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FINAL AGENDA

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CONFERENCE AT-A-GLANCE

15th Annual PEGS BOSTON

2019 PROGRAMS	SUNDAY (APRIL 7)	MONDAY-TUESDAY (APRIL 8-9)	WEDNESDAY-THURSDAY AM (APRIL 10-11)	THURSDAY PM-FRIDAY (APRIL 11-12)
ENGINEERING	PRE-CONFERENCE SHORT COURSES	Display of Antibodies	TUESDAY DINNER SHORT COURSES: Engineering Antibodies	THURSDAY DINNER SHORT COURSES: Engineering Bispecific Antibodies
ONCOLOGY		Antibodies for Cancer Therapy	Advancing Bispecific Antibodies and Combination Therapy to the Clinic	Clinical Progress of Antibody-Drug Conjugates
IMMUNOTHERAPY		Improving Immunotherapy Efficacy and Safety	CAR Ts, TCRs and TILs	Agonist Immunotherapy Targets
EXPRESSION		Difficult-to-Express Proteins	Optimizing Protein Expression	Protein Expression System Engineering
ANALYTICAL		Characterization of Biotherapeutics	Biophysical and Structural Analysis	Analytical Support for Drug Product Development
IMMUNOGENICITY & BIOASSAYS		Immunogenicity Case Studies and Clinical Management	Immunogenicity Assessment and Regulatory Approval of Biologics	Optimizing Bioassays for Biologics
FUSIONS & CONJUGATES		Fusion Protein Therapeutics	Engineering Antibody-Drug Conjugates	Clinical Progress of Antibody-Drug Conjugates
EMERGING THERAPEUTICS AND TECHNOLOGIES		Emerging Indications for Therapeutic Antibodies	Oncolytic Viral Therapy	Genome Editing with CRISPR: Towards Novel Research, Translational and Clinical Applications
Training SEMINARS By Cambridge Healthtech Institute		Intro to Protein Engineering	Next-Generation Sequencing for Antibody Discovery and Engineering	Intro to Immunogenicity
		Intro to Structure-Based Drug Design and Development	Intro to Immunology for Drug Discovery Scientists	Genome Editing with CRISPR: Towards Novel Research, Translational and Clinical Applications
		Intro to Bispecifics: History, Engineering, and Application	Statistics 101 for Assay Validation	
		Intro to Bioprocessing		

"The PEGS meeting is an outstanding conference, which continues to provide a uniquely high level of technical discourse on the development of protein therapeutics, which has become harder to find at other large conferences."

Chief Scientific Officer, Shattuck Labs, Inc.

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PLENARY KEYNOTE SESSION

MONDAY, APRIL 8 | 4:00PM

Vision for How Immunotherapy Will Shape Future of Cancer Care

Immunotherapy is considered by many as a pillar of cancer care today, but in many ways we have only scratched the surface. Our knowledge and understanding of the complexities of immunotherapy and its mechanisms continue to evolve. The future of cancer care will be defined by our ability to systematically identify and implement opportunities for combination therapy to improve and standardize patient response.

Leena Gandhi, MD, PhD

Vice President, Immuno-Oncology Medical Development, Lilly Oncology

Dr. Gandhi graduated from the NYU School of Medicine and completed her residency at MGH, and fellowship at Dana-Farber Cancer Institute (DFCI) and MGH. She worked as a thoracic oncologist and Phase I oncologist at DFCI and served as Director of Clinical Trials in the thoracic oncology program from 2013- 2016. She joined NYU Perlmutter Cancer Center as Associate Professor of Medicine and the Director of Thoracic Medical Oncology in 2016. She has worked on Phase I, II and III trials of novel targeted therapies and immunotherapies in lung cancer, with a focus on evaluating potential biomarkers of response. She has been a lead investigator in clinical trials that helped define the use of PD-L1 as a biomarker of response to PD-1 inhibition in non-small cell lung cancer. Dr. Gandhi most recently served as the lead investigator on the KEYNOTE-189 study, establishing combination chemotherapy and immunotherapy a standard of care in initial treatment for most NSCLC. On June 25, 2018, Dr. Gandhi joined Lilly Oncology to lead immuno-oncology medical development.

YOUNG SCIENTIST KEYNOTE

The Lassa Virus Glycoprotein: Stopping a Moving Target

Lassa virus causes ~5000 deaths from viral hemorrhagic fever every year in West Africa. The trimeric surface glycoprotein, termed GPC, is critical for infection, is the target for neutralizing antibodies, and a major component of vaccines. Structural analysis of Lassa GPC bound to antibodies from human survivors reveals a major Achilles heel for the virus and provides the needed template for development of immunotherapeutics and improved vaccines.

Kathryn Hastie, PhD

Staff Scientist, Immunology and Microbiology,
The Scripps Research Institute

Dr. Hastie studied Ecology and Environmental Biology, Molecular Biology and Biochemistry at the University of Colorado, Boulder. She then joined Erica Ollmann Saphire's group at The Scripps Research Institute and completed her graduate studies in October 2011. As a Staff Scientist in the Ollmann Saphire Lab, Dr. Hastie conducts an independently NIH-funded research project aimed at expanding structural knowledge of glycoproteins of Lassa and other arenaviruses. In addition, she serves on international task forces to steer thought about how to better elicit and detect the right responses and to deliver a much-needed vaccine for Lassa virus, which infects hundreds of thousands of under-served in West Africa every year.

THE PEGS YOUNG SCIENTIST KEYNOTE recognizes a rising star in the field of protein science who is currently in a postdoc program or who has completed a postdoc in the last five years. Nominations of candidates for this role were solicited from leading industry and academic research labs in the fall of 2018, and the final selection was made on the basis of votes from a 15-person group of scientific advisors. CHI's Young Scientist Keynotes join the company's Student Fellowships and Featured Poster Presentations as ways of supporting the increased visibility of those new to our field. Please visit the PEGS website following the 2019 meeting for details on how you can nominate a candidate for the 2020 event.

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SC SHORT COURSES *

SUNDAY, APRIL 7

MORNING, 10:00 AM - 1:00 PM

SC1: Preclinical and Clinical Assessment of Immunogenicity: Multidomain Therapeutics and New Modalities, Including Gene Therapy and CAR T
Darshana Jani, MSc, Associate Director, Global Lead Biologics, Clinical Assay Group, Global Product Development, Pfizer, Inc.
Magdalena Tary-Lehmann, MD, PhD, CSO, Cellular Technology Limited (CTL); Adjunct Associate Professor of Pathology, Case Western Reserve University (CWRU)
Linzhi Chen, PhD, Senior Research Fellow & Bioanalytical Group Leader, Boehringer Ingelheim Pharmaceuticals
Kosalaram Goteti, PhD, Director, Site Head of Pharmacometry, EMD Serono

SC2: Translational Biotherapeutic Development Strategies Part 1: Discovery, Molecular Assessment and Early Stage Development
Juan Carlos Almagro, PhD, Founder and Director, GlobalBio, Inc.
Zhiqiang An, PhD, Professor, Chemistry; Director, Texas Therapeutics Institute, University of Texas Health Science Center at Houston
Gadi Bornstein, PhD, Senior Director, Biologics Discovery, TESARO, Inc.

SC3: Selection, Screening and Engineering for Affinity Reagents
Jonas V. Schaefer, PhD, Lab Head/Investigator II, Novartis Institutes for BioMedical Research (NIBR)
Jürgen Klattig, PhD, Scientist, R&D, MorphoSys AG

SC4: Understanding and Modulating Tumor Microenvironment for Immunotherapy
David A. Eavarone, PhD, Associate Principal Scientist, Harbour Biomed

AFTERNOON, 2:30 - 5:30 PM

SC5: *In silico* Immunogenicity Predictions (Hands-On) Workshop
Vinodh B. Kurella, PhD, Principal Scientist, Protein Engineering, Merrimack Pharmaceuticals
Daron Forman, PhD, Principal Scientist, Molecular Discovery Technologies, Bristol-Myers Squibb

SC7: Translational Biotherapeutic Development Strategies Part 2: Analytical and Clinical Considerations
Zhiqiang An, PhD, Professor, Chemistry; Director, Texas Therapeutics Institute, University of Texas Health Science Center at Houston
Scott L. Klakamp, PhD, Senior Director & Head, Biophysics, Biologics Development Sciences, Janssen BioTherapeutics
Liming Liu, PhD, Senior Principal Scientist, Pharmacokinetics, Pharmacodynamics and Drug Metabolism (PPDM), Merck Research Laboratories
An Song, PhD, Senior Vice President, Development Sciences, Immune-Onc Therapeutics, Inc.

TUESDAY, APRIL 9

DINNER, 6:00 - 8:30 PM

SC9: Introduction to Biophysical Analysis for Biotherapeutics: Development Applications
Christine P. Chan, PhD, Principal Scientist, Global Manufacturing Science & Technology, Sanofi

SC10: CAR T-Cell Therapy for Solid Tumors
Soldano Ferrone, MD, PhD, Division of Surgical Oncology, Surgery, Massachusetts General Hospital, Harvard Medical School
Moonsoo M. Jin, PhD, Professor, Biomedical Engineering, Radiology & Surgery, Molecular Imaging Innovations Institute, Weill Cornell Medical College
Tara Arvedson, PhD, Director, Oncology Research, Amgen

SC11: Developability of Bispecific Antibodies: Formats and Applications
Nimish Gera, PhD, Director, Research and Development, Mythic Therapeutics

THURSDAY, APRIL 11

DINNER, 5:45 - 8:15 PM

SC12: Design Strategies and Development of ADCs
Robert Lutz, PhD, Principal Consultant, Crescendo Biopharma Consulting

SC13: Bioassay Quality by Design
Thomas Little, PhD, President and CEO, Bioassay Sciences, Thomas A. Little Consulting

DINNER, 5:45 - 8:45 PM

SC15: Transient Protein Production in Mammalian Cells
Richard Altman, MS, Staff Scientist, Life Science Solutions, Thermo Fisher Scientific
Henry C. Chiou, PhD, Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific
Bojiao Yin, PhD, Scientist, Protein Technologies, Amgen

** Separate Registration Required.*

TS

TRAINING SEMINARS

Training SEMINARS
By Cambridge Healthtech Institute

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.

MONDAY, APRIL 8: 8:30 AM - 12:30 PM -
TUESDAY, APRIL 9: 8:30 AM - 5:25 PM

TS9A: Introduction to Protein Engineering

CHI's Introduction to Protein Engineering training seminar offers a comprehensive tutorial in the concepts, strategies and tools of protein engineering and explains the role of this discipline in the progression of biotherapeutic research and development. Learn about the selection of functional assays to monitor changes in desired properties, traditional and emerging display technologies and library design strategies. Also explore the engineering and enhancement of traditional antibodies and discuss the roles of protein engineering in the discovery, design and development of new therapeutic modalities. The class includes briefings on the expression platforms used for producing proteins for testing and for manufacture, and the rapidly emerging role of protein engineering in optimizing antibody and other protein therapeutics.

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

TS10A: Introduction to Structure-Based Drug Design and Development

CHI's Introduction to Structure-Based Drug Design and Development offers an introduction to the concepts, strategies and tools of structure-based drug design, optimization and development. The seminar consists of presentations and live demonstrations of some of the common computational tools used in the field. We will cover techniques to triage therapeutics sequences, modulate affinity, create novel constructs (such as Fc-fusions, bispecifics, and protein traps) along with increasing the manufacturability of a biologic. The class is directed at scientists new to the industry, academic scientists and career protein engineers wanting an introduction into how structure can aid in guiding experimental design.

Instructors:

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

Traian Sulea, PhD, Senior Research Officer, Human Health Therapeutics, National Research Council Canada

TS11A: Introduction to Bispecifics: History, Engineering, and Application

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

Instructor: GG. Jonah Rainey, PhD, Vice President, Antibody Therapeutics, Gritstone Oncology, Inc.

TS12A: Introduction to Bioprocessing

CHI's Introduction to Bioprocessing training seminar offers a detailed survey of the steps needed to produce today's complex biopharmaceuticals, from early development through commercial. The seminar begins with an introduction to biologic drugs and the aspects of protein science that drive the progression of analytical and process steps that follow. Then, step through the stages of bioprocessing, beginning with the development of cell lines and ending at scaling up for commercial production. Also explore emerging process technologies, facility design considerations and the regulatory and quality standards that govern our industry throughout development. The important roles of analytical methods at all stages of development as well as formulation and stability assessments in developing and gaining approval for a biopharmaceutical are also examined.

Instructors:

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

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

TS TRAINING SEMINARS CONTINUED

WEDNESDAY, APRIL 10: 8:30 AM - 5:45 PM -
THURSDAY, APRIL 11: 8:30 AM - 12:30 PM

TS9B: Next-Generation Sequencing for Antibody Discovery and Engineering

In this training seminar, participants will learn about Next-Generation Sequencing (NGS) of antibody repertoires. Part 1 will provide an introduction to the antibody repertoires, consisting of genetic background, generation of diversity, sequencing technologies and a hand-on session on the computational tools available for the analysis antibody repertoire NGS data. Part 2 will focus on the preprocessing and analysis of data. Each step of the preprocessing will be elucidated using the programming language R along with existing bioinformatics pipelines available. Repertoire analysis content will provide statistical quantification and visualization of high-dimensional data. The course will be fully interactive with case studies, participants will be able to download data and example scripts. Please bring your computer.

Instructors:

Sai Reddy, PhD, Assistant Professor, Biosystems Science and Engineering, ETH Zurich, Switzerland

Simon Friedensohn, MSc, Research Assistant, Biosystems Science and Engineering, ETH Zurich, Switzerland

TS10B: Introduction to Immunology for Drug Discovery Scientists

This 1.5-day seminar will cover the fundamentals of human immunology for an audience of scientists across different backgrounds working in pharmaceutical and biotech organizations in programs related to immunotherapy. The course will cover a historical perspective, basic mechanisms, fundamental concepts and practical approaches to developing therapeutics and their combinations to modulate the immune system. Additionally, the class will offer perspectives on how immune responses can be monitored by assessment of biomarkers and modulated through biopharmaceutical intervention. Through group activities, attendees will actively review immunological concepts as well as design functional immunological assays and read-outs.

Instructors:

Masha Fridkis-Hareli, MSc, PhD, Founder and President, ATR, LLC

Tatiana Novobrantseva, PhD, Co-Founder, Head of Research and Development, Verseau Therapeutics

TS11B: Statistics 101 for Assay Validation

This training first covers all the basic statistical concepts that are required to perform a successful assay validation, such as (non)linear models for calibration, variance component analysis, and design of experiments. We will then discuss some regulatory requirements for assay validation and discuss how to ensure regulatory compliance while also guaranteeing that the assay is fit for its intended purpose. Finally, we will combine those statistical and regulatory concepts in a case study.

Instructor: Perceval Sondag, Senior Manager, Statistics, PharmaLex

THURSDAY, APRIL 11: 1:40 - 5:20 PM -
FRIDAY, APRIL 12: 8:30 AM - 3:40 PM

TS8C: Introduction to Immunogenicity

All protein drugs generate an immunogenic response. This 1.5-day training seminar provides a practical, comprehensive overview of immunogenicity – the causes, how to assess, predict and prevent, and what to do if you observe immunogenicity during preclinical, clinical and post-market approval. The seminar begins by detailing the science behind immunogenicity, the latest international guidances, followed by assay and bioanalytical assessment strategies for traditional and emerging biologics. Other topics include predictive models and how to report immunogenicity incidents both internally and externally.

Instructors:

Bonnie Rup, PhD, Independent Consultant

Sofie Pattijn, CTO, ImmunXperts

TS9C: Genome Editing with CRISPR: Towards Novel Research, Translational and Clinical Applications

This rigorous day and a half program compiled for specialists interested in applying genome editing technologies for both basic and translational research will comprehensively review the state-of-art information on gene editing strategies and applications in various areas, such as disease modelling, drug discovery and development. Beginning from introductory level basic technology aspects, key molecular features, strengths and shortcomings of CRISPR/Cas9 systems, the instructor will advance towards sharing in-depth knowledge related to virtually all facets of present day genome editing applications, such as constructing of cell culture-based experimental platforms, engineering disease models for *in vivo* research supporting preclinical drug development workflows, rational design and functional screening of sgRNA libraries, application of CRISPR/Cas9 technology for diagnostic and therapeutic purposes and many others.

Instructor:

Serguei V. Kozlov, PhD, MBA, PMP, Principal Scientist/PM, Team Leader PTO, Center for Advanced Preclinical Research, Frederick National Laboratory for Cancer Research (NCI)

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PRESENT A POSTER AND SAVE $50

POSTER COMPETITION

Two poster awards will be given at the conference for a cash prize for best poster. Present your poster at PEGS and be automatically entered to win. One winner from each poster session will be chosen based on visual appearance of poster, clarity of concepts presented, audience engagement, technology advances and implications of the work presented.

Reasons you should present your research poster at PEGS Boston:

- Your poster will be seen by our international delegation, representing leaders from top pharmaceutical, biotech, academic and government institutions
- Receive $50 off your registration
- Your poster abstract will be published in our conference materials
- Automatically entered in the poster competition

REGISTER AND SUBMIT BY MARCH 1, 2019

STUDENT FELLOWSHIPS

PEGS SUMMIT IS PROUD TO SUPPORT AND RECOGNIZE THE SCIENTISTS OF TOMORROW!

Students are encouraged to present a research poster and qualify as a student fellow of the event.

To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by March 1, 2019.

Fellowships are limited to 25 students and submission deadlines must be met. Special pricing is available for students without a poster presentation. Full time graduate students and PhD candidates qualify for the student rate. See the event website for details.

STUDENT FELLOWSHIP DETAILS:

- Receive a poster presentation slot and a savings of over $900 on their registration fee
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ENGINEERING STREAM

- **Display of Antibodies**
- **Engineering Antibodies**
- **Engineering Bispecific Antibodies**

Engineering Novel First-in-Class Biologics

Designing platforms to lend novel functionality and improvements in developability requires a high degree of innovation to address hard to reach and difficult targets. The **Engineering stream** provides knowledge and collaboration opportunities for scientists in this highly competitive field. Display and engineering of biologics including bispecific antibodies will be highlighted for applications in oncology, immunotherapy, infectious disease, CNS, inflammation and autoimmune disorders.

21ST ANNUAL

DISPLAY OF ANTIBODIES

Engineering Novel First-in-Class Biologics

April 8-9, 2019

The Twenty-first Annual Display of Antibodies is the cornerstone conference of the PEGS Summit and convenes leaders in the field year after year. This year's meeting showcases innovation in discovery, design and engineering of biologics through molecular evolution using phage, yeast and other display methodologies. The proliferation of novel constructs is possible through methods to improve library design, pharmacological and biophysical properties to create drug molecules with greater potency, modes of action, target specificity and activity than previously achievable.

SUNDAY, APRIL 7

Recommended Short Course*

SC3: Selection, Screening and Engineering for Affinity Reagents

Separate registration required.* ***Click here* *or see page 5 for course details.*

MONDAY, APRIL 8

7:00 am Registration and Morning Coffee

NEW APPLICATIONS FOR PHAGE DISPLAY

8:30 Chairperson's Opening Remarks

Gregory A. Weiss, PhD, Professor, Chemistry, Molecular Biology & Biochemistry, University of California, Irvine

8:40 Protein-Directed Evolution in Genomic Contexts Using Mutagenesis and CRISPR/Cas9

Michael Krogh Jensen, PhD, Senior Researcher & Co-Principal Investigator, Technical University of Denmark, Novo Nordisk Foundation Center for Biosustainability

Here we describe a method for robust directed evolution using mutagenesis in genomic contexts. The method employs error-prone PCR and Cas9-mediated genome integration of mutant libraries of 300-600 bp-sized donor variants into genomic sites with efficiencies reaching 98-99% and >100K variants from a single transformation. To validate the method for directed evolution, we engineered two essential enzymes in the mevalonate pathway of *Saccharomyces cerevisiae*. Taken together, our method extends on existing CRISPR technologies by facilitating efficient mutagenesis of hundreds of nucleotides in cognate genomic contexts.

9:10 Constructing a Synthetic Biology Toolbox Using Phage Display Parts

C. Ronald Geyer, PhD, Professor, Pathology and Lab Medicine, University of Saskatchewan

Antibody phage display is a powerful strategy for producing antibody fragments that can be used as parts for constructing synthetic antibody-like devices. Here we describe the construction and selection of antibody fragment libraries and the assembly of selected antibody parts into devices useful for antibody therapy, imaging, and diagnostics.

9:40 Development of a Complex T7 Phage Display Library for Discovery of Biomarkers of Lung Diseases

Lobelia Samavati, MD, Associate Professor of Medicine, Department of Medicine, Center for Molecular Medicine and Genetics, Wayne State University School of Medicine

Chronic respiratory diseases of unknown etiology share similarities with various inflammatory and infectious diseases including tuberculosis. Currently, there is no test available to discriminate between active TB and sarcoidosis or between active, latent TB and other respiratory diseases. Using a high throughput method, we developed two T7 phage display cDNA libraries derived from mRNA isolated from bronchoalveolar lavage (BAL) cells and leukocytes of sarcoidosis patients. We combined these two libraries with two other libraries derived from embryonic lung fibroblasts and human monocytes, to build a complex library. Our studies indicate that our complex library contains diverse clones that can distinguish sera from healthy controls, sarcoidosis, cystic fibrosis and tuberculosis.

10:10 Networking Coffee Break

10:50 KEYNOTE PRESENTATION: Engineering Membrane Proteins with Phage Display

Gregory A. Weiss, PhD, Professor, Chemistry, Molecular Biology & Biochemistry, University of California, Irvine

Phage display offers a power tool for remodeling proteins – their binding, catalysis, solubility and other properties. However, the technique has largely been confined to soluble proteins. My laboratory has demonstrated that membrane proteins can also be displayed on the phage surface. In this talk, I'll describe the limitations of membrane protein phage display and applying the approach to solubilize and engineer membrane proteins with powerful new functions.

11:20 Cytosolic Delivery of Proteins by Bioreversible Esterification

Ronald T. Raines, PhD, Firmenich Professor of Chemistry, Department of Chemistry, Massachusetts Institute of Technology

The surface of mammalian cells is highly anionic. Accordingly, Coulombic repulsion prevents anionic molecules from entering cells. We have tuned the reactivity of a diazo compound to elicit the efficient O-alkylation of carboxylic acids in water. Such esterification enables proteins (including a Fab fragment) to traverse the plasma membrane directly, like a small-molecule prodrug. As with prodrugs, the nascent esters are substrates for endogenous esterases that regenerate native proteins.

11:50 Generating Pairs of Affinity Reagents for Sandwich Assays through MegaSTAR
Brian K. Kay, PhD, Professor & Head, Biological Sciences, University of Illinois, Chicago
The 'sandwich' assay is a robust, flexible and sensitive test that is widely employed in clinical diagnostics for monitoring human health and disease. Unfortunately, identifying pairs of antibodies takes time and luck. We have recently developed a method to discover pairs of recombinant affinity reagents part of the phage-display process. We will present results of applying MegaSTAR to cell signaling proteins and biomarkers of heart disease.

12:20 pm High Quality Antibodies for Therapeutic Applications
Vera Molkenthin, PhD, Chief Scientist, AbCheck
AbCheck discovers and optimizes human antibodies for therapeutic applications leveraging several proprietary platforms including *in vitro* and *in vivo* technologies. AbCheck will present new technological developments regarding its versatile human antibody discovery and optimization platform with a focus on Rabbit Mass Humanization and AbAccelTM.. Both technologies can be combined with AbCheck's yeast display platform AbSieveTM and deliver high quality leads with subnanomolar affinities and good stabilities which are compatible with different antibody designs including bispecifics.

12:50 Luncheon Presentation I: Integrated Solutions for Antibody Discovery and Beyond
Sponsored by LakePharma
Hua Tu, PhD, CEO and Founder, LakePharma
LakePharma focuses on providing complete solutions from antibody discovery to GMP manufacturing. In this talk, the biotech company will share its experience and case studies in antibody discovery and engineering using display technology. The presentation provides solutions for the common problems encountered by display technology as well as rapid development to clinical manufacturing.

1:20 Luncheon Presentation II: Bruteforcing Hard Targets with Computationally Immuno-Engineered SuperHuman 2.0
Sponsored by distributed bio
Jacob G. Glanville, PhD, Co-founder & CSO, Distributed Bio Inc.
Over the last decade, the iterative analysis and computational optimization of antibody repertoires has resulted in a 1000x improvement in antibody library functional sequence diversity. Here, we present a series of case studies against traditionally hard targets that demonstrate the practical consequences of optimized library diversity. In GPCRs, we show a combination of a large library and high-throughput sequencing enables routine recovery of antibodies, including functionally active antibodies, against GPCRs like CXCR5.

1:50 Session Break

2:00 Synthetic DNA Technologies Enable Antibody Discovery and Optimization
Sponsored by TWIST BIOSCIENCE
Aaron Sato, PhD, CSO, Twist Bioscience
Utilizing its proprietary DNA writing technology to create oligo pools, genes, and synthetic libraries, Twist Pharma, a division of Twist Bioscience, provides the biotechnology industry with an end-to-end antibody discovery solution. This solution includes (1) a panel of high diversity synthetic antibody libraries, (2) a proprietary human anti-GPCR antibody phage display library focused on this validated target class, and (3) a Twist Antibody Optimization (TAO) platform for antibody affinity and developability optimization.

2:30 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks
Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, AstraZeneca

4:10 Vision for How Immunotherapy Will Shape Future of Cancer Care
Leena Gandhi, MD, PhD, Vice President, Immuno-Oncology Medical Development, Lilly Oncology
Immunotherapy is considered by many as a pillar of cancer care today, but in many ways we have only scratched the surface. Our knowledge and understanding of the complexities of immunotherapy and its mechanisms continue to evolve. The future of cancer care will be defined by our ability to systematically identify and implement opportunities for combination therapy to improve and standardize patient response.

4:55 The Lassa Virus Glycoprotein: Stopping a Moving Target
Kathryn Hastie, PhD, Staff Scientist, Immunology and Microbiology, The Scripps Research Institute
Lassa virus causes ~5000 deaths from viral hemorrhagic fever every year in West Africa. The trimeric surface glycoprotein, termed GPC, is critical for infection, is the target for neutralizing antibodies, and a major component of vaccines. Structural analysis of Lassa GPC bound to antibodies from human survivors reveals a major Achilles heel for the virus and provides the needed template for development of immunotherapeutics and improved vaccines.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:15 End of Day

TUESDAY, APRIL 9

8:00 am Registration and Morning Coffee

ENGINEERING SMALL PROTEINS AND CONSTRAINED PEPTIDES

8:25 Chairperson's Remarks
K. Dane Wittrup, PhD, J.R. Mares Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

8:30 Yeast Display of Post-Translationally Modified Polycyclic Peptides
Wilfred A. van der Donk, PhD, Richard E. Heckert Endowed Chair in Chemistry, Director of Graduate Studies, Howard Hughes Medical Institute Investigator, Department of Chemistry, University of Illinois
Ribosomally synthesized and post-translationally modified peptides (RiPPs) constitute a large class of natural products with vast structural diversity. Lanthionine-containing peptides (lanthipeptides) are examples of this growing class. They contain multiple thioether crosslinks installed post-translationally by a single enzyme that typically forms 2-5 rings with high control over regio- and chemoselectivity. This presentation will discuss use of the biosynthetic machinery to display libraries of such polycyclic peptides.

9:00 Integrating Computational Design with Screening in Mammalian Cells for Novel Peptide Therapeutics
Philip M. Kim, PhD, Associate Professor, The Donnelly Centre for Cellular and Biomolecular Research, Departments of Molecular Genetics and Computer Science, University of Toronto
I will present our technology platform that integrates computational library design with modern in-cell selection strategies to uncover novel peptide therapeutics. I will cover a number of different library designs and selection methodologies, including selections for phenotype or using genetic reporter systems and cell sorting, as well as methods to obtain highly stable mirror image peptides.

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9:30 Platforms for the Generation and Screening of Cyclic Peptide Libraries
Ali Tavassoli, PhD, Professor, Chemical Biology, University of Southampton

Cyclic peptide libraries have demonstrated significant potential when employed against challenging targets such as protein-protein interactions. SICLOPPS is a genetically encoded method for the intracellular generation of cyclic peptide libraries of over a hundred million members. SICLOPPS libraries can be interfaced with a variety of cell-based assays. Here, we will report the use of this approach for the identification of inhibitors of a variety of challenging targets.

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

NOVEL TECHNOLOGIES

10:45 Chairperson's Remarks
Jennifer R. Cochran, PhD, Shriram Chair of Bioengineering; Professor of Bioengineering, and (by courtesy) Chemical Engineering, Stanford University

10:50 Specificity and Polyreactivity: Designing Antibodies Against Receptor Families for Desired Reactivity
Christilyn Graff, PhD, Director, Antibody Discovery and Engineering, Biogen

Targeting receptor families can present a challenge depending on the level of sequence and structural homology. From highly conserved to more divergent families, *in vitro* display libraries can be used to focus the antibody response to the desired specificity. Antigen optimization, in concert with knowledge of ligand/receptor interactions across the family, can also be used to direct the response. This talk will highlight our efforts to isolate antibodies that are either highly specific or polyreactive, in order to better understand the implication of targeting one or more members of the receptor family.

11:20 A Platform Enabling High-Throughput Functional Screening of Antibody Libraries
Ryan Kelly, PhD, Research Scientist, xCella Biosciences

We present a novel platform for rapid antibody discovery based on cell binding and functional activity readouts. Our microcapillary array technology allows us to screen antibody libraries, displayed on or secreted by yeast and mammalian cells, using a wide variety of assay formats. This proprietary hardware and software platform combined with xEmplar™, our human-inspired synthetic antibody library, have enabled the isolation of antibodies against multiple clinically relevant targets.

11:50 A Novel Strategy for the Generation of Yeast Surface Display Antibody Fab Libraries
Stefan Zielonka, PhD, Group Leader & Principal Scientist, Protein Engineering & Antibody Technologies, Discovery Technologies, Global Research and Development, Merck KGaA

Yeast surface display emerged as a promising platform technology for antibody engineering. Still, generation of libraries comprising heavy chain as well as light chain diversities is a cumbersome process involving multiple steps. We recently implemented a focused approach for the construction of Fab antibody libraries using type IIs restriction enzymes. This method seems to be valid for the generation of YSD diversities with adequate qualities.

12:20 pm Luncheon Presentation I: Highly Specific Claudin6 Antibodies for Targeting Solid Tumors
Sponsored by integral molecular
Benjamin Doranz, PhD, MBA, President and CEO, Integral Molecular

Claudin6 is upregulated in tumors, but unlike other claudins, is not expressed in normal tissue. Using our MPS Antibody Discovery platform, we have discovered lead candidate antibodies that bind unique residues on Claudin6 (creating novel IP) and do not bind any other membrane protein in the human proteome.

Specificity Profiling and High-Resolution Epitope Mapping of mAbs Targeting Membrane Proteins
Duncan Huston-Paterson, DPhil, Product Manager, Integral Molecular

Specificity testing across the proteome de-risks lead selection and has been applied to hundreds of mAbs using our Membrane Proteome Array of 5,300 membrane proteins. Conformational epitopes generate novel IP and mechanistic insights, and we have mapped >1,000 such epitopes with >95% success rate using our Shotgun Mutagenesis platform.

12:50 Luncheon Presentation II: Efficient Membrane Protein Targeting Antibodies Discovery Using Synthetic Antibody Libraries and CIS Display
Sponsored by isogenica
Guy Hermans, PhD, CSO, Isogenica Ltd.

Isogenica's IlamdA™ library is a highly diverse, fully synthetic VHH library. It can be used to discover VHHs in phage display format, as well as through our proprietary CIS display selection process. In this talk, we will briefly discuss the benefits this library design brings and illustrate some of the unique benefits of VHH technology over conventional antibodies. Also, we will share recent data demonstrating isolation of VHHs to membrane proteins.

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

NGS IN NATURAL AND ARTIFICIAL ANTIBODY REPERTOIRES

2:00 Chairperson's Remarks
Andrew R.M. Bradbury, MB BS, PhD, CSO, Specifica, Inc.

2:05 Using Structural Information to Aid *in silico* Therapeutic Design from Next-Generation Sequencing Repertoires of Antibodies
Charlotte Deane, PhD, Professor of Structural Bioinformatics & Head of Department, Department of Statistics University of Oxford; Head of the Oxford Protein Informatics Group, University of Oxford

We have built the freely available Observed Antibody Space database of over half-a-billion antibody sequences. Using this data, I will show how predicted structural information can enrich data from next-generation sequencing experiments. In particular, ABOSS, our novel method for filtering Ig-seq data, which considers the structural viability of each sequence and TAP, our novel therapeutic antibody profiler that provides five computational developability guidelines.

2:35 Analysis of Human Antibody Repertoires
Eline T. Luning Prak, MD, PhD, Associate Professor, Department of Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania

This talk will focus on different methods for the analysis of antibody repertoires including RNA- and DNA-based methods in bulk populations as well as single cell analysis. I will describe the strengths and limitations of each method and which methods are most useful for different types of research questions.

3:05 Rational Library Design for the Affinity Maturation of Antibodies
Sponsored by fusionantibodies
Richard Buick, PhD, CTO, Fusion Antibodies plc

A case study will be shown for the affinity maturation of an anti-Cathepsin S antibody by rational library design followed by molecular docking of variants in a step-wise combinatorial fashion.

DISPLAY OF ANTIBODIES continued

Sponsored by VACCINEX

3:20 Use of Mammalian Virus Display to Select Antibodies Specific for Complex Membrane Antigens

Ernest Smith, PhD, CSO, Senior VP, Research, Vaccinex, Inc

We have developed a technology to enable direct incorporation of multipass membrane proteins such as GPCRs and ion channels into the membrane of a mammalian virus. Antigen expressing virus can be readily purified and used for antibody selection using either vaccinia, phage or yeast display methods. This method is rapid, does not require any detergents or refolding, and can be applied to multiple cell types in order to maximize protein expression and to provide properly folded protein that is necessary for antibody selection.

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

4:25 Shaping of Primary Ig Repertoires

Duane R. Wesemann, MD, PhD, Principal Investigator, Assistant Professor of Medicine, Harvard Medical School; Associate Physician, Brigham and Women's Hospital

B cell immunoglobulin (Ig) repertoire composition shapes immune responses. The generation of Ig diversity begins with Ig variable region exon assembly from gene segments, random inter-segment junction sequence diversity, and combinations of Ig heavy and light chain. This generates vast preemptive sequence freedom in early developing B lineage cell Ig genes that can anticipate a great diversity of threats. This freedom is met with large restrictions that ultimately define the naïve (i.e. preimmune) Ig repertoire. Activation-induced somatic hypermutation (SHM), which further diversifies Ig V regions, is also met with strong selection that shapes Ig affinity maturation. While individual repertoire features, such as affinity for self and competition for foreign antigen, are known to drive selection, the selection filters themselves may be regulatable. Large sequence freedom coupled with strong selection for each diversification process provides flexibility for demand-driven regulation to dynamically balance antigen recognition capacities and associated autoimmune risks according to host needs. We use single B cell culture, antibody specificity testing, and deep Ig sequencing analysis to investigate Ig tolerance filter porosity.

4:55 Going Directly from Sequence to Clone: Isolation of Antibodies after Identifying Them by NGS

Fortunato Ferrara, PhD, Vice President, Specifica, Inc.

Going easily from sequence to clones presently represents the primary bottleneck in the full exploitation of next-generation sequencing (NGS) applied to *in vitro* antibody selection. We have devised and tested a number of different methods to generate antibody clones identified by NGS. This talk will describe the success we obtained with the different methods, how effective they were to reach into the abundance rank, and the affinities and binding properties of antibodies derived at different abundance depths.

5:25 End of Display of Antibodies

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC11: Developability of Bispecific Antibodies: Formats and Applications

Separate registration required.* ***Click here* *or see page 5 for course details.*

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20TH ANNUAL

ENGINEERING ANTIBODIES

New Science and Technologies for the Discovery and Engineering of Next-Generation Biotherapeutics

April 10-11, 2019

The field of protein engineering is at an exciting point in its development, with new generations of therapeutic antibodies now progressing through development and into the market, great advances in protein science and discovery technology and a body of clinical evidence that can be used to inform the development of safe, highly effective therapies for unmet medical needs. The PEGS Engineering Antibodies conference explores case examples of the most significant emerging technologies used by protein engineers working at the discovery and design stages to quickly and efficiently craft biotherapeutics directed at the most elusive targets and biological functions.

TUESDAY, APRIL 9

Recommended Short Course*

SC11: Developability of Bispecific Antibodies: Formats and Applications

Separate registration required.* ***Click here* *or see page 5 for course details.*

WEDNESDAY, APRIL 10

7:15 am Registration and Morning Coffee

7:25 - 8:25 PANEL DISCUSSION: Women in Science – Inspired Professional and Personal Stories

Moderator: Women in Bio, Boston Chapter

Panelists:

Susan Richards, PhD, Presidential Scientific Fellow, Translational Medicine Early Development, Sanofi R&D

Joanna Brewer, PhD, Vice President, Platform Technologies, AdaptImmune

Additional Panelists to be Announced

DEEP SEQUENCING AND B-CELL CLONING IN ANTIBODY DISCOVERY

8:30 Chairperson's Opening Remarks

Jane Seagal, PhD, Principal Research Scientist, Global Biologics, AbbVie

8:40 Antibody Affinity and Repertoires from Single Antibody-Producing Cells

Pierre Bruhns, PhD, Professor, Antibodies in Therapy & Pathology, Pasteur Institute, France

The antibody response represents the circulating fraction of antibodies produced by plasma blasts and plasma cells. Weak to lack of expression of membrane-bound antibody prevents conventional technologies to assess their antibody specificity/ polyreactivity, affinity and repertoires on a single cell level. We circumvented this issue by using single-cell compartmentalization in droplet microfluidics and characterized plasmablasts and plasma cells following immunization or autoimmune antibody responses in mice and humans.

9:10 Microfluidic Technology to Identify and Isolate Antigen-Specific T Cells

Julie Brouchon, PhD, Postdoctoral Associate, Weitz Lab, Harvard University

Isolation of antigen-specific T cells is fundamental to study autoimmune diseases and to develop immunotherapies. Unfortunately, these cells are rare and cannot be easily identified by surface markers. We overcome these challenges by compartmentalizing cells into microfluidic droplets and performing a functional assay relying on T cell-target cell interaction and subsequent fluorescent detection of cytokine secretion. In one day, we can screen several million cells to isolate live, antigen-specific T cells.

9:40 High Throughput Antibody Discovery in the Digital Age

Jane Seagal, PhD, Principal Research Scientist, Global Biologics, AbbVie

The constantly growing demand for novel therapeutic biologics drives technology innovation enabling efficient antibody discovery. Optimization and 'digitalization' of antibody discovery workflows is essential for successful identification of antibodies against challenging targets and the sampling diverse antibody repertoires. In this talk, automated platform technologies enabling both hybridoma and single B cell workflows are presented highlighting the integration of sequence information, screening data, and informatics for large panels of antibodies.

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

10:15 Women in Science Speed Networking in the Exhibit Hall

ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING IN ANTIBODY DISCOVERY

10:55 Antibody Discovery and Engineering Using Deep Learning

Sai Reddy, PhD, Assistant Professor, Biosystems Science and Engineering, ETH Zurich, Switzerland

Deep learning, as a part of a family of tools related to artificial intelligence, is an emerging field of information and computer science that uses large data sets to extract features and representations. Antibody discovery and engineering is reliant on experimental platforms of high-throughput expression and screening of libraries. Here, I will describe how we are applying deep learning to augment the discovery and engineering of antibodies by moving beyond experimental screening.

11:25 KEYNOTE PRESENTATION: Implementing Artificial Intelligence in Biotherapeutic Discovery and Development

Philip Tagari, PhD, Vice President, Research, Amgen

The very rapid "democratization" of machine learning provides a broad range of opportunities in the complete lifecycle of therapeutics discovery and development. Strategies and examples will be discussed in molecule design and selection, manufacturability assessment, novel prognostic biomarkers, clinical trial design and "beyond the medicine".

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11:55 Machine Learning in Computational Biology to Accelerate Heterologous Protein Production
Elizabeth Brunk, PhD, Postdoctoral Research Fellow, Systems Biology Research Group, University of California, San Diego
Standardized, multi-omics datasets are becoming increasingly available, but major impediments prevent the realization of impact of big data resources. Modern machine learning methods bring the promise of leveraging large-scale omics data to make accurate predictions. Here, I present recent efforts on the development of appropriate *in silico* tools and cross-disciplinary training resources, which are paramount for further progress in big data science.

12:25 pm Biologics by Design: Incorporating Physics-based Methods into Prediction Models for Protein Stability and Binding Affinity
Sponsored by SCHRÖDINGER
Eliud Oloo, PhD, Senior Principal Scientist, Schrödinger
Combining experiment with physics-based computational approaches and Machine Learning is emerging as a promising strategy for advancing the discovery of biologic treatments, including monoclonal antibodies, vaccines, and enzyme replacement therapies. To develop effective statistical correlations and learned predictive models applicable to the design and optimization of biologics, it is important to take into account structure-based features. Structural properties are however often difficult and expensive to obtain by experiment. We describe physics-based computational methods that narrow this gap by calculating properties derived from structure and simulation, thus complementing experimental measurements.

12:55 Luncheon Presentation I: Build Better Biologics with Machine Learning and Synbio
Sponsored by ATUM
Claes Gustafsson, PhD, CCO, Co-Founder, ATUM
This presentation will showcase how ATUM combines recent developments in genome engineering, automation, big data and product analytics to increase efficiency of engineering and developability of biologics and cell lines. Cell lines generated using the LeapIn® transposase combined with optimized vector constructs, proprietary codon optimization and QSAR-based protein engineering allow for an information rich and efficient optimization of mAbs, bispecifics, CAR-T molecules, and the increasingly complex biologics approaching the market place.

