlations of ADA data between animal studies and human clinic trials. We will also present a case study with de-immunogenicity of Humira showed that ADA titers in mouse were reduced by 90%.

12:45 Session Break

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

Engineering Next-Generation Cancer Immunotherapies

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

IMMUNOTHERAPY COMBINATIONS

2:00 Chairperson's Remarks

Stephen Beers, Ph.D., Associate Professor, Cancer Immunology and Immunotherapy, University of Southampton, United Kingdom

2:05 Update on Clinical Progress of Immunotherapy Combinations

Gregory Daniels, M.D., Ph.D., Professor, Medicine, Moores Cancer Center, University of California, San Diego

Tumors development occurs in the context of a functioning immune system with intrinsic and extrinsic growth pathways dynamically shaping a pro-tumor microenvironment. Tumor response to current therapies depend upon the quantitate and qualitative presence of the natural immune response. I will discuss examples of combination immune therapy in solid tumors that overcome the barriers in generating an anti-tumor response.

2:35 Rational Combination of Oncolytic Virus and Checkpoint Therapy

Jason DeVoss, Ph.D., Senior Scientist, Oncology, Amgen

3:05 Transition to BuzZ Sessions

3:15 BuzZ Sessions with Refreshments

BuzZ sessions

Join your peers and colleagues for interactive roundtable discussions.

Please see page 78 for additional information.

EMERGING PATHWAYS AND TARGETS FOR CANCER IMMUNOTHERAPY

4:30 Epigenomic Mapping to Discover Novel Immunotherapy Targets

Pandurangan Vijayanand, M.D., Ph.D., Associate Professor, Vaccine Discovery, La Jolla Institute for Allergy and Immunology

5:00 The Importance of Fc Receptor Interactions for OX40 Agonists and Their Ability to Drive Tumor Ag-Specific T Cell Expansion

Andrew Weinberg, Ph.D., Judy Ann Hartmann Endowed Chair for Cancer Immunology Research, Robert W. Franz Cancer Research Center

OX40 agonists have been shown to increase T cell effector function, proliferation and survival. These T cell stimulating properties are important to enhance anti-tumor therapeutic efficacy. We have found that Fc receptor interactions are important for the agonist properties of these OX40 targeting Abs, which appear to be completely independent of Treg depletion. Recently we have found that OX40 agonists can expand tumor reactive T cells within the cancer microenvironment.

5:30 Targeted Mass Spectrometry for Cancer Antigen Discovery

Paul Armistead, M.D., Ph.D., Associate Professor, Medicine, Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill

Mass spectrometry based identification of HLA-bound, cancer antigens is essential for many immunotherapeutic strategies; however, standard non-targeted methods are insensitive and inadequate for the discovery of previously undefined peptides (e.g., neoantigens). These problems can be overcome, however, by optimizing mass spectrometers for the targeted detection of specific antigens. Targeting approaches that we have adopted involve differential ion mobility spectrometry for target enrichment and parallel reaction monitoring for target confirmation.

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

Sponsored by NANOTEMPER

7:15 Close of Day

TUESDAY, JANUARY 9

8:00 am Registration and Morning Coffee

NOVEL IMMUNOTHERAPIES

8:30 Chairperson's Remarks

G. Jonah Rainey, Ph.D., Executive Director, Research, MabVax Therapeutics Holdings, Inc.

8:35 Pritumumab, the First Therapeutic Antibody for Glioma Patients

Mark C Glassy, PhD, Chairman, Nascent Biotech; Visiting Scholar, Translational Neuro-Oncology, Moores Cancer Center, University of California, San Diego

Gliomas are a particularly aggressive form of brain cancer for which immunotherapy may hold promise. Pritumumab is a natural human IgG1kappa monoclonal antibody developed from a B lymphocyte isolated from a regional draining lymph node of a patient with cervical carcinoma. Here we review data on the development and characterization of Pritumumab, and review clinical trials data assessing immunotherapeutic effects of Pritumumab for glioma patients.

9:05 Efficacy of CAR-T Cells and Other Immunotherapies

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

Parameters that could affect efficacy of CAR-T cells and other immunotherapies including affinity, epitope location, surface expression and concentration of target cell surface associated antigen will be discussed as well as possible underlying mechanisms. Specific examples will be presented including an update on the high efficacy of the anti-CD22 CARs based on the scFv m971 as well as newly developed BiKEs targeting the HIV-1 envelope glycoprotein.

9:35 Featured Poster Presentation: Identification of Breast Cancer Subtypes by Phenotypic Antibody Selection

Kristine Kim, PhD, Professor, Department of Systems Immunology, College of Biomedical Science, Kangwon National University, Korea

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

Engineering Next-Generation Cancer Immunotherapies

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

11:00 A New Immunomodulatory Strategy of Releasing Immunosuppression in the Tumor Microenvironment

Carolyn R. Bertozzi, PhD, Professor, Chemistry, Howard Hughes Medical Institute, Stanford University

Cancer therapy has been revolutionized by inhibiting immune-checkpoints to harness the power of the immune system in fighting cancer. Immune-checkpoint inhibitors have proved to achieve a durable response in a subset of cancer patients. However, most patients are still resistant to these first generation I/O drugs. Enormous effort is pursued to identify new immunomodulatory strategies. We describe a novel approach of blocking an immunosuppression pathway involved in innate and adaptive response.

11:30 Achieving Broad Tumor Coverage by Targeting Cancer Carbohydrate Antigens: Lessons from the Clinic Accelerate Development of Additional Targets

G. Jonah Rainey, Ph.D., Executive Director, Research, MabVax Therapeutics Holdings, Inc.

Glycans are promising therapeutic targets present on broad tumor types. We are clinically developing an anti-sialyl Lewis A (sLea) naked antibody (MVT-5873), immunoPET imaging agent (MVT-2163), and radioimmunoconjugate (MVT-1075). Here we describe a fully human antibody against another cancer glycan, Tn (GalNAc alpha-O-Ser/Thr), which shows minimal overlap with sLea by tumor microarray. We compare translational learnings from anti-sLea programs and describe how they have guided development of our anti-Tn effort.

12:00 pm Featured Poster Presentation: Engineering Adenosine Deaminase 2 for Cancer Immunotherapy Development

Lin Wang, Ph.D., Principal Scientist, Halozyme Therapeutics, Inc.

Adenosine is an endogenous immunosuppressant that binds to adenosine receptor checkpoints. Abnormally high level of adenosine contributes to a highly immunosuppressive tumor microenvironment (TME). We hypothesized that adenosine deaminase 2 (ADA2), a human enzyme that catalyzes the deamination of adenosine, could be administered at therapeutic levels to deplete high level of TME adenosine and stimulate anti-tumor immune activity. This talk will present data that supports our hypothesis.

12:30 Session Break

12:45 Luncheon Presentation: Identification of Novel Receptor Targets and Specificity Screening of Biotherapeutics

Sponsored by RETROGENIX SPOTTING YOUR TARGET

Alex Kelly, Business Development Manager, Retrogenix Limited

Human cell microarray screening enables the discovery of primary cell surface receptors and off-targets for a variety of biotherapeutic molecules, including peptides, antibodies and proteins, as well as CAR T and other cell therapies. Case studies will demonstrate the utility of the technology in identifying novel immunotherapy targets as well as in specificity screening for biotherapeutics to aid safety assessment and provide critical data to support IND submissions.

1:15 Close of Engineering Next-Generation Cancer Immunotherapies Conference

JANUARY 9-10 | 5TH ANNUAL

Antibody-Drug Conjugates

Engineering for Clinical Success

The Fifth Annual Antibody-Drug Conjugates conference reveals the engineering that has brought about today's ADC revolution, and examines how to design safe and effective therapeutics. Exploring options for selecting new targets and ensuring potency will be discussed, along with strategies for advancing ADCs to the clinic. A special focus on fighting cancer will be highlighted including tumor penetration. Analyzing ADCs to explore conjugation, stability, and payloads will also be addressed in this leading ADC event.

TUESDAY, JANUARY 9

1:00 pm Registration

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

IMPROVING THERAPEUTIC INDEX

2:00 Chairperson's Opening Remarks

Ian Schwartz, MS, CMC Expert, Antibody Drug Conjugate and Upstream/Downstream Process Development, Tech Transfer, and Manufacturing Ops, Sartorius Stedim Biotech

KEYNOTE PRESENTATION

2:05 Case Study: Translational Safety of Antibody Drug Conjugates -- Opportunities to Mitigate Clinical Toxicities and Improve Therapeutic Index (TI)

Rakesh Dixit, Ph.D., DABT, Vice President, R&D, MedImmune/AstraZeneca

I discuss preclinical toxicity models of safety assessment, translational safety and therapeutic index, and clinical development of ADCs using precision medicine approaches.

2:45 Improved Therapeutic Window with Antibody Linked Pyrrolobenzodiazepine Dimers That Is Enhanced by PARP Inhibitor in BCA Mutant Tumors

Haihong (Helen) Zhong, Ph.D., Senior Scientist, Oncology Research, MedImmune, Inc.

One of the major challenges to ADCs is how to improve therapeutic index. PBDs are DNA-damaging agents that have potent cytotoxicity against a broad spectrum of tumors. In preclinical efficacy and safety studies including a "mouse PDX trial", PBD-based ADC as a single agent or in combination with PARPi demonstrated enhanced anti-tumor acitivity in BRCA mutant tumors. Furthermore, the combination was better tolerated than monotherapy, indicating an improved therapeutic index.

3:15 Computational Exploration of Mechanistic Determinants of ADC Pharmacokinetics Using QSP Modeling Strategies

Sponsored by applied biomath

John Burke, Ph.D., Co-Founder, President, CEO, Applied BioMath, LLC

The pharmacokinetics of ADC therapeutics typically show a discrepancy between PK of total antibody and of conjugated antibody, carrying one or more payload molecules. This discrepancy is often attributed to deconjugation, however recent evidence suggests that underlying mechanisms may be more complex. This presentation will demonstrate a computational approach to understand the impact of DAR and resulting changes in molecular properties on overall PK and relative payload disposition as observed in preclinical and clinical studies.

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

NEXT-GEN ADC STRATEGIES

4:30 From Cells to ADCs: A Magnetic Bead-Based Workflow for Antibody Capture and Conjugation

Paul Gianella, Ph.D., Postdoctoral Research Fellow, Amgen, Inc.

Magnetic beads are a useful research tool for manipulation and isolation of cells or proteins of interest due to their ability to be fuctionalized with a variety of affinity reagents and ease of handling. Here, we developed a process that demonstrates the speed and ease of use of magnetic beads for highly efficient purification and conjugation of cysteine-engineered antibodies from cell culture to final antibody conjugate products in a single workflow.

5:00 Exploring Higher Order Structure of ADCs with Biophysical Characterization Techniques

David Chiu, Ph.D., Scientist, Analytical Sciences, Seattle Genetics

Conformational changes to a biotherapeutic can impact product stability, safety, and efficacy, making higher order structure (HOS) characterization fundamentally important. Multiple biophysical techniques, each with their own capabilities and limitations, are required to elucidate HOS. ADCs can present unique biophysical analytical challenges, and as a case study, the biophysical characterization of a cysteine-conjugated ADC with a drug-to-antibody ratio of 8 will be presented.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

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

WEDNESDAY, JANUARY 10

8:00 am Registration and Morning Coffee

FIGHTING CANCER WITH ADCs

8:30 Chairperson's Remarks

Floris Van Delft, Ph.D., Founder & CSO, SynAffix BV

FEATURED PRESENTATION

8:35 Targeted Protein Therapeutic Drug Design in Oncology

Jeannick Cizeau, Ph.D., Director, Research, Viventia Bio, Inc.

Targeted protein therapeutics, or TPTs, are recombinant proteins composed of targeting moieties genetically fused via a short peptidic linker to cytotoxic protein payloads. A fit-for-purpose design approach is utilized to overcome specific challenges inherent to antibody drug conjugates currently in use for the treatment of solid cancers. An overview of drug design for both local and systemically deliverable TPTs will be presented.

9:05 Targeting Solid Tumors with Antibody-Drug Conjugates: An Update

Dimiter S. Dimitrov, Ph.D., Senior Investigator, Center for Cancer Research, NCI/NIH

Therapy of solid tumors continues to be a major challenge. We have been developing several antibody-drug conjugates (ADCs) to solid tumors including lung, colon and breast cancer, and neuroblastoma. The ADCs were generated by site-specific conjugation through glycans and conjugated to PBD dimers. They were tested *in vitro* and in mouse models and showed promise for further evaluation in humans. Potential problems related to toxicity and efficacy will be discussed.

9:35 Accelerate Development of Bioconjugates

Tyler Gable, Ph.D., Technology and Application Consultant, Bio and Reaction Engineering, METTLER TOLEDO AUTOCHEM

Rapid, reproducible, and data-rich process understanding Design of Experiment (DoE) can achieve accelerated process development of antibody and protein-conjugates. Gain confidence in the precise control of drug substance process with repeatable reactions under reproducible conditions. Examine two recent industry case studies utilizing automated bioconjugate workstations to eliminate process induced aggregates, improve product distribution and monomeric drug substance composition, optimize raw material consumption, efficiency and reduce overall process time.

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

INNOVATING LINKER & PAYLOAD TECHNOLOGIES

10:50 Understanding Stability of ADCs Utilizing Deconjugation of Small Molecule Drugs

Colin Medley, Ph.D., Senior Scientist, Small Molecule Pharmaceutical Sciences, Genentech, Inc.

This presentation will highlight our recent efforts to use deconjugation of the payload of ADCs to better understand the stability and degradation pathways for the linker drug portion of ADCs. We have developed methods of enzymatic and chemical deconjugation that have proved effective for analyzing ADCs comprised of different linker drugs and different antibodies.

11:20 Balancing Selectivity and Efficacy of Bispecific EGFR x c-MET Antibodies and Antibody-Drug Conjugates

Carolin Sellmann, Ph.D., Scientist, Protein Engineering and Antibody Technologies, Merck KGaA

Therapies targeting EGFR often suffer from toxicities due to basal EGFR expression in normal tissue and may face limited efficacy through c-MET activation. Hence, we aim to construct bispecific EGFR x c-MET antibodies employing affinity-optimized binding moieties to balance both high selectivity and anti-tumor efficacy and to evaluate their potential for an innovative antibody-drug conjugate approach.

11:50 Development and Optimization of Antibody-Drug Conjugates Armed with DNA Damaging Payloads

Julia Gavrilyuk, Ph.D., Principal Research Scientist, Chemistry Lead, Discovery Chemistry, Abbvie StemcentRx, Inc.

Highly potent DNA damaging payloads present unique challenges in prediction of corresponding ADCs *in vivo* efficacy and toxicological profile based on limited *in vitro* evaluation. Unexpected experimental findings in the course of development and optimization of calicheamicin and pyrrolobenzodiazepine based ADCs will be presented.

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

12:50 Session Break

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

SITE-SPECIFIC CONJUGATION

2:00 Chairperson's Remarks

Julia Gavrilyuk, Ph.D., Principal Research Scientist, Chemistry Lead, Discovery Chemistry, Abbvie StemcentRx, Inc.

2:05 Optimized Site-Specific Antibody-Glucocorticoid Conjugation for Targeted Delivery of Novel Glucocorticoids to Ag+ Cells

Amy Han, Ph.D., Director, Chemistry, Regeneron Pharmaceuticals

We optimized transglutaminase-mediated site-specific conjugations, and our site-specific antibody glucocorticoid (GC) conjugates selectively delivered GCs to Ag+ cells with > 500-fold selectivity over non-target cells *in vitro*, and demonstrated excellent stability *in vivo*. Specifically delivering GCs to disease-affected cells via an ADC could potentially reduce the systemic side effects of non-targeted GC therapy.

2:35 HydraSpace Technology: A Versatile Ionic Spacer to Further Empower Glycan-Conjugated (GlycoConnect) Antibody-Drug Conjugates

Floris Van Delft, Ph.D., Founder & CSO, SynAffix BV

Conjugation and spacer technology constitute key components of antibody-drug conjugates (ADCs). We here demonstrate that manufacturability and stability of our "GlycoConnect" technology, based on site-specific conjugation of payload through the native glycan, is further enhanced by a novel spacer technology ("HydraSpace"). Moreover, head-to-head *in vivo* assessment versus all main-stream conjugation technologies, including based on cysteine engineering, indicate a major improvement in pharmacokinetics, efficacy and safety, hence significantly enhanced therapeutic index.

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

OVERCOMING PRODUCTION CHALLENGES

4:00 Early and Late-Stage Development and Manufacturing Challenges for ADCs

Robert Herbst, Ph.D., Director, Process Development and Engineering, ImmunoGen, Inc.

4:30 Strategy to Advance ARX788 ADC from Development to Clinical Manufacturing

Yun Bai, Ph.D., Director, Ambrx, Inc.

ADC technology transfer and manufacturing can be very challenging, especially for CMOs in a different

country with different cGMP and clinical filing regulations. This presentation will focus on various strategies used in ARX788 ADC technology transfer project for multi-country clinical filing.

5:00 Blocking Salt Release with Precision

James R. Prudent, Ph.D., President & CEO, Centrose LLC

Extracellular drug conjugates (EDCs) act at the cell surface, do not internalize and do not release free drug. This talk will describe anti-cancer EDCs that induce irreversible cell swelling. Swelling is a highly evolved system that induces stress, disrupts gradients, and activates the immune system. This talk will discuss how triggered irreversible swelling can be induced in a cancer specific manner and why this is important.

5:30 - 6:45 Networking Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Antibody-Drug Conjugates Conference

JANUARY 11-12 | 7TH ANNUAL

Bispecific Antibody Therapeutics

Engineering Multi-Specificity

The Seventh Annual Bispecific Antibody Therapeutics conference explores the challenges of engineering multi-specificity to achieve more effective therapies that bind to at least two molecular targets simultaneously. These next-generation antibody formats are showing efficacy in the efforts to conquer cancer and other diseases. Case studies will highlight novel engineering approaches that address safety, stability, enhanced targeting, and manufacturability, as well as breakthrough development technologies and strategies.

THURSDAY, JANUARY 11

7:45 am Registration and Morning Coffee

CREATING NEXT-GENERATION THERAPIES

8:15 Chairperson's Opening Remarks

David E. Szymkowski, Ph.D., Vice President, Cell Biology, Xencor, Inc.

KEYNOTE PRESENTATION

8:20 The Rise of Bispecific Antibodies as Drugs

Paul J. Carter, Ph.D., Staff Scientist and Senior Director, Antibody Engineering, Genentech, Inc.

Bispecific antibodies are emerging as drugs with two such molecules approved for human therapy and over 50 more in clinical development. We developed a robust method for production of bispecific IgG in single mammalian host cells to support the clinical development of these complex hetero-tetrameric molecules. Additionally, we established high-resolution mass spectrometry methods to facilitate the characterization and quantitation of bispecific antibodies and other complex biologics.

9:00 Examples of Development Strategies for Next-Generation Therapeutics

Nicola Beaucamp, Ph.D., Head, Process Research, Pharma Research and Early Development, Roche Innovation Center Munich, Roche Diagnostics GmbH

A number of novel antibody formats have been advanced into the clinic by Roche pRED. In order to discover and develop differentiated monoclonal antibodies, Roche's strategy is based on engineering technologies which bear several challenges for technical development. Examples will be presented on how the development processes were adapted to deliver these new format molecules in the best quality and quantity for clinical studies.

9:30 Engineering IgM CH2 Domain as a Versatile Building Block for the Construction of Various Multi-Specific Antibodies

Jijie Gu, Ph.D., Research Fellow and Function Head, Immunology Discovery, AbbVie Bioresearch Center

Multi-specific antibodies hold great promise as one of the approaches for developing next generation antibody-based therapeutics. We engineered IgM2 CH2 domain from a homodimeric domain to a CH1/CK like heterodimeric domain. Engineered IgM CH2 domain can be used as a versatile building block for the construction of various multi-specific antibody formats to enable various novel therapeutic concepts.

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

11:00 Tailoring Processing of Amyloid Precursor Protein as a Therapeutic for Alzheimer's Disease

Michael Sierks, Ph.D., Professor, Chemical Engineering, Arizona State University

Generation of beta-amyloid from the amyloid precursor protein is a key step in the progression of Alzheimer's disease. We have designed a bispecific antibody that inhibits toxic amyloidogenic processing of the amyloid precursor protein while simultaneously catalyzing formation of a neuroprotective fragment. We show that the bispecific antibody provides excellent therapeutic benefit in a mouse model of AD.

11:30 Design and Evaluation of Next-Generation Biologics for Cancer Immunotherapy

Christopher Smith, Ph.D., Senior Scientific Consultant, Biologics, Genedata

Bi- and multi-specific antibodies, Ab-cytokine fusion proteins, non-Ig scaffolds, chimeric antigen receptors (CARs), engineered TCRs and TCR-based bispecific constructs can provide significant advantages for use in cancer immunotherapy. However, as highly engineered molecules they pose new design, engineering, cloning, expression, purification, and analytics challenges. Genedata Biologics enables the automated design, screening, production, and testing of large panels of these candidate therapeutic molecules and includes 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

FIGHTING CANCER

2:00 Chairperson's Remarks

Eric Smith, Ph.D., Director, Bispecific Antibdies, Regeneron Pharmaceuticals, Inc.

FEATURED PRESENTATION

2:05 Non-Engineered Multi-Specific Antibodies

Marie Kosco-Vilbois, Ph.D., CSO, NovImmune SA

The κλ body continues to embody an innovative design to incorporate multi-specificity into a human framework devoid of any mutation, foreign sequences or linkers. κλ bodies exploit light chain diversity, conferring different specificities into >1500 targeting arms directed against >15 targets. The format's simplicity makes manufacturing from research to clinical easily scalable and ensures high purity and stability. The first κλ bodies are designed to exploit the innate immune checkpoint, CD47, safely yet effectively, by targeting phagocytosis of cancer cells specifically to B cell malignancies and solid tumors.

2:35 Bispecific Antibodies for Dual Immune Checkpoint Blockade

David E. Szymkowski, Ph.D., Vice President, Cell Biology, Xencor, Inc.

Combinations of checkpoint-blocking antibodies are more efficacious then single inhibitors, but generate greater immune-related toxicities. We reasoned that a bispecific antibody could achieve dual blockade to selectively target tumor-reactive lymphocytes, improving safety and efficacy. We generated multiple dual-checkpoint inhibitors including XmAb20717 (anti-PD1 x anti-CTLA4) that display compelling *in vivo* activity relative to combinations of monospecific antibodies, suggesting that checkpoint bispecifics may have clinical advantages for the treatment of cancer.

3:05 SELECTED POSTER PRESENTATION: COBRA (Conditional Bispecific Re-Directed Activation) Platform of Protein Therapeutics for Cancer Treatment

Maia Vinogradova, Ph.D., Director, Protein Sciences, Maverick Therapeutics

COBRA platform allows to design bispecific T-cell engaging protein therapeutics with a reduced risk of potential on-target cytotoxicity. COBRAs are multidomain proteins comprising the familiar scaffolds of the antibody repertoire, but not of the immunoglobulin type. We demonstrated the conditional protease dependent activity of our molecules in proof-of-concept T-cell dependent cytotoxicity assays.

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

4:15 Development of T Cell Redirecting Fully Human Bispecific Antibodies

Eric Smith, Ph.D., Director, Bispecific Antibodies, Regeneron Pharmaceuticals, Inc.

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

4:45 Co-Stimulation of Immune Cells in the Tumor Microenvironment via Bispecific DART and TRIDENT Molecules

Gundo Diedrich, Ph.D., Associate Director, Antibody Engineering, MacroGenics, Inc.

Targeting costimulatory receptors on immune cells with agonistic antibodies is a promising strategy in cancer therapy. To limit the immune activity to tumors, while sparing effects on normal tissue, we generated bispecific DART and TRIDENT molecules targeting several tumor antigens together with the costimulatory receptor, CD137. T cell agonistic activity by these molecules was strictly dependent on the expression of the tumor antigens. Preclinical development of these proteins will be addressed.

5:15 The Benefits of Bispecific mAb2 Antibodies Targeting EGFR and HGF

Kin-Mei Leung, Ph.D., Principal Scientist, Drug Discovery, F-star Biotechnology, Ltd.

F-star's Modular Antibody Technology™ platform was utilized to generate bispecific molecules that bind to Epidermal Growth Factor Receptor (EGFR) and Hepatocyte Growth Factor (HGF). The EGFR/HGF mAb^2 inhibit cell proliferation *in vitro* and show anti-tumor activity in patient-derived xenograft (PDX) models *in vivo*. The mAb^2 molecules show superior inhibition of tumor growth compared to combination treatments in tumors with specific molecular profiles suggesting novel biology of the bispecific.

5:45 Close of Day

FRIDAY, JANUARY 12

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast

BUZZ sessions

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

Table Moderator: Nicola Beaucamp, Ph.D., Head, Process Research, Pharma Research and Early Development, Roche Innovation Center Munich, Roche Diagnostics GmbH

ENGINEERING IMPROVED PROPERTIES WITH NEXT-GEN TECHNOLOGIES

9:00 Chairperson's Remarks

Marie Kosco-Vilbois, Ph.D., CSO, NovImmune SA

9:05 Identification and Quantitation of DuoBody Bispecific IgG1 Using Mass Spectrometry and Automated Data Processing and Analysis Workflow

Ewald Van den Bremer, Ph.D., Senior Scientist, Genmab A/S

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

9:35 bisFabs: Tools for Rapidly Screening Hybridoma IgGs for Their Activities as Bispecific Antibodies

Bushra Husain, Ph.D., Senior Scientific Researcher, Genentech, Inc.

Bispecific antibodies enable therapeutics with novel mechanisms of actions. To expedite the screening of hybridoma clones for their potential as bispecific antibodies, we developed procedures to chemically crosslink Fabs obtained from hybridomas with different isotypes. The resulting crosslinked F(ab')2s (bisFabs) were compared for their biological activities to the counterpart molecules reformatted into the full-length IgG. Results showed bisFabs and full-length IgGs had comparable activities, validating the predictive value of bisFabs.

JANUARY 11-12 | 7TH ANNUAL

Bispecific Antibody Therapeutics

Engineering Multi-Specificity

10:05 From the Bench to the Clinic: Developing Next-Generation ADAPTIR Molecules

David Bienvenue, Senior Director, Protein Sciences, Aptevo Therapeutics

The presentation will highlight the activity, stability and manufacturability of ADAPTIR bispecifics and will include recent data for a lead preclinical candidate, APV0436, which targets CD123 and CD3. APV0436 has shown potent biological activity in preclinical studies and is rapidly advancing towards first-in-human clinical trials.

10:35 Coffee Break with a Poster Pavilion

See page 4 for details

11:15 An IgM-Based Bispecific Platform for Enhanced T Cell and Complement Dependent Cytotoxicity on Low Antigen Expressing Cells

Ramesh Baliga, Ph.D., Vice President, Discovery Biology, IGM Biosciences

IGM Biosciences has built a unique bispecific platform based on a CD3 epsilon binding single chain Fv domain fused to the IgM joining chain. Our CD20 targeted IgM bispecific antibody IGM-2323 binds CD20 antigen greater than 1000X better, and shows functional effects such as CDC greater than 100X better than corresponding IgG's. Moreover, it shows T cell dependent cytotoxicity even on cells with very low cell surface expression of CD20 (Namalwa).

