22ND ANNUAL

PepTalk

JANUARY 16-20, 2023 | SAN DIEGO, CA

HILTON SAN DIEGO BAYFRONT & VIRTUAL

THE PROTEIN SCIENCE AND PRODUCTION WEEK

2023 PROGRAMS

Click on pipeline title to view full agenda

- ANTIBODY DISCOVERY & ENGINEERING
- BISPECIFIC ANTIBODY DEVELOPMENT
- CHARACTERIZATION OF BIOTHERAPEUTICS & VACCINES
- CELL & GENE THERAPY
- BIOTHERAPEUTIC EXPRESSION & PRODUCTION
- PROCESS TECHNOLOGY & INNOVATION
- TS TRAINING SEMINARS

RESERVE YOUR SPOT DECEMBER 2

ADVANCE SAVINGS UP TO $200

> "Being in person again was a real game-changer, and I met plenty of new friends and collaborators. The talks were excellent as always, and I have a lot of new information and ideas to bring home."
>
> *David W., The Ohio State University*

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ABOUT THE EVENT

Advancing Research and Innovation in Protein Science

PepTalk unites a global community of leading protein science, biopharma, and technology experts in the field of biotherapeutics research and development.

Join more than 1,000 participants in San Diego and online on January 16-20 for extensive learning and opportunities. Hear from some of the most influential and thought provoking speakers in the industry, gain insight into emerging strategies, innovative technologies, and best practices to move your research to the next level, and collaborate with your peers and build your network in a friendly atmosphere.

CONFERENCE PROGRAMS feature keynote presentations, case studies and new unpublished data from influential leaders in academia and industry.

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

BUZZ SESSION BREAKOUT GROUPS initiate discussions about current research and trends.

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

POSTER SESSIONS showcase cutting-edge, ongoing research – over 100 posters will be presented!

ON-DEMAND ARCHIVE of presentations to access on your own time.

PLENARY SESSION

Fireside Chat: Supporting and Driving Biotech: Past, Present, and Future

Wednesday, January 18 | 9:00 am-10:15 am

Innovation can refer to something new, such as an invention, or the development and introduction of new practices. The end result is often a new product, but it can also be a new practice, procedure, or way of thinking. Change and challenges are often what inspire innovation and propel us forward into new ways of thinking and doing. This Fireside Chat convenes long term supporters of PepTalk: The Protein Science and Production Week who will be exploring the following:

- Success stories
- Serendipitous discoveries
- Current projects
- Future developments

CHI-PepTalk.com #PTK23

REGISTER EARLY & SAVE!

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22nd Annual
PEPTALK

January 16-20-2023 | San Diego, CA
HILTON SAN DIEGO BAYFRONT AND ONLINE

2023

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CONFERENCE PROGRAMS

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CONFERENCE AT-A-GLANCE

PepTalk 2023

THE PROTEIN SCIENCE AND PRODUCTION WEEK

click pipeline or track titles to view full agenda

- ANTIBODY DISCOVERY & ENGINEERING
- BISPECIFIC ANTIBODY DEVELOPMENT
- CHARACTERIZATION OF BIOTHERAPEUTICS & VACCINES
- CELL & GENE THERAPY
- BIOTHERAPEUTIC EXPRESSION & PRODUCTION
- PROCESS TECHNOLOGY & INNOVATION
- TS TRAINING SEMINARS *In-Person Only*

Monday, January 16 - Tuesday, January 17 (am)	Tuesday, January 17 (pm) - Wednesday, January 18	Thursday, Janaury 19 - Friday, January 20
Intelligent Antibody Discovery Part I	Intelligent Antibody Discovery Part II	Creative Protein Engineering
Recommended Training Seminar: Intro to Bispecific Antibodies	Developability of Bispecific Antibodies	Safety and Efficacy of Bispecific Antibodies, ADCs and Combination Therapy
Characterization of Biotherapeutics	Characterizing Protein Aggregates and Impurities	Characterization and Development of Vaccines
Cell Therapy Analytics & Manufacturing	Gene Therapy Analytics & Manufacturing	*Recommended Training Seminar:* Intro to CMC for Biotech Cell & Gene Therapy Products
Cell Line Engineering and Development	Recombinant Protein Expression and Production	Optimizing Workflows in Protein Production Laboratories
Higher-Throughput Bioproduction	*Recommended Training Seminar:* Biomanufacturing 101	Advanced Purification and Recovery
Intro to Bispecific Antibodies Intro to Antibody Engineering Intro to Machine Learning for Biologics Design	Biomanufacturing 101 Antibody Deep Sequencing and Single Cell Analysis	Intro to CMC for Biotech Cell & Gene Therapy Products Biostatistics Basics for CMC Scientists and Data Reviewers

Your Safety is Our Top Priority

To ensure maximum safety, CHI has instituted mandatory health and safety protocols for all attendees, exhibitors, speakers, and staff who attend in person. Attendees who cannot participate because of this policy, or due to travel restrictions, are encouraged to participate using our highly praised virtual event platform. Our virtual events are designed to provide you with an in-person experience at your convenience, anywhere, anytime. We are actively following news and recommendations around COVID-19. These protocols are subject to change as we continue to learn more. All in-person attendees must: Have a negative COVID-19 test result from an FDA-authorized over-the-counter antigen test within 24 hours prior to arriving at the event. **You will be asked about your results at registration. CHI recommends all attendees: Have an updated COVID-19 vaccination and wear a mask in public spaces at the event.**

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Training SEMINARS

By Cambridge Healthtech Institute

IN-PERSON ONLY

MONDAY, JANUARY 16, 2023 9:00 - 6:00 PM | TUESDAY, JANUARY 17, 2023 8:45 - 12:40 PM

TS2A: Introduction to Bispecific Antibodies

Instructor:

G. Jonah Rainey, PhD, Senior Director, Protein Engineering, Eli Lilly and Company

Introduction to Bispecific Antibodies will be organized as an informative and practical guide to getting up to speed on critical aspects of bispecific antibody therapeutics. Topics will include historical successes, failures, and lessons learned. Specific practical instruction will span mechanisms of action, engineering, developability, regulatory considerations, and translational guidelines. Perspectives on the ideal implementation of bispecifics as targeted and immunomodulatory approaches will be discussed.

TS7A: Introduction to Antibody Engineering

Instructors:

Andrew R.M. Bradbury, PhD, CSO, Specifica, Inc.

James D. Marks, MD, PhD, Professor and Vice Chairman, Department of Anesthesia and Perioperative Care, University of California, San Francisco (UCSF); Chief of Performance Excellence, Zuckerberg San Francisco General Hospital and Trauma Center (ZSFG)

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 providing ample opportunities to discuss technology with instructors.

TS8A: Introduction to Machine Learning for Biologics Design

Instructors:

Christopher R. Corbeil, PhD, Research Officer, Human Health Therapeutics, National Research Council Canada

Francis Gaudreault, PhD, Research Officer, Human Health Therapeutics, National Research Council Canada

This course offers an introduction to the concepts, strategies, and machine learning methods used for biologics design. It consists of presentations and demonstrations of the methods used in the field, covering techniques such as triaging sequences, modulating affinity, and designing antibody libraries, along with increasing manufacturability. The course is directed at scientists new to the field and protein engineers wanting an introduction to how machine learning can aid in guiding biologics design.

TUESDAY, JANUARY 17, 2023 1:30 - 5:30 PM | WEDNESDAY, JANUARY 18, 2023 :00 - 5:45 PM

TS6B: Biomanufacturing 101: An Overview on Animal Cell Culture Technology from Cell Line Development to Scale-Up Strategies

Instructor:

Kamal A. Rashid, PhD, President, International Biotechnology Associates

In this seminar, we will take an in-depth look at modern cell culture techniques from a frozen stock to bioreactor design and operations. Cell line development, characterization, and scale-up strategies will be discussed in detail. Special emphasis will be placed on media design and optimization for specific clones to be utilized in production of biologics. We will highlight the significance of proper handling of cells in culture to avoid contamination and batch failure. Upstream processing of therapeutic proteins, monoclonal antibodies, and vaccines will be presented. After the completion of this seminar, the participants will have a clear understanding of the principles and techniques utilized in culturing animal cells for production of biologics, quality control of a cell culture laboratory, and types of contaminants of cells in culture with special emphasis on mycoplasma detection. They will learn scale-up strategies for suspension and anchorage-dependent cells utilizing stirred-tank bioreactors, hollow fiber bioreactors, and microcarrier cell culture technology.

THURSDAY, JANUARY 19, 2023 8:30 - 5:00 PM | FRIDAY, JANUARY 20, 2023 9:00 - 12:30 PM

TS4C: Introduction to CMC for Biotech, Cell & Gene Therapy Products

Instructor:

Kevin Zen, PhD, Executive Director, Chemistry Manufacturing and Controls, AnaptysBio, Inc.

The chemistry manufacturing and controls (CMC) of biologics is a multidiscipline technical operation of bioprocess, analytics, dosage formulation and cGMP manufacturing/testing for DS/DP release and stability to treat human diseases. This interactive training course will provide a comprehensive CMC overview of therapeutic biological products. It introduces a variety of therapeutic modalities including recombinant proteins, monoclonal antibodies (Mab), and cell and gene therapy (CGT) in the context of IMPD and IND regulatory filing. Attendees will learn scientific, technical, and operational aspects of overall biologics CMC activities as well as quality compliance and regulatory requirement. The instructor will present common pitfalls and share the best industry practices. Numerous real-world regulatory queries/comments from health authorities worldwide will be exemplified as case studies during the training course.

CHI Training Seminars Offer:

- 1.5-day instruction
- Morning and afternoon refreshments (as applicable; specific times included in the onsite agendas)
- Registered Attendees Receive:
- A hard copy handbook for the specific seminar of registration (limited additional handbooks are available for non-registered attendees)

CHI requests that Training Seminars not be interrupted once they have begun. We ask that attendees commit to attending the entire program to not disturb the hands-on style instruction being offered to other participants.

ANTIBODY DISCOVERY & ENGINEERING

PepTalk's **Antibody Discovery & Engineering** pipeline offers a forum for protein scientists working to quickly and efficiently discover and develop differentiated biotherapeutics for unmet medical needs. Two tracks are dedicated to the discipline of intelligent antibody discovery, with the first exploring new capabilities in the core technologies of next-generation sequencing and single cell analysis, and the second considering the integration of these tools into computational and machine learning models. The week concludes with a full track dedicated to creative approaches to engineering novel modalities and resolving significant targeting challenges.

PEPTALK

JANUARY 16-17

Intelligent Antibody Discovery Part One

AGENDA

JANUARY 17-18

Intelligent Antibody Discovery Part Two

AGENDA

JANUARY 19-20

Creative Protein Engineering

AGENDA

JANUARY 16-17, 2023 | Cambridge Healthtech Institute's 2nd Annual

INTELLIGENT ANTIBODY DISCOVERY: PART ONE

Next-Generation Technologies for Repertoire Sequencing and Single Cell Interrogation

SUNDAY, JANUARY 15

4:00 pm Pre-Conference Registration (Indigo Foyer)

MONDAY, JANUARY 16

7:00 am Registration and Morning Coffee (Indigo and Aqua Foyer)

9:00 Organizer's Welcome Remarks

ROOM LOCATION: Aqua Salon C

ADVANCING THE CAPABILITIES OF REPERTOIRE SEQUENCING

9:05 Chairperson's Opening Remarks

Lindsay Cowell, MS, PhD, Associate Professor; Peter O'Donnell Jr. School of Public Health; Department of Immunology, School of Biomedical Sciences; Population Science Program, Simmons Comprehensive Cancer Center; UT Southwestern Medical Center

9:10 KEYNOTE PRESENTATION: Near-Term Vision for Applications of Machine Learning in Biopharmaceutical R&D

Tommaso Biancalani, PhD, Director and Senior Scientist, AI/ML, Genentech, Inc.

How can AI help drug discovery? A short answer is "by making sense of large datasets." Indeed, new technologies have recently enabled the collection of massive amounts of data, which crucially needs AI-based analysis to translate this data into actionable insights. In the talk, I will describe two paradigmatic examples of how AI facilitates target discovery via analysis of sequencing data, and drug discovery by enabling molecular virtual screens.

9:50 Near-Comprehensive Exploration of Antigen and Antibody Functional Sequence Space Using Deep Mutational Scanning

Timothy A. Whitehead, PhD, Associate Professor, Chemical & Biological Engineering, University of Colorado, Boulder

Massively parallel, high-throughput measurements of protein function are essential for deep learning approaches promising to revolutionize antibody engineering. In this talk, I will describe our latest technologies enabling near-comprehensive exploration of functional sequence space. I will show the mapping of antibody escape mutants for the SARS-CoV-2 Spike RBD. Then, I will describe our antibody yeast display Fab platform which allows tracking of simultaneous heavy and light chain mutations.

10:20 Networking Coffee Break (Indigo and Aqua Foyer)

10:45 Combining NGS and Proteomics for Immune Repertoire Profiling

Jiwon Lee, PhD, Assistant Professor, Dartmouth College

Antibody repertoire established from previous exposures can persist in circulation and exert a major influence on the nature of subsequent responses. However, determining the relative contributions from pre-existing and newly-elicited antibodies can be difficult. We combine B cell repertoire sequencing with liquid-chromatography tandem mass-spectrometry proteomics to identify and quantify individual antibody clonotypes across multiple time points for in-depth analysis of the immunological memory and longevity of antibody responses in circulation.

11:15 Integrating NGS and Single-Cell Technologies with Machine Learning

Lindsay Cowell, MS, PhD, Associate Professor; Peter O'Donnell Jr. School of Public Health; Department of Immunology, School of Biomedical Sciences; Population Science Program, Simmons Comprehensive Cancer Center; UT Southwestern Medical Center

There has been a surge of interest in the potential of adaptive immune receptor repertoires to serve as a source of diagnostic and prognostic biomarkers. In this talk, I will discuss machine learning approaches for discovering repertoire sequence patterns that distinguish individuals with a shared clinical phenotype or outcome from control groups. Examples will include B cell and T cell receptor repertoires in autoimmune disease and cancer, respectively.

11:45 Rapid and Efficient Discovery of Antibodies Using LIBRA-seq

Andrea Shiakolas, PhD, Postdoctoral Researcher, Pathology, Microbiology, and Immunology, Vanderbilt University Vaccine Center

Antibody discovery relies on screening tools for prioritization of candidates for downstream characterization; the process is generally inefficient. To overcome these obstacles, we developed LIBRA-seq, which maps antibody sequences to antigen specificity using next-generation sequencing. We extended LIBRA-seq to include ligand blocking for the evaluation of antibody functionality at the screening step. Overall, LIBRA-seq presents a general platform with applications to virtually any area targeting the identification of antibody candidates.

12:15 pm Extending the Specifica Generation 3 Platform to Affinity Maturation

Andrew Bradbury, MB BS, PhD, CSO, Specifica

The Specifica Generation-3 Library Platform is based on highly developable clinical scaffolds, into which natural CDRs purged of sequence liabilities are embedded. The platform directly yields highly diverse, high affinity, developable, drug-like antibodies, as potent as those from immune sources, with minimal need for downstream optimization. This talk will discuss extension of the Platform to lead antibody improvement, with simultaneous enhancement of both affinity and developability.

12:45 Enjoy Lunch on Your Own

1:55 Session Break

HIGH-THROUGHPUT FUNCTIONAL ASSAYS

2:00 Chairperson's Remarks

Karyn McFadden, PhD, Senior Scientist, Amgen, Inc.

2:05 Computational + Experimental = A New Platform for the Discovery of Epitope-Specific Nanobodies

Xing Xu, PhD, Postdoctoral Researcher, Chemistry, University of Cambridge, United Kingdom

In silico design is emerging as an alternative way to generate nanobodies, facilitating the discovery of nanobodies that target epitopes with pre-determined biological functions. However, binding affinity of designed nanobodies is hardly optimal, limiting their practical application. Herein, we report a novel pipeline that integrates computer-guided rational design and *in vitro* selection from a synthetic library to identify epitope-specific nanobodies with improved binding affinity and developability.

2:35 High-Throughput Screening Platforms to Improve Antibody Discovery against Diverse Drug Targets

Brandon DeKosky, PhD, Phillip and Susan Ragon Career Development Professor of Chemical Engineering, MIT Core Member, The Ragon Institute of Massachusetts General Hospital, Massachusetts Institute of Technology, and Harvard

Antibody discovery technologies have made rapid progress against simple targets like soluble ectodomains, but discovery remains difficult against proteins like diverse/broad viral families, disordered proteins, and membrane proteins, delaying new antibody drug development against difficult targets. Here we will share case studies of effective library-scale approaches to engineer new antibodies against the disordered malaria circumsporozoite protein (CSP), broad HIV-1 viral strains, and against membrane protein targets.

ROOM LOCATION: Indigo and Aqua Foyer

BuzZ Sessions

3:05 Find Your Table and Meet the BuzZ Sessions Moderator

3:10 BuzZ Sessions with Refreshments (IN-PERSON ONLY)

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.
Please continue to check the BuzZ Session page on our conference website for detailed discussion topics and moderators.

BuzZ Table 1: Deep Profiling of Ab Sequence-function Relationships by Deep Sequencing

Timothy A. Whitehead, PhD, Associate Professor, Chemical & Biological Engineering, University of Colorado, Boulder

BuzZ Table 8: Implementation Challenges for Machine Learning as a Tool for Antibody Discovery

Christopher Negron, PhD, Principal Research Scientist, AbbVie, Inc.

IMPROVING THE RESOLUTION AND RANGE OF SINGLE-CELL ANALYSIS

4:30 Immune Repertoire Characterization from the Peripheral Blood of Mice

Karyn McFadden, PhD, Senior Scientist, Amgen, Inc.

In this talk, we will discuss a new process for the single cell characterization of antigen-specific B cells from humanely sampled peripheral blood of living mice. We leverage this protocol to screen the sequence diversity of the immune repertoire during immunization and used the information to steer the immune response toward our design goal.

5:00 Dynamic Imaging of T Cells for Infectious Diseases and Cancer Immunotherapy

Mohsen Fathi, PhD, Head of Technology, CellChorus, Inc.

Characterizing immune response during disease or profiling genetically modified immune cells for cancer treatment has enabled new challenges in quantifying functional immune response. Here, I describe two examples using the dynamic single-cell technology platforms we developed to address these problems: (1) the use of integrated dynamic and transcriptional single-cell profiling to identify clinical response biomarkers for T cell therapy; (2) the nature of the cytotoxic T cell responses elicited upon SARS-CoV-2 infection.

5:30 Application of Peptide Microarrays to Analyze Differences in Epstein-Barr Virus Antibody Epitopes across a Diverse Sample Set

Chris Diehnelt, PhD, Founder & CEO, Robust Diagnostics LLC

Epstein-Barr virus (EBV) infects over 80% of the population and periodically reactivates causing antibody response to EBV containing epitopes that mimic host proteins and epitope response differences could be important to understanding the disease. We developed an EBV epitope peptide microarray to resolve epitope level differences in IgG and IgM responses in a COVID +/- cohort.

6:00 Welcome Reception in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

YOUNG SCIENTIST MEET UP

Young Scientist Meet Up

Iris Goldman, Production, Cambridge Innovation Institute

7:30 Close of Day

CITY WALK MEET UP

BREAKOUT DISCUSSION: City Walk Meet Up

Kevin Brawley, Associate Project Manager, Production Operations & Communications, Cambridge Innovation Institute

TUESDAY, JANUARY 17

8:15 am Registration and Morning Coffee (Indigo and Aqua Foyer)

ROOM LOCATION: Aqua Salon C

EMERGING PLATFORMS AND CAPABILITIES

8:45 Chairperson's Remarks

Christopher Negron, PhD, Principal Research Scientist, AbbVie, Inc.

8:50 NGS-Based Antibody Discovery from Phage Libraries Enables Deeper Repertoire Mining of Antigen-Specific Antibodies

Ankit Mahendra, PhD, Principal Scientist, Antibody Platform, Large Molecule Research, Sanofi USA

We have developed a comprehensive process of NGS-based analysis of phage panning to follow the enrichment of antibody sequences along the different panning rounds. To obtain information on cognate chain pairs we used long-read PacBio sequencing method and developed an NGS analysis pipeline to analyze the enrichment of paired VH/VL sequences of antibodies. Our results indicated a 125% increase in identifying novel antibody sequences over traditional panning method.

9:20 From Structure to Sequence: Antibody Discovery Using cryoEM

Andrew Ward, PhD, Professor, Integrative Structural and Computational Biology, Scripps Research Institute

Antibody discovery of specific, quaternary epitopes of membrane proteins can be a difficult process. Here, we have devised a novel approach to harness cryoEM and generate many heterogeneous polyclonal antibody-antigen complexes at high resolution in a single experiment. By combining these data with B cell receptor repertoire analysis we circumvent the need to isolate individual B cells and generate monoclonal antibodies against specific epitopes for further characterization.

9:50 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

10:30 An *in silico* Method to Assess Antibody Fragment Polyreactivity

Edward Harvey, PhD, Postdoctoral Researcher, Biological Chemistry and Molecular Pharmacology, Harvard Medical School

Polyreactive antibodies compromise screening pipelines and are generally intractable for clinical development. We designed experiments using a synthetic camelid antibody fragment ('nanobody') library to enable machine learning models to accurately assess polyreactivity from protein sequence (AUC>0.8). Our models provide quantitative metrics that predict the effect of amino acid substitutions on polyreactivity. We experimentally tested their performance on three nanobody scaffolds, where over 90% of predicted substitutions successfully reduced polyreactivity.

11:00 Identifying mAb Sequence and Structure Features for Developability Assessment

Christopher Negron, PhD, Principal Research Scientist, AbbVie, Inc.

With over 100 approved antibody-based therapeutics, the format is a well-established starting point for drug discovery. Despite this success, lead antibodies may suffer from undesired molecular properties. Thus, we present the Therapeutic Antibody Developability Analysis (TA-DA). A tool built by testing hundreds of sequence- and structure-based descriptors at differentiating clinical antibodies from non-natively paired human repertoire antibodies.

11:30 Talk Title to be Announced

Speaker to be Announced

11:45 Accelerated Antibody Discovery: The Intersection of Hyper-Throughput™ and Function-First Screening

Shawn Manchester, VP of Products, Triplebar

Triplebar discovers antibodies produced by mammalian expression hosts by directly measuring the function of millions of variants each day using miniaturized cell-based assays in our proprietary Hyperthroughput (HyTS) microfluidics platform. We simultaneously screen for function and developability, and avoid time-consuming reformatting from different screening modalities. We aim to find solutions for the most difficult targets, including GPCR agonists and membrane proteins, by using our function-first approach.

12:00 pm Session Break and Transition to Luncheon Presentation

12:10 Incorporating Biological Intelligence with Computational Tools to Generate Highly-Specific Therapeutic Antibodies

Todd Pettingill, Vice President, Business Development and Strategy, OmniAb, Inc.

The OmniAb antibody discovery platform leverages ***in vivo*** powered Biological Intelligence and Computational Tools to generate, recover and optimize high-quality therapeutic candidates. OmniAb antibodies have been used by partners in a variety of modalities towards a variety of targets. The four-species platform provides access to a diverse range of potential therapeutic antibody candidates. A single license provides access to OmniAb's wide range of antibody discovery technologies and services.

12:40 Close of Intelligent Antibody Discovery Part 1

JANUARY 17-18, 2023 | Cambridge Healthtech Institute's 2nd Annual

INTELLIGENT ANTIBODY DISCOVERY: PART TWO

Integrating Next-Generation Discovery Tools, Transitioning to Computational Design and Machine Learning

TUESDAY, JANUARY 17

12:45 pm Registration (Indigo Foyer)

1:00 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

1:30 Organizer's Welcome Remarks

ROOM LOCATION: Aqua Salon C

1:35 Chairperson's Remarks

Qing Chai, PhD, Research Advisor, BioTechnology Discovery Research, Eli Lilly & Co.

1:40 KEYNOTE PRESENTATION: Deep Learning in Antibody Engineering

Jeffrey J. Gray, PhD, Professor & Research Mentor & Outreach Advisor, Chemical & Biomolecular Engineering, Johns Hopkins University

Deep learning (DL) is transforming the field of structural molecular biology, but antibodies present additional challenges due to their unique evolutionary mechanisms and their reliance on loops and interfaces. I will share how we address these challenges through our recent DL algorithms (IgFold, IgLM, FvHallucinator) for antibody structure prediction, library generation, and antibody design. I will close with a discussion of the prospects for artificial intelligence-based antibody engineering.

CASE STUDIES OF CURRENT APPLICATIONS OF MACHINE LEARNING

2:20 Benchmarking of Machine Learning Approaches for Antibody-Antigen Binding Prediction

Victor Greiff, PhD, Associate Professor, Immunology, University of Oslo

The unavailability of large-scale datasets hinders the ground-truth-based benchmarking of antibody-antigen binding prediction. We developed the Absolut! software that enables generation of synthetic lattice-based 3D-antibody-antigen binding structures with ground-truth access to conformational paratope, epitope, and affinity. We confirmed that accuracy-based rankings of ML methods trained on experimental data hold for ML methods trained on Absolut!-generated data. The Absolut! framework enables real-world relevant benchmarking of ML strategies for biotherapeutics design.

2:50 Presentation to be Announced Machine Learning in Support of Library Design with Improved Biophysical Properties

Tushar Jain, PhD, Principal Scientist, Computational Biology, Adimab LLC

Specificity, chemical stability, and manufacturability are important facets for an antibody therapeutic. We combine auto-regressive modeling on sequences from NGS repertoires and functional output across diverse targets, with models for biophysical property prediction to generate novel synthetic libraries with improved developability. We discuss the application of this approach to the development of Adimab's HCab platform generating high-affinity developable output across therapeutically relevant antigens, in a traditionally difficult modality.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

4:00 Machine Learning to Predict Pharmaceutical Properties of Candidate Biotherapeutics

Qing Chai, PhD, Research Advisor, BioTechnology Discovery Research, Eli Lilly & Co.

