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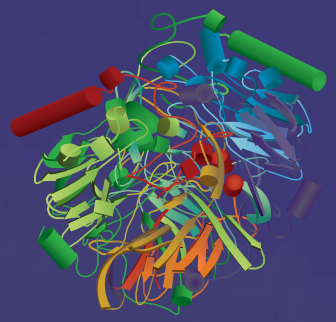

13TH ANNUAL

PEGS BOSTON

May 1-5, 2017 • Seaport World Trade Center

THE ESSENTIAL PROTEIN ENGINEERING SUMMIT

PLENARY **KEYNOTE:**

Sir Gregory Winter, Ph.D.,
FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics

EVENT **FEATURES:**

NEW Young Scientist Keynote Presentation

2,200+ Global Attendees

22 Conference Tracks

6 Training Seminars

19 Short Courses

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CONFERENCE AT A GLANCE

#PEGS17

PRE-CONFERENCE SHORT COURSES*

SUNDAY April 29	MONDAY May 1	TUESDAY May 2	WEDNESDAY May 3	THURSDAY May 4	FRIDAY May 5
	Display of Antibodies		Engineering Antibodies		Engineering Bispecific Antibodies
	Antibodies for Cancer Therapy		Advancing Bispecific Antibodies to the Clinic for Oncology		ADCs II: Advancing Toward the Clinic
	Preventing Toxicity in Immunotherapy		Adoptive T-Cell Therapy		Agonist Immunotherapy Targets
	Difficult to Express Proteins		Optimizing Protein Expression		Protein Expression System Engineering
	Characterization of Biotherapeutics		Biophysical Analysis of Biotherapeutics		Protein Aggregation and Stability
	Immunogenicity: Regulatory and Clinical Relevance		Strategies for Immunogenicity Assay Assessment		Optimizing Bioassays for Biologics
	Fusion Protein Therapeutics		ADCs I: New Targets, Payloads and Alternative Formats		ADCs II: Advancing Toward the Clinic
	Drug Discovery for Autoimmunity and Inflammation		Biologics and Vaccines for Infectious Disease		Agonist Immunotherapy Targets
		Dinner Short Courses*		Dinner Short Courses*	

Cambridge Healthtech Training SEMINARS
Comprehensive and Practical Training

Introduction to Protein Engineering	Immunology for Drug Discovery Scientists	Introduction to Structure-Based Drug Design and Development
Introduction to Immunogenicity	Regulatory Requirements Across the Product Development Lifecycle	
	Next-Generation Sequencing for Antibody Discovery & Engineering	

Separate Registration Required

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PLENARY KEYNOTE SESSION

Monday, May 1 | 4:00 - 5:40 pm

Bicycles and Bicycle Drug Conjugates: Next Generation Therapeutics

Sir Gregory Winter, Ph.D.,
FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics

Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles' unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs); a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. This presentation will describe both the Bicycle® and BDC platforms.

About

Sir Gregory Winter is the Master of Trinity College Cambridge and was until recently a member of the Medical Research Council Laboratory of Molecular Biology (LMB) in Cambridge, U.K., and has served as both Deputy and Acting Director. He was one of the early pioneers of the science of protein engineering, focusing first on enzymes (with Alan Fersht) and then antibodies. In particular he invented techniques to humanise rodent antibodies for use as therapeutics, in the course of which he helped to develop alemtuzumab/Campath-1H. Later, he developed methods to make fully human antibodies against human self-antigens using antibody libraries. His inventions are used in most of the antibody products on the market, including the humanised antibodies alemtuzumab/Campath-1H, trastuzumab/Herceptin, bevacizumab/Avastin, palivizumab/Synagis and the first human antibody (adalimumab/Humira) to be approved by the U.S. Food and Drug Administration.

Sir Gregory has also acted as an entrepreneur to translate his scientific inventions to medicines. He was a founder of Cambridge Antibody Technology (1989) and Domantis (2000) and Bicycle Therapeutics (2009); these companies pioneered the use of antibody libraries to make fully human antibody therapeutics including adalimumab/Humira and belimumab/Benlysta.

Young Scientist Keynote: Programming Proteins by Deep Sequencing and Design

Tim Whitehead, Ph.D.,
Assistant Professor, Chemical Engineering and Materials Science, Michigan State University

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 group leverages this unprecedented wealth of sequence-function information to design and engineer protein affinity, specificity, and function and to infer structural complexes of proteins. My talk will present an overview of the above and detail methodological improvements that enable the engineering work.

About

Tim Whitehead is an Assistant Professor at Michigan State University in the Departments of Chemical Engineering and Materials Science, Biomedical Engineering, and Biosystems Engineering. He has won an NSF CAREER award, holds 6 patents (5 licensed), and has published over 30 research articles in journals like Science, Nature Biotechnology, and Nature Methods.

The PEGS Young Scientist Keynote

The PEGS Boston Young Scientist Keynote recognizes a rising star in the field of protein science 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 2016, and the final selection was made on the basis of input provided by a 14-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 2017 meeting for details on how you can nominate a candidate for the 2018 meeting.

Register Online!
PEGSummit.com

Cambridge 25 YEARS HEALTHTECH Institute
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SHORT COURSES*

SUNDAY, APRIL 30

MORNING 10:00 AM - 1:00 PM

SC1: Preclinical and Clinical Immunogenicity Bioanalysis: ADCs, Multi-Domain Biotherapeutics and New Modalities
Darshana Jani, M.S., Senior Manager, Pfizer, Inc.
Seema Kumar, Ph.D., Associate Director, EMD Serono
Corinna Krinos Fiorotti, Ph.D., Business Development Manager, Bioagilytix
Priya Sriraman, Ph.D., Principal Investigator, Biotherapeutics Development, Celgene Corp

SC2: Translational Considerations for Development of Monoclonal Antibodies Part I: Focus on Early Discovery
Gadi Bornstein, Ph.D., Global Correlative Science Leader, Director, Novartis Pharmaceuticals
Enrique Escandon Ph.D., Senior Principal Scientist, DMPK and Disposition, Merck Research Laboratories
Vaishnavi Ganti, Ph.D., Associate Principal Scientist, Biologics Discovery-DMPK, Merck Research Laboratories
Veronica Juan, Ph.D., Principal Scientist, Protein Sciences, Merck Research Labs
Scott L. Klakamp, Ph.D., Principal, SKD Consulting LLC
Mohammad Tabrizi, Ph.D., Director Biologics Discovery, Merck Research Laboratories

SC3: Genomics in the Service of Cancer Immunotherapy
Zoltan Szallasi, Ph.D., M.D., Senior Research Scientist, Informatics Program; Assistant Professor, Pediatrics, Children's Hospital Boston and Harvard Medical School

SC4: The Multi-Attribute Method (MAM) for Improving Product and Process Development
Richard Rogers, Ph.D., Scientist 4, Just Biotherapeutics

SC6: *In silico* Protein Docking
Vinodh B. Kurella, Ph.D., Ph.D., Senior Scientist, Molecular Engineering Unit, Intexon Corp.
Paolo Marcatili, Ph.D., Assistant Professor, Bio & Health Informatics, Danish Technical University

AFTERNOON 2:00 - 5:00 PM

SC7: Translational Considerations for Development of Monoclonal Antibodies Part II: Focus on Nonclinical Development to the Clinic
Gadi Bornstein, Ph.D., Global Correlative Science Leader, Director, Novartis Pharmaceuticals
Enrique Escandon Ph.D., Senior Principal Scientist, DMPK and Disposition, Merck Research Laboratories
Vaishnavi Ganti, Ph.D., Associate Principal Scientist, Biologics Discovery-DMPK, Merck Research Laboratories
Veronica Juan, Ph.D., Principal Scientist, Protein Sciences, Merck Research Labs
Scott L. Klakamp, Ph.D., Vice President of Chemistry and Biochemistry, Bioptix
Mohammad Tabrizi, Ph.D., Director Biologics Discovery, Merck Research Laboratories

SC8: *In silico* Immunogenicity Predictions – A Hands-On Workshop
Vinodh B. Kurella, Ph.D., Senior Scientist, Molecular Engineering Unit, Intrexon Corp.

SC9: Target Selection for Biologics
William R. Strohl, Ph.D., President, BiStro Biotech Consulting, LLC

SC11: Adoptive Therapy with CAR T Cells
Prasad S. Adusumilli, M.D., F.A.C.S., Associate Attending and Deputy Chief, Thoracic Surgery, Memorial Sloan Kettering Cancer Center
Carl J DeSelm, M.D., Ph.D., Researcher, Immunotherapy, Memorial Sloan Kettering Cancer Center
Matthew J. Frigault, M.D., Clinical Fellow in Medicine, Dana-Farber Cancer Institute
Eric Smith, M.D., Medical Oncologist, Memorial Sloan Kettering Cancer Center

***Separate Registration Required**

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SHORT COURSES*

TUESDAY, MAY 2

DINNER 6:00 - 8:30 PM

SC12: Study Design and Statistical Data Analysis of Flow Cytometry Assays
Shuguang Huang, Ph.D., CSO, Stat4ward LLC

SC13: Phenotypic Screening Applications and Technologies
Steven Rust, Ph.D., Senior Manager, R&D, MedImmune

SC14: Overcoming the Challenges of Immunogenicity Assays, Risk Assessment and Regulatory Requirements
Jim McNally, Ph.D., Associate Director and Immunogenicity Expert, Global Early Development - Quantitative Pharmacology & Drug Disposition, EMD Serono
Bonnie Rup, Ph.D., Independent Consultant

DINNER 6:00 - 9:00 PM

SC17: Transient Protein Production in Mammalian Cells
Richard Altman, MS, Scientist, Protein Technologies, Amgen
Henry C. Chiou, Ph.D., Associate Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific
Dominic Esposito, Ph.D., Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research, Leidos Biomedical Research, Inc.
Panelist: Barry A. Morse, Ph.D., Principal Research Scientist, Biologics Research, Janssen Research and Development

THURSDAY, MAY 4

DINNER 5:45 - 8:15 PM

SC15: Critical Considerations for the Design and Development of Antibody-Drug Conjugates
Isabel Figueroa, Ph.D., Scientist, PTPK, Genentech, Inc.
Shawn Owen, Ph.D., Assistant Professor, Pharmaceutics and Pharmaceutical Chemistry; and Adjunct Professor, Internal Medicine, University of Utah

SC16: New USP Initiatives for Characterization and Release of Biologics
Maura C. Kibbey, Ph.D., Director Science & Standards, Global Biologics, US Pharmacopeia
Steven L. Walfish, Ph.D., Principal Science & Standards Liaison, US Pharmacopeia

SC18: Clinical Prospects of Cancer Immunotherapy
Gaurav Goel, M.D., Assistant Professor, Division of Medical Oncology, Medicine, University of Kentucky Markey Cancer Center

SC19: Strategic Bioassay Design and Analysis
Liming Shi, MS, MA, Senior Group Leader, Bioassay Development, Hospira, a Pfizer Company

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Cambridge HEALTHTECH Institute
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Cambridge Healthtech Training SEMINARS

Comprehensive and Practical Training

TS1: INTRODUCTION TO PROTEIN ENGINEERING| May 1-2, 2017

Day 1: May 1, 8:30am -5:30pm Day 2: May 2, 8:30am-12:30pm

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. The class is directed at scientists new to the industry or working in support roles, academic scientists and career protein scientists wanting a detailed update on the current state of the field.

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

TS2: INTRODUCTION TO IMMUNOGENICITY May 1 - May 2, 2017

Day 1: May 1, 8:30am -5:30pm Day 2: May 2, 8:30am-12:30pm

All protein drugs generate an immunogenic response. This two-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 development.

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.

Instructor:

Arno Kromminga. PhD., Senior Vice President and European Chief Scientific Officer, BioAgilytix

TS3: IMMUNOLOGY FOR DRUG DISCOVERY SCIENTISTS | May 3-4, 2017

Day 1: May 3, 8:30am-5:45pm Day 2: May 4, 8:30am-12:30pm

In this course, we will explore therapeutic approaches that harness our knowledge of the immune system to treat human disease. From vaccines to cancer (not to mention cancer vaccines!) and diabetes to IBD, we will explore how the immune system can be shaped, engineered, and harnessed by exploring specific examples of current and future therapeutics, and the immunology behind them.

Instructors:
Kevin Bonham, Ph.D., Curriculum Fellow, Microbiology and Immunobiology Department, Harvard Medical School
Matthew Woodruff, Ph.D., Postdoctoral Fellow, Emory University

TS4: REGULATORY REQUIREMENTS ACROSS THE PRODUCT DEVELOPMENT LIFECYCLE | May 3-4, 2017

Day 1: May 3, 8:30am-5:45pm Day 2: May 4, 8:30am-12:30pm

The successful development of a pharmaceutical product requires not only good science, but also compliance with FDA regulatory expectations. This course will include a comprehensive review of the Chemistry, Manufacturing and Controls (CMC) section of regulatory filings, with a focus on phase appropriate requirements.