11:45 A Novel Trifunctional Antibody Combining PD-1/PD-L1 Blockade and Targeting of a Tumor-Specific Carbohydrate Antigen

Christoph Goletz, Associate Director, Immunomodulation, Glycotope GmbH

We developed a trifunctional antibody combining PD-1/PD-L1 blocking and highly tumor-specific targeting via the novel protein/carbohydrate mixed epitope TA-MUC1 with a functional Fc part in one molecule. By focusing the checkpoint blockade to the tumor and combining multiple modes of action, that antibody has the potential to increase efficacy and broaden the patient coverage giving additional benefit compared to the respective monospecific antibody.

12:15 pm Conference Wrap-Up

Nicola Beaucamp, Ph.D., Head, Process Research, Pharma Research and Early Development, Roche Innovation Center Munich, Roche Diagnostics GmbH

12:45 Close of Conference

INNOVATIONS IN DISCOVERY & DEVELOPMENT

JANUARY 8-9

AGENDA Advancing CNS Biotherapeutics and Crossing the Blood-Brain Barrier

JANUARY 9-10

AGENDA Next-Generation Approaches to Antibody Screening and Discovery TRAINING SEMINAR

JANUARY 11-12

AGENDA Emerging Technologies for Antibody Discovery

JANUARY 8-9 | INAUGURAL

Advancing CNS Biotherapeutics and Crossing the Blood-Brain Barrier

Innovation, New Targets, Tools, Delivery and New Research Updates

CHI's Inaugural Advancing CNS Biotherapeutics and Crossing the Blood-Brain Barrier conference strives to bring you the hottest topics and biggest opportunities in discovering and developing highly efficacious therapeutic agents against CNS disorders and innovative strategies for delivering therapies across the blood-brain barrier (BBB). This new meeting will brainstorm ideas and share new research on topics such as the biologics for CNS targets and biomarkers, brain cancer, neurodegeneration, neuroinflammation, neuroimmunology, alteration of CNS/BBB barriers due to injury or disease, preclinical models, neuroimaging, tools for prediction of brain penetration, and updates from the industry.

SUNDAY, JANUARY 7

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

MONDAY, JANUARY 8

7:00 am Registration and Morning Coffee

CONSIDERATIONS FOR DISCOVERY AND DEVELOPMENT FOR CNS AND BBB THERAPIES

9:00 Welcome by Conference Organizer

Nandini Kashyap, Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks

Per-Ola Freskgard, Ph.D., Vice Director and Senior Leader, Neuroscience, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd.

KEYNOTE PRESENTATION

9:10 Efficient and Safe Biologics for Diseases of CNS

Per-Ola Freskgard, Ph.D., Vice Director and Senior Leader, Neuroscience, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd.

9:50 Clearance of Beta-amyloid is Facilitated by Apolipoprotein E and Circulating High-density Lipoproteins in Bioengineered Human Vessels

Jerome Robert, PhD, Pathology and Laboratory Medicine, Djavad Mowafaghian Centre for Brain Health, University of British Columbia

Amyloid plaques, consisting of deposited beta-amyloid (Aβ), are a neuropathological hallmark of Alzheimer's Disease (AD). Cerebral vessels play a major role in AD, as Aβ is cleared from the brain by pathways involving the cerebrovasculature, most AD patients have cerebrovascular amyloid (cerebral amyloid angiopathy (CAA), and cardiovascular risk factors increase dementia risk. Here we present a notable advance in vascular tissue engineering by generating the first functional 3- dimensioinal model of CAA in bioengineered human vessels. We show that lipoproteins including brain (apoE) and circulating (high-density lipoprotein) synergize to facilitate Aβ transport across bioengineered human cerebral vessels. These lipoproteins facilitate Aβ42 transport more efficiently than Aβ40, consistent with Aβ40 being the primary species that accumulates in CAA. Moreover, apoE4 is less effective than apoE2 in promoting Aβ transport, also consistent with the well-established role of apoE4 in Aβ deposition in AD.

10:20 Networking Coffee Break

10:45 Biologics That Already Benefit the Brain: Lessons, Mysteries, Surprises

Lois A. Lampson, Ph.D., Emeritus Associate Professor of Neurosurgery, Brigham & Women's Hospital/Harvard Medical School

Biologics that already benefit the brain include monoclonal antibodies for MS, brain metastases, and models of AD and other tauopathies. Lessons include the value of indirect effects, often involving migratory cells, with the antibody itself not crossing the BBB. Mysteries include the final effector mechanism, and the state and role of the BBB. Surprises include unorthodox specificities, such as anti-tumor antibodies that also attack normal cells.

11:15 New Targets and Biomarkers for CNS Disorders and Diseases

Servio Ramirez, Ph.D., Associate Professor, Pathology and Laboratory Medicine, Lewis Katz School of Medicine, Temple University

Extracellular microvesicles (EVs) have emerged as a novel biological phenomenon, released by virtually every cell type in the body. We have identified that brain endothelial derived EVs contain key constituents of the BBB. Our recent discoveries suggest that BBB de-stabilization during neuroinflammation triggers brain endothelial EV release which facilitates BBB breach. Thus, I will introduce concepts that could help us understand EV significance in vascular remodeling and utility as biomarkers.

11:45 PANEL DISCUSSION: Challenges and Opportunities in Discovery and Development of New CNS and BBB Therapies

Moderator:
Lois A. Lampson, Ph.D., Emeritus Associate Professor of Neurosurgery, Brigham & Women's Hospital/Harvard Medical School

Panelists:
Per-Ola Freskgard, Ph.D., Vice Director and Senior Leader, Neuroscience, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd.

Robert D. Bell, Ph.D., Senior Principal Scientist, Neurovascular Biology Lab Head, Pfizer, Inc.

Servio Ramirez, Ph.D., Associate Professor, Pathology and Laboratory Medicine, Lewis Katz School of Medicine, Temple University

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

12:45 Session Break

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

DRUG DELIVERY AND MOLECULAR TRANSPORT ACROSS BBB

2:00 Chairperson's Remarks

Torben Moos, M.D., Ph.D., DMSc, Professor, Medicine and Health Technology, Aalborg University

2:05 Brain Penetrating IgG Fusion Proteins: From Genetic Engineering to Clinical Trials in Lysosomal Storage Disorders

Ruben Boado, Ph.D., Vice President, Research & Development/Co-Founder, ArmaGen, Inc.

Lysosomal enzymes, such as iduronase (IDUA) and sulfatases, are large molecule drugs that do not cross the blood-brain barrier (BBB). The BBB-penetration of enzyme therapeutics is enabled by re-engineering the recombinant enzyme as bi-functional IgG fusion proteins, wherein the IgG domain targets a specific endogenous receptor-mediated transporter system within the BBB, such as the human insulin receptor (HIR). The enzyme

Advancing CNS Biotherapeutics and Crossing the Blood-Brain Barrier
Innovation, New Targets, Tools, Delivery and New Research Updates

therapeutic domain of the fusion protein exerts the pharmacological effect in brain once across the BBB. Several brain penetrating IgG-LSD fusion proteins have been engineered and validated. First in human proof of concept Phase II clinical trial in LSD is in progress.

2:35 Deliverable Biologics at the Blood-Brain Barrier

Torben Moos, M.D., Ph.D., DMSc, Professor, Medicine and Health Technology, Aalborg University

My presentation will cover the concepts of the blood-brain barrier (BBB) with emphasis on macromolecular transport. I will cover the restraints and probable avenues for transport of biologics through the BBB. I will place emphasis on transport of proteins with therapeutic potential. This will include targeted uptake at the BBB, the potential of induced gene therapy to the BBB, and hypotheses on further release of biologics into the brain.

3:05 Transition to BuzZ Sessions

3:15 BuzZ Sessions with Refreshments

Join your peers and colleagues for interactive roundtable discussions.

Please see page 78 for additional information.

4:30 Delivery across the BBB, Utilizing Single-Domain Antibodies and a New Receptor-Mediated Transcytosis Pathway

Kristin Kemmerich, Ph.D., Head, Antibody Generation Section, National Research Council Canada

The blood-brain barrier (BBB) regulates brain homeostasis and provides protection against pathogens and other molecules, but it also restricts the effective delivery of biotherapeutics into the CNS. Here we characterize an unexplored receptor-mediated transcytosis pathway to deliver biologics to the brain. We developed specific single-domain antibodies that can carry payload across the BBB and assessed these *in vitro* and *in vivo* to allow for PK/PD modeling.

5:00 Development of Highly Efficient BBB Transport of Antibodies to the CNS Using *in vivo* Phage Display with Single Domain VNAR to the Transferrin Receptor

Frank S. Walsh, Ph.D., CEO, Ossianix

Antibody-based molecules do not cross the BBB in amounts required for therapeutic efficacy. Receptor-mediated transporters in the luminal membrane of brain capillary endothelium offer an approach for the delivery of therapeutics to the brain. Using a combination of *in vitro* and *in vivo* phage display technology, we isolated a panel of cross species binders to the transferrin receptor 1 (TfR1) from synthetic single domain VNAR libraries. At therapeutic (2 mg/kg) doses delivered by tail vein injection, high levels (>5% brain/plasma ratio) of the bispecific antibodies were found in the brain after 18 hours.

5:30 Blood-Brain Barrier Penetrating Dual Specific Binding Proteins for Treating Brain and Neurological Diseases

Kangwen Deng, Ph.D., Senior Scientist, Biologics, AbbVie

Blood-brain barrier (BBB), which consists mainly of specialized brain capillary endothelial cells, is a physical and physiological barrier that controls very efficiently and selectively the entry of compounds from blood into the CNS, and protects nervous tissue from harmful substances and infectious agents present in circulating blood. While naturally protective, the BBB provides a challenge for drug development as most of the small organic molecule drugs and nearly all biologic therapeutics do not cross the BBB to therapeutically relevant concentrations. Here, we will describe the generation and expression of DVD-Ig proteins which are capable of binding specific disease targets in the brain. The levels and localization of DVD-Ig proteins, which were injected systemically, were assessed by two orthogonal methods. Results showing the uptake, retention as well as the elevated functional activity of DVD-Ig proteins in the brain will be demonstrated.

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

Sponsored by TEMPER

7:15 Close of Day

TUESDAY, JANUARY 9

8:00 am Registration and Morning Coffee

IMAGING, PRECLINICAL TOOLS, MODELS AND TRANSLATIONS STRATEGIES

8:30 Chairperson's Remarks

Miroslaw Janowski, M.D., Ph.D., Associate Professor, Radiology, Johns Hopkins University

8:35 Extremely Fast Clinical MRI for Predicting and Real-Time Monitoring of Intra-Arterial Opening of the Blood-Brain Barrier

Miroslaw Janowski, M.D., Ph.D., Associate Professor, Radiology, Johns Hopkins University

MRI guidance enables opening of the blood-brain barrier (BBB) using intra-arterial route in a predicted and precise fashion. However, the monitoring of the process of BBB opening was difficult, as the real-time EPI MRI pulse sequence was not capable of visualizing the marker of BBB permeability. Here, we show that extreme speed of MRI reconstruction using the new GPU set-up allows turning other pulse sequences into real-time mode and visualize the process of BBB opening.

9:05 Nanobodies to Cross the Blood-Brain Barrier

Yessica Wouters, Researcher, VIB & KU Leuven Center for Brain & Disease Research

9:35 Sponsored Presentation *(Opportunity Available)*

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

JANUARY 8-9 | INAUGURAL

Advancing CNS Biotherapeutics and Crossing the Blood-Brain Barrier

Innovation, New Targets, Tools, Delivery and New Research Updates

11:00 The Blood Meningeal Barrier (BMB) Orchestrates the Development of Neuroinflammatory Responses

Jorge Iván Alvarez, Ph.D., Assistant Professor, Department of Pathobiology, University of Pennsylvania

To address how CNS endothelium drives neuroinflammation, we established a novel human model of the BMB and BBB. We found that the BMB immunological fingerprint induces a proinflammatory phenotype on migrating lymphocytes and promotes B cell aggregates that mirror their distribution within the meningeal compartment during multiple sclerosis. Our findings highlight the heterogeneity of the CNS vascular beds, how they regulate leukocyte function and demonstrate that the BMB niche is more conducive to promote neuroinflammation.

11:30 Intranasal Administration as a Method to Target Therapeutics to the CNS

Jeffrey Lochhead, Ph.D., Research Assistant Professor, Department of Pharmacology, University of Arizona

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 Advancing CNS Biotherapeutics and Crossing the Blood-Brain Barrier Conference

JANUARY 9-10 | INAUGURAL

Next-Generation Approaches to Antibody Screening and Discovery TRAINING SEMINAR

Training SEMINARS By Cambridge Healthtech Institute

TUESDAY, JANUARY 9 - WEDNESDAY, JANUARY 10

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

Instructor: David Bramhill, Ph.D., Founder, Bramhill Biological Consulting, LLC

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

Attendees will learn about:

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

INSTRUCTOR BIOGRAPHY

David Bramhill, Ph.D., Founder, Bramhill Biological Consulting, LLC

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

JANUARY 11-12 | 3RD ANNUAL

Emerging Technologies for Antibody Discovery

Exploring the Intersection of Display Technologies, Next-Generation Sequencing and Informatics for the Discovery of Next-Generation Biotherapeutics

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 – and that the biotherapeutics against these are selected and engineered to minimize development risk. For 2018, Cambridge Healthtech Institute's Third Annual Emerging Technologies for Antibody Discovery conference considers the intersection of traditional display based screening and selection approaches with next-generation tools such as immune repertoire sequencing, *in silico* modeling and high-resolution imaging.

THURSDAY, JANUARY 11

7:45 am Registration and Morning Coffee

8:15 Chairperson's Opening Remarks
Andrew Bradbury, Ph.D., CSCO, Specifica, Inc.

KEYNOTE PRESENTATION

8:20 Remodeling of Cell Surfaceomes in Cancer
James A. Wells, Ph.D., Professor, Pharmaceutical Chemistry, University of California, San Francisco

The cell surface proteome (surfaceome) is the primary hub for cells to communicate with the outside world. My lab studies how the surfaceome is remodeled in cancer. We find the new set of proteins promote enhanced cell growth and detachment from native tissues allowing metastasis. Our primary goal is to systematically understand how cancer cells remodel their membrane proteomes (surfaceomes) during cancer transformation and develop antibodies to detect and attack them.

FUNCTIONAL SCREENING

9:00 Combining Screening with Phenotypic Selection in Antibody Phage Display
Marcin Paduch, Ph.D., Pipeline Director, Recombinant Antibody Network, University of Chicago

State-of-the-art methods for generating recombinant antibodies do not necessarily allow for targeting the particular cellular phenotype posing a fundamental challenge. A set of next generation high-throughput technologies that allow for phenotypic selection has to be developed. Intimate knowledge of conformation states and biochemistry of antigens can be exploited to mimic native-like environments and create the possibility of trapping physiologically-relevant states otherwise not accessible by current methods.

9:30 Phage-Displayed Ubiquitin Variant (UbV) Libraries to Rapidly Identify Potent and Highly Selective Protein-Based Inhibitors Targeting E3 Ligases and Deubiquitinases
Wei Zhang, Ph.D., Mitacs Elevate Fellow, University of Toronto, Canada

E3 ligases and deubiquitinases regulate diverse cellular processes and are implicated in numerous human diseases. However, targeting these enzymes potently and specifically remains a big challenge. We thus devised a screening platform to develop protein-based modulators for ubiquitin proteasome system components. I will report how we design the ubiquitin variant (UbV) library to generate inhibitors and activators for E3 ligases (RING and HECT family) and deubiquitinases (viral and human origin).

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

11:00 Efficient B Cell Cloning and Antibody Engineering Platform for Rare Ab Generation
Feng Shu, Ph.D., Senior Researcher, Chugai Pharmabody Research, Singapore

Here we describe a high throughput antibody identification system by single B cell cloning, which can generate and evaluate a large number of antibodies with high diversity to identify the rare antibodies with required properties such as pH dependency. A robust antibody engineering system is also introduced, where thousands of antibodies with designed mutations can be generated and evaluated in 2 weeks' time to further accelerate the antibody discovery process.

Sponsored by RAPID NOVOR

11:30 Antibody Protein Sequencing with Mass Spectrometry
Mingjie Xie, MSc, MBA, CEO, Rapid Novor Inc

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

12:00 pm Session Break

Sponsored by protein simple

12:15 Luncheon Presentation I: Next-Generation Capillary Electrophoresis Technology for Protein Analysis
Wei-Chiang Chen, Ph.D., Scientist, Analytical Development, Biogen

Recombinant adeno-associated virus (AAV) is a promising platform in human gene therapy. AAV vectors contain a protein outer shell called capsid, which is comprised of 60 subunits containing three viral proteins. To confirm the purity of the AAV capsids, we developed a CE-SDS method on the Maurice platform, which automates analysis of 96 samples in one batch. This assay demonstrates good separation of viral proteins (LOQ at 5e11 vg/ml), and comparable results with SDS-PAGE gels.

12:45 Presentation to be Announced

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

ADVANCES IN DISPLAY TECHNOLOGIES AND LIBRARY DESIGN

2:00 Chairperson's Remarks
Nicolas Fischer, Ph.D., Head, Research, Novimmune SA, Switzerland

2:05 Enhancing the Chemical Versatility of Yeast Display
James Van Deventer, Ph.D., Assistant Professor, Chemical and Biological Engineering, Tufts University

We have established a version of yeast display that supports the integration of chemical groups into displayed proteins using noncanonical amino acid incorporation. We are currently investigating

strategies for positioning chemical groups within antibodies in order to enhance and change the molecular recognition capabilities of these proteins. This talk will highlight our recent progress in constructing, evaluating, and screening "hybrid" structures with potential applications in the tumor microenvironment.

2:35 How Big Are Antibody Libraries Really? And Are We Accessing the Full Diversity?

Andrew Bradbury, Ph.D., CSO, Specifica, Inc.

In vitro antibody libraries have been used to generate antibodies against many different therapeutic lead targets. Analyses indicate that one would expect to select 1-3 antibodies from a 1e7 library. However, this does not appear to scale to larger libraries with diversities estimated to be >1 billion, suggesting that libraries are less diverse than thought or selection methods do not tap the full diversity. This talk discusses the use of NGS to explore these issues and the application of NGS to the creation of improved antibody libraries.

3:05 Sponsored Presentation *(Opportunity Available)*

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

4:15 Dual Display Technology for "In Format" Selection and Screening of Bispecific Antibodies

Nicolas Fischer, Ph.D., Head, Research, Novimmune SA, Switzerland

The desired biological activity of bispecific antibodies is often dependent on the adequate geometry of the two antibody binding sites, thus requiring extensive combinatorial testing of isolated antibodies. Being able to evaluate candidates 'in format' as early as possible would greatly facilitate the development of bispecific antibodies. To achieve that goal, we have developed methodologies that allow 'in format' phage display selection and screening of candidates early in discovery.

4:45 Synthetic Human Antibody Fragment Libraries for CAR T Cell Therapy

Thomas J. Van Blarcom, Ph.D., Associate Research Fellow, Rinat Laboratories, Oncology Research and Development, Pfizer, Inc.

Unlike most therapeutic antibodies, CAR T cells are typically generated with single chain variable fragment (scFv) antibodies. In this study, we present a human synthetic scFv antibody library that we use to simplify the generation and testing of large panels of antibodies for use as CAR T cells. The CAR T cells generated from these antibodies had desirable phenotypes and demonstrated robust and specific cytotoxic activity *in vitro*.

5:15 Highly Multiplexed Cell Surfaceomics Using Genetically Barcoded Antibody-Phage

Samuel Pollock, Researcher, Pharmaceutical Chemistry, University of California, San Francisco

Cells express thousands of different surface proteins that can be used for their classification. We present a surface proteomic method using genetically barcoded antibodies called Phage-antibody Next Generation Sequencing. We use PhaNGS to reveal changes in surface protein abundance in the contexts of drug resistance, adaptation to oncogenes, and on the single-cell level. Linking selective, genetically encoded binders to NGS enables direct, multiplexed protein detection, comparable to RNAseq for mRNA.

5:45 Close of Day

FRIDAY, JANUARY 12

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast

BuzZ sessions

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

Table Moderator: James Van Deventer, Ph.D., Assistant Professor, Chemical and Biological Engineering, Tufts University

Table Moderator: Marcin Paduch, Ph.D., Pipeline Director, Recombinant Antibody Network, University of Chicago

INTEGRATED DISCOVERY PLATFORMS

9:00 Chairperson's Remarks

Sagar Kathuria, Ph.D., Senior Scientist, Protein Engineering, Sanofi Genzyme

9:05 Generation of Mono and Bispecific Antibodies from Immunized Transgenic Rodents and the Potential to Engineer Multi-Specific Entities Using Common Light Chain Paratopes

Simon Krah, Ph.D., Senior Scientist, Protein Engineering and Antibody Technologies, Merck KGaA, Germany

We demonstrate that by using Yeast Surface Display (YSD), a more effective coverage of the antibody diversity generated during the course of an immunization can be realized in comparison to classical hybridoma technology. Moreover, we show that bispecific antibodies can also be readily engineered via such YSD approaches in combination with the application of common light chains. In addition, we established a methodology which facilitates the tedious and time-consuming process of YSD library generation.

9:35 Discovery Platform for Antibody Generation and Screening for Different Applications

Anne Marcil, Team Lead, Monoclonal Antibodies, National Research Council, Canada

The National Research Council of Canada has a strong history in target discovery, antibody generation and characterization, resulting in the production of new antibodies against hundreds of targets. An overview of our antibody discovery pipeline which includes bioinformatics and MS analysis for target discovery, monoclonal, single-domain and antibody library screening, *in vitro* screening for function (ADCs, Blood-brain barrier crossers, electrophysiology, etc.) and *in vivo* screening will be presented.

JANUARY 11-12 | 3RD ANNUAL

Emerging Technologies for Antibody Discovery

Exploring the Intersection of Display Technologies, Next-Generation Sequencing and Informatics for the Discovery of Next-Generation Biotherapeutics

10:05 A Patient-Centric Function F.I.R.S.T™ Approach to Cancer Immunotherapy Discovery

Björn Frendéus, Ph.D., CSO, Bioinvent, Sweden

We have developed a patient-centric phenotypic discovery approach (F.I.R.S.T) that utilizes primary cancer patients' cells from the initial steps of isolating antibodies from a naïve human antibody library through POC studies and subsequent identification of targeted receptors. A lead candidate which blocks FcgRIIB internalization and acts in synergy with rituximab to boost responses and help overcome resistance in the background of emerging targeted therapies as well as conventional chemotherapy *in vivo*, is now in clinical phase testing.

10:35 Coffee Break with a Poster Pavilion

See page 4 for details

11:15 Tool and Platform Development for Antibody Developability Assessment and Mitigation

Sagar Kathuria, Ph.D., Senior Scientist, Protein Engineering, Sanofi Genzyme

Antibodies have emerged as very successful biological drugs in the recent past. The growth of this industry has highlighted a need for a comprehensive set of non-redundant assays and corresponding threshold values to identify likely candidates early during research and prioritize their development. We make use of several high-throughput biophysical and biochemical tools for antibody characterization towards achieving this goal. Results from some test cases will be discussed.

11:45 High Content Confocal for Antibody Selection and Potency Screening

Tianyi Wang, Ph.D., Scientist, R&D, Sorrento Therapeutics

This talk outlines applications of high content confocal and cell-by-cell metrics for selection and potency of antibodies with applications toward intracellular targets. 3D spheroids and high content confocal *in vitro* system are used to screen the phenotypic effects of selected intracellular-targeting antibodies. 3D spheroids, by mimicking tumor microenvironment, are a better predictor of clinical potential of antibody therapeutics. Our method proposes multiparametric analyses of spheroids to elucidate mechanism of action.

12:15 pm Conference Wrap-Up

Tilman Schlothauer, Ph.D., Principal Scientist, Biochemical and Analytical Research, Large Molecule Research, Roche Innovation Center Munich

12:45 Close of Conference

FORMULATION & STABILITY

JANUARY 8-9

AGENDA Optimizing Biologics Formulation Development

JANUARY 9-10

AGENDA Lyophilization and Emerging Drying Technologies

JANUARY 11-12

AGENDA Protein Aggregation and Emerging Analytical Tools

JANUARY 8-9 | 10TH ANNUAL

Optimizing Biologics Formulation Development

A Best Practices Exchange for Resolving the Challenges of Formulating Novel Biologic Drug Products

Cambridge Healthtech Institute's Tenth Annual Optimizing Biologics Formulation Development conference is an essential international gathering of analytical and formulation scientists from leading industry companies, offering an exchange of scientific developments and emerging technologies in an environment that encourages discussion with colleagues. For 2018, the conference focuses on a set of best practices for resolving key formulation development challenges. Each talk in the program will be presented by a different industry or academic group to ensure the widest possible range of perspectives.

SUNDAY, JANUARY 7

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

MONDAY, JANUARY 8

7:00 am Registration and Morning Coffee

A PRODUCT-CENTRIC VIEW OF FORMULATION DEVELOPMENT

9:00 Welcome by Conference Organizer

Kent Simmons, Senior Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks

Tarik Khan, Ph.D., Group Leader, Late-Stage Pharmaceutical and Processing Development, F. Hoffmann-La Roche Ltd., Switzerland

KEYNOTE PRESENTATION

9:10 An End to End Approach to Formulation Development: Considerations from Cell Line to Drug Product Process Development

Kapil Gupta, Ph.D., Associate Director, Protein Pharmaceutical Development, Biogen

Development of high concentration stable formulations requires an end to end approach. Product heterogeneity and process impurities generated from upstream process can impact drug product stability and might not be solved by formulation optimization. An integrated development approach is needed by balancing bioreactor productivity, yield, quality attributes and drug product stability to ensure success. This talk will highlight this concept using some recent case studies.

9:50 Present and Future Trends in Biotherapeutic Device-Mediated Delivery Technologies

Didier Pertuy, Vice President, Global Drug Device Integrated Development & Device Strategy, Sanofi, France

Biotherapeutic device-mediated delivery is dominated by self-injectable devices like prefilled syringes, pens and auto-injectors. Next incremental step should be Large Volume Devices driven by dosing frequency reduction and low device-ability profile of new formats. In parallel, emerging mHealth-enabling technology is bringing new opportunities for smarter devices and integrated care solutions. Even though longer-term evolution stays difficult to predict some potential trends could be considered.

10:20 Networking Coffee Break

CO-FORMULATION AND CO-ADMINISTRATION

10:45 The Challenges and Considerations of Protein and Peptide Coformulations

Rebecca Davis-Harrison, Ph.D., Research Scientist, BioTechnology Discovery Research, Eli Lilly and Company

The coformulation of two therapeutic peptides and/or proteins into a single dose is an emerging area of biological therapeutics and brings additional complexity to the already complex field of protein formulations. Preserving the physiochemical integrity of each molecule often requires that formulation conditions needed for one be applied simultaneously to the other. Analytical methods must also be able to detect changes in either molecule in this more complex environment.

11:15 Challenges in mAb Combination Drug Products: A CMC Overview

Jiali Du, Ph.D., Scientist, Formulation Sciences, MedImmune

The use of two mAbs in combination to improve treatment outcomes, and increase patient convenience and compliance is receiving increased scientific interest. This talk will provide a CMC outlook on challenges when formulating mAb combinations. Case studies of challenges during in-use stability, development of formulation and presentations, analytical characterization, and fill/finish processes will be discussed.