Computational approaches are transforming therapeutic antibody discovery on speed and success. Among them, knowledge-based machine learning becomes a powerful tool enabling virtual screening of thousands of sequences for desired properties. This talk will discuss the development of prediction models, as well as the effective utilization of prediction algorithms to speed up quality hits discovery.

4:30 Fueling ML-Assisted Antibody Discovery and Optimization with High-Throughput Protein-Protein Interaction Data

Randolph Lopez, PhD, CTO and Co-Founder, A-Alpha-Bio

Current antibody development methods are limited by the availability of large datasets of antibody-antigen binding data. In this talk, we demonstrate how large datasets of multi-dimensional antibody-antigen data and associated machine learning models enable the discovery and optimization of antibodies with desired affinity, cross-reactivity, epitope, and bio-developability. We introduce A-Alpha Bio's protein-protein interaction database with over 100M protein-protein interactions and describe initial work towards developing a generalizable antibody-antigen binding model.

5:00 Applications of Deep Learning for *De Novo* Protein Optimization

Kelly Duong, PhD, Machine Learning Research Engineer, Computational Protein Design, Neoleukin Therapeutics, Inc.

Exploring the vast sequence space is a major challenge in designing ***de novo*** proteins. Optimizing for one trait often comes at the expense of another. Utilizing pre-trained language models and graph neural networks, we show that ***de novo*** cytokine mimetics that express well, fold into the desired structure, are thermostable and bind to their desired targets can be generated at a much higher success rate than with traditional physics-based simulation.

5:30 Close of Day

WEDNESDAY, JANUARY 18

8:30 am Registration and Morning Coffee (Indigo and Aqua Foyer)

ROOM LOCATION: Aqua Salon CDE

9:00 Organizer's Remarks

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

9:10 Plenary Fireside Chat: Supporting and Driving Biotech: Past, Present, and Future

Moderator: Julie Ames, Vice President, Corporate Communications, Biocom California

Innovation can refer to something new, like an invention, or the development and introduction of new practices. The end result is often a new product, but it can also be a new practice, procedure, or way of thinking. Change and challenges are often what inspire innovation and propel us forward into new ways of thinking. This Fireside Chat will explore the following:

- Success stories
- Serendipitous discoveries
- Current projects
- Future developments

Panelists:
Amy K. Butler, PhD, President, Biosciences, Thermo Fisher Scientific
Taegen Clary, Vice President, Marketing, Unchained Labs
Jonathan Haigh, PhD, MBA, Vice President, Process Development, Fujifilm Diosynth Biotechnologies
Craig R. Monell, PhD, Vice President, Sales, Marketing & Business Development, BioLegend, Inc.

10:15 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

ROOM LOCATION: Aqua Salon C

NEXT-GENERATION APPLICATIONS OF MACHINE LEARNING

11:00 Chairperson's Remarks

James Bowman, PhD, Head, Discovery, AI Proteins

11:05 Developing Deep Learning Models to Accelerate Molecular Dynamics Simulations for Antibody Drug Development

Pin-Kuang Lai, PhD, Assistant Professor, Department of Chemical Engineering and Materials Science, Stevens Institute of Technology

In this talk, we will present our recent development by combining a high-throughput molecular dynamics simulation platform and neural networks to accelerate the prediction of antibody biophysical properties, including solvent accessible surface area, charge, and hydrophobicity. These models, requiring only protein sequences, can accelerate the prediction of antibody biophysical properties from hours using supercomputers to seconds using laptops, an essential advantage for screening antibody drug candidates.

11:35 Integrating Antibody Sequencing Results with AI for Development of Predictive and Generative Algorithms

Simon Kelow, PhD, Scientist, Structure & Computational, Prescient Design, a Genentech Company

Antibody sequencing data has grown exponentially concomitant with the discovery and engineering of next-generation sequencing technologies. Generative machine learning models have the potential to learn complex relationships between sequences and benefit from large, heterogeneous sequence datasets. Here we describe advances in generative modeling of antibody sequences towards antibody design and property prediction, with a focus on incorporating structural information *via* structure prediction software.

12:05 pm Lunch on Your Own

12:35 Enjoy Lunch on Your Own

1:45 Session Break

TOWARD *DE NOVO* DESIGN

2:00 Chairperson's Remarks

Brian Hie, PhD, Science Fellow, Biochemistry, Stanford University School of Medicine

2:05 *De novo* Designed Miniproteins Have Big Potential for Therapeutic Development

James Bowman, PhD, Head, Discovery, AI Proteins

Miniproteins are a powerful yet underutilized therapeutic modality. They are only 30-90 amino acids in length, yet they adopt a folded tertiary structure like a much larger protein; this structure enables miniproteins to bind with high affinity and specificity to their targets. Miniproteins found in nature are very challenging to engineer to bind new targets. We solved this problem using computational *de novo* design, finally unlocking miniproteins for therapeutic development.

2:35 Biopharmaceutical Informatics: How to Discover and Develop Biotherapeutics *in silico*

Sandeep Kumar, PhD, Distinguished Research Fellow, Computational Biochemistry and Bioinformatics, Boehringer Ingelheim Pharmaceuticals

In this talk, I shall introduce my strategic vision of Biopharmaceutical Informatics and how it can be used to discover developable biotherapeutics.

3:05 Application of a Generative Adversarial Network for the Design of Antibody Display Libraries

Rutilio Clark, PhD, Scientific Director, Antibody Discovery and Optimization, Just - Evotec Biologics

We constructed two antibody display libraries using a Generative Adversarial Network (GAN) machine learning algorithm. ML pattern recognition of IgG human repertoire has enabled application of V(D)J-gene diversity of CDRs and frameworks into our Just Humanoid Antibody Library (J.HAL). The phage Fab library exhibited success in multiple discovery campaigns and is currently undergoing diversity expansion to improve success rates. The yeast VHH library has demonstrated value for novel therapeutic discovery.

PepTalk Plaza: Speed Networking

IN-PERSON ONLY: Speed Networking

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

MACHINE LEARNING IN STRUCTURAL BIOLOGY

4:15 Structure-Based Generative Model for *in silico* Binder Design

Possu Huang, PhD, Assistant Professor, Bioengineering, Stanford University

We developed a deep learning-based protein-protein interface (PPI) design pipeline that leverages a generative model (Ig-VAE) for 3D protein generation. This novel strategy uses neural networks' capabilities in capturing dynamic structures to create a fully flexible structural docking process for PPI design. The approach can sample protein conformations at an unprecedented speed and optimize structures for predefined functions. I will describe our current results on designing epitope-specific protein binders.

4:45 Assessing the Quality of Antibody-Antigen Models Using AlphaFold

Francis Gaudreault, PhD, Research Officer, Human Health Therapeutics, National Research Council Canada

AlphaFold has revolutionized the structure prediction of proteins alone or in the complex. The need for co-evolutionary sequence constraints for structure prediction limits its use against antibody-antigen complexes. We predicted the structure of antibody-antigen complexes using traditional physics-based protein-protein docking tools. We evaluated the ability of AlphaFold in the quality assessment of models. Our results highlight that AlphaFold can rescue poorly-ranked models and better discriminate good-quality models from decoys.

EXPERIMENTAL VALIDATION

5:15 Efficient Evolution of Human Antibodies from General Protein Language Models and Sequence Information Alone

Brian Hie, PhD, Science Fellow, Biochemistry, Stanford University School of Medicine

We show that deep learning algorithms known as protein language models can evolve human antibodies with high efficiency, despite providing the models with no information about the target antigen, binding specificity, or protein structure, and also requiring no additional task-specific finetuning or supervision. Screening 20 or fewer language-model-guided variants of seven antibodies over just two rounds of evolution, we improved binding affinities up to 160-fold across diverse viral antigens.

5:45 Networking Reception in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

WOMEN IN SCIENCE MEET UP AT PEPTALK PLAZA

Women in Science Meet Up at PepTalk Plaza

Christa Cortesio, PhD, Senior Scientist and Group Lead, Protein Science, Protein Biochemistry & Analytics Core, Kite Pharma

Michelle R. Gaylord, MS, Principal Scientist, Protein Expression Lead, Velia, Inc.

7:00 Close of Intelligent Antibody Discovery Part 2

JANUARY 19-20, 2023 | Cambridge Healthtech Institute's 2nd Annual

CREATIVE PROTEIN ENGINEERING

Strategies for Engineering Complex New Modalities

THURSDAY, JANUARY 19

8:00 am Registration and Morning Coffee (Indigo and Aqua Foyer)

8:30 Organizer's Welcome Remarks

ROOM LOCATION: Aqua Salon C

8:35 Chairperson's Opening Remarks

Yuan Cheng, PhD, Senior Principal Scientist, Therapeutic Discovery, Amgen, Inc.

8:40 KEYNOTE PRESENTATION: Evolvability and Developability in Synthetic Scaffolds

Benjamin J. Hackel, PhD, Associate Professor, Chemical Engineering & Materials Science, University of Minnesota

Synthetic miniproteins are compelling scaffolds for binding ligands with advantageous modularity, physiological transport, and efficient synthesis. We have evaluated the evolvability and developability of >50 miniprotein libraries systematically varied across topology, framework, and paratope location. We evolved binders to eight targets and measured proxies of solubility, expression, and stability for millions of scaffold variants. The result elucidates biophysical factors that dictate miniprotein scaffold performance thereby empowering library and clone design.

NEXT-GENERATION CONJUGATES AND FUSIONS

9:20 Toll-Like Receptor Agonist Antibody Conjugate for Targeted Immune Activation

Min Li, PhD, Director, Protein Science, Tallac Therapeutics Inc

Tallac Therapeutics focuses on novel therapeutics engaging both innate and adaptive anti-tumor immunity. We developed a novel Toll-like Receptor Agonist Antibody Conjugate (TRAAC) platform to deliver a potent TLR9 agonist (T-CpG) for targeted immune activation *via* systemic administration. TRAAC molecules targeting either immune cell receptors or tumor-specific antigens demonstrated robust immune modulation and potent single-agent anti-tumor activity in preclinical settings, suggesting therapeutic potential across multiple solid tumor malignancies.

9:50 Comparing Potential Bispecific Formats of Trastuzumab and a Humanized OKT3

Donmienne Leung, PhD, Head of Protein Engineering, Absolute Antibody

Not every antibody can be combined to produce well-behaved multi-specifics. The valency and geometry of each design can determine the production, target engagement and ultimately the requisite biological functions. In this case study, we selected two established antibody therapeutics, trastuzumab and a humanized OKT3 to produce 20 different bispecific formats to compare the feasibility of each format.

10:05 Expression Platform for Producing Flexible and Novel Bispecific Modalities at Pandemic Speed

Sean Taylor, PhD, BD Executive, Business Development, GenScript

The expression of modified antibodies has opened the door for generation of new and powerful treatment options. The challenges associated with augmenting expression, controlling glycosylation and assuring appropriate assembly, folding and solubility of novel disease-specific antibodies have increased dramatically. We describe a novel platform to overcome the pitfalls of next generation antibody design with results demonstrating the production and purification of bispecific antibodies with native and modified glycosylation in weeks.

10:20 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

11:00 Discovery of a Bispecific GIPR Antagonist Antibody and GLP-1 Peptide Conjugate (AMG 133) for the Treatment of Obesity

Yuan Cheng, PhD, Senior Principal Scientist, Therapeutic Discovery, Amgen, Inc.

Gastric inhibitory polypeptide receptor (GIPR) plays a role in regulation of body weight and GLP-1 receptor agonists are known to control blood glucose levels. We will present the discovery of a novel GIPR antagonistic antibody and GLP-1 peptide conjugate (AMG 133) that demonstrated robust body weight reduction and significant improvement of metabolic parameters in preclinical models. AMG133 also displayed efficacy and tolerability in the Phase I clinical trial.

11:30 Enhancing the Anti-Tumor Efficacy of Bispecific T Cell Engagers *via* Cell Surface Glycocalyx Editing

Peng Wu, Professor, Chemical Physiology, Scripps Research Institute

We developed BiTE-sialidase fusion proteins that enhance tumor cell susceptibility to BiTE-mediated cytolysis by T cells *via* selective desialylation at the T cell-tumor cell interface that results in better immunological synapse formation. BiTE-sialidase fusion proteins exhibit superior efficacy both *in vitro* and *in vivo* when compared to BiTEs alone.

12:00 pm Enjoy Lunch on Your Own

1:10 Ice Cream Break in the Exhibit Hall and Last Chance for Poster Viewing (Indigo Ballroom)

DESIGNING MULTI-SPECIFICS FOR FUNCTION

2:00 Chairperson's Opening Remarks

Pawel Stocki, PhD, Vice President, Research, Ossianix, Inc.

2:05 Engineering CD28 Bispecific Antibodies and Cytokine Mimetics to Treat Solid Tumors

Gregory L. Moore, PhD, Senior Director, Protein Engineering, Xencor, Inc.

T cells require multiple signals (TCR engagement, costimulation, cytokines) for optimal activation, survival, and differentiation. However, T cells and positive signals are found sparingly in solid tumors. Traditional bispecific T cell engagers provide only TCR engagement (CD3) and may drive an incomplete anti-tumor response. We engineered CD28 bispecific antibodies and cytokine mimetics capable of providing T cells with additional signals and show that they provide enhanced activity over traditional bispecifics.

2:35 From Dual Targeting Fabs to Tri- and Tetravalent IgGs

Janina Speck, PhD, Science and People Lead, LMR Discovery, Roche, Germany

The DutaFab platform delivers fully human bispecific Fab molecules, which are structurally indistinguishable from a conventional monospecific Fab and can be reformatted into diverse antibody formats as required. Heavy and light chains both contribute to each of the two adjacent paratopes, which can be maturated independently to high affinities and combined in a modular way. Unique MoAs are achievable by either simultaneous or mutual exclusive binding to the two targets.

3:05 Networking Refreshment Break (Aqua Foyer)

ENGINEERING FOR TUMOR, TISSUE, AND ORGAN SPECIFICITY

3:30 Guided Antibody Tumor Engagers (TwoGATE): A Sophisticated and Differentiated Approach for T Cell Redirection in Solid Tumors

Kenneth J Simon, PhD, Senior Director, Biology, Revitope Oncology

Harnessing the immune system has revolutionized cancer treatment. However, on-target off-tumor toxicities limit their therapeutic potential. Revitope is developing a new class of cancer therapeutics

engineered with a split anti-CD3 paratope that enables targeting each inactive half-paratope to a different antigen on the same tumor cell. TwoGATE have pM potency *in vitro*, potently regress tumors *in vivo*, are well-tolerated in non-human primates, and have highly favorable developability properties.

4:00 Targeting KRas G12C Covalent Inhibitors in MHC I Complexes for Immunotherapy

Peter Rohweder, PhD, Researcher, University of California, San Francisco

Here we report that KRAS G12C mutant cells treated with the covalent inhibitor ARS1620 present ARS1620-modified peptides in MHC-I complexes. Using ARS1620-specific antibodies identified by phage display, we show that these haptenated MHC-I complexes can serve as tumor-specific neoantigens and that a bispecific T cell engager construct based on a hapten-specific antibody elicits a cytotoxic T cell response against KRAS G12C cells, including those resistant to direct KRAS G12C inhibition.

4:30 Development of Brain Delivery Shuttles Based on TfR1 Specific VNAR Antibodies – Translation to Primates

Pawel Stocki, PhD, Vice President, Research, Ossianix, Inc.

Poor brain delivery is a major hurdle in the development of biological therapeutics for neurologic diseases because of poor Blood-Brain Barrier (BBB) penetration. Numerous BBB shuttles based on single domain VNAR antibodies were developed by Ossianix. These include TXP1 which was demonstrated to penetrate the brain with high efficiency when inject at a low therapeutic dose in non-human primates with an over 30-fold increase in comparison to the control.

5:00 Close of Day

FRIDAY, JANUARY 20

7:30 am Registration (Indigo Foyer)

ROOM LOCATION: Indigo and Aqua Foyer

BuzZ Sessions

8:00 BuzZ Sessions with Continental Breakfast (IN-PERSON ONLY)

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.

Please continue to check the BuzZ Session page on our conference website for detailed discussion topics and moderators

BuzZ Table 4: VHH: Challenges & Opportunities

Andre Teixeira, PhD, Head, Antibody Libraries, Specifica, Inc.

ROOM LOCATION: Aqua Salon C

NOVEL SCAFFOLDS

9:00 Chairperson's Remarks

Elissa Leonard, PhD, Postdoctoral Fellow, Biomedical Engineering, Johns Hopkins University

9:05 Drug-Like VHH Straight from Naive Library Selections

Andre Teixeira, PhD, Head, Antibody Libraries, Specifica, Inc.

Developing VHH for medical use involves many engineering steps after immunization to humanize, affinity-mature, remove liabilities, and engineer Protein A binding. Improving one characteristic often impairs another. We devised a new library that enables bypassing many of these processes: human liability-free CDR1-2 are inserted into clinical VHH scaffolds (humanized) and filtered for Protein A binding. These are combined with >10^8 CDR3 and are able to yield VHH with drug-like characteristics.

9:35 Antibody Invertase Fusion Protein Enables Quantitative Detection of SARS-CoV-2 Antibodies Using Widely Available Glucometers

Elissa Leonard, PhD, Postdoctoral Fellow, Biomedical Engineering, Johns Hopkins University

Rapid, cost-effective, and widely available diagnostics are needed to monitor and mitigate the spread of SARS-CoV-2 and future outbreaks. An engineered antibody-enzyme fusion protein recognizes SARS-CoV-2-specific patient antibodies and catalyzes the conversion of sucrose to glucose, allowing quantification of antibodies against disease antigens using commercial glucometers. Engineering of the detection antibody, as well as a substation of the capture antigen, are expanding the applications and efficacy of this diagnostic.

10:05 Computational Peptide Design for Diverse Structures and Functions

Gaurav Bhardwaj, PhD, Assistant Professor, Medicinal Chemistry, University of Washington

Developing peptide binders against intracellular proteins and protein-protein interfaces remains a challenge with current methods and scaffolds. We recently developed computational methods to design peptides with enhanced membrane permeability and oral bioavailability. We are further integrating our computational methods with high-throughput peptide synthesis to design peptide binders for antibiotic, antiviral, and other therapeutic applications. Overall, these methods present avenues for binding intracellular targets currently considered "undruggable" or "difficult to drug."

10:35 Networking Coffee Break (Aqua Foyer)

11:00 Affibody-mediated Targeting of HER3 and EGFR for Cancer Therapy

Stefan Ståhl, PhD, Professor, Molecular Biotechnology, KTH Royal Institute of Technology, Sweden

We evaluated affibody-based concepts for bivalent and bispecific targeting of HER3 and EGFR. For HER3 in mice, we demonstrated efficient tumor growth inhibition. For EGFR, we developed an affibody-based prodrug concept with conditional targeting conferred by an anti-idiotypic affibody masking domain, and activation by cancer-associated proteases, to achieve impressive selective tumor-targeting in tumor-bearing mice. Will be further present how cytotoxic compounds conjugated to the affibody constructs improve their therapeutic efficacy.

11:30 Novel Ultra-Stable Peptide Therapeutics for Cancer Treatment

Julio A. Camarero, PhD, Professor, Pharmacology and Pharmaceutical Sciences, USC

We developed a cell-based screening of genetically encoded libraries of cyclotides for Hdm2/HdmX antagonists that has allowed the selection of a bioactive cyclotide, MCo-52-2. This cyclotide was able to bind the RING domains of both HdmX and Hdm2 and inhibit the formation of the RING-mediated Hdm2/HdmX complex. This bioactive cyclotide was also shown to have high ***in vivo*** activity in two murine models of colorectal carcinoma.

12:00 pm PANEL DISCUSSION: Development Challenges for Novel Biotherapeutic Scaffolds Development Challenges for Novel Biotherapeutic Scaffolds

Moderator: Elissa Leonard, PhD, Postdoctoral Fellow, Biomedical Engineering, Johns Hopkins University

Panelists:

Gaurav Bhardwaj, PhD, Assistant Professor, Medicinal Chemistry, University of Washington

Julio A. Camarero, PhD, Professor, Pharmacology and Pharmaceutical Sciences, USC

Stefan Ståhl, PhD, Professor, Molecular Biotechnology, KTH Royal Institute of Technology, Sweden

Andre Teixeira, PhD, Head, Antibody Libraries, Specifica, Inc.

12:30 Close of PepTalk

BISPECIFIC ANTIBODY DEVELOPMENT

The **Bispecific Antibody Development** pipeline will feature 3 consecutive units for a comprehensive look at the bispecific antibody pipeline. The Introduction to Bispecific Antibodies Training Seminar will be an informative and practical guide to getting up to speed on bispecific antibodies, including mechanisms of action, engineering, developability, regulatory considerations, and translational guidelines. The Developability of Bispecific Antibodies track will showcase how platforms and engineering along with identifying favorable drug-like properties including half-life, pk/pd, immunogenicity, stability, and manufacturability can be considered early on to optimize chances for success of multi-specific drug candidates. Lastly, the Safety and Efficacy of Bispecific Antibodies, ADCs and Combination Therapy track will review clinical results and milestones of emerging constructs and identify the key parameters for success and safety of these novel formats.

PEPTALK

JANUARY 16-17

Training Seminar: Introduction to Bispecific Antibodies

AGENDA

JANUARY 17-18

Developability of Bispecific Antibodies

AGENDA

JANUARY 19-20

Safety and Efficacy of Bispecific Antibodies, ADCs and Combination Therapy

AGENDA

REGISTER EARLY & SAVE!

TABLE OF CONTENTS

MONDAY, JANUARY 16, 2023 9:00 - 6:00 PM | TUESDAY, JANUARY 17, 2023 8:45 - 12:40 PM

TS2A: INTRODUCTION TO BISPECIFIC ANTIBODIES

Introduction to Bispecific Antibodies will be organized as an informative and practical guide to getting up to speed on critical aspects of bispecific antibody therapeutics. Topics will include historical successes, failures, and lessons learned. Specific practical instruction will span mechanisms of action, engineering, developability, regulatory considerations, and translational guidelines. Perspectives on the ideal implementation of bispecifics as targeted and immunomodulatory approaches will be discussed.

TOPICS TO BE COVERED:

- A brief history of bispecific antibodies: 60 years of progress with critical advances and key pioneers
- Bispecific applications and powerful mechanisms of action
- Engineering bispecific antibodies: 100 formats and counting
- Bispecific-specific considerations in preclinical development and regulatory landscape
- Developability, manufacturing, and analytical considerations
- Clinical experience, translation, and regulatory approval
- Current trends and future opportunities in regulating immune checkpoints, cell-based therapies, and personalized approaches

INSTRUCTOR BIOGRAPHY:

G. Jonah Rainey, PhD, Senior Director, Protein Engineering, Eli Lilly and Company

Jonah Rainey holds a PhD in Biochemistry from Tufts University and completed postdoctoral training at the University of Wisconsin and the Salk Institute. He has engaged in discovery, research, and development of bispecific antibodies for more than 15 years. He is an inventor on several patents describing novel bispecific platforms and current clinical candidates that exploit these platforms as well as an author on almost 30 publications. Jonah contributed to research and early development leading to multiple clinical candidates from Phase I and through approved products and led many advanced preclinical programs in oncology, infectious disease, autoimmunity, and other therapeutic areas. Previous industry experience includes MacroGenics, MedImmune/AZ, Oriole Biotech, Gritstone Oncology, and Alivamab Discovery Services. Currently, Jonah is a Senior Director in Protein Science at Eli Lilly & Co.

Cambridge Healthtech Institute Training Seminars offer real-life case studies, problems encountered and solutions applied, and extensive coverage of the basic science underlying each topic. Experienced Training Seminar instructors offer a mix of formal lectures, interactive discussions and activities to help attendees maximize their learning experiences. These immersive trainings will be of value to scientists from industry and academic research groups who are entering new fields – and to those working in supporting roles that will benefit from an in-depth briefing on a specific aspect of the industry.

JANUARY 17-18, 2023 | Cambridge Healthtech Institute's 12th Annual

DEVELOPABILITY OF BISPECIFIC ANTIBODIES

Connecting Platforms, Formats, Engineering and Manufacturing for Multi-Specifics

TUESDAY, JANUARY 17

12:45 pm Registration (Indigo Foyer)

1:00 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

1:30 Organizer's Welcome Remarks

ROOM LOCATION: Aqua Salon C

1:35 Chairperson's Remarks

Qing Chai, PhD, Research Advisor, BioTechnology Discovery Research, Eli Lilly & Co.

1:40 KEYNOTE PRESENTATION: Deep Learning in Antibody Engineering

Jeffrey J. Gray, PhD, Professor & Research Mentor & Outreach Advisor, Chemical & Biomolecular Engineering, Johns Hopkins University

Deep learning (DL) is transforming the field of structural molecular biology, but antibodies present additional challenges due to their unique evolutionary mechanisms and their reliance on loops and interfaces. I will share how we address these challenges through our recent DL algorithms (IgFold, IgLM, FvHallucinator) for antibody structure prediction, library generation, and antibody design. I will close with a discussion of the prospects for artificial intelligence-based antibody engineering.

ROOM LOCATION: Aqua Salon D

MACHINE LEARNING AND COMPUTATIONAL DESIGN FOR CANDIDATE SELECTION

2:19 Chairperson's Remarks

Harald Kolmar, PhD, Professor and Head, Institute for Organic Chemistry and Biochemistry, Technische Universität Darmstadt

2:20 Machine Learning Prediction of Antibody Aggregation and Viscosity at High Concentration

Neil Mody, Associate Director, Early-Stage Formulation Sciences, Biopharmaceutical Development, AstraZeneca

2:50 Next-generation HCAb-based multi-specific platform

Musheng Bao, PhD, Head of Biology, Nona Biosciences

HCAb Harbour Mice® have been developed that generate fully human heavy chain only antibodies and nanobodies that can be utilized for bi/multi-specific antibody develpment and other applications such as cell therapy, antibody-drug conjugates and targeted lipid nanoparticles. As a showcase, HCAb Harbour Mice® were used to efficiently identify high affinity CLDN18.2-specific HCAbs and 4-1BB-specific agonistic and cross-link dependent HCAbs that are ideal for TAA x 4-1BB bispecific antibody development.