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

TS5: NEXT-GENERATION SEQUENCING FOR ANTIBODY DISCOVERY AND ENGINEERING | May 3-4, 2017

Day 1: May 3, 8:30am-5:45pm Day 2: May 4, 8:30am-12:30pm

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

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

TS6: INTRODUCTION TO STRUCTURE-BASED DRUG DESIGN AND DEVELOPMENT | May 4-5, 2017

Day 1: May 4, 1:40pm- 5:20pm Day 2: May 5, 8:30am-3:40pm

CHI's Introduction to Structure-Based Drug Design and Development training seminar offers an introduction to the concepts, strategies and tools of structure-based drug design and development. This seminar will consist of presentations, breakout problem solving sessions and live demonstrations of some of the common computational tools used in the field. 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, Ph.D., Research Officer, Human Health Therapeutics, National Research Council Canada
Traian Sulea, Ph.D., Senior Research Officer, Human Health Therapeutics, National Research Council Canada

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

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

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

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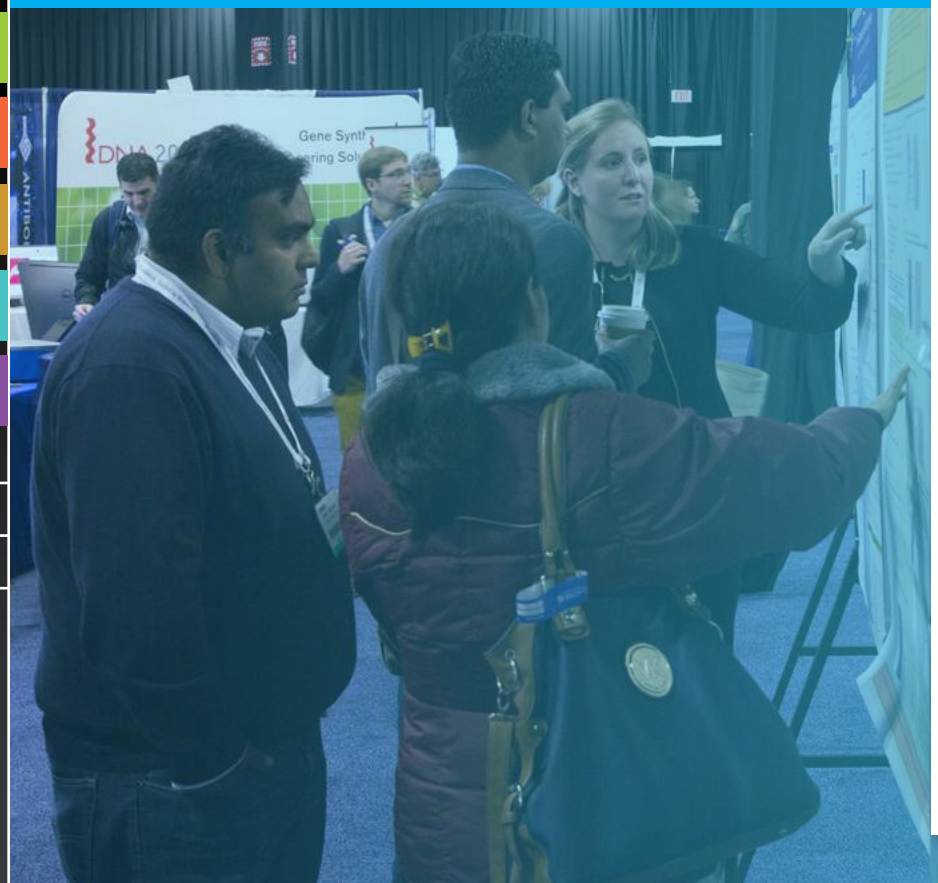
STUDENT FELLOWSHIP

Present Your Poster to 2,200+ Protein Engineering Researchers

Full time graduate students and Ph.D. candidates are encouraged to apply for the PEGS conference Student Fellowship. Fellows will receive a poster presentation slot and a savings of over $900 on their registration fee. Applications are due by **February 3, 2017.**

STUDENT FELLOWSHIP DETAILS:

- Interested students must complete the below application for the 2017 Student Fellowship
- Fellows are required to present a scientific poster. A poster title and abstract are due at the time of the application.
- All applications will be reviewed by the scientific review committee and the accepted students will be notified no later than February 17, 2017 if they were accepted for the 2017 Student Fellowship
- Accepted 2017 Student Fellows will receive a discounted conference rate of $295*, which must be paid in full by March 10, 2017. Credit card information is requested at the time of the application and will be charged upon application approval.
- This fellowship is limited to 20 students and is for the Premium Conference Package, May 1-5, 2017. Excludes Short Courses.
- All accepted 2017 Student Fellows will be asked to help promote the conference onsite at their college, and throughout their social media networks.
- Students not accepted for the 2017 Student Fellowship, can register at a discounted rate $595*, and will not be required to present a poster
- ADDED BONUS! Poster competition features cash prizes. (Open to all poster presenters)



PRESENT A POSTER

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

REASONS YOU SHOULD PRESENT YOUR RESEARCH POSTER AT THIS CONFERENCE:

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

POSTER COMPETITION!

Two poster awards will be given at the conference for a cash prize for best poster. Winners will be chosen by delegate voting onsite using the program guide app. 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. See program guide for details. Good luck!

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 17, 2017**.

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ENGINEERING STREAM

- Display of Antibodies
- Engineering Antibodies
- Engineering Bispecific Antibodies

Recommended Short Courses*

SC3: Genomics in the Service of Cancer Immunotherapy

SC9: Target Selection for Biologics
**Separate registration required, please see page 5-6 for course details.*

MONDAY, MAY 1

7:00 am **Registration and Morning Coffee**

From Library to Structure and Back: Mapping Receptor Ligand Interaction by Phage Display

8:30 **Chairperson's Remarks**
Gregory A. Weiss, Ph.D., Professor, Chemistry, Molecular Biology & Biochemistry, University of California, Irvine

8:40 **KEYNOTE PRESENTATION: Targeting Dynamic Protein Targets for Structural and Functional Insight**
Charles S. Craik, Ph.D., Professor, Pharmaceutical Chemistry, University of California, San Francisco
Fabs that recognize 3D protein conformations against proteins with high conformational entropy and large hetero-oligomeric complexes can enable subnanometer resolution in single particle cryo-electron microscopy. Once engineered, these Fabs can probe dynamic complex assembly in cells. Examples will be presented where Fabs are accelerating both structural and functional studies of dynamic and complex protein targets to accelerate their understanding and validation as bona fide therapeutic targets.

9:10 **Protein Engineering of Phage-Antibody Complexes for Biomarker Detection**
Jennifer Cha, Ph.D., Norviel Associate Professor, Chemical & Biological Engineering, University of Colorado, Boulder
This talk will highlight our recent efforts at using protein engineering to build covalent crosslinks between bacteriophage and the Fc portion of monoclonal antibodies. The phage-antibodies are used to target and bind specific analytes while the phage genome is genetically modified to generate amplified signals in real time with specific primers.

9:40 **Bio-Inspired Phage Material Assembly and Applications**
Seung-Wuk Lee, Ph.D., Professor, Bioengineering, University of California, Berkeley; Faculty Scientist, Biological Systems and Engineering, Lawrence Berkeley National Laboratory
I will demonstrate a facile biomimetic process to create functional nanomaterials utilizing M13 phage. A single-step process produces long-range-ordered films showing multiple levels of hierarchical organization. Using the self-assembly processes, we have created various biomimetic supramolecular nanostructures. The resulting materials show distinctive optical and photonic properties. Through the directed evolution of the phages, I will show how resulting materials can be utilized as functional nanomaterials for biomedical and biosensor applications.

10:10 **Coffee Break**

Cytoplasmic Delivery

10:45 **Chairperson's Remarks**
K. Dane Wittrup, Ph.D., J.R. Mares Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

10:50 **Cytosol-Penetrating IgG Antibody and Its Application for Directly Targeting Disease-Associated Cytosolic Proteins**
Yong-Sung Kim, Ph.D., Professor, Molecular Science and Technology, Graduate School; Professor, Applied Chemistry and Biological Engineering; Director, Pioneer Research Center for iMab, Ajou University
The ability of an IgG-format antibody to reach the cytosol of target mammalian cells from outside of cells is highly desired for diverse purposes. In this talk, I will introduce the cytosol-penetrating antibody, named cytotransmab, and its application for directly targeting disease-associated cytosolic proteins after systematic administration.

11:20 **Precision Delivery of Proteins into the Cytosol of Cells**
Amy Rabideau, Ph.D., Scientist, Moderna Therapeutics
There are a number of methods to deliver bioactive peptides and proteins into mammalian cells for biotechnological purposes. Most approaches do not allow for routine precision delivery of chemical entities such as mirror image peptides and intrabodies. Here, we present a macromolecular delivery platform based on an engineered bacterial transport machine that allows for facile delivery of bioactive variants to the cytosol of cells. We show the delivered cargo can disrupt protein-protein interactions in cancer cells and induce cell death. Further, we show targeted delivery of a RAS/RAP specific protease to pancreatic cells.

Display of Antibodies

11:50 Rapid Screening of Cyclotide-Based Libraries against Intracellular Protein-Protein Interactions

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

The cyclotide scaffold has a tremendous potential for the development of therapeutic leads based on their extraordinary stability and potential for grafting and molecular evolution applications. We will show an example, where a large cyclotide-based genetically encoded library was used to screen for low nanomolar inhibitors of the Hdm2-HdmX complex. We will also present different strategies to improve the cellular uptake and pharmacokinetic profiles of bioactive cyclotides.

12:20 pm Further Advancements for Human Antibody Discovery

Sponsored By AB CHECK

Vera Molkenthin, Ph.D., Chief Scientist, AbCheck s.r.o.

AbCheck has developed Mass Humanization to generate humanized libraries. This approach utilizes batch cloning of CDR3 immune repertoires from immunized rabbits into selected human frameworks containing specifically diversified CDR1 and CDR2 regions. For selecting high affinity binders from the resulting, highly diverse library, AbCheck routinely applies Phage or Yeast Display under various conditions. In this talk, AbCheck will present new technological developments regarding its human antibody discovery and optimization platform.

12:50 Luncheon Presentation I: Antibody Library Display on a Mammalian Virus: Application to both Soluble and Complex Membrane Antigens

Sponsored By VACCINEX

Ernest S. Smith, Ph.D., Senior Vice President, Research & CSO, Vaccinex, Inc.

We have developed an antibody discovery platform that enables efficient expression of a library of antibodies in IgG format on the surface of both a mammalian virus and the cell surface, enabling rapid selection of high quality antibodies. We have also modified this technology to enable the direct incorporation of multipass membrane proteins into the viral membrane. Antigen expressing virus can be readily purified and used for antibody selection.

1:20 Luncheon Presentation II: The Use of Biosensor Display Libraries in Antibody Discovery

Sponsored By INNOVATIVE TARGETING SOLUTIONS

Paul Kang, CSO, Discovery Research, Innovative Targeting Solutions

Cell-based biosensors are extremely sensitive and can be used to detect a diverse range of biological targets. The presentation will describe the use of V(D)J recombination mediated *de novo* antibody sequence diversification, mammalian display and antigen dependent signaling based biosensors to generate a powerful new antibody discovery platform, Biosensor Display. Antibody based cell biosensor libraries will provide unparalleled access to traditionally challenging multi-pass membrane targets, such as GPCRs and ion channels, in their native environments.

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

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

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

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

4:10 Bicycles and Bicycle Drug Conjugates: Next Generation Therapeutics

Sir Gregory Winter, Ph.D., FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics

Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles' unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs); a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. This presentation will describe both the Bicycle® and BDC platforms.

4:55 Young Scientist Keynote: Programming Proteins by Deep Sequencing and Design

Tim Whitehead, Ph.D., Assistant Professor, Chemical Engineering and Materials Science, Michigan State University

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 group leverages this unprecedented wealth of sequence-function information to design and engineer protein affinity, specificity, and function and to infer structural complexes of proteins. My talk will present an overview of the above and detail methodological improvements that enable the engineering work.

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

6:55 End of Day

TUESDAY, MAY 2

8:00 am Registration and Morning Coffee

Emerging Applications and Platforms for Novel Screening

8:25 Chairperson's Remarks

Jennifer Cochran, Ph.D., Hitachi America Associate Professor, Bioengineering and Chemical Engineering, Stanford University

8:30 Genetically-Encoded Libraries of Chemically-Modified Peptides

Ratmir Derda, Ph.D., Assistant Professor, Chemistry, University of Alberta

Genetically-encoded (GE) libraries of polypeptides are one of the major sources of discovery of biological drugs. They are often limited to handling of structures made of 20 natural amino acids. We use GE-libraries of peptides as a starting material for multi-step organic synthesis to produce GE-molecules that combine peptide scaffolds with variable, genetically-encoded "unnatural" modifications. These libraries allow attacking unsolved problems in molecular recognition and

Display of Antibodies

discovery of ligands for "undruggable targets" such as carbohydrate binding proteins.

9:00 Reprogramming Immunity with Engineered Interleukin-2 Antibodies

Jamie Spangler, Ph.D., Postdoctoral Fellow, Garcia Lab, Molecular & Cellular Physiology and Structural Biology, Stanford University School of Medicine

Interleukin-2 (IL-2) is a multi-functional cytokine that regulates immune homeostasis, but its concurrent promotion of both immune effector cells and regulatory T cells has limited its efficacy as an immunotherapeutic. Certain anti-IL-2 antibodies selectively direct cytokine activity toward particular cell subsets, presenting an exciting opportunity for targeted therapy. We elucidated the molecular mechanisms through which antibodies bias cytokine function and built on our insights to engineer promising cytokine-targeted antibody therapeutics.

9:30 Synthetic Human Antibody Fragment Libraries for CAR T Cell Therapy

Thomas J. Van Blarcom, Ph.D., Associate Research Fellow, Rinat Laboratories, Bio-Therapeutics Division, Pfizer Inc.

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

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

EMERGING APPLICATIONS AND PLATFORMS FOR NOVEL SCREENING (Continued)

10:45 Chairperson's Remarks

David Lowe, Ph.D., Senior Director, R&D, Antibody Discovery and Protein Engineering, MedImmune Ltd.

10:50 Transpo-mAb: Transposon-Mediated B Cell Display and Functional Screening of Full-Length IgG Libraries

Roger R. Beerli, Ph.D., CSO, NBE-Therapeutics AG

Transpo-mAb is a novel and highly efficient non-viral antibody discovery and engineering platform, allowing for the efficient display of full-length antibodies on the surface of B lymphocytes. Due to a built-in switch between surface and secreted expression, functional screening can be seamlessly integrated into the antibody discovery workflow. Several examples, including the direct identification of mAbs suitable as backbones of antibody drug conjugates, will be presented.

Engineering Novel Functionalities into Variable Regions

11:20 Chairperson's Remarks

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

11:25 Computational Design and Experimental Validation of Antibodies with Increased Affinity

Roland L. Dunbrack, Jr., Ph.D., Professor, Institute for Cancer Research, Program in Developmental Therapeutics, Fox Chase Cancer Center

We have developed an antibody design computational protocol, implemented in Rosetta, that is based on our clustering of CDR structures (doi:10.1016/j.jmb.2010.10.030). The program replaces CDRs with loops of different lengths and conformations and performs sequence design on the inserted CDR to improve binding. In benchmarking, we are able recapitulate native antibodies. We have designed new CDRs for two antibodies and were able to increase the experimental binding affinity 2-50 fold.