11:45 Case Study: Clinical In-Use Stability Evaluation: Co-Administration of Two Antibody Therapeutics

Zhen Wu, Ph.D., Senior Scientist, AbbVie

Concomitant IV administration of drugs, if clinically feasible, is a convenient approach for the patients and may offer competitive advantage. In this presentation, co-administration of two antibody therapeutics will be presented as an example. Both drugs were diluted in an IV bag and an in-use study was performed to evaluate dose solution stability. The approach taken to adapt the analytical methods and overcome the analytical challenges will be discussed.

12:15 pm See Stability in Hi-Def with Hunky

Sponsored by UNCHAINED LABS

Greg Manley, Ph.D., Senior Applications Specialist, Unchained Labs

Developing biologics requires identifying ideal constructs and assessing a wide range of formulation space to ensure stability and minimize aggregation. Assessing ΔG is a powerful approach for the quantitative assessment of conformational stability and aggregation. Unchained Labs automates the tedious and manual task of determining ΔG, allowing for quantitative stability and aggregation assessment throughout biologic development. We'll discuss how automated chemical denaturation can be used with more traditional approaches to assess stability.

12:45 Session Break

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

JANUARY 8-9 | 10TH ANNUAL

Optimizing Biologics Formulation Development

A Best Practices Exchange for Resolving the Challenges of Formulating Novel Biologic Drug Products

CELL AND GENE THERAPIES

2:00 Chairperson's Remarks

Arun Alphonse Ignatius, Ph.D., Principal Scientist, Pfizer

2:05 Formulation Development for AAV-Based Gene Therapy Products

Arun Alphonse Ignatius, Ph.D., Principal Scientist, Pfizer

Over the past few years, adeno-associated viruses (AAV) have evolved significantly with few products moving into late stage clinical development, and many others in early trials showing significant promise in the clinic. However, there are significant challenges that remain primarily due to the rapid transition into industry. This presentation will use case studies to showcase some of the challenges and considerations in the formulation development for AAVs.

2:35 Biophysical Characterization of mRNA Loaded Lipid Nanoparticles Formulations

Flaviu Gruia, Ph.D., Principal Scientist, Drug Product Analytical Development, Moderna Therapeutics

Developing a delivery vehicle capable of transporting the mRNA cargo to its intended target is a key challenge that should be addressed during development of mRNA-based products. Lipid nanoparticles represent a class of non-viral delivery systems that show potential in this space. The presentation will review some analytical development aspects, with specific examples of techniques that are valuable for biophysical characterization of nanoparticle formulations. Selected case studies will be included.

3:05 Transition to BuzZ Sessions

3:15 BuzZ Sessions with Refreshments

BuzZ sessions

Join your peers and colleagues for interactive roundtable discussions.

Please see page 78 for additional information.

PROTEIN FORMULATION CHALLENGES

4:30 Formulation Challenges for Low and High Concentration Proteins

Shiang Gwee, Scientist, Drug Product Sciences, MacroGenics, Inc.

DART® molecules are bi-specific antibody-based proteins developed for immuno-oncology indications. These molecules are manufactured using conventional antibody platforms, and demonstrate comparable product quality and stability to conventional antibodies. Increased potency and lower dose requirement of certain bi-specific molecules present challenges for intravenous administration in early stage development. Case studies will be presented of approaches for IV administration of low/high concentration protein formulations that highlight these challenges.

5:00 Pulse Proteolysis: A Novel High-Throughput Tool for Formulation Screening

Lavanya Iyer, Ph.D., Research Investigator, Bristol-Myers Squibb

Biologics formulation selection is typically based on shelf-life stability data obtained over months. In this work, a novel analytical method called Pulse Proteolysis was used to rank-order formulations, based on resistance to proteolysis. The results demonstrate that formulations could be rank-ordered based on T-zero stability, as measured by pulse proteolysis. The high correlation with storage stability indicates that pulse proteolysis could prove to be a useful tool for formulation screening.

5:30 Characterization and Control of Interfacial Antibody Adsorption and Aggregation

Ian Shieh, Ph.D., Scientist, Genentech

Exposure to interfaces can accelerate aggregation of antibody therapeutics during manufacture, transportation, and administration. Controlling interfacial antibody adsorption is critical to limiting aggregation. A panel of mAbs was characterized by multiple surface-sensitive techniques to predict their risk of interfacially mediated aggregation. We also measured and visualized antibody coadsorption with surfactant at the air-water interface to understand the protective mechanisms of the surfactants included in antibody formulations.

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

Sponsored by MO TEMPER

7:15 Close of Day

JANUARY 8-9 | 10TH ANNUAL

Optimizing Biologics Formulation Development

A Best Practices Exchange for Resolving the Challenges of Formulating Novel Biologic Drug Products

TUESDAY, JANUARY 9

8:00 am Registration and Morning Coffee

PREFORMULATION STUDIES

8:30 Chairperson's Remarks

Rebecca Davis-Harrison, Ph.D., Research Scientist, BioTechnology Discovery Research, Eli Lilly and Company

8:35 Non-Ideal Colligative Properties in High Concentration Mab Solutions and Impact to Biopharmaceutical Manufacturing

William Callahan, Senior Scientist, Amgen

Osmolality measurement is routinely used to monitor physical properties of protein formulations. In this work, osmolality of high concentration protein solutions was found to either drift to higher than expected values or to be immeasurable due to a failure to freeze in the freezing point depression (FPD) osmometer. This presentation highlights the problem inherent in determining osmolality of high concentration protein solutions and that caution must be taken in interpreting these measurements.

SURFACTANTS AND EXCIPIENTS

9:05 Challenges and Solutions in Polysorbate Degradation

Steven LaBrenz, Ph.D., Scientific Director, Cell and Developability Sciences, PDMS, Janssen R&D

Polysorbate degradation events in biopharmaceuticals are becoming more understood, moving beyond the original autooxidation work of Donbrow. Understanding degradation processes, relating that knowledge to actual conditions of use and controlling degradation events involving polysorbate are essential to developing a stable protein formulation. When controlling for external effectors that lead to issues in a protein formulation, degradation events involving polysorbate can be controlled.

Sponsored by FUJIFILM Diosynth

9:35 Molecular Knowledge and Experience as the Driving Forces Behind Successful Protein Formulation Development

Katherine Bowers, Ph.D., Principal Scientist, Group Leader, Analytical and Formulation Development, FUJIFILM Diosynth Biotechnologies

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

11:00 Poloxamer 188 as an Alternative Surfactant

Tarik Khan, Ph.D., Group Leader, Late-Stage Pharmaceutical and Processing Development, F. Hoffmann-La Roche Ltd., Switzerland

Polysorbates have long been the workhorse surfactant for stabilizing biologics. However, due to their susceptibility to degradation there is a clear desire to identify alternative surfactants. Poloxamer 188 (P188) is one such stable surfactant that has been successfully utilized in the formulation of biologics. This talk will highlight real formulation/stability data as well as mechanistic characterization of how P188 stabilizes biologics by interfacial activity and solution behavior.

11:30 Prospects for the Identification and Application of Excipient Mixtures and Novel Excipients

Miko Schleinitz, PhD Student, Biochemical and Chemical Engineering, Technical University, Dortmund, Germany

Classically, novel excipients and excipient mixtures are identified based on heuristic approaches often neglecting synergetic effects and hindering transferability of the results to novel formulations. It is thus desired, to develop a physically-sound method to identify excipient mixtures and novel excipients based on modeling/predicting the intermolecular interactions in solution. This allows for considering the mutual influence of multi-excipient systems and to determine the optimal excipient mixture circumventing cost-intensive screening methods.

Sponsored by Albumedix

12:00 pm Formulation of Hard-to-Stabilize Biopharmaceuticals

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

Modern biopharmaceuticals are changing. Increasingly, the industry is shifting towards more complex biological molecules intensifying formulation challenges requiring more advanced excipients. Human albumin is well known to stabilize proteins through a variety of roles, therefore recombinant human albumin is a promising stabilizer for hard-to-formulate biopharmaceuticals. We present data on the use of Albumedix® Recombumin® as a stabilizing agent across several different stress tests showing its versatility as an advanced excipient.

12:30 Session Break

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

1:15 Close of Optimizing Biologics Formulation Development Conference

JANUARY 9-10 | 11TH ANNUAL

Lyophilization and Emerging Drying Technologies

Formulation and Process Optimization, Models, QbD, Delivery and Devices

The popular Eleventh Annual Lyophilization and Emerging Drying Technologies conference covers latest trends and challenges in lyophilization and emerging drying technologies. This conference will feature in-depth case studies, new and unpublished data and discussions on developing scientifically sound freeze dried formulation, process optimization for biologics and vaccines. It will also present cutting edge research and case studies on freeze/thaw and formulation challenges, drying in cartridges, storage stability, 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 9

1:00 pm Registration

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

PREDICTION OF STABILITY IN FREEZE DRIED PRODUCTS: NEW TOOLS AND STRATEGIES

2:00 Chairperson's Opening Remarks

Elizabeth M. Topp, Ph.D., Dane O. Kildsig Chair and Department Head, Department of Industrial and Physical Pharmacy, Purdue University

KEYNOTE PRESENTATION

2:05 Hydrogen Deuterium Exchange in Lyophilized Solids: Correlation with Protein Stability

Elizabeth M. Topp, Ph.D., Dane O. Kildsig Chair and Department Head, Department of Industrial and Physical Pharmacy, Purdue University

Solid-state hydrogen deuterium exchange with mass spectrometric analysis (ssHDX-MS) provides high resolution structural information for proteins in lyophilized solids. Recent studies with a lyophilized monoclonal antibody (mAb) show that deuterium incorporation is highly correlated with chemical and physical stability on storage, and will be presented here.

2:45 Prediction of Protein Stability in Lyophilized Formulations: Miscibility, Mobility, and Microenvironmental pH

Eric J. Munson, Ph.D., Patrick DeLuca Endowed Professor, Department of Pharmaceutical Sciences, College of Pharmacy, University of Kentucky

The stabilization of proteins in lyophilized matrices requires that the protein and cryoprotectant, such as sucrose or trehalose, be in intimate contact with each other and have reduced mobility in the matrix, and that the buffer maintains the optimized solid-state ionization (i.e., pH equivalent). We have been using solid-state NMR spectroscopy to show that the stability of the protein, especially against aggregation, requires that the protein and cryoprotectant remain intimately mixed and relatively immobile.

3:15 Roles for Antifreeze Polypeptides in Optimizing Lyophilization Formulations and Protecting Stability of Proteins

Xin Wen, Ph.D., Professor, Department of Chemistry and Biochemistry, California State University, Los Angeles

In this talk, we will discuss the potential use of antifreeze polypeptides (AFPs) in optimizing lyophilized formulations and protecting stability proteins. Naturally produced by many cold-adapted organisms including fish, insects, and plants, AFPs are known for their ability to inhibit ice growth and recrystallization efficiently. We have demonstrated that AFPs can also control the crystallization of carbohydrates and nucleosides and protect proteins under extreme temperatures.

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

4:30 Predicting Stability of Freeze Dried Proteins Using Materials Dynamics

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

I will describe efforts in our lab towards understanding the fundamental connection between picosecond timescale, molecular length scale motions and protein degradation processes in lyophilized formulations. I will also discuss our efforts in developing benchtop methods to rapidly predict protein stability using this fundamental understanding.

5:00 New Tools for Prediction of Stability of Freeze Dried Products - A Cold Perspective

Miguel Ângelo Rodrigues, Ph.D., Researcher and Invited Professor, Chemical Engineering, Instituto Superior Técnico, University of Lisbon

Reactions that can compromise stability and quality of the freeze dried products happen within the ice structure. However, it's difficult to correlate parameters with results, because of the complexity and intricate relation between thermodynamic and kinetic variables leading to cryoconcentration, cold-denaturation, precipitation or aggregation. Experimental and modeling approaches were developed to understand and anticipate some of these mechanisms, which can assist the development of more rational formulations and optimized freeze drying procedures.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

5:45 - 8:45 Dinner Short Courses*

See page 5 for details

** Separate registration required*

WEDNESDAY, JANUARY 10

8:00 am Registration and Morning Coffee

MODELS AND TOOLS FOR PROCESS DESIGN, SCALE-UP AND TECHNOLOGY TRANSFER

8:30 Chairperson's Remarks

Xiaofeng Lu, Ph.D., Principal Research Scientist, Pharmaceutical Development, AbbVie, Inc.

8:35 Optimizing the Vial Heat Transfer Coefficient for Pharmaceutical Freeze Drying: A Case Study Illustrating a New Press-Blow Technique for the Manufacturing of Molded Vials

Tim Wenzel, Scientist, Ph.D. Candidate, University of Erlangen GILYOS GmbH on behalf of Henning Gieseler, Ph.D., CSO, Pharmaceutical Development, GILYOS GmbH

The vial heat transfer coefficient (Kv) serves as a key parameter to assess the total heat flow to a

Lyophilization and Emerging Drying Technologies

Formulation and Process Optimization, Models, QbD, Delivery and Devices

vial during primary drying. The present case study discusses the heat transfer characteristics of a vial manufactured by a blow-blow and new press-blow process, and subsequently discusses the impact of such a design and manufacturing features on Kv. The results clearly suggest a significant impact of the manufacturing technique on Kv.

9:05 Freeze Drying of a Low Tg' and High Fill Protein Drug Product: The Critical Role of Freezing on Primary Drying Process Performance and Final Product Quality Attributes

Xiaofeng Lu, Ph.D., Principal Research Scientist, Pharmaceutical Development, AbbVie, Inc.

Development of an efficient and robust freeze drying cycle was challenging for low Tg' and high fill protein drug product. A regular freezing protocol resulted in a long primary drying process and undesired product appearance. In this presentation, the critical role of freezing conditions on primary drying process performance and product quality attributes will be demonstrated. An effective freezing protocol will be recommended to achieve an efficient primary drying process and desired product quality attributes.

9:35 Emerging Drying Techniques for Manufacturing of Pharmaceutical Biologics

Qi (Tony) Zhou, Ph.D., Assistant Professor, Industrial and Physical Pharmacy, Purdue University

Traditional lyophilization is a batch and time-consuming process with low energy consumption efficiency. There are increasing interests to develop emerging drying techniques that have higher processing efficiency and lower costs while maintain product quality. A few drying techniques have been attempted such as spray drying and spray freeze drying. This talk will discuss the advantages and disadvantages of these emerging drying techniques for the application of biologics.

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

10:50 Use of Model in Process Design and Scale-Up: A Case Study Using Lab, Pilot and GMP Equipment

Alina Alexeenko, Ph.D., Professor, School of Aeronautics and Astronautics, Purdue University

In this presentation, we will discuss use of model in process design and scale up. We will present a case study of freeze-drying cycle variations for lyophilizers of different scale and cleanroom environment using a typical protein formulation.

11:20 Lyophilization Development of a High Concentration Antibody Formulation: Technology Transfer from Lab to Pilot Plant

Akhilesh Bhambhani, Ph.D., Principal Scientist & Group Leader, New Technologies-Vaccine Drug Product Development, Merck & Co., Inc.

Recommendations for a successful scale-up of a high concentration mAb will be shared with emphasis on a) formulation characterization, b) product and process design space, c) significance of engineering runs and d) robust manufacturing process.

11:50 Process Monitoring by Mass Spectrometry during Freeze Drying

Jason Stewart, BS, Senior Associate Scientist, Pharmaceutical Research and Development, Pfizer, Inc.

Mass spectrometry has emerged as a key technology for the detection of trace levels of silicone oil in freeze drying chamber. With the capability of measuring low molecular mass gasses such as water and nitrogen, mass spectrometry positions itself to be a powerful tool for monitoring the entire drying process.

12:20 pm Lyophilisation of High Concentration Protein Formulations: Excipient Selection and Challenges

Valeria Gervasi, PhD Candidate, School of Pharmacy, Synthesis & Solid State Pharmaceutical Centre,University College Cork

The design of lyophilisation process for high concentration protein formulations can be challenging due to the necessity of employing products with high total solute concentration, resulting in high cake resistance. Excipient selection and modelling approaches, as well as the identification of critical parameters for the optimization of the lyophilisation process, can aid the efficient manufacture of a stable product with prolonged shelf-life.

12:50 Session Break

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

ADVANCES IN ICE NUCLEATION, VISUAL INSPECTION AND RECONSTITUTION CHALLENGES

2:00 Chairperson's Remarks

2:05 Secondary Ice Nucleation as the True Driver for Product Heterogeneity When Controlling Ice Nucleation in Pharmaceutical Freeze Drying

Tim Wenzel, Scientist, Ph.D. Candidate, University of Erlangen GILYOS GmbH

The common ground for controlled ice nucleation technologies in freeze drying is that they can only control primary nucleation. However, formation of the ice network throughout the product solution determines the overall drying performance and product quality. To obtain optimum homogeneity, secondary nucleation and ice crystal growth must be controlled post primary nucleation. Impact factors and appropriate process set-up for two pressure-dependent nucleation technologies will be discussed.

2:35 Methods to Reduce the Reconstitution Time of High Concentration Lyophilized Protein Therapeutics

Jacob Luoma, Engineer II, Pharmaceutical Processing and Technology Development, Genentech

There is increasing interest in producing high concentration lyophilized protein therapeutics. Since reconstitution time increases as protein concentration increases, the product may become inconvenient to use in the clinic if reconstitution time is not addressed. This talk will review methods that Genentech has evaluated for reducing reconstitution time.

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

4:00 SELECTED POSTER PRESENTATION: CFD Simulation and Verification for Local Pressure over Vials During Lyophilization at Laboratory Scale

Tatsuhiro Kodama, Ph.D. Visiting Scholar, Birck Nanotechnology Center, Purdue University

Lyophilization and Emerging Drying Technologies

Formulation and Process Optimization, Models, QbD, Delivery and Devices

4:30 Characterization of Universal Stabilized Stem Flu Vaccine Candidates

Sashikanth Banappagari, Ph.D., Scientist II, Formulation Development, Vaccine Production Program/VRC/NIAID/NIH

The purpose of this project is to elicit responses across multiple strains, looking towards a pandemic flu vaccine. This study describes advanced biophysical characterization of stabilized stem constructs of HA-Ferritin by CD, DSC, FTIR, Fluorescence and 2D UV-vis spectroscopy. These methods can contribute to understanding the basal physicochemical properties for optimal formulation development and monitoring vaccine quality that pertains to product comparability studies during development.

5:00 Considerations for Assessment of Particles in Biologics Originating from Packaging and Standardization Initiatives

Diane Paskiet, MS, Director of Scientific Affairs, Scientific Affairs and Technical Services, West Pharmaceutical Services

It is critical to understand the types and sources of particulates in biologic products and how their presence may affect product quality and patient safety. The linkage between particles, biologic formulation and packaging development involves understanding contributions from all sources. This presentation will provide insight into measurements of particles originating from packaging components, comparison of data from various technologies and USP standardization initiatives.

5:30 - 6:45 Networking Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Lyophilization and Emerging Drying Technologies Conference

JANUARY 11-12 | 9TH ANNUAL

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 in biopharmaceuticals. This conference will feature in-depth discussion on mechanisms of aggregation, new tools for detection and quantitation of aggregates. It will also discuss mechanistic understanding of protein aggregation and present case studies on prevention of particle formation by engineering and formulation approaches, aggregation in ADCs, bispecifics, impact of aggregation on production, aggregates as a factor for immunogenicity, and approaches for improvement of biophysical properties of protein solutions.

THURSDAY, JANUARY 11

7:45 am Registration and Morning Coffee

MECHANISM, PREDICTION AND OVERCOMING PROTEIN AGGREGATION

8:15 Chairperson's Opening Remarks

Thomas Laue, Ph.D., Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

KEYNOTE PRESENTATION

8:20 Light-Induced Protein Disulfide Degradation: Product Characterization

Christian Schoneich, Ph.D., Distinguished Professor and Chair, Pharmaceutical Chemistry, University of Kansas

Protein biotherapeutics can degrade via a manifold of physical and chemical degradation mechanisms. We will show here, that light exposure of therapeutic disulfide-containing proteins can lead to > 60 different products, generated via novel cross-linking and fragmentation mechanisms. Some of these reactions may be catalyzed by metal impurities such as iron or tungstate, which can be present in pre-filled glass syringes. Mechanistically, product formation can be rationalized by light-induced generation of radicals and reactive oxygen species.

9:00 Protein Solvation: Preventing Aggregation by Forming a Tighter 'Shield' around a Protein

Thomas Laue, Ph.D., Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

For proteins to aggregate, they need to come into contact. The hydration/solvation shell around proteins can block protein-protein contacts. This talk will focus on what factors impact the strength of the solvation shell.

9:30 Characterizing and Inhibiting Glucagon Fibrillation

Elizabeth M. Topp, Ph.D., Dane O. Kildsig Chair and Department Head, Department of Industrial and Physical Pharmacy, Purdue University

Glucagon, a peptide hormone, is currently marketed in lyophilized form for treating severe hypoglycemia. The lyophilized form is necessary because glucagon rapidly fibrillates in solution. This presentation summarizes computational and experimental studies of the mechanisms of glucagon fibrillation, and presents novel glucagon derivatives that resist fibrillation.

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

11:00 Design of Stable and Aggregation Resistant Single-Domain Antibody Biotherapeutics

Jamshid Tanha, Ph.D., Senior Research Officer, Human Health Therapeutics Portfolio, National Research Council Canada

Various approaches for improving the stability of VH and VL single-domain antibodies have been described. Here we zoom in on one particular approach, namely disulfide engineering approach, which improves the stability of VHs and VLs. The approach appears to be universally applicable across all VHs and VLs and may also apply to scFvs, Fabs, mAbs and their derivatives.

11:30 Automated, Low Volume Assessment of Stability Parameters in Protein Formulations

Sponsored by Malvern Panalytical

Kevin Mattison, Principal Scientist, Bioscience, Malvern PANalytical

Measuring key stability parameters of a protein formulation is critical in the early stage development of biopharmaceutical products. At this early stage the quantity of drug substance available for testing is limited, requiring these tests be performed on very small sample volumes. The Viscosizer TD system is an automated platform to characterize the stability of formulations. The system provides automated, low volume measurement of Viscosity, Hydrodynamic Size, Stokes Radius, and the Diffusion Interaction Parameter (kD).

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

NEW TOOLS AND STRATEGIES FOR HTS SCREENING

2:00 Chairperson's Remarks

Wayne F. Reed, Ph.D., Professor, Physics, Tulane University

2:05 Recent Progress in Light Scattering Determination of Aggregation Rates with Small Samples in Parallel Format

Wayne F. Reed, Ph.D., Professor, Physics, Tulane University

Monitoring protein aggregation via simultaneous multiple sample light scattering in real time allows rapid, parallel determination of aggregation rates (AR), which are directly related to protein stability for different formulations. Recent progress beyond AR includes: interpretation of non-linear light scattering signatures in terms of mechanisms, relationship of AR to GPC data, distinguishing small populations of large aggregates from large populations of small aggregates, and considerations of reproducibility and predictability of aggregation.

Protein Aggregation and Emerging Analytical Tools

Mechanism, Prediction, Screening, Immunogenicity and Formulation Challenges

2:35 High Throughput, Low Volume Subvisible Particle Screening

Sponsored by halo labs

Bernardo Cordovez, Ph.D., President, Halo Labs

Halo labs will present a subvisible particle screening tool, the HORIZON, with detailed explanation of its Backgrounded Membrane Imaging (BMI) technology. A comparative analysis between HORIZON and flow imaging will be presented and key performance indicators including sample volume, throughput, dynamic range, instrument repeatability will be evaluated.

2:50 Protein (In)stability and Analytical Tools for Monitoring Aggregation

Vasco Filipe, Ph.D., Lab Head, Pharmaceutical Development Biologics, Sanofi

Drug product development of therapeutic proteins involves a complex selection and optimization process aimed at making proteins manufacturable, stable and deliverable. Avoiding protein aggregation is one of the main concerns. Choosing the right formulation and setting up good strategies to monitor, predict and avoid protein aggregation during the various steps of the process is crucial. Formulation development considerations and analytical tools used to monitor protein aggregation will be presented.

3:05 Sifting through the Noise-Utilizing Light Scattering for Rapid Formulation Development

Sponsored by WYATT TECHNOLOGY

Lynette Schroeter, Crystalomics, Group Lead, Formulations Development, Althea CMO

Delivering high concentration, low viscosity biotherapeutics to patients is an attractive option for innovator companies. Althea's Crystalomics® technology delivers formulated protein crystal suspensions subcutaneously, whereby the crystals dissolve readily with no adverse effect. Light scattering analysis, particularly rapid screening utilizing the Wyatt Technology Dynapro® Plate Reader II, is critical to rapidly optimizing formulation conditions and characterizing the protein pre and post crystallization.

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

FORMULATION, PROCESS AND MANUFACTURING STRATEGIES TO OVERCOME AGGREGATION

4:15 Formulation, Process and Manufacturing Strategies to Prevent and Overcome Aggregation Challenges in Early and Late Stage Development

Sreedhara Alavattam, Ph.D., Principal Scientist and Senior Group Leader, Genentech

Aggregation remains a challenge during protein process development. Aggregation during production, purification and product handling can have potential impacts on immunogenicity. The talk will cover various aspects of decreasing aggregates and potentially remediate the aggregation during handling of drug products in the clinical setting.

4:45 Particulate Formation during Fill & Finish Operations

Cheng Her, Ph.D., Postdoctoral Research Fellow, Carpenter Lab, Pharmaceutical Sciences, University of Colorado-Denver, Anschutz Medical Campus

As the final step before the drug product reaches the patient, it is vital that a fill & finish operation mitigate both particulate formation and aggregation. It was the aim of this study to have a more comprehensive look at particulate formation during fill & finish operations, from the tubing and pumps used, to the storage and handling of the drug product after fill & finish operations.

5:15 PANEL DISCUSSION: Preventive and Analytical Approaches for Reduction and Removal of Aggregates that Work

Moderator:

Wayne F. Reed, Ph.D., Professor, Physics, Tulane University

Panelists:

Bernardo Cordovez, President, Halo Labs

Cheng Her, Ph.D., Postdoctoral Research Fellow, Carpenter Lab, Pharmaceutical Sciences, University of Colorado-Denver, Anschutz Medical Campus

Sophia Kenrick, Ph.D., Senior Applications Scientist, Wyatt Technology

Sreedhara Alavattam, Ph.D., Principal Scientist and Senior Group Leader, Genentech

Wei Qi, Ph.D., Scientist, Pre-Pivotal Drug Product, Amgen

5:45 Close of Day

FRIDAY, JANUARY 12

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast

BuzZ sessions

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

Table Moderator: Thomas Laue, Ph.D., Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

IMMUNOGENICITY, DEVELOPABILITY, EXCIPIENTS, AND STABILITY

9:00 Chairperson's Remarks

Nathan H. Joh, Ph.D., Scientist, Attribute Sciences, Amgen

9:05 High Molecular Weight Species of a Therapeutic Antibody is Chemically Modified, Lacks Distinct Structure, and Shows No Increased Risk of Immunogenicity in Model Systems

Nathan H. Joh, Ph.D., Scientist, Attribute Sciences, Amgen

High-molecular-weight (HMW) species from monoclonal antibody drug substance was investigated to elucidate structure, chemical modifications, and potential risk of immunogenicity. Higher levels of oxidized methionine and tryptophan were observed in HMW compared to monomer. HMW species lacked a well-defined molecular structure. Little to no risk of immunogenicity was observed for HMW in multiple immune model systems, including heterozygous transgenic mice,

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human peripheral blood mononuclear cells, and engineered immune cells.