3:05 Better Data, Faster: High-Throughput Assays for Bispecific Antibody Evaluation "

James Geiger, Ph.D., Sr. Product Specialist, PerkinElmer

Bispecific antibodies, with their ability to bind to two distinct antigens, or two epitopes on one antigen, have shown great promise for many complex diseases. Here we discuss high-throughput approaches to assess bispecific antibody binding activity, potency in cell-mediated toxicity, and antibody fragmentation.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

4:00 Computational Prediction of Developability Parameters of Antibodies

Marc Oeller, Graduate Student, Chemistry, Univ of Cambridge

Poor developability parameters are among the major causes of attrition in antibody discovery programs, in part because it is challenging to assess them experimentally in a high-throughput manner. The availability of large databases of antibody sequences and developability measurements is making it possible to develop computational methods to predict these parameters from their amino acid sequences. I will present methods to achieve this goal.

4:30 Pushing the Boundaries of Multifunctional Biologics Design

Stephen J. Demarest, PhD, CSO, Tentarix Biotherapeutics

Our teams have utilized innovative computational protein design algorithms and protein subunit-based screening approaches to generate bifunctional biologics with antibody-like biophysical properties. More recently, we have pushed these boundaries to generate multifunctional biologics with the goal of achieving highly specific cellular targeting of various functionalities.

5:00 Close of Day

WEDNESDAY, JANUARY 18

8:30 am Registration and Morning Coffee (Indigo and Aqua Foyer)

ROOM LOCATION: Aqua Salon CDE

9:00 Organizer's Remarks

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

9:10 Plenary Fireside Chat: Supporting and Driving Biotech: Past, Present, and Future

Moderator: Julie Ames, Vice President, Corporate Communications, Biocom California

Innovation can refer to something new, like an invention, or the development and introduction of new practices. The end result is often a new product, but it can also be a new practice, procedure, or way of thinking. Change and challenges are often what inspire innovation and propel us forward into new ways of thinking. This Fireside Chat will explore the following:

- Success stories
- Serendipitous discoveries
- Current projects
- Future developments

Panelists:

Amy K. Butler, PhD, President, Biosciences, Thermo Fisher Scientific

Taegen Clary, Vice President, Marketing, Unchained Labs

Jonathan Haigh, PhD, MBA, Vice President, Process Development, Fujifilm Diosynth Biotechnologies

Craig R. Monell, PhD, Vice President, Sales, Marketing & Business Development, BioLegend, Inc.

10:15 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

ROOM LOCATION: Aqua Salon D

SELECTING THE RIGHT FORMAT AND BUILDING BLOCKS USING DEVELOPABILITY

11:00 Chairperson's Remarks

Harald Kolmar, PhD, Professor and Head, Institute for Organic Chemistry and Biochemistry, Technische Universität Darmstadt

11:05 One Size Does Not Fit All: Navigating the Multi-Dimensional Space to Optimize T Cell Engaging Protein Therapeutics

Fan Yang, PhD, Associate Research Fellow, Molecular Discovery, Pfizer Inc.

T cell-engaging antibodies represent a promising class of bispecifics in immuno-oncology. Here we leverage the two well-characterized modalities within Pfizer, diabody-Fc, and full-length IgG2, and a series of engineered cell lines, to interrogate how we might use bispecific antibodies to modulate T cell activation while using T cell-redirected cytotoxicity and cytokine release as two primary readouts. We demonstrated the possibility of decoupling cytotoxicity and cytokine release if one optimizes inter-membrane distance.

11:35 The Influence of Configuration on Bispecific Antibody Physiochemical Properties, Pharmacokinetics, and Disposition

Amita Datta-Mannan, PhD, Senior Research Scientist, Drug Disposition Development, Eli Lilly & Co.

BsAbs often exhibit a broad range of pharmacokinetic (PK) behavior. Optimization of the neonatal Fc receptor (FcRn) interactions and removal of undesirable physiochemical properties have been used to improve the 'pharmacokinetic developability' for mAb therapeutics, yet there is a sparsity of such information for BsAbs. The present work evaluated the influence of FcRn interactions and inherent physiochemical properties on the PK of BsAb formats with different fusion partners and configurations.

12:05 pm A Semi-Mechanistic Pharmacology Model of ATG-101, a PD-L1/4-1BB Bispecific Antibody for Treatment of Solid Tumors

applied biomath

Kas Subramanian, PhD, Executive Director, Modeling, Applied BioMath

• ATG-101 is a bispecific Ab that crosslinks tumor-expressed PD-L1 to T-cell-expressed 4-1BB, selectively activating T-cells infiltrating solid tumors while inhibiting immune checkpoints
• The pharmacologically active complex that corresponds to efficacy consists of the drug bound to both PD-L1 and 4-1BB, which, while difficult to measure directly, can be predicted using mechanistic modeling
• By predicting PD-L1 RO and trans-cell complex formation, the model provides a rational basis for clinical dose selection

12:35 Enjoy Lunch on Your Own

OPTIMIZING BISPECIFIC ANTIBODIES FOR DEVELOPMENT

2:00 Chairperson's Remarks

Harald Kolmar, PhD, Professor and Head, Institute for Organic Chemistry and Biochemistry, Technische Universität Darmstadt

2:05 Attenuating CD3 Affinity in a PSMAxCD3 Bispecific Antibody Enables Killing of Prostate Tumor Cells with Reduced Cytokine Release

Pranjali Dalvi, PhD, Senior Scientist, Amgen

T cell redirecting antibodies have gained momentum in cancer immunotherapy with limitations in the clinic due to toxicities associated with CRS. We developed AMG 340, an anti-CD3xPSMA for the treatment of mCRPC that exhibited killing of PSMA+ tumor cells comparable to a positive control with the same anti-PSMA but stronger anti-CD3 arm, but significantly reduced cytokine secretion compared to the positive control, potentially having a better clinical outcome for patients.

2:35 POSTER HIGHLIGHT: Mosaic Biosciences' Yeast Display Antibody Platform Optimizes for Multiple Characteristics in Parallel

Eric Furfine, PhD, Co-CEO & CSO, Mosaic Biosciences, Inc.

3:05 An Integrated Approach for Assessing Immunogenicity Risk of Biotherapeutics

Sivan Cohen, PhD, Senior Principal Scientist, Genentech

Immunogenic responses, such as generation of anti-drug antibodies (ADA), against biotherapeutic products may have detrimental effects on drug safety, efficacy, and pharmacokinetics. Clinical trials are aimed at directly examining the ADA response in patients, but what if we could predict immunogenicity before clinical trials begin and mitigate those immunogenicity risks? This presentation will focus on *in silico* and *in vitro* tools to assess immunogenicity risk of monospecific and bispecific biotherapeutics.

PepTalk Plaza: Speed Networking

IN-PERSON ONLY: Speed Networking

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

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

BISPECIFIC ADCs FOR ONCOLOGY

4:14 Chairperson's Remarks

Nimish Gera, PhD, Vice President, Biologics, Mythic Therapeutics

4:15 Challenges and Opportunities with Development of Bispecific ADCs for Cancer

Rakesh Dixit, PhD, President & CEO, Bionavigen

4:45 Zymeworks ZW49

Stuart D. Barnscher, BSc, Director, Preclinical Programs, ADC Therapeutic Development, Zymeworks, Inc.

The biparatopic format of zanidatamab zovodotin enables enhanced tumour cell binding, internalization, and payload delivery compared to a monospecific HER2-targeting ADC. Zanidatamab zovodotin induces *in vitro* hallmarks of immunogenic cell death (ICD) in a HER2-dependent manner. Taken together, the differentiated properties of zanidatamab zovodotin compared to other HER2+ targeted therapies, supported progression to the clinic where durable responses have been observed in heavily pretreated HER2+ patients.

5:15 IMGN151: A Biparatopic Antibody Drug Conjugate (ADC) Targeting Folate Receptor Alpha (FRa)

Olga Ab, PhD, Associate Director, Translational Sciences, ImmunoGen, Inc.

FRa is a clinically-validated ADC target. The scientific rationale of a next-generation FRa-specific IMGN151, its design, and preclinical activity will be discussed.

5:45 Networking Reception in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

WOMEN IN SCIENCE MEET UP AT PEPTALK PLAZA

Women in Science Meet Up at PepTalk Plaza


Christa Cortesio, PhD, Senior Scientist and Group Lead, Protein Science, Protein Biochemistry & Analytics Core, Kite Pharma

Michelle R. Gaylord, MS, Principal Scientist, Protein Expression Lead, Velia, Inc.

7:00 Close of Developability of Bispecific Antibodies

JANUARY 19-20, 2023 | Cambridge Healthtech Institute's Inaugural

SAFETY AND EFFICACY OF BISPECIFIC ANTIBODIES, ADCS, AND COMBINATION THERAPY

THURSDAY, JANUARY 19

8:00 am Registration and Morning Coffee (Indigo and Aqua Foyer)

8:30 Organizer's Welcome Remarks

ROOM LOCATION: Aqua Salon D

RECENT ADVANCES IN BISPECIFIC, ADCs, AND THEIR COMBINATIONS

8:35 Chairperson's Opening Remarks
Rakesh Dixit, PhD, President & CEO, Bionavigen

8:40 KEYNOTE PRESENTATION: Efficacy and Safety of Bispecifics, ADCs, and Combination Therapies in War against Deadly Cancers
Rakesh Dixit, PhD, President & CEO, Bionavigen

In the last decade, tremendous progress has been made to improve overall survival due to cancer and related illnesses; however, most cancers still remain deadly and therapeutic challenges are fierce. This keynote lecture will discuss the unprecedented progress in the development of innovative bispecifics, ADCs, and combination therapies in the war against cancers. A special focus will be on the safety challenges of bispecifics, immunotherapies, ADCs, and their combinations.

9:20 Cevostamab, a FcHR5xCD3 Bispecific Antibody for the Treatment of Relapse/Refractory Multiple Myeloma
Suzanne M. Trudel, MSc, MD, Affiliate Scientist, Medicine, Princess Margaret Hospital

Fc receptor-homologue 5 (FcRH5) is a cell surface antigen of unknown function enriched on malignant plasma. Cevostamab (BFCR4350A), is a humanized IgG Fc antibody, targeting FcRH5 and CD3 on T cells that is undergoing clinical evaluation in relapsed/refractory multiple myeloma. Preclinical data supporting the clinical application of this novel bispecific antibody in multiple myeloma as well as the safety profile and efficacy in relapsed/refractory disease will be discussed.

9:50 Novel Format Conjugates and Multi-Specific Antibodies Produced by Chemical Site-Specific Conjugation: AJICAP
Yutaka Matsuda, PhD, Project Manager, ADC, Ajinomoto Bio-Pharma Services

Site-specific chemical conjugation technology (termed AJICAP®) is a simplified manufacturing process without using antibody engineering. We attempted to use site-specific conjugation technology to produce bispecific and trispecific antibodies with a new shape. The development of the unique methodology to produce homogeneous DAR = 1 conjugates enabled the production of homogeneous multispecific antibodies without a difficult purification process. Initial applications of AJICAP technology to novel format conjugates are also discussed.

10:20 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

11:00 Amivantamab – EGFR x cMet Bispecific Antibody with the Activities that Show 1 + 1 > 2
Mark L. Chiu, PhD, CSO, Tavotek Biotherapeutics

A review of amivantamab, a bispecific antibody (BsAb) targeting the epidermal growth factor receptor (EGFR) and mesenchymal-epithelial transition factor (MET) pathways, will be presented. Specific focus on patients with non-small cell lung cancer. The unique mechanisms of action can provide benefits to patients with malignancies associated with aberrant EGFR and MET signaling. A new generation molecule using cMet x EGFR x VEGF will be highlighted for unmet medical needs.

11:30 Trispecific Antibodies
Ronnie R Wei, PhD, Head, Biologics Discovery, Modex Therapeutics

Most diseases involve an interplay of multiple biological pathways. Effective therapies for cancers and viral infections may require combinatorial intervention. Carefully designed strategies could elicit novel mechanisms to achieve better efficacy and/or improved risk/benefit. I will present how we achieved exceptional breadth and potency against HIV and SARS-CoV-2 in a single molecule using the trispecific antibody technology, which may lead to improved prevention and treatment approaches for these diseases.

12:00 pm Enjoy Lunch on Your Own

1:10 Ice Cream Break in the Exhibit Hall and Last Chance for Poster Viewing (Indigo Ballroom)

2:00 Chairperson's Remarks
Rakesh Dixit, PhD, President & CEO, Bionavigen

2:05 Tebentafusp: A Novel gp100-Directed TCR-CD3 Bispecific for the Treatment of Metastatic Uveal Melanoma
Koustubh Ranade, PhD, Head, Translational Medicine, Immunocore LLC

ImmTACs are bispecific proteins comprised of an affinity-enhanced T cell receptor recognizing tumor antigens in the context of HLA fused to a T cell-activating anti-CD3 domain. Tebentafusp, a gp100-directed immTAC, is the first TCR bispecific to demonstrate overall survival benefit in a solid tumor, and is approved for the treatment of metastatic uveal melanoma. I will discuss mechanism of action of tebentafusp and challenges and opportunities for TCR bispecifics.

EMERGING BISPECIFICS: SAFETY AND EFFICACY CHALLENGES

2:35 On-Target Toxicity Associated with an Anti-CD70 Bispecific T Cell Engager Molecule in Cynomolgus Monkeys
Tod Harper, PhD, DABT Principal Scientist, Translational Safety, Amgen, Inc.

CD3 bispecific T cell engager molecules have great potential to treat cancer. Nevertheless, dependent on the targeted tumor antigen, the mechanism of action that drives efficacy may also contribute to on-target/off-tumor toxicities. Here we illustrate how a thorough understanding of expression and upregulation is needed to fully address putative liabilities associated with on-target/off-tumor activity of CD3 bispecific molecules using an anti-CD70 half-life extended BiTE molecule as a case example.

3:05 Networking Refreshment Break (Aqua Foyer)

3:30 Bispecific Antibodies for Hematologic Malignancies: Clinical Development, Therapeutic Applications, and Recent Clinical Trials
Priya Hays, PhD, Technical Writer, Science Writer, Hays Documentation Specialists, LLC

Bispecific antibodies are composed of two monoclonal antibodies that engage T cells with tumor cell antigens and lead to tumor cell lysis. The most common types fall into the category of bispecific T cell engagers, or BiTEs, that have the canonical CD3-CD19 bispecific construct. Blinatumomab is the first bispecific antibody that received FDA approval for relapsed refractory B cell precursor acute lymphoblastic leukemia.

4:00 Teclistamab (BCMA x CD3 Bispecific) in Relapsed/Refractory Multiple Myeloma
Carlyn Tan, MD, Hematologic Oncologist, Hematology & Oncology, Memorial Sloan Kettering Cancer Center

Teclistamab is a novel BCMA x CD3 T cell-redirecting bispecific antibody developed for the treatment of multiple myeloma (MM). We will review the safety and efficacy of teclistamab as a single agent and in combination with various standard myeloma regimens from recent clinical trials, describe strategies to manage teclistamab-specific toxicities and side effects, and discuss challenges and future approaches for RRMM with the development of multiple BCMA-directed therapies.

4:30 Close of Day

FRIDAY, JANUARY 20

7:30 am Registration (Indigo Foyer)

ROOM LOCATION: Indigo and Aqua Foyer

BuzZ Sessions

8:00 BuzZ Sessions with Continental Breakfast

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.
Please continue to check the BuzZ Session page on our conference website for detailed discussion topics and moderators

BuzZ Table 6: Bispecific Antibodies from Bench to the Clinic

Priya Hays, PhD, Technical Writer, Science Writer, Hays Documentation Specialists, LLC

- Clinical development and efficacy of BiTEs and BCMAs in hematologic malignancies
- Immune related adverse events
- Beyond CD3-CD19 epitopes: Dual affinity BsAbs and tandem diabodies
- Combination and sequential therapies

BuzZ Table 7: The Challenges and Opportunities for Treating Low HER2 Expressing Cancers

Rakesh Dixit, PhD, President & CEO, Bionavigen

Robert J. Lutz, PhD, CSO, Iksuda Therapeutics

- Challenges of developing effective therapies against low HER2-cancers
- Unprecedented activity of Enhertu (Trastuzumab Deruxtecan), a HER2 targeting ADC in low HER2 breast cancer, ASCO recognition and FDA approval
- New and upcoming therapies to treat Enhertu refractory low HER2 expressing tumors

ROOM LOCATION: Aqua Salon D

INNOVATIVE ADCs: MITIGATION OF TOXICITY TO IMPROVE EFFICACY

9:00 Chairperson's Remarks

Rakesh Dixit, PhD, President & CEO, Bionavigen

9:05 Novel Tumor-Selective ADC Designs for Improved Therapeutic Index

Robert J. Lutz, PhD, CSO, Iksuda Therapeutics

Novel linker-payload chemistries take advantage of upregulated enzymes in cancer cells to improve the tumor-selectivity of ADC activation. Increased tumor-selectivity allows the exploration of high potency payloads to improve efficacy and tolerability. Case studies demonstrating marked differentiation of the new ADC designs compared to traditional ADC benchmarks will be presented.

9:35 A CD79b Targeting ADC with Superior Anti-Tumor Activity and Tolerability

Bernd Schlereth, PhD, Chief Development Officer, Araris Biotech AG

The Araris' site-specific and 1-step linker conjugation technology aims at generating safe and highly efficacious ADCs without the need for antibody engineering. We developed a very stable anti-CD79b-MMAE ADC with this technology which shows a significantly improved efficacy and tolerability compared to polatuzumab-vedotin in preclinical models. Our ADC may represent a safe and efficacious treatment option for patients with diffuse large B cell lymphoma (DLBCL) and indolent lymphoma.

10:05 Making Amanitin Available for the Clinic – Engineering a Therapeutic Window into a Poison

George Badescu, PhD, Vice President, Business Development, Heidelberg Pharma AG

Amanitin is a member of the amatoxin group of natural poisons, which occur in the death cap mushroom (Amanita phalloides). Our strategy is to use an ADC approach to engineer a therapeutic window into amanitin. The first amanitin-based ADC (HDP-101) is directed against BCMA and is currently undergoing clinical development for multiple myeloma.

10:35 Networking Coffee Break (Aqua Foyer)

11:00 Protein Engineering of Avidity Effects to Improve the Therapeutic Window of Antibody Drug Conjugates

Greg M. Thurber, PhD, Associate Professor, Chemical Engineering & Biomedical Engineering, University of Michigan

Antibody Drug Conjugates (and Bispecific Antibodies) interact with their targets, including immune cells, through multivalent interactions with receptors. These interactions can be designed computationally and tested experimentally to develop enhanced therapies. Here, we discuss how these multivalent interactions, also known as avidity affects, can be tuned with combination therapy to improve intratumoral drug distribution and target specificity for increased efficacy and reduced toxicity.

11:30 PANEL DISCUSSION: Learning from the Successes and Failures of ADCs, Bispecifics, and Combinations

Moderator: Rakesh Dixit, PhD, President & CEO, Bionavigen

The panel discussion with Q&A will include learnings from the successes and failures of ADCs, bispecifics, and their combinations.

Panelists:

Nimish Gera, PhD, Vice President, Biologics, Mythic Therapeutics

Tod Harper, PhD, DABT Principal Scientist, Translational Safety, Amgen, Inc.

Greg M. Thurber, PhD, Associate Professor, Chemical Engineering & Biomedical Engineering, University of Michigan

Carlyn Tan, MD, Hematologic Oncologist, Hematology & Oncology, Memorial Sloan Kettering Cancer Center

12:30 pm Close of Safety and Efficacy of Bispecific Antibodies, ADCs, and Combination Therapy

CHARATERIZATION OF BIOTHERAPEUTICS & VACCINES

The **Characterization of Biotherapeutics & Vaccines** pipeline features three back-to-back popular conferences on critical topics such as analytical and characterization tools for protein aggregation, stability assessment, detection, and control of contaminants and impurities in biotherapeutics and vaccines for COVID-19 and other diseases. These conferences will feature case studies, new and unpublished data, interactive discussions, panel discussions on strategies and tools for characterization, risk assessment, and mitigation for protein aggregates, particles, and impurities arising from products, excipients, processes, and packaging in novel biologics and vaccines and mRNA therapies.

PEPTALK

JANUARY 16-17

Characterization of Biotherapeutics

AGENDA

JANUARY 17-18

Characterizing Protein Aggregates and Impurities

AGENDA

JANUARY 19-20

Characterization and Development of Vaccines

AGENDA

REGISTER EARLY & SAVE!

TABLE OF CONTENTS

JANUARY 16-17, 2023 | Cambridge Healthtech Institute's 9th Annual

CHARACTERIZATION OF BIOTHERAPEUTICS

Improving Prediction, Screening, and Characterization of New Biologics

SUNDAY, JANUARY 15

4:00 pm Pre-Conference Registration (Indigo Foyer)

MONDAY, JANUARY 16

7:00 am Registration and Morning Coffee (Indigo and Aqua Foyer)

9:00 Organizer's Welcome Remarks

ROOM LOCATION: Aqua Salon D

MAKING BETTER DECISIONS EARLY

9:05 Chairperson's Opening Remarks

Peter M. Tessier, PhD, Albert M. Mattocks Professor, Pharmaceutical Sciences & Chemical Engineering, University of Michigan

9:10 KEYNOTE PRESENTATION: Drug-Like Antibodies Generated Using Yeast-Display Screening and Machine Learning

Peter M. Tessier, PhD, Albert M. Mattocks Professor, Pharmaceutical Sciences & Chemical Engineering, University of Michigan

Therapeutic antibody development requires the selection and engineering of molecules with high affinity and other drug-like biophysical properties. Here, we demonstrate the use of yeast-display selections and machine learning to greatly simplify the identification of antibodies with co-optimal levels of affinity and multiple key biophysical properties (non-specific binding, self-association, and stability).

9:50 Library-Scale Characterization of Protein Developability

Benjamin J. Hackel, PhD, Associate Professor, Chemical Engineering & Materials Science, University of Minnesota

Protein developability is a critical attribute yet often not evaluated until late in the product pipeline because of challenges in high-throughput characterization. We have developed a platform for library-scale characterization of multiple developability metrics for millions of protein variants and coupled these data with a convolutional neural network to advance understanding of the sequence-developability landscape.

10:20 Networking Coffee Break (Indigo and Aqua Foyer)

MAKING BETTER DECISIONS EARLY, CONT.

10:45 Making Better Decisions Earlier

Michael S. Marlow, PhD, Director Biologics CMC Research, Biotherapeutics Discovery, Boehringer Ingelheim Pharmaceuticals, Inc.

Bringing together advances in sequencing, bioinformatics, automation, and data analysis, we have codified and streamlined the selection and characterization of diverse hit libraries assembled from various discovery platforms. This talk will describe our process for generating extensive manufacturing and physicochemical 'drug-like properties' alongside kinetic and cell-based data to objectively identify lead molecules for optimization. The consistency and scale of our operation facilitate data science initiatives to enhance the overall approach.

11:15 A Modular Approach for Glycoengineering Therapeutic Antibody Variable Domains

Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

We developed a workflow that introduces atypical glycosylation into antibody Fv domains. We show that this approach can modulate the function and extend the *in vivo* half-life of antibodies without adversely affecting developability metrics, presenting a general glycoengineering framework for enhancing antibody performance early in the drug development process.

11:45 Assessing New and Sensitive Mass Spectrometry-Based Techniques to Rapidly Characterize Protein Therapeutics

Dhanashri Bagal, Principal Scientist, Discovery Attribute Sciences, Amgen, Inc.

Low material consumptive and rapid analytics performed on early-stage engineering panels of protein therapeutic candidates can inform on protein stability and developability. Herein we examine sensitive and robust mass spectrometry-based methods using online capillary SEC and HIC – LC/MS to inform on protein attributes such as aggregation and mispairing. We will also discuss a sensitive N-terminal chemical tagging and rpLC-MS/MS-based approach to accurately identify low-level proteolytic clips.

12:15 pm Tackling the Peptide Isomer Impurity Challenge with High-Resolution Ion Mobility Mass Spectrometry

Heidi Vitrac, Senior Market Development Scientist, MOBILion Systems, Inc

The pace of therapeutic peptide drug development has significantly increased over the last decade. To improve peptide therapeutic biological function and pharmacokinetics, several strategies have been employed, including amino acid substitution, incorporation of unnatural amino acids, amino acid modifications and cyclization. High-resolution ion mobility mass spectrometry improves therapeutic peptide impurity analysis with its ability to resolve complex mixtures of D&L amino acid isomers, deamidations and positional isomers in the gas phase.

12:45 Enjoy Lunch on Your Own

1:55 Session Break

ASSAYS AND ANALYTICAL TOOLS

2:00 Chairperson's Remarks

Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

2:05 Development of an SPR-Based Binding Assay for Characterization of Anti-CD20 Antibodies to CD20 Expressed on Extracellular Vesicles

Xiangdan Wang, PhD, Senior Principal Scientist, BioAnalytical Sciences, Genentech, Inc.

Characterization of anti-CD20 antibody binding to CD20 is critical to the development of anti-CD20 therapeutics. While SPR is widely used to characterize therapeutics binding to their targets, its application to the characterization of anti-CD20 therapeutics has been limited by challenges of obtaining recombinant or native full-length CD20 suitable for ligand binding assays. We report a novel SPR-based assay enabling elucidation of binding kinetics and affinity for anti-CD20 antibody to EV-expressed CD20.

2:35 Biosimilars – New Strategies to Explore Emerging Markets

Dinakar Panati, PhD, Head, Regulatory Affairs & Business, Epygen Biotech, Private Ltd.

Emerging markets with low biologic-treatment rates and affordability barriers that impede patients' access to expensive, innovative medicines present attractive opportunities for biosimilars. Companies can design targeted pricing models for each product and country. Here we discuss how pharma companies can unlock their potential to enter emerging markets, their regulatory pathways, pricing, affordability, and competitive landscapes.