1:55 Session Break

FAST AND NIMBLE ANTIBODY DISCOVERY AND DEVELOPMENT

2:10 Chairperson's Remarks
Gregory C. Ippolito, PhD, Research Assistant Professor, Molecular Biosciences, LIVESTRONG Cancer Institute, The University of Texas at Austin

2:15 Lessons Learned on Rapid Discovery from the DARPA Pandemic Prevention Platform (P3)
Gregory C. Ippolito, PhD, Research Assistant Professor, Molecular Biosciences, LIVESTRONG Cancer Institute, The University of Texas at Austin
The DARPA P3 program is focused on the rapid discovery, production, and delivery of antibody countermeasures to halt infectious disease outbreaks in 60 days or less. Four P3 performer teams were chosen to deploy distinct technologies for antibody discovery related to this effort. Lessons learned shall be discussed.

2:45 Case Study of Antibody Discovery and Development from a Small and Nimble Biotech
Abhishek Datta, PhD, Director, Antibody Discovery & Engineering, Scholar Rock
Since its inception 6 years ago, Scholar Rock has successfully executed multiple antibody drug discovery campaigns, including one for its lead antibody, SRK-015 that is currently in the clinic. In this presentation, Scholar Rock discusses a case study wherein the combination of an accelerated naïve discovery and optimization campaign, coupled with development/availability of an *in vivo* model that enabled rapid pharmacodynamic read-out, led to the successful identification of an antibody candidate.

3:15 Fast and Deep: Rapid High-Throughput Antibody Discovery from Deep Mining of Natural Immune Repertoires
Kevin Heyries, PhD, Co-Founder, Business Development and Strategy Lead, AbCellera
AbCellera's antibody discovery platform can screen millions of single antibody secreting cells in less than a day using multistep and multiplexed secretion assays and high-throughput imaging. We will demonstrate how this technology is being applied to rapid identification of antibodies from humans exposed to viral pathogens under the DARPA Pandemic Prevention Platform (P3) project and how these capabilities can be applied to difficult membrane protein targets.

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

THURSDAY, APRIL 11

8:00 am Registration and Morning Coffee

EMERGING TECHNOLOGIES IN ANTIBODY ENGINEERING

8:30 Chairperson's Remarks
Christoph Spiess, PhD, Senior Scientist, Antibody Engineering, Genentech

8:35 A Paradigm Shift: Moving from Traditional Screening towards Data Driven Antibody Design
Kristin Brown, Director, Protein Design and Informatics, GlaxoSmithKline
Machine learning, artificial intelligence, and *in silico* design are phrases that have had high visibility in the news and scientific papers over the last few years. Effectively incorporating these techniques within antibody discovery has the potential to transform how we design antibodies. This transformation requires a shift in how we design experiments to generate relevant data. I will be discussing different strategies that enable this change in paradigm.

9:05 New High-Throughput Technologies to Design and Optimize Non-Antibody Scaffolds
Gabriel Rocklin, PhD, Assistant Professor, Department of Pharmacology & Center for Synthetic Biology, Northwestern University
Optimizing the therapeutic suitability of protein scaffolds remains an unsolved challenge. We have developed a multiplexed mass spectrometry approach to assay thousands of *de novo* designed scaffolds for properties that are inaccessible to other high-throughput techniques, including stability against protein degradation and aggregation, the extent of conformational fluctuations, and the efficiency of intracellular delivery. Data from these large-scale assays enables us to optimize these properties in *de novo* scaffold design.

9:35 Merck's BRAIN – "Biologics Research All-in-One": Building a Request System for Quality Control of Purified Proteins
Erin Williams, Associate Lab, Head, Quality Control, Protein Sciences - Quality Control, EMD Serono
We have established a global data and workflow platform at Merck for increasing the efficiency of our antibody discovery, protein production, and quality

ENGINEERING ANTIBODIES continued

control processes. We share examples of how the use of this platform has transformed our daily research work, e.g., in organizing and performing QC of produced proteins, including standard and bispecific antibodies, and how it supports discovery and engineering groups using B-cell cloning workflows and engineering of (SEED) bispecific antibodies.

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

OPTIMIZING ANTIBODY TARGETING AND SPECIFICITY

11:05 Using Deep Sequencing Datasets to Tailor Specificity

Tim Whitehead, Associate Professor, Department Chemical and Biological Engineering, University of Colorado, Boulder

Next-generation sequencing has presented protein scientists with the ability to observe entire populations of molecules before, during, and after a high-throughput screen or selection for function. My talk will present an overview of how we can leverage this large amount of sequence-function information to program antibody specificity in typical antibody discovery workflows. I will also present on how we use NGS to mimic evolutionary landscapes of neutralizing, specific anti-Influenza antibodies.

11:35 Engineering of a T-Cell Dependent Bispecific Antibody to Broaden the Therapeutic Index for Solid Tumors

Christoph Spiess, PhD, Senior Scientist, Antibody Engineering, Genentech

The lack of tumor-specific targets for solid tumors is a challenge for the successful and safe targeting of T-cell dependent bispecific (TDB) antibodies. By fine-tuning the avidity driven binding to HER2, we engineered an anti-HER2/CD3 TDB that selectively binds and kills HER2 overexpressing tumor cells with high potency, while sparing cells with normal expression levels. The underlying concept may expand to other targets and applications that require an improved therapeutic index.

12:05 pm Intratumoral Delivery and Retention of Cytokines and Agonist Antibodies

K. Dane Wittrup, PhD, C.P. Dubbs Professor, Chemical Engineering and Biological Engineering; Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

Despite broad efforts, delivery of immune agonistic payloads via systemic administration is plagued by poor therapeutic indices, due to extensive off-target exposure. We are examining the fundamental micropharmacokinetic issues involved in intratumoral administration and find that bispecific constructs that are retained in particular subdomains of the tumor, as defined by extracellular matrix composition, can exert profound therapeutic effects while largely sparing from systemic exposure or toxicity.

12:35 End of Engineering Antibodies

Recommended Short Course*

SC12: Design Strategies and Development of ADCs

Separate registration required. **Click here or see page 5 for course details.*

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10TH ANNUAL

ENGINEERING BISPECIFIC ANTIBODIES

Improving Therapeutic Properties for Oncology and Beyond

April 11-12, 2019

The world of bispecific strategies, formats and clinical results has been gearing up over the past several years. Now in its tenth year, the Engineering Bispecific Antibodies conference was the first one in the community to address the vast challenges and exciting new engineering and manufacturing advances that are enabling the next generation of improved bispecific antibodies. Come see for yourself why this field is leading a transformation beyond oncology to many other areas of medicine.

THURSDAY, APRIL 11

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

BISPECIFICS FOR CNS AND COMPARTMENTAL DELIVERY

1:40 Chairperson's Opening Remarks
Mahiuddin Ahmed, PhD, CSO, Y-mAbs Therapeutics

1:50 Emerging Technologies for Delivery of Biotherapeutics and Gene Therapy across the Blood–Brain Barrier
Danica Stanimirovic, PhD, Research Director, Translational Bioscience, National Research Council Canada

2:20 Co-Targeting Ephrin Receptor Tyrosine Kinases A2 and A3 in Cancer Stem Cells Reduces Growth of Recurrent Glioblastoma
Sheila K. Singh, MD, PhD FRCS(C), Pediatric Neurosurgeon, McMaster Children's Hospital, Interim Division Head, Neurosurgery, Hamilton Health Sciences; Director, McMaster Surgeon Scientist Program, Professor of Surgery, McMaster University; Principal Investigator, Stem Cell and Cancer Research Institute, McMaster University; Senior Canada Research Chair in Human Cancer Stem Cell Biology, Michael DeGroote Centre for Learning and Discovery

Recurrent glioblastoma (rGBM) remains vastly understudied with few biological targets for therapeutic development. In our present study, we identify that co-expression of EphA2 and EphA3 functionally marks a potent glioblastoma stem cells (GSC) population in rGBM. We developed a EphA2/EphA3 bispecific-antibody (BsAb) and demonstrate that treatment with the BsAb reduces rGBM tumor burden. Therefore, we present the development of rational therapeutic approaches against biologically relevant targets in rGBM.

2:50 BBB Transport Vehicle (TV): A Novel Brain Delivery Platform
Mark Dennis, PhD, Fellow, Denali Therapeutics

The BBB Transport Vehicle (TV) enables the delivery of large molecule therapeutics to the brain for the treatment of neurological diseases. The TV platform contains an engineered Fc domain that binds the transferrin receptor and utilizes receptor-mediated transcytosis to cross the BBB. This platform can be formatted for efficient delivery of both antibodies (ATV) and enzymes (ETV) across the BBB.

3:20 The Journey to 'the' Antibody: Accessing a Versatile Toolbox
Sponsored by FairJourney Biologics
María González Pajuelo, CSO, FairJourney Biologics

To maximize the possibility to select "the" antibody, at FJB we have taken antibody discovery to an unprecedent level by creating a versatile toolbox that allows the selection by phage display of antibody fragments of different species from large naïve and immune repertoires. Ultimately these fragments can be engineered and converted to mono- and bi-specific formats that are produced in CHO cells

3:50 Networking Refreshment Break

4:20 T Cell Engineering to Overcome Tumor Heterogeneity and Microenvironment Inhibition in Brain Tumors
Sujith K. Joseph, PhD, Scientist, Pediatrics Hematology-Oncology, Center for Cell and Gene Therapy, Baylor College of Medicine

Successful T cell immunotherapy depends on overcoming tumor heterogeneity and microenvironment inhibition. Use of multivalent CAR T-cells demonstrate advantage when targeting highly heterogeneous brain tumors. Additionally, grafting an intrinsic checkpoint reversal receptor (CPR) to CAR T-cells can help them overcome the inhibitory effects of brain tumor microenvironment.

4:50 Tissue-Specific Delivery of Antibodies: Improving Efficacy by Putting Antibodies at the Site of Action
Martin Jack Borrok, PhD, Scientist II, AstraZeneca

Upon vascular administration, bio-therapeutics become broadly distributed throughout the body with only a fraction of dosed drugs reaching the intended organ or tissue target. By targeting existing transport systems in the lungs (and other organs), we can improve both the delivery and efficacy of therapeutics that act within these tissues while concurrently reducing unintended interactions in tissues not being targeted.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC12: Design Strategies and Development of ADCs
Separate registration required.* ***Click here* *or see page 5 for course details.*

FRIDAY, APRIL 12

8:00 am Morning Coffee

BISPECIFIC ANTIBODIES FOR IMMUNOTHERAPY: SEEING CLINICAL RESULTS

8:30 Chairperson's Remarks
Ertan Eryilmaz, PhD, Senior Scientist, Takeda

8:35 Blockade of Multiple Checkpoint Receptors with Bispecific DART® Molecules
Gundo Diedrich, PhD, Director, Antibody Engineering, MacroGenics

Therapeutic blockade of immune checkpoint pathways with monoclonal antibodies has provided remarkable anti-tumor activity, translating to a significant improvement in overall survival in subsets of cancer

ENGINEERING BISPECIFIC ANTIBODIES continued

patients. Dual blockade of checkpoint pathways with bispecific antibodies may further enhance clinical benefits. The development of two bispecific DART molecules targeting PD-1 and LAG-3 (MGD013) or PD-1 and CTLA-4 (MGD019) will be presented.

9:05 Tumor-Localized Activation of the Immune System Using Antibody-Anticalin® Fusion Proteins

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

4-1BB (CD137), a key costimulatory immunoreceptor, is a highly promising therapeutic target for the treatment of cancer. We utilized the Anticalin technology to develop 4-1BB-bispecific fusion proteins for tumor-localized activation of the immune system to overcome toxicity and efficacy limitations of current 4-1BB-targeting antibodies. We describe the characterization of PRS-343, a 4-1BB/HER2-targeting bispecific, and the *in vitro* and *in vivo* preclinical data supporting the ongoing first-in-patient trial of this drug candidate. Beyond PRS-343, the versatility of the Anticalin platform allows for the generation of a wide range of bispecifics for localized T-cell activation, including a high level of flexibility in molecular geometry and target valency to optimize good drug-like properties and superior efficacy of drug candidates generated within this therapeutic protein class.

9:35 XPAT-T cell Engagers – A Novel Format to Mitigate the On-Target, Off-Tumor Problem

Sponsored by AMUNIX

Volker Schellenberger, PhD, President and Chief Technology Officer, Research & Discovery, Amunix Pharmaceuticals, Inc.

Amunix developed a novel format of highly-selective bispecific T cell engagers based on our proprietary XPAT platform (XTENylated Protease Activatable in Tumor). XTENylation provides long *in vivo* half-life and universal masking applicable to any antibody. T cell activation is >10,000 fold reduced prior to local proteolysis in the tumor microenvironment. *In vivo* studies in xenografts and non-human primates demonstrate >100x improved therapeutic window relative to conventional T cell engagers such as BiTEs.

10:05 Networking Coffee Break

INFECTIOUS DISEASE APPLICATIONS

10:30 Chairperson's Remarks

Ertan Eryilmaz, PhD, Senior Scientist, Takeda

10:35 Rational Design of a Trispecific Antibody Targeting the HIV-1 Env with Elevated Anti-Viral Activity

Zhi-Yong Yang, PhD, Director, Synthetic & Immune Biology, Sanofi

We engineered trispecific antibodies that allow a single molecule to interact with three independent HIV-1 envelope determinants. These trispecific antibodies exhibited higher potency and breadth than any single anti-HIV-1 antibody and showed protective efficacy in an animal model of HIV-1 infection. Trispecific antibodies thus constitute a platform to engage multiple therapeutic targets through a single protein and could be applicable for diverse diseases including infections, cancer and autoimmunity.

11:05 Beyond Blinatumomab: Antiviral Activity of BiTE® Antibody Constructs Targeting HIV

Johannes Brozy, PhD, Senior Associate Scientist, BiTE® Technology, Amgen Research (Munich) GmbH

HIV is a chronic infection well controlled with the current cART. However, a cure for HIV is still lacking. Here, we show *in vitro* and *ex vivo* data that a BiTE antibody construct targeting HIV gp120 resulted in substantially reduced HIV replication. In addition, these BiTE antibody constructs display efficient killing of gp120-expressing cells and inhibited replication in *ex vivo* HIV-infected PBMCs or macrophages.

11:35 Human and Bispecific Antibodies as Immunotherapies for Chikungunya Virus

Jonathan R. Lai, PhD, Professor, Department of Biochemistry, Albert Einstein College of Medicine

Chikungunya virus (CHIKV) is a widespread mosquito-borne alphavirus that causes a severe and persistent arthralgia. We describe the use of single B-cell sorting to identify protective monoclonal antibodies that target the two envelope glycoproteins, E1 and E2, from convalescent CHIKV patients. Viral escape studies revealed the sites of susceptibility on both E1 and E2. This information was then used to engineer novel bispecific antibodies that enable simultaneous targeting of multiple epitopes in a single agent. These antibodies have strong potential for use as immunotherapies to prevent or treat CHIKV infection.

12:05 pm Presentation to be Announced

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Networking Refreshment Break

ENGINEERED FCs IN BISPECIFICS: DRIVING DESIRED PK, ACUTE ACTIVITY AND LONG-TERM BIOLOGICAL CONSEQUENCES

1:25 Chairperson's Remarks

G. Jonah Rainey, PhD, Vice President, Antibody Therapeutics, Gritstone Oncology, Inc.

1:40 The Astonishing Diversity of Fc Domain Functions and the Development of Novel Fc Engineered IgG Variants

Stylianos Bournazos, PhD, Research Assistant Professor, Laboratory of Molecular Genetics and Immunology, Rockefeller University

2:10 Engineering Fc of BiSAbs to Restore and Extend Half-Life

Clifford William Sachs, PhD, Director, Research and Development, Toxicology, AstraZeneca

A systematic evaluation of pharmacokinetics (PK) of Bispecific IgG scaffolds and parental monoclonal antibodies (mAbs) in cynomolgus monkeys identified sites of ScFv attachment and immunogenicity of parental mAbs as key determinants of PK. Across scaffolds, introduction of half-life extension mutations in the Fc portion of the BiS increased half-life by 2 to 5-fold. Collectively, these data identified structural considerations and engineering approaches to facilitate development of Bispecific IgG scaffolds.

2:40 Modulating Functionality in Bispecifics – Towards Better Therapeutics

Martin Steegmaier, PhD, Head of Discovery, Large Molecule Research, Roche Pharma Research and Early Development (pRED), Roche Innovation Center Munich

Therapeutic performance of recombinant antibodies relies on two independent mechanisms: antigen recognition and Fc-mediated antibody effector functions. Interaction of Fc-fragment with different FcR triggers antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity and determines pharmacokinetic half-life. Engineered hIgG Fc domains with completely abolished FcγR and C1q interactions, and with unaffected FcRn interactions and Fc stability have been previously described by us. The impact of antibody Fc engineering, however, goes beyond the modulation of the affinity or functionally of the interaction with various FcRs or the neonatal Fc receptor (FcRn). Specifically in the context of bispecific antibody engineering, the Fc functionality needs to be matched with the often-unique mode of action of the bispecific therapeutic to provide a unique PK profile or to match the requirement for effector function according

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ENGINEERING BISPECIFIC ANTIBODIES continued

to biological needs and safety requirements. Antagonistic antibodies can also be turned into agonists by switching the format and functionality of the Fc moiety. Examples of tailoring Fc functionality will be given for bispecific molecules currently being developed for immunological, ophthalmological and neuroscience indications.

3:10 EAGLE, A Novel Bispecific-Like Platform and Immunomodulatory Strategy

James Broderick, MD, CEO and Founder, Palleon Pharmaceuticals Inc.

Glyco-immune checkpoints have emerged as a novel mechanism of immune regulation of both innate and adaptive immunity and cancer immune escape. We have developed a novel bispecific-like platform named EAGLE (Enzyme-Antibody Glyco-Ligand Editing) with robust anti-tumor efficacy (~50% complete regression) in syngeneic EMT6 tumor models as a monotherapy. Here we reported how different bispecific-like configurations impact biological activity, pharmacokinetics, and toxicity of EAGLEs preclinically.

3:40 End of Conference

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ONCOLOGY STREAM

- Antibodies for Cancer Therapy
- Advancing Bispecific Antibodies and Combination Therapy to the Clinic
- Clinical Progress of Antibody-Drug Conjugates

Advancing Antibody Therapeutics to the Clinic

Antibody therapies are advancing to clinical development for cancer and results to date are extremely encouraging. The oncology stream will focus on identifying emerging targets, investigating novel constructs including ADCs and bispecific antibodies, and highlighting approaches for combination therapies. The **Oncology stream** will explore the latest trends and comparing strategies and recent successes from discovery to preclinical and clinical development.

9TH ANNUAL

ANTIBODIES FOR CANCER THERAPY

Driving Breakthrough Therapies

April 8-9, 2019

Antibodies have great specificity and potency to be directed against cancer. The latest wave of novel antibody designs leverages our current knowledge of the tumor microenvironment and immune cell populations and our understanding of biology for selective targeting. Don't miss the Ninth Annual Antibodies for Cancer Therapy conference for a meeting of the great thought leaders in the field to share creative ideas and advance clinical progress.

SUNDAY, APRIL 7

Recommended Short Course(s)*

SC2: Translational Biotherapeutic Development Strategies Part 1: Discovery, Molecular Assessment and Early Stage Development

SC7: Translational Biotherapeutic Development Strategies Part 2: Analytical and Clinical Considerations

Separate registration required.* ***Click here* *or see page 5 for course details.*

MONDAY, APRIL 8

7:00 am Registration and Morning Coffee

OPENING KEYNOTE SESSION

8:30 Chairperson's Opening Remarks

Soldano Ferrone, MD, PhD, Division of Surgical Oncology, Surgery, Massachusetts General Hospital

8:40 Using Tumor Reactive mAb and IL2 to Sequentially Engage Innate and Adaptive Anti-Tumor Immunity

Paul M. Sondel, MD, PhD, Reed and Carolee Walker Professor of Pediatrics, Human Oncology, and Genetics, and Director of Research, UW Division of Pediatric Hematology, Oncology and BMT, UW Carbone Cancer Center and American Family Children's Hospital, University of Wisconsin

We are developing immunotherapy regimens to eliminate advanced-large immunologically "cold" tumors in immunocompetent mice. In some models, local radiation therapy combined with intratumoral tumor-reactive mAb+IL2 can eradicate large established tumors with T-cell memory, enabling the tumor to be an *in situ* vaccine. In mice with two tumors of the same type, immunosuppression from the distant tumor can be overcome by inhibition of Treg cells. Clinical translation is being pursued.

9:10 Role of HLA Antigen Presentation in Resistance to Immune Checkpoint Blockade

F. Stephen Hodi, MD, Professor, Medicine, Harvard Medical School; Professor, Medical Oncology, Dana-Farber Cancer Institute; Sharon Crowley Martin Chair, Melanoma, Dana-Farber Cancer Institute

Tumor mutational burden correlates with response to immune checkpoint blockade in multiple solid tumors, although in microsatellite-stable tumors this association is of uncertain clinical utility. Here we uniformly analyzed whole-exome sequencing (WES) of 249 tumors and matched normal tissue from patients with clinically annotated outcomes to immune checkpoint therapy including radiographic response across multiple cancer types to examine additional tumor genomic features that contribute to selective response. Our analyses identified genomic correlates of response beyond mutational burden, including somatic events in individual driver genes, certain global mutational signatures, and specific HLA-restricted neoantigens. However, these features were often interrelated, highlighting the complexity of identifying genetic driver events that generate an immunoresponsive tumor environment. This study lays a path forward in analyzing large clinical cohorts in an integrated and multifaceted manner to enhance the ability to discover clinically meaningful predictive features of response to immune checkpoint blockade.

9:40 The Next Era of Cancer Therapeutics: Defining Biologic Problems, Engineering Solutions

Daniel Chen, MD, PhD, CMO, IGM Biosciences

The opportunity for therapeutics that turn on or off a singular target has largely been explored. However, advancements in our understanding of cancer, immune biology, and protein/cellular engineering approaches begin to define what seemed like science fiction only a few years ago. The spatial temporal coordination of modulating different biologies and cell types within emerging cancer immunotherapy will be explored.

10:10 Networking Coffee Break

TARGETING B7/H3: COMPARISON OF DIFFERENT APPROACHES

10:45 Chairperson's Remarks

Soldano Ferrone, MD, PhD, Division of Surgical Oncology, Surgery, Massachusetts General Hospital

10:50 Genetic Alteration of the Bispecific Antibody Platform to Create Trispecific NK Cell Engagers (TriKes) Targeting B7-H3

Daniel A. Vallera, PhD, Lion Scholar and Professor, Director, Section on Molecular Cancer Therapeutics; Professor of Therapeutic Radiology, University of Minnesota Masonic Cancer Center

TriKEs are trispecific natural killer (NK) cell engagers and novel immunotherapeutic drugs. A first-generation TriKE consisting of two antibody scFV fragments each recognizing NK cells and AML cells was cross-linked with cytokine IL-15. Recently, TriKes have been vastly improved by conversion of the scFVs to camelid framework. We will discuss xenograft studies of first generation TriKE, testing of the improved camelid TriKE, and clinical batch status. We will also discuss TriKEs targeting B7-H3 for solid tumor therapy.

11:20 Past, Present and Future of Omburtamab for the Treatment of B7H3(+) Tumors

Mahiuddin Ahmed, PhD, CSO, Y-mAbs Therapeutics

Omburtamab is a murine IgG1 that is under clinical

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investigation for compartmental radioimmunotherapy of B7-H3(+) tumors. Omburtamab labeled with 131- or 124-Iodine can be delivered directly into 1) the brain ventricles for pediatric neuroblastoma patients with CNS/leptomeningeal metastases,

2) the pons for diffuse intrinsic pontine glioma, and 3) the peritoneum for desmoplastic small round cell tumors. New versions of omburtamab (177-Lutetium conjugate and humanized sequence) are currently under pre-clinical development.

11:50 MGC018: A Duocarmycin-Based Antibody Drug Conjugate Targeting B7-H3

Deryk Loo, PhD, Director, Targeted Therapeutics and Site Operations, MacroGenics, Inc.

MGC018 is an ADC comprised of the cleavable linker-duocarmycin payload, valine-citrulline-seco DUocarmycin hydroxyBenzamide Azaindole (DUBA), conjugated to a humanized anti-B7-H3 antibody through interchain disulfides. MGC018 demonstrated antitumor activity *in vivo* toward B7-H3-expressing tumor xenografts at clinically relevant doses. MGC018 was tolerated in cynomolgus monkeys at exposure levels exceeding those required for antitumor activity. Our findings support clinical development of MGC018 to evaluate its potential as a therapeutic for B7-H3-expressing solid cancers.

12:20 pm Streamlined Discovery and Production of Therapeutic Antibodies

Sponsored by ICOSAGEN

Meelis Kadaja, PhD, MBA, Director of Business Development, Icosagen Cell Factory

We take advantage of the universal HybriFree antibody discovery engine to efficiently discover therapeutic antibodies by direct cloning from B-cells of immunized rabbit, chicken, human, or dog. HybriFree method is further powered by our patented QMCF expression platform to produce high-quality recombinant protein antigens and antibodies cost-effectively for pre-clinical research (including afucosylated antibodies for enhanced ADCC). Technologies and case studies will be presented and discussed.

12:50 Luncheon Presentation I: Accelerating Antibody Candidate Discovery and Development with Innovative Humanized Mouse Models

Sponsored by BIOCYTOGEN

Qingcong Lin, PhD, CEO, Biocytogen Boston Corp

The talk will present you Biocytogen services for your antibody discovery with case study, from *in vivo* efficacy and toxicity, to *in vitro* PD/PD analysis of your antibody candidates, using Biocytogen IO target humanized mouse models, B-NDG based CART, and PBMC/CD34+ human immune reconstituted mouse models, CD3e humanized models.

1:20 Luncheon Presentation II: Robust and Reproducible Target-Biology Based Bioassays for Characterization and Potency Measurement of Biologics Targeting Checkpoint Modulators

Sponsored by eurofins | DiscoverX

Jane Lamerdin, PhD, Director, Research & Development, Eurofins Pharma Discovery Services

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, AstraZeneca

4:10 Vision for How Immunotherapy Will Shape Future of Cancer Care

Leena Gandhi, MD, PhD, Vice President, Immuno-Oncology Medical Development, Lilly Oncology

Immunotherapy is considered by many as a pillar of cancer care today, but in many ways we have only scratched the surface. Our knowledge and understanding of the complexities of immunotherapy and its mechanisms continue to evolve. The future of cancer care will be defined by our ability to systematically identify and implement opportunities for combination therapy to improve and standardize patient response.

4:55 The Lassa Virus Glycoprotein: Stopping a Moving Target

Kathryn Hastie, PhD, Staff Scientist, Immunology and Microbiology, The Scripps Research Institute

Lassa virus causes ~5000 deaths from viral hemorrhagic fever every year in West Africa. The trimeric surface glycoprotein, termed GPC, is critical for infection, is the target for neutralizing antibodies, and a major component of vaccines. Structural analysis of Lassa GPC bound to antibodies from human survivors reveals a major Achilles heel for the virus and provides the needed template for development of immunotherapeutics and improved vaccines.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:15 End of Day

TUESDAY, APRIL 9

8:00 am Registration and Morning Coffee

MESOTHELIN-TARGETED THERAPIES IN SOLID TUMORS

8:25 Chairperson's Remarks

Mitchell Ho, PhD, Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute, NIH

8:30 A Two-in-One Approach to Target Solid Tumors – CAR T-Cells and Checkpoint Blockade

Prasad S. Adusumilli, MD, FACS FCCP, Deputy Chief and Associate Attending, Thoracic Surgery; Director, Mesothelioma Program; Head, Solid Tumors Cell Therapy, Cellular Therapeutics Center (CTC), Memorial Sloan-Kettering Cancer Center; Associate Professor, Cardiothoracic Surgery, Weill Cornell Medical Center

The presentation will focus on cell-intrinsic and extrinsic methods in overcoming checkpoint blockade in cellular immunotherapy.

9:00 Immunotoxins Targeting Mesothelin for Cancer Therapy

Raffit Hassan, MD, Senior Investigator & Chief, Thoracic and GI Malignancies Branch, Center for Cancer Research, National Cancer Institute, NIH

Mesothelin is a tumor differentiation antigen with limited expression on normal mesothelial cells but is highly expressed in many cancers. LMB-100 is an anti-mesothelin immunotoxin (anti-mesothelin Fab linked to PE toxin) currently in clinical trials for treating patients with malignant mesothelioma and pancreatic cancer. Our efforts are focused on improving anti-tumor efficacy of LMB-100 by decreasing its immunogenicity as well as combination studies with chemotherapy and immune checkpoint inhibitors.

9:30 Pancreatic Cancer Therapy with Mesothelin-Redirected Chimeric Antigen Receptor T Cells and Overcoming Barriers to their Efficacy

Mark O'Hara, MD, GI Malignancy Oncologist, University of Pennsylvania

Pancreatic ductal adenocarcinoma (PDA) is characterized by its highly immunosuppressive tumor microenvironment (TME) that limits T cell infiltration and induces T cell hypofunction. Delivery of mesothelin-redirected chimeric antigen receptor T cell (meso-CAR T cell) therapy in pancreatic cancer patients has been feasibile and safe, and though some efficacy has been demonstrated, antitumor

activity remains modest. Our efforts are focused on improving efficacy of meso-CAR T cells, including tumor-directed infusion of meso-CAR T cells, genome-editing of CAR T cells, and combining meso-CAR T cells with an oncolytic adenovirus expressing TNF-α and IL-2.

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

ADDRESSING DIFFICULT TARGETS: BCMA, CLL1 & CD123

10:45 Chairperson's Remarks
Horacio G. Nastri, PhD, Senior Director, Antibody Biotherapeutics, Incyte Corporation

10:50 Preclinical Validation of B-Cell Maturation Antigen (BCMA) as a Target for T-Cell Immunotherapy of Multiple Myeloma
Dexiu Bu, MD, PhD, Investigator III, Exploratory Immuno-Oncology, Novartis Institute for Biomedical Research

Chimeric antigen receptor (CAR) targeting BCMA is an attractive approach for treating multiple myeloma. We screened a set of novel, fully human scFv binding domains to BCMA. Using a series of *in vitro* and pre-clinical *in vivo* studies, we identified a scFv with high specificity for BCMA and robust anti-myeloma activity. This BCMA-specific CAR is currently being evaluated in a Phase Ib clinical study in relapsed and refractory MM patients.

11:20 Tumor-Specific Carbohydrate Antigens as Preferable Targets for Novel Bispecific Immunotherapeutics Targeting Solid Tumors
Anika Jäkel, PhD, Director, Preclinical Pharmacology & Cancer Immunology, Glycotope GmbH

Carbohydrates on the surface of cancer cells represent preferable targets for bispecifics due to their unique tumor-specificity with lack of inaccessibility on normal tissues and broad indication coverage. We demonstrate that carbohydrates are valuable targets for different bispecific approaches by creating a carbohydrate-targeted IL-15-based immunocytokine and a bispecific T-cell engager. Both molecules are able to stimulate an array of effector cell responses *in vitro* and *in vivo* and are suitable agents for mono or combinatorial therapy of solid tumors.

11:50 Disrupting the CD47-SIRPα Anti-Phagocytic Axis by a Humanized Anti-CD47 Antibody is an Efficacious Treatment for Malignant Pediatric and Adult Brain Tumors
Sharareh Gholamin, MD, PhD Candidate, Division of Biology and Biological Engineering, California Institute of Technology

Morbidity and mortality associated with pediatric malignant primary brain tumors remain high in the absence of effective therapies. Macrophage-mediated phagocytosis of tumor cells via blockade of the anti-phagocytic CD47-SIRPα interaction using anti-CD47 antibodies has shown promise in preclinical xenografts of various human malignancies. We demonstrate the effect of a humanized anti-CD47 antibody, Hu5F9-G4, on five aggressive and etiologically distinct pediatric brain tumors: group 3 medulloblastoma (primary and metastatic), atypical teratoid rhabdoid tumor, primitive neuroectodermal tumor, pediatric glioblastoma, and diffuse intrinsic pontine glioma. Hu5F9-G4 demonstrated therapeutic efficacy *in vitro* and *in vivo* in patient-derived orthotopic xenograft models. Intraventricular administration of Hu5F9-G4 further enhanced its activity against disseminated medulloblastoma leptomeningeal disease. Notably, Hu5F9-G4 showed minimal activity against normal human neural cells *in vitro* and *in vivo*, a phenomenon reiterated in an immunocompetent allograft glioma model. Thus, Hu5F9-G4 is a potentially safe and effective therapeutic agent for managing multiple pediatric central nervous system malignancies.

12:20 pm Luncheon Presentation I: Harbour Biomed's Fully Human Transgenic HCAb Mouse Technology Presents a Specialized Platform to Develop a New Class of Biologics as Therapeutics Against Cancer And Immunological Diseases
Sponsored by HARBOUR BIOMED
Frank Grosveld, PhD, Founding CSO, Platform Technology, Harbour BioMed

HBM's transgenic Harbour Mice™ were used to produce Heavy Chain Only Antibodies "HCAbs" wherein the mouse VH loci were replaced with selected human VH genes, concurrent with the CH1 gene deletion. These refinements give us the flexibility of designing multitude of single molecule formats capable of targeting one or more antigens molecule driven by *in vivo* biology to develop the NextGen Tx. Here we present one such example of HBM4003, an anti-cancer immunotherapy with high affinity and robust function, currently in preclinical development, leading to potentially exceptional efficacy and safety profile.

12:50 Luncheon Presentation II: Alternative Strategies to Control Light Chain Diversity in Transgenic Chickens
Sponsored by OmniAb
Kathryn Ching, PhD, Senior Scientist, Ligand

OmniChicken® V gene diversity in B cells can be controlled through rational design of synthetic pseudogenes inserted into the Ig loci. One design, for the purpose of conventional HxL antibodies, results in extensive diversity focused in CDR regions, and the other design, for the purpose of common light chain antibody development, results in minimal diversity across the entire V region

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

EMERGING TARGETS

2:00 Chairperson's Remarks
Mitchell Ho, PhD, Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute, NIH

2:05 Anti-BCMA Recombinant Immunotoxins Are Highly Active Agents for Myeloma Therapy
Ira H. Pastan, MD, Co-Chief, Laboratory of Molecular Biology; NIH Distinguished Investigator; Head, Molecular Biology Section

BCMA is highly expressed in myeloma cells and is an excellent target for myeloma therapy. We produced mAbs that recognize BCMA, but not other family members, and used them to make RITs that kill myeloma cell lines and patient cells. To evaluate anti-tumor activity, we prepared H929 cells expressing luciferase. Untreated mice survived 40 days, whereas treated mice were tumor-free at 90 days.

2:35 Immune-Based Therapies in AML/MDS
Naval G. Daver, MD, Associate Professor, Leukemia Department, MD Anderson Cancer Center

3:05 Antibody Protein Sequencing with Mass Spectrometry
Sponsored by RAPID NOVOR
Mingjie Xie, CEO, Rapid Novor, Inc.

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

3:20 Next Generation of Antibody Drugs with Long Lasting Efficacy
Sponsored by ABMAX
Le Sun, PhD, CEO & President AbMax Biotechnology Co., Ltd.

In this presentation, we will show 1) the successful development of Me-better by removing the strong B-cell epitopes in the FRs of Humira; 2) the improvement of stability and great reduction of *in vivo* ADA by engineering the Fc of Tecentriq's with better biological activity.

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

EMERGING TARGETS (CONT.)

Chairperson's Remarks
Mitchell Ho, PhD, Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute, NIH

4:25 Development of Next Generation Immune Modulators
René Hoet, PhD, CSO, Imcheck Therapeutics

Imcheck Therapeutics, an emerging biotech, develops antibodies to novel targets in immuno-oncology and potentially autoimmune diseases. The presentation will cover the progress of development of two first-in-class therapeutic antibodies (an anti-BLTA and an anti-BTN3) that have a positive effect on proliferation of gamma delta T cells and inhibition of tumor growth that are developed towards the clinic in 2020. In addition, the company identified an additional set of novel targets that are in the antibody validation stage for treatment in immune-oncology and potentially autoimmunity.

4:55 Phase I CD123 CAR T Cell Trial in Adults with Relapsed/Refractory AML
Elizabeth Budde, MD, PhD, Assistant Professor, Department of Hematology & Hematopoietic Cell Transplantation, City of Hope

5:25 Strategies and Challenges for Targeting CD47 to Enhance Antitumor Immunity
David D. Roberts, PhD, Senior Investigator, Head, Biochemical Pathology Section, Laboratory of Pathology, CCR, NCI

The resistance of many cancers to current immune checkpoint inhibitors might be overcome by identifying additional checkpoint molecules that enable tumors to evade immune surveillance. CD47 is a ubiquitously expressed receptor for thrombospondin-1 and the counter-receptor for signal-regulatory protein-α. The latter interaction prevents innate immune clearance of tumor cells that express elevated levels of CD47. Preclinical and clinical development of antibodies and other methods for targeting CD47 will be discussed.

5:55 End of Antibodies for Cancer Therapy: Driving Breakthrough Therapies

5:30 Registration for Dinner Short Courses

Recommended Short Course*
SC10: CAR T-Cell Therapy for Solid Tumors
Separate registration required. **Click here or see page 5 for course details.*

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7TH ANNUAL

ADVANCING BISPECIFIC ANTIBODIES AND COMBINATION THERAPY TO THE CLINIC

Creating the Killer Combo

April 10-11, 2019

One of the leading areas of antibody research is bispecific antibodies. The Seventh Annual Advancing Bispecific Antibodies and Combination Therapy to the Clinic conference will review recent preclinical and clinical results on a variety of bispecific and multi-specific constructs. Thought leaders in the community will review progress and discuss the best strategies for improving targeting, safety and efficacy for applications in immuno-oncology, oncology, CNS and infectious disease.

TUESDAY, APRIL 9

Recommended Short Course*

SC11: Developability of Bispecific Antibodies: Formats and Applications

Separate registration required.* ***Click here* *or see page 5 for course details.*

WEDNESDAY, APRIL 10

7:15 am Registration and Morning Coffee

7:25 - 8:25 PANEL DISCUSSION: Women in Science – Inspired Professional and Personal Stories

Moderator: Women in Bio, Boston Chapter

Panelists:

Susan Richards, PhD, Presidential Scientific Fellow, Translational Medicine Early Development, Sanofi R&D

Joanna Brewer, PhD, Vice President, Platform Technologies, AdaptImmune

Additional Panelists to be Announced

WHAT IS WORKING IN THE CLINIC: NEW INNOVATIONS IN BISPECIFIC ANTIBODIES

8:30 Chairperson's Opening Remarks

Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, AstraZeneca

8:40 Bringing the Tumor-Directed CTLA-4 x OX40 Bispecific Antibody, ATOR-1015, into the Clinic

Charlotte Russell, MD, PhD, CMO, Alligator Bioscience AB

ATOR-1015 is a bispecific antibody targeting CTLA-4 and OX40, designed as a next-generation CTLA-4 antibody with improved benefit-risk profile. The dual targeting directs the effect to the tumor area, allowing ATOR-1015 to induce enhanced anti-tumor effects with expected lower systemic toxicity compared to CTLA-4 monotherapy. The mode-of-action is a combination of effector T-cell activation and regulatory T cell depletion. ATOR-1015 is planned to enter clinical phase in 2018.

9:10 Design Meets Biology – Engineering a PD-1/CTLA-4 Bispecific Antibody to Improve Both Safety and Efficacy

Yariv Mazor, PhD, Senior Scientist, Antibody Discovery & Protein Engineering, AstraZeneca

MEDI5752 is a monovalent bispecific IgG1 antibody (DuetMab), targeting the two clinically validated receptors, PD-1 and CTLA-4. The bispecific antibody introduces novel MOAs that may provide an improved therapeutic index when compared to the two monotherapies and mAb combinations. MEDI5752 is currently being clinically evaluated for safety and efficacy.

9:40 A Versatile Modular Bispecific Antibody Platform, BiXAb, for the Development of Innovative Therapeutics

Eugene Zhukovsky, PhD, CSO, Biomunex Pharmaceuticals

BiXAb platform has a tetra-Fab IgG1 antibody structure and enables plug-and-play bispecific antibody formatting from any pair of monospecific mAbs. BiXAb antibodies possess excellent manufacturability in CHO cells and superior drug-like properties (stability, lack of aggregation, predictable PK). We will illustrate the properties of this bispecific antibody platform by presenting two case studies, in which BiXAbs target either solid tumors or hematological malignancies.

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

10:15 Women in Science Speed Networking in the Exhibit Hall

10:55 KEYNOTE PRESENTATION: The Need for More Effective Combination Therapies

Ronald Herbst, PhD, Vice President and Head, Oncology Research, AstraZeneca

Combination approaches are key to improving clinical response. From preclinical immune-oncology mouse models to patients enrolled in clinical trials, novel high throughput technologies enable us to understand the mechanisms underlying the complex interactions between the immune system and cancer, identify predictive biomarkers for the patients who will most likely benefit from current immunotherapies, avoid immune-related adverse events, and guide the future combination cancer immunotherapy.

11:25 Bispecific Antibodies for Cancer-Directed Blockade of the PD-1/PD-L1 Immune Checkpoint

Prof. Dr. Wijnand Helfrich, Professor of Translational Surgical Oncology, Department of Surgery, University Medical Center Groningen

On-target/off-tumor activity of current PD-L1-blocking antibodies potentially reduces tumor accretion and promotes autoimmune-related toxicity. Therefore, we constructed human bispecific antibody (bsAb) PD-L1xEGFR which simultaneously binds to PD-L1 and EGFR resulting in enhanced avidity towards PD-L1+/EGFR+ cancer cells. Importantly, PD-L1xEGFR blocks PD-1/PD-L1 interaction in an EGFR-directed manner, blocks oncogenic EGFR-signaling, and promotes ADCC of EGFR+ tumor cells. BsAb PD-L1xEGFR may be useful to enhance selectivity, efficacy and safety of PD-1/PD-L1 checkpoint inhibition.