9:35 Evaluation and Development of Screening Methods for Antibody Developability Assessment

Nikolai Lorenzen, Ph.D., Large Protein Biophysics, Novo Nordisk A/S

Biophysical screening is widely used in early phase development of monoclonal antibodies to guide selection of molecules with a high potential to reach clinical testing. Using the *in silico* solubility predictor CamSol we have designed a modelsystem of antibody variants displaying a range of solubilities. I will present how selected biophysical measures as e.g. AC-SINS, CIC, PEG precipitation and diffusion interaction parameter predict for formulation relevant measures for this modelsystem.

10:05 Counting and Sizing Protein Aggregates Down to 0.15 um at High Concentrations by Focused-Beam SPOS

Sponsored by

David Nicoli, Ph.D., Vice-President, Research & Development, Particle Sizing Systems LLC

Protein aggregates as small as 0.15-um can be counted/sized at concentrations 100-1000X higher than is possible with light scattering sensors of conventional design, using a novel focused-beam single-particle optical sizing (SPOS) technique. Adding a second sensor that combines light obscuration and scattering extends the upper particle size limit to 200 microns. Analysis can be made on sub-mL samples, including those of high viscosity, and the sample is conserved following analysis.

10:35 Coffee Break with a Poster Pavilion

See page 4 for details

11:15 Understanding the Mechanism of Interaction between Leachates and Proteins and Its Impact on Drug Product Quality

Heather Flores, BS, Scientist, Technical Development Scientist, Late Stage Pharmaceutical Development, Genentech, Inc.

Chemical impurities that leach from product contacting material have long been assessed for potential toxicological effects. More recently, however, several instances of interaction of leachables and/or impurities with the active pharmaceutical ingredient or other formulation components have been reported. Understanding the mechanisms by which leachates interact with biomolecules is key in assessing the potential impact to drug product quality and associated safety and efficacy concerns.

11:45 Late Breaking Presentation

12:15 pm Conference Wrap-Up

Thomas Laue, Ph.D., Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

12:45 Close of Conference

ANALYTICS & IMPURITIES

JANUARY 8-9

AGENDA Characterization of Biotherapeutics

JANUARY 9-10

AGENDA Detection and Characterization of Particulates and Impurities

JANUARY 11-12

AGENDA Bioprocess Analytics

JANUARY 8-9 | 4TH ANNUAL

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 Fourth Annual Characterization of Biotherapeutics conference will present new tools, strategies and case studies on analytical development and characterization of mAbs, ADCs, and other novel protein formats, biosimilars, HOS, and developability. We invite you to present a poster and attend to join with colleagues in this discussion of the key challenges and solutions improving predication, screening and characterization of biologics.

SUNDAY, JANUARY 7

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

MONDAY, JANUARY 8

7:00 am Registration and Morning Coffee

CHARACTERIZATION OF NEW BIOTHERAPEUTICS

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

9:05 Chairperson's Opening Remarks
Alexey Rak, Ph.D., Head of Bio Structure and Biophysics, Integrated Drug Discovery, Sanofi R&D

KEYNOTE PRESENTATION

9:10 Novel Low-Protein Consuming High Throughput Biophysical Methods for mAbs, ADCs and Multi-Specific Biologics Characterization
Alexey Rak, Ph.D., Head of Bio Structure and Biophysics, Integrated Drug Discovery, Sanofi R&D
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 novel biophysical methods nano-Diffrential Scanning Fluorimetry (nanoDSF), MicroScale Thermophoresis (MST) and kinetic stability experiments that we are applying in our biologics discovery and development for mAbs, ADCs and multi-specific biologics. The examples of the demonstrated effectiveness of the novel integrated biophysical methods will be presented and discussed.

9:50 Analytical Characterization of Next-Generation Antibody-Based Therapeutics
Tasneem Bahrainwala, PhD, Analytical Sciences Mass Spectrometry Group Leader, MacroGenics, Inc.
DART® molecules are bispecific antibody-based proteins developed for a variety of indications including immune-oncology, and are designed to simultaneously bind to two targets. These versatile molecules have the potential for improved efficacy and safety profile through enhanced selectivity and recruitment of specialized effector cells. This presentation will discuss analytical characterization strategies using this novel class of molecules and other antibody molecules as case studies.

10:20 Networking Coffee Break

10:45 Effects of Chemical Degradation on Higher Order Structure, Conformational Stability, Physical Instabilities, and Biological Properties of an IgG1 mAb
Dinen Shah, Department of Pharmaceutical Sciences (Krishna Mallela Lab), University of Colorado Denver Health Sciences Center
Oxidation is a critical challenge during the life cycle of any therapeutic protein. In this study, we probed the effect of oxidation on the structure, stability, aggregation, and function of a therapeutic IgG1 monoclonal antibody (mAb-8). In particular, we examined whether the extent of protein destabilization, aggregate formation, and loss of specific protein activity can be correlated with the site and extent of oxidation.

11:15 Composition and Thermal Stability of Adsorbed Vaccines
Marina Kirkitadze, Ph.D., Deputy Director, Head of Biophysics and Conformation Unit, Analytical R&D Biochemistry, Sanofi Pasteur, Canada
The focus of this presentation is a characterization of adsorbed vaccine consisting of several protein antigens and new adjuvant. The applicability of several biophysical methods (FTIR, Raman, DSF) to characterize vaccine components in the final drug product without desorption.

11:45 Analytical QbD Applied to the Development of a Robust Reversed Phase Separation Method to Monitor Free Drug Related Impurities in an ADC
Kevin Strozyk, Sr. Research Associate, Analytical Sciences, Seattle Genetics
Quality by Design (QbD) allows for a systematic approach to method development with predefined objectives while leveraging prior method understanding. Here we present a case study for the development of a robust reversed phase UPLC separation to accurately and precisely quantify free drug related impurities (FDRI) in an ADC using components of analytical QbD including the use of an Analytical Target Profile (ATP), prior knowledge, and Design of Experiment (DoE).

12:15 pm Expanding the Role of Circular Dichroism (CD) in Higher Order Structure (HOS) Characterization of Bio-therapeutics – Forced Degradation Studies of mAbs
Sponsored by AppliedPhotophysics
Helen Wu, Ph.D., Senior Scientist, Boehringer Ingelheim Pharmaceuticals Inc
Expanding the Role of Circular Dichroism (CD) in Higher Order Structure (HOS) Characterization of Bio-therapeutics – Forced Degradation Studies of mAbs

12:45 Session Break

1:00 Luncheon Presentation: Glycans before Lunch: Rapid N-Glycan Sample Preparation Workflows for Screening and Characterization of Biotherapeutics
Sponsored by PROzyme
Aled Jones, Senior Product and Applications Manager, ProZyme
The structure of N-linked glycans can play a critical role in the pharmacology of therapeutic proteins, potentially affecting immunogenicity, pharmacokinetics and pharmacodynamics. This makes the characterization of N-glycans an essential part of the biotherapeutic development process. We present 3 rapid N-glycan sample preparation and analysis workflows: Gly-X with InstantPC or 2-AB Express labeling for glycan characterization by liquid chromatography, and Gly-Q for rapid screening using an integrated system with capillary electrophoresis.

JANUARY 8-9 | 4TH ANNUAL

Characterization of Biotherapeutics

Improving Prediction, Screening and Characterization of New Biologics

HIGH-THROUGHPUT SCREENING, IMMUNOASSAY AND BIOCHEMICAL ASSAY

2:00 Chairperson's Remarks
Czeslaw Radziejewski, Ph.D., Senior Principal Research Scientist, Biophysical Chemistry, AbbVie

2:05 Relationship between kinetic Stability and Structural Rigidity of IgG1 mAbs as Monitored by Resistance to SDS Induced Denaturation
Haripada Maity, Ph.D., Research Advisor, Formulation Development, CMC Development, Eli Lilly and Company

2:35 Deciphering the Root-Causes for Atypical PK of mAbs and Complex Biologics by Protein Engineering
Thomas E. Kraft, Ph.D., Postdoctoral Scientist, Large Molecule Research, Roche Diagnostics GmbH

Therapeutic antibodies with nearly identical Fc domains show >10-fold differences in clearance. We systematically identified properties of the Fv domain that can cause atypical pharmacokinetic behavior. Using protein engineering, we created Fab mutants with defined biophysical properties and tested them in biochemical PK prediction assays and for *in vivo* clearance. Our results are highly relevant for predicting and improving *in vivo* PK based on biophysical properties and biochemical assay data.

3:05 Transition to BuzZ Sessions

3:15 BuzZ Sessions with Refreshments
Join your peers and colleagues for interactive roundtable discussions.
Please see page 78 for additional information.

BIOSIMILARS, COMPARABILITY, HIGHER ORDER STRUCTURE & BIOPHYSICAL CHARACTERIZATION

4:30 Selection and Sensitivity of Biophysical Techniques in Characterization of Higher Order Structure of Proteins
Haripada Maity, Ph.D., Research Advisor, Formulation Development, CMC Development, Eli Lilly and Company

A strong correlation among higher order structure (HOS), conformational stability, and functional properties is generally observed for proteins. Characterization of HOS is primarily performed by different biophysical techniques. The selection and sensitivity of these techniques is very important, and may depend on protein to protein. This presentation will discuss the sensitivity and limitations of different techniques used in the characterization of proteins of different sizes, and the number of intrinsic chromophores under a variety of stress conditions.

5:00 Biologics Characterization and Comparability
Yemin Xu, Ph.D., Senior Regulatory Scientist, Regulatory Science, Regeneron

Biologics development is the fastest growing pharmaceutical market. Biologics development and licensing application require thorough physicochemical and biological characterization. Across development stages, analytical comparability exercises are commonly required when changes are implemented into the manufacturing process. Analytical comparability plays a crucial role to demonstrate that pre- and post-change products are comparable and have no adverse impact on safety, identity, purity, or efficacy of the product.

5:30 Biophysical Studies of Multivalent Antibody-Antigen Complexes
Czeslaw Radziejewski, Ph.D., Senior Principal Research Scientist, Biophysical Chemistry, AbbVie

This presentation will describe electron microscopy studies of various complexes that are formed when TNF alpha interacts with anti-TNF monoclonal antibodies.

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

7:15 Close of Day

TUESDAY, JANUARY 9

8:00 am Registration and Morning Coffee

DEVELOPABILITY ASSESSMENT AND ANALYTICAL CHARACTERIZATION

8:30 Chairperson's Remarks
Haripada Maity, Ph.D., Research Advisor, Formulation Development, CMC Development, Eli Lilly and Company

8:35 Developability Assessment to Support Pre-Candidate Selection of Biotherapeutics
Jonathan S. Kingsbury, Ph.D., Principal Scientist, Global Pharmaceutical Development Biologics, Sanofi

Developability/deviceability is a critical pipeline support activity, the results of which are used to focus the field of potential candidate molecules. Such assessments can be conducted in diverse ways, with different testing compositions and timing. The benefits of a multi-checkpoint strategy for candidate credentialing completed at different stages throughout the early discovery/development timeline will be discussed. In addition, the defining qualities of a comprehensive, process-relevant assessment strategy will be discussed and explained using examples. The use of the resulting data to enable decision making for pre-candidate selection using empirical benchmarks will be highlighted.

9:05 Case Study: Light-Induced Covalent Histidine Adducts on A IgG1 Molecule: Reaction Pathways and Influencing Factors
Ming Lei, Ph.D., Associate Scientist, Protein Analytical Chemistry, Genentech

Light is known to induce many reactions on protein residues such as tryptophan (Trp), cysteine (Cys) and histidine (His). In this work, light-induced His-adducts were found on a monoclonal antibody (mAb-1) formulated in His-containing buffer. The reaction pathways and influencing factors such as solvent accessibility and the concentrations of common surfactants are thoroughly investigated.

9:35 Selected Poster Presentation: Detection of a Host-Cell Protein Impurity-Hamster Phospholipase B-Like 2 (PLBL2) in Therapeutic Monoclonal Antibodies
Sheetal Mehta, Research Scientist, Analytical Department, Bristol Myers Squibb Co.

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

JANUARY 8-9 | 4TH ANNUAL

Characterization of Biotherapeutics

Improving Prediction, Screening and Characterization of New Biologics

11:00 Structural Characterization of SDS-Solubilized Proteins by ESI-MS

Cheng Zhao, Ph.D., Principal Scientist, Abbott Laboratories

The diversity and increasing complexity of new protein formats requires a change from former platform approaches often applied for antibodies, to project specific strategies. The developability assessment concept applied at Novartis combines information about early process development, aggregation propensity, stability, solubility, physicochemical properties and immunogenicity of potential candidates. This integrated approach prior to lead selection provides a thorough yet resource efficient approach. The presentation will provide an overview about the concept and provide selected case studies.

11:15 Selected Poster Presentation: Membrane-based Protein A Purification Device Offers High Dynamic Binding Capacity and Short Residence Time

Chao Zheng Ph.D., Senior Scientist, Department of Biotherapeutics Discovery, Boehringer Ingelheim

11:30 PANEL DISCUSSION: Application of New Analytical Tools and Mass Spectroscopy for Characterization of Biologics

Moderator:

Haripada Maity, Ph.D., Research Advisor, Formulation Development, CMC Development, Eli Lilly and Company

Panelists:

Jonathan S. Kingsbury, Ph.D., Principal Scientist, Global Pharmaceutical Development Biologics, Sanofi

Thorsten Lorenz, Ph.D., Global Head Developability Assessment, Integrated Biologics Profiling, Novartis Pharma AG

Ming Lei, Ph.D., Senior Research Associate, Protein Analytical Chemistry, Genentech

12:00 pm Rapid Development of Anti-Idiotypic Binders Using a Novel Affinity Scaffold

Sponsored by Avacta LIFE SCIENCES

Matt Johnson, Ph.D., CSO, Avacta Life Sciences

Affimer® proteins are next-generation affinity scaffolds, offering highly specific and stable binders, with great potential for the generation of novel biotherapeutics and renewable research and diagnostics tools. We produced highly-specific anti-idiotypic Affimers, for Trastuzumab, anti-CTLA4, anti-CD20 and anti-TNFa antibodies, via a 12-week development process. The resulting Affimer® binders can be used

12:30 Session Break

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

1:15 Close of Characterization of Biotherapeutics Conference

JANUARY 9-10 | 4TH ANNUAL

Detection and Characterization of Particulates and Impurities

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

Particles and impurities can arise from the products and/or during any stage of bioprocessing or from the delivery devices and primary packaging. These impurities have the 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 Fourth 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 such as subvisible particles, host cell proteins, extractables and leachables, impurities from excipients and raw materials, glass and other particles, etc.

TUESDAY, JANUARY 9

1:00 pm Registration

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

GUIDANCE, PARTICLES, AGGREGATES AND IMMUNOGENICITY

2:00 Chairperson's Opening Remarks
Maura Kibbey, Ph.D., Director, Global Biologics, U.S. Pharmacopeia

KEYNOTE PRESENTATION

2:05 Anticipating Aggregation Propensity of Proteins at Early Formulation Development Stage: How to Support a Data-Based Approach for Immunogenicity Risk Assessment
Joël Richard, Ph.D., Vice President, Peptides, CMC & Engineering, Ipsen

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

2:45 USP Standards to Monitor and Characterize Impurities in Biologics
Maura Kibbey, Ph.D., Director, Global Biologics, U.S. Pharmacopeia

The United States Pharmacopeial Convention (USP) is an independent scientific organization that protects public health through standards for medicines and their ingredients. As biological science contributes to more advanced therapies, standards continue to play a critical role in drug development and manufacturing. This talk will highlight new quality standards for demonstration of method performance, as well as measurement and characterization of impurities in peptides and biologics.

3:15 Best Practices and Strategies for Host Cell Protein ELISAs
Sponsored by CYGNUS TECHNOLOGIES
Eric Bishop, MBA, MSc, Vice President, Research & Development, Cygnus Technologies

Regulatory agencies around the world expect sponsors to have a good understanding of the HCP profile of their Drug Product. Knowing that low HCP results are due to HCP content and not due to an insensitive HCP ELISA is key. Talk will focus on current best practices and strategies to effectively demonstrate that an HCP ELISA is fit for purpose. (Selection of the best antibodies, assay design / qualification, and the integration of orthogonal methods.)

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

4:30 Assessment of Immunogenic Risk Posed by Biologic Aggregation
Michael Swanson, Ph.D., Senior Scientist, Merck

Aggregated therapeutic antibodies have the potential to induce an immune response. Elucidation of the mechanism of responses to aggregated antibodies could mitigate the immunogenic risk. Utilizing cell-based *in vitro* models, we investigated the role of different innate immune receptors in responses to aggregated antibody. By comparing the ability of aggregated antibody and natural ligands to activate different receptors, we were able to begin to determine the relative risk posed by aggregates.

5:00 PANEL DISCUSSION: Strategies and Experience with Managing Regulatory Expectation for Particles and Impurities for Early and Late Stage Submissions
Moderator:
Maura Kibbey, Ph.D., Director, Global Biologics, U.S. Pharmacopeia
Panelists:
Jonas Hoeg Thygesen, Ph.D., Area Specialist, R&D - Microanalysis Centre, Novo Nordisk Pharmatech
Joël Richard, Ph.D., Vice President, Peptides, CMC & Engineering, Ipsen

5:30 Close of Day

5:30 - 5:45 Short Course Registration

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

WEDNESDAY, JANUARY 10

8:00 am Registration and Morning Coffee

HOST CELL PROTEIN AND PROCESS IMPURITIES

8:30 Chairperson's Remarks
Joël Richard, Ph.D., Vice President, Peptides, CMC & Engineering, Ipsen

8:35 Late Breaking Presentation

9:05 Quantitation of Affinity Ligand Leachate in Processing Samples – Why Commercial Kits Fail and What You Can Do About It
Xiaohui Lu, Ph.D., Senior Scientist, BioPharma Development, Biogen

9:35 Identification and Quantification of HCPs in mAbs, Recombinant Proteins and Biosimilars by Mass Spectrometry
Sponsored by CAPRION
Michael Schirm, Ph.D., Associate Director, Research & Development, Proteomics, CAPRION BIOSCIENCES INC.

Gel-free, label-free mass spectrometry (MS) enables identification and quantitation of total and individual HCP in biotherapeutic products, and represents an orthogonal method to ELISA. Examples will be presented showing use of semi-quantitative HCP discovery (LC-MS/MS) and absolute quantitation of HCP (LC-MRM/MS), as applied to monitoring

JANUARY 9-10 | 4TH ANNUAL

Detection and Characterization of Particulates and Impurities

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

of process changes/improvements, scale-up, batch uniformity, clearance, and comparison of Biosimilars vs Innovators. Caprion's HCP platform features customizable organism/process-specific databases, highly controlled analytical processes and reproducible robust detection (to ~1ppm).

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

FORMULATION, RAW MATERIALS, EXCIPIENTS AND E&L IMPURITIES

10:50 Understanding Mechanism of Interaction between E&L and Proteins to Minimize Risk on Product Safety and Quality Attributes

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

Plastic components are commonly used in the manufacture of drug-device combination products. The identification of the extractable and leachable (E&L) impurities from the device components form the basis for toxicology assessments. However, significant challenges remain with the quality evaluation of the therapeutic proteins. E&L impurities may interact with certain biological products, thus compromising the quality attributes (e.g. protein aggregates and structural modifications). This presentation will attempt to show how safety and quality evaluations can be bridged through the principles of Cramer classification in relation to adverse outcome pathway.

11:20 Identification of Micro Steel Particles Using Energy Dispersive X-ray Spectroscopy Coupled with Multivariate Statistics

Jonas Hoeg Thygesen, Ph.D., Area Specialist, R&D - Microanalysis Centre, Novo Nordisk Pharmatech

Regulatory agencies call for identification and characterization of any intrinsic, inherent or extrinsic particles present in pharmaceuticals. USP <1787> outlines methods and strategies for particle identification and characterization. Scanning Electron Microscopy (SEM) and Energy Dispersive X-ray Spectroscopy (EDS) are two of the methods discussed in USP <1787>. This presentation will show how SEM and EDS in combination with multivariate statistics enable rapid identification of both visible and subvisible steel particles.

11:50 New NMR Methods for Fast and Efficient Analysis of Trace Leachables and Impurities in Biologics

Ken Skidmore, Technical Development Scientist, Protein Analytical Chemistry, Genentech

Analyzing process pools and drug product for a broad spectrum of impurities is challenging. We will discuss three key NMR techniques we use for process development and regulatory filings: suppression of protein drug signals, while leaving impurity signals intact; quantitation by 2D NMR in complex matrices; and the use of CRAFT NMR, a powerful new technique which resolves the signals of trace impurities from those of protein and formulation components.

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

12:50 Session Break

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

FORMULATION, RAW MATERIALS, EXCIPIENTS AND E&L IMPURITIES (CONT.)

2:00 Chairperson's Remarks

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

2:05 Challenges in Subvisible Particle Characterization

Miguel Saggu, Scientist, Late Stage Pharmaceutical Development, Genentech

This presentation will address challenges in subvisible particle analysis in biopharmaceutical formulations. It will discuss case studies to demonstrate how to address challenges in particle analysis using state-of-the-art particle analysis.

2:35 Protein-Excipient Interactions Evaluated via NMR Studies in Polysorbate-Based Multi-Dose Protein Formulations: Influence on Antimicrobial Efficacy and Potential Study Approach

Riccardo Torosantucci, Ph.D., Head of Laboratory Formulation Development, Pharmaceutical Development Biologics, Sanofi-Aventis Deutschland GmbH

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

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

4:00 SELECTED POSTER PRESENTATION: CFD Simulation and Verification for Local Pressure over Vials During Lyophilization at Laboratory Scale

Tatsuhiro Kodama, Ph.D. Visiting Scholar, Birck Nanotechnology Center, Purdue University

4:30 Characterization of Universal Stabilized Stem Flu Vaccine Candidates

Sashikanth Banappagari, Ph.D., Scientist II, Formulation Development, Vaccine Production Program/VRC/NIAID/NIH

The purpose of this project is to elicit responses across multiple strains, looking towards a pandemic flu vaccine. This study describes advanced biophysical characterization of stabilized stem constructs of HA-Ferritin by CD, DSC, FTIR, Fluorescence and 2D UV-vis spectroscopy. These methods can contribute to understanding the basal physicochemical properties for optimal formulation development and monitoring vaccine quality that pertains to product comparability studies during development.

5:00 Considerations for Assessment of Particles in Biologics Originating from Packaging and Standardization Initiatives

Diane Paskiet, MS, Director of Scientific Affairs, Scientific Affairs and Technical Services, West Pharmaceutical Services

It is critical to understand the types and sources of particulates in biologic products and how their presence may affect product quality and patient safety. The linkage between particles, biologic formulation and packaging development involves understanding contributions from all sources. This presentation will provide insight into measurements of particles originating from packaging components, comparison of data from various technologies and USP standardization initiatives.

5:30 - 6:45 Networking Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Detection and Characterization of Particulates and Impurities Conference

JANUARY 11-12 | 2ND ANNUAL

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 Second Annual Bioprocess Analytics conference addresses statistical analysis strategies including multivariate data analysis (MVDA), quality by design (QbD), process analytical technology (PAT) and multi-attribute method (MAM), allowing for optimized and informed control of bioprocessing.

THURSDAY, JANUARY 11

7:45 am Registration and Morning Coffee

PROCESS TO PRODUCT

8:15 Chairperson's Opening Remarks

Gyun Min Lee, Ph.D., Professor, Biological Sciences, KAIST

KEYNOTE PRESENTATION

8:20 Integrating Cell Culture with Magnetic Protein A Bead-Trap Technology Accelerates Antibody Purification

John K. Kawooya, Ph.D., Director, Biologics Optimization, Discovery Research, Amgen

Antibody engineering produces large numbers of molecules (200-500 molecules at 30-50ml each) which require purification, analysis and screening for potency, binding, pharmacodynamics, pharmacokinetics, manufacturability, expression levels and stability in order to select leads. Ever since its inception over 30 years ago, the AKTA system combined with Protein A agarose columns has remained the "workhorse" of antibody purification from cell cultures. However, the inability of this system to process multiple samples in parallel coupled with both its limiting flow rates, its requirement for multiple FTEs to remove cells and particulate from each sample prior to loading together with the potential for sample swapping errors and cross contaminations – all impose major bottlenecks in expediting large purified panels of molecules. In this presentation, I show how a single FTE with parallel Magnetic Protein A bead-trap technology accelerates delivery of high-quality purified antibodies in high yield directly from small (30ml-5liters) to large (25-liter wave-bag) crude cell cultures without centrifugation or filtration.

9:00 Speed to IND: Alignment and Acceleration of Critical Early Phase Activities

Kyle Zingaro, Ph.D., Development Scientist II, Early Stage Development, Alexion Pharmaceuticals

Speed to IND is the current battle cry across early phase biologics development. Despite some risks, new technologies and workflow alignment can afford faster and better decisions during this crucial phase of new product development. This is especially true across the Discovery and Process Development handoff. We present new data and approaches to improve that handoff and detail the impact on timelines and quality of molecules and cell lines in early phase development.

9:30 "Lost in Translation": Bridging the Gap between Academia and Biotech

Tsafi Danieli, Ph.D., Director, BioGiv Excubator & Head, Protein Expression Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem

One of the most difficult and frustrating aspects of basing a startup company on academic findings is translating and transferring academic findings to biotech language. This procedure is often frustrating to both parties and requires psychological skills as well as critical review of the research. Working in the interphase between academia and industry, there are several preemptive strikes we can take to avoid some of the major pitfalls.

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

11:00 Proteomic Analysis of Host Cell Protein Dynamics in the Culture Supernatants of Therapeutic Protein-Producing CHO Cells

Gyun Min Lee, Ph.D., Professor, Biological Sciences, KAIST

Host cell proteins (HCPs) accumulate extracellularly during the cultures of recombinant CHO (rCHO) cells, potentially impairing product quality. HCPs accumulated extracellularly in batch and fed-batch cultures of rCHO cell lines were identified and quantified by mass spectrometry. This dataset of HCPs provides insights into determining the appropriate target proteins to be removed during both the cultures and purification steps for ensuring good therapeutic protein quality.

11:30 Using SUREscan™ to Survey Genetic Changes in Stable CHO Cell Lines *Sponsored by* SELEXIS

Pierre-Alain Girod, CSO, Selexis

CHO cells are the most frequently applied host-cell system for industrial protein therapeutic manufacturing. Rapid generation of high-producing clones that don't lose expression capability over time has been a major industry focus. Using SUREscan™ with next-generation sequencing (NGS), we can quickly analyze whole genomes of any cell line, improving traceability of Research Cell Banks (RCBs). In contrast to other CHO published data, we will show that SUREtechnology Platform™ generates RCBs with chromosomally stable lineages.