11:55 Antibody Discovery Using Natural and Nature-Emulating Diversity Libraries

Eunice Zhou, Ph.D., Associate Adjunct Professor, Anesthesia, University of California, San Francisco

Naïve human antibody CDR sequences were collated and used to design non-redundant synthetic CDRs matching the naturally occurring diversities. These synthetic non-redundant CDRs were inserted into the well expressing V-gene frameworks, and displayed to construct phage Ab library. Such phage Ab library was used to isolate high quality renewable antibodies (rAbs), which are essential reagents for determining how proteins function under normal and pathophysiological conditions.

Sponsored By TaKaRa

12:20 pm Facilitating Novel Antibody Discovery and Engineering with a Membrane-Based Antibody Purification Workflow

Keren Drori, Ph.D., Product Manager II, Protein Science, Takara Bio USA

There is a constant need for faster, more efficient antibody and protein purification processes at any scale. High-capacity membrane technologies allow for purification directly from complex matrices, such as cell supernatants, in minutes. This new approach also provides highly purified and concentrated antibodies and his-tagged proteins, even from samples containing additives not compatible with other purification technologies. This talk will review several applications including purification of a GPCR, hybridoma screening, and purifying secreted protein.

Sponsored By aptaIT

12:50 A New Next-Generation Sequencing Analysis Tool for Improved Identification of Peptide and Antibody Ligands

Michael Blank, Ph.D., CSO, Research & Development, AptaIT GmbH

AptaIT's new desktop software is an intuitive and user-friendly tool enabling the improved identification of B-cell receptors or ligands from biopanning experiments. Individual selection rounds or defined stages of the immune response, which are digitalized by NGS, can be analyzed at very high resolution. The software provides results in form of comprehensible, interactive graphs and tables and allows a systematic reduction of big data down to a number of relevant sequences for subsequent experimental testing.

Display of Antibodies

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

NGS with Display: Phage, Yeast and Bacterial

2:00 Chairperson's Remarks
David Lowe, Ph.D., Senior Director, R&D, Antibody Discovery and Protein Engineering, MedImmune Ltd.

2:05 Mapping the Targets of Antibody Repertoires for Diagnostic and Therapeutic Development
Patrick S. Daugherty, Ph.D., President & CSO, Serimmune Inc.; Adjunct Professor, University of California, Santa Barbara

The functional composition of antibody repertoires, as defined by the collection of unique antigen-epitope binding specificities, remains obscure. The convergence of display library technologies, robust NGS technology, and computational advances has provided an opportunity to characterize the diversity of antigen epitope binding specificities present within antibody repertoires in health and disease. This digital serology approach provides a new tool to support diagnostics, vaccine and therapeutic development.

2:35 Bacterial Surface Display for Antibody Engineering and Stratification of Patients
Johan Rockberg, Ph.D., Assistant Professor, Proteomics and Nanobiotechnology, KTH - Royal Institute of Technology

There is a need for precise classification of responsive patients for their safe and cost-effective treatment. We use bacterial display for structural epitope mapping of the approved drug eculizumab to C5 identifying six residues essential for binding, some which were present as germlines of non-responding patients. Instead we show potential of another drug (OmCI) for these groups. Personal medicine and antibody engineering using gram-positive display will be covered.

3:05 High-Throughput Screening for Antibody Discovery Using Mirrorball
Sponsored by ttplabtech
Christyne Kane, Ph.D., Senior Scientist, AbbVie Bioresearch Center, Inc.

3:20 High-Fidelity Next-Generation Sequencing of Full Variable Region of Antibody Libraries
Sponsored by CELEMICS
Hyoki Kim, Ph.D., President and CEO, Celemics Inc.

NGS-based antibody library analysis faces key issues of sequencing error rate, short read length and need of gene synthesis for binding assay. In this talk, we will discuss our newly developed technology that enables to obtain accurate read of antibody libraries and provides the corresponding scFv gene for binding assay.

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

4:25 Next-Generation Sequencing of mRNA Display Selections
Martin Wright, Ph.D., Associate Director, Selection Technologies, Bristol-Myers Squibb

Applications of NGS with mRNA display selection will be discussed. This will include methods to recover low-abundance sequences from a diverse population and additional methods for rapid optimization of antibodies and other polypeptides.

4:55 Hierarchy and Extremes in Selections from Antibody Libraries
Clément Nizak, Ph.D., Research Scientist, Laboratory of Biochemistry, CNRS-ESPCI

Efficient selection requires sufficiently diverse libraries, but merely counting the number of different clones does not fully characterize a library's selective potential. We analyzed phage display selection outcome by high-throughput sequencing to quantitatively characterize selective potentials. They follow simple statistical laws, which can be interpreted with extreme value theory, and show a marked hierarchy between libraries. We provide a quantitative approach to measure the selective potential of a library.

5:25 End of Display of Antibodies

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC13: Phenotypic Screening Applications and Technologies
**Separate registration required, please see page 5-6 for course details.*

Recommended Short Courses*

SC13: Phenotypic Screening Applications and Technologies

SC14: Overcoming the Challenges of Immunogenicity Assays, Risk Assessment and Meeting Regulatory Requirements
**Separate registration required, please see page 5-6 for course details.*

WEDNESDAY, MAY 3

7:30 am Registration and Morning Coffee

8:30 Chairperson's Remarks
Robin Barbour, Head, Antibody and Assay Development, Research, Prothena Biosciences

8:40 KEYNOTE PRESENTATION: New High-Throughput Model for Optimizing Antibody Affinities
Frederick Alt, Ph.D., Charles A. Janeway Professor of Pediatrics, Boston Children's Hospital; Professor of Genetics, Harvard Medical School; Director, Program in Cellular and Molecular Medicine, Boston Children's Hospital

We will describe our new approach to utilize natural primary and secondary mechanisms of antibody optimization *in vivo* to improve therapeutic antibodies. We use genetically modified ES cells to rapidly generate chimeric mice that extensively diversify a given therapeutic antibody. Following immunization, variant therapeutic antibodies with superior properties to the prototype can be selected. We validated this system by substantially improving the antigen binding affinity of an existing therapeutic antibody.

High Resolution Imaging and Structural Biology

9:10 Novel Mechanism of Antigen Recognition by Extremely Specific Synthetic Antibodies
Shohei Koide, Ph.D., Professor, Biologics Design, Langone Medical Center, New York University

Creating molecular recognition interfaces that discriminate subtle chemical differences remains a major challenge in protein engineering. We have generated synthetic antibodies against histone tails that cleanly discriminate the difference of a single methyl group, arguably the smallest difference in antigens. Crystal structures and mechanistic studies revealed a surprising mechanism underlying their exquisite specificity, which has led to the design of new antibody formats suitable for achieving exceptional specificity.

9:40 Electron Microscopy Structures of Dual Variable Domain Immunoglobulin (DVD-Ig1) and its Complex with Target Antigen
Paul Matsudaira, Ph.D., Professor, Dept. of Biological Sciences, National University of Singapore

A dual variable domain immunoglobulin, DVD-Ig1, forms 1:2 and 2:2 complexes with its antigen, TNFα. Our negative stain TEM studies show that DVD-Ig1 displays flexibility with different angles between the Fab arms and dynamics by the two Fab's outer domains: without TNFα (DVD-Ig1 alone) and with TNFα (DVD-Ig1/TNFα complexes). In addition, the structures of these molecules and complexes were studied using single particle cryoEM and preliminary findings will be discussed.

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

Deep Sequencing and B-Cell Screening

10:55 Droplet Microfluidics in High-Throughput Antibody Discovery and Vaccine Development
Christoph Merten, Ph.D., Group Leader Microfluidics, European Molecular Biology Laboratory (EMBL)

We have developed droplet-based microfluidic platforms for the discovery of therapeutic antibodies. The technology allows the direct screening of >1 million primary, non-immortalized plasma cells (optionally from humans) in a single experiment and also facilitates assays for the effect of antibodies on target cells (e.g. modulating GPCRs). In a complementary approach we use the technology to derive vaccine candidates starting with neutralizing antibodies against pathogens such as HIV.

11:25 Germline-Encoded Neutralization of a *Staphylococcus Aureus* Virulence Factor by the Human Antibody Repertoire
Andy Yeung, Ph.D., Associate Research Fellow, Rinat-Pfizer

We employed single-B cell cloning, phage display, high-throughput sequencing, epitope mapping, and crystallography to characterize in detail the humoral immune response to the staphylococcal protein IsdB. We show that in all donors a heavily biased use of two immunoglobulin heavy chain germlines generated ultra-high affinity neutralizing antibodies. Interestingly, the binding is primarily driven by the germline-encoded CDR-H2, with a binding mechanism nearly identical for each antibody derived from different donors.

11:55 Antibody Specificity Profiling by Combining NGS with a Plug-and-(Dis)play Hybridoma Platform
Sai Reddy, Ph.D., Assistant Professor, Biosystems Science and Engineering, ETH Zurich

In this presentation, I will show how we are combining this NGS-based analysis with a novel mammalian hybridoma display platform for antibody screening and discovery. Specifically, we use NGS to identify candidate antigen specific clones from immunized repertoires, we then integrate these antibody clonal libraries into our hybridoma platform using CRISPR-Cas9 genome editing. Flow cytometry is

Engineering Antibodies

then used to screen and isolate antigen-specific antibodies.

12:25 pm CHO Cell Line Engineering for Enhanced Productivity and Stability

Sponsored By SELEXIS

Pierre-Alain Girod, Ph.D., CSO, Selexis

Stable, high quality production cell lines secreting optimal levels of recombinant protein require stable integration of the recombinant DNA, elevated gene transcription, optimized secretion and metabolic machinery to handle the increased protein loads along with cellular phenotypic stability. Using the extensive transcriptomic and FISH-RNA/DNA data we have generated for our CHO-K1 cell line (CHO-M), we will describe how we are significantly boosting production capabilities and cell line stability of our CHO-M cell line.

12:55 Luncheon Presentation I: The Trianni Mouse: Best-In-Class Technology for Human Antibody Discovery

Sponsored By TRIANNI

David Meininger, Ph.D., Chief Business Officer, Trianni, Inc.

The Trianni Mouse is the only human transgenic antibody discovery platform offering a complete heavy, kappa and lambda repertoire in a single organism. Sequences of the variable domain exons are human while all genetic machinery are of mouse origin. The platform is seen as best-in-class by multiple Big Pharma and other licensees subsequent to extensive validation and benchmarking. Additional strains in development include Plasma Ig, Autoimmune/All Epitope and a "true" Bispecific.

1:25 HuMab Chickens: The Next Generation Antibody Discovery Platform

Sponsored By CRYSTAL BIOSCIENCE

Bill Harriman, Ph.D., CEO, Crystal Bioscience

Transgenic rodents producing human sequence antibodies are widely accepted as a reliable source of therapeutic candidates. However, their repertoires are limited by their evolutionary similarity to humans. Crystal Bioscience has expanded the repertoire of transgenic animals by engineering HuMab chickens producing fully human sequence, high affinity mAbs. In addition to revealing novel epitopes and, therefore novel IP, the Crystal Platform yields mAbs recognizing murine orthologs of human antigens that facilitate pre-clinical studies.

1:55 Session Break

Mechanisms of Action

2:10 Chairperson's Remarks

Elizabeth England, Scientist, Antibody Discovery and Protein Engineering, MedImmune

2:15 Counteracting Tumor Evasion of Antibody Immunity by a Novel Therapeutic Strategy

Zhiqiang An, Ph.D., Professor and Robert A. Welch Distinguished University Chair in Chemistry, University of Texas Health Science Center at Houston

Immune suppression is recognized as a hallmark of cancer and this notion is largely based on studies on cellular immunity. Our recent studies have demonstrated a potential new mechanism of cancer suppression of immunity by impairment of antibody effector function mediated by proteolytic enzymes in the tumor microenvironment. Furthermore, we are exploring strategies to restore the lost functions to the damaged antibodies, which represent potentially new directions in cancer immunotherapy.

2:45 Discovering Antibodies to a Moving Target

Elizabeth England, Scientist, Antibody Discovery and Protein Engineering, MedImmune

MedImmune has shown that IL-33 forms disulphide bonds, resulting in large conformational changes. This occurs rapidly, posing a challenge in identifying antibodies that inhibit the action of IL-33. Through innovative use of mutant forms of IL-33 and appropriate design of screening campaigns, a highly potent inhibitor of IL-33 was identified, a testament to how understanding of target structure and biology is key to the identification of potential therapeutic drug candidates.

3:15 llamdA™ Next Generation VHH Library: Combining Immune Functionality with Synthetic Diversity

Sponsored By isogenica

Guy Hermans, Ph.D., CSO, Isogenica Limited

3:30 Improving Developability with Protein Surface Charge and Hydrophobic Patch Analysis

Sponsored By CHEMICAL COMPUTING GROUP

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

We describe a computational method for identifying and measuring hydrophobic and charged patches on the surface of the protein structure. An analysis of protein complexes in the PDB suggests that hydrophobic patches play an important role in binding. Their application to reducing aggregation, improving solubility, and epitope mapping is demonstrated.

4:00 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, MAY 4

8:00 am Morning Coffee

Computational Modeling for Antibody Engineering

8:30 Chairperson's Remarks

Ruud de Wildt, Ph.D., Director, Head, Antibody Selections, Biopharm, GlaxoSmithKline

8:35 Modeling and Docking Antibody Structures with Rosetta

Jeliazko Jeliazkov, Research Assistant, Molecular Biophysics, Johns Hopkins University

Structures of antibodies in complex with their antigens can give insight into therapeutic mechanisms and suggest improved antibody designs. We have developed computational methods (1) to create atomically accurate models of antibodies from their sequences and (2) to dock those models to antigens. This talk will present the methods, critically analyze their accuracy, and demonstrate

Engineering Antibodies

applications to large-scale repertoire analysis as well as Celiac disease and pulmonary hypertension.

9:05 Computational Design of *de novo* Anti-Influenza Minibinder Proteins

Christopher Pirie, Ph.D.,CEO, Virvio, Inc.

Rosetta computational design can create proteins that target neutralizing epitopes on Influenza hemagglutinin. These designed proteins bind like broadly neutralizing antibodies, but in a smaller molecule that is both more manufacturable and stable. In animal models they inhibit the function of hemagglutinin and prevent viral infectivity. These computationally designed binders represent a new class of protein therapeutics for infectious diseases.