ROOM LOCATION: Indigo and Aqua Foyer

BuzZ Sessions

3:05 Find Your Table and Meet the BuzZ Sessions Moderator

3:10 BuzZ Sessions with Refreshments (IN-PERSON ONLY)

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.
Please continue to check the BuzZ Session page on our conference website for detailed discussion topics and moderators

BuzZ Table 2: Beyond Injectable mAb Drug Products

Christopher Mensch, Director, Drug Product, IGM Biosciences, Inc.

- Delivery Technologies for New Routes
- Dosage Form & Formulation Considerations
- Analytical Characterization

FORMULATION, CHARACTERIZATION, AND DEVELOPABILITY

4:30 How Does Biologics Formulation Evolve into a High-Throughput Workflow?

Hanlin Ouyang, Senior Scientist, Merck & Co., Inc.

The talk will focus on how we transformed a completely non-HT biologics formulation workflow in the late-stage drug product development into an HT and HT-compatible one in the lab from sample prep to sample analytics. Since the study was designed by JMP, the talk will also demonstrate how we evolved our own mindset to leverage the power of DOE and statistics.

5:00 Impact of Surfactant Excipients on Protein Behavior in Extensional Flow

Michelle Calabrese, PhD, Assistant Professor, Department of Chemical Engineering and Materials Science, University of Minnesota

We examine the extensional flow properties with model ovalbumin protein (OVA) and commonly used polysorbate excipients (PS20, PS80), which despite similarities in structure, cause pronounced differences in flow behavior. While undesirable elasticity is observed in some high-concentration formulations, polysorbate-containing solutions are more promising than solutions containing higher molecular weight polymeric excipients. Understanding excipient flow behavior can help formulate protein medications with greater shelf stability and tolerance to adverse flow effects.

5:30 Presentation to be Announced

6:00 Welcome Reception in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

YOUNG SCIENTIST MEET UP

Young Scientist Meet Up

Iris Goldman, Production, Cambridge Innovation Institute

7:30 Close of Day

CITY WALK MEET UP

BREAKOUT DISCUSSION: City Walk Meet Up

Kevin Brawley, Associate Project Manager, Production Operations & Communications, Cambridge Innovation Institute

TUESDAY, JANUARY 17

8:15 am Registration and Morning Coffee (Indigo and Aqua Foyer)

ROOM LOCATION: Aqua Salon D

CHARACTERIZATION OF PROTEIN AND PEPTIDE FORMULATIONS

8:45 Chairperson's Remarks

Devinder K. Ubhi, PhD, Principal Scientist, Analytical Development & Formulations, IGM Biosciences

8:50 Development of an Intranasally Administered IgM Antibody

Devinder K. Ubhi, PhD, Principal Scientist, Analytical Development & Formulations, IGM Biosciences

An IgM antibody (IGM-6268) was engineered to specifically target the RBD of SARS-CoV-2 spike protein, with enhanced avidity and potent variant neutralization compared to an IgG antibody. Since administration at the site of infection has the potential for prophylactic and treatment efficacy, IGM-6268 was evaluated for aerosolization targeting the nasal cavity. Development of a stabilizing formulation was paired with Teleflex MAD300 Nasal device delivery characterization, for rapid advancement into clinic.

9:20 A Universal Method for Refractive Index Increment and Extinction Coefficient Determination of Macromolecules

Nicholas Larson, PhD, Scientist, Biogen

Determination of extinction coefficients is critical to reliably measure the concentration of biomacromolecules. Most existing methods to measure extinction coefficients are designed for specific types of molecules (e.g. protein, DNA). We demonstrate a universal method for measuring the extinction coefficient of any biomolecule. Case studies on the application to protein-DNA conjugates and virus particles will be discussed.

9:50 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

ROOM LOCATION: Aqua Salon D

CHARACTERIZATION OF CELL THERAPY AND NOVEL BIOLOGICS

10:30 Latest Analytical Methods for Characterization of Virus Particles in Cell and Gene Therapy Products

Tim Menzen, PhD, CTO & Pharmacist, Coriolis Pharma Research GmbH

Cell and gene therapy using viral vectors promises to overcome unmet needs in therapy of severe diseases. These viral vectors provide an analytical challenge during product development and stability assessment as they contain proteins, nucleic acids, and in some cases also a lipid membrane. The talk will provide an overview of latest analytical methods for virus particle characterization and show recent results from, e.g., analytical ultracentrifugation.

11:00 Development for and Characterization of Intraorganelle Localization of Peptide, Protein, and Oligo Conjugated Actives

Jay Sarkar, PhD, Visiting Scholar, Stanford University

Conjugated peptide sequences redefine targeted delivery through their dual nature as both physical and informational constructs. Their physical properties are exploited through their gross electrochemical interactions with cellular structures, most notably the cell membrane. While their informational properties can be harnessed through the cell's endogenous protein trafficking logic. We will discuss this utility and how to design and characterize their localization of drug actives to and even within organelle targets.

11:30 Mass Photometry - an analytical technology for biomolecular characterization

Gabriella Kiss, Director of Global Strategic Accounts, Business Development, Refeyn Inc.

Quantification of empty/full ratio of capsids in AAV preparations is a major bottleneck in characterizing recombinant AAV samples. Samux^{MP} is a mass photometer, tailored specifically to measure empty/full ratios of AAVs. In this talk, we will demonstrate capabilities of the Samux^{MP} in characterizing AAV samples in less than 5 mins. We will show that it can differentiate between empty, partially filled and full AAV capsids, and that it is serotype agnostic.

11:45 Simultaneous Quantification of Expression Levels and Affinities of Membrane Proteins without Purification or Calibration

Sebastian Fiedler, PhD, Head of Applications, Applications, Fluidic Analytics

We introduce a membrane protein affinity and concentration assay for working with unpurified membrane proteins in a native lipid-bilayer environment. To demonstrate our approach, we quantified both the expression level of endogenous HER2 in a breast cancer cell line and its affinity to trastuzumab. The method is quick and easy to use and has the potential to be expanded from cell lines to tissues and tumor biopsies.

12:00 pm Session Break and Transition to Luncheon Presentation

12:10 Luncheon Presentation to be Announced

Speaker to be Announced

12:40 Close of Characterization of Biotherapeutics

JANUARY 17-18, 2023 | Cambridge Healthtech Institute's 14th Annual

CHARACTERIZING PROTEIN AGGREGATES AND IMPURITIES

Strategies and Tools for Detection and Characterization of Aggregates and Impurities in Biologics

TUESDAY, JANUARY 17

12:45 pm Registration (Indigo Foyer)

1:00 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

1:30 Organizer's Welcome Remarks

ROOM LOCATION: Aqua Salon E

IMPORTANT CONSIDERATION FOR DEVELOPMENT OF NOVEL BIOTHERAPEUTICS

1:35 Chairperson's Opening Remarks

Susumu Uchiyama, PhD, Professor, Biotechnology, Osaka University

1:40 KEYNOTE PRESENTATION: Optimizing Drug Product Presentation and Manufacturing Processes for Gene Therapy Products

Sandeep Yadav, PhD, Senior Director, Drug Product Formulation & Fill/Finish, Sangamo Therapeutics

Biotechnology companies are extensively leveraging AAV to deliver therapeutic DNA for genomic medicine applications. Some of the notable challenges are extremely low titers, limited manufacturing lots to develop process knowledge, and complex analytical methodologies required to characterize AAV systems leading to higher cost of goods (COGs). We discuss developing and optimizing DP formulation/presentations and manufacturing strategies to support patient safety, healthcare provider convenience, and reducing COGs to enable patient accessibility.

2:20 Latest Developments in Particulate Impurity Characterization Technologies for Biologics

Bruce A. Kerwin, PhD, Principal, Kerwin Biopharma Consulting LLC

Within the talk, novel approaches for the characterization of particulate impurities in biologics will be presented and compared to state-of-the-art technologies for submicron and subvisible particle analysis. Besides new analytical technologies, the integration of machine learning for data analysis will be presented.

2:50 Trehalose and Sucrose: Essential Components of Platform Biopharma Formulations and COVID 19 applications

Pfanstiehl

Sudhakar Voruganti, Dr., Director, Business Development, Pfanstiehl

- Introduction of Pfanstiehl and its high quality/purity GMP components
- Commercial Biotherapeutics Stabilized with Trehalose and Sucrose
- Examples for utilizations and functionalities of Sucrose and Trehalose in Covid 19 related formulations and applications
- Essential components of a "Platform Biopharma Formulation"
- Understanding important physicochemical properties of Trehalose and Sucrose
- Purity, Quality, Consistency in Pfanstiehl's Trehalose and Sucrose

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

GUIDANCE, STANDARDS, AND TOOLS FOR AGGREGATES AND IMPURITIES

4:00 USP Standards and Tools for Impurities Analysis in Biotherapeutics

Kevin L. Carrick, Director, Global Biologics, USP

The monitoring and control of process-related impurities is an important element in process development and product manufacturing. USP has developed standards and tools to assist in the quantitation of host cell DNA and host cell proteins. This presentation will cover USP standards, documentary and reference standards, for host cell DNA quantitation, and new reference materials in development to support quantitation of host cell proteins.

4:30 Advances in Methods for Detection, Characterization, and Enumeration of Process and Product-Related Particles

Richard Cavicchi, PhD, Research Physicist, Biomolecular Measurement Division, Material Measurement Laboratory, National Institute of Standards and Technology

Identification, counting, and minimization of particles continue to be important for the safety and efficacy of biotherapeutics. Protein aggregates, which can arise as pure protein or nucleated on other particle types, present unique measurement challenges. While the standard methods used for lot release are still based on light obscuration methods from the 1990s, significant advances have resulted in improved capabilities over a wide size range. Recent developments will be discussed.

5:00 Standards for Particle Detection: From Nanometers to Visible

Dean C. Ripple, PhD, Group Leader, Bioprocess Measurements Group, NIST

I will present strategies for the use of particle reference materials, discussing their strengths and limitations. Both the properties of interest in reference material and its use vary substantially from the size range of nanometers to visible. Reference materials developed for size and count are also now finding use for new technologies and methods, such as AI analysis of particle images.

5:30 Close of Day

WEDNESDAY, JANUARY 18

8:30 am Registration and Morning Coffee (Indigo and Aqua Foyer)

ROOM LOCATION: Aqua Salon CDE

9:00 Organizer's Remarks

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

9:10 Plenary Fireside Chat: Supporting and Driving Biotech: Past, Present, and Future

Moderator: Julie Ames, Vice President, Corporate Communications, Biocom California

Innovation can refer to something new, like an invention, or the development and introduction of new practices. The end result is often a new product, but it can also be a new practice, procedure, or way of thinking. Change and challenges are often what inspire innovation and propel us forward into new ways of thinking. This Fireside Chat will explore the following:

- Success stories
- Serendipitous discoveries
- Current projects
- Future developments

Panelists:

Amy K. Butler, PhD, President, Biosciences, Thermo Fisher Scientific

Taegen Clary, Vice President, Marketing, Unchained Labs

Jonathan Haigh, PhD, MBA, Vice President, Process Development, Fujifilm Diosynth Biotechnologies

Craig R. Monell, PhD, Vice President, Sales, Marketing & Business Development, BioLegend, Inc.

10:15 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

ROOM LOCATION: Aqua Salon E

SURFACTANTS AND AGGREGATION

11:00 Chairperson's Remarks

Christian Schoeneich, PhD, Takeru Higuchi Distinguished Professor & Chair, Pharmaceutical Chemistry, University of Kansas Lawrence

11:05 A Mechanistic Understanding of Monoclonal Antibody Interfacial Protection by Hydrolytically Degraded Polysorbate 20 and 80 under IV Bag Conditions

Aadithya Kannan,PhD, Technical Development Principal Scientist, Genentech

Polysorbates (PS) are used to reduce monoclonal antibody (mAb) aggregation at hydrophobic interfaces. PS can hydrolyze over time to generate free fatty acid (FFA) degradants, primarily lauric acid for PS20 and oleic acid for PS80. This talk discusses key differences in the effect on aggregation of a surface-active mAb by degraded PS20 and PS80, using surface tension studies, static storage behavior, colloidal, and conformational stability of mAbs with degraded PS.

11:35 Photolytic and Oxidative Degradation of Polysorbates in Common Buffers

Christian Schoeneich, PhD, Takeru Higuchi Distinguished Professor & Chair, Pharmaceutical Chemistry, University of Kansas Lawrence

The chemical degradation of polysorbate continues to present a challenge for the development of stable protein formulations. Free radical-mediated mechanisms play a central role in oxidative polysorbate degradation. Polysorbate oxidation can target polysorbate monomers or polysorbate micelles. Here, we show that intra-micellar oxidation reactions dominate polysorbate oxidation even when initiated with hydrophilic oxidants. We further show that specific buffer-derived radicals can play a critical role in polysorbate oxidation.

12:05 pm Manufacturing physically stable proteins starting from cell line development

Dikran Khachadourian, Field Application Scientist, Halo Labs

Cell line development (CLD) is a critical aspect of drug development. However, data supporting the stability of secreted proteins during CLD is scarce. Bridging the gap between CLD and developability allows biomanufacturers to pre-screen samples for immunogenic subvisible protein aggregates. In this talk, we present Aura PTx, an instrument that enables low volume, high-throughput subvisible particle imaging, counting, sizing, and identification to generate stable biologic candidates from CLD through product release.

12:35 Session Break and Transition to Luncheon Presentation

12:45 LUNCHEON PRESENTATION: Tackle Stability and Viscosity of Your Biologic with Unchained Labs Solutions

Andre Mueller, PhD, Marketing Manager, Biologics Solutions, Unchained Labs

Unchained Labs is all about unleashing solutions to tackle the increasing complexity of screening biologics and the ever-growing challenge to select the best candidate or formulation.
Join my talk to see examples of how Uncle monitors protein stability in thermal ramps or during storage, and how Honeybun rapidly measures viscosity of multiple samples in mere minutes.

1:45 Session Break

CONSIDERATION DURING PRODUCT DEVELOPMENT & MANUFACTURING

2:00 Chairperson's Remarks

Danny K. Chou, PharmD, PhD, President, Biopharmaceutical Characterization and Formulation Development, Compassion BioSolution, LLC

2:05 Rescuing Catastrophic Aggregation – Formulation and Delivery Considerations to Enable Pulmonary Administration of IgM Drug Product in Early Development

Christopher Mensch, Director, Drug Product, IGM Biosciences, Inc.

The degree of protein purity and aggregation are well-established critical quality attributes requiring careful monitoring during the development of monoclonal antibody Drug Products. A strategic approach was utilized to rapidly rescue soluble and insoluble aggregation and enable pulmonary delivery of IgM mAb Drug Product. Key formulation and delivery considerations to enable Early Development activities will be described.

2:35 Characterization and Disruption of Ultra-Low Affinity HCP-mAb Interactions

Shrenik Mehta, PhD, Technical Development Scientist, Pharmaceutical Development Department, Genentech, Inc.

3:05 Real-Time Detection of Protein Aggregation – Practical Strategies for Implementation during Product Development and Manufacturing

Danny K. Chou, PharmD, PhD, President, Biopharmaceutical Characterization and Formulation Development, Compassion BioSolution, LLC

The goal of this presentation is to provide an update on the most recent developments in real-time detection and monitoring of protein aggregation. The focus is on emerging orthogonal methods that may be implemented during product development as well as during large-scale manufacturing.

PepTalk Plaza: Speed Networking

IN-PERSON ONLY: Speed Networking

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

4:15 Biophysical Characterization of mAb-Excipient Interactions

Subhashchandra Naik, PhD, Senior Research Scientist, Comera Life Sciences

Monoclonal antibodies at high concentrations interact with each other and with excipients by a variety of mechanisms. We can modulate these interactions by using excipients to change the properties of drug products. Here we look at a few excipients and how they affect mAb formulations.

4:45 Strategies for Addressing Challenges of High Concentration Formulation Development: A 150 mg/mL mAb Case Study

Benjamin R. Clarkson, PhD, Scientist II, Formulation Development, NIH/NIAID/VRC Vaccine Production Program

Development of formulations for high concentration (100+ mg/mL) biotherapeutics poses numerous technical and logistical challenges during formulation and process development. As illustrated in a case study of the development of a 150 mg/mL monoclonal antibody formulation, strategic use of data generated at lower concentrations, utilization of certain predictive assays for stability at high concentrations, and careful molecule selection can enable rapid development of stable high concentration formulations.

5:15 Succinate Buffer in Biologics Products: Real-World Formulation Considerations, Processing Risks, and Mitigation Strategies

Anvay Ukidve, PhD, Scientist, Formulation and Process Development, Sanofi

Succinate acid/succinate system has an excellent buffering capacity at acidic pH values (4.5-6.0). However, its use in formulating drug products is largely limited due to risk of its components crystallizing and the consequent pH shifts. Physicochemical behavior of succinate system was characterized under pharmaceutically representative conditions. mAbs formulated in de-risked succinate buffer maintained a good stability profile during typical pharmaceutical processing and storage, bolstering their wider use in drug products.

5:45 Networking Reception in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

WOMEN IN SCIENCE MEET UP AT PEPTALK PLAZA

Women in Science Meet Up at PepTalk Plaza


Christa Cortesio, PhD, Senior Scientist and Group Lead, Protein Science, Protein Biochemistry & Analytics Core, Kite Pharma

Michelle R. Gaylord, MS, Principal Scientist, Protein Expression Lead, Velia, Inc.

7:00 Close of Characterizing Protein Aggregates and Impurities

JANUARY 19-20, 2023 | Cambridge Healthtech Institute's Inaugural

CHARACTERIZATION AND DEVELOPMENT OF VACCINES

Development, Analytics, and Manufacturing of COVID Vaccines, mRNA Vaccines and Beyond

THURSDAY, JANUARY 19

8:00 am Registration and Morning Coffee (Indigo and Aqua Foyer)

8:30 Organizer's Welcome Remarks

ROOM LOCATION: Aqua Salon E

UPDATES ON COVID-19 VACCINES AND BOOSTERS

8:35 Chairperson's Opening Remarks

Alois Jungbauer, PhD, Professor & Head, Biotechnology, Institute of Bioprocess Science and Engineering, University of Natural Resources and Life Sciences (BOKU)

8:40 KEYNOTE PRESENTATION: Personalized Vaccinology: Missed Opportunities during COVID-19; Is It Too Late Now?

John Mattison, Operating Partner/Chief Medical Information Officer, Arsenal Capital Partners

The COVID pandemic offered a fantastic opportunity to expand our knowledge base, but there was little T cell research from pharma associated with new vaccine development. As the pandemic subsides, there may still be time for critical research more broadly on personalizing vaccine strategies across a variety of risk cohorts, including Long COVID sufferers who often experience deterioration of symptoms post-vaccine.

9:20 Presentation to be Announced

9:50 Level up your tools for the development and characterization of lipid nanoparticle vaccines

Martha Perez, PhD, Director of Marketing, LNP Solutions, Unchained Labs

Lipid nanoparticles (LNPs) are a valuable tool in the repertoire of vaccine delivery vectors, but LNP development is a complex process. Screening formulations, controlling the size and quality of the LNPs, getting rid of organic solvents, and characterization require significant and tedious work. Level up your tools with Nunchuck, Stunner, Unagi, and Uncle to make the perfectly-sized LNPs, characterize size and quality, buffer exchange and concentrate samples, and analyze stability.

10:20 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

11:00 Manufacturing and Analytical Challenges in Pandemic Vaccine Development

Nikolai Petrovsky, PhD, Research Director, Vaxine Pty Ltd.; Professor of Medicine, Flinders University

The rapid development of safe and effective vaccines is a key requirement to conquering any pandemic. Recombinant proteins remain amongst the most reliable and safest approaches but face challenges in design, manufacture, structural characterization, analytical analysis, and delivery. The examples of the 2009 influenza pandemic and 2019 COVID-19 pandemic highlight the many challenges faced when compressing development of a novel pandemic vaccine into months rather than decades.

11:30 PANEL DISCUSSION: Lessons Learned from COVID-19 Vaccine Development to Take Forward

Moderator: Alois Jungbauer, PhD, Professor & Head, Biotechnology, Institute of Bioprocess Science and Engineering, University of Natural Resources and Life Sciences (BOKU)

Panelists:

John Mattison, Operating Partner/Chief Medical Information Officer, Arsenal Capital Partners

Sabrina Leslie, PhD, Associate Professor, Physics and Astronomy Department, The University of British Columbia

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

12:30 Enjoy Lunch on Your Own

1:10 Ice Cream Break in the Exhibit Hall and Last Chance for Poster Viewing (Indigo Ballroom)

DEVELOPMENT AND STABILITY OF VACCINES, mRNA, AND GENOMIC-BASED VACCINES

2:00 Chairperson's remarks

Gautam Sanyal, PhD, Principal Consultant, Vaccine Analytics, LLC

2:05 Advances in Characterization and Formulation Development of Vaccines

Prashant Kumar, PhD, Scientific Assistant Director, Pharmaceutical Chemistry, University of Kansas, Lawrence

This presentation will focus on providing an overview of high-throughput analytical characterization and formulation development considerations for new vaccine candidates targeted for use in low- and middle-income countries (LMICs). Case studies with live-virus vaccine candidates will highlight implementing state-of-the-art selective and stability-indicating assays to enable expeditious formulation development to enhance vaccine access in LMICs.

2:35 Analytical Characterization of mRNA Vaccines

Gautam Sanyal, PhD, Principal Consultant, Vaccine Analytics, LLC

This talk will include analytical strategies for quantitative evaluation of CQAs of mRNA vaccine drug substances and drug products with a view to speedy batch release of high quality vaccines. Strategies for addressing the challenges with evaluating integrity of each mRNA construct and potency of each antigen in a multivalent mRNA vaccine will be discussed.

3:05 Networking Refreshment Break (Aqua Foyer)

3:30 Analytical Tools to Support Vaccine Quality

Kevin L. Carrick, Director, Global Biologics, USP

Appropriate quality assessment is an important element of vaccine development and manufacturing. The USP-NF contains general information and best practices on the quality assessment of vaccines. This presentation will cover General Chapters in the USP-NF that support vaccines and new efforts to develop additional tools for vaccine quality assessment.

4:00 Single-Particle Imaging to Quantitate Biophysical Properties of mRNA Lipid Nanoparticles and Engineer Improved Vaccines

Sabrina Leslie, PhD, Associate Professor, Physics and Astronomy Department, The University of British Columbia

We present a quantitative single-particle imaging platform that enables simultaneous measurements of the size, mRNA-payload, and dynamic properties of vaccines in cell-like conditions. We investigate the dependence of mRNA-lipid-nanoparticle structure and fusion dynamics on formulation, using commercially available formulations. These measurements are made on confined, freely diffusing particles, and during reagent-exchange such as in response to solution pH, in order to emulate intracellular dynamics in a controlled setting.

4:30 Size Characterization of Vaccine Antigens: Ensemble vs Single Particle Analysis Approach

Rahul Misra, PhD, Scientist, Biophysics and Process Analytical Technology, Sanofi

Single particle analysis approach involves tunable resistive pulse sensing technology which measures the size of individual particles passing through a nanopore and claims to provide more accurate particle size distribution data. Particle concentration analysis is also based on single-particle measurements thereby ensuring highly accurate calculations compared to the ensemble-based approach. The present study performs the comparative analysis of size distribution of vaccine antigens to evaluate the performance of these methods.

5:00 Close of Day

FRIDAY, JANUARY 20

7:30 am Registration (Indigo Foyer)

ROOM LOCATION: Indigo and Aqua Foyer

BuzZ Sessions

8:00 BuzZ Sessions with Continental Breakfast

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.
Please continue to check the BuzZ Session page on our conference website for detailed discussion topics and moderators

BuzZ Table 3: High-Capacity Chromatography Material for Virus Purification

Alois Jungbauer, PhD, Professor & Head, Biotechnology, Institute of Bioprocess Science and Engineering, University of Natural Resources and Life Sciences (BOKU)

ROOM LOCATION: Aqua Salon E

ANALYTICS AND CMC OF mRNA VACCINES AND BEYOND

9:00 Chairperson's Remarks

Prashant Kumar, PhD, Scientific Assistant Director, Pharmaceutical Chemistry, University of Kansas, Lawrence

9:05 Development of RNA Vaccines and Therapeutics Enabled by Lipid Nanoparticles

Mano Manoharan, PhD, Distinguished Scientist & Senior Vice President, Innovation Chemistry, Alnylam Pharmaceuticals

The regulatory approval of ONPATTRO, a lipid nanoparticle-based short-interfering RNA drug for the treatment of polyneuropathies induced by hereditary transthyretin amyloidosis, paved the way for the clinical development of many nucleic acid-based therapies including the approved mRNA vaccines, enabled by nanoparticle delivery. The chemistry and biology principles behind the discovery, development and targeting based on LNP technology will be discussed.

9:35 Evaluation of *in vivo* Delivery, Kinetics of Protein Translation, and Immunogenicity of Self-Amplifying and Non-Amplifying mRNA Formulated with Cationic Nanolipoprotein Particles

Wei He, PhD, Biomedical Scientist, Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory

Messenger RNA (mRNA) has great potential as a therapeutic or vaccine agent. We generated cationic nanolipoprotein particles (c-NLPs) to complex with traditional non-amplifying mRNA or self-amplifying mRNA (SAM) for *in vivo* delivery, evaluating protein expression relative to a lipid nanoparticle (LNP)-based delivery vector over 22 days. Furthermore, SAM formulated with c-NLPs or LNPs induced robust immune response against a variety of viral and bacterial antigens.

10:05 Measurement of Adenovirus-Based Vector Heterogeneity

Shaleem I. Jacob, PhD, Research Fellow, Biochemical Engineering, University College London

In-process quality attribute data collected during Adenovirus vector manufacturing has focused on particle concentration and infectivity ratios (based on viral genome: cell-based infectivity), and data suggests only a fraction of viral particles present in the final vaccine product are efficacious. Here we examine the product heterogeneity of two Adenovirus viral vectors, Chimpanzee adenovirus (ChAdOx1) and Human adenovirus Type 5 using TEM and MS.