12:00 pm Session Break

12:15 Luncheon Presentation: Get Your High Protein Concentrations Right on the Money with Lunatic *Sponsored by* UNCHAINED LABS

Thomas Martens, Principal Scientist, Unchained Labs

Stop quantifying proteins one by one hoping that your old reader is getting the numbers right. Get rid of that dilution step you always need to measure 200 mg/ml IgG or even higher. Come learn about how Lunatic gets rid of all dilutions, eliminates any risk of cross contamination and accurately measures protein concentration at high throughput and high concentrations. We'll talk about how lunatic:

- measures either 16 or 96 samples in one run
- uses only 2 µL for each measurement
- needs only 5 minutes
- Requires no dilutions

JANUARY 11-12 | 2ND ANNUAL

Bioprocess Analytics

Data Measurement, Monitoring and Modeling Allow Informed Control of Bioprocesses

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

ANALYTICAL WORKFLOWS AND MODELING

2:00 Chairperson's Remarks

Tsafi Danieli, Ph.D., Director, BioGiv Excubator & Head, Protein Expression Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem

2:05 Novel Hybrid Modeling Approaches for QbD: Getting More from the Combination of Fundamental Knowledge and Statistical Methods

Moritz von Stosch, Ph.D., Senior Manager, Fermentation, Technical R&D, GSK Vaccines

The combination of fundamental knowledge with statistical methods is referred to as hybrid modeling. These models have been shown to 1) provide better extrapolation properties, 2) have lower data requirements, and 3) are more efficient to develop than models based on a single knowledge source. This talk introduces novel hybrid methods that work more coherently with small datasets and estimate their own prediction quality, such being optimal for the development of the process design space in the context of QbD.

2:35 Phase-Appropriate Analytics

SiowFong Wee, Ph.D., Director, Formulation, Analytical & Bioassay, Aptevo Therapeutics

It can be a struggle to decide how much analytics is considered sufficient for product quality evaluation and characterization to support a project that is in the early development stage. Phase-appropriate analytics to support 'clone-to-clinic' will be presented in this talk.

3:05 Integration of ambr High-Throughput Bioreactor Systems into the USP Development Workflow and into the Data Acquisition, Management and Analysis System

Timo Frensing, Ph.D., Senior Scientist, Cell Culture Research, Roche Diagnostics GmbH

To enable a high-throughput USP development we implemented a semi-automated workflow to connect ambr® bioreactors (Sartorius, Germany) via a Fluent® pipetting robot (Tecan, Switzerland) to the Cedex Bio HT Analyzer (Roche Diagnostics, Germany) for an accurate sample processing and sophisticated process analytics. Thereby, all systems are integrated in our data acquisition, management and analysis system to ensure an efficient data processing.

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

CELL LINE DEVELOPMENT

4:15 Lost in Translation: On the Formation of Protein Sequence Variants

Zhongqi Zhang, Ph.D., Scientific Director, Attribute Sciences, Process Development, Amgen

With modern mass spectrometry and appropriate informatics tools, a large number of low-level sequence variants in therapeutic proteins are detected and quantified. This large collection of information allows for a deeper understanding of the mechanism for the formation of sequence variants, thereby facilitating optimization of cell line and cell culture process to minimize them.

4:45 The Stability of CHO Genome: Essential for Cell Line Characterization or Not?

Noriko Yamano, Ph.D., Senior Scientist, Manufacturing Technology Association of Biologics; Guest Academic Staff, Graduate School of Engineering, Osaka University

The chromosomes in CHO cells frequently cause genomic variations, due to genetic instability. Distribution and stability of chromosomes were examined in CHO-DG44 cells, and two cell lines expressing different numbers of chromosomes were isolated from the original CHO-DG44 cell line to investigate the effect of aneuploid cells on recombinant protein production. In addition, gene expression profiles between cells with disparate chromosome numbers have been compared by mRNA-seq analysis.

5:15 High-Throughput Screening of Transfection Efficiency of dTtaPS Reagent Library, and Its Application for Transient Production of Proteins in Micro Bioreactors

Harsh Jain, Ph.D., Visiting Associate, FDA

5:45 Close of Day

FRIDAY, JANUARY 12

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast

BuzZ sessions

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

Table Moderator: Diane Paskiet, MS, Director of Scientific Affairs, Scientific Affairs and Technical Services, West Pharmaceutical Services

Table Moderator: Moritz von Stosch, Ph.D., Senior Manager, Fermentation, Technical R&D, GSK Vaccines

PRODUCT CHARACTERIZATION AND ANALYTICS

9:00 Chairperson's Remarks

Moritz von Stosch, Ph.D., Senior Manager, Fermentation, Technical R&D, GSK Vaccines

9:05 Characterization of mAbs Using Charge Variant Analysis Coupled to High Resolution Native Mass Spectrometry

Jonathan Bones, Ph.D., Principal Investigator, Characterisation and Comparability Laboratory, National Institute for Bioprocessing Research and Training

Charge variant analysis (CVA) of biopharmaceuticals is required under ICH Q6B. Issues arise when a new peak is identified in the CVA profile. Here, the development of high resolution charge variant analysis coupled directly to native high resolution mass spectrometry is described that facilitates the intact mass analysis of minor charge variants with high mass accuracy. Application to the characterization of mAbs and other recombinant proteins is described under normal conditions and during forced degradation studies.

JANUARY 11-12 | 2ND ANNUAL

Bioprocess Analytics

Data Measurement, Monitoring and Modeling Allow Informed Control of Bioprocesses

9:35 Utilizing High-Throughput Lab Automation and Analytics, Advanced Data Management and Multivariate Statistical Analysis to Define the Formulation Design Space for Biotherapeutics

Michael Siedler, Ph.D., Head, NBE High-Throughput and Advanced Formulation Sciences, Drug Product Development, AbbVie Deutschland GmbH & Co. KG

We discuss adaption and miniaturization of standard analytical methods to be used for 96 and 384 well plates, transition to a data-centric strategy, and implementation of advanced data management to effectively integrate and analyze screening data (including metadata). We also discuss multivariate parameter analysis and statistical modeling to calculate the formulation design space, hence assuring safety and efficacy of new products.

10:05 The Use of Method Performance Monitoring as a Component of a Comprehensive Product Control Strategy

Juma Bridgewater, Ph.D., Senior Scientist, Analytical Sciences and Technology, Bristol-Myers Squibb

Method performance monitoring is a critical component of a comprehensive pharmaceutical product control strategy. It comprises the real-time trending of sample-independent method metrics to assess the performance of methods used to control process parameters, raw material, intermediate, DS and DP quality attributes. MPM detects deterioration in method performance and maintains consistent quality of the data used for product control.

10:35 Coffee Break with a Poster Pavilion

See page 4 for details

HIGHER-THROUGHPUT SYSTEMS

11:15 High-Throughput Automations and Optimizations for Improved Binder Generation and Validation

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

While recombinant binder selection pipelines by now work in rather high-throughput, the screening of suitable affinity reagents and especially the validation of their essential features for the final applications is still laborious and time-intensive. To optimize the efficiency of these processes, we have improved already existing and developed novel methods to efficiently test candidates for their suitability, e.g., regarding their specificity.

11:45 High-Throughput Characterization of Hydrolytic Enzymes in Low Volume and Closed Systems

Nigel F. Reuel, Ph.D., Assistant Professor, Chemical and Biological Engineering, Iowa State University

Hydrolytic enzymes play a significant role in biologic and synthetic processes. The ability to better characterize these enzymes would enable shorter development times and better products. This talk will detail two recent developments for hydrolytic enzyme characterization: 1) a carbon nanotube-based optical sensor that allows for quantitative measurement in <20ul volumes and 2) a resonant antenna sensor that passively transmits its response in the 1-100MHz range, enabling detection within closed, opaque systems.

12:15 pm Conference Wrap-Up

Richard Altman, MS, Scientist, Protein Technologies, Amgen

Haiyan Jiang, Ph.D., Principal Scientist, Biologics Research, Janssen BioTherapeutics, Janssen R&D

Diane Paskiet, MS, Director of Scientific Affairs, Scientific Affairs and Technical Services, West Pharmaceutical Services

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

Moritz von Stosch, Ph.D., Senior Manager, Fermentation, Technical R&D, GSK Vaccines

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12:45 Close of Conference

PROCESS TECHNOLOGIES & PURIFICATION

JANUARY 8-9

AGENDA Single-Use Technologies and Continuous Processing

JANUARY 9-10

AGENDA Protein Purification and Recovery

JANUARY 11-12

AGENDA Higher-Throughput Protein Production and Characterization

JANUARY 8-9 | 5TH ANNUAL

Single-Use Technologies and Continuous Processing

Advancing Bioprocessing through Technological Innovation

Cambridge Healthtech Institute's Fifth Annual Single-Use Technologies and Continuous Processing conference will once again gather technology and equipment providers, end users, and regulators to discuss innovative approaches to current challenges, update companies on the trends in technology, share case studies on successful implementation, and ultimately identify how to derive as much value as possible from these technological advances.

SUNDAY, JANUARY 7

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

MONDAY, JANUARY 8

7:00 am Registration and Morning Coffee

CONTINUOUS PROCESSING: CONSIDERATIONS, IMPLEMENTATION AND ENABLING TECHNOLOGIES

9:00 Welcome by Conference Organizer
Kip Harry, Senior Conference Director, Cambridge Healthtech Institute

9:05 Chairperson's Opening Remarks
Dennis Powers, Director, Sales Engineering, G-CON Manufacturing

KEYNOTE PRESENTATION

9:10 A Fully Automated Biopharmaceutical Manufacturing Plant: Process Design, Modeling, and Control
Richard D. Braatz, Ph.D., Edwin R. Gilliland Professor of Chemical Engineering, Massachusetts Institute of Technology
This presentation describes the strategy used in the design of a fully automated small-footprint biopharmaceutical manufacturing plant that produces multiple biologics. Dynamic models are constructed for the design of the equipment for the unit operations and their operations including the real-time control of biologic drug production. An opportunity is the use of a "virtual" plant for the dynamic operations of the entire end-to-end biomanufacturing process. The virtual plant can guide the selection of a control strategy for each critical quality attribute (CQA), design of startup and shutdown operations, and control systems design.

9:50 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.

10:20 Networking Coffee Break

10:45 A Single-Use Strategy to Enable Manufacturing of Affordable Biologics
Renaud Jacquemart, Ph.D., BioPharma Downstream Process Specialist, Natrix Separations
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 Integrated Continuous Manufacturing Progress and the Life Sciences Industry "Fad or Reality"
Robert Dream, Ph.D., Managing Director, HDR Company LLC

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**

ADVANCES IN SINGLE-USE TECHNOLOGIES

2:00 Chairperson's Remarks
Adam Goldstein, MSc, Principal Scientist, Global Technology, Roche/Genentech

2:05 Technology Advances in Single-Use Technologies
Adam Goldstein, MSc, Principal Scientist, Global Technology, Roche/Genentech
This presentation will focus on challenges single-use applications currently have and may have in the future of biomanufacturing. I will also discuss advances in single-use technologies, with particular emphasis on bulk freeze applications.

2:35 Challenges Faced by the End Users during the Qualification of SUS
Ben Jeyaretnam, E&L Analytical Lead, Sanofi
Recently the pharmaceutical industry has been increasingly using single-use systems (SUS). Before a SUS can be used in the manufacturing process, it needs to be qualified for use by a predetermined process. This presentation will discuss a variety of challenges that the end user faces during the qualification process. Complexity of SUS, varying quality of vendor data, component change management, changing regulatory expectations,

E&L study execution, analytical challenges, and the potential impact of unexpected E&L study results will be presented.

3:05 Transition to BuzZ Sessions

3:15 BuzZ Sessions with Refreshments

BuzZ sessions

Join your peers and colleagues for interactive roundtable discussions.

Please see page 78 for additional information.

4:30 Selected Presentation

5:00 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.

5:30 Single-Use Considerations for the High-Yield Production of Glyco-Optimized Biopharmaceuticals with Human Cells in Perfusion Bioreactors

Steffen Kreye, Ph.D., Associate Director, USP, Glycotope GmbH

The GlycoExpress® (GEX®) technology displays a set of human cell lines for the production of glyco-optimized human biopharmaceuticals. Case studies for GEX® processes will be highlighted with special focus on single-use applicability, continuous processing and product quality. In a first section, data of a process transfer from a 200 L stainless steel to a 1000 L single-use bioreactor for a continuous cell culture application will be discussed. As a second part, a 10 mL down-scale system for perfusion cultivation in a single-use microbioreactor will be introduced and its application for process development evaluated.

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

Sponsored by MINO TEMPER

7:15 Close of Day

TUESDAY, JANUARY 9

8:00 am Registration and Morning Coffee

BIOPROCESS ANALYTICS FOR SINGLE-USE SYSTEMS AND CONTINUOUS PROCESSING

8:30 Chairperson's Remarks

Jonathan Bones, Ph.D., Principal Investigator, Characterisation and Comparability Laboratory, National Institute for Bioprocessing Research and Training

8:35 SU Sensors on FlexAct UD, a SU Platform for UF/DF: In-Process Testing and Evaluation of Robustness

Nikhil Ramsubramaniam, Ph.D., Senior Scientist, Merck

9:05 Continuous Chromatography for the Improvement of the Purification of Proteins and Peptides

Thomas Müller-Späth, Ph.D., Senior Scientist, Institute for Chemical and Bioengineering, ETH Zürich

Continuous chromatography processes allow a number of improvements in the downstream processing of biomolecules including increase in throughput, improved stationary phase utilization, improved yield and reduced buffer consumption. In this talk a brief overview of the different process concepts including CaptureSMB and MCSGP is presented and their strengths and weaknesses with respect to different applications is discussed. The concepts are also reviewed in the context of integration into continuous downstream manufacturing. The application examples of monoclonal antibody Protein A capture using a twin-column countercurrent CaptureSMB process and polishing using a twin-column MCSGP process are discussed in greater detail.

9:35 SELECTED POSTER PRESENTATION: The Utilization of a Novel Online Cell Quantitation Microscopic Technology in Cell Culture Process Development

Jianxin Sun, PhD, Senior Scientist, Boehringer Ingelheim

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

11:00 Large-Scale Extractable and Leachable Analysis of Single-Use Bioreactors for Biopharmaceutical Manufacture

Jonathan Bones, Ph.D., Principal Investigator, Characterisation and Comparability Laboratory, National Institute for Bioprocessing Research and Training

This presentation will describe the characterization of extractables and leachables from disposable bioreactors within a public-private partnership.

11:30 Presentation to be Announced

12:00 pm PANEL DISCUSSION: Advances in Bioprocess Technologies and Analytics

Moderator:

Jonathan Bones, Ph.D., Principal Investigator, Characterisation and Comparability Laboratory, National Institute for Bioprocessing Research and Training

Panelists:

Nikhil Ramsubramaniam, Ph.D., Senior Scientist, Merck

Thomas Müller-Späth, Ph.D., Senior Scientist, Institute for Chemical and Bioengineering, ETH Zürich

12:30 Session Break

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

1:15 Close of Single-Use Technologies and Continuous Processing Conference

JANUARY 9-10 | 10TH ANNUAL

Protein Purification and Recovery

Streamlining & Innovating Processes

The Tenth Annual Protein Purification and Recovery conference examines the strategies that efficiently lead to pure protein for research or therapeutic use. As the most costly and time-consuming process in the manufacture of protein-based therapies, purification poses continual challenges for streamlining steps and cutting costs. Challenges are multiplied when purifying complex molecules, such as membrane proteins or antibody-drug conjugates. This leading purification meeting explores how experts are optimizing processes to reach project goals in a timely way. Along with innovating 'traditional' technologies such as affinity tags, Protein A, and chromatography, leaders will also address alternatives and breakthroughs.

TUESDAY, JANUARY 9

1:00 pm Registration

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

ANTIBODY PURIFICATION

2:00 Chairperson's Opening Remarks
Christopher H. Gray, Ph.D., Team Leader, Structural Biology, Drug Discovery Program, CRUK Beatson Institute

KEYNOTE PRESENTATION

2:05 Introduction of a Disruptive Technology into a Highly Regulated Industry: A Brief History with Lessons Learned
David Wood, Ph.D., Professor, Professor, Chemical & Biomolecular Engineering, The Ohio State University
Over the past 20 years, we and others have worked to develop a highly disruptive self-cleaving tag technology for the biopharmaceutical industry. As we draw closer to this goal, it is worthwhile to consider the larger picture of how we have adapted our goals and approaches to this highly regulated and rapidly developing industry. This talk will cover the history and most recent developments of this technology in this context.

2:45 Optimization of an IgG-Binding, Protein A-Based Purification Matrix
Sophia Hober, Ph.D., Professor, Molecular Biotechnology, KTH Royal Institute of Technology
Presented here is an engineered protein based on the Protein A-derived Z domain, to which a calcium-binding EF-loop has been introduced. The new protein domain, ZCa, is shown to have a calcium dependent binding to IgG and can be used to purify antibodies with elution by EDTA at pH 5.5, providing a very valuable new tool for antibody and Fc-fusion protein purification. The process of the development, its function as well as the molecular explanation of its behavior will be discussed.

3:15 SELECTED POSTER PRESENTATION: Designing a State-of-the-Art Sample Management Facility to Empower Research
Katharine Heeringa, Scientific Researcher, Protein Sciences, Genentech, Inc.
Biomolecular Resources Sample Management (BMR-SM) at gRED is a state-of-the-art facility supporting all of research at Genentech, acting as both a nucleic acid and protein repository and a nucleic acid production facility. BMR-SM leverages bioinformatics and automation to support multiple users and at multiple access points with a diverse range of products and comprehensive sample and process tracking. We seek to build a core biologic molecule repository and nucleic acid production group that can expand and adapt to an ever-changing research environment.

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

4:30 An Introduction to HisMAB: An Antibody-Based Affinity Purification System for His Tagged Proteins
Jiansheng Wu, Ph.D., Principle Scientific Manager, Protein Chemistry, Genentech, Inc.
Ni based methods have been well established for the purification of his tagged proteins for decades. They usually have high binding capacity at relatively low cost. However, due to the low selectivity of Ni resin, sometimes it is difficult to purify His tagged proteins with poor expression. In my lab, we have developed a new antibody based affinity system for the purification of His tagged proteins. The antibody called HisMAB binds to his tagged proteins at high affinity. It has very high specificity toward his tagged proteins. In this talk, we will share our experience using the antibody. HisMAB is best suited for the purification of secreted his tagged proteins expressed by BEVS and mammalian systems.

5:00 Co-Elution of Host Cell Proteins (HCP) with Monoclonal Antibodies and Their Potential Immunogenicity Risk Assessment
Qingchun Zhang, Ph.D., Senior Scientist, Process Development, Amgen, Inc.
Recent advances in mass spectrometry allow the identification and quantification of individual HCPs. These advancements now make it possible to characterize HCPs in the presence of mAbs and to collect data to perform a risk assessment of individual HCP impurities. A comprehensive comparison of HCP subpopulations across different mAbs was conducted and the potential immunogenicity risk of commonly observed HCPs was investigated using both *in silico* prediction and an *in vitro* PBMC-based assay.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

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

WEDNESDAY, JANUARY 10

8:00 am Registration and Morning Coffee

INNOVATING PROCESSES

8:30 Chairperson's Remarks
Sophia Hober, Ph.D., Professor, Molecular Biotechnology, KTH Royal Institute of Technology

JANUARY 9-10 | 10TH ANNUAL

Protein Purification and Recovery

Streamlining & Innovating Processes

FEATURED PRESENTATION

8:35 Ten-Minute Purification and Rapid Folding of Proteins by Vortex Fluidic Device

Gregory A. Weiss, Ph.D., Professor, Chemistry and Molecular Biology & Biochemistry, University of California, Irvine

Recombinant proteins often require process intensive purification and refolding steps. In collaboration with Professor Colin Raston (U. Flinders, Australia), my lab applies a vortex fluidic device for continuous flow purification and refolding of proteins. Cell lysates can be directly processed without chromatography or centrifugation steps. Furthermore, the proteins remain bioconjugated to the surface of the flow reactor, allowing in-line bioprocessing by enzymes after their recovery from lysates.

9:05 Bigger, Brighter, Faster: Accelerating Protein Production by Enhancing Soluble Yield, Monitoring Expression and Compressing Chromatography Strategies

Christopher H. Gray, Ph.D., Team Leader, Structural Biology, Drug Discovery Program, CRUK Beatson Institute

We increased output using auto-cleaving MBP fusions, elevating soluble expression while eliminating MBP from purification. Additionally, we developed systems for rapid monitoring of target expression during fermentation using a co-expressed GFP tracer. Finally, we developed multimodal style affinity chromatography for tandem tagged proteins giving high purity material in a single column without need for slow polishing steps. The net result is reliability, higher yields and accelerated delivery to downstream users.

9:35 A Quick Check of Protein Quality that Will Vastly Improve all Protein Purification and Characterization Workflows

Sponsored by NanoTemper

Peter Fung, Ph.D., Senior Manager, Product Marketing, NanoTemper Technologies

Starting with material of questionable quality for protein purification and characterization leads to irreproducible or ambiguous results. Methods such as chromatography while widely used, can also derail experiments—due to the amount of time and expertise required to perform these techniques. We present a new platform that swiftly identifies sample quality and relative functionality in minutes complementing and guiding purification and characterization workflows—making go/no go decisions easy and quick—saving time, effort and cost downstream.

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

NEXT-GEN CHROMATOGRAPHY

10:50 SELECTED POSTER PRESENTATION: Tricks to Enhance Bispecific Antibody Purification by Using Protein L Chromatography

Yuichiro Shimizu, Ph.D., Research Manager, Chugai Pharmabody Research PTE. LTD.

In this study, we have established a system to efficiently separate 4-chain bispecific antibodies (BiAb) as well as to remove certain type of by-products by using protein L chromatography. Due to its simplicity and robustness, this method can potentially be used broadly for BiAb purification with minimum engineering of amino acid sequences.

11:20 An Efficient, Ultra-High Affinity Chromatography in a One-Step Purification of Complex Proteins

Dmitry G. Vassylyev, Ph.D., Professor, Biochemistry and Molecular Genetics, University of Alabama at Birmingham

Protein purification is the basis for numerous biochemical and biomedical studies. It is particularly crucial and challenging for structural analysis and industrial protein production, where it has to meet the High-yield/High-purity/High-activity (HHH) requirement. The ultra-high affinity (CL7/Im7) purification system allows for one-step HHH-purification of a wide range of traditionally challenging proteins and might emerge as a universal high-throughput purification tool to advance biological studies and manufacturing of therapeutic proteins.

11:50 Multidimensional Chromatography Coupled with Mass Spectrometry Characterization of Species Observed in Native Separations of a Thiol-Linked Antibody-Drug Conjugate

Andrew Holloway, Senior Research Associate, Analytical Sciences, Seattle Genetics, Inc.

12:20 The Strep-tag® Technology - The Superior Tag System for the Entire Protein Production Workflow

Sponsored by iba Solutions For Life Sciences

Dennis Niermeier, MSc, IBA Lifesciences

12:50 Session Break

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

PURIFYING MEMBRANE PROTEINS

2:00 Chairperson's Remarks

Dmitry G. Vassylyev, Ph.D., Professor, Biochemistry and Molecular Genetics, University of Alabama at Birmingham

2:05 Detergent-Free Purification of Membrane Proteins Using SMA Polymer

Alice Rothnie, D.Phil., Lecturer, Biochemistry, Life & Health Sciences, Aston University

Purification of membrane proteins can be challenging due to the need to remove them from the membrane. Traditionally, this is achieved using detergents, which often cause instability and/or loss of function. A new methodology for the extraction and purification of membrane proteins uses a styrene maleic acid co-polymer (SMA) which inserts in the membrane and assembles into small discs of bilayer encircled by polymer, termed SMA lipid particles (SMALPs). These particles are stable, maintain the lipid environment of a protein and are amenable to structural and biophysical studies.

2:35 Small Affinity Tags for Efficient Purification and Recovery of Integral Membrane Receptors

Alexei Yeliseev, Ph.D., Staff Scientist, LMBB, NIH/ NIAAA

We expressed the recombinant cannabinoid receptor CB2 expressed in *E. coli* cells as well as in expi CHO cells in milligram quantities. Protein was purified by tandem affinity chromatography using

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either His tag/twin Strep-tag or His tag/EF1 tag pairs. In this work, we compare the use of single affinity and tandem affinity purification strategies. The protocols developed in our laboratory can be applied to expression and purification of other membrane receptors for structural and functional studies.

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

OVERCOMING PERSISTENT CHALLENGES

4:00 The Development of Optimised Silica Resins to Solve Complex Purification Challenges

Søren Flygenring Basset, Ph.D., Director, R&D, Novo Nordisk Pharmatech A/S

4:30 Establishing Guiding Principles to Optimize Host Cell Protein Removal during Purification Process Development

André C. Dumetz, Ph.D., Senior Scientific Investigator, Biopharm Downstream PD-3, R&D Platform Technology & Science, GlaxoSmithKline

5:00 Engineering the Beta Roll Domain for Bioseparations Applications

Scott Banta, Ph.D., Professor, Chemical Engineering, Columbia University

RTX peptide domains are intrinsically disordered and reversibly fold into the beta roll secondary structure domain specifically upon calcium addition. RTX domains created from concatenated consensus sequences reversibly precipitate with calcium addition and we have developed this for non-chromatographic protein purification. We have also engineered a face of the beta roll domain to bind to a target protein and this enables a new calcium-dependent catch and release affinity chromatography platform.

5:30 - 6:45 Networking Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Protein Purification and Recovery Conference

JANUARY 11-12 | 7TH ANNUAL

Higher-Throughput Protein Production and Characterization

Innovating Processes

High-throughput processes have come of age by transforming the traditional protein-by-protein trial-and-error approach for testing criteria and scaling up. In this leading conference, 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 to reduce the time and effort needed to successfully analyze proteins, fine tune processes, and achieve well-folded, pure protein.

THURSDAY, JANUARY 11

7:45 am Registration and Morning Coffee

NEXT-GEN HTP TOOLS AND TECHNOLOGIES

8:15 Chairperson's Opening Remarks

Allan Matte, Ph.D., Senior Research Officer, Downstream Processing & Analytics, Human Health Therapeutics, National Research Council Canada (NRC-CNRC)

KEYNOTE PRESENTATION

8:20 High-Throughput *de novo* Computational Protein Design and Its Applications

Gabriel Rocklin, Ph.D., Senior Fellow, Biochemistry & Bioengineering, University of Washington

Advances in computational protein design and DNA synthesis technology have made it possible to design and recombinantly express tens of thousands of small designer proteins (40-80 amino acids) at once, each with a novel *de novo* fold and unique functional possibilities. These proteins can be engineered to bind to targets and to resist thermal denaturation and aggregation, and we can iteratively improve these properties through cycles of large-scale design and efficient, massively parallel experimental testing.

9:00 Mitigating Developability Risks by Application of Affinity-Capture Self-Interaction Nanoparticle Spectroscopy (AC-SINS)

Craig D. Dickinson, Ph.D., Senior Research Advisor, AME, Eli Lilly and Company

9:30 Flow Cytometry – An Old Dog with New Tricks for Ultra-High Throughput Screening of Recombinant Protein Libraries

Karl E. Griswold, Ph.D., Associate Professor, Thayer School of Engineering, Dartmouth College

Flow cytometry (FC) is a powerful tool for screening recombinant protein libraries via cell surface display. However, functional screening of soluble, secreted proteins that act in-trans upon heterologous target cells is more challenging, since the genotype-phenotype link is inherently lost for such trans-interactions. Here, we describe integrated gel microdroplet-FC (GMD-FC) screens in which recombinant expression hosts are co-encapsulated with heterologous target cells in micron scale hydrogel droplets, thereby re-establishing the genotype-phenotype link and enabling FC screening of soluble, secreted protein libraries.