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SCHRÖDINGER. BIOLOGICS

9:35 Computational Approaches in Antibody Design: Identifying and Reducing Liabilities Early in the Discovery Process

David Pearlman, Ph.D., Senior Principal Scientist, Schrödinger

Computational tools that can be used in the optimization process for putative antibody drug candidates have greatly improved in the past several years. Using the BioLuminate software platform, we describe both how these calculations can be utilized for workflowed triage among multiple candidates, and how tools such as FEP can be used to suggest sequence engineering that can ameliorate identified liabilities such as aggregation propensity while maintaining affinity and stability.

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

Antibodies for Emerging Targets

11:05 Optimizing Antibodies for Targeting the Tau Protein for Alzheimer's Disease and Other Tauopathies

James A. Ernst, Ph.D., Senior Scientist, gRED, Protein Chemistry and Neuroscience, Research and Early Development, Genentech, Inc.

Tau is a prime therapeutic target for Alzheimer's disease. We discovered that in pre-clinical models *in vivo* and in cell based experiments, effector function is not required for targeting tau efficaciously with tau antibodies, and that attenuation of effector function could be advantageous. We propose that effector function status is an important consideration when designing therapeutic tau antibodies, and potentially for antibodies against other neurodegeneration targets as well.

11:35 Progress and Challenges with the Isolation and Optimization of Antibodies against Multi-Spanning Transmembrane Targets

Ruud de Wildt, Ph.D., Director, Head, Antibody Selections, Biopharm, GlaxoSmithKline

Raising antibodies to complex cellular targets such as ion channels, G-protein coupled receptors (GPCRs) and other multi-spanning membrane targets is typically very challenging due to their complex nature and limited antigen availability. This talk will describe the strategies implemented by GSK to successfully identify high potency neutralizing antibodies for such targets, using the ADIMABTM yeast-based platform and *in vivo* immunization approaches.

12:05 pm Targeting Islet Amyloid Polypeptide (IAPP) as an Immunotherapy for Type 2 Diabetes

Robin Barbour, Head, Antibody and Assay Development, Research, Prothena Biosciences

Islet Amyloid Polypeptide (IAPP) is a 37 amino acid aggregation prone peptide that is co-secreted with insulin, and the toxicity of IAPP aggregates are believed to contribute to the pathophysiology of type 2 diabetes. We used a transgenic rat model that expresses human IAPP, which presents type 2 diabetes-relevant phenotypes such as pancreatic IAPP deposition and loss of insulin-secreting beta-cells, and showed that anti-IAPP immunotherapy slowed the disease progression in this model.

12:35 End of Engineering Antibodies

Engineering Bispecific Antibodies

The Future of Immunotherapy Development

Recommended Short Courses*

SC3: Genomics in the Service of Cancer Immunotherapy

SC11: Adoptive Therapy with CAR T Cells
**Separate registration required, please see page 5-6 for course details.*

THURSDAY, MAY 4

Bispecific Antibodies for Cancer Immunotherapy

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Christian Klein, Ph.D., Discovery Oncology oDTA, Pharma Research and Early Development (pRED), Roche Glycart AG

1:50 KEYNOTE PRESENTATION: Engineering Bispecific Antibodies for Cancer Immunotherapy
Nai-Kong V. Cheung, M.D., Ph.D., Enid A. Haupt Endowed Chair, Pediatric Oncology, Memorial Sloan Kettering Cancer Center
Conventional IgG monoclonal antibodies (mAbs) utilize Fc-dependent mechanisms which are constrained by low killing potency, poor cell trafficking, and the absence of memory. Bispecific (or multi-specific) antibody (BsAb) constructs can drive polyclonal T cells into solid tumors to enhance the anti-tumor response despite the immunosuppressive tumor microenvironment. These antibodies bypass the need for prior immunization, as well as the need for tumor HLA and costimulatory molecules. For payload delivery, bsAb can also be exploited in multistep targeting to vastly improve the therapeutic ratio.

2:20 Novel Approaches in the Use of Bispecific Antibodies for Cancer Immunotherapy
Christian Klein, Ph.D., Head, Oncology Programs; Department Head, Cancer Immunotherapy Discovery, Pharma Research and Early Development (pRED), Roche Glycart AG
Cancer immunotherapy has emerged as key modality to achieve long term response in cancer therapy. A number of antibody-based cancer immunotherapies has been approved recently and/or is currently being investigated in clinical trials. This presentation will give an overview over the design and the *in vitro* and *in vivo* pharmacological properties of T cell bispecific antibodies and novel strategies introduced to enhance their activity.

2:50 Development of T Cell Redirecting Fully Human Bispecific Antibodies
Eric Smith, Ph.D., Associate Director, Bispecifics, Regeneron Pharmaceuticals
This presentation will describe Regeneron's bispecific antibody platform as well as the development of REGN1979, a fully human CD20xCD3 bispecific antibody. Characterization of the *in vitro* and *in vivo* properties of this bispecific will be discussed, along with findings from preclinical and phase 1 clinical studies. In addition, development of new T cell redirecting bispecifics for solid tumor indications will be discussed.

3:20 Design and Evaluation of Next-Generation Biotherapeutics
Maria Wendt, Ph.D., Head of Science, Biologics, Genedata
Bi- and multi-specifics, alternative scaffolds, ADCs, TCRs, CARs can provide significant advantages over traditional mAb molecules. However, as highly engineered molecules they pose new design, cloning, expression, purification, and analytics challenges. Our workflow platform employed by top biopharma companies enables the automation, engineering, production, and testing of large panels of these candidate therapeutic molecules. We demonstrate the platform's high-throughput capability when handling novel molecule-specific designs and its built-in tools for developability and manufacturability assessments.

3:50 Refreshment Break

4:20 Enhanced Affinity TCR-Based Cancer Immunotherapy: Development of Novel Targets
Adriana Gambardella, Ph.D., Senior Scientist, Autoimmune Group, Immunocore Ltd.
Immune Mobilising Monoclonal TCRs against Cancer (ImmTACTM) molecules are bispecific reagents comprising a monoclonal TCR (binding a unique tumour-associated peptide) and an anti-CD3 scFv domain (recruiting and activating T cells). ImmTAC molecules are extremely efficient and specific in recognising and enabling target cell killing. Target selection and affinity engineering of TCRs are critical steps in the development of potent ImmTAC molecules through a robust process involving in-depth molecular and cellular analyses.

4:50 PANEL DISCUSSION

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC18 Clinical Prospects for Cancer Immunotherapy
**Separate registration required, please see page 5-6 for course details.*

Engineering Bispecific Antibodies

FRIDAY, MAY 5

8:00 am Morning Coffee

Applications Outside Oncology

8:30 Chairperson's Remarks
Eric Smith, Ph.D., Associate Director, Bispecifics, Regeneron Pharmaceuticals

8:35 The "Evil Hitch-Hiker" Effect: Bispecific Antibodies to Target Viruses in Endosomes
Kartik Chandran, Ph.D., Professor, Microbiology and Immunology, Harold and Muriel Block Faculty Scholar in Virology, Albert Einstein College of Medicine
Conventional antiviral immunotherapies cannot access the exquisitely sensitive "cryptic" viral epitopes that are unmasked in endosomes during cellular invasion. To target these epitopes in Ebola virus, we developed bispecific antibodies that coopt virus particles themselves for endosomal delivery. Blockade of the endosomal virus-receptor interaction by these antibodies afforded broad antiviral efficacy *in vivo*. This approach should be widely applicable to the development of antiviral immunotherapeutics.

9:05 Preclinical Development of HIVenv x CD3 Bispecific DART® Molecules for Elimination of Latent HIV Reservoirs
Annie Lam, Ph.D., Scientist II, Antibody Engineering, MacroGenics, Inc.
The principal barrier to HIV cure is a remarkably stable reservoir of latently infected cells. To eliminate this reservoir, we generated and tested several HIVenv x CD3 bispecific DART® molecules capable of redirecting T cells against latently-infected cells. In this talk, we will discuss considerations that guide our molecular design and present data that support further development of HIVenv x CD3 DART® molecules towards clinical applications.

9:35 Bispecific CD20 x CD3 IgM with Enhanced Potency and Safety
Bruce Keyt, Ph.D., CSO, IGM Biosciences
IGM Biosciences has constructed a unique bispecific CD20xCD3 IgM. The IgM pentamer binds CD20 and a modified J-chain displays a scFv binding CD3e domain. IGM-2323 binds CD20 antigen more potently (1000x) with greater CDC (100x) compared to IgG. TDCC is effective on CD20 low B cells with reduced cytokine release profile. *In vivo* studies show low doses (3 ug/mouse) yield complete B-cell killing. These data indicate broad application for potent asymmetric bispecific IgM formats.

10:05 Coffee Break

Developing Assays for Selecting Target Combinations

10:30 Chairperson's Remarks
G. Jonah Rainey, Ph.D., Executive Director, Head of Antibody Research, MabVax Therapeutics Holdings, Inc.

10:35 Bi-and Multi-Specific Biologics for Cancer Immunotherapy: Selecting Target Combinations and Designing Biologics to Modulate Anti-Tumor T Cell Functions
Tariq Ghayur, Ph.D., Distinguished Research Fellow, Biologics, AbbVie Bioresearch Center, Inc.
The technological challenges of making bi-/multi-specific biologics are mostly solved and several formats are now in clinical development. The key challenge now is identify the right target combinations and designing the right bi-/multi-specific molecule(s) to achieve the desired outcomes. In this presentation we will describe novel approaches we have developed to identify target combinations and novel bi-/multi-specific formats to reveal novel biology and/or address key biological questions.

11:05 Tuning Bispecific Antibodies for Efficacy and Safety
Stephen J. Demarest, Ph.D., Senior Research Advisor, Protein and Antibody Engineering, Lilly Biotechnology Center
Bispecific antibodies provide more than the ability to deliver two drugs in one molecular package. They can be used to fine tune receptor binding, more precisely target specific cell types, and provide novel receptor/cellular engagements unattainable with antibody combinations. This presentation will focus on new advances in bispecific technology and novel therapeutic modalities realized through fine-tuning of bispecific antibody binding to cell surface receptors.

11:35 Overcoming Obstacles to CAR T Cell Therapy in Solid Tumors
Sujith K. Joseph, Ph.D., Staff Scientist, Department of Pediatrics Center for Cell and Gene Therapy Baylor College of Medicine
Our bispecific CAR technology, which includes a second binding domain on the CAR T cell that can lead to either an inhibitory or amplifying signal, can increase specificity of our CAR T cells for cancer cells versus normal cells. For example, a CAR T cell can be engineered such that it would be triggered in the presence of one target protein, but if a second protein is present it would be inhibited. Alternatively, it could also be engineered such that two target proteins would be required for maximal activation. These approaches may increase the specificity of the CAR for tumor relative to normal tissue.

12:05 pm Engineering Anti-PDL1 Antibody Based Bifunctional Fusion Protein and Bispecific Antibody for Enhanced Antitumor Activity
Zhenping Zhu, M.D., Ph.D., CSO and President, R&D, 3SBio, Inc.
This talk will cover the rationale for dual target engagement, describe the design and engineering the molecules and present *in vitro* and *in vivo* proof-of-concept studies.

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

1:05 Refreshment Break

Engineering Bispecific Antibodies

Compartmental Targeting and Payload Delivery Strategies

1:35 Chairperson's Remarks

Nai-Kong V. Cheung, M.D., Ph.D., Enid A. Haupt Endowed Chair, Pediatric Oncology, Memorial Sloan Kettering Cancer Center

1:40 Efficient Payload Delivery by a Bispecific Antibody-Drug Conjugate Targeting HER2 and CD63

Bart De Goeij, Scientist, Antibody Science, GenMab A.V.

To improve efficacy of antibody-drug conjugates (ADCs), we have designed a bispecific ADC, in which one binding domain would provide tumor specificity (anti-HER2), whereas the other binding domain would facilitate targeting to the lysosomal compartment (anti-CD63). The resulting bsHER2xCD63his-ADC demonstrated strong binding, internalization and lysosomal accumulation in HER2-positive tumor cells as well as potent cytotoxicity against HER2-positive tumors, which was not observed with monovalent HER2- and CD63-specific ADCs.

2:10 Increased T Cell Infiltration into Tumor Microenvironment to Overcome Checkpoint Blockade Resistance

Yang-Xin Fu, M.D., Ph.D., Mary Nell and Ralph B. Rogers Professorship in Immunology, University of Texas, Southwestern Medical Center

Targeting tumors with tumor necrosis factor superfamily member LIGHT activates lymphotoxin beta receptor signaling, leading to the production of chemokines that recruit massive numbers of T cells. Furthermore, targeting non-T cell-inflamed tumor tissues by antibody-guided LIGHT creates a T cell-inflamed microenvironment and overcomes tumor resistance to checkpoint blockade. Our data indicates that targeting LIGHT might be a potent strategy to increase the responses to checkpoint blockades and other immunotherapies in non-T cell-inflamed tumors.

2:40 Beyond TfR: Identification of Novel Targets to Facilitate Uptake of Therapeutic Antibodies into the Brain

James A. Ernst, Ph.D., Senior Scientist, gRED, Protein Chemistry and Neuroscience, Research and Early Development, Genentech, Inc.

Therapeutic antibodies have shown tremendous success in the treatment of human disease. However several physiological compartments, including the central nervous system (CNS), allow for limited penetration of large molecules. Improved transport into these compartments could extend the opportunities for therapeutic antibodies in neuro-degeneration, improving both safety and efficacy. This presentation will focus on the selection of novel targets in the vasculature to facilitate receptor-mediated transcytosis into the brain.

3:10 Balancing Selectivity and Efficacy of Bispecific EGFR x c-MET Antibodies and Antibody-Drug Conjugates

Carolin Sellmann, Ph.D., Postdoctoral Researcher, Protein Engineering and Antibody Technologies, Merck KGaA (Darmstadt, Germany); Institute of Biochemistry, Technische Universität Darmstadt

Therapies targeting the tumor-associated antigen epidermal growth factor receptor (EGFR) often suffer from toxicities due to basal EGFR expression in normal tissue. Furthermore, EGFR-directed inhibitors might struggle with limited efficacy because of c-MET mediated resistance mechanisms. Hence, we aim to construct bispecific EGFR x c-MET antibodies employing affinity-optimized binding moieties to balance selectivity and anti-tumor efficacy and to evaluate their potential for an innovative antibody-drug conjugate approach.