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11:55 Development of Novel Fully Human Bispecific Antibodies for Oncology
Eric Smith, PhD, Director, Bispecifics, Regeneron Pharmaceuticals

This presentation will describe Regeneron's bispecific platform and present pre-clinical data on several new bispecifics being developed for solid and liquid tumor indications. In addition, status updates on Regeneron's clinical stage bispecific antibodies (REGN1979, REGN4018, and REGN5458) will be presented.

12:25 pm WuXiBody™, an Innovative and Versatile Bispecific Antibody Format Opens a New Era for Therapeutic Antibody Development
Sponsored by WuXi Biologics
Jing Li, Senior Vice President, Discovery, WuXi Biologics

Bispecific antibodies are a growing area of biotherapeutics but with many development challenges. Many of the new platforms have limitations in yield, purity, stability, solubility, half-life, and immunogenicity. Thus, a one-size-fit-all solution is still desired. Aiming to solve those issues, WuXi Biologics has generated WuXiBody™, a flexible, proprietary bispecific antibody format that can reduce the development time by 6 -18 months and can decrease cost of goods by 90%.

12:55 Luncheon Presentation I: CANscript™: A Phenotypic-Based, Tumor Modeling Platform for Drug Discovery and Development
Sponsored by MITRA BIOTECH
Mark Paris, PhD, Associate Director, Translational Application, Mitra Biotech

Delineation of an intra-tumor microenvironment in a dynamic spatio-temporal setting is required owing to its clinical relevance in many cancer indications. Majority of solid cancers represent a highly complex tumor microenvironment wherein a dysregulated phenotypic context impacts treatment outcomes at a personalized level. We have developed and validated an ex-vivo platform technology (CANscript™) using patient material (tumor, autologous ligands and immune cells) to predict tumor efficacy in the clinic across several drug classes.

1:25 Luncheon Presentation II: Design and Development of Innovative Bispecific Antibodies
Sponsored by GenScript
Timothy Xia, PhD, Vice President, Biologic Discovery & Development, GenScript, Inc.
Liusong Yin, PhD, Director, Antibody Drug Discovery, GenScript, Inc.

GenScript is the world leader in biotechnology and has 15 years of experience in discovery and development services. Provides One-Stop solution, offering target discovery to IND application that aligns conformity to the regulations for applications to FDA/CFDA/EMA. Our scientists have in-depth understanding of industrial standards of biological drug discovery and development. Mature development platform that saves expenses and reduces operation risks. We offer flexible collaboration modes to fulfill a wide spectrum of customer needs. The World's top pharmaceuticals and academic Institutes use GenScript`s discovery services to accelerate basic and discovery research for target validation, lead generation, lead characterization and optimization. Our proprietary technology platforms in a variety of domains make us very competitive in the biologics space. In this talk, key discovery services will be discussed, that includes hybridoma and phage display therapeutic mAb generation against multi-transmembrane proteins, capable of making any bispecific format like single-domain monoclonal antibody (SMAB) production, humanization, developability assessment and affinity maturation. At GenScript Biologics, we pride ourselves on our flexible options for you in drug discovery and development.

1:55 Session Break

WHAT IS WORKING IN THE CLINIC: NEW INNOVATIONS IN BISPECIFIC ANTIBODIES (CONT.)

2:10 Chairperson's Remarks
Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, AstraZeneca

2:15 Preclinical and Clinical Development of Best-in-Class Anti-HER2 Bispecifics and Bispecific ADCs
Tony Polverino, PhD, Executive Vice President of Early Development and CSO, Zymeworks, Inc.

ZW25 is a bispecific antibody directed against two distinct epitopes (biparatopic) on HER2 that has been successfully engineered using the Azymetric™ IgG1 antibody scaffold. In clinical studies, ZW25 is well tolerated and has demonstrated promising single-agent anti-tumor activity in heavily pretreated HER2-expressing breast, gastric, and other cancers. Preclinical development of ZW49, a biparatopic antibody-drug conjugate based on the unique design of ZW25 and armed with our proprietary ZymeLink™ cytotoxic payload, will also be discussed.

2:45 Development of a Novel T-Cell Engager Platform Based on DARPin® Molecules
Sebastian Grimm, PhD, Senior Scientist, Lead Generation, Molecular Partners AG

T-cell-engaging therapies have shown high therapeutic efficacy in hematological malignancies and promising early clinical data in solid tumors. Favorable biophysical properties and high format flexibility enable T-cell engager formats that may address limitations of current engagers in the clinic, such as tumor selectivity or antigen coverage. We have developed a flexible T-cell engager platform based on Designed Ankyrin Repeat Proteins binding to human CD3. The characterization of different multispecific formats with tailored serum half-life will be presented.

3:15 Highlighted Poster Presentation: Efficient *in vivo* Tumor Clearance and Minimal Cytokine Release with a Novel T-Cell Engaging Bispecific Antibody Platform
Speaker to be Announced, TeneoBio Inc.

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

THURSDAY, APRIL 11

8:00 am Registration and Morning Coffee

BISPECIFIC ANTIBODIES OFF THE BEATEN PATH: FUSIONS, NON-ANTIBODY SCAFFOLDS, ETC.

8:30 Chairperson's Remarks
Frank Comer, PhD, Senior Scientist, AstraZeneca

8:35 KEYNOTE PRESENTATION: Overview of Bispecific Antibodies
Roland Kontermann, PhD, Professor, Biomedical Engineering, Institute of Cell Biology and Immunology, University of Stuttgart

Bispecific antibodies have experienced a dramatic interest and growth for therapeutic applications, with more than 70 molecules in clinical development, e.g. in oncology, immuno-oncology, but also for non-oncology applications. An overview will be given on the making of bispecific antibodies and the various therapeutic concepts and applications, e.g. for dual targeting strategies, retargeting of immune effector cells, and substitution therapy by mimicking the function of natural proteins.

ADVANCING BISPECIFIC ANTIBODIES AND ACOMBINATION THERAPY TO THE CLINIC continued

9:05 M7824, a Novel Therapeutic Inhibiting PDL1 and Sequestering TGF-Beta

James L. Gulley, MD, PhD, FACP, Chief, Genitourinary Malignancies Branch, Head, Immunotherapy Group, GMB Director, Medical Oncology Service, Center for Cancer Research, NCI, NIH

M7824 is a first-in-class bifunctional fusion protein composed of a TGFβ trap fused to an anti-PD-L1 antibody. A first-in-human dose escalation study demonstrated safety, saturation of peripheral PD-L1 and sequestration of all released plasma TGFβ1, -β2, and -β3 throughout the dosing period at doses >1 mg/kg. M7824 1200 mg IV has been tested in multiple cohorts including in HPV-associated cancers (ORR 35%) and NSCLC (ORR 28% with ORR 41% in patients with ≥1% of tumor cells PDL1+).

9:35 Highlighted Poster Presentation: CB307, a Novel T-Cell Costimulatory Humabody Therapeutic for PSMA-Positive Tumours

Brian McGuinness, PhD, Senior Director, Business Development, Crescendo Biologics Ltd.

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

11:05 A Highly Efficacious Antibody Mixture against MET-Dependent Tumors

Thomas Tuxen Poulsen, PhD, Principal Scientist, Symphogen A/S

Activation of the receptor tyrosine kinase MET is associated with poor clinical outcome in certain cancers. To target MET more effectively, we developed the antagonistic antibody mixture Sym015 consisting of two humanized antibodies directed against non-overlapping epitopes of MET. Sym015 is well tolerated and strongly inhibits growth of MET-dependent preclinical tumor models. An ongoing clinical trial of Sym015 demonstrates promising signals of clinical activity in a subset of MET-dependent patients.

11:35 Engineering Bispecific Antibodies for Specific Targeting of Tumor Cells

Rajkumar Ganesan, PhD, Director, Antibody Engineering, Janssen Biotherapeutics

Bispecific antibodies can redirect immune cells such as natural killer cells or cytotoxic T cells to lyse tumor cells by releasing the pro-apoptotic agents. Excessive levels of released cytokines can lead to a series of immune-related adverse events. To circumvent toxicity issues, we adopted several design strategies such as modulation of binding affinity, geometry and valency to engineer bispecifics antibodies to discriminate healthy versus tumor cells.

12:05 pm Oncolytic Vaccines to Augment BiTE Efficacy against Solid Tumors

Christine E. Engeland, MD, PhD, Head of Laboratory, Virotherapy, National Center for Tumor Diseases

Challenges in treating solid tumors with bispecific antibodies include increasing response rates and decreasing toxicity. We have developed tumor-selective oncolytic vectors for delivery of immunomodulators to avoid systemic exposure and mitigate toxicity. Furthermore, vector-mediated oncolysis serves as an *in situ* tumor vaccine, inducing synergistic anti-tumor immune responses. This talk highlights the versatility of our vector system and avenues for clinical translation.

12:35 End of Advancing Bispecific Antibodies and Combination Therapy to the Clinic

Recommended Short Course*

SC12: Design Strategies and Development of ADCs

Separate registration required.* ***Click here* *or see page 5 for course details.*

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9TH ANNUAL

CLINICAL PROGRESS OF ANTIBODY-DRUG CONJUGATES

Advancing Novel ADC Platforms and Combinations to the Clinic

April 11-12, 2019

Antibody-drug conjugates (ADCs) continue to emerge as a strong and promising strategy for target cancer therapy. Companies are leveraging on lessons learned from first- and second-generation trials to inform on next-generation ADC designs. PEGS Boston's Ninth Annual Clinical Progress of Antibody-Drug Conjugates invites investigators to share their latest results from preclinical and clinical trials, lessons learned to inform drug design & dosing, and strategies to improve safety, efficacy and patient outcomes.

THURSDAY, APRIL 11

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

STRATEGIES TO INFORM DRUG DESIGN & DOSING, AND IMPROVE PATIENT OUTCOMES

1:40 Chairperson's Opening Remarks
Thomas Held, MBA, Vice President, ADC Task Force, Daiichi Sankyo

1:50 Single-Cell PK/PD of Antibody-Drug Conjugates and Immuno-Oncology Agents to Design More Effective Therapies
Greg Thurber, PhD, Assistant Professor, Chemical Engineering and Biomedical Engineering, University of Michigan

Antibody-drug conjugates and checkpoint inhibitors are powerful agents in the treatment of cancer. However, the delivery and distribution of these agents in the tumor microenvironment is complex. We are using single-cell measurements within the tumor to inform better decisions on drug design and dosing.

2:20 Chemo-Enzymatic Glycan Conjugation of Toxic Payloads: Clinical-Stage GlycoConnect™ ADCs Demonstrate Superior Therapeutic Index
Sander van Berkel, PhD, Director, R&D Operations, Synaffix B.V.

The native glycan of monoclonal antibodies is evolving as a privileged site to generate ADCs with a significantly improved therapeutic index, as corroborated by a multitude of studies in rodents and NHPs. While the first clinical studies with a GlycoConnect™ ADC are now underway (NCT03700294), we will discuss how mAb glycan structure correlates with therapeutic index, as well as aspects of CMC supply chain and regulatory considerations towards IND filing.

2:50 Developing Antibody-Drug Conjugates as Targeted Conditioning Agents for Bone Marrow Transplant
Charlotte McDonagh, PhD, Vice President, Head, Biotherapeutics, Magenta Therapeutics

Many diseases can be cured by a bone marrow transplant. Prior to transplant, patients are conditioned by removing their own bone marrow stem cells using toxic, non-selective chemotherapy and radiation. Many patients suffer serious side effects, and others refuse a transplant. This presentation will highlight preclinical development of antibody-drug conjugates that may be safer, targeted agents for patient preparation with the aim of extending the use of curative bone marrow transplant and improving patient outcomes.

3:20 Development and Clinical Updates on Sacituzumab Govitecan
Robert Iannone, MD, MSCE, Head, R&D, CMO, Immunomedics

3:50 Networking Refreshment Break

IMPROVING THE SAFTEY AND EFFICACY OF ADCs

4:20 Preclinical Study of Liver Injury Induced by T-DM1: Molecular Mechanisms of T-DM1-Induced Hepatotoxicity
Wen Jin Wu, MD, PhD, Senior Investigator, OBP, CDER, FDA

Hepatotoxicity is one of the serious adverse events associated with T-DM1. We show that T-DM1 is internalized upon binding to cell surface HER2, resulting in DM1-associated cytotoxicity, including disorganized microtubules, nuclear fragmentation/multiple nuclei, and cell growth inhibition. Based on our data, we propose that T-DM1-induced upregulation of TNFa enhances the liver injury that may be initially caused by DM1-mediated intracellular damage. In addition, a novel target that mediates T-DM1-induced hepatotoxicity will also be discussed.

4:50 POSTER HIGHLIGHT: Exploring the Ever-Evolving Bioanalytical Strategy for ADCs from Discovery to the Clinic
Edit Tarcsa, PhD, Director, Drug Metabolism & Pharmacokinetics, AbbVie

ADCs are complex therapeutic modalities with the possibility of forming multiple analytes *in vivo*. A wide variety of assays and multiple analytical platforms had been utilized for their characterization. How do we chose what is appropriate to support decision making at the various stages of a project and how does one go by balancing speed, quality and available reagents. Since the key questions to answer during drug discovery (ADC optimization), versus late stage development are usually very different, therefore the analytes and assays appropriate to answer those questions could also be different. A few case studies and a bioanalytical decision tree will illustrate the issues.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC12: Design Strategies and Development of ADCs
Separate registration required. **Click here or see page 5 for course details.*

FRIDAY, APRIL 12

8:00 am Morning Coffee

8:30 Chairperson's Remarks
Greg Thurber, PhD, Assistant Professor, Chemical Engineering and Biomedical Engineering, University of Michigan

Cambridge HEALTHTECH Institute
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8:35 KEYNOTE PRESENTATION:
The House of Vedotins
Robert J. Lechleider, MD, Senior Vice President, Clinical Research, Seattle Genetics
Antibody-drug conjugates have proven effective in treating an array of cancers. Among the most active drug-linker combinations is monomethyl-auristatin E (MMAE) coupled to a targeting antibody via a valine-citrulline linker. MMAE conjugates have shown activity in heme and solid tumors using a number of targeting antibodies. The role and future of MMAE drug conjugates in the treatment of cancer will be discussed.

PRECLINICAL UPDATES AND PROOF-OF-CONCEPT

9:05 A Novel Antibody-Drug Conjugate Targeting ADAM9-Expressing Solid Tumors Demonstrates Potent Preclinical Activity
Stuart Hicks, PhD, Director, Pipeline R&D, ImmunoGen
ADAM9 is a cell surface protein that belongs to the ADAM (a disintegrin and metalloproteinase) family of proteases and is overexpressed in multiple solid tumor indications. IMGC936 is a novel ADAM9-targeting ADC comprised of a high-affinity humanized antibody site-specifically conjugated to DM21, a next-generation linker-payload that combines a maytansinoid microtubule-disrupting payload with a stable peptide linker. IMGC936 shows compelling efficacy in ADAM9-positive xenograft models and was well-tolerated following repeat dosing in cynomolgus monkeys making IMGC936 a promising therapeutic candidate to target a wide range of ADAM9-expressing tumors.

9:35 CD163 as a Target for Directing ADCs to Macrophages in Cancer and Inflammation – Preclinical Proof of Concept
Jonas Heilskov Graversen, PhD, Associate Professor, Molecular Medicine, University of Southern Denmark
We have validated the macrophage specific internalization receptor CD163 as an ADC target in cancer and inflammation. PoC studies in mice, rats and pigs show a strongly reduced (50-fold) effective dose for anti-inflammatory effect when targeting dexamethasone to macrophages (endotoxemia and NASH models). In cancer we observe substantially increased infiltration of effector T-cells and T-cell dependent tumor regression in a murine anti-PD-1 resistant melanoma model when eradicating tumor associated macrophages by toxin targeting.

10:05 Networking Coffee Break

CLINICAL DEVELOPMENT AND LESSONS LEARNED

10:35 Amanitin-based Antibody-Drug-Conjugates as New Therapeutic Modalities for Cancer Therapy
George Badescu, PhD, VP Scientific Affairs, Heidelberg Pharma
Antigen-Targeted Amanitin-Conjugates (ATACs) represent a new class of ADCs using the payload Amanitin. This payload introduces a novel mode of action into oncology therapy, the inhibition of RNA polymerase II. The technology platform includes Amanitin supply, site-specific conjugation, demonstrated safety profile and biomarker. HDP-101 is the first ATAC directed against BCMA entering Phase I trials by the end of 2019.

11:05 Targeting Breast Cancer with Antibody-Drug Conjugates
Aditya Bardia, MD, MPH, Assistant Professor, Medicine, Harvard Medical School
Chemotherapy is the mainstay of management of multiple solid tumors, but can be associated with considerable adverse effects. Conceptually, antibody-drug conjugates can be utilized for targeted delivery of toxic payloads to cancer cells. However, antigen selection of antigen and tumor heterogeneity are significant challenges in clinical development of novel antibody-drug conjugates. In this presentation, we will review potential therapeutic strategies and the clinical development of antibody-drug conjugates in breast cancer.

11:35 Discovery of Next-Generation ADCs: Preclinical and Clinical Development of AVID100, an EGFR-Targeting ADC
Maureen O'Connor-McCourt, PhD, CSO, Forbius
AVID100 is an EGFR-targeting ADC which was designed by screening a library of anti-EGFR ADCs against both tumor and normal cells expressing EGFR. This approach enabled us to identify AVID100, which exhibited a very promising therapeutic index in preclinical studies. AVID100 recently completed a successful phase 1 clinical program and a phase 2 study has been initiated. Importantly, only modest skin toxicity was observed, as predicted by our preclinical data.

12:05 pm [Fam-] Trastuzumab Deruxtecan (DS 8201) Clinical Development Update
Thomas Held, MBA, Vice President, ADC Task Force, Daiichi Sankyo

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Networking Refreshment Break

1:35 Chairperson's Remarks
Maureen O'Connor-McCourt, PhD, CSO, Forbius

NEXT-GENERATION ADCS

1:40 Next-Generation ADCs: Considerations and Examples
Marc Damelin, PhD, Executive Director, Head of Biology, Mersana Therapeutics, Inc.
I will discuss considerations for the discovery and development of next-generation ADCs as informed by learnings from the field's collective experience. Topics will include target selection, molecular design, and preclinical pharmacology.

2:10 Targeting CD74 with a Novel Antibody-Drug Conjugate, STRO-001 for Treatment of B-Cell Malignancies
Arturo Molina, MD, MS, FACP, CMO, Sutro Biopharma

2:40 Antibody-Drug Conjugates Targeting Tumor Stromal Cells
Brad St. Croix, PhD, Head, Tumor Angiogenesis Unit, Mouse Cancer Genetics Program, National Cancer Institute
Targeting the tumor stromal cells in addition to tumor cells with ADCs is a promising anti-cancer strategy. CD276 and TEM8 are variably expressed in a variety of cancers and to different extents on tumor stromal cells and tumor cells. Both CD276-ADC-PBD and TEM8-ADC-MMAE eradicated large established tumors and metastases and improved long-term overall survival in several different mouse models of cancer. The mechanistic basis for the efficacy of these agents will be discussed, along with implications for other vascular-targeted ADCs

3:10 Tisotumab Vedotin – A Novel Tissue Factor-Targeting Antibody-Drug Conjugate for the Treatment of Advanced Solid Tumors
Jeffrey Harris, PhD, Associate Director, Translational Research, Genmab
Tisotumab vedotin (TV) is an antibody-drug conjugate (ADC) that binds and interferes with tissue factor signaling, has potent anti-tumor activity *in vitro* and *in vivo*, and minimal effect on pro-coagulant activity. TV is efficiently internalized to the lysosome of the cell, making it an optimal ADC. TV is currently being tested in multiple clinical trials evaluating the safety, tolerability, and anti-tumor activity in patients with previously treated and advanced metastatic solid tumors.

3:40 End of Conference

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IMMUNOTHERAPY STREAM

- **Improving Immunotherapy Efficacy and Safety**
- **CAR Ts, TCRs and TILs**
- **Agonist Immunotherapy Targets**

Developing Next-Generation Targeted Cancer Immunotherapies

The **Immunotherapy stream** focuses on the latest science, modalities and targeting strategies driving the development of immunotherapies for solid and liquid tumors. Part One examines strategies for demonstrating T cell activity, combinations, preventing toxicology, dosing, and targeting the tumor microenvironment. Part Two focuses on developing and engineering adoptive cell therapies for solid and liquid tumors, especially CAR Ts, TCRs, NKs, and TILs, as well as new targets of interest. Finally, Part Three examines new clinical and preclinical data in agonist immunotherapy targets, as well as the biology and mechanisms of these emerging therapies of interest. Together, these three units will provide a focused look at how industry is applying new science and technology in developing the next generation of targeted cancer immunotherapies.

4TH ANNUAL

IMPROVING IMMUNOTHERAPY EFFICACY AND SAFETY

Developing Targeted, Safe Immunotherapies

April 8-9, 2019

Immunotherapies represent a step-change in cancer treatment, yet questions still remain around their efficacy, targeting and toxicity. Cambridge Healthtech Institute's Improving Immunotherapy Efficacy and Safety conference details the latest developments in immunotherapy, including established and emerging targets and modalities, new engineering strategies, combinations, biomarkers, effective preclinical models and strategies to mitigate toxicity and recent clinical developments. Examples will come from the world of checkpoint inhibitors, adoptive T cell therapy and combinations. We will also investigate manipulating the tumor microenvironment and emerging IO targets.

SUNNDAY, APRIL 7

Recommended Short Course(s)*

SC2: Translational Biotherapeutic Development Strategies Part 1: Discovery, Molecular Assessment and Early Stage Development

SC7: Translational Biotherapeutic Development Strategies Part 2: Analytical and Clinical Considerations

Separate registration required. **Click here or see page 5 for course details.*

MONDAY, APRIL 8

7:00 am Registration and Morning Coffee

EMPOWERING THE IMMUNE SYSTEM

8:30 Chairperson's Opening Remarks
Michael Curran, PhD, Assistant Professor, Department of Immunology, MD Anderson Cancer Centre

8:40 Evolutionary Dynamics of the Immune Response to Cancer: Implications for Immunotherapy
Brad Nelson, PhD, Co-Director, Immunotherapy Program, BC Cancer Agency

Human cancers evolve over time and space and under various selective pressures, resulting in a high degree of intratumoral heterogeneity (clonal diversity) within individual patients. Using ovarian cancer as an example, I will review our current understanding of the mechanisms used by the human immune system to contend with intratumoral heterogeneity and discuss immune-based strategies that might address this challenge in a clinically impactful way.

9:10 Development of Pegilodecakin, a PEGylated IL-10
Martin Oft, MD, Senior Vice President, Preclinical and Clinical R&D, ARmo Biosciences, a Wholly Owned Subsidiary of Eli Lilly

9:40 A Multiantigen-Targeting Cytotoxic CD4+ T Cell Approach for Treating B Cell Malignancies
Baochun Zhang, MD, PhD, Assistant Professor of Medicine, Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School

Many B-cell tumors lose MHC-I expression, allowing their escape from recognition by CD8+ cytotoxic T-lymphocytes (CTLs). CD19-targeted chimeric antigen receptor (CAR)-T cell therapy bypasses the need of MHC-mediated recognition but produces durable remissions in less than half of treated patients. Here, we present a novel approach for generating CD4+ CTLs for targeting B-cell malignancies through a wide range of endogenous tumor antigens.

10:10 Networking Coffee Break

ADVANCES IN CHECKPOINT INHIBITORS AND IO COMBINATIONS

10:45 Chairperson's Remarks
Brad Nelson, PhD, Co-Director, Immunotherapy Program, BC Cancer Agency

10:50 KEYNOTE PRESENTATION: PD-1 Antibodies Are Transforming Cancer Treatment Both as Mono and Combination Therapy
Roy Baynes, MD, PhD, Senior Vice President, Global Clinical Development & CMO, Merck Research Labs

Pembrolizumab was initially studied in a known immune responsive cancer – melanoma. A high response rate prompted exploration of addressable malignancies. A big data enabled, biologically informed phase 2 screening program was conducted across some 30 major malignancies. Monotherapy activity is being progressively defined across lines of therapy by tumor type and also in histology agnostic biomarker informed populations. Precision medicine tools have been used to explore potential resistance biology thereby informing combination therapy choices and development. A number of effective combinations have already been identified.

11:20 Best-in-Class PD-1 Pathway Blockade with Efficacy against Cold Tumors
Michael Curran, PhD, Assistant Professor, Department of Immunology, MD Anderson Cancer Centre

To address the therapeutic limitations of both PD-1 and PD-L1 blockade, we have developed novel, fully human antibodies which block binding of both PD-ligands to PD-1, as well as of PD-L1 to B7-1. The *in vitro* efficacy of these therapeutics equals or exceeds that of pembrolizumab; however, when armed with effector function *in vivo*, these antibodies can regress both PD-1 sensitive "hot" and PD-1 resistant "cold" syngeneic tumors.

IMPROVING IMMUNOTHERAPY EFFICACY AND SAFETY continued

11:50 Third-Generation Immune Checkpoint Inhibitors and Development of AB154, a Clinical-Stage TIGIT Antibody

Joanne B.L. Tan, PhD, Research Fellow, Arcus Biosciences, Inc.

TIGIT and DNAM-1 (CD226), expressed on lymphocytes, compete for intra-tumoral ligand CD155. TIGIT induces immune suppression, whereas DNAM-1 mediates immune activation. AB154 is a sub-nanomolar TIGIT mAb that activates T and NK cell function, as shown in multiple *in vitro* assays. A flow cytometry-based assay that quantifies TIGIT occupancy by AB154 in blood is being utilized to guide dose selection in the ongoing dose escalation clinical study in cancer patients.

12:20 pm Industrializing IO Therapeutic Discovery Platforms: Multispecifics, Engineered TCRs and CARs

Andrew Lynch, PhD, Scientific Consultant, Biologics, Genedata

Novel classes of bio-molecules are currently evaluated for their use in cancer immunotherapy. Bi- and multi-specific antibodies, Ab-cytokine fusion proteins, non-Ig scaffolds, chimeric antigen receptors (CARs), engineered TCRs and TCR-based bispecific constructs promise significant advantages. However, these highly engineered molecules pose new challenges in design, engineering, cloning, expression, purification, and analytics. We present an infrastructure that addresses these challenges and enables the industrialization of these various novel therapeutic platforms.

12:50 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, AstraZeneca

4:10 Vision for How Immunotherapy Will Shape Future of Cancer Care *Leena Gandhi, MD, PhD, Vice President, Immuno-Oncology Medical Development, Lilly Oncology*

Immunotherapy is considered by many as a pillar of cancer care today, but in many ways we have only scratched the surface. Our knowledge and understanding of the complexities of immunotherapy and its mechanisms continue to evolve. The future of cancer care will be defined by our ability to systematically identify and implement opportunities for combination therapy to improve and standardize patient response.

4:55 The Lassa Virus Glycoprotein: Stopping a Moving Target

Kathryn Hastie, PhD, Staff Scientist, Immunology and Microbiology, The Scripps Research Institute

Lassa virus causes ~5000 deaths from viral hemorrhagic fever every year in West Africa. The trimeric surface glycoprotein, termed GPC, is critical for infection, is the target for neutralizing antibodies, and a major component of vaccines. Structural analysis of Lassa GPC bound to antibodies from human survivors reveals a major Achilles heel for the virus and provides the needed template for development of immunotherapeutics and improved vaccines.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:15 End of Day

TUESDAY, APRIL 9

8:00 am Registration and Morning Coffee

NK CELLS, SWITCHABLE CAR Ts

8:25 Chairperson's Remarks

Saad J. Kenderian, PhD, Assistant Professor, Medicine and Oncology, Mayo Clinic College of Medicine

8:30 NK Cells: Growing up to Become Safe and Efficacious Cellular Therapeutics?

Hans Klingemann, MD, PhD, Vice President, Research and Development, NantKwest, Inc.

The continuously proliferating NK-92® cell line has been developed into an off-the-shelf, broadly cytotoxic NK cell therapeutic platform. aNK and haNK® have completed Phase I studies, while HER2 taNK® for glioma is currently accruing patients. Further genetic modifications of the haNK platform include additional CARs as well as homing receptors and molecules that can positively affect the tumor microenvironment.

9:00 Enhancing the Efficacy of T Cell-Based Immunotherapy Through Fucosylation

Gheath Al-Atrash, DO, PhD., Associate Professor of Medicine, Section of Transplant Immunology

Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center

The homing of adoptively transferred cytotoxic T lymphocytes (CTL) to tumor tissue is a major limiting factor to the efficacy of adoptive cellular therapy (ACT) for cancer. This challenge may be overcome through fucosylation, a process whereby fucosyltransferases (FTs) add fucose groups to cell surface glycoproteins. *Ex vivo* fucosylation enhances CTL homing to malignant bone marrow and solid tumor tissue and appears promising in improving the efficacy of ACT.

9:30 Dual-Switch CAR-NK Cells; Inducible and Targeted Anti-Tumor Efficacy with Safety

J. Henri Bayle, PhD, Director of Molecular Biology, Research and Development, Bellicum Pharmaceuticals

Natural Killer (NK) lymphocytes possess innate anti-tumor activity useful as an allogeneic CAR cell therapy with reduced GvHD risk relative to alpha beta T cells. To overcome poor NK cell expansion *in vivo*, we utilized a molecular switch that relies on rimiducid-directed dimerization of inducible MyD88/CD40 (iMC) to control cell proliferation and cytotoxicity *in vitro* and *in vivo*. Moreover, rapamycin-inducible Caspase-9 (iRC9) provided an orthogonally regulated safety switch.

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

IMPROVING IMMUNOTHERAPY EFFICACY AND SAFETY continued

MITIGATING CAR T TOXICITIES

10:45 Chairperson's Remarks
Kathleen McGinness, PhD, Senior Director, Platform Technologies, Unum Therapeutics

10:50 Novel Strategies to Mitigate Toxicities after Chimeric Antigen Receptor T Cell Therapy
Saad J. Kenderian, PhD, Assistant Professor, Medicine and Oncology, Mayo Clinic College of Medicine

Despite the impressive responses after chimeric antigen receptor T (CAR T) cells in hematological malignancies, their application is limited by the development of cytokine release syndrome (CRS). The lack of relevant preclinical models for CRS after CAR T cell therapy is a significant limitation for the development interventions to treat or prevent CRS. In this presentation, we will review relevant preclinical models of human CRS after CART cell therapy and efforts to develop and optimize preventative strategies.

11:20 The Myeloid System in Cytokine Release Syndrome
Theodoros Giavridis, PhD, Center for Cell Engineering, Memorial Sloan Kettering Cancer Center

We recently described the first mouse model for Cytokine Release Syndrome (CRS) elicited by anti-CD19 CAR T cell therapy, which recapitulates multiple aspects of clinical CRS. In this model we established that CRS is the result of a tripartite interaction between CAR T cells, macrophages and the tumor microenvironment. Novel insights into the interplay between the actors of CRS will inform future considerations for CAR T cell therapy.

11:50 Next Generation Approaches for Increased Safety and Efficacy of CAR T Cells
Daniel J. Powell Jr., PhD, Associate Professor of Pathology and Laboratory Medicine, University of Pennsylvania

T cells engineered to express chimeric antigen receptors can mediate durable cancer regression in some patients with certain forms of cancer but safety and durability issues exist and the lack of efficacy in other cancer types is yet to be resolved. I will discuss the use of modified CAR T cells approaches that allow for quantitative and qualitative control of T cell activity to address safety concerns, as well as the provision of accessory molecules that either boost efficacy or limit CAR-associated toxicities.

12:20 pm Luncheon Presentation I: Target Specificity Screening of CAR T Cells Using Human Cell Microarray Technology
Sponsored by RETROGENIX™ SPOTTING YOUR TARGET.
Alex Kelly, US Business Development Manager, Retrogenix Limited

Human cell microarray screening enables the discovery of both primary cell surface receptors as well as potential off-targets for a variety of biologics including: peptides, antibodies, proteins, CAR T and other cell therapies. Case studies will demonstrate the utility of the technology in identifying novel, druggable targets as well as in specificity screening for antibodies, scFvs and CAR T cells to aid safety assessment and provide key data to support IND submissions.

12:50 Luncheon Presentation II: *(Sponsorship Opportunity Available)*

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

CAR T FOR SOLID TUMORS, NON-VIRAL GENOME TARGETING

2:00 Chairperson's Remarks
Daniel J. Powell Jr., PhD, Associate Professor of Pathology and Laboratory Medicine, University of Pennsylvania

2:05 Development of CAR-T Cell Therapeutics for Solid Tumor
Zonghai Li, PhD, CSO, CARSgen

Great success has been made in CAR-T cell therapeutics for the treatment of blood cancer such as acute lymphoblastic leukemia while rare improvement has been made for solid tumor treatment. In this talk, we will summarize the current global progress of CAR-T cell therapeutics for solid tumor and share the thoughts and strategies of CARsgen to develop CAR-T cell therapeutics for the treatment of solid tumor.

2:35 Bolt-On Transgenes Improve Engineered T Cell Function in Solid Tumor
Kathleen McGinness, PhD, Senior Director, Platform Technologies, Unum Therapeutics

The immunosuppressive features within solid tumors present unique challenges to the success of engineered T cell therapies. We have employed a "bolt-on" strategy to overcome key immunosuppressive mechanisms by co-expressing over 100 different novel transgenes in T cells bearing chimeric receptors. We have identified several bolt-on transgenes that modulate T cell metabolism or costimulation and impart enhanced function to chimeric receptor T cells in preclinical models of solid tumor malignancies.

3:05 UTG-4D; Developing the Most Rapid Patient Tumor Model *in vitro*
Sponsored by Premas Biotech
Prabuddha Kundu, PhD, Co-Founder & Managing Director, Premas Biotech Pvt Ltd

UTG-4D, universal tissueoid generator, is the most rapid *in vitro* representation of the *in vivo* patient tumors. We have developed scaffolds for growing patient samples or tumor cell lines, or cell lines and converting them into rapidly growing 3D tissueoid models, which can be studied, dosed and therapeutic determination can be performed. Hundred's of tissueoids have been grown with >90% success rates. The model device scaffolds enable rapid growth, within 24-48 hrs reproducibly.

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

4:25 Reprogramming Human T Cell Function and Specificity with Non-Viral Genome Targeting
Theodore Roth, MD, PhD Student, Department of Microbiology and Immunology, University of California

Cellular therapies using human T cells are opening new chapters in cancer and autoimmune disease therapy. These living drugs can be genetically engineered to acquire new therapeutic functions. However, current methods to insert new genetic material into human T cells require viral vectors, slowing research and hindering therapeutic development. We have developed a non-viral methodology for the targeted integration of large DNA sequences in human T cells that has enabled rapid therapeutic reprogramming of T cell function and specificity.

4:55 Cell Therapies for HIV
Conrad Russel Cruz, PhD, Director, Translational Research Laboratories, Center for Emerging Technologies in Immune Cell Therapy, Children's National Hospital

5:25 End of Improving Immunotherapy Safety and Efficacy Program

5:30 Registration for Dinner Short Courses

Recommended Short Course*
SC10: CAR T-Cell Therapy for Solid Tumors
Separate registration required.* ***Click here* *or see page 5 for course details.*

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6TH ANNUAL

CAR Ts, TCRs AND TILs

Latest Innovations and Developments in Adoptive Cell Therapy

April 10-11, 2019

Novel gene editing technologies and a greater understanding of cancer biology could unleash the full power of CAR T in both blood and solid tumors. But which therapies will succeed? Cambridge Healthtech Institute's Sixth Annual CAR Ts, TCRs and TILs conference focuses on the latest research, protein engineering and clinical strategies driving the development of adoptive cell therapies across a wide range of indications. Clinical progress with Chimeric Antigen Receptors (CAR), T Cell Receptors (TCR), Tumor Infiltrating Lymphocytes (TIL), and NK cells will be addressed as well as new strategies for commercialization will be reviewed.

TUESDAY, APRIL 9

Recommended Short Course*

SC10: CAR T-Cell Therapy for Solid Tumors

**Separate registration required, please see page 5 for course details.*

WEDNESDAY, APRIL 10

7:15 am Registration and Morning Coffee

7:25 - 8:25 PANEL DISCUSSION: Women in Science – Inspired Professional and Personal Stories

Moderator: Women in Bio, Boston Chapter

Panelists:

Susan Richards, PhD, Presidential Scientific Fellow, Translational Medicine Early Development, Sanofi R&D

Joanna Brewer, PhD, Vice President, Platform Technologies, AdaptImmune

Additional Panelists to be Announced

CAR T MECHANISMS, RESISTANCE AND NOVEL TARGETS

8:30 Chairperson's Opening Remarks

Bob Valamehr, PhD, Chief Development Officer, Fate Therapeutics

8:40 KEYNOTE PRESENTATION: Mechanisms of CAR Treatment Success and Failure Based on Clinical Experience in Lymphoma and Leukemia

Adrian Bot, PhD, Vice President, Translational Sciences, Kite Pharma, a Gilead Company

As CAR T cell therapy is now standard of care in certain B cell malignancies, novel data point to mechanistic aspects related to treatment success or failure, essential to advance next-generation therapies. In this presentation, we cover factors influencing clinical outcomes: product T cell fitness, integrating the number and polyfunctionality of specialized T cell subsets, tumor burden and immune microenvironment, and biological aspects intrinsic to the cancerous process.

9:10 Resistance to CART19 Therapy: Mechanisms and Novel Therapeutic Strategies

Marco Ruella, MD, Clinical Instructor, Associate Director, Dr. June's Laboratory, Center for Cellular Immunotherapies, Perelman School of Medicine, University of Pennsylvania

Chimeric Antigen Receptor T cell (CAR T) have generated impressive clinical results for CD19+ B cell leukemia and lymphoma. However, a significant subset of patients still does not respond or eventually relapses. I will discuss the mechanisms of resistance to CART19 and present future developments.

9:40 Novel Targets and Technologies for CAR T Cells in Multiple Myeloma and Acute Myeloid Leukemia

Michael Hudecek, PhD, Program Leader, Max Eder Research Group, CAR T-Cell Engineering, Department of Medicine II, University of Hudecek

Translational research in CAR T cell immunotherapy involves a rapidly increasing portfolio of novel target antigens, CAR designs, and technologies to enhance safety, efficacy and physician control. This talk will review the latest developments from our program including novel targets in hematology and oncology, and novel technologies for high-throughput screening, ultra-fast manufacturing, and real-time control over CAR T cells after administration *in vivo*.

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

10:15 Women in Science Speed Networking in the Exhibit Hall

10:55 Targeting TCR-β Constant Domain for Immunotherapy of T Cell Malignancies

Shimobi Onuoha, PhD, Head, Protein Engineering, Autolus

Unlike B cell depletion, pan-T cell aplasia is prohibitively toxic. We report a new targeting strategy based on the mutually exclusive expression of T cell receptor β-chain constant domains 1 and 2 (TRBC1 and TRBC2). Unlike nonselective approaches targeting the entire T cell population, TRBC-targeted immunotherapy could eradicate a T cell malignancy while preserving sufficient normal T cells to maintain cellular immunity.

OFF-THE-SHELF CAR Ts

11:25 FEATURED PRESENTATION: Allogeneic CAR T: The Next Revolution in Cell Therapy

Barbra Sasu, PhD, CSO, Allogene

While allogeneic CAR T research is at an earlier stage, encouraging Phase 1 clinical data demonstrates the promise of this therapy for more patients. The talk will highlight the clinical data available to date and the overall research strategy to develop a pipeline of allogeneic CAR T therapies across a range of hematological and solid tumor indications.

11:55 Gene Edited Off-the-Shelf Immunotherapies

Andre Choulika., PhD., Chairman & CEO, Cellectis

Cambridge HEALTHTECH Institute
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12:25 pm The Functional Capacity of Immune Cells Predicts Clinical Outcome Across IO Therapies
Sponsored by isoplexis
Will Singleterry, PhD, Director, Business Development, IsoPlexis

Using single cell proteomics to measure the functional capacity or 'fitness' of immune cells has correlated with and been predictive of clinical outcome in CAR-T, TIL, Cancer Vaccine and Checkpoint Inhibitor therapy. This talk will review several of these data sets and discuss applications of IsoPlexis' single cell technology.

12:40 Mammalian Display Antibody Discovery for Integral Membrane Proteins
Sponsored by Oxford Genetics
Nathan Robertson, PhD, Antibodies, Oxford Genetics

Through co-expression of integral membrane targets and scFv molecule libraries in a mammalian cells we show that cells that exhibit self-labelling can be purified and lead molecules identified via NGS analysis. Lead candidates are then suitable for either CAR-T or antibody reformatting.

12:55 Luncheon Presentation I: Genetically Modified Cell Lines for Immuno-Oncology Cell-Based Assay Development
Sponsored by MilliporeSigma
Stacey Ward, PhD, Senior Research & Development Scientist, Cell Design Studio, MilliporeSigma

MilliporeSigma's Cell Design Studio™ cell line engineering service offering is the premier research partner for generating customized cell-based assays and immunotherapy research models. Our team has generated new monoallelic HLA panel expression cell lines and tumor-associated antigen panels, which express individual tumor antigens at varying levels in biologically-relevant cell lines. In this presentation, we will discuss the breadth of these lines and discuss their utility in immuno-oncology and therapeutic testing.

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

1:55 Session Break

OFF-THE-SHELF CAR Ts (CONT.)