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

11:00 High-Throughput Protein Production within the Swedish Human Protein Atlas Project

Hanna Tegel, Ph.D., Scientist and Group Leader, Biotechnology, Proteomics and Nanobiotechnology, KTH Royal Institute of Technology

Within the Swedish Human Protein Atlas project, an antibody-based proteomics effort with focus on protein profiling in human tissues and cells, a protein production pipeline has been set up to handle hundreds of proteins per week. The challenges we met when setting up this pipeline and the solutions we have chosen will be discussed and presented.

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

HTP PURIFICATION

2:00 Chairperson's Remarks

Nigel F. Reuel, Ph.D., Assistant Professor, Chemical and Biological Engineering, Iowa State University

2:05 Integrated High-Throughput Purification Platforms for Bio-Therapeutics R&D

Allan Matte, Ph.D., Senior Research Officer, Downstream Processing & Analytics, Human Health Therapeutics, National Research Council Canada (NRC-CNRC)

Early-stage screening campaigns for therapeutic antibody development involve the purification of hundreds of antibody samples, often produced in CHO or HEK transient expression systems with a range of titers and volumes. To meet this challenge, we have implemented a number of high-throughput purification platforms capable of rapidly generating sub-milligram to hundreds of milligrams of purified products. Redundancies in purification platforms and integration with in-process analytics is required to achieve this outcome.

2:35 Development of an Automated Mid-Scale Parallel Protein Purification System for Antibody Purification and Affinity Chromatography

Brian Hall, Ph.D., Principal Scientist, Biologics, Merck & Co.

To address the need for higher throughput affinity purification of samples 20ml-100ml we modified a 4 channel SPE system with switching valves and holding loops to perform affinity purification using commercially available columns and micro-titer deep well blocks. The system has the capacity to purify 24 samples using a single-step affinity purification protocol or a two-step protocol consisting of affinity chromatography followed by desalting/buffer exchange.

3:05 SELECTED POSTER PRESENTATION: Automated Procedures for Large-Scale Purification of Human GTPase KRas and Raf1 Cystine Rich Domain (CRD)

Simon Messing, Ph.D., Scientist II, Leidos Biomedical Research/RAS initiative

Here, we show a fully automated protein purification strategy for the large-scale production of the G domain of KRas, and one of its effectors, the cysteine rich domain of RAF1. This strategy includes five purification steps, which includes TEV protease-mediated affinity tag cleavage, Ni2+ affinity, ion exchange, and size exclusion chromatography. This automated approach provides distinct advantages to previous manual workflows, by reducing typical large-scale purification from 3-4 days down to 1.5 days. This saving in run time and workload significantly reduces protein production as a rate-limiting step in the processes of drug discovery.

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

HTP ANTIBODY PRODUCTION

4:15 Medium-Scale Higher Throughput Purification and Characterization of Antibody Therapeutics and Bispecific Antibodies

Haiyan Jiang, Ph.D., Principal Scientist, Biologics Research, Janssen BioTherapeutics, Janssen R&D

4:45 High-Throughput Production of Antibodies Using Yeast and Mammalian Cells

Juergen Nett, Ph.D., Director, High Throughput Expression, Adimab, LLC

High-throughput, small-scale production of antibodies is an essential part of a discovery workflow. After isolation from a large yeast-based antibody library, Adimab directly expresses large panels of full-length IgGs in 96-well and 24-well format. Protein purification is accomplished in a plate-based format using liquid handling platforms. The same semi-automated process is also compatible with IgGs expressed in mammalian hosts. Process setup, attributes, and output will be reviewed.

5:15 High-Quality Antibodies Targeting Protein Post-Translational Modification Sites through Affinity and Specificity Engineering

Yongku Cho, Ph.D., Assistant Professor, Chemical and Biomolecular Engineering, University of Connecticut

Developing high affinity and specificity antibodies targeting protein post-translational modification sites remains a challenge. Using human tau as a model protein, we show that antibodies engineered for high affinity alone often lose their specificity. Using a novel approach to screen for improved specificity, we engineered picomolar affinity clones with no detectable off target binding. The new methods developed may be useful for setting a quantitative standard for characterizing antibody specificity.

5:45 Close of Day

FRIDAY, JANUARY 12

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast

BuzZ sessions

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

Table Moderator: Haiyan Jiang, Ph.D., Principal Scientist, Biologics Research, Janssen BioTherapeutics, Janssen R&D

ASSESSING AND ENSURING DEVELOPABILITY

9:00 Chairperson's Remarks

Gabriel Rocklin, Ph.D., Senior Fellow, Biochemistry & Bioengineering, University of Washington

9:05 Platformization of Multi-Specific Protein Engineering I: From *in silico* Design and Bulk Modular Cloning to Automated Deconvolution of Variant Libraries

Joerg Birkenfeld, Ph.D., Section Head, High Throughput Biologics, R&D Biologics Research/ Protein Therapeutics, Sanofi-Aventis Deutschland GmbH

The success rate to identify a multi-specific lead molecule with favorable drug-like properties increases with the number of variants tested. We report here the establishment of a novel, automated platform process for the fast generation of large panels of multi-specific variants (up to 10,000). Our high-throughput process integrates emerging cloning technologies with state-of-the-art automation and workflow supporting bioinformatics based on Genedata Biologics Database.

9:35 High-Throughput Methods for Protein Stability Prediction and Formulation Challenges Identification

Smita Raghava, Ph.D., Senior Scientist, Sterile Formulation Sciences, Merck & Co.

Successful development of biologics requires development of orthogonal tools to meet the challenge of rapidly and accurately assessing protein solution stability using limited material. This presentation will focus on combination of high-throughput technologies and assays for formulation and drug product development of biologics, such as monoclonal antibodies (mAbs) and mAb-based modalities. The overview of tools, their novel implementation, and relationship to commonly conducted "stability studies" will be further discussed using examples of high-throughput workflows, pre-formulation screening, and formulation development/optimization.

10:05 HTP Method for Affinity Determination in Complex Matrices by Solution Equilibrium Analysis Using Meso Scale Discovery Technology

Eilyn R. Lacy, Ph.D., Principal Scientist, Janssen BioTherapeutics (JBIO), Janssen Research & Development, LLC

The determination of antigen-antibody affinity is essential in the development of biotherapeutics and high throughput methods for affinity analysis in physiologically relevant and complex matrices are

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Higher-Throughput Protein Production and Characterization

Innovating Processes

needed. We developed a high throughput method for affinity determination in neat serum by solution equilibrium analysis using Meso Scale Discovery technology (MSD-SEA). The results highlight the potential of the MSD-technology for HTP analysis of high affinity therapeutic candidates using physiologically relevant matrices.

10:35 Coffee Break with a Poster Pavilion

See page 4 for details

11:15 High-Throughput Automations and Optimizations for Improved Binder Generation and Validation

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

While recombinant binder selection pipelines by now work in rather high-throughput, the screening of suitable affinity reagents and especially the validation of their essential features for the final applications is still laborious and time-intensive. To optimize the efficiency of these processes, we have improved already existing and developed novel methods to efficiently test candidates for their suitability, e.g., regarding their specificity.

11:45 High-Throughput Characterization of Hydrolytic Enzymes in Low Volume and Closed Systems

Nigel F. Reuel, Ph.D., Assistant Professor, Chemical and Biological Engineering, Iowa State University

Hydrolytic enzymes play a significant role in biologic and synthetic processes. The ability to better characterize these enzymes would enable shorter development times and better products. This talk will detail two recent developments for hydrolytic enzyme characterization: 1) a carbon nanotube-based optical sensor that allows for quantitative measurement in <20ul volumes and 2) a resonant antenna sensor that passively transmits its response in the 1-100MHz range, enabling detection within closed, opaque systems.

12:15 pm Conference Wrap-Up

Richard Altman, MS, Scientist, Protein Technologies, Amgen

Haiyan Jiang, Ph.D., Principal Scientist, Biologics Research, Janssen BioTherapeutics, Janssen R&D

Diane Paskiet, MS, Director of Scientific Affairs, Scientific Affairs and Technical Services, West Pharmaceutical Services

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

Moritz von Stosch, Ph.D., Senior Manager, Fermentation, Technical R&D, GSK Vaccines

12:45 Close of Conference

BIOTHERAPEUTIC EXPRESSION & PRODUCTION

JANUARY 8-9

AGENDA Engineering Genes and Hosts

JANUARY 9-10

AGENDA Recombinant Protein Expression and Production

JANUARY 10-11

AGENDA CHO Cell Lines

JANUARY 11-12

AGENDA Optimizing Expression Platforms

JANUARY 8-9 | 10TH ANNUAL

Engineering Genes and Hosts

Exploring Strategies in Systems Engineering and Synthetic Biology

The mandate of "faster, better, less expensive" resonates with recombinant protein expression and production researchers. Thus, protein expression scientists are exploring new engineering tools including synthetic biology and systems engineering. However, many variables still must be considered during the engineering process, including verification and sequence analysis of the gene or protein of interest, codon optimization, vector construction and clone/host selection. Ultimately, as with any new system, these tools must be weighed against traditional expression and production strategies to achieve the desired quantity and quality.

Cambridge Healthtech Institute's Tenth Annual Engineering Genes and Hosts conference continues the tradition of applying effective engineering strategies for protein expression and production research leading to functional protein products. Learn from seasoned, savvy researchers as they share their real-world experiences, applications and results.

SUNDAY, JANUARY 7

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

MONDAY, JANUARY 8

7:00 am Registration and Morning Coffee

SYNTHETIC BIOLOGY

9:00 Welcome by Conference Organizer

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

9:05 Chairperson's Opening Remarks

Mark Welch, Ph.D., Vice President, Research and Development, ATUM (formerly DNA2.0)

KEYNOTE PRESENTATION

9:10 Forward Genome Engineering

Ryan T. Gill, Ph.D., Slade Professor, Chemical and Biological Engineering, University of Colorado

I discuss new technologies and approaches that are enabling the engineering of biological systems at scales of 100,000s of designer mutations in parallel.

FEATURED PRESENTATION

9:50 A Semi-Synthetic Organism that Stores and Retrieves Increased Genetic Information

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

We have examined numerous unnatural nucleotides bearing mainly hydrophobic nucleobase analogs that pair based on packing and hydrophobic interactions rather than H-bonding. More recently, we have engineered *E. coli* to import the requisite unnatural triphosphates and shown that DNA containing the unnatural base pair is efficiently replicated, transcribed, and translated within the cell, resulting in the first semi-synthetic organism that stores and retrieves increased information.

10:20 Networking Coffee Break

10:45 Codon and Codon Context Optimization in Synthetic Gene and Gene Library Design

Dimitris Papamichail, Ph.D., Assistant Professor, Computer Science, The College of New Jersey

Advances in *de novo* synthesis of DNA and computational gene design methods make possible the customization of genes and gene libraries by direct manipulation of features such as codon and codon context bias. I present computational methods to design genes with desired codon and codon context content, and low-cost gene variant libraries for high-throughput experimentation.

11:15 Synthetic Biology for Natural Product Biosynthesis

Christopher Boddy, Ph.D., Professor & Director, Biochemistry Program, University of Ottawa

Synthetic biology approaches are dramatically impacting the scientific community's ability to heterologous express complex natural product biosynthetic pathways, revolutionizing the discovery and characterization of these pathways as well as the development the natural products they encode. In this presentation we will highlight new strategies for heterologous expression of bacterial biosynthetic pathways, focusing on the violacein biosynthetic pathway, and examine methods to harness biosynthetic pathways for overproduction of natural products, using nonulosonic acid biosynthetic pathways.

11:45 Data-Driven Approaches for Rapid Scale-Up of Bioproducts

Derek Abbott, Ph.D., Director, Analytics, Amyris, Inc.

Optimization of microbial production of any product requires repeated iterations of the design-build-test-analyze engineering cycle to achieve economic viability. The presentation covers details of the automated platforms that enable Amyris scientists to rapidly cycle through a data-driven strain improvement process. Additionally, we present our vision for how the industry can leverage these platforms to positively impact the bioeconomy by dramatically reducing the cost and time to market for a variety of molecules.

12:15 pm SELECTED POSTER PRESENTATION: A High Throughput Approach to Construct Generation and Expression Screening for Recombinant Protein Production

Christine Kugel, Scientific Researcher, Biomolecular Resources, Genentech, Inc.

12:45 Session Break

1:00 Luncheon Presentation I: A Systematic Approach to Address Development and Production Challenges for Complex Biologics

Sponsored by ATUM

Claes Gustafsson, Ph.D., CCO & Founder, ATUM (formerly DNA2.0)

By using design of experiment (DoE) methodologies coupled with machine learning, transient transfection has been optimized to yield milligram levels of purified proteins in just a few days. Stable cell lines can be created in weeks to generate proteins at the gram scale. Case studies showing how these methods have been applied to multiple targets including soluble secreted proteins and integral membrane proteins will be presented.

JANUARY 8-9 | 10TH ANNUAL

Engineering Genes and Hosts

Exploring Strategies in Systems Engineering and Synthetic Biology

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

GENOME ENGINEERING

2:00 Chairperson's Remarks

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

2:05 CRISPR/Cas Tools for Host Cell Improvement in the Baculovirus-Insect Cell System

Donald L. Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming

One of my group's major efforts has focused on engineering protein glycosylation pathways in the baculovirus-insect cell system (BICS) to create new systems capable of producing "humanized" recombinant glycoproteins. We report development of novel CRISPR/Cas9 tools for site-specific genome editing in the BICS. We then describe the use of these new tools to enhance our glycoengineering efforts by targeting an endogenous *Spodoptera frugiperda* (Sf) glycogene, which antagonizes human-type glycan elongation.

2:35 New Strategies of CRISPR/Cas9-Based High-Throughput Functional Genomic Screening

Dongxin Zhao, Ph.D., Postdoctoral Fellow, Prashant Mali Lab, Department of Bioengineering, University of California, San Diego

Cancer is a complex disease of which targetable vulnerabilities are the consequence of reprogramming of genetic architecture driven by various genetic mutations. Dissection of genetic interactions in a systematic way would provide unprecedented insights in drug discovery. Applying the new powerful CRISPR/Cas9 technology, we developed a combinatorial screening platform which allows for both high-throughput mapping of synthetic lethality and quantification of cancer cell type-specific interactions in metabolic circus.

3:05 Transition to BuzZ Sessions

3:15 BuzZ Sessions with Refreshments

BuzZ sessions

Join your peers and colleagues for interactive roundtable discussions.

Please see page 78 for additional information.

4:30 Mammalian Display: Antibody Discovery, Affinity Maturation and Developability Screening in IgG Format

Mike Dyson, Ph.D., CTO, IONTAS, Ltd.

Using directed integration of antibody genes by CRISPR/Cas9 and TALE nucleases, we have constructed large libraries in mammalian cells containing a single antibody gene/cell. This has permitted construction of millions of monoclonal stable cell lines displaying IgG antibodies on their surface from which antibodies have been selected by flow cytometry for specificity, binding affinity, species cross-reactivity and expression level. Expression in production cell lines also enables high-throughput developability screening.

5:00 RNA Structural Determinants of Optimal Codons Revealed by MAGE-Seq

Eric Kelsic, Ph.D., Staff Scientist, George Church Laboratory, Wyss Institute, Harvard Medical School

To understand the determinants of codon choice across a gene, we generated 12,726 *in situ* codon mutants in the *Escherichia coli* essential gene infA and measured their fitness with MAGE-seq. Correlating predicted 5' RNA structure with fitness revealed that codons even far from the start of the gene are deleterious if they disrupt the native 5' RNA conformation. Our results shed light on natural codon distributions and should improve engineering of gene expression for synthetic biology applications.

5:30 PANEL DISCUSSION: CRISPR/Cas Genome Editing for Protein Expression

CRISPR/Cas has emerged as a powerful tool for engineering the genome in diverse organisms. However, there are also financial and legal considerations in using this tool. Hear this panel of experts discuss the pros and cons of CRISPR/Cas genome editing and its role in enhancing desired protein expression.

Moderator:

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

Panelists:

Mike Dyson, Ph.D., CTO, IONTAS, Ltd.

Donald L. Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming

Eric Kelsic, Ph.D., Staff Scientist, George Church Laboratory, Wyss Institute, Harvard Medical School

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

Dongxin Zhao, Ph.D., Postdoctoral Fellow, Prashant Mali Lab, Department of Bioengineering, University of California, San Diego

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

Sponsored by MO TEMPER

7:15 Close of Day

Engineering Genes and Hosts

Exploring Strategies in Systems Engineering and Synthetic Biology

TUESDAY, JANUARY 9

8:00 am Registration and Morning Coffee

CASE STUDIES IN ENHANCING EXPRESSION SYSTEMS

8:30 Chairperson's Remarks
Henry C. Chiou, Ph.D., Associate Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific

FEATURED PRESENTATION

8:35 Engineering Cell Factories for Protein Production
Bjørn Voldborg, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark
We have engineered cell-based factories for protein production, using state-of-the-art technologies combined with high-throughput genome engineering, *in silico* modeling, deep -omics analysis and big data analysis. Our main focus is CHO cells, where we have generated a panel of CHO cell lines, with optimized phenotypes generating tailormade PTMs, improved bioprocess and product quality, etc.

9:05 SKIK Tag Increasing the Expression of Hard-to-Express Proteins and Its Application to Antibody Screening from Single B Cells
Teruyo Ojima-Kato, Ph.D., Researcher, Meijo University
A novel tag sequence SKIK can drastically increase the expression of hard-to-express proteins in *Eschericha coli in vivo* and *in vitro* protein synthesis systems without affecting its activity in most cases. We used the peptide for a novel antibody production from single B cells by RT-PCR, PCR and cell-free protein synthesis, because the amount of protein expressed can be highly improved and normalized for better evaluation of Fab synthesized.

9:35 Engineering a CHO K1 Toolbox for Reliable High Titer Protein Expression
Sponsored by horizon
Mario Pereira, Ph.D., Senior Scientist, Horizon Discovery
Aside from single gene knockouts to allow for metabolic selection systems, the CHO host remains largely unchanged. I will present how we have used a combination of techniques including genome engineering approaches such as CRISPR and rAAV to improve the biomanufacturing capacity of our GS knockout CHO K1 cell line.

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

11:30 Establishing Protein Production without Reinventing the Wheel: ProteinData.Cloud
Peter Nollert, Ph.D., Business Director, Research and Development, Bio Data Bridges
Establishing viable paths for recombinant protein sample production is typically inefficient due to the commonly applied laborious trial-and-error approach. ProteinData.Cloud is a platform to access and share otherwise invisible experimental recombinant protein production information. Researchers find engineered vector sequences, positive and negative recombinant expression trials and purification detail, apply and improve recombinant protein production strategies to their own targets to improve protein production yield and purity.

12:00 pm Unlock *Pichia* – Novel Strategies and Molecular Tools to Enhance Protein Expression
Sponsored by VTU technology
Iskandar Dib, Ph.D., Principal Scientist DSP & Analytics, VTU Technology GmbH
Pichia pastoris is an established, safe and highly competitive expression host with strong and effective secretory capacities often resulting in double-digit g/l levels of recombinant protein. Recent research has brought about new exciting technologies increasing the potential of this already powerful yeast production host. An extended molecular toolbox addresses challenges in protein folding and secretion and facilitates the expression of more complex proteins, thus maximizing yields without compromising product quality.

12:30 Session Break

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

1:15 Close of Engineering Genes and Hosts Conference

JANUARY 9-10 | 20TH ANNUAL

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 9

1:00 pm Registration

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

OPTIMIZING PRODUCTION PLATFORMS

2:00 Chairperson's Opening Remarks
Mark Arbing, Ph.D., Core Facility Director, UCLA-DOE Institute, University of California, Los Angeles

KEYNOTE PRESENTATION

2:05 Combining Biophysical Analytics with NGS-Based Genetic Characterization and Gene Editing Technologies to Improve mAb Producing CHO Cell Lines
Holger Thie, Ph.D., Associate Director, Molecular Biology, Early Stage Bioprocess Development, Boehringer Ingelheim Pharma GmbH & Co. KG

This study demonstrates how state-of-the-art technologies foster the development of production cell lines by gaining a more holistic understanding of these cells to ensure high performance and product quality. Here, the process is shown from the detection of an unfavorable molecule property (remarkable differences in N-linked glycosylation between two production clones derived from the same CHO cell line), the identification of the genetic background by NGS and how this can be fixed by applying gene editing technologies.

2:45 Hosts, Partners, and Accessories: Keys to Productive Protein Production
Mark Arbing, Ph.D., Core Facility Director, UCLA-DOE Institute, University of California, Los Angeles

Successful production of recombinant proteins requires an appropriate expression host and careful consideration of protein expression conditions. Important factors to consider are the origin of the target protein, the context in which the target protein natively exists, and additional factors (e.g., chaperones) that may be required for proper folding of the target protein.

3:15 A Chemically-Defined Baculovirus-Based Expression System for Enhanced Protein Production in Sf9 Cells
Sponsored by ThermoFisher SCIENTIFIC
Jonathan Zmuda, Ph.D., Director, Cell Biology, Research & Development, Thermo Fisher Scientific

The Baculovirus Expression Vector System (BEVS) is one of the major platforms for recombinant protein production. Unlike mammalian systems, insect systems rely on yeastolate-containing media that can exhibit significant variability in cell growth and protein expression. Here, we present the development of a novel Sf9-based Baculovirus expression system based on a high-density, chemically-defined medium, a high-expressing Sf9 cell line and enhancers that allow for consistent protein production with improvements in titers compared to traditional workflows.

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

4:30 Redirecting Bacterial Microcompartment Systems to Improve Expression of Toxic Proteins
Mimi Cho Yung, Ph.D., Biomedical Staff Scientist, Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory

Recombinant expression of toxic peptides/proteins remains a challenging problem. We redirected recombinant bacterial microcompartment (BMC) systems in *Escherichia coli* to shield the toxicity and enhance the expression of lysis protein E from bacteriophage ϕX174. Ultimately, our recombinant system achieved a ~7-fold improvement in protein yield compared to prior reports. Ongoing efforts to express antimicrobial peptides within encapsulin microcompartments to enhance their recombinant expression will also be discussed.

5:00 Development of Diatoms (Algae) as Therapeutic Protein Expression Systems
Mark Hildebrand, Ph.D., Research Scientist and Director, Marine Biology Research Division, Scripps Institution of Oceanography, University of California, San Diego

We have developed microalgae called diatoms as protein expression systems, particularly for vaccine production. We use a novel inducible promoter that suppresses expression during growth (enabling expression of toxic proteins), and induces under nutrient-induced growth cessation – increasing yields by enabling channeling of energy and metabolites into protein synthesis. Diatom silica cell walls are an effective adjuvant, and the system is an all-in-one package of adjuvant and slow-release particulate antigen.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

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

WEDNESDAY, JANUARY 10

8:00 am Registration and Morning Coffee

CELL-FREE SYSTEMS

8:30 Chairperson's Remarks

Feras Hatahet, Ph.D., Scientist, Protein Technologies, Amgen

8:35 Protein Production Platform for Rational Design Engineering

Takanori Kigawa, Ph.D., Team Leader, Quantitative Biology Center, RIKEN

We have established a protein production platform based on cell-free technologies, which can produce milligram quantities of a hundred kinds of newly generated mutant proteins within a day totally without recombinant DNA technology. By using this platform, time and labor consuming site-directed mutagenesis and subsequent mutant protein expression/purification are dramatically accelerated. Therefore, this platform is highly useful for protein engineering with rational design approaches.

9:05 Membrane Protein Production and Characterization in Tailored Lipid Environments

Frank Bernhard, Ph.D., Lab Leader, Institute of Biophysical Chemistry, Goethe University Frankfurt

Using proprietary cell-free expression platforms, we synthesize membrane proteins directly into supplied preformed nanoparticles containing defined lipid compositions. The process has been optimized for preparative scale production yielding up to 100 µM concentrations of membrane protein containing nanoparticles in the reactions. We show applications of GPCRs, ion channels, transporters as well as of large assemblies and demonstrate the complete detergent-free structural analysis of membrane proteins by crystallization and NMR.

Sponsored by premas biotech partners in discovery

9:35 Oral Insulin: Significant COGs Reduction via Innovative Process Development and Production for Late Stage Clinical Trials

Prabuddha K Kundu, Ph.D., Cofounder, Executive Director, Premas Biotech

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

ANTIBODY PRODUCTION IN *E. COLI*

10:50 SPEAKER CANCELLATION: Rapid Screening of Cyclotide-Based Libraries against Intracellular Protein-Protein Interactions

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

We report novel methods for the biosynthesis of natively folded MCoTI-based cyclotides inside live *E. coli* cells using split protein splicing units. The cyclotide MCoTI-cylotides are potent trypsin inhibitors recently isolated from the seeds of *Momordica cochinchinensis*, a plant member of the *cucurbitaceae* family. Biosynthesis of genetically encoded cyclotide-based libraries opens the possibility of using single cells as microfactories where the biosynthesis and screening of a particular inhibitor can take place in a single process within the same cellular cytoplasm. The cyclotide scaffold has tremendous potential for the development of therapeutic leads based on its extraordinary stability and potential for grafting applications. We show an example, where a large cyclotide-based genetically encoded library was used to screen for low nanomolar antagonists for the Hdm2-HdmX RING-mediated E3 ligase activity. We also present different strategies to improve the cellular uptake and pharmacokinetic profiles of bioactive cyclotides.

11:20 Super Secretory Production of Recombinant Antibody Fragments by Precisely Controlled Fed-Batch Culture of *E. coli*

Yoichi Kumada, Ph.D., Associate Professor, Department of Functional Chemistry, Kyoto Institute of Technology

Large-scale production of single-chain Fv antibodies by recombinant *E. coli* was investigated. Periplasmic secretion signal, pel B reader was often effective for leaking proteins to supernatant, while most of them were aggregated as inclusion body in flask culture. When the fed-batch culture was performed by Jar fermenter with tightly regulated DO control system, the scFvs expressed were highly secreted to the culture supernatant. Consequently, final concentration of scFv reached at more than 4g/L, and solubility of scFv was approx. 50%. These results potentially suggested that precisely regulated fed-batch fermentation is a promising way for secretory production of target recombinant proteins.

11:50 Soluble Expression of Antibody Fragments in the Cytoplasm of *E. coli*

Feras Hatahet, Ph.D., Scientist, Protein Technologies, Amgen

E. coli is widely used for the production of proteins of pharmaceutical importance. However, the production of soluble functional proteins can be hampered when disulfide bonds are required. We demonstrate the feasibility of producing single chain variable fragments (scFv) of antibodies and multi-chain peptides in the cytoplasm of genetically altered *E. coli*. This approach is potentially quite useful for assessing the convertibility of antibodies into multi-specific antibody formats containing scFvs.

12:20 Enjoy Lunch on Your Own

CHO CELL DEVELOPMENT FOR EFFICIENT PROTEIN PRODUCTION

2:00 Chairperson's Remarks

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

2:05 Optimizing Expression of Proteins in CHO through a Systems Biology Approach

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

In our lab, we are mapping out the cell pathways controlling CHO cell growth, protein synthesis, and protein glycosylation. Here I discuss our work in which we have developed computational models to predict the cell costs for protein synthesis and identify how to improve protein synthesis through media and genetic modifications.