3:40 End of Conference

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ONCOLOGY STREAM

- Antibodies for Cancer Therapy
- Advancing Bispecific Antibodies and Combination Therapy to the Clinic
- Antibody-Drug Conjugates II: Advancing Toward the Clinic

Antibodies for Cancer Therapy

Creating the Next Generation of Winning Strategies

Recommended Short Courses*

SC2: Translational Considerations for Development of Monoclonal Antibodies Part I: Focus on Early Discovery

SC7: Translational Considerations for Development of Monoclonal Antibodies Part II: Focus on Nonclinical Development to the Clinic

**Separate registration required, please see page 5-6 for course details.*

MONDAY, MAY 1

7:00 am Registration and Morning Coffee

Emerging Targets

8:30 Chairperson's Remarks

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

8:40 CAR-T Strategies Targeting Hematologic and Solid Malignancies

David G. Maloney, M.D., Ph.D., Medical Director, Cellular Immunotherapy; Leonard and Norma Klorfine Endowed Chair for Clinical Research, Fred Hutchinson Cancer Research Center; Professor, Medicine, Oncology, University of Washington

The recent successes of CD19-specific chimeric antigen receptor (CAR)-modified T cell immunotherapy are built on a foundation provided by previous generations of preclinical and clinical studies. Despite the many differences in CAR design, manufacturing strategies, and clinical delivery that make comparisons between clinical trials difficult to interpret, we are beginning to identify patterns that will inform future generations of the optimal design of CAR-T cell immunotherapy trials.

9:10 Beyond CD19: Alternative and Multispecific Immunotherapeutic Targeting Strategies to Overcome Leukemic Resistance to CAR Therapy

Terry J. Fry, M.D., Investigator and Head, Hematologic Malignancies Section, Pediatric Oncology Branch, National Cancer Institute

CD19 antigen loss may occur in approximately one third of patients achieving remission following CD19-targeted chimeric antigen receptor expressing T cell (CAR-T) therapy. Dr. Fry will discuss results from a CD22-targeted CAR-T trial demonstrating successful remission induction in patients relapsing after CD19 CAR-T cell therapy. He will then discuss the preclinical development of multispecific immunotherapeutic targeting approaches to prevent leukemic resistance due to antigen-loss.

9:40 Concerted Antibody Drug and Target Discovery by Phage Display

Christoph Rader, Ph.D., Associate Professor, Immunology, The Scripps Research Institute

The paucity of suitable targets for monoclonal antibodies and their derived entities, including antibody-drug conjugates, bispecific antibodies, and chimeric antigen receptor T cells, currently limits their broader utility for cancer therapy. To complement bottom-up target discovery strategies based on genomics and proteomics, we developed novel top-down, target agnostic approaches that are based on whole-cell selections of antibody libraries from immune and naïve antibody repertoires by phage display.

10:10 Coffee Break

10:50 KEYNOTE PRESENTATION: Immunotherapy – The Need for Novel Targets?

Laszlo Radvanyi, Ph.D., Senior Vice President and Global Head, The Immuno-Oncology Translational Innovation Platform at EMD Serono (a business of Merck KGaA, Darmstadt, Germany)

Despite the impact on overall response rates (ORRs) made by the new immuno-oncology agents, there are huge unmet needs in a number of difficult-to-treat cancers. While precision medicine and combination treatments may offer potential to further increase ORRs from checkpoint inhibitors to 40–50%, novel immunotherapy approaches may further unlock new mechanisms that attack cancer cells. This presentation will overview different approaches and where the next significant advances may come from.

11:20 Development on Novel Therapeutic Antibodies for Cancer Derived from Single Human B Cells

Edward F. Patz, Jr., M.D., James and Alice Chen Professor, Radiology; Professor, Pharmacology and Cancer Biology, Radiology, Duke University Medical Center

In an effort to develop novel therapeutic antibodies against a tumor specific antigen, we isolated and expressed DNA sequences from single, sorted B cells obtained from patients with autoantibodies against the relevant target. A recombinant antibody was then produced in mammalian cells, and shown to cause tumor growth inhibition *in vivo*. This strategy represents an alternative paradigm in antibody drug discovery.

11:50 Target Selection in Antibody Therapy Development

Bin Liu, Ph.D., Professor, Anesthesia, University of California, San Francisco

One of the most challenging tasks in antibody therapy development is target selection. In addition to tumor specificity, other factors need to be considered to maximize the therapeutic window. We will describe some of our approaches for cell surface target discovery and our experience in translational development of human antibodies binding to selected targets.

Antibodies for Cancer Therapy

12:20 pm Cancer Biotherapeutics - Affimers: A Novel Scaffold for Biotherapeutics

Sponsored By Avacta LIFE SCIENCES

Amrik Basran, Ph.D., CSO, Therapeutics, Avacta Life Sciences

Affimers® are a new protein scaffold with great potential for the generation of biotherapeutics. Based on the protease inhibitor Stefin A, large diverse libraries have been created by engineering in peptide loops into the scaffold backbone. Using phage display, we have identified competitive binders to a ranage of targets, including the immune check point, PD-L1. We have shown that the scaffold is amenable to being engineered with a range of half-life extension technologies.

12:50 The Better Biologic

Sponsored By distributed bio

Jacob Glanville, Ph.D., CSO, Distributed Bio Inc

The better biologic: bypassing traditional monoclonal developability and engineering barriers in the rapid developing of an IO portfolio of biosuperiors.

1:20 Session Break

2:20 Problem-Solving Breakout Discussions

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

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

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

4:10 Bicycles and Bicycle Drug Conjugates: Next Generation Therapeutics

Sir Gregory Winter, Ph.D., FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics

Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles' unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs); a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. This presentation will describe both the Bicycle® and BDC platforms.

4:55 Young Scientist Keynote: Programming Proteins by Deep Sequencing and Design

Tim Whitehead, Ph.D., Assistant Professor, Chemical Engineering and Materials Science, Michigan State University

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 group leverages this unprecedented wealth of sequence-function information to design and engineer protein affinity, specificity, and function and to infer structural complexes of proteins. My talk will present an overview of the above and detail methodological improvements that enable the engineering work.

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

6:55 End of Day

TUESDAY, MAY 2

8:00 am Registration and Morning Coffee

Anti-PD1 Therapy and Resistance Mechanisms in the Treatment of Malignant Diseases

8:25 Chairperson's Remarks

Soldano Ferrone, M.D., Ph.D., Division of Surgical Oncology, Surgery, Massachusetts General Hospital

8:30 CD19-Targeted CAR T Cell Therapies in the Lab and in the Clinic

Marco Davila, M.D., Ph.D., Associate Member, Blood and Marrow Transplantation, H. Lee Moffitt Cancer Center and Research Institute

A major advance for T cell therapy is the chimeric antigen receptor (CAR), which is a single chain variable fragment (scFv) fused to the signal domains of a T cell receptor (TCR). We review the clinical experience with CD19-targeted CAR T cells in patients with B cell malignancies and recent pre-clinical studies that suggest new directions in CAR design that can enhance function CAR T cell function in patients.

9:00 Combined Inhibition of IDO1 and PD-1 as an Effective Therapeutic Strategy in Cancer

Peggy Scherle, Ph.D., Vice President, Preclinical Pharmacology, Incyte Corporation

Antibodies to checkpoint receptors have demonstrated unprecedented efficacy in a broad range of tumors types and represent a new paradigm in cancer treatment focused on inhibition of mechanisms that suppress anti-tumoral immunity. Indoleamine-2,3-dioxygenase-1 (IDO1) has also emerged as an immunotherapy target due to its role in regulating T-cell responses. Preclinical and early clinical data will be described that support the combination of IDO1 inhibition with antibodies to checkpoint receptors.

9:30 Clinical Features and Response to Systemic Therapy in a Historical Cohort of Advanced or Unresectable Mucosal Melanoma

Paul B. Chapman, M.D., Attending Physician and Section Head, Department of Medicine, Memorial Sloan Kettering Cancer Center; Professor of Medicine, Weill Cornell Medical College

There is little data available regarding the pattern of first metastases in resected mucosal melanomas (MMs) as well as the response of advanced MM to cytotoxic therapy. A retrospective, single-institution cohort was assembled of all patients with advanced/unresectable MM between 1995 and 2012 who had received systemic therapy with available imaging.

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

Antibodies for Cancer Therapy

New Generation of Targeting Approaches for Immunotherapy

10:50 Bispecific Antibodies for T Cell Recruitment and Dual Checkpoint Blockade

John R. Desjarlais, Ph.D., CSO, Xencor, Inc.

Xencor's bispecific antibody platform utilizes a strongly hetero-dimerizing Fc domain and a scFv-Fab-Fc format to create high-yield and highly developable bispecific antibodies. We will discuss application of the platform to create of a pipeline of T cell-redirecting CD3 bispecifics that have compelling *in vivo* activity, and a series of bispecific antibodies that selectively target double-checkpoint-positive T cells to promote stronger T cell activation. Several checkpoint pairs, including PD1 x CTLA4, promote enhanced T cell activation *in vitro* and *in vivo*.

11:20 Breaking Symmetry: Towards a New Generation of Bispecific Antibodies

Luis Alvarez-Vallina, Ph.D., Associate Professor, Engineering, Aarhus University

For many applications, asymmetric configurations where one antigen is bound multivalently and another is bound monovalently may be advantageous. Recently, we have developed a technology platform that allows the rapid and efficient engineering of mono and multispecific tandem trimerbodies with defined stoichiometry and controlled orientation of the antigen binding domains.

11:50 Novel Insights on the Effect on Anti-PDL1 on the NK and Myeloid Cells in the Tumor Microenvironment

Yan Qu, Ph.D., Senior Principal Scientist, Pfizer

Antibodies blocking PD-1/PD-L1 axis have been designed as either hIgG4 or as an engineered hIgG1 isotypes which has low or no binding to the FcγR. Because PD-L1 can be expressed on activated T cells, in-depth understanding of PDL1's expression pattern within the tumor microenvironment is required for optimal isotype selection. Our recent preclinical data suggest that the effects of PD-L1 blockade on NK and myeloid suppressor cells in the tumor microenvironment are antibody isotype dependent.

Sponsored By OmniAb

12:20 pm Luncheon Presentation: OmniRat, OmniMouse, Omniflic: Transgenic Animals for the Generation of Fully Human Antibodies

Christel Iffland, Ph.D., Vice President, Antibody Technologies, Ligand

OmniAb® includes three transgenic animals for generation of human antibodies. OmniRat® and OmniMouse® generate antibodies with human idiotypes as effectively as wildtype animals make rat antibodies. OmniFlic® is an engineered rat with a fixed light chain for the development of bi-specific antibodies. OmniAb antibodies have been generated with more than 100 therapeutic targets. The first OmniAb antibody entered phase I trials in 2016.

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

Single Domain Antibodies, Novel Scaffolds and Antibody Fragments

2:00 Chairperson's Remarks

Horacio G. Nastri, Ph.D., Senior Director, Antibody Biotherapeutics, Incyte Corporation

2:05 Synergy Generates Picomolar Potency and a High Resistance Barrier in Combinectin: A Novel Trispecific HIV-1 Entry Inhibitor with Clinical Promise

Jonathan H. Davis, Ph.D., Principal Scientist, Protein Design, Bristol-Myers Squibb

We have designed a biological HIV-1 entry inhibitor with three linked active domains (two Adnectins and a helical peptide) that have separate inhibitory actions. Each of the individual components has an EC50 in the low nM range, but when fused into a single molecule, two different synergistic mechanisms enhance the potency by up to 100-fold or more, with a concomitant boost in the resistance barrier. We describe the design and optimization of the Combinectin, and discuss the general principal of how symmetric and asymmetric synergy can be used and combined to create extremely potent therapeutics.

2:35 Integrin-Targeted Combination Immunotherapy Using Fusion Proteins

Jennifer Cochran, Ph.D., Hitachi America Associate Professor, Bioengineering and Chemical Engineering, Stanford University

We have adapted an engineered integrin-binding peptide-Fc fusion to recruit immune cell effector functions to tumors. The co-administration of peptide-Fc fusion and an immune stimulating cytokine results in significant control of tumor growth in several tumor models, including melanoma and colon carcinoma, which is further enhanced by checkpoint blockade inhibitors.

3:05 Ultra-Deep Screening of Natural Antibody Repertoires Using High-Content Single-Cell Selection Assays

Carl Hansen, Ph.D., President & CEO, AbCellera

AbCellera's microfluidic platform enables deep screening of natural immune repertoires using a wide array of single-cell selection assays including multiplexed binding, species cross-reactivity, ligand blocking, and various cell-based assays. The combination of screening throughput and multi-step selection assays improves the diversity and speed of lead candidate generation.

Sponsored By HARBOUR BIOMED

3:20 Applying Novel Mice Platforms to Generate Fully |Human Antibodies for Global Biotherapeutic Innovation

Liang Schweizer. Ph.D., CSO, Harbour BioMed

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

Antibodies for Cancer Therapy

Emerging Companies and Novel Approaches

4:20 Chairperson's Remarks
Janice M. Reichert, Ph.D., Executive Director, The Antibody Society and Editor-in-Chief, mAbs

4:25 Antibody Coupled T Cell Receptor (ACTR): A New Modality for Naked Antibodies
Seth Ettenberg, Ph.D., CSO, Unum Therapeutics
Immunotherapy is a promising option for cancer treatment. Recent results of clinical trials specifically manipulating a patient's own T-cell response provide compelling evidence and clinical benefit. T-cells engineered to express an Antibody Coupled T-cell Receptor (ACTR), the ectodomain of CD16 fused to costimulatory and CD3z signaling domains, exert powerful cytotoxicity against tumor cells *in vitro* and *in vivo*. This approach allows for the production of a single cellular product to be combined with many different tumor-targeting antibodies, creating a universal T-cell product.

4:40 Bstrongximab, a Novel Antibody-Drug-Conjugate Targeting Metastatic and Aggressive Cancers
W. Mike Schopperle, Ph.D., CEO, CureMeta LLC
Almost all solid tumor patient deaths are due to metastatic cancer. CureMeta is a biotech company developing novel antibody-based therapeutics to treat and cure patients with metastatic cancers. We are generating novel antibodies and potent ADCs specific to embryonic targets which are not expressed in normal healthy tissues but are re-expressed in aggressive and metastatic cancer. Bstrongximab is the lead drug in CureMeta's pipeline.