2:10 Chairperson's Remarks
Adrian Bot, PhD, Vice President, Translational Sciences, Kite Pharma, a Gilead Company

2:15 Rejection-Resistant T Cell Platform for an Off-the-Shelf Therapy
Maksim Mamonkin, PhD, Instructor, Center for Cell and Gene Therapy, Baylor College of Medicine

'Off-the-shelf' (OTS) T cell products pre-manufactured from healthy donors are readily available and less costly than autologous products, offering similar therapeutic potency. However, immune rejection by host T- and NK-cells may limit the persistence of OTS cells and compromise their anti-tumor activity. We engineered alloimmune defense receptors (ADRs) that enable OTS T cells to recognize and eliminate alloreactive lymphocytes resulting in complete protection from immune rejection while retaining full functionality.

2:45 Translation of Pluripotent Cell-Derived T and NK Cells as a Cornerstone Approach for Off-the-Shelf Cancer Immunotherapy
Bob Valamehr, PhD, Chief Development Officer, Fate Therapeutics

Pluripotent cell technology represents a powerful approach to make cell-based immunotherapies available to a wide range of patients through the generation of a consistent and renewable "off-the-shelf" source of cellular therapeutics. I will discuss our progress towards developing unique and effective strategies to create a renewable source of genetically engineered "off-the-shelf" T and NK cells with augmented function. Updates on IND filings and FIH progress will also be given.

3:15 Epitope Identification and Clinical Immune Monitoring in Gene Therapy and Immune Oncology Programs
Sponsored by ProImmune
Emilee Knowlton, PhD, Immunology, Sales Specialist, Sales, ProImmune, Inc.

Epitope discovery is a crucial element in the development of vaccine candidates and drug therapeutics. In the Immune-oncology space, identifying neoepitopes and tumor-associated antigens provide new targets for cancer diagnostics and enable the tracking of patient responses to treatment. ProImmune provides industry-leading tools for antigen characterization, epitope mapping and immune monitoring. In this presentation, case studies will be shared that detail how ProImmune's integrated platform has identified novel epitopes in the immune-oncology field.

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

Cambridge HEALTHTECH Institute
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THURSDAY, APRIL 11

8:00 am Registration and Morning Coffee

CAR NK CELLS, TCRs AND TILs

8:30 Chairperson's Remarks
Adrian Bot, PhD, Vice President, Translational Sciences, Kite Pharma, a Gilead Company

8:35 Combining Innate and Adaptive Immunity: NK Receptors for CAR T Cell Therapy
Simon Bornschein, PhD, Scientist, Celyad

The success of CAR T therapy against B-cell malignancies generated high expectations for all cancers, but the target remains the challenge. NKG2D binds to 8 different ligands present on a broad range of tumors yet largely absent on healthy tissue indicating a potential breadth of applicability of the approach. Our approache to exploring the therapeutic power of NKG2D CAR T cells in the autologous (CYAD-01) and allogeneic (CYAD-101) setting will be discussed.

9:05 Gene Editing of Stem Cells for Universal SPEAR T-Cell Therapy
Joanna Brewer, PhD, Vice President, Platform Sciences, AdaptImmune

Adoptive T cell therapy using autologous material for CAR and TCR therapies show considerable promise. However, an off-the-shelf product will speed up the time to treat patients and provide a consistent and unlimited source of therapeutic cells. Stem cells are also amenable to genetic modification, allowing them to remain hidden from the immune system for long-term persistence of differentiated T cells expressing enhanced affinity TCRs.

9:35 Sponsored Presentation *(Opportunity Available)*

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

11:05 Expanding the Tractable Tumor Target Universe with T Cells Carrying Engineered TCRs
Iulia Diaconu, PhD, Associate Director, Immunotherapy, Bluebird Bio

11:35 Tumor Infiltrating Lymphocytes Therapy for Solid Tumors
Chantale Bernatchez, PhD, Assistant Professor, Department of Melanoma Medical Oncology - Research, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

In TIL therapy T cells are grown from solid tumor samples and expanded to large numbers *ex vivo* to be infused back to the patient. The therapy has been very successful in metastatic melanoma with a 42% clinical response rate at our institution and others with most of the responses being durable. Despite great results we are at this point investigating why the other half of the patients would not respond. Through molecular and immunological assays we are trying to define biomarkers that could predict response to therapy. Another focus of our research is to test the efficacy of TIL therapy in other solid tumor types.

12:05 pm Advancements in Tumor Infiltrating Lymphocytes in Treatment of Solid Tumors
Kelly DiTrapani, VP, Medical Affairs, Iovance Biotherapeutics

Iovance is developing TIL, a one-time cell therapy treatment that leverages and enhances the body's natural defenses against certain solid tumors. TIL is being investigated in several multi-center Phase 2 clinical trials and preliminary results have demonstrated safety and efficacy in melanoma, head and neck and cervical cancer patients. While available immunotherapies for solid tumors, such as anti-PD-1 antibodies have shown promise, additional agents are needed for patients who may progress on such therapies or are intolerant.

12:35 End of CAR Ts, TCRs and TILs

Recommended Short Course*

SC14: Subvisible Protein Particles in Immunogenicity: Measurement, Characterization and Impact
Separate registration required. **Click here or see page 5 for course details.*

5TH ANNUAL

AGONIST IMMUNOTHERAPY TARGETS

Stepping on the Gas with Costimulatory Agents

April 11-12, 2019

The immunotherapies industry is currently dominated by antagonist antibodies such as PD-1 and CTLA-4. However, it is clear that antagonists alone are not enough to elicit response in the majority of patients, hence a rising interest in agonists targets. CHI's Agonist Immunotherapy Targets conference will examine these modalities and their treating disease. Agonists showing the most promise, including OX40, CD27, GITR, and 4-1BB, will be covered in clinical case studies by examining the data as well as the biology and mechanisms. Emerging agonists, including TNFR receptors, ICOS, STING, and VISTA will also be discussed. Focus will be given throughout to potential combination immunotherapies to ensure durable antitumor response. Overall, this event will emphasize strategies for target discovery to ensure continued growth and success for immunotherapies.

THURSDAY, APRIL 11

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

LATEST DEVELOPMENTS IN AGONIST IMMUNOTHERAPY - CYTOKINES AND OX40 TARGETS

1:40 Chairperson's Opening Remarks
Karin Enell Smith, PhD., Senior Scientist, Immuno-oncology, Alligator Bioscience

1:50 KEYNOTE PRESENTATION:
Harnessing Potent Cytokine Agonist Pathways by Polymer Engineering to Develop Novel Immune Therapeutic Agents
Loui Madakamutil, PhD, Vice President, Head of Discovery, Nektar Therapeutics
We have engineered cytokines using polymer technology to enable viable medicines. NKTR-214 is in Phase 3 clinical trials and a key example of how polymer conjugation can bias the well-known IL-2 receptor pathway to favor CD8 T cell tumor infiltration over Tregs. On the other hand, NKTR-358 selectively grows T regs *in vivo*. Finally, NKTR-255, an IL-15 receptor agonist stimulates NK cells. Each agent is conjugated in unique ways to elicit desirable and controlled pharmacological and immunological outcomes.

2:20 Agonists in Combination Immunotherapy
William L. Redmond, PhD, Associate Member, Laboratory of Cancer Immunotherapy, Director, Immune Monitoring Laboratory, Providence Portland Medical Center
Our previous studies helped elucidate the mechanisms by which OX40 agonist immunotherapy plus checkpoint blockade synergized with a novel cancer vaccine to boost the function of killer CD8 T cells and cause tumor regression. We are investigating how combination immunotherapy restores the function of killer CD8 T cells that have been paralyzed, or rendered anergic, by tumors. Additional studies seek to understand the mechanisms by which immunotherapy enhances the efficacy of conventional treatments, such as radiation therapy, with the goal of providing a path for rapid translation to the clinic.

2:50 OX40: Is Timing Everything?
Brendan Curti, MD, Robert W. Franz Chair for Clinical Research, Earle A. Chiles Research Institute, Providence Cancer Institute
We now have FDA-approved checkpoint immunotherapy for many stage III and IV cancers, but administration of immunotherapy before surgery has not been as extensively investigated. A clinical trial of the neoadjuvant administration of an agonist antibody to OX40, a T cell co-stimulatory agent, will be discussed, along with changes in tumor infiltrating CD39+CD103+ T cells that we hypothesize are relevant to achieving effective anti-tumor immunity.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Networking Refreshment Break

4:20 Agonist Bispecific Antibodies Delivering the Next Immuno-Oncology Breakthrough
Mihriban Tuna, PhD, Vice President, Drug Discovery, F-star Biotechnology, Ltd.
Targeting T cell costimulatory pathways can strongly activate the immune system due to the broad expression of receptors such as OX40 and CD137 across multiple immune cell types. However, Fcg receptor (FcgR)-mediated crosslinking is often required for the activity of monoclonal antibodies, and we hypothesise that this likely limits clinical activity due to the inherently low affinity of Fc:FcgR interactions, as well as the potential for FcgR-mediated depletion of T cells through ADCC. Here we will present novel bispecific antibody programmes that do not rely on FcgR binding, but instead crosslink using their two target binding sites.

4:50 Development of SIRPa-Fc-CD40L for Cancer Immunotherapy
Taylor Schreiber, PhD, CSO, Research & Development, Shattuck Labs, Inc.
The CD47/SIRPa axis functions to enhance antigen cross-presentation within the context of anti-tumor immunity, which holds promise for the treatment of immune-neglected tumors. The subset of dendritic cells which are the most potent antigen cross-presenters express CD40, and stimulation of CD40 enhances activation of CD8+ lymphocytes by these cells. SIRPa-Fc-CD40L has demonstrated superiority to CD47/SIRPa blocking antibodies, CD40 agonist antibodies, and antibody combinations in both rodent and non-human primate studies, which position this compound to provide unique benefits to human cancer patients.

5:20 End of Day

5:20 Registration for Dinner Short Courses
Separate registration required. **Click here or see page 5 for course details.*

FRIDAY, APRIL 12

8:00 am Morning Coffee

TNF AND 4-1BB AGONIST TARGETS

8:30 Chairperson's Remarks
Christopher Thanos, PhD, CEO, Actym Therapeutics

AGONIST IMMUNOTHERAPY TARGETS continued

8:35 The Appeal of The TNFR2 Target for Immunotherapy: Tregs and Tumor Oncogenes
Denise L. Faustman, MD, PhD, Director of Immunobiology, Massachusetts General Hospital, Associate Professor of Medicine, Harvard Medical School

Immune checkpoint inhibitors have revolutionized cancer therapy but can exhibit variable efficacy. TNFR2 is a signaling molecule found on a subset of potent Treg cells that activates the proliferation of these cells. TNFR2 is also abundantly expressed on the surface of many human tumors as an oncogene. We propose blocking TNFR2 might target abundant TNFR2+ tumor-infiltrating Tregs and directly kill TNFR2-expressing tumors. TNFR2 inhibitors might also potentially constitute safer and more targeted immunotherapy.

9:05 Development of TNF Superfamily Agonists
Andreas Raue, PhD, Associate Director, Research, Merrimack Pharmaceuticals

Members of the TNF superfamily of costimulatory receptors have emerged as promising immuno-oncology targets, and agonistic antibodies are currently being evaluated clinically. Here, we describe our STIMULI platform, which consists of novel multispecific and multivalent TNF receptor agonists, engineered to provide more precise activation of immune cell subsets.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Networking Coffee Break

10:35 IGM Antibodies with Very Potent Agonism to DR-5 Induced Apoptosis and as Anti-Tumor Agents
Bruce Keyt, PhD, CSO, IGM Biosciences

IGM Biosciences has anti-DR5 antibodies prepared as IgG and IgM. Anti-DR5 as IgM exhibits very potent and robust tumor cell killing *in vitro* and *in vivo*. IgM has broad anti-cancer bioactivity against various epithelial and hematologic tumors, both as established tumor cell lines as well as PDX cells *in vitro*. *In vivo* studies show very strong positive results in single agent treatment or in combinations with chemotherapy. Primate models show very low to no evidence of toxicity. We are scaling these antibodies for IND enabling studies and FIH human trials.

11:05 ATOR-1017, A 4-1BB Antibody Developed for Tumor Directed Immunotherapy of Cancer
Peter Ellmark, PhD, Vice President, Discovery, Alligator Bioscience

ATOR-1017 is a 4-1BB agonistic IgG4 antibody designed for optimal efficacy and safety. The agonistic activity of ATOR-1017 depends on engagement with certain FcγRs, and it will thereby induce a tumor directed immune activation in patients with tumors co-expressing these FcγRs and 4-1BB. The preclinical data package supports a favorable safety/efficacy profile. Clinical studies with ATOR-1017 are planned for 2019.

11:35 Structure of the 4-1BB/4-1BBL Complex and Distinct Binding and Functional Properties of Utomilumab and Urelumab
Javier Chaparro-Riggers, PhD, Senior Director, Protein Engineering, Pfizer

4-1BB is an inducible costimulatory receptor expressed on activated T cells. Two agonist antibodies, utomilumab (PF-05082566) and urelumab (BMS-663513), demonstrate distinct activities in the clinic. To understand these differences, we solved structures of the human 4-1BB/4-1BBL complex, the 4-1BBL trimer alone, and 4-1BB bound to utomilumab or urelumab. Additionally, cell-based assays demonstrate utomilumab is a milder agonist than urelumab. Collectively, our data provide a deeper understanding of the 4-1BB signaling complex, providing a template for future development of next generation 4-1BB targeted biologics.

12:05 pm CB307, A Novel T-Cell Agonist Humabody Therapeutic for PSMA-Positive Tumours
James Legg, PhD, Vice President, Research and Development, Crescendo Biologics

Crescendo Biologics has initiated clinical development of CB307 a novel bispecific Humabody VH targeting CD137 (4-1BB) and prostate specific membrane antigen (PSMA). The talk will describe the identification, mechanism of action and preclinical characterisation of the CB307 drug candidate. The benefits of using the modular Humabody VH platform, rather than an IgG format to develop this molecule will be discussed, including optimal (monovalent) engagement of both targets with small VH domains and the avoidance of Fc receptor interactions. The unique design of CB307 enables highly potent and tumour selective T-cell co-stimulation.

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Networking Refreshment Break

4-1BB, TLR AND STING AGONIST TARGETS

1:35 Chairperson's Remarks
Christopher Thanos, PhD, CEO, Actym Therapeutics

1:40 CTX-471, a Novel Agonistic Antibody Targeting CD137
Ugur Eskiocak, PhD, Associate Director, Translational Immunology & Immunopharmacology, Compass Therapeutics

CTX-471 is a fully human IgG4 agonist of CD137 (4-1BB) that binds to a unique epitope and displays a differentiated pharmacology and toxicology profile. *In vitro*, CTX-471 increased IFN-γ production by human T cells in an FcγR-dependent manner, displaying an intermediate level of activity between two clinical-stage anti-CD137 antibodies. *In vivo*, CTX-471 exhibited curative monotherapy activity in CT26, A20, and EMT-6 models.

2:10 ImmunoSTATs: A Novel Biologics Therapeutic Platform for Antigen-Specific Immunotherapy
Anish Suri, PhD., Cue Biopharma

ImmunoSTATs are proprietary biologics that incorporate, in a single molecular framework, key signals needed to selectively modulate antigen-specific T cells: namely, the pMHC-complex and relevant co-stimulatory/co-inhibitory signals, dependent upon the disease indication. The lead clinical candidate CUE-101 is comprised of HLA-A*0201, genetically bound to a HPV16 epitope (E7 protein, peptide 11-20), along with affinity-attenuated human interleukin-2 to selectively activate and expand HPV16 E711-20-specific CD8+ T cells for HPV-driven malignancies.

2:40 A Novel Systemically Delivered STING Pathway Agonist Therapy Demonstrates Robust Anti-Tumor Efficacy in Multiple Murine Cancer Models
Christopher Thanos, PhD, CEO, Actym Therapeutics

Delivery of immunotherapy to directly activate tumor-resident immune cells is required to elicit durable anti-tumor immunity. To this end, we have generated an immunotherapy platform that allows for tumor-specific delivery of engineered RNAi towards any tumor/immune target of interest (alone or in combination). For our initial RNAi target selection, a therapy targeting TREX1 was designed. TREX1 is a 3' exonuclease immune checkpoint that degrades cytosolic DNA, thereby preventing it from binding cGAS and activating the STING pathway.

3:10 Beyond PD1: Targeting STING and Other Novel Pathways
Anthony Desbien, PhD., Senior Scientist, Translation Immunology, Aduro Biotech

3:40 End of Conference

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EXPRESSION STREAM

- **Difficult-to-Express Proteins**
- **Optimizing Protein Expression**
- **Protein Expression System Engineering**

Meeting Growing Demands for Viable Protein

The burgeoning field of protein science, and the resultant biological products, places ever growing demands on protein expression. Increasingly, researchers need to produce quality protein faster and in larger quantities to meet industry's rising demands. Protein scientists must delve into genomic structure and function in order to understand and engineer expression systems, elucidate protein function and behavior, and overcome protein's intrinsic challenges, such as aggregation and misfolding. Membrane and other especially troublesome proteins pose even greater difficulties, yet hold considerable promise and rewards. The week-long **Expression Stream** focuses on productivity, from genes and clones, through production systems, and includes an examination of Difficult-to-Express Proteins along with breakthrough strategies and technologies in the pursuit of viable proteins.

14TH ANNUAL

DIFFICULT-TO-EXPRESS PROTEINS

Overcoming Expression Challenges

April 8-9, 2019

Proteins are each unique and bring unique challenges when attempting to tame them into submission. CHI's Fourteenth Annual Difficult-to-Express Proteins conference examines the challenges researchers encounter when striving for high-yield production of "difficult-to-express" proteins (DTEPs), and the strategies and technologies that have proven successful in overcoming those challenges. Some of the difficulties encountered include solubility, proper folding, inability to crystallize, aggregation and formation of inclusion bodies. Researchers employ a range of problem-specific solutions to achieve expression, including genetic modifications, manipulating how a target protein is produced, and employing protein tags. In addition, the identification of DNA coding sequences along with the use of high-throughput approaches has brought about significant improvements. The "Difficult-to-Express Proteins" conference provides the latest developments in improving yield for DTEPs through Case Studies and breakthrough data.

SUNDAY, APRIL 7

Recommended Short Course(s)*

SC3: Selection, Screening and Engineering for Affinity Reagents

SC6: Introduction to Host Cell Proteins (HCPs)

Separate registration required.* ***Click here* *or see page 5 for course details.*

MONDAY, APRIL 8

7:00 am Registration and Morning Coffee

INNOVATING PROCESSES FOR DTEPs

8:30 Chairperson's Opening Remarks

Nicola Burgess-Brown, PhD, Principal Investigator, Biotechnology, Nuffield Department of Medicine, Structural Genomics Consortium, University of Oxford

8:40 KEYNOTE PRESENTATION: A High-Throughput Platform to Express All Human Cell Surface Proteins

James Love, PhD, COO, Protein Production, Institute for Protein Innovation

Generating open-source monoclonal antibodies against every extracellular and secreted protein in humans, has required the development of expression platforms capable of generating high quality antigens and antibodies in HT format. Classes of proteins show somewhat uniform characteristics in 'expressibility' and even recalcitrant proteins, such as integral membrane proteins can be processed by rescue pathways if necessary. This talk will outline methods that have proven fruitful and present future areas for investigation.

9:10 Use of a Protein Engineering Strategy to Overcome Limitations in the Production of "Difficult to Express" Recombinant Proteins

Alan Dickson, PhD, Professor, Biotechnology; Director, Centre of Excellence in Biopharmaceuticals (COEBP), University of Manchester

Domain engineering opens the potential to manufacture novel recombinant products with innovative functions. Intellectual shuffling of protein domains/parts can be frustrated by the quality control processes in current cell factories. This presentation will focus on our recent work that has localised the sites of limitation of production of model 'difficult to express' proteins and development of molecular interventions that enhance production of a desired recombinant protein.

9:40 Teaching an Old Dog New Tricks: Making CHO Cell Line Development Ready for the Difficult-to-Express Protein Challenge

Simon Fischer, PhD, Head, BPAD Cell Line Development, Bioprocess & Analytical Development, Boehringer Ingelheim Pharma GmbH & Co. KG

The number of DTE therapeutic proteins appearing in drug development pipelines of pharmaceutical companies has increased dramatically. To address challenges in DTE protein expression, novel cell line development strategies need to be implemented. Being an old workhorse within the industry, CHO cells still represent the predominant production host for large-scale manufacturing. In this talk, we will present new technologies in cell line and molecule engineering to enhance CLD for DTE proteins in the future.

10:10 Networking Coffee Break

BACULOVIRUS & INSECT CELLS

10:45 Chairperson's Remarks

Gargi Roy, MSc, Scientist, Antibody Discovery and Protein Engineering, AstraZeneca

10:50 Production of Human Integral Membrane Proteins Using Baculovirus and BacMam

Nicola Burgess-Brown, PhD, Principal Investigator, Biotechnology, Nuffield Department of Medicine, Structural Genomics Consortium, University of Oxford

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

11:20 13 Years of Baculovirus Protein Expression in a Core Facility: Evolution of an Ultra-Short Protocol

Sabine Suppmann, PhD, Head, Recombinant Protein Production, Biochemistry Core, Max Planck Institute of Biochemistry

In the last three decades, the Baculovirus expression vector system (BEV) has evolved to one of the most widely used eukaryotic systems for heterologous protein expression. Despite the significant improvements introduced during the past years, the BEV system still has major drawbacks, primarily the time required to generate recombinant virus and

DIFFICULT-TO-EXPRESS PROTEINS continued

virus instability for certain target proteins. We have established and validated an ultra-short BEV protocol that also eliminates the risk of virus decay.

11:50 Tools for Studying the RAS/RAF/MEK Pathway: Using the BEVS to Produce Complexes and Native Proteins

William Gillette, PhD, Principal Scientist, RAS Reagents Core; Deputy Director, Protein Expression Laboratory, Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research (FNL)

This talk will focus on progress in producing proteins involved in the RAF activation pathway that are suitable for *in vitro* structural and biochemical studies. Recent advances in using the BEVS to overcome stability issues and producing complexes, as well as more biologically accurate KRAS proteins will be highlighted.

12:20 pm 9g/l in 90 Hours: Development of C1 into a Next-Generation Therapeutic Protein Production System

Sponsored by DYADIC

Ronen Tchelet, Vice President, Research & Development, Dyadic International, Inc.

This presentation will show the results of the development of the filamentous fungus Myceliophthora thermophila C1 into a next-generation therapeutic protein production system.

12:35 Expression, Purification and Characterization of Difficult to Express Membrane Proteins

Sponsored by ThermoFisher SCIENTIFIC

Anass Jawhari, PhD, CSO, Calixar

This talk will focus on strategies for optimizing expression levels of membrane proteins using the Expi293 and ExpiCHO expression systems. Additionally, an introduction to newly developed Expi293 engineered cell lines combined with CALIXAR patented technology to improve quality and quantity of challenging membrane proteins will be provided. A case study of KCC2 production and characterization will be further described.

12:50 Luncheon Presentation I: The Beacon™ Platform for the Rapid Discovery of Rare Antibodies to Difficult Targets

Sponsored by Berkeley Lights

Anupam Singhal, PhD, Technology Development, Berkeley Lights, Inc.

The search of biologics to novel therapeutic targets is hampered by current antibody discovery technologies that are laborious, time-consuming, and generate limited diversity. Here, I will demonstrate how Berkeley Lights' Beacon® platform's automated plasma cell antibody discovery workflow mines the vast immune repertoire to identify B cells producing rare, functional antibodies to difficult therapeutic targets in under 24 hours. The Beacon platform links phenotype-to-genotype at the single-cell level, simplifying downstream sequencing, cloning, and bioinformatics analysis.

1:20 Session Break

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, AstraZeneca

4:10 Vision for How Immunotherapy Will Shape Future of Cancer Care

Leena Gandhi, MD, PhD, Vice President, Immuno-Oncology Medical Development, Lilly Oncology

Immunotherapy is considered by many as a pillar of cancer care today, but in many ways we have only scratched the surface. Our knowledge and understanding of the complexities of immunotherapy and its mechanisms continue to evolve. The future of cancer care will be defined by our ability to systematically identify and implement opportunities for combination therapy to improve and standardize patient response.

4:55 The Lassa Virus Glycoprotein: Stopping a Moving Target

Kathryn Hastie, PhD, Staff Scientist, Immunology and Microbiology, The Scripps Research Institute

Lassa virus causes ~5000 deaths from viral hemorrhagic fever every year in West Africa. The trimeric surface glycoprotein, termed GPC, is critical for infection, is the target for neutralizing antibodies, and a major component of vaccines. Structural analysis of Lassa GPC bound to antibodies from human survivors reveals a major Achilles heel for the virus and provides the needed template for development of immunotherapeutics and improved vaccines.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:15 End of Day

8:00 am Registration and Morning Coffee

MEMBRANE PROTEINS

8:25 Chairperson's Remarks

Shahram Misaghi, PhD, Senior Scientist, Cell Culture, Genentech, Inc.

8:30 Structures Suggest a Mechanism for Energy Coupling by a Family of Organic Anion Transporters

Robert M. Stroud, PhD, Professor, Biochemistry and Biophysics, Pharmaceutical Chemistry, Macromolecular Structure Group (MSG), University of California, San Francisco (UCSF)

Members of the solute carrier 17 family use divergent mechanisms to concentrate organic anions. Membrane potential drives uptake of the principal excitatory neurotransmitter glutamate into synaptic vesicles, whereas closely related proteins use electroneutral cotransport to drive efflux from the lysosome. To identify the common features of ionic coupling by the SLC17 family, we determined the structure of *E. coli* D-galactonate/H+ symporter DgoT in two states: one open to the cytoplasmic side, and the other open to the periplasmic side with substrate bound. The structures identify residues of a proton translocation pathway conserved from bacteria to mammals. Functional analysis suggests that a transition in the role of H+ from flux coupling to allostery may underlie the divergence in energy source.

9:00 Modulation of STEAP2 Conformation by the Cholesterol Content of Cellular Membrane: An In-Depth Study of Conformational Epitope Located in the Second Extracellular Loop

Haruki Hasegawa, PhD, Principal Scientist, Biologics – Protein Technology, Amgen, Inc.

Leveraging a newly-identified mAb that recognizes a conformation-sensitive epitope nested in the second extracellular loop of human STEAP2, we demonstrate that the epitope formation is dependent on the cholesterol content of the membrane in which STEAP2 was embedded. Membrane permeabilization step and membrane cholesterol extraction treatment both abrogated cell surface staining of STEAP2 expressing cells. Given the preexisting difference in cholesterol content among different cellular membranes, STEAP2 conformation appears to undergo compartment-specific modulation during secretory and endocytic trafficking.

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9:30 Tag-on-Demand – Exploiting 'Switchable' Expression Technology for the Enrichment of High-Expressing Membrane Protein Cell Lines
Zachary T. Britton, PhD, Scientist, Antibody Discovery and Protein Engineering, AstraZeneca

Poor expression and detection of membrane protein therapeutic targets have hampered drug discovery and screening efforts. To address this, we have developed the "Tag-on-Demand" approach that exploits 'switchable' expression of 'tagged' and 'untagged' membrane proteins in response to non-natural amino acid supplementation. Expression of 'tagged' membrane proteins facilitate detection and selection steps, and expression of 'untagged' native proteins can be used directly in whole-cell drug discovery efforts. Validation of this approach using model membrane proteins will be presented.

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

MEMBRANE PROTEINS – DETERGENTS & SOLUTIONS

10:45 Chairperson's Remarks
Shahram Misaghi, PhD, Senior Scientist, Cell Culture, Genentech, Inc.

10:50 A High-Throughput Approach for Kinetics of Membrane Protein-Detergent Interactions
Liviu Movileanu, PhD, Professor, Physics, Syracuse University

Interfacial interactions of the membrane protein-detergent complex (PDC) have implications in protein function, structure, stability, and dynamics. Current methods for examining kinetics of the PDC require high amounts of protein and are low throughput. I will talk about our recent developments on an approach for acquiring details of these interactions in a scalable fashion. Further improvements of this semi-quantitative method will impact physical and chemical biology of membrane proteins.

11:20 Peptidisc: A Simple Solution for Capturing Membrane Proteins without Detergent
Franck Duong, PhD, Professor and Principal Investigator, Biochemistry & Molecular Biology, University of British Columbia

The peptidisc is a straightforward "one fits all" method that allows capture of membrane proteins into functional, heat-stable, water-soluble particles. Addition of lipids or engineering of the scaffold is not necessary. The flexibility of the peptidisc is suited for trapping proteins of various fold, size, architecture and the reconstitution process can be embedded directly within the membrane protein purification protocol.

11:50 Exploration of New Methods to Improve and Streamline Expression of Difficult Membrane Proteins to Support Drug Discovery
Noel J. Byrne, MSc, Associate Principal Scientist and Lead, Expression Group, Target Protein Design, Merck Research Laboratories

Integral membrane proteins represent more than 60% of current drug targets. Despite the clinical significance, therapeutic agents that target membrane proteins have been difficult to develop. Poor expression in recombinant systems is the most critical challenge to producing functional integral membrane proteins for antibody discovery, structural and functional studies. The results from the exploration of different technologies for the streamlined, efficient mammalian expression of several GPCRs and Ion Channels through stable cell-line generation and transient expression (DNA and BacMam) will be presented.

12:20 pm Luncheon Presentation I: Expi293 Transient Protein Expression System: New Tools for Structural Biology and Difficult to Express Proteins *Sponsored by* ThermoFisher SCIENTIFIC
Jon Zmuda, PhD, Director of Cell Biology, R&D, Thermo Fisher Scientific

In this presentation, we demonstrate the performance of a new range of Expi293 components, including engineered Expi293 cell lines (e.g. GNTI-, Inducible and Inducible/GNTI- Expi293 cell lines) to allow for regulated expression and/or glycosylation of proteins, as well as an Expi293 Methionine-Deficient System for metabolic labeling of proteins for NMR or multiwavelength anomalous dispersion (MAD). Together, these new tools significantly enhance the ability of researchers to produce difficult to express proteins for structural biology analyses.

12:50 pm Luncheon Presentation II: Engineered Selexis CHO Cell Lines for Improved Recombinant Protein Production *Sponsored by* SELEXIS
Ghislaine Arib, PhD, Genomic Director, Selexis SA

Biologics development requires stable, high-producing cell clones yielding high-quality product over years. These clones need stable chromosomal integration, elevated transcription plus optimized metabolic & secretion. Selexis CHO cell line generation combines the SURE technologyPlatform™ with precise selection of clones with desirable traits and manipulation of specific genes. This approach allows the isolation of desired clones that are rare events in cell populations and has led to remarkable progress in optimized product quality & titers

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

BREAKTHROUGH TECHNOLOGIES TO SUPPORT DTEPs

2:00 Chairperson's Remarks
William Gillette, PhD, Principal Scientist, RAS Reagents Core; Deputy Director, Protein Expression Laboratory, Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research (FNL)

2:05 FEATURED PRESENTATION:
MicroED: Cryo-Electron Diffraction of 3D Microcrystals
Brent Nannenga, PhD, Assistant Professor, Chemical Engineering, Arizona State University

The growth of large well-ordered crystals is often a barrier to high-resolution biomolecular structure determination. The cryo-electron microscopy technique of microelectron diffraction, or MicroED, is capable of determining high-resolution structures from extremely small microcrystals, promising to overcome this obstacle. In this presentation, the MicroED technique and representative structures will be described, as well as new improvements aimed at structure determination of difficult targets.

2:35 Development of a High-Yielding Expression Platform for the Introduction of Non-Natural Amino Acids
Gargi Roy, MSc, Scientist, Antibody Discovery and Protein Engineering, AstraZeneca

We developed an expression technology that enables site-specific incorporation of non-natural amino acids (nnAA) in a protein sequence. Fully functional, high yielding IgG, in a continuous perfusion process, was produced in hosts stably expressing an orthogonal tRNA synthetase/tRNA pair. These host platforms hold promise to overcome the expression challenges that have encumbered the developability of this technology for manufacturing of antibody drug conjugates and other protein conjugates.

DIFFICULT-TO-EXPRESS PROTEINS continued

3:05 GS Xceed® Gene Expression Toolbox: Overview and the Introduction of New Tools

Sponsored by Lonza Pharma & Biotech

Peter O'Callaghan, PhD, Principal Scientist, Research & Development, Lonza Pharma & Biotech

In this presentation, we will share an overview of the GS Xceed® Gene expression toolbox will be presented with a focus on new tools that have recently been added. Alongside this some new in-house research will be presented showing the benefit of applying control circuits to boost protein expression.

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

ANTIBODY EXPRESSION

4:25 Utilizing a Regulated Targeted Integration (RTI) Cell Line Development (CLD) Approach to Systematically Investigate What Makes an Antibody Difficult to Express

Shahram Misaghi, PhD, Senior Scientist, Cell Culture, Genentech, Inc.

A regulated target integration (RTI) system was used to analyze causes of low protein expression for a difficult-to-express antibody (mAb-A). Based on our findings, both antibody heavy chain and light chain subunits of mAb-A independently contributed to its low expression. RTI pools, generated by swapping antibody chains or point-mutations, confirmed that LC expression triggered ER stress and accumulation of intracellular BiP, while HC molecules had impaired degradation and clearance.

4:55 Expression of Multivalent Antibodies that Can Cross the BBB and Detect Aggregates in Amyloid Diseases with Expi293 Cells and PEI

Sofia Stenler, PhD, Scientist, Pharmaceutical Biosciences, Protein Drug Design, Uppsala University

I will describe a method of expressing antibodies and bispecifics in EXPI293 cells with PEI. The method is cheap and reliable. We have used the method to express bispecific antibodies that can pass the BBB 80 times better than unmodified antibodies. The antibodies bind monovalently despite having two binding domains and this is what facilitated the high uptake. We have shown that the antibodies can be used to treat or diagnose neurodegenerative diseases.

5:25 End of Difficult-to-Express Proteins

5:30 Registration for Dinner Short Courses

Recommended Short Course*

SC9: Introduction to Biophysical Analysis for Antibody Discovery & Development

Separate registration required. **Click here or see page 5 for course details.*

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9TH ANNUAL

OPTIMIZING PROTEIN EXPRESSION

Enhancing Expression Systems

April 10-11, 2019

Expression of heterologous proteins presents many challenges; and understanding expression systems is key. The Ninth Annual Optimizing Protein Expression conference delves into protein expression by examining and enhancing expression systems, including CHO, and other mammalian systems, *E. coli*, yeast, and baculovirus. What is the best expression system for expressing your protein of choice? Ease and cost of scale-up must be considered to ensure successful bottom-line results. Experts will share case studies and disclose data, while divulging details of expression systems' underlying mechanisms. Comparing and contrasting systems will also be featured to increase understanding in the quest for greater productivity.

TUESDAY, APRIL 9

Recommended Short Course*
SC9: Introduction to Biophysical Analysis for Antibody Discovery and Development

Separate registration required.* ***Click here* *or see page 5 for course details.*

WEDNESDAY, APRIL 10

7:15 am Registration and Morning Coffee

7:25 - 8:25 PANEL DISCUSSION: Women in Science – Inspired Professional and Personal Stories
Moderator: Women in Bio, Boston Chapter
Panelists:
Susan Richards, PhD, Presidential Scientific Fellow, Translational Medicine Early Development, Sanofi R&D
Joanna Brewer, PhD, Vice President, Platform Technologies, AdaptImmune
Additional Panelists to be Announced

PROTEIN PRODUCTION STRATEGIES

8:30 Chairperson's Opening Remarks
Philippe Billiald, PharmD, PhD, Professor, Biochemistry, University Paris-Sud & Acticor Biotech

8:40 KEYNOTE PRESENTATION: Early Process Development: Challenges and Opportunities for Emerging Therapies
Nicola Beaucamp, PhD, Head, Process Research, Roche Innovation Center Munich, Pharma Research and Early Development, Roche Diagnostics GmbH
A number of new molecules, different from standard antibody structures, have been advanced into clinics by Roche pRED. In order to discover and develop differentiated biologics, Roche's strategy is based on engineering technologies leading to new formats and processes which bear several challenges and many opportunities for technical development towards the clinic and beyond.

9:10 Site-Specific Biotinylation of Secreted Proteins in Mammalian Cells *in vivo* – Made Viable!
Mark Trautwein, PhD, Senior Scientist, Pharmaceuticals R&D, Preclinical Research, Expression Technologies, Bayer AG
Site-specific biotinylation of secretory target proteins is desirable to achieve *in vivo* during protein expression in mammalian cells. However, conventional techniques like the AviTag suffer from serious losses in expression yields, preventing their applicability as a generic approach. In this presentation, I will describe how we have optimized a protein tag to solve the problem and achieve this goal.

9:40 SoluPro™, A Groundbreaking *E. coli* Platform for Next-Generation Antibody Scaffolds and Protein TherapeuticsAntibody Therapeutics
Sponsored by AbSci
Johan Kers PhD, Vice President, Research, AbSci
SoluPro™, a game-changing *E. coli* expression platform that eliminates the formation of inclusion bodies, increases plant efficiencies, and drastically reduces COGs and CapEx outlay. Employing proprietary assays to optimize for product titer, function, and quality, SoluPro™ produces correctly folded, active protein, at groundbreaking titers in less than 3 months. The platform can produce a wide range of complex proteins including full-length antibodies (4 g/L), Fabs (4.4g/L), and insulin (>20g/L) in 48 hours or less.

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

10:15 Women in Science Speed Networking in the Exhibit Hall

OPTIMIZING CHO-BASED EXPRESSION

10:55 Combining Biophysical Analytics with Next-Generation Sequencing for Deep Characterization of mAb Producing CHO Cell Lines
Holger Thie, PhD, Senior Manager, Technology and Innovation, Biologics Development, Boehringer Ingelheim Pharma GmbH & Co. KG

11:25 Engineering CHO Cell Lines for the Production of Hard-to-Produce Proteins
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark
Using our high-throughput cell line engineering platform, we have engineered CHO cells able to produce therapeutic proteins that have previously not been possible to produce in CHO cells. This approach may result in improved therapeutic proteins with better biological properties, such as increased half-life, improved activity, etc.

11:55 Importance of Appropriately Glycosylated Species, and Modulation Efforts, to Achieve Desired Post-Translational Modifications in CHO-Derived Monoclonal Antibodies
Gaurav Chauhan, MS, Associate Principal Scientist, BioProcess Development, Merck & Co., Inc.
The glycosylation profile of the monoclonal

OPTIMIZING PROTEIN EXPRESSION continued

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antibodies has major impact on the efficacy and safety of the drug and is therefore an important parameter to control during protein production. Since glycosylation is an important parameter for IgG function, several strategies to modify glycosylation profiles of human IgG or to select the most efficient glycoforms have been explored. Further, considerable efforts have been made to understand how these glycoforms can be modulated as desired. I would like to present on current understandings of such efforts.

12:25 pm New Tools for Screening & Harvesting Solutions for CHO & HEK293 Cells, for both Transient and Stable Cells

Sponsored by THOMSON Solutions That Work INSTRUMENT COMPANY

Samuel Ellis, Vice President, Thomson Instrument Company

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

12:55 Luncheon Presentation I: Scaling Flexibility with Fed-Batch Expression in 96-Well Plates and Shaken Single-Use Bioreactors

Sponsored by Kuhner shaker

Annie Ngo, Technical Scientist, Kuhner Shaker Inc

Simple and unique, Kuhner Shaken Bioreactors (SB) mimic shake flask conditions for robust and scalable process development. From advanced 96-well fed-batch screening plates to single-use disposables of 2500L w/v, orbital shaking scales easily based on kLa and mixing time. Shaken processes offer further advantages of low-shear stress and less foaming – especially beneficial for sensitive cell types. Here we present data for small scale controlled-release fed-batch and data from users of the 3L-12L SB10 bioreactor.

1:25 Luncheon Presentation II: Generation of High-Yielding Stable Pools Expressing Difficult Target Proteins Through Maxcyte's Transfection System®

Sponsored by MaxCyte

Kevin Guay, Associate Scientist, Jounce Therapeutics

The transient transfection of Human Embryonic Kidney (HEK) cells has long been a workhorse for protein production. Often, however, these reagents suffer from poor yields and high amounts of aggregate formation. Furthermore, multiple production runs can introduce different post-translation modification patters, which could potentially lead to discrepancies in protein activity. We have employed the route of stable-pool generation to mitigate these issues, providing a great tool for programs in all stages of drug development.

1:55 Session Break

GENETICALLY ENGINEERING CHO CELLS

2:10 Chairperson's Remarks

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

2:15 Generation of Superior Host Cell Lines for Biomanufacturing

Margaret Lai, MS, Investigator II, Novartis Institutes for BioMedical Research

CHO cells are the most widely used host for large-scale production of recombinant therapeutic proteins. Using transcriptomic approaches, we have identified target genes involved in productivity and product quality. Subsequently, a variety of novel parental CHO cell lines were generated applying cell line engineering techniques as ZFN or TALEN. These novel knockout CHO cell lines are superior in respect to productivity and/or product quality.

2:45 Achieving Predictable Recombinant Gene Expression in CHO Cells Using CRISPR-Mediated Genome Engineering

Nuša Pristovšek, PhD, Postdoctoral Researcher, The Novo Nordisk Foundation Center for Biosustainability (CFB), Technical University of Denmark

Chinese hamster ovary (CHO) cells are one of the major hosts for production of complex therapeutic proteins. Efficient synthetic biology tools are of great interest to improve production in CHO cell factories. Here, our latest development of these tools will be demonstrated. Together with high-throughput technologies and systems biology approaches, synthetic biology can pave the way toward accelerated generation of desirable CHO cell factories with predicted culture performance.