JANUARY 9-10 | 20TH ANNUAL

Recombinant Protein Expression and Production

Achieving Quality and Quantity

2:35 Optimizing Biologics by Cell-Based Glycan Display

Claus Kristensen, Ph.D., CEO, GlycoDisplay Aps

Glycan structures are important for efficacy and distribution of biologics. Optimization of glycans has been hampered by inefficient technologies for glyco-engineering in mammalian cells. Now GlycoDisplay offers technologies allowing development of novel glyco-optimized biologics. GlycoDisplay has applied targeted cell engineering to generate cell lines with different glycosylation capacities. By expressing a drug candidate protein in panels of glycoengineered cell lines, followed by screening novel glyco-optimized leads are identified.

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

4:00 Overexpression of Ebola Virus Envelope GP1 Protein

Zhongcheng Zou, Ph.D., Staff Scientist, Structural Immunology Section, Lab of Immunogenetics, NIAID/NIH

To elucidate the role of the mucin-like domain of GP1 in Ebola-host attachment and infection and to facilitate vaccine development, we constructed a GP1 expression vector containing the entire attachment region. Cysteine 53 of GP1 was mutated to serine to avoid potential disulfide bond mispairing. Stable expression clones using codon optimized open reading frame were developed in human 293-H cells with yields reaching ~ 25 mg of GP1 protein per liter of spent medium.

4:30 Using GlycoExpress to Overcome Production Limitations for Difficult-to-Express Proteins

Lars Stöckl, Ph.D., Director, Glycoprotein Development and PTM Analytics, Glycotope GmbH

Even though productivity for CHO systems has remarkedly improved over the last years, some biopharmaceuticals like bispecific constructs or complex glycoproteins remain very challenging. We present case study data from clone and upstream perfusion development for the human GlycoExpress cell line, which overcomes productivity limitations.

5:00 Expression of Recombinant Blood Coagulation Factor VIII: Importance for Human Healthcare and Approaches to Improve the Protein's Yield and Quality

Andrey G. Sarafanov, Ph.D., Chemist, Principal Investigator, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration (FDA)

Deficiency in factor VIII (FVIII) results in abnormal bleeding (Hemophilia A), which is treated by infusions of FVIII. However, the FVIII production is challenging as the protein is expressed at low levels both in plasma (0.3 nM) and heterologous systems. The presentation overviews approaches to improve FVIII production, in particular, re-design of the protein and its gene, optimization of the protein expression and purification, and selection of test methods.

5:30 - 6:45 Networking Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Recombinant Protein Expression and Production Conference

JANUARY 10-11 | 4TH ANNUAL

CHO Cell Lines

Enhancing Expression, Performance & Process

CHO cells' rapid rise in production prominence is due to their adaptability to various culture conditions, gene plasticity, and ability in proper folding, posttranslational modifications, and glycosylation of desired proteins. Thus, advances in CHO cell lines and culture continue to significantly improve biotherapeutic production. This achievement is due to progress in engineering stable and transient cell lines, enhancing cell culture conditions and performance, as well as optimizing process development. When all are accomplished, higher-production titers and better product quality result. 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 10

1:00 pm **Registration**

ENHANCING EXPRESSION THROUGH ENGINEERING

2:00 **Chairperson's Opening Remarks**

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

2:05 **Optimizing Expression of Proteins in CHO through a Systems Biology Approach**

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

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Glycan structures are important for efficacy and distribution of biologics. Optimization of glycans has been hampered by inefficient technologies for glyco-engineering in mammalian cells. Now GlycoDisplay offers technologies allowing development of novel glyco-optimized biologics. GlycoDisplay has applied targeted cell engineering to generate cell lines with different glycosylation capacities. By expressing a drug candidate protein in panels of glycoengineered cell lines, followed by screening novel glyco-optimized leads are identified.

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5:30 - 6:45 **Networking Reception in the Exhibit Hall with Poster Viewing**

6:45 **Close of Day**

THURSDAY, JANUARY 11

7:45 am **Morning Coffee**

IMPROVING PRODUCT QUALITY THROUGH PROCESS

8:15 **Chairperson's Remarks**

Gyun Min Lee, Ph.D., Professor, Biological Sciences, KAIST

KEYNOTE PRESENTATION

8:20 **Integrating Cell Culture with Magnetic Protein A Bead-Trap Technology Accelerates Antibody Purification**

John K. Kawooya, Ph.D., Director, Biologics Optimization, Discovery Research, Amgen

Antibody engineering produces large numbers of molecules (200-500 molecules at 30-50ml each) which require purification, analysis and screening for potency, binding, pharmacodynamics, pharmacokinetics, manufacturability, expression levels and stability in order to select leads. Ever since its inception over 30 years ago, the AKTA system combined with Protein A agarose columns has remained the "workhorse" of antibody purification from cell cultures. However, the inability of this system to process multiple samples in parallel coupled with both its limiting flow rates, its requirement for multiple FTEs to remove cells and particulate from each sample prior to loading together with the potential for sample swapping errors and cross contaminations – all impose major bottlenecks in expediting large purified panels of molecules. In this presentation, I show how a single FTE with parallel Magnetic Protein A bead-trap technology accelerates delivery of high-quality purified antibodies in high yield directly from small (30ml-5liters) to large (25-liter wave-bag) crude cell cultures without centrifugation or filtration.

JANUARY 10-11 | 4TH ANNUAL

CHO Cell Lines

Enhancing Expression, Performance & Process

9:00 Speed to IND: Alignment and Acceleration of Critical Early Phase Activities

Kyle Zingaro, Ph.D., Development Scientist II, Early Stage Development, Alexion Pharmaceuticals

Speed to IND is the current battle cry across early phase biologics development. Despite some risks, new technologies and workflow alignment can afford faster and better decisions during this crucial phase of new product development. This is especially true across the Discovery and Process Development handoff. We present new data and approaches to improve that handoff and detail the impact on timelines and quality of molecules and cell lines in early phase development.

9:30 "Lost in Translation": Bridging the Gap between Academia and Biotech

Tsafi Danieli, Ph.D., Director, BioGiv Excubator & Head, Protein Expression Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem

One of the most difficult and frustrating aspects of basing a startup company on academic findings is translating and transferring academic findings to biotech language. This procedure is often frustrating to both parties and requires psychological skills as well as critical review of the research. Working in the interphase between academia and industry, there are several preemptive strikes we can take to avoid some of the major pitfalls.

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

11:00 Proteomic Analysis of Host Cell Protein Dynamics in the Culture Supernatants of Therapeutic Protein-Producing CHO Cells

Gyun Min Lee, Ph.D., Professor, Biological Sciences, KAIST

Host cell proteins (HCPs) accumulate extracellularly during the cultures of recombinant CHO (rCHO) cells, potentially impairing product quality. HCPs accumulated extracellularly in batch and fed-batch cultures of rCHO cell lines were identified and quantified by mass spectrometry. This dataset of HCPs provides insights into determining the appropriate target proteins to be removed during both the cultures and purification steps for ensuring good therapeutic protein quality.

11:30 Using SUREscan™ to Survey Genetic Changes in Stable CHO Cell Lines

Sponsored by SELEXIS

Pierre-Alain Girod, CSO, Selexis

CHO cells are the most frequently applied host-cell system for industrial protein therapeutic manufacturing. Rapid generation of high-producing clones that don't lose expression capability over time has been a major industry focus. Using SUREscan™ with next-generation sequencing (NGS), we can quickly analyze whole genomes of any cell line, improving traceability of Research Cell Banks (RCBs). In contrast to other CHO published data, we will show that SURE technology Platform™ generates RCBs with chromosomally stable lineages.

12:00 pm Session Break

12:15 Luncheon Presentation: Get Your High Protein Concentrations Right on the Money with Lunatic

Sponsored by UNCHAINED LABS

Thomas Martens, Principal Scientist, Unchained Labs

Stop quantifying proteins one by one hoping that your old reader is getting the numbers right. Get rid of that dilution step you always need to measure 200 mg/ml IgG or even higher. Come learn about how Lunatic gets rid of all dilutions, eliminates any risk of cross contamination and accurately measures protein concentration at high throughput and high concentrations. We'll talk about how lunatic:

- measures either 16 or 96 samples in one run
- uses only 2 µL for each measurement
- needs only 5 minutes
- Requires no dilutions

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

PROTEIN PRODUCTION: TRANSIENT, STABLE OR BOTH?

2:00 Chairperson's Remarks

Saurabh Sen, Ph.D., Principal Scientist, Biotherapeutics Discovery, Boehringer Ingelheim

2:05 A High-Density CHO-S Transient Transfection System: Comparison of ExpiCHO and Expi293

Tadas Panavas, Ph.D., Senior Principal Scientist, Biotherapeutics Molecule Discovery, Boehringer Ingelheim Pharmaceuticals, Inc

Chinese Hamster Ovary (CHO) cells are the principal mammalian host used for stable cell line generation and biotherapeutic protein production. Until recently, production of milligrams to grams of protein in CHO transient systems was challenging. To overcome such challenges, we evaluated the ExpiCHO system, a high-density CHO-S transient transfection system, and compared it to the Expi293 and FreeStyle MAX CHO transient systems. Detailed analysis was performed on protein titer, monodispersity, enzyme activity, and posttranslational modifications.

2:35 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.

3:05 Sponsored Presentation *(Opportunity Available)*

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

4:15 Lost in Translation: On the Formation of Protein Sequence Variants

Zhongqi Zhang, Ph.D., Scientific Director, Attribute Sciences, Process Development, Amgen

With modern mass spectrometry and appropriate informatics tools, a large number of low-level sequence variants in therapeutic proteins are detected and quantified. This large collection of information allows for a deeper understanding of the mechanism for the formation of sequence variants, thereby facilitating optimization of cell line and cell culture process to minimize them.

4:45 The Stability of CHO Genome: Essential for Cell Line Characterization or Not?

Noriko Yamano, Ph.D., Senior Scientist, Manufacturing Technology Association of Biologics; Guest Academic Staff, Graduate School of Engineering, Osaka University

The chromosomes in CHO cells frequently cause genomic variations, due to genetic instability. Distribution and stability of chromosomes were examined in CHO-DG44 cells, and two cell lines expressing different numbers of chromosomes were isolated from the original CHO-DG44 cell line to investigate the effect of aneuploid cells on recombinant protein production. In addition, gene expression profiles between cells with disparate chromosome numbers have been compared by mRNA-seq analysis.

5:15 High-Throughput Screening of Transfection Efficiency of dTtaPS Reagent Library, and Its Application for Transient Production of Proteins in Micro Bioreactors

Harsh Jain, Ph.D., Visiting Associate, FDA

5:45 Close of CHO Cell Lines Conference

JANUARY 11-12 | 5TH ANNUAL

Optimizing Expression Platforms

Tools for Effective Expression, Production & Purification

The utilization of engineered therapeutic proteins for basic research, clinical diagnostics and therapy continues to expand. Consequently, protein expression laboratory researchers face challenges in efficient expression, production, and purification even while improving quantity and quality and minimizing time and cost. Transient protein production (TPP) has the advantage of speed and limiting risk while stable transfection – the longer and more complex process – has the advantage of producing long-term expression of the biotherapeutic of interest. The rapidly increasing need for recombinant proteins necessitates further improvements in both technologies.

Cambridge Healthtech Institute's Fifth Annual Optimizing Expression Platforms conference convenes protein expression specialists who share their experiences of the differences, tradeoffs, and improvements in producing recombinant proteins in transient or stable production systems, and who investigate their advantages and disadvantages and when to use both.

THURSDAY, JANUARY 11

7:45 am Registration and Morning Coffee

TRANSIENT PROTEIN PRODUCTION

8:15 Chairperson's Opening Remarks

Richard Altman, MS, Scientist, Protein Technologies, Amgen

KEYNOTE PRESENTATION

8:20 Integrating Cell Culture with Magnetic Protein A Bead-Trap Technology Accelerates Antibody Purification

John K. Kawooya, Ph.D., Director, Biologics Optimization, Discovery Research, Amgen

Antibody engineering produces large numbers of molecules (200-500 molecules at 30-50ml each) which require purification, analysis and screening for potency, binding, pharmacodynamics, pharmacokinetics, manufacturability, expression levels and stability in order to select leads. Ever since its inception over 30 years ago, the AKTA system combined with Protein A agarose columns has remained the "workhorse" of antibody purification from cell cultures. However, the inability of this system to process multiple samples in parallel coupled with both its limiting flow rates, its requirement for multiple FTEs to remove cells and particulate from each sample prior to loading together with the potential for sample swapping errors and cross contaminations – all impose major bottlenecks in expediting large purified panels of molecules. In this presentation, I show how a single FTE with parallel Magnetic Protein A bead-trap technology accelerates delivery of high-quality purified antibodies in high yield directly from small (30ml-5liters) to large (25-liter wave-bag) crude cell cultures without centrifugation or filtration.

9:00 Transient Antibody Production: How to Generate Higher Titers

Saurabh Sen, Ph.D., Principal Scientist, Biotherapeutics Discovery, Boehringer Ingelheim

The presentation covers topics on optimizing efficient expression and production even while improving quantity and quality and minimizing time and cost. Our Transient Gene Expression (TGE) technology for transient protein production (TPP) has significant advantages by using lesser amounts of coding DNA by 70-80% -- and using 50% less transfection reagent. For research purposes, we have an improved TGE protocol with significant advantage of speed, higher yields and lower costs.

9:30 Advances and Challenges in Transient Plant-Based Therapeutic Protein Production

Karen McDonald, Ph.D., Professor, Chemical Engineering, University of California, Davis

Plants are an excellent host for transient production of therapeutic proteins due to their high expression levels, rapid development timescales, short batch production times, flexibility, robustness, scalability, biosafety, and economics. A variety of transient expression systems/platforms and glycoengineered plant host lines have been developed and commercial-scale facilities have been built. Current work in the area of transient production of recombinant proteins in plant cell suspension cultures will be presented.

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

11:00 Fundamentals of Baculovirus Expression and Applications

Christopher Kemp, Ph.D., President, Kempbio

The baculovirus expression vector system (BEVS) is a major protein expression platform for the production of research and therapeutic grade proteins. BEVS supports the expression of proteins in both insect and mammalian cell hosts and the high efficiency and reproducibility of viral transduction allows the expression of difficult proteins. This presentation focuses on applications of BEVS for the expression of proteins and protein complexes in insect and mammalian cells.

11:30 Accelerated Protein Production via Transient Cell Engineering

Sponsored by MaxCyte

Enrique Miranda Rota, Ph.D., Research Associate, MaxCyte, Inc., University College London Cancer Institute

Biotherapeutic protein development groups are often faced with producing a wide variety of proteins with varying and often complex requirements. Our presentation describes a fully scalable, cGMP compliant, transient cell engineering strategy along with a streamlined purification process that allows us to generate large quantities of purified biotherapeutic proteins quickly to satisfy the needs of our collaborators without having to do labor and time intensive stable clone generation or produce large cell collections.

12:00 pm Session Break

12:15 Luncheon Presentation I: New Tools for Screening & Harvesting Solutions for CHO & HEK293 Cells, for Both Transient and Stable Cell

Sponsored by THOMSON INSTRUMENT COMPANY

Sam Ellis, Vice President, Thomson Instrument Company

Evaluation of different transfection tools, product

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

12:45 **Luncheon Presentation II** *(Sponsorship Opportunity Available)*

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

CHO CELLS: TRANSIENT, STABLE OR BOTH?

2:00 **Chairperson's Remarks**
Saurabh Sen, Ph.D., Principal Scientist, Biotherapeutics Discovery, Boehringer Ingelheim

2:05 **A High-Density CHO-S Transient Transfection System: Comparison of ExpiCHO and Expi293**
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2:35 **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.

3:05 **Difficult to Express Proteins: Novel Plasmid Technology to Significantly Increase Product Yield in CHO Cells**
Sponsored by BATAVIA biosciences
Marco Cacciuttolo, Ph.D., Head of Operations, Batavia Biosciences
Yield is still an area that requires significant improvement for many promising recombinant proteins and antibodies. Novel vector technology enables rapid generation of stable, CHO cell lines able to provide at least 10-fold more product per cell.

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

4:15 **Lost in Translation: On the Formation of Protein Sequence Variants**
Zhongqi Zhang, Ph.D., Scientific Director, Attribute Sciences, Process Development, Amgen
With modern mass spectrometry and appropriate informatics tools, a large number of low-level sequence variants in therapeutic proteins are detected and quantified. This large collection of information allows for a deeper understanding of the mechanism for the formation of sequence variants, thereby facilitating optimization of cell line and cell culture process to minimize them.

4:45 **The Stability of CHO Genome: Essential for Cell Line Characterization or Not?**
Noriko Yamano, Ph.D., Senior Scientist, Manufacturing Technology Association of Biologics; Guest Academic Staff, Graduate School of Engineering, Osaka University
The chromosomes in CHO cells frequently cause genomic variations, due to genetic instability. Distribution and stability of chromosomes were examined in CHO-DG44 cells, and two cell lines expressing different numbers of chromosomes were isolated from the original CHO-DG44 cell line to investigate the effect of aneuploid cells on recombinant protein production. In addition, gene expression profiles between cells with disparate chromosome numbers have been compared by mRNA-seq analysis.

5:15 **High-Throughput Screening of Transfection Efficiency of dTtaPS Reagent Library, and Its Application for Transient Production of Proteins in Micro Bioreactors**
Harsh Jain, Ph.D., Visiting Associate, FDA

5:45 **Close of Day**

FRIDAY, JANUARY 12

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast

BuzZ sessions

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

Table Moderator: Richard Altman, MS, Scientist, Protein Technologies, Amgen

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

TECHNOLOGIES TO ESTABLISH EFFICIENT PRODUCTION & PURIFICATION

9:00 Chairperson's Remarks

Gabriel Rocklin, Ph.D., Senior Fellow, Biochemistry & Bioengineering, University of Washington

9:05 Platformization of Multi-Specific Protein Engineering I: From *in silico* Design and Bulk Modular Cloning to Automated Deconvolution of Variant Libraries

Joerg Birkenfeld, Ph.D., Section Head, High Throughput Biologics, R&D Biologics Research/ Protein Therapeutics, Sanofi-Aventis Deutschland GmbH

The success rate to identify a multi-specific lead molecule with favorable drug-like properties increases with the number of variants tested. We report here the establishment of a novel, automated platform process for the fast generation of large panels of multi-specific variants (up to 10,000). Our high-throughput process integrates emerging cloning technologies with state-of-the-art automation and workflow supporting bioinformatics based on Genedata Biologics Database.

9:35 High-Throughput Methods for Protein Stability Prediction and Formulation Challenges Identification

Smita Raghava, Ph.D., Senior Scientist, Sterile Formulation Sciences, Merck & Co.

Successful development of biologics requires development of orthogonal tools to meet the challenge of rapidly and accurately assessing protein solution stability using limited material. This presentation will focus on combination of high-throughput technologies and assays for formulation and drug product development of biologics, such as monoclonal antibodies (mAbs) and mAb-based modalities. The overview of tools, their novel implementation, and relationship to commonly conducted "stability studies" will be further discussed using examples of high-throughput workflows, pre-formulation screening, and formulation development/optimization.

10:05 HTP Method for Affinity Determination in Complex Matrices by Solution Equilibrium Analysis Using Meso Scale Discovery Technology

Eilyn R. Lacy, Ph.D., Principal Scientist, Janssen BioTherapeutics (JBIO), Janssen Research & Development, LLC

10:35 Coffee Break with a Poster Pavilion

See page 4 for details

11:15 High-Throughput Automations and Optimizations for Improved Binder Generation and Validation

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

While recombinant binder selection pipelines by now work in rather high-throughput, the screening of suitable affinity reagents and especially the validation of their essential features for the final applications is still laborious and time-intensive. To optimize the efficiency of these processes, we have improved already existing and developed novel methods to efficiently test candidates for their suitability, e.g., regarding their specificity.

11:45 High-Throughput Characterization of Hydrolytic Enzymes in Low Volume and Closed Systems

Nigel F. Reuel, Ph.D., Assistant Professor, Chemical and Biological Engineering, Iowa State University

Hydrolytic enzymes play a significant role in biologic and synthetic processes. The ability to better characterize these enzymes would enable shorter development times and better products. This talk will detail two recent developments for hydrolytic enzyme characterization: 1) a carbon nanotube-based optical sensor that allows for quantitative measurement in <20ul volumes, and 2) a resonant antenna sensor that passively transmits its response in the 1-100MHz range, enabling detection within closed, opaque systems.

12:15 pm Conference Wrap-Up

Richard Altman, MS, Scientist, Protein Technologies, Amgen

Haiyan Jiang, Ph.D., Principal Scientist, Biologics Research, Janssen BioTherapeutics, Janssen R&D

Diane Paskiet, MS, Director of Scientific Affairs, Scientific Affairs and Technical Services, West Pharmaceutical Services

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

Moritz von Stosch, Ph.D., Senior Manager, Fermentation, Technical R&D, GSK Vaccines

12:45 Close of Conference

ALTERNATIVE EXPRESSION & PRODUCTS

JANUARY 8-9

AGENDA Engineering Genes and Hosts

JANUARY 9-10

AGENDA Biocatalysis and Bio-Based Chemical Production

JANUARY 11-12

AGENDA Microbial Production

JANUARY 8-9 | 10TH ANNUAL

Engineering Genes and Hosts

Exploring Strategies in Systems Engineering and Synthetic Biology

The mandate of "faster, better, less expensive" resonates with recombinant protein expression and production researchers. Thus, protein expression scientists are exploring new engineering tools including synthetic biology and systems engineering. However, many variables still must be considered during the engineering process, including verification and sequence analysis of the gene or protein of interest, codon optimization, vector construction and clone/host selection. Ultimately, as with any new system, these tools must be weighed against traditional expression and production strategies to achieve the desired quantity and quality.

Cambridge Healthtech Institute's Tenth Annual Engineering Genes and Hosts conference continues the tradition of applying effective engineering strategies for protein expression and production research leading to functional protein products. Learn from seasoned, savvy researchers as they share their real-world experiences, applications and results.

SUNDAY, JANUARY 7

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

MONDAY, JANUARY 8

7:00 am Registration and Morning Coffee

SYNTHETIC BIOLOGY

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

9:05 Chairperson's Opening Remarks
Mark Welch, Ph.D., Vice President, Research and Development, ATUM (formerly DNA2.0)

KEYNOTE PRESENTATION

9:10 Forward Genome Engineering
Ryan T. Gill, Ph.D., Slade Professor, Chemical and Biological Engineering, University of Colorado

I discuss new technologies and approaches that are enabling the engineering of biological systems at scales of 100,000s of designer mutations in parallel.

FEATURED PRESENTATION

9:50 A Semi-Synthetic Organism that Stores and Retrieves Increased Genetic Information
Floyd Romesberg, Ph.D., Professor, Chemistry, The Scripps Research Institute

We have examined numerous unnatural nucleotides bearing mainly hydrophobic nucleobase analogs that pair based on packing and hydrophobic interactions rather than H-bonding. More recently, we have engineered *E. coli* to import the requisite unnatural triphosphates and shown that DNA containing the unnatural base pair is efficiently replicated, transcribed, and translated within the cell, resulting in the first semi-synthetic organism that stores and retrieves increased information.

10:20 Networking Coffee Break

10:45 Codon and Codon Context Optimization in Synthetic Gene and Gene Library Design
Dimitris Papamichail, Ph.D., Assistant Professor, Computer Science, The College of New Jersey

Advances in *de novo* synthesis of DNA and computational gene design methods make possible the customization of genes and gene libraries by direct manipulation of features such as codon and codon context bias. I present computational methods to design genes with desired codon and codon context content, and low-cost gene variant libraries for high-throughput experimentation.

11:15 Synthetic Biology for Natural Product Biosynthesis
Christopher Boddy, Ph.D., Professor & Director, Biochemistry Program, University of Ottawa

Synthetic biology approaches are dramatically impacting the scientific community's ability to heterologous express complex natural product biosynthetic pathways, revolutionizing the discovery and characterization of these pathways as well as the development the natural products they encode. In this presentation we will highlight new strategies for heterologous expression of bacterial biosynthetic pathways, focusing on the violacein biosynthetic pathway, and examine methods to harness biosynthetic pathways for overproduction of natural products, using nonulosonic acid biosynthetic pathways.

11:45 Data-Driven Approaches for Rapid Scale-Up of Bioproducts
Derek Abbott, Ph.D., Director, Analytics, Amyris, Inc.

Optimization of microbial production of any product requires repeated iterations of the design-build-test-analyze engineering cycle to achieve economic viability. The presentation covers details of the automated platforms that enable Amyris scientists to rapidly cycle through a data-driven strain improvement process. Additionally, we present our vision for how the industry can leverage these platforms to positively impact the bioeconomy by dramatically reducing the cost and time to market for a variety of molecules.

12:15 pm SELECTED POSTER PRESENTATION: A High Throughput Approach to Construct Generation and Expression Screening for Recombinant Protein Production
Christine Kugel, Scientific Researcher, Biomolecular Resources, Genentech, Inc.

12:45 Session Break

1:00 Luncheon Presentation I: A Systematic Approach to Address Development and Production Challenges for Complex Biologics

Sponsored by ATUM

Claes Gustafsson, Ph.D., CCO & Founder, ATUM (formerly DNA2.0)

By using design of experiment (DoE) methodologies coupled with machine learning, transient transfection has been optimized to yield milligram levels of purified proteins in just a few days. Stable cell lines can be created in weeks to generate proteins at the gram scale. Case studies showing

how these methods have been applied to multiple targets including soluble secreted proteins and integral membrane proteins will be presented.

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

GENOME ENGINEERING

2:00 **Chairperson's Remarks**

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

2:05 **CRISPR/Cas Tools for Host Cell Improvement in the Baculovirus-Insect Cell System**

Donald L. Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming

One of my group's major efforts has focused on engineering protein glycosylation pathways in the baculovirus-insect cell system (BICS) to create new systems capable of producing "humanized" recombinant glycoproteins. We report development of novel CRISPR/Cas9 tools for site-specific genome editing in the BICS. We then describe the use of these new tools to enhance our glycoengineering efforts by targeting an endogenous *Spodoptera frugiperda* (Sf) glycogene, which antagonizes human-type glycan elongation.

2:35 **New Strategies of CRISPR/Cas9-Based High-Throughput Functional Genomic Screening**

Dongxin Zhao, Ph.D., Postdoctoral Fellow, Prashant Mali Lab, Department of Bioengineering, University of California, San Diego

Cancer is a complex disease of which targetable vulnerabilities are the consequence of reprogramming of genetic architecture driven by various genetic mutations. Dissection of genetic interactions in a systematic way would provide unprecedented insights in drug discovery. Applying the new powerful CRISPR/Cas9 technology, we developed a combinatorial screening platform which allows for both high-throughput mapping of synthetic lethality and quantification of cancer cell type-specific interactions in metabolic circus.

3:05 **Transition to BuzZ Sessions**

3:15 **BuzZ Sessions with Refreshments**

BuzZ sessions

Join your peers and colleagues for interactive roundtable discussions.

Please see page 78 for additional information.

4:30 **Mammalian Display: Antibody Discovery, Affinity Maturation and Developability Screening in IgG Format**

Mike Dyson, Ph.D., CTO, IONTAS, Ltd.