VACCINE BIOPROCESSING AND MANUFACTURING

10:35 Networking Coffee Break (Aqua Foyer)

11:00 Purification of COVID-19 and Influenza Virus-Like Particles by Non-Woven Material

Alois Jungbauer, PhD, Professor & Head, Biotechnology, Institute of Bioprocess Science and Engineering, University of Natural Resources and Life Sciences (BOKU)

Non-woven material represents the next-generation of chromatography material with special features for bionanoparticles separation. The architecture of this bed allows the processing of large particles and molecules without diffusional limitation. This is exemplified by separation of COVID-19 and influenza virus-like particles.

11:30 Lipid Nanoparticles for Overcoming Biological Barriers to mRNA Delivery

Michael Mitchell, PhD, Skirkanich Assistant Professor of Innovation, Department of Bioengineering, University of Pennsylvania

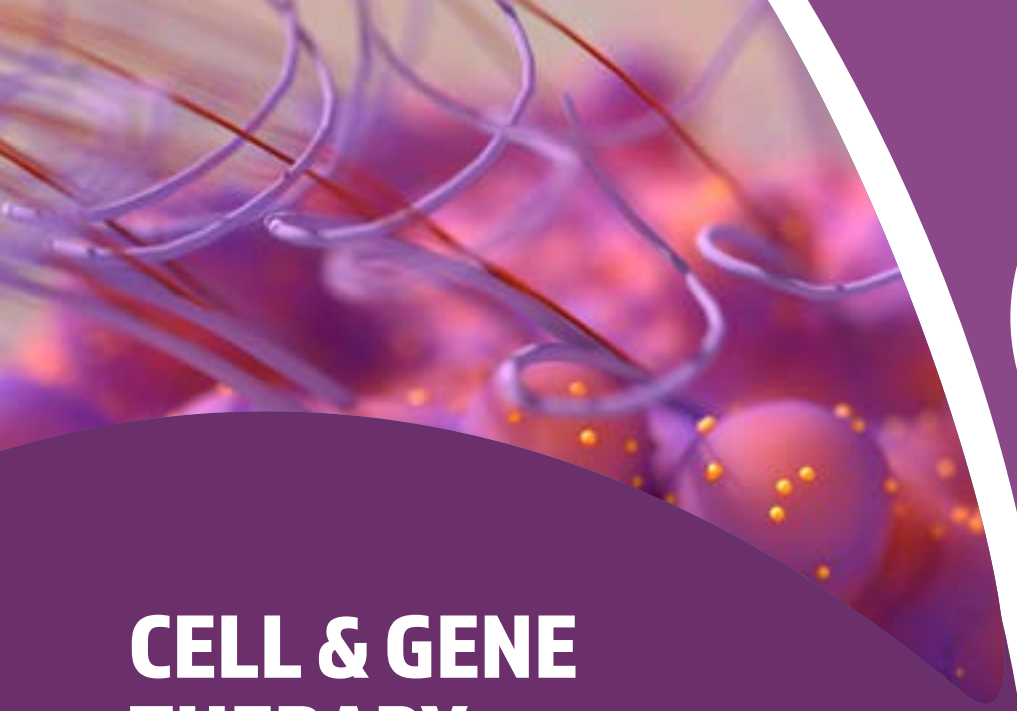
In this talk, I will discuss our efforts towards the development of lipid and polymer-based nanoparticles that enable the delivery of nucleic acid therapeutics to target cells and tissues ***in vivo***. Furthermore, I will describe new therapeutic strategies utilizing these nanoparticles to (i) reprogram immune cells for cancer immunotherapy applications, (ii) in utero mRNA delivery for treating disease before birth.

12:00 pm COVID-19 Vaccines: Technology Transfer and Licensing Facilitated Rapid Deployment

Elizabeth R. Nesbitt, Senior International Trade Analyst, Office of Industry & Competitiveness Analysis, U.S. International Trade Commission

The rapid deployment of three COVID-19 vaccines authorized for use in the United States in 2020 and 2021 involved substantial firm-level collaboration to rapidly complete the multidimensional matrix of steps along the entire global value chain from discovery to commercialization. Key enabling factors included quickly establishing and expanding international supply chains meeting regulatory requirements and the vaccine owners' rapid technology transfer to firms in developing and developed countries.

12:30 Close of PepTalk



CELL & GENE THERAPY

The **Cell & Gene Therapy** pipeline features two back-to-back conferences and a foundational training seminar on the critical challenges facing the analysis, characterization, quality control, scale-up, and manufacture of cell and gene therapies. Some of the topics to be discussed include product and process characterization, critical quality attributes, analytical toolbox, product development, process development, and scale-up, and the role of CDMOs.

PEPTALK

JANUARY 16-17

Cell Therapy Analytics & Manufacturing

AGENDA

JANUARY 17-18

Gene Therapy Analytics & Manufacturing

AGENDA

JANUARY 18-19

Training Seminar: Introduction to CMC for Biotech Cell & Gene Therapy Products

AGENDA

JANUARY 16-17, 2023 | Cambridge Healthtech Institute's 4th Annual

CELL THERAPY ANALYTICS & MANUFACTURING

CMC and Characterization Strategies, Analytical Tools, Process Development, and Scale-Up

SUNDAY, JANUARY 15

4:00 pm Pre-Conference Registration (Indigo Foyer)

MONDAY, JANUARY 16

7:00 am Registration and Morning Coffee (Indigo and Aqua Foyer)

9:00 Organizer's Welcome Remarks

ROOM LOCATION: Aqua Salon F

APPROACHES FOR CAR Ts

9:05 Chairperson's Opening Remarks
Kelly Kemp, PhD, Senior Director CMC, ViaCyte, Inc.

9:10 KEYNOTE PRESENTATION: A Tool Box for Next-Generation Chimeric Antigen Receptors
Preet M. Chaudhary, MD, PhD, Professor & Chief Hematology & Director, Blood & Marrow Transplant, University of Southern California

Chimeric Antigen Receptors (CAR) can redirect T cells to selectively kill tumor cells in an MHC independent manner. However, there are several limitations to this approach including toxicities (e.g., cytokine release syndrome and neurotoxicity), tonic signaling resulting in CAR-T cell exhaustion and lack of persistence, and lack of efficacy against solid tumor. The talk will describe a toolbox for the generation of next-generation chimeric antigen receptors.

9:50 *In vivo* Reprogramming of CAR T Cells Using Targeted LNPs
Viktor Lemgart, Research Fellow, Tidal Therapeutics, a Sanofi Company

Tidal Therapeutics has developed a new technology that allows the generation of Chimeric Antigen Receptor-expressing T cells directly *in vivo*. The technology uses *in vitro* translated synthetic mRNA that is formulated in lipid nanoparticles. The LNPs are specifically targeted to circulating T cells to transiently express disease-specific receptors on the surface.

10:20 Networking Coffee Break (Indigo and Aqua Foyer)

CELL THERAPY PROCESS DEVELOPMENT, CMC, AND ANALYTICS

10:45 Analytical Challenges and Strategies for the Development of Allogeneic Cell-Based Therapeutics
Kelly Kemp, PhD, Senior Director CMC, ViaCyte, Inc.

Cell therapy products tend to be novel and can be more complex compared to other biologics, presenting a number of analytical challenges. With few standardized methods available, we must be innovative and define our own best practices. Considerations for analytical development and for the characterization of cellular therapies will be discussed.

11:15 Viral Vector Production Improvements for Cell Therapy
Gabriel Byrne, PhD, Scientist III, Gene Therapy Process Development, Sangamo Therapeutics

A handful of vendors now supply nearly every component necessary for bioprocessing – from designer cell lines and specialized media through bioreactors and columns. While these systems are presented as an ideal solution, designed to maximize yield, shorten time, and simplify supply logistics, it is worthwhile to explore selecting and testing each component individually. Here we present work done by Sangamo's process development team, increasing viral vector titers in bioreactors.

11:45 PANEL DISCUSSION: Emerging Challenges in Cell Therapy Analytics and CMC
Moderator: Kelly Kemp, PhD, Senior Director CMC, ViaCyte, Inc.
Panelists:
Preet M. Chaudhary, MD, PhD, Professor & Chief Hematology & Director, Blood & Marrow Transplant, University of Southern California
Tracy Zhao, Field Application Scientist, Tech Support, Acrobiosystems
Steven J. Kattman, PhD, Executive Director, Sana Biotechnology, Inc.
Viktor Lemgart, Research Fellow, Tidal Therapeutics, a Sanofi Company

12:15 pm Products & Services Across Cell Therapy Research & Development
Tracy Zhao, Field Application Scientist, Tech Support, ACROBiosystems

There're many different types of cancer therapies in the clinical space, and Immunotherapies are a novel one. A subsection of immunotherapies is cell therapy, modify immune cells to have better effects and safety. ACRO offers multiple types of products. Including beads, cytokines, target proteins, antibodies, ELISA kits, etc. To support each phase of your cell therapy journey. Our products promote the efficacy of cell therapy and potency, preserving research budgets.

12:30 Presentation to be Announced

12:45 Enjoy Lunch on Your Own

1:55 Session Break

ROLE OF ACADEMIA AND CDMOs IN DEVELOPMENT AND MANUFACTURING

2:00 Chairperson's Remarks
Steven J. Kattman, PhD, Executive Director, Sana Biotechnology, Inc.

2:05 The Role of Academic Centers in Cell Therapy Development
Matthew B. Seefeldt, PhD, Executive Director & Research Instructor, Cell Therapy & Manufacturing, University of Colorado

The purpose of this talk will be to walk through the design and build-out of a multi-product GMP manufacturing facility in an academic setting. The talk would review both the technical design considerations as well as business components to ensure staffing and Phase I compliance.

2:35 Reprogramming Natural Killer Cells for Immunotherapy of Cancer
Sandro Matosevic, PhD, Assistant Professor, Department of Industrial and Physical Pharmacy, Purdue University

Natural killer (NK) cell infiltration into and anti-tumor immunity against solid tumors is often low. Functional and metabolic impairment of NK cells is induced by the suppressive microenvironment of solid tumors due to, among others, hypoxia, metabolites, such as adenosine, and the expression of inhibitory NK checkpoints. Here, we discuss our work in redirecting NK cells to overcome immunosuppressive solid tumor by genetically rewiring their functional and immunometabolic responses.

ROOM LOCATION: Indigo and Aqua Foyer

BuzZ Sessions

3:05 Find Your Table and Meet the BuzZ Sessions Moderator

3:10 BuzZ Sessions with Refreshments (IN-PERSON ONLY)

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.
Please continue to check the BuzZ Session page on our conference website for detailed discussion topics and moderators

BuzZ Table 3: Cell Therapy Drug Product Development

Steven J. Kattman, PhD, Executive Director, Sana Biotechnology, Inc.

- Process considerations for manufacturing autologous and allogeneic cell therapy products
- Drug product considerations for hematological malignancies and solid tumor indications
- Clinical vs commercial supply chain needs: Integrated drug product design

BuzZ Table 7: Cell Therapy Process Development

Kelly Kemp, PhD, Senior Director CMC, ViaCyte, Inc.

- Selection of raw materials
- Increasing cell yields
- Demonstrating comparability

PROCESS DEVELOPMENT, SCALE-UP, AND MANUFACTURING

4:30 Cell Culture Process Scale-Up Challenges for Commercial-Scale Manufacturing of Allogeneic Pluripotent Stem Cell Products

Brian Lee, PhD, CEO, PBS Biotech, Inc.

Human induced pluripotent stem cells (hiPSCs) have enormous promise. However, their potential can be bottlenecked due to unique challenges related to scalable manufacturing of high-quality hiPSCs for clinical and commercial purposes. PBS Biotech, with its innovative single-use bioreactors, provides scalable solutions to its global customers that enable them to scale up production of their therapeutic cells, with some entering various phases of clinical trials

5:00 Unique Challenges in The Development and Manufacture of Pluripotent Stem Cell-Derived Cell Therapies

Steven J. Kattman, PhD, Executive Director, Sana Biotechnology, Inc.

Pluripotent Stem Cell (PSC)-derived cell therapies provide unprecedented opportunities to address unmet and seemingly intractable diseases. However, the development of cell therapy products derived from PSCs pose unique manufacturing challenges, including selection of starting cell lines, application of developmental biology, scaling, product profile, and cryopreservation. Here we will discuss these challenges and approaches to generate PSC-derived cardiomyocytes as a novel cell therapy to address heart failure.

6:00 Welcome Reception in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

YOUNG SCIENTIST MEET UP

Young Scientist Meet Up

Iris Goldman, Production, Cambridge Innovation Institute

7:30 Close of Day

CITY WALK MEET UP

BREAKOUT DISCUSSION: City Walk Meet Up

Kevin Brawley, Associate Project Manager, Production Operations & Communications, Cambridge Innovation Institute

TUESDAY, JANUARY 17

8:15 am Registration and Morning Coffee (Indigo and Aqua Foyer)

ROOM LOCATION: Aqua Salon F

STRATEGIES FOR PRODUCT DEVELOPMENT OF CELL THERAPIES

8:45 Chairperson's Remarks

Jay Sarkar, PhD, Visiting Scholar, Stanford University

8:50 Challenges and Opportunities in Cell Therapy Drug Product Development

Bharathi Vellalore, PhD, Senior Scientist, Biotherapeutics Drug Product Development, Janssen

- Overview of drug product development from formulation, fill-finish, and storage, to delivery
- Formulation and process considerations to improve end-to-end drug product stability
- Integrated drug product design to suit clinical and commercial supply chain needs

9:20 Selected Poster Presentation: CD47 Expression Is Required for CAR T Cell Persistence *In Vivo*

Alexandra Beckett, PhD Candidate, Biomedical Sciences, St. Jude Children's Research Hospital

We previously developed CD47-specific chimeric antigen receptor (CV1-CAR) T cells that overcome fratricide by downregulating CD47 expression. While CV1-CAR T cells are specific and exert potent antitumor activity ***in vitro***, loss of cell surface CD47 prevented their persistence ***in vivo*** due to macrophage mediated phagocytosis. Our results support current interests in CD47 overexpression to enhance adoptive cell transfer strategies.

9:50 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

ROOM LOCATION: Aqua Salon D

CHARACTERIZATION OF CELL THERAPY AND NOVEL BIOLOGICS

10:30 Latest Analytical Methods for Characterization of Virus Particles in Cell and Gene Therapy Products

Tim Menzen, PhD, CTO & Pharmacist, Coriolis Pharma Research GmbH

Cell and gene therapy using viral vectors promises to overcome unmet needs in therapy of severe diseases. These viral vectors provide an analytical challenge during product development and stability assessment as they contain proteins, nucleic acids, and in some cases also a lipid membrane. The talk will provide an overview of latest analytical methods for virus particle characterization and show recent results from, e.g., analytical ultracentrifugation.

11:00 Development for and Characterization of Intraorganelle Localization of Peptide, Protein, and Oligo Conjugated Actives

Jay Sarkar, PhD, Visiting Scholar, Stanford University

Conjugated peptide sequences redefine targeted delivery through their dual nature as both physical and informational constructs. Their physical properties are exploited through their gross electrochemical interactions with cellular structures, most notably the cell membrane. While their informational properties can be harnessed through the cell's endogenous protein trafficking logic. We will discuss this utility and how to design and characterize their localization of drug actives to and even within organelle targets.

11:30 Mass Photometry - an analytical technology for biomolecular characterization

Gabriella Kiss, Director of Global Strategic Accounts, Business Development, Refeyn Inc.

Quantification of empty/full ratio of capsids in AAV preparations is a major bottleneck in characterizing recombinant AAV samples. Samux^{MP} is a mass photometer, tailored specifically to measure empty/full ratios of AAVs. In this talk, we will demonstrate capabilities of the Samux^{MP} in characterizing AAV samples in less than 5 mins. We will show that it can differentiate between empty, partially filled and full AAV capsids, and that it is serotype agnostic.

11:45 Simultaneous Quantification of Expression Levels and Affinities of Membrane Proteins without Purification or Calibration

Sebastian Fiedler, PhD, Head of Applications, Applications, Fluidic Analytics

We introduce a membrane protein affinity and concentration assay for working with unpurified membrane proteins in a native lipid-bilayer environment. To demonstrate our approach, we quantified both the expression level of endogenous HER2 in a breast cancer cell line and its affinity to trastuzumab. The method is quick and easy to use and has the potential to be expanded from cell lines to tissues and tumor biopsies.

12:00 pm Session Break and Transition to Luncheon Presentation

12:10 Luncheon Presentation to be Announced

Speaker to be Announced

12:40 Close of Cell Therapy Analytics & Manufacturing

JANUARY 17-18, 2023 | Cambridge Healthtech Institute's 4th Annual

GENE THERAPY ANALYTICS & MANUFACTURING

CMC Strategies, Tools, Process Development, and Scale-Up Considerations for Gene Therapies

TUESDAY, JANUARY 17

12:45 pm Registration (Indigo Foyer)

1:00 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

1:30 Organizer's Welcome Remarks

ROOM LOCATION: Aqua Salon E

IMPORTANT CONSIDERATION FOR DEVELOPMENT OF NOVEL BIOTHERAPEUTICS

1:35 Chairperson's Opening Remarks

Susumu Uchiyama, PhD, Professor, Biotechnology, Osaka University

1:40 KEYNOTE PRESENTATION: Optimizing Drug Product Presentation and Manufacturing Processes for Gene Therapy Products

Sandeep Yadav, PhD, Senior Director, Drug Product Formulation & Fill/Finish, Sangamo Therapeutics

Biotechnology companies are extensively leveraging AAV to deliver therapeutic DNA for genomic medicine applications. Some of the notable challenges are extremely low titers, limited manufacturing lots to develop process knowledge, and complex analytical methodologies required to characterize AAV systems leading to higher cost of goods (COGs). We discuss developing and optimizing DP formulation/presentations and manufacturing strategies to support patient safety, healthcare provider convenience, and reducing COGs to enable patient accessibility.

2:20 Latest Developments in Particulate Impurity Characterization Technologies for Biologics

Bruce A. Kerwin, PhD, Principal, Kerwin Biopharma Consulting LLC

Within the talk, novel approaches for the characterization of particulate impurities in biologics will be presented and compared to state-of-the-art technologies for submicron and subvisible particle analysis. Besides new analytical technologies, the integration of machine learning for data analysis will be presented.

ROOM LOCATION: Aqua Salon F

2:50 Strategies to Propel Your Viral Vector Therapy from Lab to Clinic

FUJIFILM Diosynth Biotechnologies

Hung Nguyen, PhD, Global Program Design, Manager, FUJIFILM Diosynth Biotechnologies

Gene Therapies continue to offer promising avenues as curative therapies for unmet patient needs; however, developers of these life-changing therapies often face various challenges on their journey to the clinic, including compressed timelines and high costs. FUJIFILM Diosynth Biotechnologies provides a flexible AAV development and manufacturing platform that can help our partners navigate these challenges by streamlining the critical path from pre-clinical and clinical development through commercialization.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

ANALYTICAL TOOLS AND CMC STRATEGIES FOR GENE THERAPIES

4:00 Analytical Assessment of AAV-Based Gene Therapy: Best Practices and Lessons Learned

Jerome Jacques, PhD, Principal Scientist, United States Pharmacopeia

Gene therapies offer tremendous promise to address human disease, but their complexity and diversity present unique challenges to those seeking to standardize materials and methods. Therefore, the USP is working with stakeholders to respond to the needs by developing both documentary and physical reference standards. We will discuss existing documentary standards that apply to gene therapies and provide an update on new standards under development to support AAV-based gene therapies.

4:30 Analytics for AAV-Based Gene Therapy Products

Santoshkumar L. Khatwani, PhD, Director, Analytical Development, Sangamo Therapeutics

Demonstrating Analytical Comparability in Gene Therapy:
1. Challenges of demonstration analytical comparability
2. Best practices for analytical comparability
3. Case study in gene therapy

5:00 Biophysical Characterizations of AAV Vectors with Small Volume

Susumu Uchiyama, PhD, Professor, Biotechnology, Osaka University

Biophysical characterizations of AAV vectors are necessary for understanding the quality of purified AAV vectors. I will introduce characterization methods that can be performed with small amount of AAV vectors and will contribute to the improvement of the manufacturing process.

5:30 Close of Day

WEDNESDAY, JANUARY 18

8:30 am Registration and Morning Coffee (Indigo and Aqua Foyer)

ROOM LOCATION: Aqua Salon CDE

9:00 Organizer's Remarks

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

9:10 Plenary Fireside Chat: Supporting and Driving Biotech: Past, Present, and Future

Moderator: Julie Ames, Vice President, Corporate Communications, Biocom California

Innovation can refer to something new, like an invention, or the development and introduction of new practices. The end result is often a new product, but it can also be a new practice, procedure, or way of thinking. Change and challenges are often what inspire innovation and propel us forward into new ways of thinking. This Fireside Chat will explore the following:
- Success stories
- Serendipitous discoveries
- Current projects
- Future developments

Panelists:

Amy K. Butler, PhD, President, Biosciences, Thermo Fisher Scientific

Taegen Clary, Vice President, Marketing, Unchained Labs

Jonathan Haigh, PhD, MBA, Vice President, Process Development, Fujifilm Diosynth Biotechnologies

Craig R. Monell, PhD, Vice President, Sales, Marketing & Business Development, BioLegend, Inc.

10:15 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

ROOM LOCATION: Aqua Salon F

ANALYTICAL TOOLS AND CMC STRATEGIES FOR GENE THERAPIES, CONT.

11:00 Chairperson's Remarks

Jerome Jacques, PhD, Principal Scientist, United States Pharmacopeia

11:05 AAV Characterization with Multiwavelength Analytical Ultracentrifugation

Amy Henrickson, Research Associate, Biochemistry, University of Lethbridge

Multi-wavelength analytical ultracentrifugation offers two highly precise and orthogonal characterization methods in one experiment to identify the ratio of any loading state of AAVs, ranging between empty capsids to overfilled capsids. In this talk, I will present examples, and discuss the experimental approaches used to characterize viral vectors and their nucleic acid cargo load by multi-wavelength analytical ultracentrifugation.

11:35 Mass Spectrometry Applications in Cell & Gene Therapy

Jill Bradley-Graham, PhD, Scientist, BioAnalytics Characterization, Sanofi Genzyme

We are performing extensive MS method development to characterize critical quality attributes in gene and cell therapy products, not only proteins but lipids and oligonucleotides as well. Utilizing new MS technologies for protein analysis, we are gaining a better understanding of post-translational modifications on gene and cell therapy products as well as investigating critical structure/function relationships.

12:05 pm Improving titer and impurity analysis for gene therapy products on the Gyrolab® platform

GYROS PROTEIN Technologies

Emily Menesale, Scientist II, Ultragenyx

Many types of analytical assays are needed in the support of gene therapy product development. Immunoassays are one such platform that are used to measure attributes such as capsid titer and impurity levels. Typical ELISAs are hands-on and time-consuming. We describe the development of automated immunoassays on the Gyrolab® platform. These assays not only increase efficiency, but also produce high quality data needed to support process development and product release.

12:20 Presentation to be Announced

12:35 Session Break and Transition to Luncheon Presentation

12:45 LUNCHEON PRESENTATION: Scalable, High Titer Production of AAV in the Gibco CTS AAV Production System

ThermoFisher SCIENTIFIC

Chao Yan Liu, Sr. R&D Manager, Cell Biology, Thermo Fisher Scientific

We present data on the Gibco™ CTS™ AAV-MAX Production System, a suspension based AAV production system that allows for scalable, high titer AAV production using a clonal 293F-derived cell line and chemically defined reagents. The AAV-MAX system delivers titers of ≥5x10^{10} viral genomes per mL (vg/mL) across multiple serotypes, with excellent scalability from multi-well plates to stirred tank bioreactors, making it an ideal platform for clinical and commercial production of AAV.

1:45 Session Break

PROCESS CHARACTERIZATION

2:00 Chairperson's Remarks

Vikas Bhat, PhD, Associate Director, Process Development, BioMarin Pharmaceutical, Inc.

2:05 Orthogonal Analytics to Monitor Quality Attributes of AAV Capsids to Support Efficient Process Development

Vikas Bhat, PhD, Associate Director, Process Development, BioMarin Pharmaceutical, Inc.

Process development for adeno-associated virus (AAV) manufacturing faces unique challenges given the complex nature of the molecule. Biomarin employs multiple biochemical and biophysical techniques to overcome these challenges in order to optimize process development efforts with the ultimate goal of innovating in the field of AAV production for the benefit of our patients.

2:35 Process Design and Characterization to Enable Production of AAV-Based Gene Therapy for Clinical Use

Benson Gikanga, Associate Director, Cell & Gene Therapy Formulation, Sangamo Therapeutics

Many challenges faced by CGT products impact process design, characterization, and validation of manufacturing processes. Specifically, the complexity of these modalities coupled with scarcity of material for use in knowledge building studies makes it hard to reduce studies needed for launch. The need to justify scale-down models and surrogates used poses additional challenges. This presentation will explore such challenges using a few case studies.

PROCESS, SCALE-UP, AND MANUFACTURING CONSIDERATIONS

3:05 High-Throughput Chromatography Studies to Risks in Gene Therapy Clinical Manufacturing

Matthew Petroff, PhD, High-Throughput Process Development Lead, Spark Therapeutics, Inc.

Challenges of AAV downstream processing – including high levels of product variants and complex characterization – are exacerbated by pressures for early implementation of process innovations. We show high-throughput case studies for early assessment of platform fit, process optimization, and process sensitivity. Together these generate optimization and risk assessments early in development, reducing risks of process changes in large-scale manufacturing.

PepTalk Plaza: Speed Networking

IN-PERSON ONLY: Speed Networking

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

4:15 Cytosolic miRNA-Inducible Nuclear Translocation of CRISPR Protein for Disease-Specific Genome Modification

JiMin Lee, PhD, Assistant Professor, KAIST

Harnessing the innate mechanism of mRNA decay by disease-specific endogenous miRNA, our platform enables the development of new gene therapies that restore normal function in patients' cells. We applied the mRNA bridge mimetics platform to Cas9 protein to confer it the ability to translocate into the nucleus via cleavage of the nuclear export signal. This system performed programmed gene editing *in vitro* and *in vivo*.