3:15 Scaling Up and Scaling Out: Pushing the Boundaries of Transient Protein Production

Sponsored by absolute antibody

Ian Wilkinson, PhD, CSO, Absolute Antibody, Ltd.

Whilst transient yields have improved drastically in the last decade, scalable systems are time-consuming and costly to implement. Absolute Antibody has developed systems which scale up and scale out protein expression and purification, enabling the rapid and cost-effective production of milligram to gram quantities of large panels of proteins.

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

THURSDAY, APRIL 11

8:00 am Registration and Morning Coffee

COMPARE/CONTRAST EXPRESSION SYSTEMS

8:30 Chairperson's Remarks
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

8:35 Microbial or Mammalian Cells for Expression of Therapeutic Antibody Fragments: Making the Choice with the End in Mind
Philippe Billiald, PharmD, PhD, Professor, Biochemistry, University Paris-Sud & Acticor Biotech

Because antibody fragments are usually aglycosylated proteins, many host cell expression platforms can be used for production, including bacteria, yeast and mammalian cells. However, all these expression systems are not equivalent in terms of cell line development, culture time, product quality and cost of production. We will report differences that may have to be considered before pharmaceutical development and moving forward to the clinic.

9:05 Using Non-Coding RNA for Improving Recombinant Protein Expression and Growth from Mammalian Cells and Microorganisms
Joseph Shiloach, PhD, Director, Biotechnology Core Lab, NIDDK, NIH

Non-coding RNAs, including microRNA and siRNA in eukaryotes, and small RNA in prokaryotes, are regulatory molecules that can affect protein expression through interactions with specific sections of the host mRNA in mammalian cells, and mRNA and proteins in bacteria. The utilization of mammalian microRNA and siRNA to enhance growth and protein expression from HEK and CHO cells and affecting *E. coli* metabolism using bacterial small RNA will be presented.

9:35 Sponsored Presentation *(Opportunity Available)*

9:50 Overcoming Limitations of Conventional Tag Systems – Strep-Tactin®XT Applications
Sponsored by iba
Dennis Karthaus, MSc, IBA Lifesciences

The Strep-Tactin®XT:Twin-Strep-tag®-purification system enables protein purification at high yields and purity under physiological conditions. Providing the highest binding affinity among all affinity tag systems, the technology fulfills the demands of mammalian expression systems (e.g. Expi) and is well suited for downstream applications like SPR.

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

NON-MAMMALIAN EXPRESSION SYSTEMS

11:05 Rational Engineering of an Improved Secretion Signal for *Pichia pastoris*
Benjamin Glick, PhD, Professor, Molecular Genetics and Cell Biology, University of Chicago

The yeast *Pichia pastoris* is widely employed to secrete heterologous proteins. Typically, the N-terminal portion of pre-pro-alpha-factor is used as a secretion signal. This secretion signal promotes posttranslational translocation into the ER, so proteins that fold in the cytosol are poorly secreted. The alpha-factor pro region can also promote aggregation in the ER. We applied cell biological principles to address both issues. The resulting improved secretion signal confers dramatic benefits.

11:35 Titer Estimation for Quality Control (TEQC) Method: A Practical Approach for Optimal Production of Protein Complexes Using the Baculovirus Expression Vector System
Yuichiro Takagi, PhD, Associate Professor, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine

The baculovirus expression vector system (BEVS) is becoming the method of choice for expression of many eukaryotic proteins and protein complexes. However, what influences the overall production of proteins or protein complexes remains largely unclear. We developed the Titer Estimation for Quality Control (TEQC) method, which enables researchers to quantitatively optimize protein expressions utilizing BEVS in a highly reproducible fashion.

12:05 pm BryoTechnology: Large-Scale GMP-Manufacturing of Glyco-Designed Proteins with Moss
Andreas Schaaf, PhD, CSO, Greenovation Biotech GmbH

BryoTechnology, i.e., moss-based production of biopharmaceuticals, has evolved into a GMP manufacturing technology with products already in clinical development. While leveraging the mosses advantages, comparability to mammalian cell-based technologies was a priority in process development. Today's moss process relies on the latest single-use technologies and follows the established routines of mammalian cell-based production. Thus, moss-based production fits easily into existing cleanroom environments and offers rapid changeover and flexible configuration.

12:35 End of Optimizing Protein Expression

5:45-8:45 pm Recommended Short Course*
SC15: Transient Protein Production in Mammalian Cells
Separate registration required.* ***Click here* *or see page 5 for course details.*

5TH ANNUAL

PROTEIN EXPRESSION SYSTEM ENGINEERING

Gene to Cell Line

April 11-12, 2019

CHI's Fifth Annual Protein Expression System Engineering conference examines the functioning of the cellular machinery harnessed during protein biosynthesis, and how to engineer hosts to efficiently express a protein of interest. The intricate steps required to achieve properly folded protein will be discussed, including verification and sequence analysis of the gene, codon optimization, vector construction, selecting and optimizing a clone, and selecting a host system. In addition, engineering host cells to sustain expression for longer time periods will be discussed, along with overcoming cellular stress response to produce and secrete functionally active recombinant proteins.

THURSDAY, APRIL 11

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

SYNTHETIC BIOLOGY & GENETIC ENGINEERING

1:40 Chairperson's Opening Remarks

Susan Sharfstein, PhD, Professor, Nanobioscience, Nanoscale Science and Engineering, SUNY Polytechnic Institute

1:50 KEYNOTE PRESENTATION:

Mammalian Synthetic Biology: Foundations and Application to Cell Line Engineering

Ron Weiss, PhD, Professor, Biological Engineering, Massachusetts Institute of Technology (MIT)

In this research, we appropriate from established engineering fields proven design principles such as abstraction, standardization, modularity, and computer aided design. But we also spend considerable effort towards understanding what makes synthetic biology different from all other existing engineering disciplines and discovering new design rules that are effective for the biological substrate. Building on this foundation, I will describe our recent application of synthetic biology tools and principles towards the improvement of cell line engineering and biomanufacturing.

2:20 Communicating with and Controlling Gene Expression via Redox-Linked Bioelectronics

William E. Bentley, PhD, Robert E. Fischell Distinguished Chair, Engineering; Inaugural Director, Robert E. Fischell Institute for Biomedical Devices, Chemical and Biomolecular Engineering, University of Maryland, College Park

We are developing tools of "biofabrication" that enable facile assembly of biological components within devices, including microelectronic devices, that preserve their native biological function. We have created redox-based synthetic biology to sample, interpret and report on biological information contained in molecular communications circuitry. We have also developed synthetic genetic circuits that enable electronic actuation of gene expression. These tools enable unparalleled means to control genetic circuits, creating new and exciting means to actuate and control biology.

2:50 Steering N-Glycosylation of Recombinant Proteins Using Systems Engineering

Michael J. Smanski, PhD, Assistant Professor, Biochemistry, Molecular Biology & Biophysics, Biotechnology Institute, University of Minnesota

Chinese Hamster Ovary cells are used for industrial production of protein-based therapeutics (i.e. 'biologics'), but systems-level genetic engineering of beneficial traits is slow, difficult, and empirically-guided. We exploit systems- and synthetic-biology approaches to design, build, and screen multi-gene constructs that rationally perturb the post-translational glycosylation of a secreted Immunoglobulin G (IgG) towards high galactose incorporation. Our approach allows for rapid hypothesis testing and quantification of synergistic behavior from genetic perturbations.

3:20 Fusion Partners for Robust Peptide Production in Pseudomonas Fluorescens

Sponsored by PFEnex

Diane Retallack, PhD, Senior Director, Upstream Processing and Intellectual Property, Pfenex

3:50 Networking Refreshment Break

4:20 A Multi-Landing Pad DNA Integration Platform for Mammalian Cell Engineering

Liliana Wroblewska, PhD, Principal Scientist, Biomedicine Design, Pfizer, Inc.

Reliable, large-scale engineering of CHO cells through precise insertion of large amounts of heterologous DNA into well-characterized genomic loci would have broad applications for mammalian synthetic biology, recombinant protein production, and biomanufacturing. Using multi-gene payload vectors, cell lines with multiple landing pads, and recombinase technology, we demonstrated controlled integration of up to nine copies of a monoclonal antibody (about 100 kb of heterologous DNA), and a corresponding linear increase in antibody expression.

4:50 Implementing Next-Generation Sequencing for DNA-Based Sequence Variant Analysis of Recombinant Proteins

Ulrich Göpfert, PhD, Principal Scientist, Cell Line & Molecular Development, Roche Innovation Center Munich

Sequence variants are unintended amino acid substitutions in biopharmaceuticals, which can either be due to the manufacturing process or mutations of the transgene. Transgene mutations are permanent properties of affected cell lines and may give rise to critical quality attributes. Therefore, mutated cell lines need to be identified and excluded from development. We will share our experience with next-generation sequencing as an efficient and highly sensitive method to detect DNA-based sequence variants.

5:20 End of Day

5:20 Registration for Dinner Short Courses

5:45-8:45 pm Recommended Short Course*

SC15: Transient Protein Production in Mammalian Cells

Separate registration required.* ***Click here* *or see page 5 for course details.*

FRIDAY, APRIL 12

8:00 am Morning Coffee

ANALYZING & IMPROVING PRODUCTIVITY

8:30 Chairperson's Remarks
Christopher H. Gray, PhD, Staff Scientist & Team Leader, Structural Biology, Drug Discovery Program, CRUK Beatson Institute

8:35 FEATURED PRESENTATION:
Methylation Analysis of Cell Lines with Varying Productivities
Susan Sharfstein, PhD, Professor, Nanobioscience, Nanoscale Science and Engineering, SUNY Polytechnic Institute
DNA methylation plays a critical role in regulating gene expression, and it is well known that the CMV promoter contains a CpG island that is subject to silencing by methylation. Using a novel next-generation sequencing approach, we have analyzed the methylation status of the CMV promoter for cell lines with varying productivity to provide insight into the role of methylation in control of transgene expression.

9:05 Improving Cytidine and Adenine Base Editors by Expression Optimization and Ancestral Reconstruction
Luke Koblan, PhD, Scientist, Chemical Biology, Chemistry & Chemical Biology, Harvard University
Base editors enable targeted single-nucleotide conversions in genomic DNA. The usefulness of base editors for research and therapeutic applications strongly depends on the efficiency with which they modify target nucleotides. Optimizations to improve editor expression, nuclear localization, and the component deaminase domain enable substantially improved editing by both cytidine and adenine base editors in a variety of mammalian cell types. BE4max, AncBE4max, and ABEmax represent the current state-of-the-art base editors.

9:35 Development and Production of Biologics Beyond Antibodies
Sponsored by cevec
Ulrich Kettling, Vice President, Business Development, CEVEC Pharmaceuticals GmbH
While antibodies have become standard, now more and more complex, glycosylated proteins get into the focus of biopharma research, as cell therapy reagents and therapeutics. While such complex proteins represent a large portion of the human proteome they are notoriously difficult to express in CHO or microbials. The presentation discusses the CAP cell lines and CAP-Go expression platform which are specifically designed for production of high-end biologics with authentic post-translational modifications and tailor-made glycosylation patterns.

10:05 Networking Coffee Break

10:35 Synonymous Codon Selection for Enhanced Yield of Functional Proteins
Patricia Clark, PhD, John Cardinal O'Hara, C.S.C. Professor, Chemistry & Biochemistry, University of Notre Dame
Historically, "optimizing" a gene for heterologous expression consisted of substituting rare codons with synonymous common codons. This strategy can increase the amount of protein produced but at the expense of adversely affecting the yield of active, functional protein. This talk will focus on our recent discoveries regarding rare codon distribution in naturally occurring coding sequences and rational strategies for rare codon placement to enhance folding yield.

11:05 Cell-Free Synthetic Biology for Therapeutics, Sensing, and Remediation
David Karig, PhD, Associate Professor, Systems and Synthetic Biology, Bioengineering, Clemson University
Cell-free protein expression systems offer a number of advantages for implementing synthetic biology applications. They simplify system composition and tuning, avoid evolution away from the intended function, and alleviate safety concerns associated with the spread of engineered living cells. Key developments in the preservation and ruggedization of cell-free reagents will enable therapeutics production in the field as well as environmental sensing and remediation.

11:35 Identification of ADP-Ribosylation by Tandem Mass Spectrometry
Guy Poirier, PhD, Professor, Faculty of Medicine, Scientific Advisor, Proteomics Platform CHU of Quebec, Université Laval
We have developed a new method to identify all the ADP-ribosylation sites independent of the acceptor amino acid. This method uses tandem mass spectrometry amenable to CID or other modes of fragmentation. The mass spectrometry signature is very unique and is stable in any mode of fragmentation.

12:05 pm Production of Antimicrobial Peptides Using Protein-Cage Carrier Proteins
Mimi Cho Yung, PhD, Staff Scientist, Biosciences and Biotechnology Division, Physical and Life Sciences Directorate, Lawrence Livermore National Laboratory (LLNL)
The bioproduction of antimicrobial peptides (AMPs) in bacterial expression systems remains a challenging problem due to host toxicity and proteolysis. We will discuss our recent efforts to engineer encapsulin nanocompartment systems to enhance expression of AMPs in *Escherichia coli*.

12:35 Luncheon Presentation: Strategies to Increase the Speed of Cell Line Generation for Biomanufacturing Whilst Maintaining Performance
Sponsored by FUJIFILM Diosynth Biotechnologies
Fay Saunders, PhD, Head, Mammalian Cell Culture, PD, FUJIFILM Diosynth Biotechnologies
Increasing efforts are focused towards reducing the time taken to move from gene to GMP manufacturing. In this study we demonstrate how to leverage (i) host cell line directed evolution strategies to improve bioprocess relevant phenotypes and increase mAb titres up to 2-fold; and (ii) key technology enablers that allow intensification of cell line development timelines.

1:05 Networking Refreshment Break

IMPROVING EXPRESSION SYSTEMS

1:35 Chairperson's Remarks
David Karig, PhD, Associate Professor, Systems and Synthetic Biology, Bioengineering, Clemson University

1:40 Molecular Approaches that Improve Soluble Protein Yields from Bacterial Expression Systems
Christopher H. Gray, PhD, Staff Scientist & Team Leader, Structural Biology, Drug Discovery Program, CRUK Beatson Institute
Expression systems targeting well folded products often employ contradictory strategies, pushing production with strong promoters and codon-enhanced cDNAs, while simultaneously slowing the process by titrating back inducing reagents or culture temperature. Often, elevated total expression levels aren't matched by a similar increase in the recovery of soluble protein. We compare a series of alterations to key codons and expression-vector sequence elements that attenuate protein production rates and maximise soluble recovery.

2:10 Engineering CHO Metabolic Essential Gene for Efficient and High Expressing Clones Suited for Perfusion Processes
Hatim Motiwala, PhD, Head, Cell Line Engineering and Bio-Analytical Sciences, Enzene Biosciences Limited
A double knock-out cell line for two important metabolic genes was created using CRISPR/Cas. This allows for a strong clonal selection of a monomeric or dimeric protein. The cell line is also tested in continuous upstream process for significantly higher expression.

2:40 Recombinant (Membrane) Protein Production in Yeast

Roslyn M. Bill, DPhil, Professor, Biotechnology; Associate Dean, Research, Aston University

My lecture will focus on methods that are available for protein synthesis in yeasts, which are an important source of recombinant eukaryotic membrane proteins. I will provide an overview of approaches to optimize the expression plasmid, host cell and culture conditions, as well as the extraction and purification of functional protein for further study.

3:10 Development of the Filamentous Fungus *Myceliophthora thermophila* C1 into a Next-Generation Therapeutic Protein Production System

Anne Huuskonen, MSc, Research Scientist, VTT Technical Research Centre of Finland, Ltd.

We are utilizing the vast protein production capability of the filamentous fungus *Myceliophthora thermophila* to construct a highly potent therapeutic protein production platform. Superb productivities of full-length antibodies, up to 2.5 g/l/day, have been reached. We have also successfully produced several difficult-to-express proteins such as bispecific antibodies and vaccine proteins in titers superior to other expression systems. Our work also aims at humanizing the glycosylation pathway of this fungus, and the first steps in this research line have been successful.

3:40 End of Conference

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ANALYTICAL STREAM

- **Characterization of Biotherapeutics**
- **Biophysical and Structural Analysis**
- **Analytical Support for Drug Product Development**

Best Practices and Solutions for Analytical Characterization, Biophysical/Structural Analysis and Drug Product Development for Next-Generation Biotherapeutics

The **Analytical Stream** focuses on the application of biochemical, biophysical and structural characterization tools to help gain a detailed knowledge of proteins from discovery through all the stages of development, and for 2019 presents a new meeting exploring the analytical challenges of drug product development. This three-meeting stream offers a range of best practice case studies from industry and academic perspectives on the characterization of new modalities (including CAR-Ts and gene therapy), emerging analytical methods and responses to regulatory requirements related to analytical characterization.

9TH ANNUAL

CHARACTERIZATION OF BIOTHERAPEUTICS

Exploring the Analytical Challenges of Today's Complex Biologics

April 8-9, 2019 | Seaport World Trade Center | Boston, MA

As new product formats progress through development and into the regulatory process, the role of analytical characterization is taking on new meaning. Very new modalities present challenges to both analytical scientists and regulatory agencies alike, and this steep learning curve requires a near-constant cycle of adaptation and innovation. The agencies are requiring sponsors to provide ever more complex data across a wide range of analytical methods, and instrumentation suppliers are striving to support this new era with unique product features, software and feature combinations. The PEGS Characterization of Biotherapeutics conference explores the progression of analytical development for an exciting range of emerging modalities and offer a case study forum for those working in the field to share ideas, experiences and solutions that support the preclinical and clinical development of new biotherapeutics.

SUNDAY, APRIL 7

Recommended Short Course(s)*
SC2: Translational Biotherapeutic Development Strategies Part 1: Discovery, Molecular Assessment and Early Stage Development
SC7: Translational Biotherapeutic Development Strategies Part 2: Analytical and Clinical Considerations
Separate registration required. **Click here or see page 5 for course details.*

MONDAY, APRIL 8

7:00 am Registration and Morning Coffee

CHARACTERIZATION OF COMPLEX FORMATS

8:30 Chairperson's Opening Remarks
William C. Motel, PhD, Director, Regulatory Affairs, IQVIA Global Regulatory Affairs

8:40 Identifying Early Production Truncated Drug Candidates by Top-Down Mass Spectrometry
Zhe Zhang, PhD, Senior Scientist, Novartis Institutes for BioMedical Research

Mass spectrometry has shown to be a powerful tool to characterize different therapeutic protein formats. With intact MS and peptide mapping, identification and site-specific characterization can be achieved. Top-down mass spectrometry, however, can provide added value, for example avoiding digestion and artifact generation, sequence coverage on special regions, etc. Two case studies from different projects found truncation problem in early production stage. MS, especially Top-down MS, was able to provide sequencing information with high efficiency, quick turnover and independency.

9:10 Characterization of Novel and Complex Antibody Formats
Markus Haberger, PhD, Senior Scientist, Roche, Germany

The number of novel biotherapeutic antibody-based formats in drug development is continuously increasing. Characterization of these formats is challenging. Since established physiochemical and mass spectrometric methods show limited capabilities for characterization of product related impurities, new analytical strategies have to be developed. Here, we present a native MS based analytical approach which successfully assisted in the elucidation of size and charge variants of complex antibody formats such as bispecific antibodies or antibody fusion proteins.

9:40 Expanding Role of Mass Spectrometry in Development of Biotherapeutics
Dhaval Nanavati, PhD, Senior Scientist, AbbVie

The versatility of mass spectrometer has made it the prevailing analytical platform for understanding the distribution, target interaction, off target interaction of biotherapeutics. The role of mass spectrometry in dissecting post translational modified variants of a putative target is also critical in identification of unique targets and development of novel bio therapeutics. In this work, we show specific examples of enhanced foot print of mass spectrometry in early stages of development of biotherapeutics.

10:10 Networking Coffee Break

REGULATORY CHALLENGES

10:50 The Regulatory Path for Breakthrough Designations and Orphan Drugs
William C. Motel, PhD, Director, Regulatory Affairs, IQVIA Global Regulatory Affairs

The U.S. Food and Drug Administration (FDA) offers several special designations to aid in progression of a drug's approval. The orphan drug designation specifically targets products that treats a rare disease or condition affecting fewer than 200,000 Americans, while the breakthrough therapy designation applies to a drug that is aimed at treating a serious or life-threatening disease or that may demonstrate substantial improvement over existing therapies.

11:20 CMC Analytical Strategies Designed for Regulatory Dialog Intended for Early Phase IND Filings
Vaneet K. Sharma, PhD, Manager, Analytical Development, Vaccine Development & Manufacturing, International AIDS Vaccine Initiative (IAVI)

This presentation will outline phase appropriate CMC analytical strategies intended for successful regulatory submissions, especially for exploratory and phase 1 programs. A case study will be presented to demonstrate the application of the regulatory accepted phase appropriate analytical characterization to support HIV vaccine development.

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11:50 KEYNOTE PRESENTATION: Planning the Extent and Timing of Analytical Studies: What is the Risk to Benefit Impact in Relation to Drug Development Stage?

Jennifer F. Nemeth, PhD, SCPM, Director, Biophysics, Structural Characterization, Biologics Discovery Sciences, Janssen Research & Development

New biologic drug development is costly, and where money is spent impacts a company's pipeline. Upfront spend can allow for quicker Go/NoGo decisions or while limited development allows for a faster path to PoC. This talk will focus on the benefits/risks of applying analytical assays before vs after New Molecular Entity Declaration, and which assay were found to be the most impactful for selection to justify the spend and time.

12:20 pm ProteinMentor Developability Assessment: Case Studies for Therapeutic Proteins

Sponsored by proteindynamic SOLUTIONS

Belinda Pastrana, PhD, CEO, Protein Dynamic Solutions

Two case studies will be presented on developability analysis of therapeutic proteins. An array-based biophysical platform was used for deamination assessment, stability and higher order structure determination. Drug substance and drug products were evaluated and the data generated can be used for computational modeling for logic-driven protein design.

12:35 Cryo-EM Unveils Antibody-Mediated Neutralization Mechanism of Enteroviruses

Sponsored by BIORTUS

Xiaodong Yan, PhD, Executive Director, Biortus Biosciences Co., Ltd.

Cryo-electron microscopy (cryo-EM) becomes a very powerful tool for epitope-mapping. We hereby present near-atomic cryo-EM structures of three Enteroviruses (CVA6, CVA10 and D-68) and their immune complexes. The ensemble of structures reveals molecular mechanisms of antibody-mediated neutralization and will facilitate the development of effective vaccines and therapeutics against Enterovirus infections.

12:50 Luncheon Presentation I: Boost Your Protein Quantification with Same-Time Quality

Sponsored by UNCHAINED LABS

Lisa Adamiak, PhD, Product Manager, Marketing, Unchained Labs

There are many reasons to assess the quality of protein samples prior to downstream analysis, such as comparing batches of purified material, changing formulation conditions, or checking the integrity of thawed or stressed samples. With Stunner, you can now perform painless quality checks by determining the concentration, hydrodynamic size, and polydispersity at the same time with just 2 µL of sample, enabling you to move on to the next steps in your workflow with confidence.

1:20 Luncheon Presentation II: MS-Based Characterization of Biotherapeutics and HCPs in Production Bioprocesses Using a Single Software Platform

Sponsored by Genedata

Xiaojuan Li, PhD, Associate Principal Scientist, Protein Mass Spectrometry Department, Merck & Co., Inc

This presentation describes application of automated MS data processing workflows for intact mass analysis, released N-glycan analysis, and peptide mapping that provide efficient, in-depth characterization of biotherapeutic products. In addition, we present a workflow that automatically detects and quantifies host cell proteins in bioprocess monitoring while reducing the number of false positive identifications.

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, AstraZeneca

4:10 Vision for How Immunotherapy Will Shape Future of Cancer Care

Leena Gandhi, MD, PhD, Vice President, Immuno-Oncology Medical Development, Lilly Oncology

Immunotherapy is considered by many as a pillar of cancer care today, but in many ways we have only scratched the surface. Our knowledge and understanding of the complexities of immunotherapy and its mechanisms continue to evolve. The future of cancer care will be defined by our ability to systematically identify and implement opportunities for combination therapy to improve and standardize patient response.

4:55 The Lassa Virus Glycoprotein: Stopping a Moving Target

Kathryn Hastie, PhD, Staff Scientist, Immunology and Microbiology, The Scripps Research Institute

Lassa virus causes ~5000 deaths from viral hemorrhagic fever every year in West Africa. The trimeric surface glycoprotein, termed GPC, is critical for infection, is the target for neutralizing antibodies, and a major component of vaccines. Structural analysis of Lassa GPC bound to antibodies from human survivors reveals a major Achilles heel for the virus and provides the needed template for development of immunotherapeutics and improved vaccines.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:15 End of Day

TUESDAY, APRIL 9

8:00 am Registration and Morning Coffee

CELL AND GENE THERAPY

8:25 Chairperson's Remarks

Qin Zou, PhD, Group Leader, Analytical Research and Development, Pfizer Inc.

8:30 Regulatory Expectations for Gene Therapy CMC Information

Michelle Joubert, Scientist, Analytical Development, Sanofi

An increasing number of gene therapy products are entering clinical development, and several approvals are anticipated in the near future. As a consequence of this intense activity, regulatory guidance has evolved to become more specific for these advanced therapies. This was highlighted by the recent publication by the FDA of several draft guidance documents for cell and gene therapies. We will discuss current thinking for gene therapy CMC packages and expectations for an IND filing. We will also share experiences and feedback we have encountered.

9:00 Application of Analytical Ultracentrifugation: from Protein Therapeutics to Gene Therapy

Qin Zou, PhD, Group Leader, Analytical Research and Development, Pfizer Inc.

This presentation will intend to provide an overview on using analytical ultracentrifugation in biotherapeutic development. Specific case studies will be provided to highlight these applications to various modalities. A stage-tailored strategy in using the technology during drug development is discussed.

9:30 Leveraging High-Dimensional '-omics' Technologies for Comprehensive Profiling of CAR T Cells to Resolve Drug Product Complexity

Eric S. Alonzo, PhD, Scientist, Process and Analytical Development, bluebird bio

Clinical-grade CAR T cell drug products contain a heterogenous mixture of phenotypically and functionally distinct cells. Such heterogeneity necessitates innovative and comprehensive strategies to characterize CAR T cell therapy investigational drug products. A case study will be presented to demonstrate how high dimensional '-omics' is used in CAR T manufacturing and beyond to

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resolve drug product complexity and identify potentially key clinical correlates.

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

10:50 Analytical Challenges During CAR T Process Development

Ken Prentice, Independent Consultant

11:20 Challenges Associated with Manufacturing and Release of Autologous Cell Therapy Products

Kuldip Sra, PhD, Senior Director, CRISPR Therapeutics

An autologous cell therapy product to treat B cell malignancies was approved in the USA in 2017 and in the EU in September 2018. Since cell therapy products manufacturing takes 6-7 days and to deliver the final product to sick patient within 2-3 wks of leukophoresis, rapid and robust analytical methods must be adapted to release final products in less than one week.

11:50 Lentiviral Vector Engineering and Characterization of Vector Potency for Cell Therapy

Marc-André Robert, PhD, Scientist, Technology Development, BioMarin Pharmaceuticals

Lentiviral vectors (LV) are currently investigated for cell therapy because they can integrate into the cell genome and provide sustainable gene expression. Thus, they can be used to replace a defective gene by providing a functional version of it. The model presented here is hematopoietic stem cells used to treat blood disorders. The presentation will focus on improving and characterizing the potency of LV, a critical quality attribute of LV.

12:20 pm Luncheon Presentation I: In-depth Evaluation of Maurice CE-SDS System for Method Development and QC Environment

Sponsored by proteinsimple

Pegah Abadian, PhD, Scientist II, Biologics Development (Analytical Method Development), Bristol Myers Squibb

CE-SDS method is employed in biologics DS/DP control. The SCIEX PA800+ is the current standard instrument and provides repeatable results. However, next-generation CE SDS instruments such as ProteinSimple Maurice can increase throughput and decrease cost per injection, among other benefits. This project provides an in-depth comparison of the Maurice with the PA800+ using BMS biologics assets in regard to 1) Onboard Stability, 2) Reported Purity, 3) Method Robustness, and 4) Flexibility of applying Custom Gels to QC Space.

12:50 Luncheon Presentation II: Enabling Routine and Reproducible Biotherapeutic Analysis when Data Integrity Matters

Sponsored by Waters

Henry Shion, Principal Scientist, Waters Corporation

Driven by increasing industry demand for a robust accurate mass MS system for routine biotherapeutic analysis within the process, development and quality organizations, a new small footprint bench-top LC-MS system was purposefully designed and developed to offer simplified operational modes, and optimized automation with accurate and reproducible mass measurements for proteins, peptides and released glycans. In this work, we show specific examples of deploying this compliance-ready bench-top system in late stage development of biotherapeutics.

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

CHARACTERIZATION CHALLENGES OF BISPECIFICS

2:00 Chairperson's Remarks

Zhimei Du, PhD, Director, Bioprocess, Merck & Company, Inc.

2:05 Domain Characterization of Protein Therapeutics *In Vivo* by Multiplexed NanoLC-HRMS Approaches

Jessy Fan, PhD, Scientist, Amgen

Next generation protein therapeutics are designed to enable enhanced pharmacology, greater selectivity, and altered drug disposition for an overall improved therapeutic profile. Engineering efforts entail addition of nonconventional domains that require robust characterization of molecular instabilities. Online multiplexed Peptide Immuno-affinity Enrichment (PIE) LC-MS workflow enables simultaneous assessment of molecular integrities through detection of individual domains of the therapeutic proteins. Case studies presented herein demonstrate different properties of therapeutic proteins *in vivo*.

2:35 The Roadmap of Bispecific Recombinant Protein Drug Development

Zhimei Du, PhD, Director, Bioprocess, Merck & Company, Inc.

Bispecific recombinant proteins are emerging fields in biological drug development. These new modalities have significantly expanded the functions of conventional mAbs as biotherapeutics. There are many protein scaffolds in bispecifics field. Besides targeting two antigens simultaneously, different molecule designs have very different features and challenges in bioactivity, pharmacokinetics, and manufacturability. We will discuss challenge details and solutions in various CMC development areas that directly impact product yield and product qualities.

3:05 A Platform Approach to Manage Developability and Manufacturability Risks of Biologics Molecules

Amanda Fitzgerald, PhD, Senior Scientific Consultant, Biologics, Genedata

We present a workflow system that enables systematic developability and manufacturability assessments, using both *in silico* and high throughput analytical confirmatory methods, over the entire biologics R&D process from initial discovery all the way to final candidate selection. We show use cases for mAbs and other complex multi/bispecific formats and discuss building predictive developability models utilizing this system. We also present the underlying molecule and task management needed for analytical organizations to accomplish this.

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

ADCS AND CONJUGATED PROTEINS

4:25 Characterization of Antibody Drug Conjugates

Liqiang (Lisa) Zhou, PhD, Senior Scientist, Protein Analytics, AbbVie

Antibody-drug conjugates (ADCs) are becoming an increasingly important class of biotherapeutics. Different levels of heterogeneity contributed by mAbs and the conjugated drugs lead to complexity in ADC characterization. In-depth understanding of the physicochemical properties of ADCs is essential to drug development and process control. A wide variety of analytical methods have been used in the characterization of an interchain cysteine-conjugated ADC, with particular focus on the charge variants and size variants.

4:55 Impurity characterization, Control Strategy and Specification Justification in Small Molecules (Payload and Linker)

Jane Zhao, PhD, Principal Scientist, Immunogen

DM4 and Sulfo-SPDB are payload and linker in the ADC manufacturing process of mirvetuximab soravtansine drug substance. Impurities in these two small molecule intermediates are well characterized and specified with acceptance criteria that are based on manufacturing capability, downstream clearance and clinical exposure. Impurity fate mapping and trending in each step of the synthetic route and during process development and PAR studies enable better control of impurities and hence improve product quality.

5:25 End of Characterization of Biotherapeutics

5:30 Registration for Dinner Short Courses

Recommended Short Course*

SC9: Introduction to Biophysical Analysis for Biotherapeutics: Development Applications

Separate registration required. **Click here or see page 5 for course details.*

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7TH ANNUAL

BIOPHYSICAL AND STRUCTURAL ANALYSIS

Implementing Emerging Technologies for Improved Product Quality and Accelerated Development Timelines

April 10-11, 2019

Biophysical and structural analysis is now playing increasingly important roles in the discovery and development of next generation biotherapeutics. Developability assessment is now standard practice across the industry, and understandings gained at this step are now being applied in the optimization of candidates at early stages of the pipeline. Higher resolution tools are enabling better understandings of how to characterize and control aggregation and particulates and are increasingly allowing these methods to be used in a quantitative, rather than qualitative way. The PEGS Biophysical and Structural Analysis conference brings together an international audience of protein scientists and analytical specialists to explore the latest technologies and methods for problem solving in this dynamic field and identify ways of optimizing the studies performed in support of regulatory filings and manufacturing.

TUESDAY, APRIL 9

Recommended Short Course*
SC9: Introduction to Biophysical Analysis for Biotherapeutics: Development Applications
Separate registration required. **Click here or see page 5 for course details.*

WEDNESDAY, APRIL 10

7:15 am Registration and Morning Coffee

7:25 - 8:25 PANEL DISCUSSION: Women in Science – Inspired Professional and Personal Stories
Moderator: Women in Bio, Boston Chapter
Panelists:
Susan Richards, PhD, Presidential Scientific Fellow, Translational Medicine Early Development, Sanofi R&D
Joanna Brewer, PhD, Vice President, Platform Technologies, AdaptImmune
Additional Panelists to be Announced

CHARACTERIZING HIGHER ORDER STRUCTURE

8:30 Chairperson's Opening Remarks
Jessy Fan, PhD, Scientist, Amgen

8:40 Characterization of Therapeutic Proteins by Circular Dichroism Spectroscopy: Application to Process Comparability and Establishment of Critical Quality Attributes
Gurusamy Balakrishnan, PhD, Scientist, Bristol-Myers Squibb
Circular dichroism (CD) spectroscopy is a widely used technique for assessing protein higher order structure (HOS) but remains difficult to assess HOS with high fidelity due to lack of sensitivity towards subtle structural perturbations. This presentation will discuss these challenges and an effective experimental method for CD measurements with the relevant examples from analytical comparability for process change and forced degradation studies for establishing critical quality attributes.

9:10 Ion Mobility Spectrometry Mass Spectrometry (IMS-MS) for HOS Characterization
Brandon Ruotolo, PhD, Professor, Chemistry, University of Michigan
The next generation of medicines will rely heavily upon our ability to quickly assess the structures and stabilities of large, complex macromolecular machines, as well as the influence of large libraries of conformationally-selective small molecule binders and protein-based biotherapeutics. Such endeavors are nearly insurmountable with current tools. In this presentation, I will discuss recent developments in ion mobility-mass spectrometry (IM-MS) technology that seek to bridge this gap.

9:40 KEYNOTE PRESENTATION: The Underestimated Power of Well-Established Methods to Assess Protein Higher Order Structure
Alejandro Carpy, PhD, Senior Scientist, Large Molecule Research, Roche Diagnostics GmbH, Germany
Proper higher order structure (HOS) is essential for the function and stability of biologics. A large number of biochemical or biophysical methods are available to assess HOS, which differ in sensitivity and specificity. We will show that approaches based on combination of conventional methods such as bioassays or liquid chromatography, which are used for batch release, are well-suited and sufficient to assess HOS, especially during early clinical development.

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

10:15 Women in Science Speed Networking in the Exhibit Hall

IMPLEMENTING THE MULTI-ATTRIBUTE METHOD (MAM)

10:55 MAM Method Development and Qualification
Jihong Wang, PhD, Principal Scientist, AstraZeneca
Several multi-attribute monitoring methods (MAM) have been developed in the biopharmaceutical industry in recent years. We reported MAM method based on Quadrupole Dalton (QDa) mass detector to selectively monitor and quantitate PTMs in a therapeutic monoclonal antibody. In this talk, case studies will be presented on applications and implementation of QDa-based QC friendly MAM methods from supporting process characterization to product release.

11:25 Implementing the Multi-Attribute Method in a Multi-Site Analytical Development Organization: Successes and Challenges
Kristin Boggio, PhD., Senior Scientist, Protein Mass Spectrometry, Pfizer
Biotherapeutics development requires thorough understanding of product quality attributes (PQAs) to ensure that clinical materials meet the desired safety/efficacy profile. Numerous routine assays are used to characterize and monitor PQAs; however, execution

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of multiple methods becomes time and resource intensive, often providing indirect measurements of biologically-relevant PQAs. We have incorporated the mass spectrometry-based multi-attribute method at various stages in non-GMP product development to monitor multiple PQAs within a single experiment.

11:55 Development of MS-Based Multi-Attribute Methods for ADC Process Support
Lintao Wang, Ph.D., Associate Director, Analytical and Pharmaceutical Development, ImmunoGen, Inc.
Antibody-drug conjugates (ADCs) are complex anti-cancer biomolecules that have multiple quality attributes. A mass spectrometry based multi-attribute method (MAM) was developed for monitoring quality attributes (such as deamidation, oxidation, glycosylation, disulfide mispairing, etc.) to support process development of an ADC with engineered cysteine linkage.

12:25 pm A Three-Pronged Characterization Tool That Makes Unstable Proteins Cry "Uncle"
Sponsored by UNCHAINED LABS
Kevin Lance, PhD, Product Manager, Marketing, Unchained Labs
Optimizing protein stability and developing the best formulations for avoiding aggregation is important throughout the biologics development pathway. Uncle's unique combination of static light scattering, dynamic light scattering, and fluorescence gives you the flexibility needed to tease out the right answers and understand the whole story.

12:55 Luncheon Presentation I: The Perfect Recipe for Protein Characterization Starts with Tycho and Knowing Protein Quality
Sponsored by NANOTEMPER
Peter A. Fung, Senior Manager Product Marketing, NanoTemper Technologies
Starting with material of questionable quality for protein purification and characterization leads to irreproducible or ambiguous results. Tycho tells you so much about the quality of your protein—its presence, purity, concentration, functionality and similarity — in a single experiment. These can all be measured simply by determining whether your protein is structurally intact or properly folded. Tycho fits into any step of a purification or characterization workflow to easily monitor protein quality and help researchers to get more consistent results.

1:25 Luncheon Presentation II: High Throughput Low Volume Subvisible Particle Analysis
Sponsored by halo labs
John Proctor, PhD, Vice President, Marketing, Halo Labs
Subvisible particle analysis is a key predictor of protein drug stability and an essential drug product quality metric. Currently it is almost impossible to obtain this vital info during early stage formulation development. Come see how the new HORIZON system from Halo Labs uses Backgrounded Membrane Imaging (BMI) to measure subvisible particles, including translucent protein aggregates. The measurement is fully automated for up to 96 samples and uses 1/10th the volume of other techniques.

1:55 Session Break

METHODS AND INSTRUMENTS

2:10 Chairperson's Remarks
Brandon Ruotolo, PhD, Professor, Chemistry, University of Michigan

2:15 Leveraging Force Degraded Material to Increase the Throughput of Peptide Map Characterization
Romesh Rao, Research Associate, Analytical Sciences, Seattle Genetics
Appropriately degraded samples can increase the throughput of peptide map characterization by facilitating data analysis. Post-translational modifications (PTMs) in a highly degraded sample were identified and site localized, enabling rapid, site-specific assignments of PTMs during subsequent analysis of nominal samples by comparison. This approach can also support lower resolution, higher throughput workflows.

2:45 PULSE-SPR and its Applications in Developability Assessment
Li Zhou, PhD, Senior Scientist, Global Biologics, AbbVie
Downstream purification of therapeutic antibodies requires candidates to be stable under various stress conditions such as low pH. Here we report a high throughput method that measures protonation induced unfolding of ligand binding sites for stability evaluation by surface plasmon resonance, or PULSE SPR.

3:15 Advances in High-Throughput Screening for Development and Formulation of Biologics
Sponsored by WYATT TECHNOLOGY
John Champagne, PhD, Senior Applications Scientist, Northeast Regional Manager, Sales, Wyatt Technology
Light scattering addresses many key analytical challenges in drug nanoparticle R&D, including accurate size distributions, conformation, payload, and formulation. We review light scattering fundamentals and then present examples illustrating how. Wyatt's unique light scattering instrumentation facilitates rapid and effective development of controlled release vehicles including liposomes, VLPs, polymer-encapsulated nanoparticles, and nanogels.

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

THURSDAY, APRIL 11

8:00 am Registration and Morning Coffee

SPECTROMETRY METHODS

8:30 Chairperson's Remarks
Iain D. G. Campuzano, Principal Scientist, Discovery Attribute Sciences, Amgen

8:35 Cutting-Edge Chromatographic, Electrophoretic and Mass Spectrometry of mAbs, Fc-Fusion Proteins and ADCs
Alain Beck, PhD, Senior Director, Biologics CMC and Developability, Pierre Fabre Laboratories, France
Developability and comparability assessment of current and next generation of biologics such as engineered mAbs, Fc-fusion proteins, BsAbs and 2 or 3G-ADCs requires state-of-the-art analytical and structural methods. Case studies will be presented based on native and ion mobility MS, multi-level 2- to 4 LC-MS, multiplexed Top and Middle-Down MS, multiple fragmentation techniques, comprising high energy collisional-, electron-transfer and ultraviolet photo-dissociation (HCD, ETD and UVPD) and CE-MS.