Using directed integration of antibody genes by CRISPR/Cas9 and TALE nucleases, we have constructed large libraries in mammalian cells containing a single antibody gene/cell. This has permitted construction of millions of monoclonal stable cell lines displaying IgG antibodies on their surface from which antibodies have been selected by flow cytometry for specificity, binding affinity, species cross-reactivity and expression level. Expression in production cell lines also enables high-throughput developability screening.

5:00 **RNA Structural Determinants of Optimal Codons Revealed by MAGE-Seq**

Eric Kelsic, Ph.D., Staff Scientist, George Church Laboratory, Wyss Institute, Harvard Medical School

To understand the determinants of codon choice across a gene, we generated 12,726 *in situ* codon mutants in the *Escherichia coli* essential gene infA and measured their fitness with MAGE-seq. Correlating predicted 5' RNA structure with fitness revealed that codons even far from the start of the gene are deleterious if they disrupt the native 5' RNA conformation. Our results shed light on natural codon distributions and should improve engineering of gene expression for synthetic biology applications.

5:30 PANEL DISCUSSION: **CRISPR/Cas Genome Editing for Protein Expression**

CRISPR/Cas has emerged as a powerful tool for engineering the genome in diverse organisms. However, there are also financial and legal considerations in using this tool. Hear this panel of experts discuss the pros and cons of CRISPR/Cas genome editing and its role in enhancing desired protein expression.

Moderator:

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

Panelists:

Mike Dyson, Ph.D., CTO, IONTAS, Ltd.

Donald L. Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming

Eric Kelsic, Ph.D., Staff Scientist, George Church Laboratory, Wyss Institute, Harvard Medical School

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

Dongxin Zhao, Ph.D., Postdoctoral Fellow, Prashant Mali Lab, Department of Bioengineering, University of California, San Diego

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

Sponsored by MO TEMPER

7:15 **Close of Day**

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

CASE STUDIES IN ENHANCING EXPRESSION SYSTEMS

8:30 **Chairperson's Remarks**

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

FEATURED PRESENTATION

8:35 **Engineering Cell Factories for Protein Production**

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

We have engineered cell-based factories for protein production, using state-of-the-art technologies combined with high-throughput genome engineering, *in silico* modeling, deep -omics analysis and big data analysis. Our main focus is CHO cells, where we have generated a panel of CHO cell lines, with optimized phenotypes generating tailormade PTMs, improved bioprocess and product quality, etc.

JANUARY 8-9 | 10TH ANNUAL

Engineering Genes and Hosts

Exploring Strategies in Systems Engineering and Synthetic Biology

9:05 SKIK Tag Increasing the Expression of Hard-to-Express Proteins and Its Application to Antibody Screening from Single B Cells

Teruyo Ojima-Kato, Ph.D., Researcher, Meijo University

A novel tag sequence SKIK can drastically increase the expression of hard-to-express proteins in *Eschericha coli in vivo* and *in vitro* protein synthesis systems without affecting its activity in most cases. We used the peptide for a novel antibody production from single B cells by RT-PCR, PCR and cell-free protein synthesis, because the amount of protein expressed can be highly improved and normalized for better evaluation of Fab synthesized.

9:35 Engineering a CHO K1 Toolbox for Reliable High Titer Protein Expression

Sponsored by horizon

Mario Pereira, Ph.D., Senior Scientist, Horizon Discovery

Aside from single gene knockouts to allow for metabolic selection systems, the CHO host remains largely unchanged. I will present how we have used a combination of techniques including genome engineering approaches such as CRISPR and rAAV to improve the biomanufacturing capacity of our GS knockout CHO K1 cell line.

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

11:30 Establishing Protein Production without Reinventing the Wheel: ProteinData.Cloud

Peter Nollert, Ph.D., Business Director, Research and Development, Bio Data Bridges

Establishing viable paths for recombinant protein sample production is typically inefficient due to the commonly applied laborious trial-and-error approach. ProteinData.Cloud is a platform to access and share otherwise invisible experimental recombinant protein production information. Researchers find engineered vector sequences, positive and negative recombinant expression trials and purification detail, apply and improve recombinant protein production strategies to their own targets to improve protein production yield and purity.

12:00 pm Unlock *Pichia* – Novel Strategies and Molecular Tools to Enhance Protein Expression

Sponsored by VTU technology

Iskandar Dib, Ph.D., Principal Scientist DSP & Analytics, VTU Technology GmbH

Pichia pastoris is an established, safe and highly competitive expression host with strong and effective secretory capacities often resulting in double-digit g/l levels of recombinant protein. Recent research has brought about new exciting technologies increasing the potential of this already powerful yeast production host. An extended molecular toolbox addresses challenges in protein folding and secretion and facilitates the expression of more complex proteins, thus maximizing yields without compromising product quality.

12:30 Session Break

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

1:15 Close of Engineering Genes and Hosts Conference

JANUARY 9-10 | 2ND ANNUAL

Biocatalysis and Bio-Based Chemical Production

Biocatalysis, Enzyme and Metabolic Engineering, and Synthetic Biology

Advances in protein engineering, the advent of new chemistries and custom-made biocatalysis are leading to broader industrial enzyme across a range of industries, including pharma, fine chemicals and agriculture. Coupled with advances in systems and synthetic biology, the opportunities to create sustainable, scalable and cost-effective chemical production are greater than ever.

CHI's Second Annual Biocatalysis and Bio-Based Chemical Production conference tackles the latest advances in biocatalysis, metabolic and enzyme engineering, and synthetic biology, with dedicated sessions on new chemistries, protein engineering and novel applications of enzymes across a range of industries.

TUESDAY, JANUARY 9

1:00 pm Registration

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

NEW ADVANCES IN BIOCATALYSIS

2:00 Chairperson's Opening Remarks
David Rozzell, Ph.D., Senior Vice President, Biocatalysis, Provivi

KEYNOTE PRESENTATION

2:05 The Discovery of a New Enzyme 'Reductive Aminase'
Nicholas Turner, Ph.D., Professor, Chemical Biology, University of Manchester

The reductive aminase from Aspergillus oryzae (AspRedAm) is an NADP(H)-dependent oxidoreductase that has been shown to catalyse the enantioselective reductive coupling of a remarkably broad set of ketones and aldehydes with different amines, ranging from primary/secondary amines to ammonia, in up to >98% conversion and with >98% enantiomeric excess. The AspRedAm wild-type biocatalyst has been applied to reductive amination reactions on a preparative-scale, displaying total turnover numbers up to 32,000.

2:45 From Novel Enzymes to *de novo* Pathways and Designer Strains
Alexandre Zanghellini, Ph.D., CEO, Arzeda

Our ability to design cell factories to produce valuable chemicals requires the "recombination" not only of existing but also designer enzymes into novel metabolic pathways to achieve entirely new metabolic function. To this end, Arzeda is developing high-throughput computational methodologies to exploit natural enzyme latent catalytic promiscuity to rapidly design new catalysts. Successful applications of this approach will be presented.

3:15 Sponsored Presentation *(Opportunity Available)*

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

4:30 Bioinformatics and Machine Learning Methods to Accelerate Enzyme Engineering
James Lalonde, Ph.D., Senior Vice President, R&D, Codexis

Enzyme engineering has benefited from technological advances in the design, testing, and analysis of variant libraries. Molecular modeling methods inform library design, while automation (particularly for sequencing) accelerates testing, and machine learning algorithms facilitate elucidation of complex structure-function relationships. Integration of such advances will be presented, along with case studies highlighting efficient enzymatic synthesis of active pharmaceutical ingredients.

5:00 Genomic Mining of Aldehyde Deformylating Oxygenates Defines Structural Features that Enable Engineering of Function
Justin Siegel, Ph.D., Assistant Professor, Biochemistry & Molecular Medicine, UC Davis Genome Center

I will discuss the combination of genomic mining, structural biology, and machine learning to determine the structural features that enable soluble aldehyde deformylating oxygenase (ADO) activity. These features were then used to introduce ADO's activity into the small subunit of ribonucleotide reducatase.

5:30 Close of Day

5:30 - 5:45 Short Course Registration

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

WEDNESDAY, JANUARY 10

8:00 am Registration and Morning Coffee

NEW ENZYME SCREENING, DISCOVERY, DESIGN AND DEVELOPMENT — CASE STUDIES

8:30 Chairperson's Remarks
David Weiner, Ph.D., Vice President, Technology & Product Development, BASF Enzymes, LLC

8:35 Accelerating the Application of Biocatalysis for Drug Discovery and Development
Douglas Fuerst, Ph.D., Director, GSK Fellow, Advanced Manufacturing Technologies, GlaxoSmithKline

Advances in biocatalysis and directed evolution are increasing the number of opportunities to apply enzymes and cells in the synthesis of pharmaceutical compounds. This presentation will describe the approach being advanced at GlaxoSmithKline across both drug discovery and development highlighted with several relevant case studies.

9:05 Biocatalysis: An Enabling Technology for Rapid Chemical Process Development
Jacob Janey, Ph.D., Associate Director, BMS

Biocatalysis has long been recognized as a key, green chemical technology in the design of robust, efficient manufacturing routes for active pharmaceutical ingredients. It also represents an important tool for the rapid execution of "fit-for-purpose" campaigns to fund supplies of development compounds' early clinical studies.

JANUARY 9-10 | 2ND ANNUAL

Biocatalysis and Bio-Based Chemical Production

Biocatalysis, Enzyme and Metabolic Engineering, and Synthetic Biology

This talk will focus on informative case studies from BMS's Chemical and Synthetics Development organization where bespoke biocatalysts have served as a critical enabling technology for innovative synthetic route development.

9:35 Sponsored Presentation *(Opportunity Available)*

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

10:50 Towards a Synthetic Biology Platform for Natural Product Discovery

Charles Moore, Ph.D., Research Investigator, Novartis

The maturation of DNA sequencing technologies coupled with the rapid emergence of synthetic biology has turned (meta)genome mining into an attractive avenue to acquire novel chemical starting points to facilitate early lead discovery. We present our experiences from a multi-year effort to design and implement a natural product discovery pipeline based on principles of synthetic biology. This effort has permitted us to understand where bottlenecks reside and potentially how they could be addressed going forward.

11:20 Enzyme Engineering for Regioselective Hydroxylation in a Whole Cell Environment

Toni Lee, Ph.D., Senior Scientist, Biocatalysis, Provivi

Membrane-bound enzymes present unique challenges to protein engineers. We are currently generating (Z)-11-hexadecenol from the alkene using an oleaginous cell catalyst expressing membrane-anchored P450 alkane or fatty acid hydroxylases. Using a medium-throughput whole-cell screen, we detected hydroxylase homologs or single point mutants with improved regioselectivity for hydroxylating the desired terminus of the alkene. These findings have application to the production of lepidopteran sex pheromones for use in agricultural pest control.

11:50 The Potential of Biocatalysis for the Synthesis of Small Drugs: Exploiting the Promiscuity of Nucleoside and Nucleotide Phosphorylases

Peter Neubauer, Ph.D., Professor, Department of Bioprocess Technology, Institute of Biotechnology, Technische Universität Berlin

We develped a broad portfolio of recombinantly expressed thermophilic enzymes with wide substrate promiscuity by novel efficient parallel expression and purification strategies. They are efficient in the synthesis of a wide range of halogenated nucleosides by one-pot transglycosylation reactions. Also, we established an enzymatic phosphorylation cascade from nucleosides to nucleotides. These tools provide a solid basis for the efficient synthesis of a wide range of novel substances.

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

12:50 Session Break

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

STRAIN, ENZYME AND METABOLIC ENGINEERING

2:00 Chairperson's Remarks

Yoram Barak, Ph.D., Biosciences Innovation Manager, BASF Enzymes, LLC

2:05 Genome-Scale Engineering: A New Frontier in Metabolic Engineering

Huiman Zhao, Ph.D., Departments of Chemical and Biomolecular Engineering, Chemistry, and Biochemistry, Bioengineering, Institute for Genomic Biology, and Center for Biophysics and Computational Biology, University of Illinois

Advances in reading, writing and editing genomes have greatly expanded our ability to reprogram biological systems at the resolution of a single nucleotide and on the scale of a whole genome. In this talk, I will highlight our recent work in the development of new molecular parts and tools for genome-scale engineering and our attempt in automating the design, build and test cycle for strain development.

2:35 Engineering Cofactor Selectivity: Some New Ideas for an Old Problem

Scott Banta, Ph.D., Professor, Chemical Engineering, Columbia University

Engineering cofactor selectivity in dehydrogenases has been an important engineering goal for more than 25 years. We have been engineering just about every aspect of the NAD(H)-dependent thermostable alcohol dehydrogenase D (AdhD) from Pyrococcus furiosus. I will discuss recent insights into the engineering of the cofactor selectivity of this enzyme, including the introduction of an intrinsically disordered peptide into the active site to tune cofactor selectivity by calcium addition.

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

4:00 Bringing Some Structure to Biocatalysis - Designing Genetically Programmable Biocatalytic Systems

Stefan Lutz, Ph.D., Professor and Department Chair, Department of Chemistry, Emory University

Protein-based nanocompartments represent robust carrier matrices for the assembly of artificial biocatalytic nanoreactors. Challenges related to ineffective permeability of metabolites due to small pores in the protein shell and lacking exterior surface functionality are addressed through protein engineering, enabling the creation of tailored carriers that can serve as highly versatile scaffold with excellent control over spatial organization of (bio)catalysts.

4:30 Combining Genome-Scale Modeling and Adaptive Laboratory Evolution to Optimize Enzymes and Whole Cells

Adam Feist, Ph.D., Project Scientist, Systems Biology Research Group, University of California

Constraint-based modeling is a predictive approach which can be utilized to drive metabolic engineering through simulating strain designs and integrating omics measurements. Adaptive laboratory evolution is a powerful experimental technique that, unlike rational engineering, is conducted without a priori knowledge on how beneficial traits would arise and therefore can result in unintuitive biological mechanisms. These two technologies can be combined to predict and acquire strains with beneficial industrial biotechnology capabilities.

5:00 The Role of Synthetic Biology in Creating New Pathways and Products

Srivatsan Raman, Ph.D., Assistant Professor, Departments of Biochemistry & Bacteriology, University of Wisconsin-Madison

5:30 - 6:45 Networking Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Biocatalysis and Bio-Based Chemical Production Conference

JANUARY 11-12 | 2ND ANNUAL

Microbial Production

Optimizing the Expression and Production of Microbial Expressed Proteins

Microbial expression systems offer significant advantages over other hosts by providing faster development times, greater yields, and lower production costs. However, limitations around glycosylation and central metabolic pathways poses significant challenges.

Cambridge Healthtech Institute's Microbial Production conference covers the latest developments in microbial expression and production – from host strain development to metabolic engineering, assembly to scale-up, downstream processing to process characterization – with particular focus on the role of *E. coli* for biotherapeutics and novel products.

THURSDAY, JANUARY 11

7:45 am Registration and Morning Coffee

INCREASING YIELD AND EXPRESSION

8:15 Chairperson's Opening Remarks
Georg Klima, Dipl. Ing., Executive Director, Process Science, Boehringer Ingelheim RCV GmbH & Co. KG

KEYNOTE PRESENTATION

8:20 Expression of Complex Proteins in *E. coli*
Dorothea Reilly, Ph.D., Principle Scientist and Associate Director, Early Stage Cell Culture, Genentech
Genentech produces recombinant proteins for therapeutic use employing both CHO cells and *E. coli*. We have developed *E. coli* processes that are optimized for the secretion of recombinant proteins into the periplasmic space where folding and assembly can occur. This talk will describe how these approaches have enabled the production of complex protein formats.

9:00 Pfizer *E. coli* Expression Platform Part I: Development and Testing of an Integrated Cloning and Expression System
Kevin Rust, Ph.D., Principal Scientist, Bioprocess R&D, BioTherapeutics Pharmaceutical Sciences, Pfizer, Inc.

9:30 Pfizer *E. coli* Expression Platform Part II: Application of the Platform to Test Reliably and Rapidly Achieve Increased Protein Yields
Marie Caparon, Ph.D., Associate Research Fellow, Bioprocess R&D, BioTherapeutics Pharmaceutical Sciences, Pfizer, Inc.
The presentation describes the application of an *E. coli* expression platform to reliably and rapidly achieve increased protein yields. This enables the development of new production processes that are commercially viable from both a cost of goods and capacity perspective. Case studies will be presented in which the original process presented significant challenges with respect to the cost of goods and the production capacity.

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

11:00 Easy Intracellular Recombinant Protein Expression in Yeast by *Pichia pastoris* Auto-Induction
Jonas Lee, Ph.D., Scientist, Amgen
Pichia pastoris is a highly successful recombinant microbial protein expression system due to its eukaryotic components while maintaining fast growth time. Despite these advantages, protein expression methods in *P. pastoris* are still burdensome due to a need to swap entire growth media to induction media. Here we present a simple method to auto-induce *P. pastoris* using the inhibitive properties of the AOX1 promoter by residual glycerol.

11:30 Microbial Secretion by ESETEC®: A Cost-Efficient Alternative to Mammalian Cells for Non-Glycosylated Proteins
Sponsored by WACKER
Sebastian Schuck, Ph.D., Head, Business Development, Wacker Biotech GmbH
The microbial secretion technology ESETEC® offers a cost- and time-efficient alternative for the production of biologics. With straightforward strain and process development, ESETEC® combines benefits of microbial and mammalian systems. Applying cutting-edge process simulation tools, we demonstrated that Cost-of-Goods for ESETEC® manufacturing is up to 3 times lower than CHO.

11:45 Sponsored Presentation *(Opportunity Available)*

12:00 pm Session Break

12:15 Luncheon Presentation I: cGMP Biologics Production Using Corynex®: A Highly-Productive Gram-Positive Microbial Protein Secretion System
Sponsored by AJINOMOTO
Yoshimi Kikuchi, Ph.D., Executive Professional and Group Manager, Recombinant Protein Research Group, Material Development & Application Labs, Ajinomoto Co., Inc.
Corynex® is Ajinomoto's highly-productive protein expression system based on the fast-growing gram-positive bacteria C. glutamicum. The powerful and easy-to-handle platform can secrete correctly-folded proteins directly into the media with high purity and no endotoxins. These advantages allow users to avoid many manufacturing/quality pitfalls and ultimately improve profitability and timelines. We recently demonstrated successful 1000L cGMP biologics production using Corynex®.

12:45 Luncheon Presentation II *(Sponsorship Opportunity Available)*

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

HOST ENGINEERING AND STRAIN DEVELOPMENT

2:00 Chairperson's Remarks
Christoph Reese, Ph.D., Director, Microbial Fermentation, Roche Diagnostics GmbH

2:05 *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.

2:35 A Strategy for Production of Correctly Folded Disulfide-Rich Peptides in the Periplasm of *E. coli*

Natalie Saez, Ph.D., Senior Research Officer, Institute for Molecular Bioscience, The University of Queensland

Disulfide bonds generally confer favorable properties, such as high stability, to the native peptides, but can pose considerable challenges for recombinant production. Presented herein is a method for recombinant expression of disulfide-rich peptides in the periplasm of *Escherichia coli* using a cleavable, solubility-enhancing fusion tag. Examples of recombinant periplasmically-expressed disulfide-rich venom peptides of therapeutic and/or commercial interest are provided.

3:05 Approaches and High Through-Put Tools to Solve Strain and Process Development Challenges for Recombinant Proteins Expressed in *E. coli*

Sponsored by FUJIFILM Diosynth Biotechnologies

Nigel Shipston, Ph.D., Director of Program Design, FUJIFILM Diosynth Biotechnologies

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

4:15 High-Yield, Mineral Medium, Antibiotics Free *E. coli* Expression System

Christoph Reese, Ph.D., Director, Microbial Fermentation, Roche Diagnostics GmbH

The development of a mineral medium based, antibiotics free *E. coli* expression system will be presented. In a case study, we show the suitability of the expression system for the manufacturing of a recombinant enzyme in industrial scale in high yield. The system may also be utilized to express otherwise insoluble proteins. A comparison to antibiotics-based selection systems and hydrolysates-based growth media will be discussed.

4:45 Holistic Process Development Strategies for Microbial Expression

Georg Klima, Dipl. Ing., Executive Director, Process Science, Boehringer Ingelheim RCV GmbH & Co. KG

Novel biotherapeutic formats pose unique development challenges. Strategies for successful development need to holistically consider all aspects of biopharmaceutical processes such as expression strategies, novel unit operations, automated high-throughput process development, as well as scale up and transfer from bench to large-scale manufacturing. We present our holistic approach based on a HTPD toolbox to lever the complexity of manufacturing development for non-platform biotherapeutics. Integration of the whole process is also discussed.

5:15 High-Throughput Automated Protein Folding and Quantitative Assessment

Philip An, Scientist, Biologics, Amgen

Employing *E. coli* to recombinantly express a gene of interest can enable rapid and robust production; however, the proteins are often located in inclusion bodies, necessitating a folding reaction to obtain their native state. To address this in a high-throughput, quantitative manner, we developed a dense folding matrix system that employs highly integrated liquid-handling automation and a quantitative assessment system to swiftly identify effective folding conditions.

5:45 Close of Day

FRIDAY, JANUARY 12

8:00 am Registration

8:00 BuzZ Sessions with Continental Breakfast

BuzZ sessions

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

Table Moderator: Adekunle O. Onadipe, Ph.D., Associate Research Fellow, Cell Line Development, Bioprocess R&D, Pfizer

MICROBIAL BIOPROCESSING AND PROCESS CHARACTERIZATION

9:00 Chairperson's Remarks

Adekunle O. Onadipe, Ph.D., Associate Research Fellow, Cell Line Development, Bioprocess R&D, Pfizer

FEATURED PRESENTATION

9:05 Microbial Process Development in View of Industry 4.0

Peter Neubauer, Ph.D., Prof. Dr., Chair of Bioprocess Engineering, Department of Biotechnology, Technische Universität Berlin

In our lab-of-the-future concept we integrate and fully automate all wetlab techniques for the production of competent cells, DNA transformation, optimization of cultivation parameters with the analytical methods for medium components and downstream operation to analyze product activity and other quality parameters. This allows us to apply a dynamic optimal design of experiments strategy (ODoE) to create digital twins for each target protein process (mechanistic models) which can be applied for computation-based bioprocess development.

9:35 A *S. Cerevisiae* Process Characterization for Production of a Therapeutic Recombinant Protein Using a Multivariate Analysis

Juan Aon, Ph.D., Senior Manager, MCCD, RD Biopharm, R&D, GSK

10:05 Microbial Expression and Production of Pasylated Proteins and Peptides: Biobetters with Extended Half-Life and Enhanced Action

Uli Binde, Ph.D., CTO, XL-Protein

PASylation comprises the genetic fusion of biologics with a natively disordered biosynthetic polymer made of Pro, Ala and/or Ser (PAS). Such PAS sequences are highly soluble in physiological solution and stably adopt random coil conformation with an expanded hydrodynamic volume which leads to retarded kidney filtration and drastically prolonged

pharmacokinetics *in vivo*. PASfusion proteins often show improved stability, and they can be produced in a single step in microbial hosts, thus avoiding costly chemical modification steps.

10:35 Coffee Break with a Poster Pavilion
See page 4 for details

11:15 Towards a New Generation of Glycoengineered Pneumococcal Bioconjugate Vaccines
Christian Harding, Ph.D., CSO, VaxNewMo
Glyco-conjugate vaccines, consisting of a polysaccharide attached to a carrier protein, are excellent immunogens manufactured using labor-intensive chemical crosslinking steps. As an innovative alternative, VaxNewMo utilizes a glycoengineering strategy to generate "bioconjugates" in *Escherichia coli.* Key to this process is a conjugating enzyme, which attaches a polysaccharide to a protein.

11:45 Recoded *E. coli* for Incorporation of Non-Natural Amino Acids and Also for the Purpose of Genetic Isolation
Farren Isaacs, Ph.D., Assistant Professor, Molecular Cellular and Development Biology, Yale University
Genetically modified organisms (GMOs) are increasingly used in research and industrial systems to produce high-value pharmaceuticals, fuels, and chemicals. Here, we describe the construction of a series of genomically recoded organisms (GROs), 11 whose growth is restricted by the expression of multiple essential genes that depend on exogenously supplied synthetic amino acids (sAAs).

12:15 pm Conference Wrap-Up
Adekunle O. Onadipe, Ph.D., Associate Research Fellow, Cell Line Development, Bioprocess R&D, Pfizer

12:45 Close of Conference

BuzZ sessions

What's the BuzZ about?

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

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Comprehensive sponsorship packages allow you to achieve your objectives before, during, and long after the event. Signing on earlier will allow you to maximize exposure to hard-to-reach decision-makers.

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For Sponsorship and Exhibit Information, Please Contact:

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781-972-5452 jgerardi@healthtech.com

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Carol Dinerstein
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781-972-5471 dinerstein@healthtech.com

View current **Exhibitor List** and **Floor Plan**

Register as an **Exhibitor** Here

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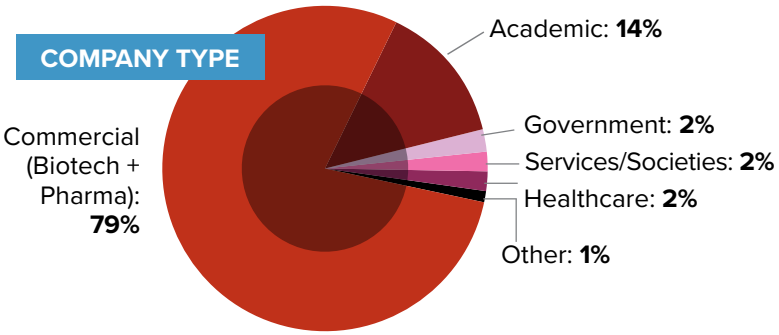

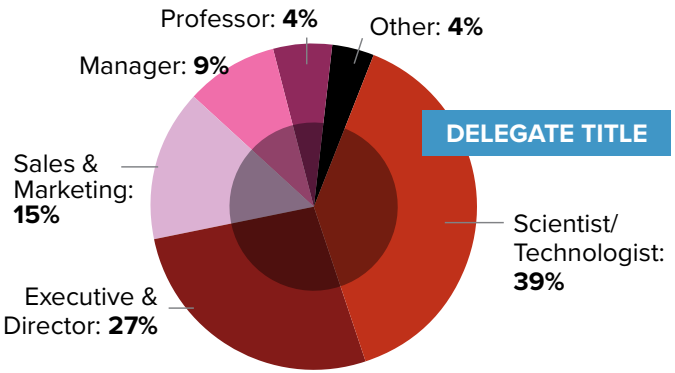

HOTEL & TRAVEL INFORMATION

Conference Venue and Hotel:
Hilton San Diego Bayfront
One Park Boulevard
San Diego, CA 92101
T: 619-564-3333

Reservations:
Visit the travel page of CHI-PepTalk.com

Discounted Room Rate:
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	Commercial	Academic, Government, Hospital-affiliated
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Tuesday, January 9 | 5:45-8:45 pm

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Poster Submission - Discount ($50 Off): Poster abstracts are due by November 10. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact jring@healthtech.com. *CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

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Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link. **Handicapped Equal Access:** In accordance with the ADA, Cambridge Healthtech Institute is pleased to arrange special accommodations for attendees with special needs. All requests for such assistance must be submitted in writing to CHI at least 30 days prior to the start of the meeting.

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