4:45 HPC-Powered AI/ML BioCAD Platform for Viral Bioengineering

Stefan N. Lukianov, PhD, CEO, Technology, Salve Therapeutics, Inc.

We are building a high-performance computing-powered bioengineering platform to mine, design, model, and test novel viral biologics. Better viral delivery methods will expand the available biologic tool kit to produce better medicines for intractable and incurable diseases. A new software platform specifically tailored to mine, design, model, and test the human virome for new therapeutic modalities will enable exploration of this therapeutic space in a safe, rapid, and cost-effective manner.

5:15 PANEL DISCUSSION: Overcoming Process and Analytics Challenges for Gene Therapies

Moderator: Vikas Bhat, PhD, Associate Director, Process Development, BioMarin Pharmaceutical, Inc.

Panelists:
Matthew Petroff, PhD, High-Throughput Process Development Lead, Spark Therapeutics, Inc.
Stefan N. Lukianov, PhD, CEO, Technology, Salve Therapeutics, Inc.
JiMin Lee, PhD, Assistant Professor, KAIST

5:45 **Networking Reception in the Exhibit Hall with Poster Viewing (Indigo Ballroom)**

WOMEN IN SCIENCE MEET UP AT PEPTALK PLAZA

Women in Science Meet Up at PepTalk Plaza


Christa Cortesio, PhD, Senior Scientist and Group Lead, Protein Science, Protein Biochemistry & Analytics Core, Kite Pharma
Michelle R. Gaylord, MS, Principal Scientist, Protein Expression Lead, Velia, Inc.

7:00 **Close of Gene Therapy Analytics & Manufacturing**

THURSDAY, JANUARY 19, 2023 8:30 AM - 5:00 PM | FRIDAY, JANUARY 20, 2023 9:00 AM - 12:30 PM

TS4C: INTRODUCTION TO CMC FOR BIOTECH, CELL & GENE THERAPY PRODUCTS

The chemistry manufacturing and controls (CMC) of biologics is a multidiscipline technical operation of bioprocess, analytics, dosage formulation and cGMP manufacturing/testing for DS/DP release and stability to treat human diseases. This interactive training course will provide a comprehensive CMC overview of therapeutic biological products. It introduces a variety of therapeutic modalities including recombinant proteins, monoclonal antibodies (Mab), and cell and gene therapy (CGT) in the context of IMPD and IND regulatory filing. Attendees will learn scientific, technical, and operational aspects of overall biologics CMC activities as well as quality compliance and regulatory requirement. The instructor will present common pitfalls and share the best industry practices. Numerous real-world regulatory queries/comments from health authorities worldwide will be exemplified as case studies during the training course.

TOPICS TO BE COVERED:

1. Diverse modality of therapeutic biological products
2. Biologics CMC activities for regulatory filing (IMPD/IND)
3. Quality by design (QbD) concept, quality target product profile (QTPP), and critical quality attributes (CQA)
4. Cell line development, process development, and manufacture of biologics, CGT DS and DP
5. Current analytical technologies to characterize product variants/impurities, process impurities (e. g. HCP), and contaminants
6. Formulation development and compatibility with container closures and injection devices
7. Reference material characterization/qualification and justification of specifications for DS/DP release and ICH stability for product expiry
8. Process validation, analytical validation, and control strategy of cGMP manufacturing
9. Manufacturing process changes during product development lifecycle: CMC comparability exercise

WHO SHOULD ATTEND:

The course is beneficial to individuals involved in biologics drug research/development, bioprocess development, analytical development, formulation development, quality control, quality assurance, regulatory affairs, project management, or related functional areas.

INSTRUCTOR BIOGRAPHY:

Kevin Zen, PhD, Executive Director, Chemistry Manufacturing and Controls, AnaptysBio, Inc.

Kevin has over 20 years of broad experience in Biologics CMC, and Strategic and Technical Operations. Prior to joining AnaptysBio, he held various positions in biologics CMC disciplines at Allergan, AstraZeneca, Becton Dickinson, and Catalent Biopharma Solutions. In addition to developing therapeutic biological products in-house, Kevin also had extensive experience working with external contract manufacturing organizations (CMO) and contract research organizations (CRO), including production cell line development, bioprocess development, DS/DP cGMP manufacturing, process characterization, process performance qualification (PPQ), formulation development by DoE, analytical procedure development and method validation, reference standard qualification, extended characterization, and CMC analytical comparability.

Cambridge Healthtech Institute Training Seminars offer real-life case studies, problems encountered and solutions applied, and extensive coverage of the basic science underlying each topic. Experienced Training Seminar instructors offer a mix of formal lectures, interactive discussions and activities to help attendees maximize their learning experiences. These immersive trainings will be of value to scientists from industry and academic research groups who are entering new fields – and to those working in supporting roles that will benefit from an in-depth briefing on a specific aspect of the industry.

BIOTHERAPEUTIC EXPRESSION & PRODUCTION

The demand for high-quality proteins for basic research, diagnostics, and therapy continues to exponentially expand. Thus, higher-throughput protein expression, production, and purification as well as more flexible expression platforms and techniques are necessary to meet the demands for both research and manufacturing pipelines. Throughout the week, the **Biotherapeutic Expression & Production** pipeline explores the newest data, innovations, and strategies to make the expression and production of these valuable proteins more efficient, effective, and trouble-free.

PEPTALK

JANUARY 16-17

Cell Line Engineering and Development

AGENDA

JANUARY 17-18

Recombinant Protein Expression and Production

AGENDA

JANUARY 19-20

Optimizing Workflows in Protein Production Laboratories

AGENDA

REGISTER EARLY & SAVE!

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JANUARY 16-17, 2023 | Cambridge Healthtech Institute's 15th Annual

CELL LINE ENGINEERING AND DEVELOPMENT

Tools for Effective Engineering of Genes, Vectors, Constructs, Clones and Hosts

SUNDAY, JANUARY 15

4:00 pm Pre-Conference Registration (Indigo Foyer)

MONDAY, JANUARY 16

7:00 am Registration and Morning Coffee (Indigo and Aqua Foyer)

9:00 Organizer's Welcome Remarks

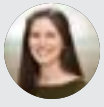
Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

ROOM LOCATION: Aqua Salon AB

EMERGING TOOLS FOR EXPANDING THE EXPRESSION TOOL KIT

9:05 Chairperson's Opening Remarks

Henry C. Chiou, PhD, Senior Director General Manager, Biosciences, Thermo Fisher Scientific



9:10 KEYNOTE PRESENTATION: Developing a Suite of High-Throughput Screens for Use in Engineering Bacterial Protein Secretion

Danielle Tullman-Ercek, PhD, Professor, Chemical and Biological Engineering; Director, Master of Biotechnology Program, Northwestern University

We present the development of a suite of high-throughput, fluorescence-based assays to probe secretion systems in bacteria. We demonstrate the utility of these screens to characterize and engineer the Salmonella enterica Type III Secretion System for the high-titer production of a variety of biochemically challenging heterologous proteins, such as growth factors, antibodies, and toxic antimicrobial peptides.

9:50 PCR-Mediated Expressions of a Gene in Triple Hosts: Yeast, *E. coli*, and Mammalian Cells

Mikiko Nakamura, PhD, Associate Professor, Department of Instrumental Analysis, Research Center for Advanced Science and Technology, Shinshu University

Escherichia coli, *Saccharomyces cerevisiae*, and mammalian culture cells are standard host organisms for genetic engineering and biological research. We developed a yeast expression plasmid that enables expression of the cloned gene in *E. coli* and mammalian cells via the transfer of PCR products amplified from the plasmid as a template. This is the first all-in-one plasmid applicable for expressions in three host organisms.

10:20 Networking Coffee Break (Indigo and Aqua Foyer)

10:45 Single Nucleotide Variants – What Can Go Wrong?

Chava Kimchi-Sarfaty, PhD, Deputy Associate Director, Research, Office of Tissues and Advanced Therapies, CBER, FDA

Single nucleotide variants (SNVs) are the underpinnings for human genomic diversity. While nonsynonymous variants are appreciated for transforming the protein sequence, synonymous variants have only lately gained increased recognition for altering mRNA structure, splicing, miRNA binding, co-translational protein folding, and protein stability. In my talk, I will show examples of single or multiple synonymous mutations in the form of codon optimization or codon recoding that can change protein attributes.

11:15 *Escherichia coli* Data-Driven Strain Design Using Aggregated Adaptive Laboratory Evolution Mutational Data

Adam M. Feist, PhD, Project Scientist, Bioengineering, University of California, San Diego

The designing of microbial genomes remains challenging due to the complexity of biology. Adaptive Laboratory Evolution (ALE) leverages nature's problem-solving processes to generate optimized genotypes currently inaccessible to rational methods. This study describes how novel strain designs can be extracted from aggregated ALE data by designing, building, and testing novel *Escherichia coli* strains. These results demonstrate how strain design efforts can be enhanced by the meta-analysis of aggregated ALE data.

11:45 Metabolic Dynamics in *Escherichia coli*-Based Cell-Free Systems

Mark Styczynski, PhD, Professor, Chemical & Biomolecular Engineering, Georgia Institute of Technology

Bacterial lysate-based cell-free systems are promising platforms for protein expression. Currently the total expression capacity of these systems can be quite limited. Here, we explore the residual metabolic network in cell-free lysates and identify the impacts of this "endogenous" metabolism on system properties including rate of protein production and final expression titers.

ROOM LOCATION: Aqua Salon E

12:15 pm Overcoming Challenges for High-Throughput Production of Diverse Custom Proteins Used in Discovery Applications

WuXi Biologics
Global Solution Provider

Jiansheng Wu, Vice President, Protein Services, WuXi Biologics

Dr. Wu will discuss the challenges in high-throughput protein production for small and large molecule drug discovery and demonstrate the parameters and design space required to generate high-quality proteins for HTS, antibody discovery, ***in vivo*** and developability studies. Supported by industry-leading platforms, our Protein team provides production services utilizing various expression systems for the generation of monoclonal, bispecific and multispecific antibodies, and other recombinant proteins.

12:45 Enjoy Lunch on Your Own

1:55 Session Break

ROOM LOCATION: Aqua Salon AB

APPLYING ALTERNATIVE EXPRESSION SYSTEMS

2:00 Chairperson's Remarks

Simon A. Messing, PhD, Scientist II, Frederick National Lab & Protein Expression Lab, Leidos Biomedical Research, Inc.

2:05 From the Lab to the Market: Making Green Algae a Competitive Player in the Biotech Industry

Yasin Torres-Tiji, PhD, University of California, San Diego

The overpopulation of the planet has caused a massive need for energy and reduced carbon, and microalgae, which are the most efficient producers within the ecosystem, can be utilized to satisfy mankind's demands. Algae biotechnology has generated varied products such as therapeutics, nutraceuticals, food, polymers, and biofuels. But to provide commercially viable bioproducts we need to advance two principal technologies: powerful genetic tools, and enhanced microalgal cultivation techniques.

2:35 Large-Scale Protein Production in *Vibrio natriegens* Can Beat *E. coli*

Simon A. Messing, PhD, Scientist II, Frederick National Lab & Protein Expression Lab, Leidos Biomedical Research, Inc.

Production of recombinant proteins in *E. coli* is the engine of many drug discovery efforts and is often the rate-limiting step. Another

bacterial host *Vibrio natriegens* has recently shown promise, as an alternative to *E. coli*. Here, we present a set of general protocols for its use. Moreover, we show that *Vibrio natriegens* can outproduce *E. coli* for certain protein reagents, and or solubilize protein where *E. coli* fails.

ROOM LOCATION: Indigo and Aqua Foyer

BuzZ Sessions

3:05 Find Your Table and Meet the BuzZ Sessions Moderator

3:10 BuzZ Sessions with Refreshments (IN-PERSON ONLY)

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.
Please continue to check the BuzZ Session page on our conference website for detailed discussion topics and moderators

BuzZ Table 4: Combining the Benefits of Academia and Industry: Get the Best of Both Worlds

Bjørn Voldborg, MSc, Head, National Biologics Facility, DTU Bioengineering, Technical University of Denmark

Is it possible to combine the efficiency, confidence., quality and focus of the industrial protein production and cell line development, with the flexibility, individualism and creativity of the academical environments at Universities?
- How to raise awareness at both ends?
- How to start-up?What are the needs?
- Funding and pricing/who will pay?
- Limitations?

BuzZ Table 6: Targeted Supplementation to Improve Protein Titer and Quality in CHO Cells

Natalie McAdams, PhD, Manager Cell Biology, BioProduction R&D, Thermo Fisher Scientific

- How can supplements be applied to a bioproduction process to boost protein titer?
- What process parameters and supplements can impact protein quality?
- Lessons learned – what process parameters or supplements can have a negative impact on performance?

EFFECTIVE EXPRESSION SCREENING

4:30 The Daft Punk Approach to Maximizing Protein Production – Faster, Better, Stronger via Leveraging Open-Source Robotics, Optimal Scaling, and High-Throughput Analytics

Lauren P. Carter, Principal Research Scientist & Engineer, Biochemistry, University of Washington

The Institute for Protein Design has developed powerful processes for computational protein design, most recently the Diffusion model, which combines structural prediction networks with generative diffusion with the ability to generate highly accurate designs optimized for soluble expression. This results in a high number of proteins requiring experimental validation. The IPD has developed methods to express, purify, and characterize these designed proteins that can keep pace with design velocity.

5:00 Using Automation to Generate High-Throughput Workflows for Higher Quality Stable Cell Line Development

Alicia Barker, Associate Scientist, Cell Line Development, Just-Evotec Biologics

The Just-Evotec Biologics CLD platform is optimized to decrease development timelines and increase throughput by using automation from transfection through RCB creation. Our high-throughput transfection method allows us to simultaneously screen 96 transfectants in stable pools to identify more manufacturable molecules with a reduced timeline. Using automation, we are capable of screening over 350 clones allowing us to identify cell lines with high productivity and favorable product quality attributes.

5:30 Coupling High-Density Data and High-Throughput Small-Scale Screening to Optimize DNA Construct Screening

Noel Byrne, Associate Principal Scientist, Structural Protein Sciences, Merck & Co., Inc.

The expression screening of large numbers of protein constructs can be automated utilizing the baculovirus expression system (BEVS) and TECAN automation. Biophysical characterization of small-scale screening samples, such as aSEC and nanoDSF, provides a more robust screening funnel with better prediction of successful clones. Expanding to an automated "midi-scale" screen allows for production of sufficient material to perform more in-depth POC studies such as Biacore, MST, and LC-MS.

6:00 Welcome Reception in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

YOUNG SCIENTIST MEET UP

Young Scientist Meet Up

Iris Goldman, Production, Cambridge Innovation Institute

7:30 Close of Day

CITY WALK MEET UP

BREAKOUT DISCUSSION: City Walk Meet Up

Kevin Brawley, Associate Project Manager, Production Operations & Communications, Cambridge Innovation Institute

TUESDAY, JANUARY 17

8:15 am Registration and Morning Coffee (Indigo and Aqua Foyer)

ROOM LOCATION: Aqua Salon AB

CHO CELL ENGINEERING AND DEVELOPMENT

8:45 Chairperson's Remarks

Bjørn Voldborg, MSc, Head, National Biologics Facility, DTU Bioengineering, Technical University of Denmark

8:50 Epigenetic Comparison of CHO Hosts and Clones Reveals Divergent Methylation and Transcription Patterns across Lineages

Meiping Chang, PhD, Principal Scientist, Process Research and Development, Merck Research Labs

The authors examine DNA methylation and transcription profiles of two different CHO hosts and the resultant production clones. Combining transcriptomics with DNA methylation data enables identification of potential processes and factors that may contribute to the differences in cell physiology between different production hosts. These differences, including epigenetic writers, readers, erasers, and effectors in turn may be important to explaining the variability in productivities of these cell lines.

9:20 Designing Biobetters using Glycoengineering

Frances Maureen Rocamora, PhD, Postdoctoral Fellow, Pediatrics, University of California, San Diego

Glycoprotein-based drugs represent the fastest-growing class of therapeutic molecules. As a key critical quality attribute of recombinant proteins, glycosylation plays a significant role in maintaining the stability, safety and efficacy of such molecules. Utilizing a platform that combines glycoengineering and systems biology, we seek to develop recombinant products that contain optimal glycan compositions and demonstrate improved biophysical characteristics and biological activity.

9:50 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

10:30 Cell Line Development to Mitigate Development Risks of a Complex Protein

Ren Liu, PhD, Principal Scientist, Discovery Interface, Merck & Co., Inc.

Expressing complex molecules such as bispecific antibodies and fusion proteins often faces challenges like low titer, poor product quality, and difficult-to-control post-translational modifications. We have tackled these challenges by engineering the expression host and vectors and optimizing the culture conditions.

11:00 Population Dynamics, Phenotypic Heterogeneity, and Age: Shifting Expression Patterns in Stable and Unstable Clonally-Derived CHO Populations

Theodore Peters, PhD, Senior Scientist, Cell Line Development, Seagen

CHO cell lines have significant phenotypic variability though derived from a single cell progenitor. This variability may lead to or be indicative of the propensity of a cell line to exhibit production instability over time. Here we characterize RNA expression from stable and unstable cell lines using single-cell RNA sequencing. Our work shows that clonally derived cell lines are a complex metapopulation of cells whose make-up changes significantly with age.

11:30 CHO Fed-Batch Strategies to Rapidly Increase MAB Titer by 100% without Sacrificing Product Quality

Severine Fagete, Vice President, Cell Line Development Services, Cell Line Services, Selexis

In the field of therapeutic antibody production, diversification of fed-batch strategies is flourishing in response to the market demand. All manufacturing approaches tend to follow the generally accepted dogma of increasing titer since it directly increases manufacturing output. Selexis has changed the parameters which influence titer and developed novel hybrid strategies that reduce timelines without compromising productivity quality.

12:00 pm Session Break and Transition to Luncheon Presentation

12:10 AmMag Quatro Plasmid Purification Made Easy

Rouba Najjar, Associate Director of US Marketing, GenScript USA, Inc.

Plasmid DNA is an essential component of molecular biotechnology applications. Large scale plasmid purification is labor-intensive, time-consuming, and often creates a process bottleneck. GenScript has developed a new automated, large-scale, high throughput plasmid purification solution, the AmMag Quatro. Designed as a scalable modular system, scientists can automate maxi-scale plasmid purification with up to four AmMag modules, each processing up to 6 maxi-prep samples, for a total of 24 samples.

12:40 Close of Cell Line Engineering and Development

JANUARY 17-18, 2023 | Cambridge Healthtech Institute's 25th Annual

RECOMBINANT PROTEIN EXPRESSION AND PRODUCTION

Employing Cell Factories to Improve Quantity and Quality

TUESDAY, JANUARY 17

12:45 pm Registration (Indigo Foyer)

1:00 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

1:30 Organizer's Welcome Remarks

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

ROOM LOCATION: Aqua Salon AB

EFFECTIVE EXPRESSION AND PRODUCTION OF UNIQUE PROTEINS

1:35 Chairperson's Opening Remarks

Oleg Brodsky, Senior Principal Scientist, Structural Biology & Protein Sciences, Pfizer Inc.

1:40 Improving Multiprotein Complex Production in Insect Cells Using Co-Expression of Chaperones and Co-Factors

Matthew R. Drew, Eukaryotic Protein Expression Lead, Protein Expression Lab, Leidos Biomedical Research, Inc.

Insect cell systems have become a vital tool in production of pharmaceutically relevant protein complexes for structural biology and drug discovery research. In many cases, in order to produce functional protein for these complexes, multiple chaperones or co-factors may be required. We discuss why co-expression is superior to co-infection, and investigate the role of specific chaperones in the production of complexes with case studies on important target proteins.

2:20 Insect Cell Manufacture for COVID-19 and Other Vaccines

Nikolai Petrovsky, PhD, Research Director, Vaxine Pty Ltd.; Professor of Medicine, Flinders University

Vaxine employed advanced technologies including artificial intelligence-assisted protein engineering, insect cell protein synthesis, and a novel adjuvant to drive development of its recombinant spike protein COVID-19 vaccine (Covax19/SpikoGen) that obtained emergency use regulatory approval in early October 2021, making this the first recombinant spike protein vaccine in the world to achieve approval, also representing the record for the fastest time from inception to approval of a protein-based vaccine.

2:50 Novel Affinity Chromatography Technology for Purification of Any Recombinant Protein

cytiva

Emma Lind, Global Product Manager, Cytiva

Presenting a novel affinity chromatography technology for the purification of any recombinant protein in research and process development workflows. This method allows the resulting pure protein to be in its native and natural state. The improved workflow will benefit researchers and process developers who purify recombinant proteins.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

4:00 Proteins against Infectious Diseases of Poverty, a Case Study - mAbs against the Scourge of Cholera

Gary L. Pierce, PhD, Executive Director, ServareGMP

4:30 geCHO, a Platform for the Production of Specific Glycoforms of Glycoproteins

Bjørn Voldborg, MSc, Head, National Biologics Facility, DTU Bioengineering, Technical University of Denmark

Glycosylation very often has a significant effect on the activity, function, and efficacy of protein-based therapeutics. Using the geCHO platform, different glycovariants of the protein-based drug candidates can be produced for research, development, and manufacturing of optimal glycoforms. The geCHO platform is also very useful for generating reagents for the studies of the effect of glycosylation on glycoproteins *in vitro* and *in vivo*.

5:00 CHO Cell Line Expressing Enterovirus 71 VLPs in a Fed-Batch Process: A New Potential Production Platform

Bich Thao Nguyen, PhD, Assistant Professor, Research, Graduate School of Engineering, Osaka University

Virus-like particles (VLPs) are potential vaccine candidates owing to their safety and ability to trigger an effective cellular and humoral immune response. To develop a VLP vaccine against hand, foot, and mouth disease, we tried producing Enterovirus 71 VLPs in Chinese Hamster Ovary (CHO) cells. In my presentation, I will demonstrate the potential of CHO cells as a promising production platform for Enterovirus 71 VLPs.

5:30 Close of Day

WEDNESDAY, JANUARY 18

8:30 am Registration and Morning Coffee (Indigo and Aqua Foyer)

ROOM LOCATION: Aqua Salon CDE

9:00 Organizer's Remarks

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

9:10 Plenary Fireside Chat: Supporting and Driving Biotech: Past, Present, and Future

Moderator: Julie Ames, Vice President, Corporate Communications, Biocom California

Innovation can refer to something new, like an invention, or the development and introduction of new practices. The end result is often a new product, but it can also be a new practice, procedure, or way of thinking. Change and challenges are often what inspire innovation and propel us forward into new ways of thinking. This Fireside Chat will explore the following:

- Success stories
- Serendipitous discoveries
- Current projects
- Future developments*Panelists:*

Amy K. Butler, PhD, President, Biosciences, Thermo Fisher Scientific

Taegen Clary, Vice President, Marketing, Unchained Labs

Jonathan Haigh, PhD, MBA, Vice President, Process Development, Fujifilm Diosynth Biotechnologies

Craig R. Monell, PhD, Vice President, Sales, Marketing & Business Development, BioLegend, Inc.

10:15 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

ROOM LOCATION: Aqua Salon AB

PREDICTING AND PERFECTING THE BEST PRODUCTION HOSTS

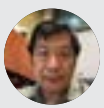
11:00 Chairperson's Remarks

Jonathan Haigh, PhD, MBA, Vice President, Process Development, Fujifilm Diosynth Biotechnologies

11:05 Prediction for Deleterious Nucleotide Variants: Challenges with Synonymous and Co-Occurring Single-Nucleotide Variants (SNVs)

Nobuko H. Katagiri, PhD, Research Scientist, Office of Tissues & Advanced Therapies, CBER, FDA

The effects of deleterious synonymous or co-occurring multiple SNVs are much more challenging to identify and predict than nonsynonymous SNVs. We have developed prediction tools for identifying deleterious synonymous SNVs. Furthermore, we have proposed a new approach that can successfully assist in accurately predicting the effect of co-occurring variants. In this talk, strategies for predicting SNVs and some approaches to predict such exceedingly challenging nucleotide variants will be discussed.



11:35 FEATURED PRESENTATION: Using Soluble GFP as a Tool in Recombinant Mammalian Protein Expression

Peter D. Sun, PhD, Chief, Structural Immunology Section, Lab of Immunogenetics, NIAID/NIH

Screening for high-level recombinant protein expression cells often requires laborsome analysis by ELISA. We report here a new method to screen for recombinant gene expression using secreted GFP. It allows high-throughput screening using a fluorescence plate reader. The expression level of a targeted recombinant protein is proportional to the GFP signals. It offers fast and cost-effective screening for recombinant protein expression clones.

12:05 pm Pelican Expression Technology Platform: A Sophisticated Toolbox Supporting Lead Development through Commercial

Diane Retallack, Senior Vice President, Platform Technologies and Innovations, Ligand Pharmacueticals

The Pelican Expression Technology is a robust, validated, cost-effective and scalable platform for recombinant protein production. An overview of how this Pseudomonas-based expression platform was developed specifically for recombinant protein production will be presented. Case studies demonstrate how the extensive Pelican toolbox of genetic elements and host strains, along with automated strain screening workflows, enable rapid and broad exploration of expression strategies to address complex and challenging disulfide-bonded protein scaffolds.

12:35 Session Break and Transition to Luncheon Presentation

12:45 Introduction of Biopharmaceutical Development and Corynex Technology to Address Challenges in Manufacturing

Hayato Nagano, Lead Researcher, Research Institute for Bioscience Products and Fine Chemicals, Ajinomoto Co., Inc.

Ajinomoto Bio-Pharma Services, as a fully integrated contract development and manufacturing organization (CDMO), offers a broad range of innovative platform technologies and end-to-end solutions for biopharmaceutical development and manufacturing. In this presentation, we will show our CDMO capability and Corynex protein expression platform technology for biopharmaceuticals, which together can improve drug substance manufacturing.