4:55 Engineering Alphabodies to Generate Potent Inhibitors of Intracellular Protein-Protein Interactions
Yvonne McGrath, Ph.D., CSO, Complix NV
The Cell Penetrating Alphabody (CPAB) is a unique protein scaffold designed to target therapeutically important intracellular PPI. We will show that CPABs targeting the anti-apoptotic protein Mcl-1 enter cancer cells *in vitro*, disrupt the Mcl-1:BAK complex thereby activating BAK and apoptotic cell death. Integration of an albumin binding domain extends the half-life of CPABs, thereby allowing for efficient tumor uptake, apoptotic cell death and tumor growth retardation *in vivo*.

5:10 Immuno-Oncology Target Selection and Monoclonal Antibody Development Process
Maloy Ghosh, Ph.D., CSO, Zumutor Biologics
Rapid scientific understanding of Immuno-oncology led to an explosion of information on drug targets. The scenario gets more complicated with recent strategies of combination therapy with almost all monoclonal antibody therapies available. We will describe our strategy of analyzing these diverse yet hugely potential targets encompassing various cancers. We have developed unique non-immune and synthetic antibody libraries and used them in antibody display technologies to develop monoclonal antibody products against multiple targets.

5:25 End of Antibodies for Cancer Therapy

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC12: Study Design and Statistical Data Analysis of Flow Cytometry Assays
**Separate registration required, please see page 5-6 for course details.*

Advancing Bispecific Antibodies and Combination Therapy to the Clinic

Creating the Killer Combo

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Recommended Short Courses*

SC3: Genomics in the Service of Cancer Immunotherapy

SC11: Adoptive Therapy with CAR T Cells
**Separate registration required, please see page 5-6 for course details.*

WEDNESDAY, MAY 3

7:30 am Registration and Morning Coffee

Advances in Bispecific Biologics and CAR T Cell Therapies

8:30 Chairperson's Remarks
Rakesh Dixit, Ph.D., DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, MedImmune

8:40 Personalized Antibody-Mediated Immunotherapy Approaches
Kipp Weiskopf, M.D., Ph.D., Resident Physician, Medicine, Brigham and Women's Hospital
Insights into myeloid development have informed us of mechanisms of programmed cell removal. The CD47/SIRPα axis, a myeloid-specific immune checkpoint, limits macrophage removal of HSCs but can be exploited by hematologic and solid malignancies. Therapeutics targeting CD47 represent a new strategy for treating cancer. Overall, an understanding of hematopoiesis and myeloid cell development has implications for regenerative medicine, hematopoietic cell transplantation, malignancy, and many other diseases.

9:10 Bi-Specific T Cell Engagers and Chimeric Antigen Receptors: T Cells Strike Back
Matthew J. Frigault, M.D., Clinical Fellow in Medicine, Dana-Farber Cancer Institute
There have been significant advances in tumor directed immunotherapy. For the last two decades, monoclonal antibodies have been on the forefront of cancer therapeutics. Despite their success they're unable to engage one of the most powerful subsets of the host immune response – T cells. With the advent of bi-specific antibodies, as well as chimeric antigen receptors, we are now able to combine the targeting specificity of monoclonal antibodies with the cytotoxic effects of cellular therapy.

9:40 A Tale of Two SpecifiCITIES: The Balancing Act of Tumor-Targeting Selectivity and Therapeutic Index in Bispecific Antibodies
Yariv Mazor, Ph.D., Senior Scientist, Antibody Engineering, MedImmune
Dual targeting of antigen double-positive cancer cells over single-positive normal tissue is believed to enhance the therapeutic efficacy, restrict major escape mechanisms and increase tumor-targeting selectivity, leading to reduced systemic toxicity and improved therapeutic index. However, the interplay of factors regulating target selectivity is not well understood and often overlooked when developing clinically relevant bispecific therapeutics. We show *in vivo* that dual targeting alone is not sufficient to endow selective tumor-targeting, and report the pivotal roles played by the affinity of the individual arms, overall avidity and format valence.

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

10:55 KEYNOTE PRESENTATION: Immunotherapy for Cancer: The Need for More Effective Combination Therapies
Ronald Herbst, Ph.D., Vice President and Head, Oncology Research, MedImmune
Combination therapies with anti-PD1/PD-L1 and anti-CTLA4 have already increased response rates in certain cancer indications, beyond checkpoint monotherapies. However, a significant subset of patients still fails to benefit from current immune therapies. New, more effective combinations, beyond checkpoint blockade, are needed to further broaden and deepen the response of cancer patients to immunotherapy.

11:55 ERY974; First-in-Class T Cell–Redirecting Bispecific Antibody Targeting Glypican-3: A Highly Tumor-Selective Antigen
Mika Sakurai, Ph.D., Biologics Discovery Dept., Chugai Pharmaceutical Co., Ltd.
T cell–redirecting antibody (TRAB) may be a solution to recent problems facing cancer immunotherapy. ERY974 is a fully IgG-type TRAB that targets glypican-3 and exhibits highly potent anti-tumor efficacy. Chugai's ART-Ig technology enables large scale production of this asymmetric and bispecific antibody. Antibody optimization, non-clinical safety, pharmacology (including combination study with other immunotherapies or chemotherapies) and design of the Phase I study will be presented.

Sponsored By applied biomath revolutionizing drug invention

12:25 pm Predicting Marketed PD-1 Dosing and Optimal PD-1 x TIM-3 Dual Targeting Approaches in Immuno-Oncology
John Burke, Ph.D., Co-Founder, President, and CEO, Applied BioMath, LLC
We will look at an example of integrating systems modeling to predict optimal drug properties targeting PD-1 and TIM3 in I/O for bispecific biologics and fixed dose combinations. We assess risk by performing an *in silico* differentiation for a bispecific vs. FDC and as part of model benchmarking we analyze why BMS and Merck anti-PD-1s therapeutic antibodies have similar dosing regimens when their affinities differ by two orders of magnitude.

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

1:55 Session Break

Advancing Bispecific Antibodies and Combination Therapy to the Clinic

Bispecifics: From Bench to Bedside

2:10 Chairperson's Remarks
Steven Coats, Ph.D., Vice President, R&D, MedImmune

2:15 Generation of BiKEs and TriKEs to Improve NK Cell-Mediated Targeting of Tumor Cells
Jeffrey S. Miller, M.D., Professor, Medicine, Division of Hematology, Oncology and Transplantation; Deputy Director, Masonic Cancer Center, University of Minnesota
We have performed clinical trials using NK cell infusions. The major limitation is their lack of specificity and their inability to proliferate when targeted, which limits their clinical efficacy. IL-15 is a cytokine critical for NK cell development and homeostasis. We have recently developed a class of molecules that combine antigen specificity and IL-15's proliferative activity together into a novel class of multifunction molecules we call trispecific killer engagers (TriKEs).

2:45 The Two Faces of Interleukin-2: Engineering towards Induction of Immune Tolerance or towards Immune Activation
Ekkehard Moessner, Ph.D., Head, Protein Engineering, Roche Pharmaceutical Research and Early Development, Roche Innovation Center Zurich

3:15 Enabling Technologies for Development and Optimization of Bi-Specific Antibodies for T-Cell Redirection
Sponsored By DiscoverX
Jane Lamerdin, Ph.D., Director, Research & Development, DiscoverX Corporation

3:30 Advancing the Discovery of Immunotherapeutics with Large Scale, Multiplexed Experiments on Cells and Proteins of Immune System
Sponsored By intellicyt
Thomas Duensing, Ph.D., CTO, IntelliCyt Corporation

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, MAY 4

8:00 am Morning Coffee

Bispecifics: From Bench to Bedside (Cont.)

8:30 Chairperson's Remarks
Steven Coats, Ph.D., Vice President, R&D, MedImmune

8:35 Bispecific Antibody Efficacy and Safety: From Research to Clinic
G. Jonah Rainey, Ph.D., Executive Director, Head of Antibody Research, MabVax Therapeutics Holdings, Inc.
MedImmune now has multiple bispecific molecules that have progressed to clinical development. As these projects mature, there have been valuable lessons learned and perspectives gained. Preclinical data will be presented for multiple projects, with clinical data demonstrating translatability to humans.

9:05 Nanobodies (Entering) in Clinical Phase: Update on their Immunogenicity
Sam Massa, Ph.D., PostDoc Scientist, VIB Center for Inflammation Research, VUB Cellular and Molecular Immunology laboratory, Vrije University Brussels
Nanobodies, the variable domain of heavy-chain only antibodies naturally occurring in camelids, are the smallest antigen-binding antibody fragments, with exceptional characteristics. Several Nanobodies are (entering) in clinical phase, some of which are discussed in this talk. Due to their sequences foreign to human, their immunogenicity is of special concern and analyzed in more detail. The latest data are presented here.

9:35 Costimulatory T-Cell Engagement by the 4-1BB/HER2 Bispecific Antibody/Anticalin Fusion Protein PRS-343
Manuela Duerr, Ph.D., Project Leader Immune-Oncology, Pieris Pharmaceuticals GmbH
Pieris used its proprietary Anticalin® platform to generate the 4-1BB-based bispecific PRS-343 (4-1BB/HER2). PRS-343 leads to efficient tumor target-dependent T-cell activation ex vivo. In a humanized mouse model, PRS-343 dose-dependently inhibits tumor growth accompanied by high tumor infiltration with human lymphocytes (hCD45+). The positive preclinical data of PRS-343 suggest a promising efficacy and safety profile in humans and its excellent developability profile support investigation of its anti-cancer activity in clinical trials.

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

Innovative Engineering Approaches to Improve Drug Efficacy

11:05 From the Bench to the Clinic: Developing Next-Generation ADAPTIR™ Molecules
Peter Pavlik, Ph.D., Principal Scientist, Molecular Biology & Protein Engineering, Aptevo Therapeutics
The ADAPTIR™ (modular protein technology) platform of bispecific protein therapeutics has unique properties compared to other bispecific antibody formats. A pipeline of ADAPTIR therapeutics is currently under development from early discovery to clinical stage, targeting both solid and hematologic malignancies. Updates will be provided on advanced ADAPTIR therapeutics, including MOR209/ES414 and ES425.

11:35 Modulating Target Binding Affinity to Minimize Immune-Related Adverse Events
Justin M. Scheer, Ph.D., Director, Antibody Engineering, Boehringer Ingelheim Pharmaceuticals, Inc.
Unprecedented durable clinical response for tumor targeting can be achieved by immunotherapy. Bispecific antibodies can specifically activate T-cells and induce tumor cell killing in an MHC-independent manner. However, by unbalancing the immune system, immunotherapies also generate dysimmune toxicities collectively termed as immune-related adverse events (IRAEs). In an attempt to minimize IRAEs and to raise the threshold for MTD (maximum tolerated dose), we've taken parallel engineering approaches to modulate binding affinity to T-cells. These

Advancing Bispecific Antibodies and Combination Therapy to the Clinic

approaches are yielding variants with a broad range of binding affinities and are being profiled to understand how they maintain the balance of efficacy and safety.

12:05 pm Engineering Manufacturable IgG-like Bispecifics for Promoting Bone Mass Accrual and Fracture Repair

Guna Kannan, Ph.D., Director, Biologics-Antibody Engineering, Pharmaceutical Development Santen Inc.

Significant progress has been made in the design and development of recombinant bispecific IgG-fusions, such as the IgG-single chain Fv, and fragment formats. However, success of full length IgG-like bispecific engineering and production without additional process manipulation is limited. This talk will review IgG-like bispecific formats, describe a manufacturable IgG-like bispecific design, and demonstrate co-inhibition of two different targets leads to synergistic bone formation in rodents and non-human primates.

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

Antibody-Drug Conjugates II: Advancing Toward the Clinic

Lessons Learned from Preclinical and Early Trials to Drive Clinical Success

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Recommended Short Course*

SC9: Target Selection for Biologics
**Separate registration required, please see page 5-6 for course details.*

THURSDAY, MAY 4

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
John Lambert, Ph.D., Executive Vice President and Distinguished Research Fellow, ImmunoGen

1:50 KEYNOTE PRESENTATION: Leveraging Antibody-Drug Conjugates to Eradicate Tumor-Initiating Cells
Alex Bankovich, Ph.D., Senior Director, Head of Late Stage Research, AbbVie Stemcentrx, LLC

Tumor-initiating cells (TICs) will remain controversial until findings in the lab translate into drugs providing clear clinical benefit to patients. Antibody drug conjugates (ADCs) are a promising class of drugs able to target and reduce the frequency of TICs in patient-derived xenografts. My company has worked to discover TIC phenotypes and to utilize methods well-suited to specifically identify cell surface proteins targetable by specific ADCs. My talk will explain the drug development path that we followed to some of our current clinical programs.

Modeling and Simulation Approaches

2:20 Novel Approaches for Modeling Pre-Clinical Activity of ADCs and Informing Biomarker Strategy
Tony D'Alessio, Ph.D., Research Investigator, Oncology Biotherapeutics, Novartis Institutes for Biomedical Research

Using PTX mouse clinical trials, we have begun to generate population-based *in vivo* activity datasets on several emerging ADC programs. By integrating response data with molecular features across these models, we are building a rich dataset for biomarker analysis. Additionally, we are employing fully syngeneic murine tumor models to profile ADC activity in immune-competent settings and characterized pharmacodynamic changes in the tumor microenvironment to inform rational combination approaches.

2:50 Predicting Clinical Success of ADCs using a Mechanistic Modeling & Simulation Approach
Alison Betts, Ph.D., Associate Research Fellow, Biomedicine Design, Pfizer

Quantitative modeling and simulation was used to analyze data on 10 ADCs in patient trials or approved for oncology indications. Clinical efficacious dose was predicted from preclinical PK/PD studies and compared with clinical MTD, recommended Phase II and clinically approved doses. Monte Carlo clinical trial simulations were performed to predict objective response rate. This information can be used to select the best ADC, to optimize clinical trial design and determine likelihood of success versus clinical standard of care.

3:20 Poster Spotlight: Glypican-3 Specific Antibody Drug Conjugate for Hepatocellular Carcinoma
Ying Fu, Ph.D., Postdoctoral Fellow, National Cancer Institute, National Institutes of Health

Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related death. Glypican-3 (GPC3) is a potential target for HCC. The hypothesis of using anti-GPC3 antibody drug conjugate to treat HCC patients has not been tested in clinical trials. Here we report the development of hYP7-PC, a humanized anti-GPC3 antibody conjugated to a highly potent DNA damaging agent through cysteine via protease-cleavable linker. hYP7-PC caused tumor remission in HCC Hep3B xenograft model.