9:05 The Application of Fourier Transform Ion Cyclotron Resonance MS and Spectral Deconvolution Algorithms within Biopharma Research
Iain D. G. Campuzano, Principal Scientist, Discovery Attribute Sciences, Amgen
Native-MS analyses for accurate antibody, protein and nanodisc MW and DAR confirmation have traditionally been performed using oa-ToF instrumentation and more recently the extended mass range Orbitrap analyzer with incremental improvements in data quality. Analysis of mAbs, ADCs, nanodiscs and a PEGylated biotherapeutics used FT-ICR MS under both native and denaturing LC-MS conditions. Also demonstrated is the use of a new parsimonious deconvolution algorithm that can efficiently deconvolve highly polydisperse MS spectra.

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9:35 Considerations of the Use of Analytical Ultracentrifugation for Characterization of AAV Gene Delivery Vectors

Sponsored by charles river

Christopher Sucato, PhD, Senior Scientist, Biophysical Characterization, Charles River

Analytical Ultracentrifugation (AUC) in the biopharmaceutical industry has traditionally been employed in the analysis of aggregation and higher order structure in protein drug products, where monomeric or dimeric protein is commonly the analyte. More recently, the rise of gene delivery vectors as a means to treat a number of conditions has opened new avenues for AUC-based characterization and QC lot release methodologies.

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

AGGREGATION AND STABILITY

11:05 Ultrafast High-Resolution Protein Analysis Unconventional Devices

Raja Ghosh, PhD, Professor, Chemical Engineering, McMaster University, Canada

High-speed, high-resolution analytical separation is one of the current needs with biopharmaceuticals. Separations using ultrafine particulate chromatographic media require ultra-high pressures which could have detrimental effects on the molecules being analyzed. In this presentation, membrane-based devices suitable for rapid, high-resolution analytical protein separation are discussed. Using these devices, high-resolution separation of proteins could be carried out in minutes at less than 1 MPa backpressure.

11:35 Effect of L-proline, L-arginine.HCl and NaCl on the Aggregation and Viscosity Behavior of High-Concentration Antibody Formulations

Chaitanya Sudrik, PhD, Postdoctoral Associate, Molecular Engineering, Massachusetts Institute of Technology

Development of subcutaneous formulations for monoclonal antibodies is hindered by several physical instabilities. In this study, we compare preferential interactions of L-proline, L-arginine.HCl and NaCl with the native state of three IgG1 mAbs that differ in their physical stability attributes. We also highlight differences amongst the excipients in terms of their effect on the aggregation and viscosity of these antibodies at high protein concentration.

12:05 pm Impact of Non-Ideal Analyte Behavior on the Separation of Protein Aggregates by Asymmetric Flow Field-Flow Fractionation

Björn Boll, Ph.D., Head, Particle Lab and Higher Order Structure Protein Analytics, Novartis Pharma AG, Switzerland

Asymmetric flow field-flow fractionation (AF4) is a valuable tool for the characterization of protein aggregates owing to its broad size range and unique separation principle. In practice, AF4 is non-trivial to use due to deviations from theory. This presentation gives an overview about non-ideal effects that influence AF4 separation including new approaches to minimize non-ideal behavior and drastically improving AF4 resolution by adjusting the mobile phase.

12:35 End of Biophysical and Structural Analysis

Recommended Short Course*
SC14: Subvisible Protein Particles in Immunogenicity: Measurement, Characterization and Impact

Separate registration required.* ***Click here* *or see page 5 for course details.*

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INAUGURAL

ANALYTICAL SUPPORT FOR DRUG PRODUCT DEVELOPMENT

Overcoming the Analytical and Formulation Challenges of a New Generation of Drug Products

April 11-12, 2019

Advances in protein science, drug combinations, delivery technology and analytical methods are supporting an unprecedented wave in novelty in the design of biologic drug products. With these new products comes the urgent need for analytical support of product development, regulatory filings and manufacturing – in ways that require a constant adaptation by analytical and formulation groups to new modalities and technologies. New for 2019, the PEGS Analytical Support for Drug Product Development conference provides a best practices exchange for scientists now working to develop these new products – or for those wishing to be prepared for forthcoming programs in their organization's pipelines.

THURSDAY, APRIL 11

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

KEY ASSAYS AND ISSUES IN DP DEVELOPMENT

1:40 Chairperson's Opening Remarks
Vijay Dhawan, PhD, Associate Director, Analytical Development, Sanofi

1:50 Developability Evaluation: Right Tools at the Right Time?
Lasse Stach, Investigator, Drug Design and Selection, GlaxoSmithKline, United Kingdom

The talk will focus on the interface between discovery and development, timing of the various developability studies and deployment of the available tools. Early lead selection of biotherapeutics requires meticulous assessment of a variety of molecule properties to minimize risk during development. However, increased complexity of non-standard protein formats requires an adaptation from former platform-based screening to project specific strategies to select quality candidates.

2:20 Approaches to Optimizing Manufacturability of Monoclonal Antibodies
Michael Anyadiegwu, PhD, Senior Scientist, Downstream Processing, Center for Process Innovation, National Biologics Manufacturing Center, United Kingdom

Molecules can fail to transition from discovery to commercialisation due to developability issues such as instability, aggregation etc. A collaborative project set out to systematically explore the developability landscape of monoclonal antibodies using experimental data. Sequences were expressed and purified allowing datasets of biochemical and biophysical quality attributes to be generated. These were then evaluated to understand more about the potential to critically assess monoclonal antibody sequences early in development.

2:50 KEYNOTE PRESENTATION: Design and Analytical Challenges of In Use Stability Studies for Biologics
Pierre Wils, PhD, Head, Biologics Formulation and Process Development, Sanofi, France

The early clinical development of highly potent biologics is usually performed by intravenous administration requiring very low starting doses and wide dose ranging. We will present case studies about in use stability studies, related to the quantification of biologics in very dilute solutions, and means to minimize protein adsorption onto the infusion material. We will also discuss trends in the preparation of infusion solutions in hospital settings.

3:20 A Platform Technology for the Rapid Generation Of Robust Anti-Idiotypic Binders for Clinical PK Assays

Sponsored by Avacta LIFE SCIENCES

Matt Johnson, CTO, Avacta Life Sciences

Affimer proteins are next-generation affinity scaffolds with great potential for the generation of both novel biotherapeutics and research tools. It is possible to generate highly-specific anti-idiotypic Affimer binders using a 14-week development process. In comparison to commercially available anti-idiotypic Fab fragments we have shown it is possible to develop high-performing antibody PK assays (and ligand binding assays) in complex samples using only a single, specific capture Affimer and generic antibody detection minimising assay complexity.

3:50 Networking Refreshment Break

4:20 Method Development and Characterization of Product Specific Host Cell Proteins
Jennifer Kessler, Senior Development Associate, MacroGenics, Inc.

Monoclonal antibodies and bispecific DART® molecules are being developed for a variety of indications including immune-oncology. These biopharmaceuticals contain residual host cell proteins (HCPs) from production cell lines that can pose a risk to product safety and stability. This presentation will discuss the development of process specific HCP methods and the characterization of product specific HCPs using this novel class of molecules and other antibody molecules as case studies.

4:50 Phase Appropriate Potency Assays: What Is Needed and When?
Sheila G. Magil, PhD, Principal Consultant, BioProcess Technology Consultants, Inc.

Regulatory expectations for potency assays include their being related to the mode of action *in vivo*. There are many ways to measure potency and what method is best also depends on the phase of development. This presentation will describe approaches to the development of acceptable potency assays throughout development including when and how to validate potency assays.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course*
SC14: Subvisible Protein Particles in Immunogenicity: Measurement, Characterization and Impact
Separate registration required. **Click here or see page 5 for course details.*

FRIDAY, APRIL 12

8:00 am Morning Coffee

DRUG PRODUCT DEVELOPMENT CHALLENGES

8:30 Chairperson's Remarks
Gerald Gellermann, PhD, Senior Fellow, Novartis, Switzerland

8:35 Dual mAb Therapies: Co-Administration and Co-Formulation Challenges and Solutions
Jasper Lin, PhD, Scientist and Group Leader, Genentech

Recently, there has been a surge of clinical trials using multiple mAbs to bring about synergistic efficacy. Sequential IV administration is burdensome for the patient, leading to interest in developing CMC solutions by means of co-administration and fixed dose combinations (FDCs). FDCs provide a great deal of promise, but also present new challenges. This talk will highlight formulation, process, and analytical challenges accompanying the development of co-administration and co-formulation strategies.

9:05 Tools for Developing a Mechanistic Understanding of Specificity in Post-Translational Modification Targeting Antibodies
Yongku Cho, PhD, Assistant Professor, Chemical and Biomolecular Engineering, University of Connecticut

Validation of antibody specificity is critical for biotherapeutics development. In particular, antibodies targeting site-specific post-translational modifications (PTMs) require utmost specificity, due to their heterogeneous and transient nature. However, recent validation efforts reveal an alarming lack of specificity in PTM-targeting antibodies. This presentation will showcase our recent efforts to overcome this problem, by understanding the origin of specificity and applying protein engineering strategies to improve specificity.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Networking Coffee Break

10:35 Bridging Discovery and Development by Early Developability Assessment
Qing Chai, PhD, Principal Research Scientist, Protein BioSciences, Eli Lilly & Co.

Biopharmaceutical development is often challenging. Among those challenges is antibody "developability," such as solubility, viscosity, manufacturability, and formulation suitability. Multidimensional developability assessment platform, including analytical methods coupled with computational approaches, was established and utilized to perform high-throughput screening at early discovery stage to facilitate the discovery, selection, and optimization of the most promising mAb molecules. Here we discuss case studies on improving mAb developability applying the principal of Quality by Design at discovery stage.

11:05 IV Set Compatibility Studies for ADCs
Alexandra (Sasha) Zaitsev, Development Associate, Analytical & Pharmaceutical Sciences, ImmunoGen

Compatibility studies with administration sets of the drug product are performed during early stage development to determine the propensity of the antibody-drug conjugate (ADC) to become altered upon contact with the infusion set materials. Possible alterations include adsorption to the infusion set, aggregation, particulate formation, etc. This presentation will discuss challenges associated with study set up and interpretation of the acquired data.

11:35 Device Considerations in Drug Product Development – Case Study of Ophthalmic Injections of Anti-VEGF Therapies
Susan Dounce, PhD, Principal SME, Prefilled Syringes, West Pharmaceutical Services

Frequent Injections into the eye can introduce particulate matter or biologic contaminants that can lead to inflammation, infection, floaters in the vision or vision loss. It is therefore critical to understand how the delivery device itself can impact the safety of the drug product so that the proper material selections are made for primary packaging to maximize patient safety. In this talk, we will explore the critical device considerations for ophthalmic drug delivery.

12:05 pm Oligomericity Status Changes and its Effects on the Stability of Proteins in Solution
Bettina Bommarius, PhD, Senior Research Scientist, Chemical and Biomolecular Engineering, Georgia Institute of Technology

We have investigated protein activity and stability as a function of the oligomeric status of a protein. Our results indicate that activity and stability correlate with a uniform oligomeric presence and that the proteins investigated can exist as a mixture of different oligomers and aggregates. Factors that influence the percentages of each given oligomer/aggregate will be presented as well as effects of oligomeric mixtures on specific activities. Protein oligomericity is an underappreciated link between protein concentration and its activity or stability.

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Networking Refreshment Break

COMPARABILITY ANALYSIS

1:35 Chairperson's Remarks
Abbie Esterman, PhD, Senior Scientist, Methods and Analytical Development, Bristol-Myers Squibb

1:40 Method Bridging: Fit or Mis-fit
Abbie Esterman, PhD, Senior Scientist, Methods and Analytical Development, Bristol-Myers Squibb

Technologies used for release and stability testing of biologics are rapidly evolving to meet the ever-increasing challenges in drug development. Consequently, one or more analytical methods will need amendment during the product life cycle. Before new methods can be filed, bridging studies are required to establish comparability and confirm the new method is fit for its intended use. Two case studies bridging novel and conventional methods for purity and charge heterogeneity analyses will be examined.

2:10 Strategies for Comparability Testing to Support Process/Product or Manufacturing Site Changes
Vijay Dhawan, PhD, Associate Director, Analytical Development, Sanofi

Accelerated timelines for clinical programs and an increased reliance on external contract manufacturers during the different project stages have resulted in an increased need to perform analytical comparability to support use of the post-change material in the clinic while avoiding non-clinical or clinical bridging studies. Approaches for establishing and executing analytical comparability plans will be discussed during the presentation.

ANALYTICAL ISSUES IN QUALITY AND PROCESS CONTROL

2:40 Development of Process and Product Understanding: Use of Prior Knowledge and Challenges for Setting of Specifications
Gerald Gellermann, PhD, Senior Fellow, Novartis, Switzerland

Applications for design space are rare as the risk benefit of a full QbD application is not clear and QbD based applications usually receive more scrutiny than traditional once. In this presentation, we will discuss the use of prior knowledge and compare consequences on specifications setting and process parameter criticality for the different development approaches.

3:10 Theoretical Constraints on Design Space for High Concentration Filling: Minimizing Clogging and Increasing Filling Precision

Richard Galas, PhD, Senior Scientist, Takeda

The fluid properties of many biologic formulations designed for pre-filled syringes are unique and create engineering challenges for filling systems. These products often clog the filling lines, causing costly delays while components are replaced. A theoretical fluid mechanics approach to the filling process was taken to define key parameters that impact filling accuracy and clogging. This approach identified a theoretical design space that minimizes filling variability and clogging.

3:40 End of Conference

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IMMUNOGENICITY & BIOASSAYS STREAM

- **Immunogenicity Case Studies and Clinical Management**
- **Immunogenicity Assessment and Regulatory Approval of Biologics**
- **Optimizing Bioassays for Biologics**

Ensuring the Safety and Efficacy of Biologics

This year's **Immunogenicity & Bioassay Stream** focuses on the latest science, technologies and strategies to ensure the safety and efficacy of novel biologics, with particular focus on immunogenicity clinical management and assay life cycles. Part One looks at new case studies and how to use immunogenicity data in clinical settings; Part Two examines immunogenicity assessment for novel biologics such as ADCs, bispecifics, CAR-T and mAbs along with an emphasis on new regulatory guideline for cell and gene therapies; and Part Three will showcase emerging technologies and strategies for day-to-day challenges when developing bioassays to evaluate potency, function and robustness of novel biologics.

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12TH ANNUAL

IMMUNOGENICITY CASE STUDIES AND CLINICAL MANAGEMENT

Interpretation and Understanding of Immunogenicity Data in Clinical Settings

April 8-9, 2019

As the immunogenicity field is moving forward, closing the gap between clinicians and assay developers is essential in the success of biologic development and accelerates the adoption of new biologic therapies in patient treatments. This year, CHI's Immunogenicity Case Studies and Clinical Management conference will focus on new case studies of novel biologics and emphasize closing this gap by providing multiple viewpoints from clinicians, technology developers and regulators on how to use immunogenicity data in clinical settings.

SUNDAY, APRIL 7

Recommended Short Course(s)*

SC1: Preclinical and Clinical Assessment of Immunogenicity: Multidomain Therapeutics and New Modalities, Including Gene Therapy and CAR T

SC5: In silico Immunogenicity Predictions (Hands-on) Workshop

Separate registration required.* ***Click here* *or see page 5 for course details.*

MONDAY, APRIL 8

7:00 am Registration and Morning Coffee

THE IMPACT OF IMMUNOGENICITY ON SAFETY AND EFFICACY

8:30 Chairperson's Opening Remarks
Sandra Garces, MD, PhD, Senior Medical Advisor for Immunogenicity, GPS Medical and Benefit-Risk Management, Eli Lilly

8:40 KEYNOTE PREESENTATION: How to Characterize ADA Responses and Assess Their Clinical Impact to Better Inform the Clinical Relevance of ADA Using a Risk-Based Approach
Sandra Garces, MD, PhD, Senior Medical Advisor for Immunogenicity, GPS Medical and Benefit-Risk Management, Eli Lilly
Practical cases will be used to better illustrate the specific questions and some of the limitations we sometimes face and to discuss potential ways to overcome challenges in pre-clinical risk assessment of expected clinical consequences according to type of biologic, disease population, drug MoA. Study designs to incorporate specific immunogenicity questions, characterization of ADA responses, type of analyses to characterize the impact on PK, on PD, efficacy and safety and risk-benefit perspective to decide if further mitigation strategies are needed will also be discussed.

9:10 Relationship Between ADA and PK Assays: Is There an Impact?
Marcela M. Araya, PhD, Principal Scientist, Group Leader, BioMedicine Design, Pfizer
The assessment of immunogenicity of therapeutics drugs is a requirement for regulatory filings. The ADA formation may have an impact on the efficacy, dosing schedules and sampling schedules. Current gaps include a limited knowledge of the effect of endogenous ADA on PK/PD profiles, and the inconsistency of reported types of ADA responses (e.g., titers, concentration, isotypes, etc). The presentation will cover the impact of immunogenicity induction on PK assays.

9:40 Applying Modeling Methodologies to Analyze the Impact of Immunogenicity on Exposure and Efficacy
Vibha Jawa, PhD, Director and Lead, Predictive and Clinical Immunogenicity, PPDM, Merck & Co Inc
Understanding immunogenicity's effect on the PK and PD of a therapeutic protein is important during drug discovery, as it allows for the identification of clinically relevant anti-drug antibody reactions. The goal of this work is to use modeling methodologies to understand the effect of immunogenicity, streamlining the early drug discovery process and informing clinical decisions.

10:10 Networking Coffee Break

RISK ASSESSMENT AND WORK FLOW PROCEDURE

10:45 Chairperson's Remarks
Vibha Jawa, PhD, Director and Lead, Predictive and Clinical Immunogenicity, PPDM,, Merck & Co Inc

10:50 Increased Immunogenicity Associated with Combination Regimens with Immune Modulatory Biologics
Jad Maamary, PhD, Associate Principal Scientist, Predictive and Clinical Immunogenicity, PPDM, Merck and Co Inc
The use of immune modulatory biologics to augment functionality of immune cells can also augment the risk of immunogenicity. The quality of such an immune response and its clinical relevance will be explored through this talk. Whether the activation of immune cells can break tolerance to otherwise tolerant sequences will also be explored.

11:20 ADA Testing in Clinical Routine: Where Are We and Where Are We Heading?
Anna Fogdell-Hahn, PhD, Associate Professor, Karolinska Institutet, Clinical Neuroscience, Clinical Neuroimmunology, Center for Molecular Medicine (CMM), Stockholm, Sweden
Whereas ADA testing is now a requirement for drugs to be approved, the use of them in clinical settings are only partially applied. This is unfortunate since it would enable identification of patients that have reacted and become tolerant against their treatment before clinical symptoms appear. In this talk I will present a feasible process for translating the ADA testing from the industry, through academy to applied clinical routine.

11:50 Post-hoc assessment of the immunogenicity of three antibodies reveals distinct immune stimulatory mechanisms
Robin E. Walsh, MS, Toxicologist, Toxicology and Immunosafety Lab, Eli Lilly & Co

In this study, we present the post-hoc analysis of three monoclonal antibodies with high immunogenicity in clinic. Two of the three antibodies were capable of eliciting a CD4[+] T cell proliferative response with multiple donors in a peripheral blood mononuclear cell (PBMC) assay, but required different experimental conditions to induce these responses. The third antibody did not trigger any T cell response in this assay. These distinct capacities to promote CD4[+] T cell responses *in vitro* were mirrored by different capacities to stimulate innate immune cells. Only one out of the three antibodies was capable of inducing human monocyte-derived dendritic cell (moDC) maturation; the second antibody promoted monocyte activation while the third one did not induce any innate cell activation *in vitro*. However, all three antibodies exhibited a moderate to high internalization by human moDCs and MHC-associated peptide proteomics (MAPPs) analysis revealed the presence of potential T cell epitopes that were later confirmed by PBMC T cell proliferation assay using peptides instead of whole antibodies. Collectively, these findings highlight the existence of distinct immune stimulatory mechanisms of immunogenic antibodies. These approaches and findings might have implications for the preclinical screening of therapeutic proteins and help lower the immunogenicity risk of therapeutic proteins.

12:20 pm Bioanalytical Strategy to support CAR-T Therapies: Where are the Challenges?
Sponsored by BioAgilytix
Corinna Fiorotti, PhD, CSO, BioAgilytix

12:50 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks
Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, AstraZeneca

4:10 Vision for How Immunotherapy Will Shape Future of Cancer Care
Leena Gandhi, MD, PhD, Vice President, Immuno-Oncology Medical Development, Lilly Oncology

Immunotherapy is considered by many as a pillar of cancer care today, but in many ways we have only scratched the surface. Our knowledge and understanding of the complexities of immunotherapy and its mechanisms continue to evolve. The future of cancer care will be defined by our ability to systematically identify and implement opportunities for combination therapy to improve and standardize patient response.

4:55 The Lassa Virus Glycoprotein: Stopping a Moving Target
Kathryn Hastie, PhD, Staff Scientist, Immunology and Microbiology, The Scripps Research Institute

Lassa virus causes ~5000 deaths from viral hemorrhagic fever every year in West Africa. The trimeric surface glycoprotein, termed GPC, is critical for infection, is the target for neutralizing antibodies, and a major component of vaccines. Structural analysis of Lassa GPC bound to antibodies from human survivors reveals a major Achilles heel for the virus and provides the needed template for development of immunotherapeutics and improved vaccines.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:15 End of Day

TUESDAY, APRIL 9

8:00 am Registration and Morning Coffee

CASE STUDIES OF BIOLOGICS

8:25 Chairperson's Remarks
Darshana Jani, PhD, Associate Director & Global Lead Biologics, Pfizer Inc

8:30 Attend Concurrent Track

9:00 Nonclinical and Clinical Immunogenicity Assessment of Bispecific Protein Therapeutics
Eric Wakshull, PhD, Principal Scientist/Group Leader, Bioanalytical Sciences, Genentech

The advent of increasingly complex and novel protein therapeutic modalities requires non-standard approaches to assessing immunogenic responses. Bispecific antibodies are one such novel modality in which two different target specificities are engineered into a single protein. This presentation will discuss our bioanalytical strategy and its implementation using two such molecule programs. These case studies will illustrate how these strategies were implemented, their outcome and impact on clinical development.

9:30 Case Study: Clinical Immunogenicity and Its Impact
Deborah Finco, PhD, President, Deborah Finco Consulting LLC

Multiple companies developed therapeutic monoclonal antibodies to the same target for lowering low-density lipoprotein (LDL). However, the immunogenicity profiles varied considerably between the different companies monoclonal antibodies. This talk will discuss the different therapeutic antibodies, the immunogenicity assays, clinical results, and the impact of immunogenicity and efficacy on one program.

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

CASE STUDIES OF BIOLOGICS (CONT.)

10:45 Chairperson's Remarks
Darshana Jani, PhD, Associate Director & Global Lead Biologics, Pfizer Inc

10:50 Immunogenicity Assessment of an Enzyme Replacement Therapy Administered via the Intracerebroventricular Route in Patients with CLN2 Disease
Anu Cherukuri, PhD, Associate Director, Immunogenicity Assessment, BioMarin Pharmaceutical Inc.

We have characterized immunogenicity of a novel ERT directly delivered to the CNS in patients with a life-threatening neurodegenerative disease. The consequences of both a systemic and CNS-specific immune response on the safety and efficacy profiles of the drug will be presented. Implications of ADA impact on systemic and CSF PK will be included. Lastly, regulatory feedback on the risk assessment approach and learnings from the program that can be applied to assess immunogenicity risks of future ICV-delivered ERT therapeutics will be presented.

11:20 Immunogenicity Testing – The Next Frontier: Gene Therapies, Nanoparticles and Beyond

Renuka Pillutla, PhD, Executive Director, Lead, Bioanalytical Sciences at Bristol-Myers Squibb

Advances in molecular engineering and our understanding of biological mechanisms are resulting in increasingly novel therapeutics. In the realm of large molecules, we have gone beyond the traditional antibody and protein therapeutics to unique modalities with innovative delivery systems. Increasing complexity of novel modalities has led to increases in the complexity of immunogenicity testing strategies. This presentation will discuss the challenges of assessing immunogenicity risk and developing appropriate testing strategies as we move into this next frontier. Two case studies will be used to illustrate some of the challenges. In one example, the therapeutic is a lipid nanoparticle that encapsulates siRNA as the active pharmaceutical ingredient. Based on a thorough assessment and careful consideration, an immunogenicity assay development strategy was developed and implemented for this complex molecule. In another example, immunogenicity considerations in gene therapy and the potential impact of pre-existing antibodies to the vector will be discussed.

POST MARKETING COMMITMENTS

11:50 PANEL DISCUSSION: Characterization and Impact of Post Marketing Commitment Requirements for New Biologics Approved by the FDA

Moderator: Susan Richards, PhD, Presidential Scientific Fellow, Translational Medicine Early Development, Sanofi R&D

Panelists:

Eric Wakshull, PhD, Principal Scientist/Group Leader, Bioanalytical Sciences, Genentech

Jack A. Ragheb, MD, PhD, Co-Chair, Immunogenicity/ Immunosafety Working Group, Senior Medical Fellow for Immunogenicity, Global Patient Safety, Eli Lilly and Company, Lilly Corporate Center

Darshana Jani, PhD, Associate Director & Global Lead Biologics, Pfizer Inc

- Gain an awareness of postmarketing requirements and commitments, how they differ and what gaps are generally addressed?
- Discuss the various immunogenicity-related commitments that have been issued by the FDA. Are there common themes? Will they provide learnings for future biologics development?
- How will the newer guidances and incorporating a risk-based immunogenic assessment approach in programs impact future PMR/PMCs?

12:20 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on your Own**

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

PRE-EXISTING ADA & IMMUNE TOLERANCE INDUCTION

2:00 Chairperson's Remarks

Sophie Tourdot, PhD, Senior Principal Scientist, Immunogenicity, Pfizer

2:05 Impact of Presence of Pre-Existing Antibodies on Immunogenicity Assessment Strategy

Joleen White, PhD, Director and Head, NBE DMPK Project Support, EMD Serono Research & Development Institute Inc.

While all biotherapeutics have the potential to induce an antidrug antibody response (ADA), for some, pre-existing ADAs are observed in drug-naïve matrix. The presence of pre-existing ADAs may influence the bioanalytical approach and data analysis, both preclinically and clinically. Clinical case studies of biotherapeutic candidates in development for Oncology or non-Oncology indications for which pre-existing ADA were detected will be presented.

2:35 The Origin of Antidrug Antibodies

Jack A. Ragheb, MD, PhD, Co-Chair, Immunogenicity/ Immunosafety Working Group, Senior Medical Fellow for Immunogenicity, Global Patient Safety, Eli Lilly and Company, Lilly Corporate Center

Many factors influence the immunogenicity of therapeutic proteins. This presentation will review basic aspects of immune tolerance and discuss the implications for the development of ADA to therapeutic monoclonal antibodies.

3:05 Sponsored Presentation *(Opportunity Available)*

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

PREEXISTING ADA & IMMUNE TOLERANCE INDUCTION (CONT.)

4:25 New Updates on the Use of Low Dose Transient Methotrexate

Lauren Bailey Flueckinger, MS, CGC, Genetic Counselor, Medical Genetics, Duke University Medical Center

Prophylactic immune tolerance induction (ITI) has been standard of care in CRIM-negative infantile Pompe disease (IPD) patients. However, the side effects and cost of rituximab has resulted in its use on in CRIM-negative IPD. We have developed an immune modulation protocol using transient low-dose methotrexate. We will present data on our experience with transient low-dose methotrexate in infantile Pompe disease.

4:55 Immune Tolerance Induction Approaches for Immunogenicity Mitigation

Sophie Tourdot, PhD, Senior Principal Scientist, Immunogenicity, Pfizer

I will talk about rationale for mitigating immunogenicity through tolerance induction (the case of ERT and gene therapy, and beyond). Current practice in the clinic (ITI, methotrexate, …) and new approaches such as antigen- specific and non-antigen specific (nanoparticles, proteasome inhibitors, anti-CD20, …) will also be discussed.

5:25 End of Immunogenicity Case Studies and Clinical Management

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*
SC14: Subvisible Protein Particles in Immunogenicity: Measurement, Characterization and Impact

Separate registration required.* ***Click here* *or see page 5 for course details.*

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12TH ANNUAL

IMMUNOGENICITY ASSESSMENT AND REGULATORY APPROVAL OF BIOLOGICS

Achieving Assay Quality and Clinical Success of Novel Biologics

April 10-11, 2019

Immunogenicity has always been a critical safety concern, especially when many biotherapeutics are becoming increasingly complex. Understanding and controlling immunogenicity-related risks are essential in the development of biotherapeutics to ensure meeting the regulatory requirements. CHI's Twelfth Annual Immunogenicity Assessment and Regulatory Approval of Biologics conference brings industry, regulatory and scientific experts together to share best practices in assessing immunogenicity of novel biologics along with biosimilar products. The session will also discuss the challenges and solutions for addressing new regulatory guidelines in assay development and validation for cell and gene therapies.

TUESDAY, APRIL 9

Recommended Short Course*
SC11: Developability of Bispecific Antibodies: Formats and Applications
Separate registration required. **Click here or see page 5 for course details.*

WEDNESDAY, APRIL 10

7:15 am Registration and Morning Coffee

7:25 - 8:25 PANEL DISCUSSION: Women in Science – Inspired Professional and Personal Stories
Moderator: Women in Bio, Boston Chapter
Panelists:
Susan Richards, PhD, Presidential Scientific Fellow, Translational Medicine Early Development, Sanofi R&D
Joanna Brewer, PhD, Vice President, Platform Technologies, AdaptImmune
Additional Panelists to be Announced

MITIGATING STRATEGIES FOR ADA CUT-POINT AND EFFECTIVENESS

8:30 Chairperson's Opening Remarks
Zhandong Don Zhong, PhD, Associate Director, Specialty Bioanalytics, Teva Pharmaceuticals

8:40 Novel, Simplified Approaches to ADA Cut Point Calculation
John Kamerud, PhD, AR Fellow, Director, Bioanalytical, Pfizer
Investigators across the industry indicate problems with very low ADA cut point factors, which can lead to elevated rates of reported positives, many of which are not biologically relevant. This talk will describe approaches to cut point calculation in which pre-existing positive samples are identified and removed, while forgoing any additional outlier analysis to retain natural variability. The resulting cut points should better reflect meaningful immunogenicity.

9:10 Strategies for Setting Cut-Points for ADA Assays in Multi-Tier vs Single-Tier Testing in a Routine Clinical Setting
Theo Rispens, PhD, Principle Investigator, Antibody structure and function, Sanquin
Immunogenicity testing may be a useful tool to assess reasons for non-response during e.g. anti-TNF therapy. Current guidelines for ADA assays focus on early stages of testing new (or biosimilar) drugs in the clinic, but may not be optimally tailored towards practical implementation of ADA testing in the context of routine care. This presentation will address different strategies for calculating cut-points in relation to single vs multi-tier assay strategies and discuss case studies comparing these different approaches

9:40 Orthogonal Approaches and Utility of ADA Assays
Soumi Gupta, PhD, Director, Immunogenicity Assessment, BioMarin Pharmaceutical Inc.
We will demonstrate using Pegvaliase (a PEGylated bacterially derived enzyme substitution therapeutic) as a case study, how to evaluate appropriateness of the ADA assays based on integrated analysis of immunological laboratory data generated by orthogonal approaches as well as clinical safety data. We will present data generated from two different ADA assays developed against Pegvaliase, one for the detection of drug-specific IgE and the other for the detection of anti-PEG IgG/IgM antibodies, alongside laboratory and clinical safety data.

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

10:15 Women in Science Speed Networking in the Exhibit Hall

IMMUNOGENICITY PREDICTION AND ASSESSMENT

10:55 Chairperson's Remarks
Kay Stubenrauch, PhD, Expert Scientist, Pharma Research & Early Development pRED, Pharmaceutical Sciences, Large Molecule Bioanalytical R&D, Roche Innovation Center Munich

10:55 FEATURED PRESENTATION: FDA's Current Thinking on Immunogenicity Assessment of Biosimilars
William Hallett, PhD, Biologist, OPQ/OBP, CDER, FDA
An overview of immunogenicity assessment of biosimilars will be presented: current landscape of biosimilar products, success rate versus failure rate and best practices to improve the quality of immunogenicity assessment for biosimilars from an FDA's perspective.

11:25 Towards a fit for purpose approach for evaluating relevant immunogenicity of mAbs in oncology human clinical trials
Mohamed Hassanein, PhD, Staff scientist, Bioanalytical Scienices, Regeneron Pharmaceuticals
Recent data from oncology trials indicated that human mAbs (h-mAbs) elicit low treatment-emergent immunogenicity. In this presentation, we will provide a tailored approach for assessing immunogenicity of therapeutic mAbs in oncology trails that factors in both the low risk profile of h-mAbs as well as the immunity status of the target population. The

IMMUNOGENICITY ASSESSMENT AND REGULATORY APPROVAL OF BIOLOGICS continued

goal of this "fit-for-purpose" approach is to provide immunogenicity data that is relevant to health-care providers and patients.

11:55 Application of Mechanistic Modelling to Prediction of Immunogenicity

Timothy Hickling, PhD, Immunogenicity Sciences Lead, Biomedicine Design, Pfizer, Inc.

This presentation will introduce an immunogenicity consortium that coordinates vitro data to predict immunogenicity in the clinic. The wide range of data is integrated into mechanistic models for prediction, PK and ADA characterization which then allows for better decision-making when translating to the clinic.

12:25 pm The Role of Product and Process-Related Impurities in the Innate Immune Response to Biotherapeutic Proteins

Sponsored by Lonza Pharma & Biotech

Noel Smith, PhD, Principal Group Leader, Applied Protein Services, Lonza Pharma & Biotech

Immunogenicity is a common problem for biotherapeutic proteins and can impact both efficacy and safety. Human *in vitro* assays are now routinely used during early development to assess the risk of a biotherapeutic protein inducing both an innate and adaptive immune response. This presentation will focus on the use of highly sensitive human primary cell assays for the assessment of product and process-related impurities that may contribute to driving an unwanted immune response.

12:55 Enjoy Lunch on Your Own

1:20 Session Break

DRUG SPECIFIC IGE ANTIBODIES

2:10 Chairperson's Remarks

Kay Stubenrauch, PhD, Expert Scientist, Pharma Research & Early Development pRED, Pharmaceutical Sciences, Large Molecule Bioanalytical R&D, Roche Innovation Center Munich

2:15 Development and Clinical Utility of a Novel Drug-Specific IgE Assay

Zhandong Don Zhong, PhD, Associate Director, Specialty Bioanalytics, Teva Pharmaceuticals

Evaluation of drug-specific IgE is important during biotherapeutic development, as anti-drug IgE formation has been reported to potentially correlate with hypersensitivity events (anaphylaxis). Nevertheless, detection of drug-specific IgE remains challenging due to its low levels in circulation, numerous potential interfering endogenous substances, and difficulty in generating a surrogate positive control. The purpose of this presentation is to demonstrate the development and clinical utility of a novel anti-drug IgE assay platform.

2:45 Detection of Drug-Specific IgE Antibodies to Biotherapeutics: Challenges and Advances

Susan Richards, PhD, Presidential Scientific Fellow, Translational Medicine Early Development, Sanofi R&D

Most focus on immunogenicity has been on the development of IgG/IgM ADA. However, a more challenging assessment is the detection of drug specific IgE antibodies. When IgE specific ADA present on the surface of mast cells or basophils is cross-linked by binding specific antigen, a series of events unfolds including the release of pharmacologic mediators leading to the symptoms experienced by patients. This can result in hypersensitivity reactions and at an extreme anaphylaxis. Sensitive and highly specific assays are needed to detect low levels of drug specific IgE ADA in the presence of total IgE and also presence of any drug specific IgG antibodies. This presentation will discuss the challenges and progress made in detecting specific IgE ADA.

3:15 Attend Concurrent Track

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

THURSDAY, APRIL 11

8:00 am Registration and Morning Coffee

NEW ASSAY FORMAT FOR IMMUNOGENICITY ASSESSMENT

8:30 Chairperson's Remarks

Theo Rispens, PhD, Principle Investigator, Antibody structure and function, Sanquin

8:35 Impact of Impurities on Bioactivity Assays

Daniela Verthelyi, PhD, Chief, Immunology Lab, Therapeutic Proteins, CDER, FDA

Product immunogenicity has emerged as one of the critical roadblocks in the development of biologics, complex generics and biosimilars. This talk will focus on the impact of process-related innate immune response modulating impurities and aggregates on the milieu where the products are delivered highlighting the complex interplay of different impurities on product immunogenicity risk.

9:05 Streamlining Preclinical and Clinical Assessment for Immunogenicity

Shara M. Dellatore, PhD, Director, Regulated Immunogenicity and Molecular Biology Bioanalytics, Merck & Co., Inc.

The titer method has been widely used for reporting immunogenicity magnitude as part of a three tiered strategy for immunogenicity assay development and validation. Through multiple case studies, we compared traditional titer to a streamlined strategy using signal-to-noise (S/N). Overall there was a strong correlation between titer and S/N methods and proved comparable for interpretation of relevant impact. The S/N approach has multiple advantages of reduced sample volume, time, resource, cost and may be a future alternative to titer-based method.

9:35 An Integrated Approach to Managing Immunogenicity Risk and Optimum Protein Design

Sponsored by ProImmune

Emilee Knowlton, PhD, Immunology, Sales Specialist, Sales, ProImmune Inc.

Integrated platforms can be used to mitigate immunogenicity risk and characterize immune responses during the drug design and development stages. ProImmune offers mutational activity mapping for optimal protein design, DC-T/T cell proliferation assays for biologic lead selection/optimization, a Mass Spectrometry assay for characterization of antigen presentation; HLA-peptide binding assays to characterize individual epitopes & undiluted whole blood cytokine storm assays.

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

11:05 Assay Strategies to Monitor Immunogenicity of New Antibody Therapeutics in Preclinical and Clinical Studies

Kay Stubenrauch, PhD, Expert Scientist, Pharma Research & Early Development pRED, Pharmaceutical Sciences, Large Molecule Bioanalytical R&D, Roche Innovation Center Munich

Bridging immunoassays are currently the predominant assay format for immunogenicity assessment. The assay allows for high throughput testing and simple implementation. However, the reliability of bridging assays can suffer in the presence of i) an oligomeric target reducing specificity or ii) residual drug reducing sensitivity. Thus, there is a need for alternative assay formats or approaches that can overcome these inherent weaknesses. In addition, some methods are introduced to further characterize ADA responses.

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11:35 Characterization of Critical Reagents Using LBA, LCMS, and Chromatography for Use in Regulated Bioanalysis

Robert Kernstock, PhD, Senior Group Leader, R&D, Immunochemistry, PPD® Laboratories

According to the new bioanalytical guidance released by the FDA in 2018, there is an expectation to characterize critical reagents for use in regulated bioanalysis. According to the guidance, characterization includes: Identity, Purity, and Stability. We have developed a menu of services to provide reagent characterization using various analytical tools such as ligand binding assays, mass spectroscopy and protein purification to provide address the guidance recommendations.

12:05 pm Preclinical Immunogenicity Assessment of Therapeutic Protein and Antibody: Applications of a Novel ADA Assay Platform Based on Capillary Electrophoresis and Immunodetection

Shuli Zhang, PhD, Principal Scientist, PPDM Global Bioanalytics, Merck Research Laboratories

Peggy Sue is a capillary-based western/immunoassay platform that can separate proteins by size or charge. It uses a HRP-conjugated secondary antibody for detection and quantitation. In his work, this platform provides comparable ADA results to traditional bridging assays with distinct advantages. These include no requirement for labeled capture and detection reagents, reduced sample volume, and valuable charge/size characterization of the immunogenic agent. Most importantly, Peggy Sue is an ideal platform for characterization of ADA specificity against complex biologics such as bispecific or multi-specific biotherapeutics.

12:35 End of Immunogenicity Assessment and Regulatory Approval of Biologics

Recommended Short Course*

SC14: Subvisible Protein Particles in Immunogenicity: Measurement, Characterization and Impact

Separate registration required. **Click here or see page 5 for course details.*

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5TH ANNUAL

OPTIMIZING BIOASSAYS FOR BIOLOGICS

Case Studies Demonstrating Successful Bioassay Development

April 11-12, 2019 | Seaport World Trade Center | Boston, MA

As the bioassay field continues to move forward, challenges are evolving from new drug formats such as antibody therapies, cell therapy and gene therapy. There are numerous considerations to keep in mind during assay development such as lifecycle management and planning for lot release. At the Fifth Annual Optimizing Bioassays for Biologics, bioassay experts will address the top challenges in bioassay design including novel technologies, increasing complex mechanisms-of-action, regulation and the application of statistics in assay development. Case studies and best practices for handling the most common issues in biological assay design will be presented. Overall, this event will showcase ways to continue moving a biologic forward in the discovery pipeline.

THURSDAY, APRIL 11

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

BUILDING A BETTER BIOASSAY

1:40 Chairperson's Opening Remarks
David Lansky, PhD, President, Precision Bioassay, Inc.

1:50 Statistical Approaches and Considerations for QbD in Bioassay Development
Ryan Yamagata, US Function Head, CMC Statistical Sciences, Vaccines Technical Research & Development, GSK

ICH Q8(R2) does not explicitly refer to analytical method development. However, a Quality by Design (QbD) approach can also be applied to bioassay development, as discussed in USP <1032>. This presentation will review relevant statistical considerations and approaches when applying QbD principles to method development and will include examples from bioassay development.

2:20 Optimization of a Complement Dependent Cytotoxicity Assay
Kristin Abrams, Scientist, Amgen, Inc.

Complement Dependent Cytotoxicity assays are used to measure complement cascade activation for many biopharmaceuticals. These assays can be used for characterization of the ability of the product to activate the complement cascade to avoid undesired safety concerns or these can be used to measure the mechanism of activation of the targeted pathway. When these assays are used as part of product release, controlling variability is imperative. When run in QC, the CDC assay exhibited a moderate degree of variability. As part of method lifecycle management, the method was closely evaluated, and minor changes were implemented which led to major improvements in assay performance. It has become clear during this assay optimization that the changes will not only significantly improve robustness, precision, and accuracy, but also increase ease of execution.