1:15 Toward Process Intensification with Methanol-Free *Pichia*

Iskandar Dib, PhD, Principal Scientist Process Development & Analytics, VALIDOGEN GmbH

VALIDOGEN's unique AOX1 promoter variants that enable methanol-free protein production at multi-gram-per-liter titers offer several advantages that go far beyond mere safety concerns. Using methanol-free production combined with other elements of VALIDOGEN's UNLOCK PICHIA toolbox, we established strategies to maximize space-time-yield and total product titer. Optimized methanol-free processes enable considerably shorter batch times and even continuous upstream processes, thus paving the way toward intensified processes for biopharma and precision fermentation.

1:45 Session Break

EXPRESSION AND PRODUCTION OF MEMBRANE PROTEINS

2:00 Chairperson's Remarks

Vincent Noireaux, PhD, Professor, Synthetic Biology and Biological Physics, University of Minnesota

2:05 The COMPPÅ Expression Platform: From Cell-Free to Bac-Mam

Renato Bruni, PhD, Senior Staff Scientist, Center on Membrane Protein Production and Analysis, New York Structural Biology Center

The Center on Membrane Protein Production and Analysis (COMPPÅ) is a resource for advanced studies on membrane proteins, emphasizing technological innovation and cutting-edge biological applications. The center offers a gene-to-structure pipeline with an emphasis on expression and purification of membrane proteins. Here we present our various expression platforms which range from a cell-free approach to several prokaryotic and eukaryotic systems.

2:35 An All-*E. coli* Cell-Free Toolbox: *in vitro* Synthesis of Soluble and Membrane Proteins

Vincent Noireaux, PhD, Professor, Synthetic Biology and Biological Physics, University of Minnesota

Cell-free transcription-translation (TXTL) has become a highly versatile multidisciplinary technology for bioengineering and synthetic biology. By enabling the rapid expression of genes and gene circuits, TXTL integrates an ever-growing variety of applications. In this talk, I will present an all-*E. coli* TXTL system, the extent of its capabilities, and the cell-free synthesis and characterization of membrane proteins.

3:05 Cell-free Scaled Production and Adjuvant Addition to a Recombinant Membrane Proteins from *Chlamydia trachomatis* and *Chlamydia muridarum* for Vaccine Development

Matthew Coleman, PhD, Senior Scientist & Group Leader, Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory

While proteins are typically produced within cells, cell-free protein synthesis (CFPS) is a versatile biological technique that takes the existing transcriptional and translational machinery from cells. The combination of CFPS with multiple nanodisc platforms enables the production of hard-to-produce membrane proteins in their native-like state. The process is scalable and adaptable. We combined these technologies, to produced multiple types of membrane bound Chlamydial proteins for characterization and vaccine studies.

PepTalk Plaza: Speed Networking

IN-PERSON ONLY: Speed Networking

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

EXPRESSION AND PRODUCTION OF ENZYMES

4:15 FEATURED PRESENTATION: Protein Expression and Purification of G-Protein Coupled Receptor Kinase 6 (GRK6), toward Structure-Based Drug Design and Discovery for Multiple Myeloma

Petra Fromme, PhD, Paul V. Galvin Professor, Chemistry & Biochemistry, Arizona State University

GRK6 is a kinase target in multiple myeloma and plays a significant role in mediating the chemotactic responses of T and B-lymphocytes. To support structure-based drug design, we describe expression and purification of three human GRK6 constructs in Sf9 insect cells. GRK6His/TEV was purified to high homogeneity and actively folded as exhibited by circular dichroism spectroscopy. The described methods will support the structure-based development of additional therapeutics against multiple myeloma.

4:45 Expression, Purification, and Activation of Recombinant Matrix Metalloproteinase Enzymes in Bacteria

Maryam Raeeszadeh-Sarmazdeh, PhD, Assistant Professor, Graduate Program Director, Chemical and Materials Engineering, University of Nevada

Matrix metalloproteinases (MMPs) have been the center of attention recently as targets to develop therapeutics that can treat diseases correlated to their overexpression. To study the MMP mechanism in solution, more facile and robust recombinant protein expression and purification methods are needed to produce active, soluble MMPs. A summary of recent methods used to overcome these challenges and improve the yields of soluble active MMPs will be discussed.

5:15 PANEL DISCUSSION: Expression, Production, and Purification of Difficult-to-Express Proteins

Moderator: Vincent Noireaux, PhD, Professor, Synthetic Biology and Biological Physics, University of Minnesota

Panelists:

Renato Bruni, PhD, Senior Staff Scientist, Center on Membrane Protein Production and Analysis, New York Structural Biology Center

Matthew Coleman, PhD, Senior Scientist & Group Leader, Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory

Petra Fromme, PhD, Paul V. Galvin Professor, Chemistry & Biochemistry, Arizona State University

Maryam Raeeszadeh-Sarmazdeh, PhD, Assistant Professor, Graduate Program Director, Chemical and Materials Engineering, University of Nevada

5:45 Networking Reception in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

WOMEN IN SCIENCE MEET UP AT PEPTALK PLAZA

Women in Science Meet Up at PepTalk Plaza

Christa Cortesio, PhD, Senior Scientist and Group Lead, Protein Science, Protein Biochemistry & Analytics Core, Kite Pharma

Michelle R. Gaylord, MS, Principal Scientist, Protein Expression Lead, Velia, Inc.

7:00 Close of Recombinant Protein Expression and Production

JANUARY 19-20, 2023 | Cambridge Healthtech Institute's Inaugural

OPTIMIZING WORKFLOWS IN PROTEIN PRODUCTION LABORATORIES

Decreasing Delivery Times of High-Quality Proteins to Support Research

THURSDAY, JANUARY 19

8:00 am Registration and Morning Coffee (Indigo and Aqua Foyer)

ROOM LOCATION: Aqua Salon AB

MANAGING AND MEETING YOUR CUSTOMER'S NEEDS

8:25 Chairperson's Opening Remarks

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

8:30 Challenges and Opportunities Supporting Early-Stage Drug Discovery Projects

Oleg Brodsky, Senior Principal Scientist, Structural Biology & Protein Sciences, Pfizer Inc.

Protein targets for small molecule drug discovery efforts are becoming increasingly more challenging. In addition, novel lead ID approaches and modalities are being utilized in order to address these challenges. Flexible and agile protein production workflows must be deployed in order to meet these project demands, as will be highlighted in this presentation.

8:50 Making Proteins for Geneticists: Life in a Small Protein Facility

Ruth L. Saxl, PhD, Protein Chemistry Scientist, Scientific Services, Jackson Laboratory

The Jackson Laboratory pioneered the use of mice as models for human disease. Today, it discovers precise genomic solutions for human diseases. JAX Protein Production and Purification Service enables the faculty to advance newly identified genes to the proteins they encode. While producing proteins, the service focuses on educating the geneticists about proteins. It strives to provide high-quality services while understanding the limits determined by being a small service.

9:10 Managing Eukaryotic Expression Platform (EEP) at the Structural Genomics Consortium

Almagul Seitova, PhD, Senior Research Associate, Structural Genomic Consortium, University of Toronto

The Eukaryotic Expression Platform is a core infrastructure platform at SGC, utilizing an optimized pipeline for the production of recombinant proteins that require eukaryotic expression machinery to obtain sufficient quantities of active and stable proteins suitable for functional and structural studies. This platform also permits the identification of the soluble forms of multiple constructs of proteins, including domains and truncated fragments as well as full-length proteins through small-scale expression screening.

9:30 Industrial Standards in an Academic Environment

Bjørn Voldborg, MSc, Head, National Biologics Facility, DTU Bioengineering, Technical University of Denmark

The National Biologics Facility at the Technical University of Denmark offers service to both academic and industrial partners within protein production, protein characterization, and cell line development. The Facility offers the advantages of a flexible and dynamic cutting-edge academic environment operating at industrial standards. The challenges of prioritizing expectations, timelines and costs with academic and industrial customers, while keeping motivation and academic mindset of the staff will be discussed.

9:50 Process Optimization for Animal-free Protein Production

Luana Ferrara, PhD, R&D Manager, Qkine Ltd

10:20 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

11:00 PANEL DISCUSSION: Protein Production Lab Challenges: Methodologies, Strategies, and the Art of Managing Multiple Projects

Moderator: Richard Altman, MS, Field Application Scientist, Life Science Solutions, Thermo Fisher Scientific

This panel will focus on the following topics:

- Lessons learned from managing a protein production workflow during a pandemic.
- Strategies on how to manage multiple "top priority" projects.
- Strategies for supporting the professional growth and career development of direct reports.
- How do we make time for technical development and process optimization?
- Troubleshooting strategies or how much time should be spent before moving to the next option?

Panelists:

David Blum, PhD, Director, Bioexpression & Fermentation Facility, Biochemistry & Molecular Biology, University of Georgia

Oleg Brodsky, Senior Principal Scientist, Structural Biology & Protein Sciences, Pfizer Inc.

Christa Cortesio, PhD, Senior Scientist and Group Lead, Protein Science, Protein Biochemistry & Analytics Core, Kite Pharma

Dominic Esposito, PhD, Director, Protein Sciences, Frederick National Laboratory

Ruth L. Saxl, PhD, Protein Chemistry Scientist, Scientific Services, Jackson Laboratory

Bjørn Voldborg, MSc, Head, National Biologics Facility, DTU Bioengineering, Technical University of Denmark

12:30 pm Session Break and Transition to Luncheon Presentation

12:40 LUNCHEON PRESENTATION: Setting Up an Effective Protein Expression Laboratory

ThermoFisher SCIENTIFIC

Steffany Dunn, Technical Specialist, Protein Expression and Delivery, Thermo Fisher Scientific

Understanding the goals and challenges of your protein expression application is critical to creating an effective protein expression laboratory. This presentation will discuss topics to consider when planning your projects across different applications, review basic concepts of mammalian protein expression to determine which system(s) will best suit your needs, as well as how to optimize your entire workflow, from cloning to analytics, to ensure the highest protein quality and yield.

1:10 Ice Cream Break in the Exhibit Hall and Last Chance for Poster Viewing (Indigo Ballroom)

STRATEGIES FOR ENHANCING THE PRODUCTION WORKFLOW

2:00 Chairperson's Remarks

Dominic Esposito, PhD, Director, Protein Sciences, Frederick National Laboratory

2:05 Protein Production and Biochemistry Support of CAR T and Cell-Based Therapeutics

Christa Cortesio, PhD, Senior Scientist and Group Lead, Protein Science, Protein Biochemistry & Analytics Core, Kite Pharma

Research and development of next-generation cell therapies are aimed at engineering safer, more potent, and effective therapies and broadening the range of indications they can target. This goal will be best achieved through a multidisciplinary approach that includes high-quality reagent proteins and biochemistry support to accelerate the acquisition of high-quality scientific data to understand drug attributes and mechanisms of action.

2:25 Implementing Kanban for Protein Expression

David Blum, PhD, Director, Bioexpression & Fermentation Facility, Biochemistry & Molecular Biology, University of Georgia

Kanban was originally developed for automobile manufacturing and is now used along with Kanban boards for project management in a variety of areas including most notably software development. Software tools are available including Trello for Kanban board management making project management across teams and locations possible. The focus of this talk will be how to employ Kanban boards to improve workflows.

2:45 The Frederick National Laboratory STAR TREC Initiative: Standardizing Methodologies for High-Quality Recombinant Protein Production

Dominic Esposito, PhD, Director, Protein Sciences, Frederick National Laboratory

Generating high-quality, reproducible recombinant proteins is a significant challenge facing the protein production field. The FNL STAR TREC initiative aims to assist in standardization of protein production SOPs and quality control, with the goal of helping to improve reproducibility and minimize financial costs and time wasted in support of basic research and early-stage drug discovery efforts.

3:05 Networking Refreshment Break (Aqua Foyer)

3:30 Utilizing a Streamlined Automated Workflow to QC Baculovirus Expression

Andrea Partridge, PhD, Senior Scientist, Computational Structural Chemistry, Merck & Co., Inc.

Challenges exist with the Baculovirus expression system including time and effort to generate, screen, and store large numbers of viruses. We have developed a streamlined process to QC new viral constructs by incorporating; 1.) Off-the-shelf automation platforms 2.) Screening miniaturization techniques and 3.) Data management platforms. This workflow accelerates viral generation through an improved screening funnel and reduces the total number of viral samples that need to be managed.

Think Tank: Production Workflow Think Tanks: Reducing Costs, Challenges, and Opportunities

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

4:30 Think Tank Report Outs: Listen and Learn

During the Think Tank interactive discussions, we shared our experiences and working solutions for end-to-end protein production workflows. Now as a collective community, let's hear from the table facilitators as they share key discussion points, strategies, and provide a wrap-up of their table's discussion. What can we take away and apply?

5:00 Close of Day

FRIDAY, JANUARY 20

7:30 am Registration (Indigo Foyer)

ROOM LOCATION: Indigo and Aqua Foyer

BuzZ Sessions

8:00 BuzZ Sessions with Continental Breakfast (IN-PERSON ONLY)

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.
Please continue to check the BuzZ Session page on our conference website for detailed discussion topics and moderators

BuzZ Table 5: Common Issues with Transient Protein Production

Richard Altman, MS, Field Application Scientist, Life Science Solutions, Thermo Fisher Scientific

Henry C. Chiou, PhD, Senior Director General Manager, Biosciences, Thermo Fisher Scientific

Dominic Esposito, PhD, Director, Protein Sciences, Frederick National Laboratory

- What are the current challenges to transient protein production?
- How has the COVID-19 pandemic affected your workflow and productivity?
- How do we optimize the whole protein expression workflow process?
- How can we maintain volumetric yields while scaling transient expression up or down?
- What cell line(s) should we use and when?
- What parameters can impact the quality or physical attributes of transiently produced proteins?

ROOM LOCATION: Aqua Salon AB

FLEXIBLE AND AGILE PROTEIN PURIFICATION AND CHARACTERIZATION WORKFLOWS

9:00 Chairperson's Remarks

Petra Fromme, PhD, Paul V. Galvin Professor, Chemistry & Biochemistry, Arizona State University

9:05 What Are the Key Considerations for Setting up and Maintaining an Effective Protein Production Laboratory?

Richard Altman, MS, Field Application Scientist, Life Science Solutions, Thermo Fisher Scientific

Protein production is more complex than just the act of expressing the protein. This presentation will review the end-to-end protein production workflow process and reflect on possibilities of how to increase the efficiency and productivity of a recombinant protein expression facility.

9:25 Large-Scale Protein Expression and Purification in Hundreds of Milligram Amounts for Time-Resolved Studies with X-Ray Free Electron Lasers

Petra Fromme, PhD, Paul V. Galvin Professor, Chemistry & Biochemistry, Arizona State University

X-ray free electron lasers probe protein structures with ultrashort x-ray pulses, thereby enabling the determination of molecular movies of molecules "at work," but large quantities of proteins in the range of hundreds of milligrams are required. We will present strategies and procedures for large-scale cell culture and protein isolation for XFEL studies that include preparation of large photosynthetic membrane protein complexes, as well as preparation of proteins from SARS-CoV-2.

9:45 Rapid Production of Highly Purified Tagless Proteins under a Simple Platform

David W. Wood, PhD, Professor, Chemical & Biomolecular Engineering, The Ohio State University

High-throughput protein production relies on affinity tags to enable purification of new targets, where tags are often left in place during initial target characterization. The production of tagless targets is now possible via a self-removing tag that functions in simple buffer systems. We will describe the use of this system to purify a variety of targets to extremely high purity with a standard protocol on a universal affinity resin.

10:05 Reimagining Protein Production Workflows to Enable Next-Generation Biologics?

Daniel Yoo, Principal Scientist, Therapeutic Discovery, Amgen, Inc.

As biologic therapeutics continue to increase in complexity, innovative approaches to candidate screening, production, characterization, and development are more important than ever. Our advanced protein production workflows incorporate novel processes, intelligent high-throughput automation, and high-quality informatics to enable robust molecule screening, selection, and scale-up. These enhancements enable advances in the speed, quality, and productivity of our biologics development pipeline.

10:35 Networking Coffee Break (Aqua Foyer)

11:00 Advancements in Protein Production Workflows to Support the Ever Increasing Demand & Complexity in Drug Discovery

Kanika Bajaj Pahuja, PhD, Scientific Manager, Protein Sciences, Genentech Inc.

This presentation will focus on the evolving needs in the protein production core facility and the creative solutions we are building to overcome and support these increasing demands. It will emphasize on the integration of our several end-to-end automated high-throughput protein expression and production workflows that leverage automation and bioinformatics tools. These approaches significantly alleviate some of the bottlenecks in protein production and accelerate the provision of key protein reagents to ambitious projects.

Think Tank: Protein Purification & Characterization – What's Next?

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

12:00 pm Think Tank Report Outs: Listen and Learn

During the Think Tank Table discussions, we shared our experiences and working solutions for protein purification and characterization workflows. Now as a collective community, let's hear from the table facilitators as they share key discussion points, strategies, and provide a wrap-up of their table's discussion. What can we take away and apply?

12:30 Close of PepTalk

PROCESS TECHNOLOGY & INNOVATION

Next-gen biopharmaceuticals are increasingly complex, including antibodies, bispecifics, ADCs, antibody fragments, vaccines, gene/cell therapies and beyond. Thus, for protein production and purification it is imperative to aim for higher-throughput, to drive automation, and to leverage digital tools to increase productivity and minimize time and cost. In the **Process Technology & Innovation** pipeline we bring together leaders from across biopharmaceutical process development to discuss challenges, showcase innovations, and share technical solutions. Attend to learn more.

PEPTALK

JANUARY 16-17

Higher-Throughput Bioproduction

AGENDA

JANUARY 17-18

Training Seminar: Biomanufacturing 101

AGENDA

JANUARY 19-20

Advanced Purification and Recovery

AGENDA

REGISTER EARLY & SAVE!

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JANUARY 16-17, 2023 | Cambridge Healthtech Institute's 12th Annual

HIGHER-THROUGHPUT BIOPRODUCTION

Analyzing & Improving Processes

SUNDAY, JANUARY 15

4:00 pm Pre-Conference Registration (Indigo Foyer)

MONDAY, JANUARY 16

7:00 am Registration and Morning Coffee (Indigo and Aqua Foyer)

9:00 Organizer's Welcome Remarks

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

ROOM LOCATION: Aqua Salon E

MONITORING, MODELING, AND ANALYTICS

9:05 Chairperson's Opening Remarks

Cinzia Stella, PhD, Senior Scientist, Tech Development, Genentech, Inc.

9:10 KEYNOTE PRESENTATION: *In silico* Facilitated Process Development of Orthogonally Selective Non-Protein A Processes for mAb Bioprocessing

Steven M. Cramer, PhD, William Weightman Walker Professor, Isermann Department of Chemical and Biological Engineering, Rensselaer Polytechnic Institute

This presentation will discuss how to combine ***in silico*** tools and high throughput screening to develop orthogonally selective non-Protein A processes for mAb bioprocessing. This approach employs data from targetted high-throughput screening of resins and conditions as inputs into ***in silico*** tools that produce a ranking of potential integrated downstream processes which are then refined at the bench scale using both mechanistic models and experiments.

9:50 Online Multi-Dimensional LC/MS: The Next-Generation PAT Tool for Real-Time Monitoring of Antibody Quality Attributes in Biopharmaceutical Processes

Cinzia Stella, PhD, Senior Scientist, Tech Development, Genentech, Inc.

Monitoring of PTMs mAbs is essential during their production in both upstream and downstream processes. However, characterization of PTMs using conventional peptide mapping procedure requires time-consuming and labor-intensive offline sample preparation steps. This work describes for the first time, the implementation of a Protein-A affinity chromatography column as the first dimension (1D) in a multi-dimensional LC setup for the automated characterization of mAb variants from harvest cell culture fluid.

10:20 Networking Coffee Break (Indigo and Aqua Foyer)

10:45 The Use of Process Analytical Technologies (PAT) to Support Continuous Manufacturing

Darby Nelson, PhD, Scientist I, Process Analytical Technology, National Resilience

Continuous manufacturing is gaining acceptance in the biopharmaceutical industry. With constant production, however, comes the need for rapid analytical techniques to ensure product quality at the production line. To address this need, we are focusing on rapid techniques for monitoring critical in-process attributes during production runs. This presentation will review approaches for at-line measurement of aggregates and bioburden to improve control of continuous processes

11:15 Integrated Process Analytical Platform for Automated Monitoring of Monoclonal Antibody N-Glycosylation

Aron Gyorgypal, PhD Candidate, Chemical & Biochemical Engineering, Rutgers University

Post-translational modification of therapeutic proteins, such as N-linked glycosylation, are critical quality attributes that affect biologics safety and efficacy, requiring close monitoring during biomanufacturing. Here we will highlight an integrated analytical tool that combines online sampling and sample preparation with a mobile HPLC allowing for fully automated and near-real-time measurement of monoclonal antibody (mAb) N-glycosylation. This toolkit can be used to monitor and control mAb glycosylation during biomanufacturing.

11:45 Benefits of Real-Time Analytics to Overcome Common Cell Culture Challenges

908devices

Graziella Piras, PhD, Director of Life Science Business Development, 908 Devices

Faster development and intensified processes are critical in biotherapeutics. Parallel bioreactors used frequently in early process development for expedited optimization also require advanced analytics to efficiently monitor CPPs and CQAs. We discuss a data-driven process optimization approach leveraging sensitive, online monitoring of key metabolites with automated feed control. We discuss how automated monitoring and control can lead to higher growth and viability, lower toxic metabolites and improved CQA.

ROOM LOCATION: Aqua Salon E

12:15 pm Overcoming Challenges for High-Throughput Production of Diverse Custom Proteins Used in Discovery Applications

WuXi Biologics
Global Solution Provider

Jiansheng Wu, Vice President, Protein Services, WuXi Biologics

Dr. Wu will discuss the challenges in high-throughput protein production for small and large molecule drug discovery and demonstrate the parameters and design space required to generate high-quality proteins for HTS, antibody discovery, ***in vivo*** and developability studies. Supported by industry-leading platforms, our Protein team provides production services utilizing various expression systems for the generation of monoclonal, bispecific and multispecific antibodies, and other recombinant proteins.

12:45 Enjoy Lunch on Your Own

1:55 Session Break

DIGITALIZATION

2:00 Chairperson's Remarks

Moritz von Stosch, PhD, Chief Innovation Officer, Datahow, Switzerland

2:05 Application of Hybrid Models and Digital Twins to Increase Understanding and Accelerate Development

Moritz von Stosch, PhD, Chief Innovation Officer, Datahow, Switzerland

Digital Twins allow us to understand the behavior of the *in silico* replicated process, to optimize or manipulate it. DTs require that the underlying models are predictive. Hybrid modeling is a cost-effective method for capturing process behavior. Due to its nature, it balances the need for data with very attractive extrapolation capabilities. We showcase how hybrid modeling rendered possible the development of DTs for challenging downstream scenarios.

2:35 Novel Sensor-integrated Proteome on Chip (SPOC) Platform for High Throughput Kinetic Interaction Analysis

Bharath Takulapalli, PhD, Founder & CEO, INanoBio

INanoBio has developed the first-of-kind protein biosensor array platform termed SPOC (sensor-integrated proteome on chip) – customizable array of >500 full-length folded proteins on gold biosensor chip. Surface plasmon resonance (SPR) outputs kinetic data with multiple quantitative parameters Rmax, Ka & Kd for each protein. Using machine learning-based analytics, SPOC can be used to resolve biological pathways/networks, characterize disease phenotypes, and discover novel biomarkers for early diagnosis and precision medicine.

ROOM LOCATION: Indigo and Aqua Foyer

BuzZ Sessions

3:05 Find Your Table and Meet the BuzZ Sessions Moderator

3:10 BuzZ Sessions with Refreshments (IN-PERSON ONLY)

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.
Please continue to check the BuzZ Session page on our conference website for detailed discussion topics and moderators

BuzZ Table 5: High Throughput—Multiplexed Technologies to Characterize Protein Interactions

Peter Bell, PhD, Senior Director, Assay & Platform Development, INanoBio

Rebecca Cook, PhD, Senior Research Scientist, INanoBio

- Comparative methods for study of protein interactions—Pros/Cons
- Challenges in expression of functional proteins for protein interactions
- Screening of hundreds to thousands of protein interactions in parallel
- Antibody screening against large panels of targets or variants—affinity, specificity
- Detection methods—discussion of readouts—MS, SPR, fluorescence, reporter assays which are best?

BREAKOUT DISCUSSION: BuzZ Table 6: Targeted Supplementation to Improve Protein Titer and Quality in CHO Cells

Natalie McAdams, PhD, Manager Cell Biology, BioProduction R&D, Thermo Fisher Scientific

- How can supplements be applied to a bioproduction process to boost protein titer?
- What process parameters and supplements can impact protein quality?
- Lessons learned – what process parameters or supplements can have a negative impact on performance?

ROOM LOCATION: Aqua Salon AB

AUTOMATION SCREENING AND SELECTION OF SUCCESSFUL CLONES

4:30 The Daft Punk Approach to Maximizing Protein Production – Faster, Better, Stronger via Leveraging Open-Source Robotics, Optimal Scaling, and High-Throughput Analytics

Lauren P. Carter, Principal Research Scientist & Engineer, Biochemistry, University of Washington

The Institute for Protein Design has developed powerful processes for computational protein design, most recently the Diffusion model, which combines structural prediction networks with generative diffusion with the ability to generate highly accurate designs optimized for soluble expression. This results in a high number of proteins requiring experimental validation. The IPD has developed methods to express, purify, and characterize these designed proteins that can keep pace with design velocity.

5:00 Using Automation to Generate High-Throughput Workflows for Higher Quality Stable Cell Line Development

Alicia Barker, Associate Scientist, Cell Line Development, Just-Evotec Biologics

The Just-Evotec Biologics CLD platform is optimized to decrease development timelines and increase throughput by using automation from transfection through RCB creation. Our high-throughput transfection method allows us to simultaneously screen 96 transfectants in stable pools to identify more manufacturable molecules with a reduced timeline. Using automation, we are capable of screening over 350 clones allowing us to identify cell lines with high productivity and favorable product quality attributes.