3:50 Refreshment Break

PKPD and Bioanalytics of ADCs in Support of Clinical Development

4:20 Relationship between the Mononuclear Phagocyte System and the Pharmacokinetics and Pharmacodynamics of Antibody Drug Conjugates in Patients
William C. Zamboni, Pharm.D., Ph.D., Associate Professor; Director, TOND2I Lab, University of North Carolina at Chapel Hill

The PKPD of carrier-mediated agents (CMA) and ADC agents are dependent on their recognition and interaction with the mononuclear phagocyte system (MPS) where the conjugated drug is cleared via interactions with the MPS. It is important to evaluate how mediators, characteristics and function of the MPS affect the PK and PD of ADCs. We will discuss: 1) pharmacologic methods to characterize ADCs *ex vivo* and *in vivo*; 2) MPS variability across patient populations; and 3) relationship between mediators, characteristics and function of the MPS and the PK and PD of ADCs in patients.

4:50 Challenges and Solutions Associated with Bioanalysis of Antibody Drug Conjugates in Support of Clinical Studies
Rafiq Islam, Ph.D., Senior Director, Bioanalytical Services, Celerion, Inc.

Since ADCs are generally complex heterogeneous mixtures of multiple species, these novel therapeutic products present unique bioanalytical challenges. Novel bioanalytical approaches and strategies including a combination of ligand-binding assays (LBA) and LC–MS-based platforms are needed to overcome challenges

Antibody-Drug Conjugates II: Advancing Toward the Clinic

unique to ADCs. This presentation will examine the different methodologies such as LBAs and LC-MS/MS methods for the bioanalysis of ADCs using Kadcyla® (ado-trastuzumab emtansine) as a case study.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC15: Critical Considerations for the Design and Development of Antibody-Drug Conjugates
**Separate registration required, please see page 5-6 for course details.*

FRIDAY, MAY 5

8:00 am Morning Coffee

Preclinical and Clinical Updates

8:30 Chairperson's Remarks
Christopher D. Thanos, Ph.D., Senior Director, Biotherapeutics Discovery, Halozyme Therapeutics

8:35 Clinical Development of ADCs: From Bench to Clinic and Back Again
Jonathan Drachman, M.D., CMO and Executive Vice President, Research and Development, Seattle Genetics
Antibody-drug conjugates are emerging as an important therapeutic option for both hematologic malignancies and solid tumors. As more clinical trials are completed, it may be possible to identify patterns that will help guide future technological advances. Lessons learned from different antigens, payloads, and early trial design will be discussed.

9:05 Antibody-Cytokine Fusion Proteins for the Therapy of Cancer and of Chronic Inflammation
Francesca Pretto, Ph.D., Head, Preclinical Research, Philogen, Inc.
Antibodies represent ideal vehicles for the delivery of cytokines to the site of disease and for the selective modulation of the immune system in pathological conditions. In this lecture, I will present preclinical and clinical data on antibody-cytokine fusion proteins that we have moved to advanced controlled clinical trials in patients with cancer or with chronic inflammatory conditions.

9:35 Pre-Clinical Development of a Novel FLT3 Targeting Antibody-Drug Conjugate Employing Site-Specific Conjugate for the Treatment of Acute Myeloid Leukemia Regardless of FLT3 Status
Nandini Rudra-Ganguly, Ph.D., Principal Scientist, Discovery Research, Agensys

10:05 Coffee Break

10:35 ImmunoGen's ADC Platform Technologies: Current Progress and Future Prospects
John Lambert, Ph.D., Executive Vice President and Distinguished Research Fellow, ImmunoGen

11:05 Update on Mersana's Antibody-Drug Conjugates: Progress into the Clinic
Donald A. Bergstrom, M.D., Ph.D., CMO, Mersana Therapeutics
XMT-1522 is a HER2-targeting ADC that induces complete regressions in models of heavily-pretreated HER2-positive breast tumors, as well as breast and non-small cell lung cancer (NSCLC) without HER2 gene amplification and lower HER2 expression. XMT-1522 entered clinical development in October 2016. XMT-1536 is a Dolaflexin ADC targeting NaPi2b that is highly active in models of NSCLC adenocarcinoma and epithelial ovarian cancer. XMT-1536 has significantly improved efficacy and tolerability compared to a monomethyl auristatin E ADC against the same target. XMT-1536 will enter clinical development in late 2017.

11:35 Treatment of Non-Hodgkin Lymphoma with the Beta-Emitting Anti-CD37 Antibody Radionuclide Conjugate Betalutin®
Jostein Dahle, Ph.D., CSO, Nordic Nanovector ASAc
177Lu-satetraxetan-lilotomab (Betalutin®) is a novel CD37-binding antibody radionuclide conjugate (ARC). CD37 is an internalizing transmembrane antigen highly expressed on most B-cell malignancies. Betalutin is currently in Phase I/II clinical development for the treatment of Non-Hodgkin lymphoma. Updated clinical and pre-clinical data will be presented.

12:05 pm Development of Novel EGFR Antibody Drug Conjugates for Solid Tumor Indications
Ed Reilly, Ph.D., Senior Research Fellow, Oncology Discovery, AbbVie
Abbvie has multiple antibody drug conjugate (ADC) programs encompassing various linker payload combinations. Several of these ADCs have advanced to clinical trials where objective responses in patients with different solid tumors have been observed. Appropriate patient selection biomarker strategies have been developed including protein, RNA and gene amplification detection methods. This presentation will focus on the development of a tumor-target specific ADC from discovery to clinical trials.

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

1:05 Refreshment Break

Novel ADC Concepts with Promising Preclinical Results

1:35 Chairperson's Remarks

Ed Reilly, Ph.D., Senior Research Fellow, Oncology Discovery, AbbVie

1:40 Synergistic Potential of Combining Antibody-Drug Conjugate and Immunotherapy for Cancer Treatment
Herren Wu, Ph.D., Senior Vice President, CTO, MedImmune, LLC.
- Race to develop combinatory cancer therapy of ADC and IO
- Promising preclinical results
- Opportunities and challenges

Antibody-Drug Conjugates II: Advancing Toward the Clinic

2:10 HTI-1511, A Novel Anti-EGFR-ADC, Demonstrates Significant Activity against KRAS- or BRAF-Mutated Tumors of Various Types In Preclinical Studies

Christopher D. Thanos, Ph.D., Senior Director, Biotherapeutics Discovery, Halozyme Therapeutics

We have previously described HTI-1511, an ADC in pre-clinical development that targets EGFR. Here we screened a panel of over 70 tumor cell lines derived from various solid tumor malignancies. Evaluations in several human xenograft tumor models and patient derived tumor models in mice demonstrated potent tumor regression. These results support further development of HTI-1511 as a possible treatment for EGFR overexpressing tumors, including those with downstream activating mutations in the KRAS/BRAF pathway.

2:40 Novel Medicines that Exploit Extracellular Protein-Protein Interactions

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

The talk will review the development of EDCs to multiple cancer-related targets and describe their extracellular mechanism which resembles necrosis. In addition, data using cynomolgus monkey models will be discussed, where a CD20-specific EDC was able to eliminate all CD20+ B-cells while having no effect on other cells or tissues. This talk will therefore describe a new level of therapeutic precision that depends on protein-protein proximity and not simply expression.

3:10 Probody Drug Conjugates for the Treatment of Cancer

Jason Sagert, Ph.D., Senior Scientist II, Oncology, CytomX Therapeutics

Probody™ Drug Conjugates (PDCs) are a class of antibody-based therapeutics that remain in a substantially inert, masked form until activated proteolytically in the tumor microenvironment. This platform allows the targeting of antigens that are highly expressed on tumor cells with high prevalence across multiple types of cancer regardless of normal tissue expression. Preclinical data supporting the development of PDCs will be presented.

3:40 End of Conference

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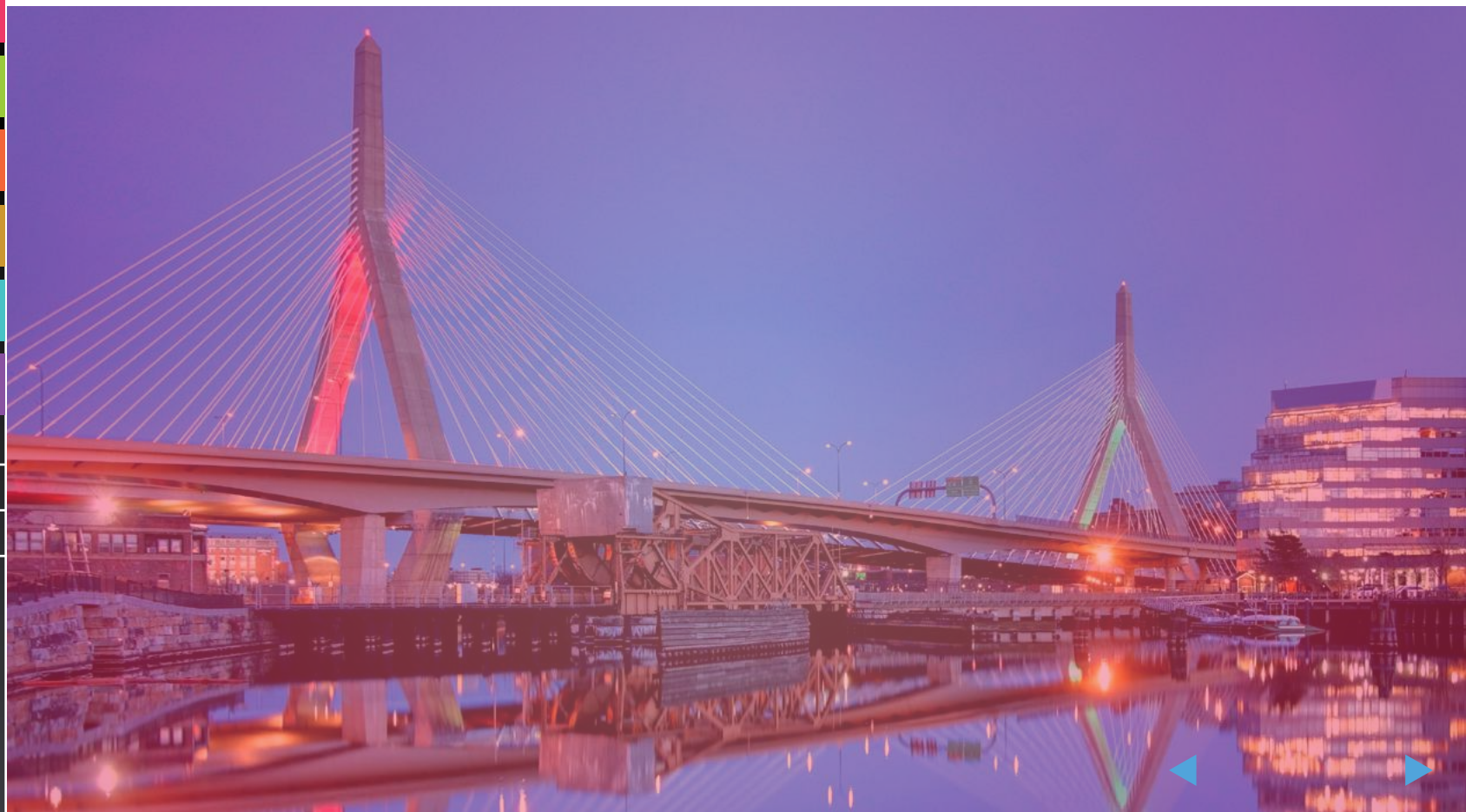
IMMUNOTHERAPY STREAM

- Preventing Toxicity in Immunotherapy
- Adoptive T Cell Therapy
- Agonist Immunotherapy Targets



Preventing Toxicity in Immunotherapy

Strategies to Advance Clinical Trials While Keeping Patients Safe

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Recommended Short Courses*

SC3: Genomics in the Service of Cancer Immunotherapy

SC11: Adoptive Therapy with CAR T Cells
**Separate registration required, please see page 5-6 for course details.*

MONDAY, MAY 1

7:00 am Registration and Morning Coffee

Building Preclinical Models

8:30 Chairperson's Remarks
Wayne Marasco, Professor, Cancer Immunology and Virology, Dana-Farber Cancer Institute

8:40 Immune Intact Preclinical Models to Understand Efficacy and Toxicity of CAR T Cells
Charles Sentman, Ph.D., Director, Center for Synthetic Immunity, The Geisel School of Medicine, Dartmouth College
The mechanisms involved in the efficacy of CAR T cells can be investigated using syngeneic tumor models with intact immune systems. CAR receptors designed to target murine tumor ligands can be used to understand the key mechanisms of action against tumors and the nature of toxicity observed in immune intact and deficient mice.

9:10 Chimeric Antigen Presenting T Cells That Change the Tumor Microenvironment
Wayne Marasco, M.D., Ph.D., Professor, Cancer Immunology and Virology, Dana-Farber Cancer Institute
The clinical effect of CART cells has been modest for the treatment of solid tumors due to several factors including the difficulty in identifying unique tumor associated antigens, inefficient homing of CART cells to tumor locations, their low persistence after infusion and their functional impairment in the immunosuppressive microenvironment. We will present our latest *in vitro* and *in vivo* CART cell data on new technology to overcome these barriers.

9:40 A Higher-Affinity Variant of a GD2-Specific CAR That Significantly Enhances Potency *in vivo* and Allows for a Novel Model of On-Target Off-Tumor Toxicity
Sarah Richman, M.D., Ph.D., Instructor, Cancer Center, The Children's Hospital of Philadelphia
On-target/off-tumor toxicity poses a major challenge in chimeric antigen receptor (CAR) T cell immunotherapy, particularly for solid tumors. The glycolipid tumor antigen GD2 is an attractive antigen with which to study on-target/off-tumor toxicity owing to its shared expression between rodents and humans and its presence on some vital normal tissues. By incorporating an affinity-enhancing mutation into a GD2-specific CAR, we have developed a model for studying on-target/off-tumor toxicity.