2:50 Strategic Ways to Meet Bioassay Performance Requirements with Modular Design and Analyses
David Lansky, PhD, President, Precision Bioassay, Inc.

Reportable values (geometric mean) of potency from bioassays of lots are compared to product specifications. Process control limits for log potency are narrower than product specifications. Assay performance requirements and their control limits (on appropriate measures of assay performance) guide assay development and monitoring. Modular design and appropriate analyses support efficient and flexible development and validation as well as alternate assay formats for alternate intended uses.

3:20 Extended Q&A with Session Speakers

3:50 Networking Refreshment Break

4:20 Improving the Robustness of a Bioassay through Outlier ID and Removal
Thomas Little, PhD, President and CEO, Bioassay Sciences, Thomas A. Little Consulting

Bioassays are known for being more variable compared to other analytical methods. Variation in the dose response is generally one of the primary root causes. The presentation will discuss within dose and between dose outlier and removal concepts and how it will impact curve fitting, confidence intervals and general bioassay performance. Four Parameter Logistics and Parallel Line Analysis type bioassays will be included in the discussion.

4:50 Strategies and Approaches for Building a Better Bioassay
Alexandra Zakharova, Head, Cell-Based Assay, BIOCAD

This presentation provides an overview of strategies and general considerations for developing MOA reflective, accurate, precise, QC-friendly and phase appropriate potency assays. Potency is a critical quality attribute of biological products. The main problem of bioassays is a very high variability. In the presentation, I will demonstrate approaches that reduce the test variability, increase consistency of analysis and significantly improve the lab efficiency.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course*
SC13: Bioassay Quality by Design
Separate registration required. **Click here or see page 5 for course details.*

FRIDAY, APRIL 12

8:00 am Morning Coffee

BEST PRACTICES

8:30 Chairperson's Remarks
Perceval Sondag, Senior Manager, Statistics, PharmaLex

8:35 FEATURED POSTER: A Case Study: Addressing Assay Curve Shifts in a Bioassay for a Late Stage Therapeutic Antibody
Tongyun (Tony) Dang, PhD, Senior Scientist, BioTherapeutics Development, Discovery, Product Development, & Supply, Janssen Research & Development

Here we present a case study involving a cell-based bioassay for an IgG1 monoclonal product that had been successfully validated and

OPTIMIZING BIOASSAYS FOR BIOLOGICS continued

transferred to multiple testing sites. During late stage development, a shift of the assay curve was identified and investigated, and a root cause was determined. Through review of historical data and evaluation of critical reagents, it was determined that a single critical reagent was responsible for the assay shift. As corrective actions, the method was updated to reduce impact on future assay shifts and the critical reagent qualification procedure was improved. Strategies are discussed to prevent future occurrences of assay curve shifts.

9:05 PANEL DISCUSSION: Best Practices to Overcome Bioassay Development Challenges

Moderator: Perceval Sondag, Senior Manager, Statistics, PharmaLex

Panelists: Gaël Debauve, PhD, Head, Bioassay Development, Analytical Sciences for Biologics, UCB

Steven Walfish, MBA, Principal Scientific Liaison, USP

Alexandra Zakharova, Head, Cell-Based Assay, BIOCAD

- Statistical considerations at each stage of bioassay development
- Challenges presented by new modalities and emerging therapies
- Best practices in ensuring quality control, lot management, and release
- Implementing new technologies and techniques in assay design and validation

10:05 Networking Coffee Break

10:35 Demystifying USP Bioassay Chapters

Steven Walfish, MBA, Principal Scientific Liaison, USP

Many companies do not have access to statistical support for bioassay design and development relying on USP General Chapters for guidance. This talk gives insights into the chapters and explains some common misconceptions with them. The importance of dilutional similarity and bioassay analysis will be highlighted.

ASSAY BRIDGING

11:05 Statistical Approaches for Successful Assay Bridging

Perceval Sondag, Senior Manager, Statistics, PharmaLex

To calculate a relative potency of a vaccine batch, a reference batch is needed. The problem is that the reference batch has a life span of 3-4 years (before running out of stock, for example), and a vaccine has a commercial life of about 30 years. Bridging studies are used to estimate a correction factor between a new and an old reference batch. Statistical methodologies for a successful bridging are widely misunderstood. This talk presents an overview of the statistical methods applied to assay bridging.

11:35 Analytical Bridging: How to Cross on the Wire Stretched Between Two Bioassay Methods? A Case Study

Gaël Debauve, PhD, Head, Bioassay Development, Analytical Sciences for Biologics, UCB

Biological products rely on a wide range of analytical methods for lot release and stability testing. As method improvement is a continued effort during lifecycle management of biopharmaceuticals, bridging studies are key to demonstrate comparability between old and new methods. Through case studies, we will attempt to clear the way, sometimes complex, allowing to conclude to method equivalence.

12:05 pm Statistical Considerations for Design and Analysis of Assay Bridging Studies

Harry Yang, Ph.D., Senior Director, Statistical Sciences, Medimmune, LLC

Biological products rely on a wide array of analytical methods for product characterization, lot release, and stability testing. As method improvement is a continued effort during the lifecycle of a biopharmaceutical product, bridging studies are often conducted to demonstrate comparability of the old and new methods. In this presentation, we discuss statistical considerations in the design and analysis of bridging studies for analytical methods.

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Networking Refreshment Break

BIOASSAYS FOR EMERGING MODALITIES

1:35 Chairperson's Remarks

Craig Kaftan, Senior Scientist, Analytical Development, Pharmaceutical Sciences, Shire HGT, a Member of the Takeda Group of Companies

1:40 Identifying and Controlling Sources of Variation in Cell-Based Potency Assays

Emily Lowe, PhD, Senior Scientist, Analytical Sciences, Kite Pharma, a Gilead Company

Cell-based potency assays are essential for engineered cell therapy products to demonstrate that drug product activity is linked to biological critical quality attributes. One of the biggest challenges in designing and executing cell-based potency assays is identifying and controlling variability. A poorly controlled and highly variable potency assay can increase invalid and re-test rates, or worse, cause a manufacturing process to appear out of control or a drug product to appear unstable. Identifying and mitigating sources of variability begins during initial assay design, as part of QbD for method development, and should continue to be a focus through life cycle management. Here, we will discuss expected and unexpected sources of variability and control strategies through presentative case studies.

2:10 Challenges in Developing Bioassays for Novel Therapeutics: Focus on Antibody Drug Conjugates

Adrienne Wildt, PhD, Associate Director, Bioanalytical Sciences, Immunogen

2:40 Cytotoxicity Assay Development for CAR-T

Ashley Mullan, Scientist, Development, Analytical Sciences, AstraZeneca

3:10 The Rare Case: Bioassay Method Development and Two Happy Customers, PD and Quality

Craig Kaftan, Senior Scientist, Analytical Development, Pharmaceutical Sciences, Shire HGT, a Member of the Takeda Group of Companies

The goal of cell-based potency methods is to provide meaningful insights into a therapeutic's structural integrity and intended physiological role. Both development and implementation come with challenges inherent when working with living organisms. Additionally, potency methods need to satisfy two very different customers, PD and Quality. For product development, the methods need to be specific, precise, robust and sensitive to be effective tools to support Process and Formulation Development and Regulatory Filings while concurrently simple in execution and management to support routine GMP lot release. However, when successful, it may come with great reward such as more comprehensive product and process understanding improving the likelihood of successful, expedient new product development.

3:40 End of Conference

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FUSIONS & CONJUGATES STREAM

- **Fusion Protein Therapeutics**
- **Engineering Antibody-Drug Conjugates**
- **Clinical Progress of Antibody-Drug Conjugates**

Bioconjugates as Therapeutics: from R&D to Clinical Development

The **Bioconjugation Stream** investigates the ongoing design and R&D efforts, along with the challenges of producing such complex bioconjugates as fusion proteins and antibody-drug conjugates, while ensuring stability, specificity and efficacy. The "Fusion Protein Therapeutics" conference examines the varying constructs achieved by combining modular building blocks to reach targets not accessible to antibodies, and discusses engineering and conjugation strategies to improve efficacy, safety and clinical success. The "Engineering Antibody-Drug Conjugates" conference reveals the exciting third-generation ADC formats, and explores new cytotoxic drugs, linkers and conjugation chemistries that enhances the homogeneity and stability of the ADC; while the "Clinical Progress of Antibody-Drug Conjugates" conference addresses ADCs in preclinical to clinical development, and showcases lessons learned to improve drug design and patient outcomes.

5TH ANNUAL

FUSION PROTEIN THERAPEUTICS

Developing and Optimizing Fusion Proteins for Oncology and Beyond

April 8-9, 2019

Chimeric fusion proteins, with their ability to extend plasma half-life and prolong therapeutic activity, offer exciting benefits over antibody-based therapeutics. Companies are intensely investigating into fusion protein therapeutics as a promising alternative to antibodies. The Fifth Annual Fusion Protein Therapeutics will explore the latest developments and future prospects of this exciting modality, by inviting researchers to present their novel fc-fusion platforms, present updates from preclinical and clinical trials, and discuss engineering and conjugation strategies to improve efficacy, safety and clinical success.

SUNDAY, APRIL 7

Recommended Short Course*

SC8: Gene Therapy Products: Phase-Appropriate Analytical Development Strategies

Separate registration required. **Click here or see page 5 for course details.*

MONDAY, APRIL 8

7:00 am Registration and Morning Coffee

NOVEL FORMATS AND APPLICATIONS

8:30 Chairperson's Opening Remarks
Celine Monnet, PhD, Head of Laboratory, Research, LFB Biotechnologies

8:40 Antibody-Cytokine Fusion Proteins: From Discovery to Pivotal Clinical Trials
Dario Neri, PhD, Professor, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology (ETH Zurich)
Antibody-cytokine fusions allow to concentrate immunomodulatory activities at the site of disease, helping spare normal tissues. I will present preclinical and clinical work, conducted in collaboration between my laboratory at ETH Zürich and Philogen in the field of cancer and of chronic inflammation.

9:10 Novel Fc Platform Development and Application for Fc-Fusion Proteins
Lu Shan, PhD, Scientist II, ADPE, AstraZeneca
Monovalent fusion proteins are often a necessary drug format for optimal structure and activity profiles. We present our novel monovalent fusion platform in target validation and lead discovery.

9:40 Redefinition of RTK Tumor Targeting: How to Design Truly Potent anti-ErbB Bispecific and Biparatopic Fusion Therapeutics
Rastislav Tamaskovic, PhD, Head, TC Facility, Biochemistry, University of Zurich
Recently, we have described major compensatory routes, which become activated in therapy of HER2-positive cancer, and developed a new class of bispecific and biparatopic anti-ErbB/Met/Axl fusion protein agents endowed with capabilities to overcome the adaptive resistance. These novel targeting vehicles achieve their superior tumoricidal activity by trapping tumor-driving receptor tyrosine kinases in inactive conformations and/or supramolecular assemblies. Analogously, we build a new platform for tumor RTK fingerprinting aimed at identifying prospective therapeutic leads and truly synergistic combination therapies.

10:10 Networking Coffee Break

10:50 KEYNOTE PRESENTATION: Preconditioning the Tumor Microenvironment to Enable Effective Immunotherapy Using Antibody Fusion Proteins
Alan Epstein, MD, PhD, Professor, Keck School of Medicine, University of Southern California
In the last 10 years, my laboratory has explored the potential of antibody fusion proteins consisting of cytokines, chemokines, and co-stimulatory molecules to alter the tumor microenvironment as a new direction of cancer immunotherapy. In addition to targeting adaptive immunity, the laboratory is currently exploring the potential application of targeted innate immunity using toll-like receptor agonists chemically linked to tumor targeting antibodies. In addition, biobetter checkpoint inhibitors are being prepared that alter immunodominant pathways required for successful immunotherapy.

11:20 Leveraging FcRn-Blocking Therapeutic Utility for Autoantibody Mediated Disease through a Minimized Affibody Fusion Format
Fredrik Frejd, PhD, CSO, Affibody AB
Several diseases are mediated by autoantibodies. Reduction of antibody plasma levels by pharmacologic interference with the neonatal FcRn receptor can reduce disease burden and save lives. Antibodies are suboptimal drugs as they rely on FcRn for long plasma half-life. ABY-039 is an FcRn blocking affibody molecule that overcomes limitations of antibody-based approaches to achieve very long half-life and outpatient subcutaneous administration. Engineering, development and clinical data will be presented.

11:50 Antibody-Targeted Superantigens and Antibody Directed Enzyme Prodrug Therapy for Improved Safety and Efficacy for Cancer Treatment
Sayed Goda, PhD, Professor, Senior Scientist, Anti-Doping Lab Qatar, Cairo University
I will present novel data for cancer treatment using Antibody Directed Enzyme Prodrug Therapy (ADEPT) and Tumor Targeted Superantigens (TTS). For ADEPT, we successfully produced an ultra-active glucarpidase that degrades MTX with a very high efficiency, and produced novel fusion with our newly discovered enzyme for targeted cancer therapy. For TTS, we successfully produced truncated superantigens with much less lethality; and novel variants of superantigens with less toxicity. We are developing cancer specific antibody-superantigen fragment fusion complex for further study.

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12:20 pm Utilizing Fusion Platforms for the Development of Efficient Hemin Scavengers Towards Therapeutic Use in Sickle Cell Disease and Other Hemolytic Disorders

Elena Karnaukhova, PhD, Research Scientist, Center for Biologics Evaluation and Research, US FDA

Detrimental effects of extracellular hemin released from hemoglobin are critically involved in hemolytic disorders. In the US alone, more than 100,000 people have homozygous sickle cell disease, however, currently there is no treatment to prevent or minimize the adverse consequences induced by the hemin release. This presentation focuses on the biophysical evaluation of hemin scavengers, utilizing fusion platforms, in collaboration with our colleagues from CSL Limited, Bio21 Institute, Parkville, Australia and University Hospital of Zurich, Switzerland.

12:50 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, AstraZeneca

4:10 *Vision for How Immunotherapy Will Shape Future of Cancer Care*

Leena Gandhi, MD, PhD, Vice President, Immuno-Oncology Medical Development, Lilly Oncology

Immunotherapy is considered by many as a pillar of cancer care today, but in many ways we have only scratched the surface. Our knowledge and understanding of the complexities of immunotherapy and its mechanisms continue to evolve. The future of cancer care will be defined by our ability to systematically identify and implement opportunities for combination therapy to improve and standardize patient response.

4:55 The Lassa Virus Glycoprotein: Stopping a Moving Target

Kathryn Hastie, PhD, Staff Scientist, Immunology and Microbiology, The Scripps Research Institute

Lassa virus causes ~5000 deaths from viral hemorrhagic fever every year in West Africa. The trimeric surface glycoprotein, termed GPC, is critical for infection, is the target for neutralizing antibodies, and a major component of vaccines. Structural analysis of Lassa GPC bound to antibodies from human survivors reveals a major Achilles heel for the virus and provides the needed template for development of immunotherapeutics and improved vaccines.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:15 End of Day

TUESDAY, APRIL 9

8:00 am Registration and Morning Coffee

ENGINEERING AND OPTIMIZATION OF FUSION PROTEINS

8:25 Chairperson's Remarks

Dario Neri, PhD, Professor, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology (ETH Zurich)

8:30 Synergistic Cytotoxicity Promoted by Human Serum Albumin Fusion Protein and Fatty Acid-Modified 5-Fluorouracil

Zhiyu Li, PhD, Associate Professor of Pharmaceutical Sciences, Director, Pharmacology and Toxicology Undergraduate Program, Department of Pharmaceutical Sciences, Philadelphia College of Pharmacy

Human serum albumin and p53-derived peptide fusion protein (rHSA-p53i) and recombinant wild type albumin (rHSA) exhibited similar biodistributions in mice; however, rHSA-p53i accumulated much more in tumor tissue. This fusion protein could also induce cytotoxicity irrespective of p53 status and display synergistic cytotoxicity with 5-fluorouracil (5FU) in cancer cells. Therefore, fatty acid-modified 5FU (FA-5FU) was synthesized to form stable non-covalent complexes with rHSA-p53i. FA-5FU showed cytotoxicity comparable with that of 5FU and FA-5FU/rHSA-p53i complexes together achieved a profound synergistic anticancer efficacy *in vitro* and *in vivo* in SJSA-1 and MDA-MB-231 xenograft mouse models.

9:00 Fc Sialylation Prolongs Serum Half-Life of Therapeutic Antibodies

Celine Monnet, PhD, Head of Laboratory, Research, LFB Biotechnologies

We demonstrated a hitherto unrecognized impact of Fc hyper-sialylation of the Asparagine 297 on the prolongation of IgG1 serum persistence. The enhanced longevity was due to the sialylated sugar moiety itself and did not modify the binding affinity to the neonatal Fc receptor (FcRn). This polarized glycosylation is achieved using a novel Fc mutation, a glutamate-residue deletion at position 294 (Del) that endows therapeutic antibodies with an up to 9-fold increase in serum lifespan.

9:30 Potential Applications of A New Recombinant Protein Format: Self-Assembling Nanoclusters for Protein Delivery and Protein Purification Purposes

Elena Garcia Fruitós, PhD, Researcher, Ruminant Production, Institute of Agriculture and Food Research and Technology

The reduction of production costs and stability improvement of recombinant soluble proteins remains a challenge. In this scenario, we have been working on the development of a new protein format based on self-assembling nanoclusters as a promising alternative in terms of stability and slow release for protein delivery and protein purification purposes. For that, we are working with endotoxin-free expression systems such as Lactococcus lactis and Lactobacillus plantarum.

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

FUSION PROTEINS FOR NON-ONOLOGY INDICATIONS

10:50 Next-Generation Antibody-Guided Enzyme Replacement Therapy for Lysosomal Diseases

Katherine Cygnar, PhD, Senior Staff Scientist, Genome Engineering Technologies, Regeneron Pharmaceuticals

Enzyme replacement therapy revolutionized treatment for lysosomal diseases, but many patients still show progressive disease on therapy mainly due to poor enzyme uptake in critical tissues. Here we show a fusion protein between the enzyme and an antibody binding an internalizing protein improves enzyme delivery to critical tissues, and completely/near-completely corrects disease phenotypes in a mouse model of Pompe disease. This platform is amenable to both protein therapeutics and gene therapy.

11:20 Platform Technology for Treatment of the Brain in Lysosomal Storage Disorders with IgG-Fusion Proteins: Preclinical and Clinical Update

Ruben Boado, PhD, Vice President, R&D and Co-Founder, ArmaGen, Inc.

Protein therapeutics can be re-engineered as brain

penetrating IgG-fusion proteins for the CNS treatment of rare disorders, like Lysosomal Storage Disorders (LSD). The BBB-penetration of enzyme therapeutics is enabled by re-engineering the recombinant enzyme as bi-functional IgG fusion proteins. The enzyme therapeutic domain of the fusion protein exerts the pharmacological effect in brain once across the BBB. Several brain penetrating IgG-LSD fusion proteins have been engineered and validated. First-in-human POC Phase II clinical trial in LSD will be discussed.

11:50 Protein Engineering by Directed Evolution to Derive ALPN-101, a Dual ICOS/CD28 Antagonist ICOSL Variant Ig Domain (vIgD)-Fc Fusion Protein for the Treatment of Inflammatory Diseases

Mark Rixon, PhD, Senior Director, Protein Therapeutics, Alpine Immune Sciences

ALPN-101 is an Fc fusion protein designed to inhibit simultaneously the CD28 and ICOS costimulatory pathways. Through directed evolution of the ICOSL extracellular variable Ig domains, Alpine Immune Sciences has engineered ALPN-101 to have increased affinity to the natural counter structure ICOS and gain of binding to the non-cognate ligand CD28. Preclinical data demonstrate superior *in vitro* and *in vivo* efficacy and corroborate the dual ICOS/CD28 antagonism of T cell costimulatory signaling.

12:20 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on your Own**

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

FUSION PROTEINS AS IMMUNOTHERAPY AGENTS

2:00 Chairperson's Remarks

Alan Epstein, MD, PhD, Professor, Keck School of Medicine, University of Southern California

2:05 Engineering Hexavalent TNFR-SF Agonists for Cancer Immunotherapy: A Unique Class of Biologics

Oliver Hill, PhD, Vice President, Molecular Biology/ Protein Engineering, Apogenix AG

Apogenix's Hexavalent TNFR-SF agonist (HERA) is based on trivalent but single-chain molecular mimics of the TNF-SF receptor binding domains fused to a dimerization scaffold. The resulting hexavalent fusion proteins are potent TNFR-SF agonists that activate distinct immune cell populations involved in the anti-tumor immune reaction thereby enabling exciting opportunities for combination treatment with other I-O drugs. The engineering details and recent results obtained for HERA-CD40L, HERA-CD27L, and HERA-GITRL will be presented.

2:35 Development of a Novel Multi-Specific Antibody Targeting PD-L1-Overexpressing Cancers by Engagement of Antigen-Committed CD8+ T Cells via the Costimulatory Receptor 4-1BB

Sebastian Meyer, PhD, COO, Numab Innovation AG

Targeting PD-L1 and 4-1BB with a multi-specific antibody format holds the promise of increased potency while improving the safety profile compared to combination therapy. Numab develops a molecule that potently blocks PD-L1/PD-1 signaling and elicits further T cell activation through its costimulatory domain. Preclinical data show efficacy on tumor growth in combination with an enhanced intratumoral CD8+ T cell activation when compared to the combination of the PD-L1 and 4-1BB modalities.

3:05 IL-DR2 Fc Is a Novel Regulator of Immune Homeostasis and Inducer of Antigen-Specific Tolerance

Stephen D. Miller, PhD, Judy Gugenheim Research Professor, Director, Interdepartmental Immunobiology Center, Microbiology-Immunology, Northwestern University Medical School

ILDR2 is a member of the Ig superfamily and has a putative role in pancreatic islet health and survival. We recently found a novel role for ILDR2 in delivering inhibitory signals to T cells. ILDR2-Fc displays a unique mode of action, combining immunomodulation, regulation of immune homeostasis, and re-establishment of Ag-specific immune tolerance via induction of regulatory T cells. These findings support the potential of ILDR-Fc as a promising therapeutic approach for the treatment of autoimmune diseases.

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

IMPROVING CYTOPLASMIC DELIVERY AND PK PROPERTIES

4:25 The Evolving Science and Long-Term Outcomes of Fc Fusion Factors

Joe Salas, PhD, Executive Director, Protein Therapeutics, Bioverativ Inc.

4:55 POSTER HIGHLIGHTS

I: Cytoplasmic Delivery of Inhibitory Antibodies

Andrew Tsourkas, PhD, Professor, Bioengineering, University of Pennsylvania

Antibodies can directly neutralize their antigen's biological activity, but their inability to cross the plasma membrane has limited them to secreted or membrane-associated targets. We have developed a site-specific bioconjugation strategy that links anionic polypeptides to native IgGs, allowing them to be complexed with lipids and polymers originally developed for nucleic acid delivery. The resulting complexes can efficiently deliver antibodies that inhibit drug targets into the cytoplasm, demonstrating that cytoplasmic antibodies are a viable new class of therapeutics.

II. Utlizing Bioorthogonal Chemistry for improving the Pharmacokinetic Properties and Inhibitory Activity of N-TIMP2

Hezi Hayun, PhD, Biotechnology Engineering, Ben Gurion University

Matrix metalloproteinases (MMPs) are a family of zinc-dependent enzymes that regulate the degradation of the extracellular matrix (ECM) components, in biological processes such as angiogenesis and wound healing. MMPs activity is regulated by natural Tissue Inhibitors of Metalloproteinases (TIMPs) that can inhibit MMP's activity, but some can also mediate activation of some pro-MMPs. Synthetic MMP inhibitors exhibit great inhibition by chelating the MMP catalytic Zn2+, but have some drawbacks such as poor pharmacokinetics and severe adverse effects, which limit their use as therapeutic drugs.Engineering approach showed that the N-terminal domain of TIMP-2 (N-TIMP2) is sufficient to inhibit MMPs activity, without leading to pro-MMP-2 activation. Thus, we have decided to use bioorthogonal chemistry to incorporate a non-canonical amino acid (NCAA) into N-TIMP2, allowing a site-specific PEGylation and a better control for this modification. We have managed to incorporate propargyl lysine (PrK) into N-TIMP2 in different positions. This residue is aimed to be conjugated with PEG-azide in a click chemistry reaction, followed by examination of the inhibition activity towards MMP-14 as well as the pharmacokinetic properties of the modified variants in *in vitro* and *in vivo* studies.

5:25 End of Fusion Protein Therapeutics

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*
SC11: Developability of Bispecific Antibodies: Formats and Applications
Separate registration required.* ***Click here* *or see page 5 for course details.*

Cambridge HEALTHTECH Institute
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9TH ANNUAL

ENGINEERING ANTIBODY-DRUG CONJUGATES

Innovations in Next-Generation ADC Design

April 10-11, 2019

In this first installment of our 2-part ADC program, PEGS Boston's Ninth Annual Engineering Antibody-Drug Conjugates invites scientists to present their design strategies to increase therapeutic index through novel payloads, alternative platforms and new linker conjugation technologies.

WEDNESDAY, APRIL 10

7:15 am Registration and Morning Coffee

7:25 - 8:25 PANEL DISCUSSION: Women in Science – Inspired Professional and Personal Stories

Moderator: Women in Bio, Boston Chapter

Panelists:

Susan Richards, PhD, Presidential Scientific Fellow, Translational Medicine Early Development, Sanofi R&D

Joanna Brewer, PhD, Vice President, Platform Technologies, AdaptImmune

Additional Panelists to be Announced

NOVEL PAYLOADS AND NEW PLATFORMS

8:30 Chairperson's Opening Remarks

Anton Neschadim, PhD, MBA, CEO, ImmunoBiochem Corporation

8:40 Enabling Silvestrol as a Novel Payload for Antibody-Drug Conjugates

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

This talk will focus on the discovery and optimization of silvestrol analogs as a novel class of antibody-drug conjugate payloads. The key learnings around drug metabolism will be discussed and how this can be avoided through engineering of the antibody or small molecule. Finally, several stable conjugates were advanced into *in vivo* studies and efficacy and safety data will be presented.

9:10 ADCs with Novel Kinesin Spindle Protein Inhibitor Payloads and a Tailor-Made Linker Chemistry

Hans-Georg Lerchen, PhD, Chief Scientist, Drug Discovery, MedChem, Bayer AG

Inhibitors of kinesin spindle protein (KSPi) have been developed as a novel payload class in antibody-drug conjugates. To increase tumor selectivity of ADC metabolism, a tumor associated protease with a unique cleavage sequence is utilized for lysosomal ADC cleavage and release of active metabolites with an appropriate profile matching the KSPi mode of action.

9:40 NAMPT Inhibitors as a Novel Payload Class for Antibody-Drug Conjugates

Chris Neumann, PhD, Principal Scientist, Medicinal Chemistry, Seattle Genetics

ADC technology is limited by the diversity of chemical payloads that retain activity in this targeted delivery format. Our group has identified NAMPT inhibitors as an ADC-compatible drug class with a distinctive mechanism targeting cellular metabolism. We report the development of a hydrophilic, cleavable linker for NAMPT inhibitors that enables targeted delivery. The favorable activity and toxicity profiles of the ADCs in preclinical models demonstrates a promising advance in the field with potential clinical utility.

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

10:15 Women in Science Speed Networking in the Exhibit Hall

10:55 Towards a Deeper Understanding of the Immune Modulatory Properties of Cytotoxic Antibody-Drug Conjugates

Tony D'Alessio, PhD, Senior Research Investigator, Oncology Biotherapeutics, Novartis Institutes for Biomedical Research

Antibody-drug conjugates (ADCs) are multi-component drugs that leverage several mechanisms of action including immune-modulation of the tumor microenvironment. Our investigations have focused on dissecting the role played by the antibody component vs. that of the payload and the specific molecular mechanisms that drive immune-modulation by anti-mitotic ADCs. Our data further our understanding of the complex pharmacodynamic changes induced by ADCs and highlight avenues for rational combination strategies.

11:25 Drug Conjugates Based on Engineered Affibody Molecules

Torbjörn Gräslund, PhD, Professor, Protein Science, KTH Royal Institute of Technology

Affibody molecules are small (58 aa), folded and robust non-Ig based affinity proteins. We have recently developed drug conjugates based on engineered affibody molecules with specific affinity for the HER2 receptor, coupled to the small molecule drug DM1. Affibody molecules allow for site-specific drug attachment and easy control over DAR. We found that the drug conjugates were potent agents for treatment of xenografted human tumors in mice.

11:55 Bispecific ADCs for Improved Tumor Targeting Specificity

David V. Liu, PhD, Director, Protein Engineering, Abbvie

The combination of two specificities against targets co-expressed on cancer cells has the potential to improve specificity of targeting and increase the therapeutic index of antibody-drug conjugates. In this presentation, data will be presented on a 1+1 bispecific antibody-drug conjugate against two cancer stem cell associated targets. The discovery, *in vitro* screening and *in vivo* validation of this construct will be presented.

Sponsored by CHEMICAL COMPUTING GROUP

12:25 pm Computational Approaches for Optimizing the Developability of Biotherapeutics

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

mAb candidates identified from high-throughput screening or binding affinity optimization often present liabilities for developability, such as aggregation-prone regions or poor solution behavior. In this work, we optimized an integrin α11 binding mAb for developability using homology modeling and rational design where reducing hydrophobic surface

patches improved HIC behavior. A retrospective data analysis demonstrates that 3D descriptors and multi-parameter models can screen candidates and enrich libraries with favorable developability properties for a range of biotherapeutics.

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

1:55 Session Break

ADCS TARGETING THE TUMOR MICROENVIRONMENT

2:10 Chairperson's Remarks
Philipp Spycher, PhD, PSI Founder Fellow, Center for Radiopharmaceutical Sciences (CRS), Paul Scherrer Institute

2:15 KEYNOTE PRESENTATION: Using Matrix Protein Affinity to Modulate the Tumor Microenvironment
Jeffrey A. Hubbell, PhD, Eugene Bell Professor in Tissue Engineering, Institute of Molecular Engineering, University of Chicago
Cancer immunotherapy with immune checkpoint inhibitors (CPI) and interleukin (IL)-2 has demonstrated clinical efficacy but is frequently accompanied with severe adverse events caused by excessive and systemic immune system activation. Here, we addressed this need by targeting both the CPI antibodies αCTLA4 + αPD-L1 and the cytokine IL-2 to tumors via conjugation or recombinant fusion to a collagen-binding domain derived from the blood protein von Willebrand factor A3 domain, harnessing the exposure of tumor stroma collagen to blood components due to the leakiness of the tumor vasculature.

2:45 Overcoming Cancer Heterogeneity with Tumor Microenvironment-Targeted Antibody-Drug Conjugates
Anton Neschadim, PhD, MBA, CEO, ImmunoBiochem Corporation
Solid tumors are evasive and heterogeneous, lacking surface tumor markers that are expressed consistently and abundantly. Unlike surface-based targets, levels of certain proteins in the cancer cell secretomes are selectively increased in the tumor microenvironment, but not normal environment. ImmunoBiochem is leveraging these targets for the selective delivery of highly-potent payloads directly to all cancer cells in the tumor, as well as various tumor-supporting cells, overcoming the challenges of heterogeneity, resistance and poor tumor penetration.

3:15 Modular coiled-coil masking domains for tumor-specific antibody activation
Vivian Trang, PhD, Scientist, Protein Sciences, Seatte Genetics
Monoclonal antibody therapeutics are powerful due to their remarkable selectivity for a chosen antigen; however, antibody therapies can still be limited by target-mediated toxicity. An emerging concept in the field of ADCs is to restrict antibody binding in a disease-specific manner by restricting binding to healthy tissues. This was previously accomplished by fusing custom masking groups to the antibody through cleavable sequences that can be activated upon hydrolysis by disease-associated proteases. Here, we describe a modular masking domain that is able to prevent antibody binding to antigen until the mask is removed using proteases. This modular approach represents an advance in the field of antibody pro-drugging as the domain can be applied to an array of therapeutic antibodies and ADCs.

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

THURSDAY, APRIL 11

8:00 am Registration and Morning Coffee

OPTIMIZING LINKERS AND CONJUGATION TECHNOLOGIES

8:30 Chairperson's Remarks
Thomas Pillow, PhD, Senior Scientist, Discovery Chemistry, Genentech

8:35 Taming Random Conjugation: A General Approach for Equimolar Conjugation of Proteins and Payloads
Sergii Kolodych, PhD, CSO, Syndivia
Multiple conjugation sites are usually available on a biomolecule. Upon conjugation, they produce a mixture of species having different degrees of conjugation (DoC). We report a general conjugation approach for achieving a defined DoC, which is virtually applicable to any biological macromolecule and payload. Applied to native antibodies, the method yields highly homogenous antibody-drug conjugates, antibody-oligonucleotide conjugates as well as bispecific scaffolds.

9:05 Disulfide Re-Bridging with Pyrrolobenzodiazepine Dimers Enable the Formation of Homogeneous, Potent and Differentiated Full-Length Antibody and Fab-Fragments Drug Conjugates
Nazzareno Dimasi, PhD, Associate Director R&D, AstraZeneca
Homogeneous full-length antibodies and Fab-fragments pyrrolobenzodiazepine conjugates with a drug to antibody ratio of one are presented. These ADCs are prepared using dual-maleimide pyrrolobenzodiazepine dimers that have been engineered to re-bridge two adjacent cysteines at the antibody hinge, at an engineered position in the CH2 domain and at the Fab cysteines forming the intrachain disulfide bond.

9:35 POSTER HIGHLIGHT: Tri-Mannosyl Antibody: A Novel Site-Specific and Dual Payload Glycoengineering Antibody Drug Conjugation Platform by Glycoengineering
Shih-Chong Tsai, PhD, Sr Research Scientist, Deputy Executive Director, Institute of Biologics Development Center for Biotechnology
We report a high efficiency glycogengineering technology by using a GnT-I (UDP N-Acetyl glucosamine transferase I) and a GnT-II (UDP N-Acetyl glucosamine transferase II) as enzymes to conjugate a tri-mannosyl core antibody and produce a novel format ADC. Our results show that a tri-mannosyl Trastuzumab 2(GlcNAc-triazole-DBCO-(PEG)4-DM1)-2(GlcNAc-triazole-DBCO-PEG4-Vc- PAB- (PEG)2-Duocarmycin SA) is generated with the conversion efficiency over 90% and 40% recovery rate. The biological activities of tri-mannosyl ADC products produced were further confirmed by the Her2 ECD binding ELISA assay and the cytotoxicity assay. Our results indicate that the tri-mannosyl ADC product does not only have a similar KD to that of commercial Kadcyla, but also has cytotoxic activities to Her2/Neu low-expression and Kadcyla-resistant cell line MDA-MB-175VI I. These studies suggest that GnT-1 and GnT-2 have very good potentials to develop a dual payload and site-specific ADC platform when a tri-mannosyl antibody is used as start material. In the future a large scale preparation will be applied.

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

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11:05 Site-Selective, Serum Stable ADCs Using Next-Generation Maleimide Linkers

James Baker, PhD, Associate Professor, Chemistry, University College London

This talk will describe the development and application of the next-generation maleimide class of reagents for the construction of ADCs. It will include a discussion of optimized dibromomaleimide and monobromomaleimide platforms for the rapid formation of robustly stable ADCs, by either rebridging the native disulfide bonds or conjugating to ThiomabsTM respectively. Insights into the application of these approaches for the construction of multispecifics will also be made, along with new enabling conjugation platforms.

11:35 Straightforward Site-Specific Payload Attachment to Native Antibodies without Antibody Engineering

Philipp Spycher, PhD, PSI Founder Fellow, Center for Radiopharmaceutical Sciences (CRS), Paul Scherrer Institute

We will introduce a new antibody-conjugation technology that enables site-specific payload attachment to native antibodies without engineering. Using this approach, well-defined ADCs can be generated directly from antibodies 'off-the-shelf' within less than two days and that have a drug-to-antibody ratio (DAR) of 2. We will provide a comprehensive set of data demonstrating that the ADCs generated with our new technology retain their binding properties, are highly cytotoxic to target over-expressing cell-lines and are stable with no drug-loss over extended periods.

12:05 pm ALT-P7: Development of HER-2 Targeting ADC for Treatment of Breast/Gastric Cancer by Use of Site-Specific Conjugation (Nexmab) Technology

Sunbae Lee, PhD, Senior Research Scientist, Alteogen

In NexMab conjugation technology, metal-ion binding peptide motif is introduced at the C-terminus of antibody heavy chain for the site-specific conjugation of payload. This talk will present the high structural stability and in intro/vivo efficacy of HER-2 targeting ADC, constructed by NexMab conjugation method with DAR 2.

12:35 End of Engineering Antibody-Drug Conjugates

Recommended Short Course*
SC12: Design Strategies and Development of ADCs

Separate registration required.* ***Click here* *or see page 5 for course details.*

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

9TH ANNUAL

CLINICAL PROGRESS OF ANTIBODY-DRUG CONJUGATES

Advancing Novel ADC Platforms and Combinations to the Clinic

April 11-12, 2019

Antibody-drug conjugates (ADCs) continue to emerge as a strong and promising strategy for target cancer therapy. Companies are leveraging on lessons learned from first- and second-generation trials to inform on next-generation ADC designs. PEGS Boston's Ninth Annual Clinical Progress of Antibody-Drug Conjugates invites investigators to share their latest results from preclinical and clinical trials, lessons learned to inform drug design & dosing, and strategies to improve safety, efficacy and patient outcomes.

THURSDAY, APRIL 11

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

STRATEGIES TO INFORM DRUG DESIGN & DOSING, AND IMPROVE PATIENT OUTCOMES

1:40 Chairperson's Opening Remarks
Thomas Held, MBA, Vice President, ADC Task Force, Daiichi Sankyo

1:50 Single-Cell PK/PD of Antibody-Drug Conjugates and Immuno-Oncology Agents to Design More Effective Therapies
Greg Thurber, PhD, Assistant Professor, Chemical Engineering and Biomedical Engineering, University of Michigan

Antibody-drug conjugates and checkpoint inhibitors are powerful agents in the treatment of cancer. However, the delivery and distribution of these agents in the tumor microenvironment is complex. We are using single-cell measurements within the tumor to inform better decisions on drug design and dosing.

2:20 Chemo-Enzymatic Glycan Conjugation of Toxic Payloads: Clinical-Stage GlycoConnect™ ADCs Demonstrate Superior Therapeutic Index
Sander van Berkel, PhD, Director, R&D Operations, Synaffix B.V.

The native glycan of monoclonal antibodies is evolving as a privileged site to generate ADCs with a significantly improved therapeutic index, as corroborated by a multitude of studies in rodents and NHPs. While the first clinical studies with a GlycoConnect™ ADC are now underway (NCT03700294), we will discuss how mAb glycan structure correlates with therapeutic index, as well as aspects of CMC supply chain and regulatory considerations towards IND filing.

2:50 Developing Antibody-Drug Conjugates as Targeted Conditioning Agents for Bone Marrow Transplant
Charlotte McDonagh, PhD, Vice President, Head, Biotherapeutics, Magenta Therapeutics

Many diseases can be cured by a bone marrow transplant. Prior to transplant, patients are conditioned by removing their own bone marrow stem cells using toxic, non-selective chemotherapy and radiation. Many patients suffer serious side effects, and others refuse a transplant. This presentation will highlight preclinical development of antibody-drug conjugates that may be safer, targeted agents for patient preparation with the aim of extending the use of curative bone marrow transplant and improving patient outcomes.

3:20 Development and Clinical Updates on Sacituzumab Govitecan
Robert Iannone, MD, MSCE, Head, R&D, CMO, Immunomedics

3:50 Networking Refreshment Break

IMPROVING THE SAFTEY AND EFFICACY OF ADCs

4:20 Preclinical Study of Liver Injury Induced by T-DM1: Molecular Mechanisms of T-DM1-Induced Hepatotoxicity
Wen Jin Wu, MD, PhD, Senior Investigator, OBP, CDER, FDA

Hepatotoxicity is one of the serious adverse events associated with T-DM1. We show that T-DM1 is internalized upon binding to cell surface HER2, resulting in DM1-associated cytotoxicity, including disorganized microtubules, nuclear fragmentation/multiple nuclei, and cell growth inhibition. Based on our data, we propose that T-DM1-induced upregulation of TNFa enhances the liver injury that may be initially caused by DM1-mediated intracellular damage. In addition, a novel target that mediates T-DM1-induced hepatotoxicity will also be discussed.

4:50 POSTER HIGHLIGHT: Exploring the Ever-Evolving Bioanalytical Strategy for ADCs from Discovery to the Clinic
Edit Tarcsa, PhD, Director, Drug Metabolism & Pharmacokinetics, AbbVie

ADCs are complex therapeutic modalities with the possibility of forming multiple analytes *in vivo*. A wide variety of assays and multiple analytical platforms had been utilized for their characterization. How do we chose what is appropriate to support decision making at the various stages of a project and how does one go by balancing speed, quality and available reagents. Since the key questions to answer during drug discovery (ADC optimization), versus late stage development are usually very different, therefore the analytes and assays appropriate to answer those questions could also be different. A few case studies and a bioanalytical decision tree will illustrate the issues.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course(s)*
SC12: Design Strategies and Development of ADCs

Separate registration required.* ***Click here* *or see page 5 for course details.*

FRIDAY, APRIL 12

8:00 am Morning Coffee

8:30 Chairperson's Remarks
Greg Thurber, PhD, Assistant Professor, Chemical Engineering and Biomedical Engineering, University of Michigan

8:35 KEYNOTE PRESENTATION: The House of Vedotins
Robert J. Lechleider, MD, Senior Vice President, Clinical Research, Seattle Genetics
Antibody-drug conjugates have proven effective in treating an array of cancers. Among the most active drug-linker combinations is monomethyl-auristatin E (MMAE) coupled to a targeting antibody via a valine-citrulline linker. MMAE conjugates have shown activity in heme and solid tumors using a number of targeting antibodies. The role and future of MMAE drug conjugates in the treatment of cancer will be discussed.