5:30 Coupling High-Density Data and High-Throughput Small-Scale Screening to Optimize DNA Construct Screening

Noel Byrne, Associate Principal Scientist, Structural Protein Sciences, Merck & Co., Inc.

The expression screening of large numbers of protein constructs can be automated utilizing the baculovirus expression system (BEVS) and TECAN automation. Biophysical characterization of small-scale screening samples, such as aSEC and nanoDSF, provides a more robust screening funnel with better prediction of successful clones. Expanding to an automated "midi-scale" screen allows for production of sufficient material to perform more in-depth POC studies such as Biacore, MST, and LC-MS.

6:00 Welcome Reception in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

YOUNG SCIENTIST MEET UP

Young Scientist Meet Up

Iris Goldman, Production, Cambridge Innovation Institute

7:30 Close of Day

CITY WALK MEET UP

BREAKOUT DISCUSSION: City Walk Meet Up

Kevin Brawley, Associate Project Manager, Production Operations & Communications, Cambridge Innovation Institute

TUESDAY, JANUARY 17

8:15 am Registration and Morning Coffee (Indigo and Aqua Foyer)

ROOM LOCATION: Aqua Salon E

AUTOMATION INSTRUMENTATION & HIGHER THROUGHPUT

8:45 Chairperson's Remarks

Steven M. Cramer, PhD, William Weightman Walker Professor, Isermann Department of Chemical and Biological Engineering, Rensselaer Polytechnic Institute

8:50 Implementation of a Fully Automated Walk-Up Residual DNA qPCR Workflow

Michele Shannon, Investigator, GlaxoSmithKline

Clearance of residual host DNA is an important part of the biopharmaceutical process as host DNA can pose a potential risk to the patient. Using the KingFisher Presto integrated into a Hamilton liquid handling system, we have automated the residual DNA assay from sample preparation through qPCR plate preparation, significantly reducing FTE labor and allowing for a walk-up system for quicker turnaround and high-throughput for residual DNA results.

9:20 LabDroid: A Highly Automated Variant Characterization Platform

Christoph Kalthoff, PhD, Director, LabDroid, Novo Nordisk A/S

Generating data on a large number of variants is crucial for advanced analytics and modeling. For this purpose, we are building LabDroid, a highly automated platform for variant characterization. Comprising eight robotic cells it can produce and characterize proteins and peptides and register all results automatically in a cloud-based repository. During this talk, we will share initial results, highlight some of our challenges, and show how we addressed them.

9:50 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

PROCESS INTENSIFICATION

10:30 Development of a High-Performance Bioreactor Process for Expression of Bi- and Multi-Specific BEAT and TREAT Antibodies

Martin Bertschinger, PhD, Director, Drug Substance Development, Ichnos Sciences

Given the need to dose bi- and multi-specific antibodies in the range of classic mAbs, expression levels similar to mAbs are required to maintain a reasonable cost of goods. The presentation describes a cell line development and upstream process created by Ichnos Sciences that allows > 5 g/L expression of bi- and multi-specific BEAT and TREAT molecules with desired product quality attributes, focusing on specific improvements such as process intensification.

11:00 Intensification Strategies: Multiple Dimensions at Different Stages for Higher-Throughput

Stefan R. Schmidt, MBA, PhD, COO & Head, Operations, BioAtrium AG

Looking at the continuum from process development to commercial production, it is obvious that different stages require different approaches. Initially, speed from gene to first clinical batch counts, later the space and time yield is relevant. This presentation gives a comprehensive overview of strategies where, how, and when to implement process intensification and quantifies the benefits like plant occupancy time and capacity optimization based on successful examples and case studies.

11:30 CHO Fed-Batch Strategies to Rapidly Increase MAB Titer by 100% without Sacrificing Product Quality

Severine Fagete, Vice President, Cell Line Development Services, Cell Line Services, Selexis

In the field of therapeutic antibody production, diversification of fed-batch strategies is flourishing in response to the market demand. All manufacturing approaches tend to follow the generally accepted dogma of increasing titer since it directly increases manufacturing output. Selexis has changed the parameters which influence titer and developed novel hybrid strategies that reduce timelines without compromising productivity quality.

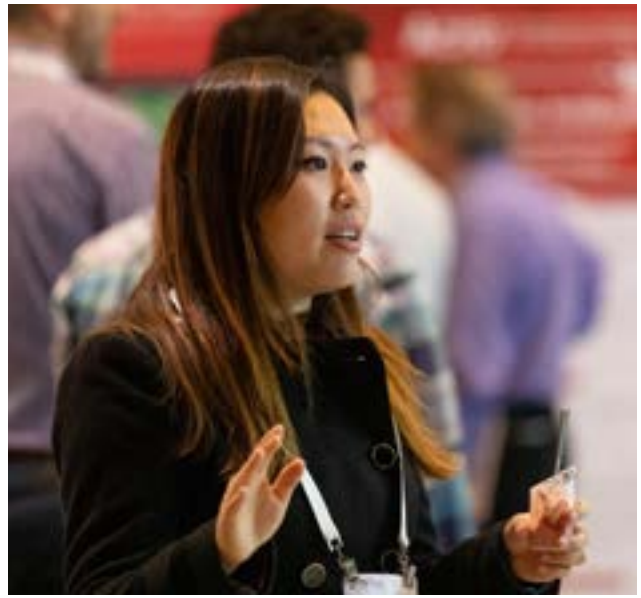
12:00 pm Session Break and Transition to Luncheon Presentation

12:10 AmMag Quatro Plasmid Purification Made Easy

Rouba Najjar, Associate Director of US Marketing, GenScript USA, Inc.

Plasmid DNA is an essential component of molecular biotechnology applications. Large scale plasmid purification is labor-intensive, time-consuming, and often creates a process bottleneck. GenScript has developed a new automated, large-scale, high throughput plasmid purification solution, the AmMag Quatro. Designed as a scalable modular system, scientists can automate maxi-scale plasmid purification with up to four AmMag modules, each processing up to 6 maxi-prep samples, for a total of 24 samples.

12:40 Close of Higher-Throughput Bioproduction



"PepTalk is the perfect place for networking and solutions from companies, organizations and universities."

TUESDAY, JANUARY 17, 2023 1:30 - 5:30 PM | WEDNESDAY, JANUARY 18, 2023 9:00 AM - 5:45 PM

TS6B: BIOMANUFACTURING 101: AN OVERVIEW ON ANIMAL CELL CULTURE TECHNOLOGY FROM CELL LINE DEVELOPMENT TO SCALE-UP STRATEGIES

In this seminar, we will take an in-depth look at modern cell culture techniques from a frozen stock to bioreactor design and operations. Cell line development, characterization, and scale-up strategies will be discussed in detail. Special emphasis will be placed on media design and optimization for specific clones to be utilized in production of biologics. We will highlight the significance of proper handling of cells in culture to avoid contamination and batch failure. Upstream processing of therapeutic proteins, monoclonal antibodies, and vaccines will be presented. After the completion of this seminar, the participants will have a clear understanding of the principles and techniques utilized in culturing animal cells for production of biologics, quality control of a cell culture laboratory, and types of contaminants of cells in culture with special emphasis on mycoplasma detection. They will learn scale-up strategies for suspension and anchorage-dependent cells utilizing stirred-tank bioreactors, hollow fiber bioreactors, and microcarrier cell culture technology.

TOPICS TO BE COVERED:

- Historical development of animal cell culture technology.
- Animal cells as factories for production of biologics.
- The importance of understanding the cell cycle for optimal productivity.
- Expression systems, transformation, and transfection assays.
- Cell line characterization and cell banking and cryopreservation.
- The importance of nutrients and media design for specific cells.
- Scale-up of cell culture and bioprocessing.
- Monoclonal antibody production.
- Viral vaccine production.
- Hollow fiber cell culture technology.
- Microcarrier cell culture technology.
- Stirred-tank bioreactors: Stainless steel and single-use systems.
- Case studies with CHO and Vero Cell lines

WHO SHOULD ATTEND:

This program is designed for scientists and engineers in the early stages of their careers who want to expand their knowledge of cell culture technology and bioprocessing. Biopharmaceutical professionals, people who work in academic institutions and government labs, along with marketers and sales personnel will benefit from the information in this Training Seminar. Downstream technicians and managers are also encouraged to attend to learn about the upstream process.

INSTRUCTOR BIOGRAPHY:

Instructor: Dr. Kamal Rashid, Professor Emeritus, Founder and President, International Biotechnology Associates

Dr. Kamal Rashid has over forty years of academic experience in research, teaching, and workforce development efforts. He has developed, directed, and implemented biotechnology/biomanufacturing training programs at Albany College of Pharmacy and Health Sciences, Worcester Polytechnic Institute, Utah State University, Penn State University, and internationally. He is an expert in animal cell culture technology and has developed and taught graduate courses in cell culture techniques and scale-up strategies for more than thirty-five years. He realized early on the importance of animal cell systems in bioprocessing and biomanufacturing as he developed the first hands-on cell culture training program for the bio-based industry in 1989, as part of a comprehensive bioprocessing training program at Penn State University. While on the faculty at Penn State, Dr. Rashid established International Biotechnology Associates as a strategic consulting partner for companies, institutions, and government agencies, helping them bring life-changing biotechnologies to people around the world. Operating on a model of collaboration, Dr. Rashid assembles and leads multidisciplinary teams to support specific client initiatives. Dr. Rashid received his undergraduate degree from University of Baghdad, Iraq, with distinction, and PhD from Penn State University with superior ranking. His major areas of research interests are in bioprocessing and genetic toxicology.

Cambridge Healthtech Institute Training Seminars offer real-life case studies, problems encountered and solutions applied, and extensive coverage of the basic science underlying each topic. Experienced Training Seminar instructors offer a mix of formal lectures, interactive discussions and activities to help attendees maximize their learning experiences. These immersive trainings will be of value to scientists from industry and academic research groups who are entering new fields – and to those working in supporting roles that will benefit from an in-depth briefing on a specific aspect of the industry.

JANUARY 19-20, 2023 | Cambridge Healthtech Institute's 14th Annual

ADVANCED PURIFICATION AND RECOVERY

Powerful Purification Platforms Serving Both Basic Research and Clinical Manufacturing

THURSDAY, JANUARY 19

8:00 am Registration and Morning Coffee (Indigo and Aqua Foyer)

8:30 Organizer's Welcome Remarks

ROOM LOCATION: Aqua Salon F

ADVANCED TECHNOLOGIES & APPROACHES

8:35 Chairperson's Opening Remarks

Jocelyn Jakubik, Senior Director, Analytical Testing and Translational Immunology, Sabin Vaccine Institute

8:40 KEYNOTE PRESENTATION: Advances in Multi-Specific Antibody Purification

John K. Kawooya, PhD, Director, Biologics Optimization and Therapeutic Discovery, Amgen, Inc.

During the last decade, major progress has been made in technical and scientific "know-how" of assembling biologically functional multi-specific antibodies (msAbs). However, many of these molecules have failed to reach patients due to a multitude of issues which include immunogenicity, toxicity, and manufacturability. In this presentation, I address the manufacturability issue and highlight current efforts being made to clear engineering side products from these molecules.

9:20 Challenges in Production of High Purity Marburg Recombinant Glycoprotein for ELISA

Jocelyn Jakubik, Senior Director, Analytical Testing and Translational Immunology, Sabin Vaccine Institute

The Marburg ELISA is starting validation using the High Purity Marburg Recombinant Glycoprotein as a coating antigen. The assay will measure Phase II human serum IgG antibody responses to Sabin's Marburg vaccine. This will be the first vaccine against this BL-4 pathogen and the coating antigen has already been used to properly measure immune response in humans and non-human primates during Sabin's Phase I trial in the USA.

9:50 SMART Cycling and Advances in Protein A Chromatography Resins

Tony Thomas, Field Application Scientist, Purification, Bioprocessing, Purolite

Jetting technology is a scalable continuous emulsification technology by which all Praesto® chromatography resins are produced. This proprietary technology results in the production of chromatography resins with a narrow, almost uniform particle size distribution, with excellent mass transfer properties that may be leveraged for process intensification. Herein, we present SMART cycling using our latest bioprocess Praesto Jetted Protein A chromatography resins.

10:20 Coffee Break in the Exhibit Hall with Poster Viewing (Indigo Ballroom)

ADVANCED TECHNOLOGIES & APPROACHES

11:00 Developing a Novel Bioprocess for a PASylated Therapeutic Enzyme Expressed in a Microbial Host Utilizing Periplasmic Release & Affinity-Free Purification

James Ware, Director, Purification Development & Tech Transfer, Pelican Expression Technology

Half-life extension of APIs has proven to be an effective way to treat patients using lower doses or less frequent dosing. Technologies to increase product half-life have evolved, introducing new challenges for traditional purification strategies. In this presentation, we share the effects of charge-shielding attributed to genetic fusion of a proline and alanine repeat polypeptide to a therapeutic enzyme, and the development of a non-traditional approach to a purification process.

11:30 PANEL DISCUSSION: Purification of AAVs

Moderator: Nick Westaway, Global Product Manager, Viral Vector Purification, Cytiva

- Chromatography as a Tool for the Purification of AAV Capsids
- Chromatographic Method Development for Enrichment of Full Capsids
- Optimization of the AAV Purification Process to Accommodate Increased Upstream Yield
- Building Reliable Workflow to Accelerate AAV Full-Capsid Enrichment Development

Panelists:

Kathy Delaria, Director, Downstream Process Development, 4D Molecular Therapeutics

Daniel Hurwit, Senior Scientist, Gene Delivery Process and Analytical Development, Bristol Myers Squibb

Sylvain Cecchini, PhD, Core Director, Associate Professor, Microbiology and Physiological Systems, UMass Chan Medical School

Ashley Craddick, Senior Director, GMP Manufacturing, Forge Biologics

12:00 pm Increasing Process Flexibility through a Novel Single-Use AEX Technology

David Chau, PhD, Global Bioprocess Application Specialist, Separation and Purification Sciences Division, 3M

AEX chromatography is considered the industry standard to remove process and/or product related impurities. However, those based on traditional quaternary ammonium (Q) functionalized ligands, may have limitations due to the narrow range of processing conditions. In this study, we explored the use of a new AEX single-use technology to overcome the limitations of traditional Q-based technology. The results show this technology can be applied across multiple modalities, simplifying the developmental approach.

12:30 Enjoy Lunch on Your Own

1:10 Ice Cream Break in the Exhibit Hall and Last Chance for Poster Viewing (Indigo Ballroom)

AFFINITY PURIFICATION & TAGS

2:00 Chairperson's Remarks

David W. Wood, PhD, Professor, Chemical & Biomolecular Engineering, The Ohio State University

2:05 New Affinity Methods for Downstream GMP Processing: Custom Resins to Cleavable Tags

David W. Wood, PhD, Professor, Chemical & Biomolecular Engineering, The Ohio State University

The success of Protein A affinity capture for mAbs has driven a search for similar methods for other proteins. The challenge has been designing affinity resins for arbitrary products with no common features. In this talk, I will compare and contrast three emerging solutions: custom affinity resins designed for single products, cleavable tags that rely on proteases, and self-removing tags that rely on inteins.

2:35 Development of Affinity Purification Platforms

Sophia Hober, PhD, Professor, School of Biotechnology, KTH Royal Institute of Technology

Due to the costly and time-consuming production of biologicals, selective affinity purification methods are desirable. For efficient and selective purification, a number of criteria are to be met. One important feature is the durability and possibility to reuse the purification matrix. Another is the possibility to avoid harsh conditions during the purification scheme. Different strategies to address these issues when developing affinity purification systems will be presented.

3:05 Networking Refreshment Break (Aqua Foyer)

3:30 Affinity Purification of Antibodies Using the Unconventional Nucleotide Binding Site

Basar Bilgicer, PhD, Professor, Chemical & Biomolecular Engineering, University of Notre Dame

In search of the next-generation chromatographic technique for antibody purification, our team has developed an affinity chromatography method using the unconventional nucleotide binding site (NBS). By generating resins that display ligands that bind to the NBS that is conserved on all immunoglobulins, we achieve purity over 99% with >99% column efficiency, supporting that NBS method provides a stable, reusable, and inexpensive alternative for purification of humanized and chimeric antibodies.

4:00 A New Vector for Expression of TwinStrep Maltose Binding Protein Tagged Proteins

Simon A. Messing, PhD, Scientist II, Frederick National Lab & Protein Expression Lab, Leidos Biomedical Research, Inc.

Immobilized metal affinity chromatography (IMAC) is the workhorse of a majority of recombinant protein purification. However, one-third to one-half of all proteins are considered metalloproteins (Ascone et al., 2003). Therefore, we designed a new vector that replaces the His-tag with a streptavidin-based affinity tag, TwinStrep. RAF1 conserved region 1 cloned into this vector showed significant improvement in folding suggesting that metal-free purification produced protein adopted a more native fold.

4:30 PANEL DISCUSSION: Protein Tag Technologies

Moderator: Richard Altman, MS, Field Application Scientist, Life Science Solutions, Thermo Fisher Scientific

Protein fusion tags are indispensable tools used to facilitate protein purification and detection, detect cellular localization of proteins, and improve protein solubility/stability.

- How do you select an affinity tag?
- Are there regulations regarding cleaving affinity tags?
- When does it make sense not to cleave the tag?
- Does the expression system impact the selection of a tag?
- Is it possible to introduce a universal approach for protein production and purification?

Panelists:

Melissa R. Thomas, PhD, Senior Principal Scientist, Biologics, Amgen, Inc.

Christa Cortesio, PhD, Senior Scientist and Group Lead, Protein Science, Protein Biochemistry & Analytics Core, Kite Pharma

Simon A. Messing, PhD, Scientist II, Frederick National Lab & Protein Expression Lab, Leidos Biomedical Research, Inc.

David W. Wood, PhD, Professor, Chemical & Biomolecular Engineering, The Ohio State University

5:00 Capture of Monoclonal Antibodies *via* Continuous Precipitation and Filtration Techniques

Gabriele Recanati, Researcher, University of Natural Resources and Life Sciences (BOKU)

A truly continuous biomanufacturing process will be presented. This is achieved by integration of a perfusion bioreactor with continuous precipitation and continuous filtration, replacing the state-of-the-art capture step for mAbs, protein A affinity chromatography. Surge tanks have been omitted *in lieu* of tubular reactors. Hereby, the residence time and the start-up/shut-down are very short, the residence time distribution very narrow. Yield, purity, and critical quality attributes are shown.

5:30 Close of Day

FRIDAY, JANUARY 20

7:30 am Registration (Indigo Foyer)

ROOM LOCATION: Indigo and Aqua Foyer

BuzZ Sessions

8:00 BuzZ Sessions with Continental Breakfast (IN-PERSON ONLY)

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.

Please continue to check the BuzZ Session page on our conference website for detailed discussion topics and moderators

BuzZ Table 1: Purification Workflows to Support Protein Engineering

Jeremy King, PhD, Senior Scientist, Amgen, Inc.

BuzZ Table 2: Scalable Non-Protein A Affinity Purification Alternatives to Bridge Research and Manufacturing

David W. Wood, PhD, Professor, Chemical & Biomolecular Engineering, The Ohio State University

ROOM LOCATION: Aqua Salon AB

FLEXIBLE AND AGILE PROTEIN PURIFICATION AND CHARACTERIZATION WORKFLOWS

9:00 Chairperson's Remarks

Petra Fromme, PhD, Paul V. Galvin Professor, Chemistry & Biochemistry, Arizona State University

9:05 What Are the Key Considerations for Setting up and Maintaining an Effective Protein Production Laboratory?

Richard Altman, MS, Field Application Scientist, Life Science Solutions, Thermo Fisher Scientific

Protein production is more complex than just the act of expressing the protein. This presentation will review the end-to-end protein production workflow process and reflect on possibilities of how to increase the efficiency and productivity of a recombinant protein expression facility.

9:25 Large-Scale Protein Expression and Purification in Hundreds of Milligram Amounts for Time-Resolved Studies with X-Ray Free Electron Lasers

Petra Fromme, PhD, Paul V. Galvin Professor, Chemistry & Biochemistry, Arizona State University

X-ray free electron lasers probe protein structures with ultrashort x-ray pulses, thereby enabling the determination of molecular movies of molecules "at work," but large quantities of proteins in the range of hundreds of milligrams are required. We will present strategies and procedures for large-scale cell culture and protein isolation for XFEL studies that include preparation of large photosynthetic membrane protein complexes, as well as preparation of proteins from SARS-CoV-2.

9:45 Rapid Production of Highly Purified Tagless Proteins under a Simple Platform

David W. Wood, PhD, Professor, Chemical & Biomolecular Engineering, The Ohio State University

High-throughput protein production relies on affinity tags to enable purification of new targets, where tags are often left in place during initial target characterization. The production of tagless targets is now possible via a self-removing tag that functions in simple buffer systems. We will describe the use of this system to purify a variety of targets to extremely high purity with a standard protocol on a universal affinity resin.

10:05 Reimagining Protein Production Workflows to Enable Next-Generation Biologics?

Daniel Yoo, Principal Scientist, Therapeutic Discovery, Amgen, Inc.

As biologic therapeutics continue to increase in complexity, innovative approaches to candidate screening, production, characterization, and development are more important than ever. Our advanced protein production workflows incorporate novel processes, intelligent high-throughput automation, and high-quality informatics to enable robust molecule screening, selection, and scale-up. These enhancements enable advances in the speed, quality, and productivity of our biologics development pipeline.

10:35 Networking Coffee Break (Aqua Foyer)

11:00 Advancements in Protein Production Workflows to Support the Ever Increasing Demand & Complexity in Drug Discovery

Kanika Bajaj Pahuja, PhD, Scientific Manager, Protein Sciences, Genentech Inc.

This presentation will focus on the evolving needs in the protein production core facility and the creative solutions we are building to overcome and support these increasing demands. It will emphasize on the integration of our several end-to-end automated high-throughput protein expression and production workflows that leverage automation and bioinformatics tools. These approaches significantly alleviate some of the bottlenecks in protein production and accelerate the provision of key protein reagents to ambitious projects.

Think Tank: Protein Purification & Characterization – What's Next?

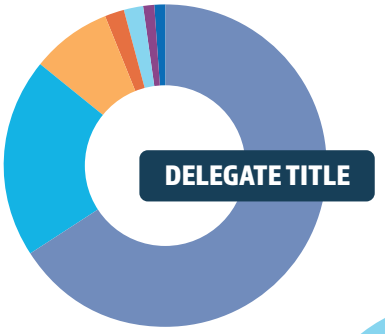
Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

12:00 pm Think Tank Report Outs: Listen and Learn

During the Think Tank Table discussions, we shared our experiences and working solutions for protein purification and characterization workflows. Now as a collective community, let's hear from the table facilitators as they share key discussion points, strategies, and provide a wrap-up of their table's discussion. What can we take away and apply?

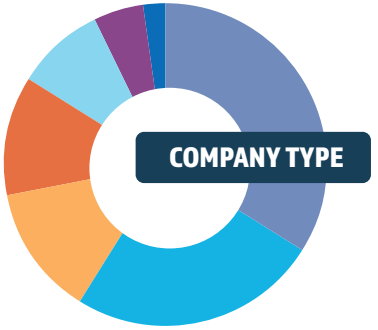
12:30 Close of PepTalk

2022 ATTENDEE DEMOGRAPHICS



DELEGATE TITLE

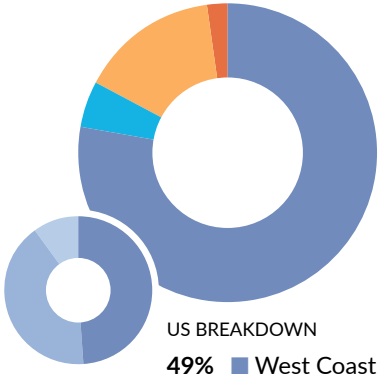
- 66% Biotech
- 20% Pharma
- 8% Academic
- 2% Healthcare
- 2% Other
- 1% Government
- 1% Services



COMPANY TYPE

- 34% Scientist/ Technologist
- 25% Sales & Marketing
- 13% Director
- 12% Executive
- 9% Manager
- 5% Professor
- 2% Assistant

GEOGRAPHIC LOCATION



- 78% United States
- 5% Europe
- 15% Asia
- 2% Rest of World

US BREAKDOWN

- 49% West Coast
- 41% East Coast
- 10% Midwest

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CHI will set up 6-8 in-person meetings during the conference, based on your selections from the advance registration list. Our staff will handle invites, confirmations and reminders, and walk the guest over to the meeting area. This package also includes a meeting space at the venue, complimentary main-conference registrations, branding, an 8'x10' exhibit space, and more.

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COMPANIES A-K

Jason Gerardi | Sr. Manager, Business Development
781-972-5452 | jgerardi@healthtech.com

COMPANIES L-Z:

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781-972-1340 | ashleyparsons@healthtech.com

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Conference Venue & Host Hotel:

Hilton San Diego Bayfront
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Discounted Room Rate: $303 s/d ** includes complimentary Wi-Fi
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PepTalk BuzZ Sessions are focused, stimulating discussions in which delegates discuss important and interesting topics related to upstream protein expression and production through downstream scale-up and manufacturing. This is a moderated discussion with brainstorming and interactive problem-solving among scientists from diverse areas who share a common interest in the discussion topic.

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

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Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure an onsite poster board and/or ensure your virtual poster presentation is included in the conference materials, your full submission must be received, and your registration paid in full by November 18, 2022.

Register and 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 materials. Please see below for more information.

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Please submit the following poster presentation materials by the poster deadline:

- Poster title
- Short text-only description for publication (70 words; about 500 characters)
- Presentation file for the virtual platform (one-page, no-audio PDF poster)

In-Person Attendees will also bring a one-page, PRINTED poster to the event for onsite viewing.

Full time graduate students and PhD candidates are encouraged to attend and present a poster. See chi-peptalk.com/posters for details.

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