PRECLINICAL UPDATES AND PROOF-OF-CONCEPT

9:05 A Novel Antibody-Drug Conjugate Targeting ADAM9-Expressing Solid Tumors Demonstrates Potent Preclinical Activity
Stuart Hicks, PhD, Director, Pipeline R&D, ImmunoGen
ADAM9 is a cell surface protein that belongs to the ADAM (a disintegrin and metalloproteinase) family of proteases and is overexpressed in multiple solid tumor indications. IMGC936 is a novel ADAM9-targeting ADC comprised of a high-affinity humanized antibody site-specifically conjugated to DM21, a next-generation linker-payload that combines a maytansinoid microtubule-disrupting payload with a stable peptide linker. IMGC936 shows compelling efficacy in ADAM9-positive xenograft models and was well-tolerated following repeat dosing in cynomolgus monkeys making IMGC936 a promising therapeutic candidate to target a wide range of ADAM9-expressing tumors.

9:35 CD163 as a Target for Directing ADCs to Macrophages in Cancer and Inflammation – Preclinical Proof of Concept
Jonas Heilskov Graversen, PhD, Associate Professor, Molecular Medicine, University of Southern Denmark
We have validated the macrophage specific internalization receptor CD163 as an ADC target in cancer and inflammation. PoC studies in mice, rats and pigs show a strongly reduced (50-fold) effective dose for anti-inflammatory effect when targeting dexamethasone to macrophages (endotoxemia and NASH models). In cancer we observe substantially increased infiltration of effector T-cells and T-cell dependent tumor regression in a murine anti-PD-1 resistant melanoma model when eradicating tumor associated macrophages by toxin targeting.

10:05 Networking Coffee Break

CLINICAL DEVELOPMENT AND LESSONS LEARNED

10:35 Amanitin-based Antibody-Drug-Conjugates as New Therapeutic Modalities for Cancer Therapy
George Badescu, PhD, VP Scientific Affairs, Heidelberg Pharma
Antigen-Targeted Amanitin-Conjugates (ATACs) represent a new class of ADCs using the payload Amanitin. This payload introduces a novel mode of action into oncology therapy, the inhibition of RNA polymerase II. The technology platform includes Amanitin supply, site-specific conjugation, demonstrated safety profile and biomarker. HDP-101 is the first ATAC directed against BCMA entering Phase I trials by the end of 2019.

11:05 Targeting Breast Cancer with Antibody-Drug Conjugates
Aditya Bardia, MD, MPH, Assistant Professor, Medicine, Harvard Medical School
Chemotherapy is the mainstay of management of multiple solid tumors, but can be associated with considerable adverse effects. Conceptually, antibody-drug conjugates can be utilized for targeted delivery of toxic payloads to cancer cells. However, antigen selection of antigen and tumor heterogeneity are significant challenges in clinical development of novel antibody-drug conjugates. In this presentation, we will review potential therapeutic strategies and the clinical development of antibody-drug conjugates in breast cancer.

11:35 Discovery of Next-Generation ADCs: Preclinical and Clinical Development of AVID100, an EGFR-Targeting ADC
Maureen O'Connor-McCourt, PhD, CSO, Forbius
AVID100 is an EGFR-targeting ADC which was designed by screening a library of anti-EGFR ADCs against both tumor and normal cells expressing EGFR. This approach enabled us to identify AVID100, which exhibited a very promising therapeutic index in preclinical studies. AVID100 recently completed a successful phase 1 clinical program and a phase 2 study has been initiated. Importantly, only modest skin toxicity was observed, as predicted by our preclinical data.

12:05 pm [Fam-] Trastuzumab Deruxtecan (DS 8201) Clinical Development Update
Thomas Held, MBA, Vice President, ADC Task Force, Daiichi Sankyo

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Networking Refreshment Break

1:35 Chairperson's Remarks
Maureen O'Connor-McCourt, PhD, CSO, Forbius

NEXT-GENERATION ADCS

1:40 Next-Generation ADCs: Considerations and Examples
Marc Damelin, PhD, Executive Director, Head of Biology, Mersana Therapeutics, Inc.
I will discuss considerations for the discovery and development of next-generation ADCs as informed by learnings from the field's collective experience. Topics will include target selection, molecular design, and preclinical pharmacology.

2:10 Targeting CD74 with a Novel Antibody-Drug Conjugate, STRO-001 for Treatment of B-Cell Malignancies
Arturo Molina, MD, MS, FACP, CMO, Sutro Biopharma

2:40 Antibody-Drug Conjugates Targeting Tumor Stromal Cells
Brad St. Croix, PhD, Head, Tumor Angiogenesis Unit, Mouse Cancer Genetics Program, National Cancer Institute
Targeting the tumor stromal cells in addition to tumor cells with ADCs is a promising anti-cancer strategy. CD276 and TEM8 are variably expressed in a variety of cancers and to different extents on tumor stromal cells and tumor cells. Both CD276-ADC-PBD and TEM8-ADC-MMAE eradicated large established tumors and metastases and improved long-term overall survival in several different mouse models of cancer. The mechanistic basis for the efficacy of these agents will be discussed, along with implications for other vascular-targeted ADCs

3:10 Tisotumab Vedotin – A Novel Tissue Factor-Targeting Antibody-Drug Conjugate for the Treatment of Advanced Solid Tumors
Jeffrey Harris, PhD, Associate Director, Translational Research, Genmab
Tisotumab vedotin (TV) is an antibody-drug conjugate (ADC) that binds and interferes with tissue factor signaling, has potent anti-tumor activity *in vitro* and *in vivo*, and minimal effect on pro-coagulant activity. TV is efficiently internalized to the lysosome of the cell, making it an optimal ADC. TV is currently being tested in multiple clinical trials evaluating the safety, tolerability, and anti-tumor activity in patients with previously treated and advanced metastatic solid tumors.

3:40 End of Conference

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- **Genome Editing with CRISPR**

Cutting-Edge Science and Technology to Deliver New Therapeutic Applications

The **Emerging Therapeutics & Technologies stream** comprises of 3 unique topics, offering an interdisciplinary approach for protein scientists from discovery, microbiology, genomics, chemistry and engineering to come together to uncover new therapeutic applications and cutting-edge technologies. Emerging Indications for Therapeutic Antibodies will reveal new targets and novel mechanisms of actions for development of next-generation therapeutics beyond oncology. New this year is the Oncolytic Viral Therapy conference, which will showcase the latest research, translational and clinical development in this fast-emerging field. The week closes with a CRISPR Genome Editing training seminar that will provide a comprehensive review of gene editing strategies and applications in disease modeling, discovery and development.

2ND ANNUAL

EMERGING INDICATIONS FOR THERAPEUTIC ANTIBODIES

R&D Advances in Non-Cancer Indications for Antibodies and Other Biotherapeutics

April 8-9, 2019

Significant scientific advances in the fields of immunology and protein science are driving the development of biotherapeutic drugs in a growing range of therapeutic areas beyond oncology. These advances are driving the identification of new and unique targets, new approaches to developing biotherapeutics for unserved medical needs, methods of binding to illusive targets and translational science for patient stratification and drug development for niche indications. The PEGS Emerging Indications for Therapeutic Antibodies conference provides a forum for research organizations with diverse portfolios to explore new science and technology in the development of a next generation of safe and effective therapeutics in an important set of emerging indications.

SUNDAY, APRIL 8

Recommended Short Course(s)*

SC2: Translational Biotherapeutic Development Strategies Part 1: Discovery, Molecular Assessment and Early Stage Development

SC7: Translational Biotherapeutic Development Strategies Part 2: Analytical and Clinical Considerations

Separate registration required.* ***Click here* *or see page 5 for course details.*

MONDAY, APRIL 8

7:00 am Registration and Morning Coffee

GPCR AND ION CHANNEL TARGETS

8:30 Chairperson's Opening Remarks

Catherine Hutchings, PhD, Independent Consultant, United Kingdom

8:40 Synthetic Antibody Fragments as Sensors and Modulators of GPCR Activation and Signaling

Arun K. Shukla, PhD, Chair, Professor and EMBO Young Investigator Intermediate Fellow, Wellcome Trust DBT India Alliance, Indian Institute of Technology, India

G protein-coupled receptors (GPCRs) constitute the largest class of cell surface receptors and they are targeted by majority of currently prescribed medicines. We have developed and characterized a series of synthetic antibody fragments through Phage Display technology platform that can report GPCR activation with spatio-temporal resolution and modulate selective functions in cellular context.

9:10 Production of Inhibitory Antibody Against Claudin-5 using Engineered Membrane Protein Antigens

Hiroyuki Takeda, Ph.D., Associate Professor and Principal Investigator, Division of Protea-Drug-Discovery Sciences, Proteo-Science Center, Ehime University, Japan

The production of antibodies against extracellular regions (ECR) of membrane proteins is notably difficult because of the low productivity and immunogenicity of membrane proteins. We overcome these problems by using protein engineering and cell-free protein production technology. Immunization of engineered claudin-5 (CLDN-5) ECR antigens induced CLDN-5 ECR-binding antibodies with a high rate. Five monoclonal antibodies against CLDN-5 ECR were produced from immunized mice, and one clone successfully inhibited CLDN-5-dependent tight junctions.

9:40 Pipeline Update on GPCR and Ion Channel Antibodies

Catherine Hutchings, PhD, Independent Consultant, United Kingdom

G protein-coupled receptors (GPCRs) and ion channels represent some of the most important target classes for therapeutic drug discovery across a wide range of diseases. The progress made by antibody-based therapeutics directed to these target classes will be reviewed outlining the breadth and diversity of antibody molecules, target opportunities in R&D and the clinical pipeline, including recent development to the expansion of opportunities afforded by next-generation modalities.

10:10 Networking Coffee Break

AUTOIMMUNITY AND INFLAMMATION

10:50 Amplifying Antibody Function with Nanomaterials for Inflammation and Autoimmune Therapy

Tarek Fahmy, PhD, Associate Professor of Biomedical Engineering and Immunobiology, Yale University

Antibody therapy (armed or unarmed) as a "magic bullet" dates back to Paul Ehlirch in the late 1800's. To date, the "magic bullet" continues to be challenging to implement in a general manner for treatment of inflammation and autoimmune disease remission. I'll discuss a paradigm-shift in amplifying antibody function using small packages called, "nanoparticles" loaded with drugs or biologics and targeted to regulatory immunity. The methodology overcomes several limitations with conventional antibody therapy.

11:20 Novel Anti-CD20 Antibodies for Treating Autoimmune Disease and Hematologic Malignancies

Alexey Misorin, Senior Research Associate, Antibody Discovery, BIOCAD, Russian Federation

We have developed monoclonal antibodies against CD20 for treating autoimmune diseases – BCD-132, and for treating hematologic malignancies – BCD-171. BCD-132 and BCD-171 interact with extracellular part of CD20 antigen with nanomolar affinity and demonstrate desirable properties *in vitro*. We will present results from a phase I study of BCD132 in which we evaluated pharmacokinetics, pharmacodynamics, safety and immunogenicity of our antibodies.

EMERGING INDICATIONS FOR THERAPEUTIC ANTIBODIES continued

11:50 KEYNOTE PRESENTATION: Lessons Learned from Humira

Jochen Salfeld, PhD, Vice President, Global Biologics; Distinguished Research Fellow, AbbVie

The presentation will focus on the evolution of therapeutic Anti-TNF approaches, the history of adalimumab and will start to answer the question how to explain some of the apparent clinical differences between the Anti-TNF agents in clinical use today. In this context the learnings about TNF biology and the mechanism of action of TNF antagonists will be discussed and how those learnings impact the development of novel therapeutics.

12:20 pm A Multiplatform Strategy for the Discovery of Modulating Antibodies Against Ion Channel Targets

Sponsored by TetraGenetics

Yelena Bisharyan, Director, External Alliances, Tetragenetics, Inc.

Identifying antibodies that block ion channels is a challenging endeavor exacerbated by difficulties in producing recombinant ion channels in amounts that support drug discovery programs. We have developed a strategy to address this challenge by combining high-level expression of these proteins with immunization of diverse species and unique screening tools.

12:35 Longitudinal, Event-Based, Same-Day Sample Collection: The Implications for Biomarker Development

Sponsored by Sanguine

Brian Neman, CEO, Sanguine Biosciences

Sanguine partners with patients and leverages their health data to accelerate your research for their condition. By working together with patients, directly, Sanguine is able to perform home visits, and to easily retrieve medical records, on their behalf. 500+ completed studies. 20/40 top pharma. 30,000+ patients.

12:50 Luncheon Presentation I: Developability: Evaluating Specificity, Immunogenicity, Functionality & Manufacturability For Lead Candidate Selection

Sponsored by ABZENA

Campbell Bunce, Senior Vice President, Scientific Operations, Abzena

Understand the latest series of *in silico* computational models, analytics, *in vitro* and *ex vivo* experiments used in developability assessment. Characterise a molecules Specificity, Immunogenicity, Safety, Functionality and Manufacturability. Data generated informs sequence, structural, formulation and process refinements to select the best candidate for manufacture.

1:20 Luncheon Presentation II: Development of Active and Passive Immunization Strategies for Preventing HIV Infection

Sponsored by GenScript

Mauricio Martins, PhD, Assistant Professor, Biology, University of Miami

Despite improvements in prevention strategies and antiretroviral therapy coverage, thousands of new HIV infections are still occurring every day, underscoring the need for effective anti-HIV immune interventions. Here I will describe how my laboratory has been developing and testing immunization strategies against HIV in rhesus macaques (RMs). In the first part of the talk, I will show how we used a new vaccine modality to elicit protective immunity against a highly pathogenic simian immunodeficiency virus (SIV) molecular clone. This vaccine regimen consisted of DNA plasmids delivered by intramuscular electroporation and replication-competent forms of rhesus monkey rhadinovirus (RRV)–a herpesvirus that establishes persistent infection in RMs. In the second part of the talk, I will go over our plans to gene therapy to prevent mother-to-child transmission (MTCT) of HIV. Specifically, we will use adeno-associated virus (AAV) vectors to transfer genes encoding HIV-specific broadly-reactive neutralizing monoclonal antibodies (bnMAbs) newborn RMs. AAV vectors have emerged as safe and versatile gene therapy tools that can transduce both dividing and non-dividing cells. Given the long lifespan of muscle cells (average: 15 years), skeletal muscle is a preferred tissue for AAV-mediated gene transfer. Thus, a single intramuscular injection of AAV/bnMAb vectors at birth might result in long-term production of bnMAbs for years, possibly decades. Achieving this outcome in infants would dramatically simplify efforts to prevent MTCT of HIV. We hope that the HIV immunization approaches described here will provide new insights into how to generate persistent immunity against HIV.

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, AstraZeneca

4:10 Vision for How Immunotherapy Will Shape Future of Cancer Care

Leena Gandhi, MD, PhD, Vice President, Immuno-Oncology Medical Development, Lilly Oncology

Immunotherapy is considered by many as a pillar of cancer care today, but in many ways we have only scratched the surface. Our knowledge and understanding of the complexities of immunotherapy and its mechanisms continue to evolve. The future of cancer care will be defined by our ability to systematically identify and implement opportunities for combination therapy to improve and standardize patient response.

4:55 The Lassa Virus Glycoprotein: Stopping a Moving Target

Kathryn Hastie, PhD, Staff Scientist, Immunology and Microbiology, The Scripps Research Institute

Lassa virus causes ~5000 deaths from viral hemorrhagic fever every year in West Africa. The trimeric surface glycoprotein, termed GPC, is critical for infection, is the target for neutralizing antibodies, and a major component of vaccines. Structural analysis of Lassa GPC bound to antibodies from human survivors reveals a major Achilles heel for the virus and provides the needed template for development of immunotherapeutics and improved vaccines.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:15 End of Day

TUESDAY, APRIL 9

8:00 am Registration and Morning Coffee

INNOVATIVE MOLECULAR AND PRODUCT FORMATS

8:25 Chairperson's Remarks

Ahuva Nissim, PhD, Professor, Antibody and Therapeutic Engineering, Biochemical Pharmacology, Queen Mary University, United Kingdom

EMERGING INDICATIONS FOR THERAPEUTIC ANTIBODIES continued

8:30 Direct Targeting Cytosolic Proteins by IgG-Format Antibody

Yong Sung Kim, PhD, Professor, Molecular Science & Technology, Ajou University, Korea

Our group recently developed a platform technology of a cytosol-penetrating antibody (cytotransmab), which in the IgG format can reach the cytosolic space of living cells owing to its endosomal escaping ability after receptor-mediated endocytosis. Based on the cytotransmab technology, we have engineered a human IgG1 format antibody, named iMab, which specifically internalizes into the cytosol of tumor cells and then selectively binds to targeted cytosolic proteins, including oncogenic Ras mutants.

9:00 Targeting Microvesicles Loaded with Drugs to Arthritic Joints Using Antibodies Specific to Arthritic Cartilage

Ahuva Nissim, PhD, Professor, Antibody and Therapeutic Engineering, Biochemical Pharmacology, Queen Mary University, United Kingdom

Microvesicles (MV) are extracellular vesicles released from the plasma membrane of cells. We loaded MV with antibody specific to damaged arthritic cartilage (anti-ROS-CII). After assessing incorporation and *in vitro* functional validation, *in vivo* localization and treatment experiments using mouse model of arthritis were successfully performed. MV targeted by anti-ROS-CII loaded with combined treatment significantly accelerated resolution of inflammation. Thus, targeted MV may be developed as a 'magic bullet' to safely treat diseases.

9:30 V565, an Oral Anti-TNFα Domain Antibody for IBD

Tim Carlton, PhD, Associate Director, Research, VHSquared, United Kingdom

V565 is an anti-TNFα domain antibody for oral administration in IBD patients, derived from a llama single domain antibody and engineered for intestinal protease resistance. *Ex vivo* biopsy studies, measuring changes in phosphoprotein levels, and oral dosing studies in man demonstrate that V565 is highly potent, stable throughout the intestine and able to penetrate the disrupted colonic mucosa and neutralize membrane and soluble TNFα at the site of active disease.

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

INFECTIOUS DISEASES

10:50 Antibody Responses to Influenza in Context

Patrick C. Wilson, PhD, Professor, Medicine & Rheumatology, Knapp Center for Lupus and Immunology Research, Committee on Immunology, University of Chicago

Influenza infections are a leading cause of death and illness. Current vaccines to influenza are insufficient because of changes in viral antigenicity. Recent work will be discussed on the characterization of human B cell and antibody responses to influenza. This work has led to key insights that should allow improvements to influenza vaccines and to identify monoclonal antibodies that could be used therapeutically.

11:20 Antibody-Antibiotic Conjugate against *Staphylococcus Aureus:* Mechanism and Modulation of Activity

Wouter Hazenbos, PhD, Scientist, Infectious Diseases, Genentech

Complicated *Staphylococcus aureus* infections can be difficult to treat, as bacteria may reside in intracellular reservoirs, limiting antibiotic access. We generated an antibody-antibiotic conjugate, comprising an antibody binding *S. aureus*, conjugated to a rifamycin-analog through a cathepsin-cleavable linker. This molecule kills *S. aureus* inside host cells, and is superior to standard antibiotics in mouse infection. Current work focuses on MOA; new technology to enhance activity; applicability to other pathogens.

11:50 Structure-Based Approaches for the Discovery of Potent Antibodies against Malaria Antigens

Jean- Philippe Julien, PhD, Canada Research Chair in Structural Immunology, The Hospital for Sick Children Research Institute

Reverse vaccinology holds promise to design effective immunogens for the development of malaria vaccines. This concept is based on interrogating B cell repertoires to identify inhibiting antibodies that will guide immunogen design. Our research focuses on characterizing protective antibodies of high potency against malaria antigens at the bottlenecks of transmission between the mosquito vector and human host. These studies also have implications for the development of antibody interventions against malaria.

12:20 pm Luncheon Presentation *(Sponsorship Opportunity Available)* or Enjoy Lunch on your Own

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

OTHER EMERGING INDICATIONS

2:00 Chairperson's Remarks

Anthony Shock, PhD, Director, Immunology Research, UCB, United Kingdom

2:05 Anti-Cytokine Therapy for Atherosclerosis

Paul M. Ridker, MD, MPH, Eugene Braunwald Professor of Medicine, Harvard Medical School; Director, Center for Cardiovascular Disease Prevention, Brigham and Women's Hospital

Recently, the Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS) has demonstrated that specific targeting of interleukin-1beta can significantly lower cardiovascular event rates with no effect on cholesterol or blood pressure. Moreover, the magnitude of clinical benefit was related to the robustness of inflammation inhibition. Thus, we now have proof of principle for the inflammation hypothesis of atherothrombisis and a signal for multiple new treatment targets.

2:35 Targeting FcRn in IgG Autoantibody-Driven Diseases

Anthony Shock, PhD, Director, Immunology Research, UCB, United Kingdom

The neonatal Fc receptor, FcRn is responsible for rescuing IgG from lysosomal degradation and is responsible for the long half-life of this protein *in vivo*, but FcRn is also responsible for recycling pathogenic IgG autoantibodies. Rozanolixizumab is a high affinity IgG4P mAb targeting FcRn, developed to specifically inhibit the recycling of IgG and is demonstrating clinical efficacy in patients with IgG autoantibody-driven diseases.

3:05 MutaMap®, a Mutational Activity Map for Optimum Protein Design

Sponsored by ProImmune

Emilee Knowlton, PhD, Immunology, Sales Specialist, Sales, ProImmune Inc.

MutaMap® is an *in vitro* assay system that helps explore the effect of substituting each amino acid in at each position in a protein sequence one by one with all 19 possible substitutions and find out the effect on protein activity. MutaMap® allows you to make informed protein engineering decisions for a range of key developability objectives, including; Improving activity/affinity, de-immunization, altering cross reactivity, improving humanization and prolonging half-life of your protein.

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

4:25 Completing the Immunity Cycle by Developing Myeloid Immunotherapies

Tatiana Novobrantseva, PhD, Co-Founder, Head of Research and Development, Verseau Therapeutics

Macrophages/DCs are biologically optimized to either induce or suppress an immune response.

EMERGING INDICATIONS FOR THERAPEUTIC ANTIBODIES continued

Targeting pro-tumorigenic macrophages has been repeatedly identified as a very important next step of development for the field of immuno-oncology. Similarly, myeloid cell suppression has been long realized to be fueling the vicious cycle of the autoimmune disease. The talk will describe Verseau Therapeutics' approaches to tweaking myeloid cell functionality in human disease.

4:55 Antagonistic Antibodies Used to Establish the Key Role for IL-13 Signaling Via the Type 2 IL-4 Receptor in Experimental Atopic Dermatitis

Itai Benhar, PhD, Professor, Molecular Cell Biology and Biotechnology. Tel-Aviv University

IL-13 and IL-4 are potent mediators of type 2-associated inflammation such as asthma and atopic dermatitis (AD) and share a receptor subunit, IL-13Ra1 which is part of IL-4R. The role of the type 2 IL-4R in AD remains to be defined. We show that oxazolone-induced AD in mice is dependent on the type 2 IL-4R and targeting of the type 2 IL-4R using an IL-13Ra1-neutralizing antibody alleviates oxazolone-induced AD.

5:25 End of Emerging Indications for Therapeutic Antibodies

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*
SC11: Developability of Bispecific Antibodies: Formats and Applications

Separate registration required. **Click here or see page 5 for course details.*

Cambridge HEALTHTECH Institute
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INAUGURAL

ONCOLYTIC VIRAL THERAPY

Engineering, Translational and Clinical Strategies

April 10-11, 2019

PEGS Boston's Inaugural Oncolytic Viral Therapy invites speakers to discuss their exciting research and development in the growing oncovirotherapy field, from mechanistic understanding of viruses and tumor biology, to engineering and optimization strategies, preclinical and translational sciences, clinical trial updates and challenges.

WEDNESDAY, APRIL 10

7:15 am Registration and Morning Coffee

7:25 - 8:25 PANEL DISCUSSION: Women in Science – Inspired Professional and Personal Stories

Moderator: Women in Bio, Boston Chapter

Panelists:

Susan Richards, PhD, Presidential Scientific Fellow, Translational Medicine Early Development, Sanofi R&D

Joanna Brewer, PhD, Vice President, Platform Technologies, AdaptImmune

Additional Panelists to be Announced

ENGINEERING NEXT-GEN ONCOLYTIC VIRUSES

8:30 Chairperson's Opening Remarks

Timothy Cripe, MD, PhD, Professor and Chief, Division of Hem/Onc/BMT, Nationwide Children's Hospital

8:40 KEYNOTE PRESENTATION: Next Generation OV and New Combinational Approaches for Treatment of Solid Tumors

Paola Grandi, PhD, CSO, Cold Genesys

In the last few years, oncolytic vectors have become one of the most promising immuno-therapy agents for the treatment of cancer. Leaders from academia and industry have made advances in vector engineering, explored advantages and limitations of preclinical models, discussed updates from combination trials, as well as shared challenges and potential strategies of systemic delivery. In this talk, I will present an overview of the Phase II clinical trial with CG0070 for the treatment of BCG-unresponsive bladder cancer.

9:10 Antibody Targeted Viruses: The Next Generation of Oncolytics

Stephen J. Russell, MD, PhD, CEO, Vyriad, Inc.

Oncolytic virus potency can be favorably impacted by concomitant immunosuppressive drug therapy to retard the host antiviral response and accelerate intratumoral spread. But without stringent targeting of virus tropism, increased OV potency is associated with an increased risk of off-target toxicity. To address this limitation, Vyriad is developing a new generation of retargeted viruses whose attachment, cell entry and cytotoxic potential are fully reprogrammed through surface display of single chain antibody targeting domains.

9:40 Oncolytic Virus Vaccines

John C. Bell, PhD, Professor, Medicine & Biochemistry, Microbiology & Immunology, Ottawa Hospital Research Institute, University of Ottawa

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

10:15 Women in Science Speed Networking in the Exhibit Hall

10:55 Engineering Viruses to Deliver their Maximum Potential: Two Examples from the Turnstone Portfolio

Caroline Breitbach, PhD, Vice President, R&D Programs and Strategy, Turnstone Biologics

An overview of the development of MG1 Maraba an SKV vaccinia oncolytic viral immunotherapy platforms will be provided. MG1 is a novel rhabdovirus engineered to express tumor antigens, thereby eliciting anti-tumor immune responses while modifying the tumor immune microenvironment. SKV is a novel engineered vaccinia platform being used to deliver multiple immune-modulatory agents. These therapeutic agents are designed to re-program the tumor microenvironment to abrogate immunosuppressive networks, thereby re-establishing endogenous anti-tumor immunity to achieve an effective *in situ* vaccination.

11:25 VSV-GP Eradicates the Tumor and Stimulates an Immune Response

Patrik Erlmann, PhD, Head, R&D, ViraTherapeutics GmbH

VSV-GP combines the tumor cell killing efficacy of Vesicular Stomatitis Virus with an enhanced safety profile, making it an excellent oncolytic virus candidate for clinical development. Here we show that VSV-GP mediated cell lysis releases tumor derived antigens, which in combination with the viral components, such as the viral RNA genome unleash a strong anti-tumor immune response.

11:55 pm POSTER HIGHLIGHT: Stealth Targeted Nano Coatings for Oncolytic Viruses for Repeat Systemic Administration

Inanc Ortac, PhD, CTO, DevaCell, Inc.

Systemic delivery and repeat administration of oncolytic viruses have been shown to be crucial for strong efficacy and anti-tumor immunity of oncolytic virotherapy. However, rapid neutralization and clearance of oncolytic viruses limits the promise of the therapy. Surface modifications of viruses such as blocking and removing immunogenic antigens often have negative impacts on the infectivity of the virus. This poster describes a novel approach, which is based on forming a removable organic/inorganic hybrid nanolayer, ONCoat™, formed around the virus surface that releases the unmoEdified virus inside the infected cell. Such encapsulation provides flexible surface functionalization to the virus while allowing viruses to be stealth to the immune system, enabling targeted syste mic delivery and repeat administration. Following application of ONCoat™, the infectivity of the virus is not negatively affected. Furthermore, virus, when released within the cell, is unmodified can still engage its own mechanisms for gene expression, replication and oncolysis.

12:25 Luncheon Presentation *(Sponsorship Opportunity Available)* or Enjoy Lunch on Your Own

1:55 Session Break

Cambridge HEALTHTECH Institute
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PRECLINICAL AND CLINICAL PROGRESS

2:10 Chairperson's Remarks
Patrik Erlmann, PhD, Head, R&D, ViraTherapeutics GmbH

2:15 Development of Patient-Derived Glioblastoma Model Systems to Predict Response to OV Therapy
Martine Lamfers, PhD, Associate Professor, Neurosurgery, Erasmus Medical Center Rotterdam

Oncolytic viral therapies are showing promising results in early clinical trials, however, response rates are suboptimal. Preclinical studies suggest that tailoring the selected OV strain to the tumor subtype may markedly improve response rates. Patient-derived model systems may offer a tool to identify the most optimal oncolytic virus for a specific patient and could aid in the design of future stratified trials for OV therapy.

2:45 Lessons Learned from a Phase I Trial of Intratumoral and Intravenous Oncolytic Herpes Virus in Children and Young Adults
Keri Streby, MD, Pediatric Oncologist, Hematology & Oncology, Nationwide Children's Hospital

3:15 Engineering Vaccinia Virus for Intratumoral Delivery to Generate "*in situ* Vaccination" against Cancer
Liang Deng, MD PhD, Associate Member, Associate Attending Physician, Memorial Sloan Kettering Cancer Center

Vaccinia virus is a large cytoplasmic DNA virus. Modified vaccinia virus Ankara (MVA) is a highly attenuated vaccinia virus, an important vaccine vector. I will discuss our published study on the intratumoral delivery of inactivated MVA to induces systemic antitumor immunity and to overcome resistance to immune checkpoint blockade.

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

THURSDAY, APRIL 11

8:00 am Registration and Morning Coffee

TARGETING THE TUMOR MICROENVIRONMENT

8:30 Chairperson's Remarks
Paola Grandi, PhD, CSO, Cold Genesys

8:35 T-SIGn Virus Approach to Cancer Gene Therapy – Driving the Tumor Cells to Express Combinations of Biological Therapeutics within the Tumor Microenvironment
Brian Champion, PhD, CSO, PsiOxus

This presentation will cover the T-SIGn oncolytic adenovirus platform: gene therapy for cancer; T-SIGn viruses for combination immunotherapy and NG-641 T-SIGn virus designed for targeting the treatment of stromal-rich cancers.

9:05 Inflaming the Tumor Microenvironment to Augment Oncolytic Virotherapy
Timothy Cripe, MD, PhD, Professor and Chief, Division of Hem/Onc/BMT, Nationwide Children's Hospital

Cancer immunotherapies hold great promise, but scores of disappointing studies highlight our relative ignorance in understanding the immunosuppressive microenvironment within solid tumors. Because of their central role in mediating immunosuppression, tumor associated macrophages (TAMs), typically "polarized" to a so-called M2-like phenotype, are thought to be an important therapeutic target. I will discuss our work to modulate TAMs and TGFb to enhance antitumor efficacy of oncolytic herpes virotherapy.

9:35 Oncolytic Herpes Simplex Virus Combinations Boosting Immunovirotherapy
Samuel D. Rabkin, PhD, Thomas A. Pappas Prof of Neurosciences, Prof of Neurosurgery (Microbiology), Harvard Medical School and Massachusetts General Hospital

Oncolytic herpes simplex virus (oHSV) acts by direct tumor cell killing and the induction of anti-tumor immune responses, immunovirotherapy. The virus can also be 'armed' with therapeutic transgenes, such as cytokines, to improve efficacy by modulating the tumor microenvironment. We will describe preclinical studies to boost immunovirotherapy using oHSV combinations with approved pharmacological agents targeting oncogenic pathways (MEK inhibitors) and the tumor microenvironment (axitinib). These combinations can interact with immune checkpoint blockade and are translatable to the clinic.

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

COMBINATION VIROTHERAPY WITH IMMUNOTHERAPY

11:05 Exploring Virotherapy/Immunotherapy Combinations for the Treatment of Glioblastoma
Sean Lawler, PhD, Assistant Professor, Managing Director, Harvey Cushing Neurosurgery Laboratories, Brigham and Women's Hospital

We have been investigating a gene therapy agent based on a non-replicating adenoviral vector to deliver the Herpes virus Thymidine kinase gene to glioblastoma by intratumoral injection. Our studies have shown that this results in high local IFNg levels, and upregulation of PD-L1 on tumor cells, microglia, and macrophages in the tumor microenvironment. Combination of immune checkpoint blockade with an anti-PD1 antibody overcomes this potential resistance mechanism and leads to a high cure rate in experimental murine glioblastoma models. This combination is now being advanced towards Phase I clinical trials in primary glioblastoma.

11:35 Oncolytic Poliovirus Combined with PD1/PDL1 Blockade for Cancer Therapy
Smita Nair, PhD, Professor, Surgery, Neurosurgery and Pathology, Duke University School of Medicine

Oncolytic poliovirus PVSRIPO targets and kills tumor cells and induces sustained type I IFN-dominant activation of antigen presenting cells, which overcomes the immunosuppressive tumor microenvironment to stimulate antitumor immunity. Preclinical data in murine models demonstrate that: 1] Intratumor PVSRIPO administration causes oncolysis and inflammation, which stimulates innate and adaptive immunity; 2] Immune activation triggers adaptive immune resistance via the PD1/PDL1 axis; 3] Blocking PD1/PDL1 with PVSRIPO eliminates adaptive resistance and potentiates durable antitumor immunity.

12:05 pm Combination of Adenovirus Oncolytic Virotherapy with CDK4/6 Inhibitors: An Unexpected and Incredible Strong Treatment Alliance
Per Sonne Holm, PhD, Head, Virotherapy Research Group, Urology, Technical University Munich

It is widely accepted that adenovirus E1A drives human cells into S-phase by displacing the Retinoblastoma (RB) proteins from E2F transcription factors to de-repress cell cycle genes and viral gene expression. However, CDK4/6 inhibitors led to strong synergistic effects with regards to viral replication and cell killing, resulting in new unexpected insights into Rb/E2F regulation of adenovirus life cycle. These new perspectives in the Rb/E2F mediated regulation of the adenoviral life cycle will have great impact for the use of oncolytic adenoviruses with cell cycle inhibitors.

12:35 End of Oncolytic Viral Therapy

THURSDAY, APRIL 11: 1:40-5:20 PM - FRIDAY, APRIL 12: 8:30 AM - 3:40 PM

Genome Editing with CRISPR:

Towards Novel Research, Translational and Clinical Applications

This rigorous day and a half program compiled for specialists interested in applying genome editing technologies for both basic and translational research will comprehensively review the state-of-art information on gene editing strategies and applications in various areas, such as disease modelling, drug discovery and development. Beginning from introductory level basic technology aspects, key molecular features, strengths and shortcomings of CRISPR/Cas9 systems, the instructor will advance towards sharing in-depth knowledge related to virtually all facets of present day genome editing applications, such as constructing of cell culture-based experimental platforms, engineering disease models for *in vivo* research supporting preclinical drug development workflows, rational design and functional screening of sgRNA libraries, application of CRISPR/Cas9 technology for diagnostic and therapeutic purposes and many others. The instructor will strive to achieve a balance between presenting theory information and conducting some practical tasks in exploring available digital resources for designing and enabling CRISPR/Cas9 studies, as well as assist in troubleshooting specific complex experimental scenarios and conduct Q&A sessions.

Instructor:
Serguei V. Kozlov, PhD, MBA, PMP, Principal Scientist/PM, Team Leader PTO, Center for Advanced Preclinical Research, Frederick National Laboratory for Cancer Research (NCI)

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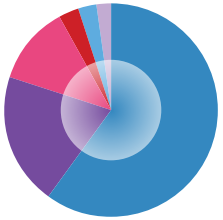
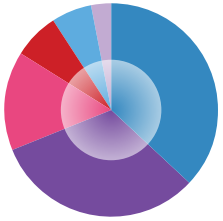
- Podcasts

2018 ATTENDEE DEMOGRAPHICS



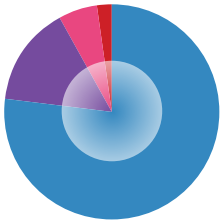
COMPANY TYPE

Biotech	60%
Pharma	20%
Academic + Government	12%
Services	3%
Healthcare	3%
Financial, Press, Societies	2%



DELEGATE TITLE

Scientist/Technologist	37%
Executive + Director	32%
Sales & Marketing	15%
Manager	7%
Professor	6%
Assistant	3%



GEOGRAPHIC LOCATION

USA	77%
Europe	15%
Asia	6%
Rest of World	2%

VIEW CURRENT EXHIBITOR LIST AND FLOOR PLAN

US BREAKDOWN

East Coast	65%
West Coast	27%
Midwest	8%

For more information on sponsorship and exhibit opportunities, please contact:

COMPANIES A-K: **Jason Gerardi**
Senior Manager, Business Development
781-972-5452 | jgerardi@healthtech.com

COMPANIES L-Z: **Carol Dinerstein**
Senior Manager, Business Development
781-972-5471 | dinerstein@healthtech.com

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PEGS BOSTON

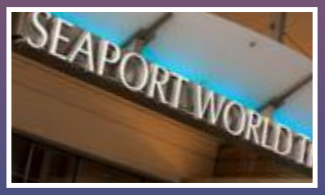
> "Well organized, as usual, but particularly in regard to the breadth of topics covered and the connections made between diciplines was nice to see – **very forward looking.**"
>
> - Research Scientist, AbbVie

EVENT FEATURES

- **22 Conferences, Training Seminars and Short Courses** covering protein and antibody engineering, cancer immunotherapy, oncology, and emerging therapeutics, and more
- **Over 350+ Speakers** representing top pharma, biotech, academia, and government institutions – In 2018 there were over 100 presentations from top 10 pharma companies
- **2,600+ International Delegates** focusing on biotherapeutic protein drug development opportunities
- **Short Courses** providing additional training and education to brush up on your knowledge or expand your horizons
- **Inspiring Keynote Presentations** from world-renowned experts and visionaries
- ***NEW*** **Women in Science** panel discussion and dedicated networking events!
- **Lively Exhibit Hall featuring 150+ companies** showcasing novel technologies and solutions
- **Poster Sessions** featuring cutting-edge, ongoing research – nearly 300 posters in 2018!
- **Valuable Networking** through breakout discussion groups, dedicated poster viewing sessions, interactive panels and more
- **1-on-1 Networking App** to easily build connections with fellow life science professional, schedule meetings and expand your network
- **Student Fellowships** offering discounted registration for young researchers looking to make a difference and share their research
- **Sponsored Talks** by leading technology and service providers showcasing new offerings

HOTEL & TRAVEL INFORMATION

Conference Venue:
Seaport World Trade Center
200 Seaport Boulevard
Boston, MA 02210



Host Hotel:
Seaport Hotel
One Seaport Lane
Boston, MA 02210
T: 1-877-SEAPORT
(1-877-732-7678)

Reservations: Go to the Travel Page of **PEGSUMMIT.com**

Discounted Room Rate: $294 s/d

Discounted Room Rate Cutoff:
March 1, 2019

Please visit the Travel Page of PEGSUMMIT.com for additional Information

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How to Register: PEGSummit.com

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Please use keycode
PEG F
when registering!

PRICING AND REGISTRATION INFORMATION

SHORT COURSE ONLY PRICING

	Commercial	Academic, Government, Hospital-affiliated
1 Short Course	$699	$349
2 Short Courses	$999	$599
3 Short Courses	$1,199	$699

CONFERENCE PACKAGE OPTIONS

PREMIUM PACKAGE
(Includes access to all Conferences & Training Seminars Monday-Friday. PLUS! Save 10% off your Short Course registration.)

Advance - Registration Rate Until March 15, 2019	$3,199	$1,699
Registrations After March 15, 2019 and On-Site	$3,399	$1,799

STANDARD PACKAGE *(Includes access to 2 conferences and/or Training Seminars. Excludes short courses.)*

Advance - Registration Rate Until March 15, 2019	$2,799	$1,349
Registrations After March 15, 2019 and On-Site	$3,049	$1,449

BASIC PACKAGE *(Includes access to 1 conference or Training Seminar. Excludes short courses.)*

Advance - Registration Rate Until March 15, 2019	$1,899	$949
Registrations After March 15, 2019 and On-Site	$2,099	$1,099

CONFERENCE DISCOUNTS

POSTER SUBMISSION - DISCOUNT ($50 OFF):
Poster abstracts are due by **March 1, 2019.** Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact jring@healthtech.com.
*CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

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

ALUMNI DISCOUNT - SAVE 20%: Cambridge Healthtech Institute (CHI) appreciates your participation at its events. As a result of the great loyalty you have shown us, we are pleased to extend to you the exclusive opportunity to save an additional 20% off the registration rate.

GROUP DISCOUNTS: Discounts are available for multiple attendees from the same organization. For more information on group rates contact David Cunningham at +1-781-972-5472 or cunningham@healthtech.com.

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

ADDITIONAL REGISTRATION DETAILS

Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link.

Handicapped Equal Access:
In accordance with the ADA, Cambridge Healthtech Institute is pleased to arrange special accommodations for attendees with special needs. All requests for such assistance must be submitted in writing to CHI at least 30 days prior to the start of the meeting.

To view our Substitutions/ Cancellations Policy, go to healthtech.com/regdetails

Video and or audio recording of any kind is prohibited onsite at all CHI events.