10:10 Coffee Break

Monitoring and Preventing Cross Reactivity

10:45 Chairperson's Remarks
Michael Postow, M.D., Medical Oncologist, Department of Medicine, Memorial Sloan Kettering Cancer Center

10:50 ImmTACTM Platform: Delivering Novel Bi-functional TCR-based Biologics for Targeted Immunotherapy
Stephen Hearty, Group Leader, Autoimmune Group, Immunocore Ltd.
Immunocore has developed a unique biologic platform through the creation of ImmTAC reagents. The ability of ImmTAC molecules to bind intracellular peptides presented in the context of HLA significantly expands the addressable antigenic landscape beyond that currently accessible to antibody based therapies. One thing that is essential to the development of ImmTAC molecules is a robust pre-clinical testing package. This presentation will expand upon how Immunocore is diversifying the ImmTAC platform to deliver novel immunotherapeutics.

11:20 Preventing Self-Reactivity of Engineered TCRs
Andrew Sewell, Ph.D., Distinguished Research Professor and Wellcome Trust Senior Investigator, Cardiff University School of Medicine
The αβ TCR repertoire is dwarfed by the vast array of potential foreign peptide-MHC complexes. Comprehensive immunity requires that each T-cell recognizes numerous peptides and thus be extremely cross-reactive. Natural central tolerance culls T-cells that have a high affinity for self peptide-MHC. TCR engineering bypasses this process and can result in dangerous self-reactivity. These toxicities can be predicted and engineered out without loss of specificity for the target antigen.

Preventing Toxicity in Immunotherapy

Toxicity in Combination Studies

11:50 A Different Way of Thinking about Toxicities of Combination Immune Checkpoint Blockade
Michael Postow, M.D., Medical Oncologist, Department of Medicine, Memorial Sloan Kettering Cancer Center
Immune checkpoint inhibition results in immune-related adverse events. We will briefly review the spectrum of toxicities seen with these agents and how clinicians approach their treatment. We will then discuss toxicity issues arising when CTLA-4 and PD-1 immune checkpoint inhibitors have been combined and how clinicians and researchers can think differently about best strategies to deliver these medications safely.

12:20 pm Human *in vitro* Skin Explant Assays for Predicting Immunotoxicity of Drugs and Cellular Therapies
Shaheda Ahmed, Ph.D, Senior Scientific Officer, Alcyomics Limited, Haematological Sciences, Institute of Cellular Medicine, The Medical School, Newcastle University
There are currently no reliable human *in vitro* assays which test for immunogenicity, sensitivity, efficacy and allergic reactions of biologics that are equivalent to *in vivo* animal testing. Here we describe a novel test named SkimuneT, a non-artificial (non-3D) human *in vitro* test which can predict allergic responses to monoclonal antibodies. SkimuneT gives a predictive readout of skin damage which also correlates with inflammatory cytokine release and T cell proliferation responses. This test allows for the improved development of therapeutic drugs and compounds by the early detection of allergic reactions and immune responses and therefore aid in the safety profiling and a reduction in the cost of potentially adverse reactions being picked up before Phase I clinical trials.

12:35 A Novel T-Cell Engaging Bispecific Antibody Platform: Maximizing Tumor Cell Cytotoxicity While Minimizing Cytokine Release
Nathan Trinklein, Ph.D., Vice President, TeneoBio
We have created a large collection of fully human anti-CD3 antibodies with diverse T-cell agonist activities. These novel T-cell agonist antibodies were identified using our unique discovery platform that screens large numbers of antibodies by combining antibody repertoire deep sequencing, high-throughput gene assembly, and recombinant expression. The CD3 antibodies we identified show diverse *in vitro* T-cell activation profiles measured by CD69 upregulation, and cytokine production. Using our discovery platform, we have also generated human antibodies targeting tumor antigens that may be combined with our unique CD3 antibodies to create bispecific molecules that mediate T-cell killing of tumor cells. Using multiple myeloma tumor cells along with primary human PBMCs, our panel of aCD3 bispecific antibodies show a spectrum of *in vitro* tumor cell killing activity with varied levels of cytokine release.

12:50 Luncheon Presentation I: Identifying Critical Receptor Targets and Off-Target Profiling Using Plasma Membrane Protein Array Technology
Sponsored By RETROGENIX
Jim Freeth, Ph.D., Managing Director, Retrogenix Limited
Human cell microarray screening enables rapid discovery of the primary cell surface receptors and off-targets of antibodies, proteins, viruses and small molecules. Case studies from pharmaceutical partners will demonstrate how this unrivalled platform has been used for: 1) Uncovering novel targets from antibody phenotypic screening approaches; 2) Identifying receptors for protein ligands in normal and disease processes, such as immune checkpoint interactions; 3) Off-target profiling of biotherapeutics including CAR T cell lines.

1:20 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

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

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks
Gregory A. Weiss, Ph.D., Professor, Chemistry, Molecular Biology & Biochemistry, University of California, Irvine

4:10 Bicycles and Bicycle Drug Conjugates: Next-Generation Therapeutics
Sir Gregory Winter, Ph.D., FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics
Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles' unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs); a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. This presentation will describe both the Bicycle® and BDC platforms.

4:55 Young Scientist Keynote: Programming Proteins by Deep Sequencing and Design
Tim Whitehead, Ph.D., Assistant Professor, Chemical Engineering and Materials Science, Michigan State University
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 group leverages this unprecedented wealth of sequence-function information to design and engineer protein affinity, specificity, and function and to infer structural complexes of proteins. My talk will present an overview of the above and detail methodological improvements that enable the engineering work.

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

6:55 End of Day

TUESDAY, MAY 2

8:00 am Registration and Morning Coffee

Safety in Cell Therapies: CAR, TCR, and TIL

8:25 Chairperson's Remarks

Preventing Toxicity in Immunotherapy

Saad Kenderian, M.D., Assistant Professor of Medicine and Oncology, Hematology, Mayo Clinic College of Medicine

8:30 Toxicities after Chimeric Antigen Receptor T Cell Therapy: Management, Prevention and Preclinical Modeling

Saad Kenderian, M.D., Assistant Professor of Medicine and Oncology, Hematology, Mayo Clinic College of Medicine

Despite the impressive responses after chimeric antigen receptor T (CART) cells in hematological malignancies, their application is limited by the development of cytokine release syndrome (CRS). While steroids and the IL-6 receptor blocker tocilizumab can generally reverse the syndrome, there is a concern that early introduction of immunosuppression can impair CART cell activity and therefore are reserved for severe CRS. The lack of relevant preclinical models for CRS after CART 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.

9:00 Biomarker Correlates and Potential Mechanisms of CAR T Cell Toxicities

Adrian Bot, M.D., Ph.D., Vice President, Translational Medicine, Kite Pharma

Treatment with CD19-directed CAR T cells can lead to durable clinical responses in lymphoma patients, but they may be associated with reversible toxicities. Biomarker analysis implicated several immune programs in the cytokine release syndrome and neurotoxicities associated with this therapeutic modality. Elucidation of mechanisms differentially involved with toxicities but dispensable for clinical activity, may allow rationale management of such toxicities, and development of next generation T cell products.

9:30 Controlling Specificity and Activity of Adoptive Cellular Therapies

Peter Emtage, CSO, Cell Design Labs

Cell Design Labs' THROTTLE Switch™ and synNotch™ technologies allow for the ability to control the intrinsic activity of CAR-Ts. THROTTLE-Switch™ achieves this using a small molecule definable mechanism while synNotch™ incorporates a logic gated decision paradigm. The application of these systems in the clinic will provide physicians with the ability to modulate safety issues like CRS and on/off target toxicities while maximizing efficacy.

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

New Technologies to Prevent and Mitigate Toxicity

10:50 Switch Mediated Control of CAR-T Cell Therapy

Travis S. Young, Ph.D., Principal Investigator, Biology, California Institute for Biomedical Research

Given the promising results for CAR-T cells in early clinical trials, along with the need for a solution to adverse effects and long-term T cell aplasia associated with its use, we have established an antibody-based control "switch" which affords tunable CAR-T cell activity. The universal design allows the same CAR to be retargeted to multiple tumor antigens to combat antigen-loss relapse mutations and to expand into multiple indications.

11:20 Harnessing T Cells to Fight Cancer with Novel Multispecific Antibodies

Jijie Gu, Ph.D., Research Fellow in Foundational Immunology & Head of Oncology Biologics Discovery at Global Biologics, AbbVie Bioresearch Center

Modulating T cells to kill tumor cells requires the better understanding of T cell biology for both efficacy and safety. In this presentation, we will discuss the development of multispecific antibody technology and how this technology could be used to design molecules to fine tune T cell functions for tumor killing.

Preventing Toxicity in Immunotherapy

11:50 ProTIA – A Novel Format of Bispecific T Cell Engagers Designed for Activation by Tumor-Associated Proteases

Volker Schellenberger, Ph.D., President and CEO, Amunix

Amunix is developing bispecific T cell activators based on our proprietary ProTIA (Protease Triggered Immune Activator) platform. ProTIA therapeutics have been engineered for activation at the tumor site by tumor-associated proteases. ProTIA molecules release their highly selective payload in the tumor microenvironment, which maximizes anti-tumor effects while minimizing systemic toxicity (compared to other bispecific molecules such as BiTEs). ProTIA molecules are based on Amunix' proprietary XTEN™ polymer technology which has been validated in hundreds of patients and through partnerships with partners such as Biogen, Lilly, Roche, Janssen, and Versartis.

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

Understanding Immune-Related Adverse Events

2:00 Chairperson's Remarks

David Teachey, M.D., Associate Professor, Pediatrics, Children's Hospital of Philadelphia

2:05 Is This Really Just "Fatigue"? - Case Series of Immune Related Hypophysitis Secondary to Immune Checkpoint Inhibitors

Misako Nagasaka, M.D., Hematology and Oncology Fellow, Oncology, Karmanos Cancer Institute

While immunotherapy targeting the PD1/L1 pathway has shown promising activity in many tumor types, immune related (IR) adverse events from these agents present a serious concern. Autoimmune hypophysitis are rare but serious IR events known to occur with PD1/PDL-1 inhibitors. The most typical presentation of autoimmune hypophysitis is "fatigue", a very common everyday complaint in the oncology clinic. Although autoimmune hypophysitis itself is rare, it will likely become more prevalent as the usage of checkpoint inhibitors increase. Early recognition and treatment of autoimmune hypophysitis is imperative in providing quality care.

2:35 Cytokine Release Syndrome after CAR T Therapy for Acute Lymphoblastic Leukemia

David Teachey, M.D., Associate Professor, Pediatrics, Children's Hospital of Philadelphia

Chimeric antigen receptor (CAR)-modified T cells with anti-CD19 specificity are a highly effective novel immune therapy for relapsed/refractory hematologic malignancies. Dramatic responses have been reported in patients with relapsed/refractory ALL. Cytokine release syndrome (CRS) is the most significant and life-threatening toxicity. The clinical presentation, management, and biology of CRS, as well as, the ability to predict which patients may develop severe CRS will be discussed.

3:05 Extended Q&A With Session Speakers

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

4:25 Efficacy and Toxicity of Targeting Shared Tissue Differentiation Antigens versus Neoepitopes

Smita Chandran, Ph.D., Senior Research Scientist, Memorial Sloan Kettering Cancer Center

Immunological targeting of neoepitopes and shared tissue-differentiation antigens can mediate complete and durable tumor regression in patients with metastatic melanoma. The expression of nonmutated self-antigens on normal tissue- a pattern that is distinct from the tumor specific expression of mutated neoantigens- can lead to undesirable on-target, off-tumor toxicity. However, directing T cells toward neoantigens that would result in tumor elimination, and not tumor escape, is critical to the efficacy of targeting mutations. Understanding the balance between efficacy and toxicity will be critical to the widespread success of cellular immunotherapies against these two classes of antigens.

4:55 Cancer Immunotherapy and Immune Related Adverse Events Oncologists' New Frontier

Ammar Sukari, M.D., Assistant Professor, Head and Neck Multi-Disciplinary Team Leader, Department of Oncology, School of Medicine , Wayne State University/ Karmanos Cancer Institute

Many researchers believe that anti-cancer immunotherapy has the potential to eventually cure many types of cancer. Despite mounting data, there are still many un-answered questions that require more research and clinical trials to answer. This presentation will address immune related toxicities and side effects of checkpoint inhibitors and the best way to manage these side effects.

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC13: Phenotypic Screening Applications and Technologies

**Separate registration required, please see page 5-6 for course details.*

Adoptive T Cell Therapy

Clinical Progress with CAR, TCR, and TIL

Recommended Short Courses*

SC3: Genomics in the Service of Cancer Immunotherapy

SC11: Adoptive Therapy with CAR T Cells
**Separate registration required, please see page 5-6 for course details.*

WEDNESDAY, MAY 3

7:30 am Registration and Morning Coffee

KEYNOTE SESSION: Neoantigens: A Framework for Personalized Immunotherapies

8:30 Chairperson's Remarks
David Gilham, Ph.D., Vice President, Research & Development, Celyad S.A.

8:40 Fully Individualized Tumor Neoantigen-Based Vaccine Approaches to Cancer Therapy
Karin Jooss, Ph.D., CSO, Gritstone Oncology, Inc.
Genetic instability in tumors generates tumor-specific neo-antigens which have been identified as the targets of new T cells in patients responding to checkpoint inhibitor therapy. Predicting neo-antigens by sequencing routine clinical biopsy material and then incorporating them into therapeutic cancer vaccines is an attractive concept being developed by Gritstone Oncology. The complexities of neo-antigen prediction will be discussed, together with insights into how vaccine vectors are selected and designed.

9:10 Discovery and Development of Novel Immunogenic Tumor Neoantigens for the Treatment of Solid Tumors
Philip M. Arlen, M.D., President and CEO, Precision Biologics, Inc.
Immunogenic Neoantigens were derived from a membrane preparation of pooled allogeneic colorectal cancer from patients undergoing surgery. Membrane fractions were isolated and tested for immunogenicity and utilized in a clinical trial in patients with chemotherapy refractory metastatic colorectal cancer. A positive correlation was observed in patients who were able to mount and sustain IgG responses to vaccine. Antibodies were screened using this vaccine and tested for sensitivity, specificity, and anti-tumor function. Neoantigens were identified in colon cancer with these functional antibodies.

9:40 How Can We Utilize Neoantigens in Personalized Therapies for Patients with Tumors Having Low Mutation Profiles?
Markus Dangl, Ph.D., Senior Vice President Research and Pre-Clinical Development, Medigene AG
One important challenge in the use of neoantigens for personalized immunotherapies is to understand whether neoantigens are accessible as targets only for tumors of high mutational burden and/or limited to patients with pre-existing neoantigen-specific T cells. Medigene uses its immunotherapy platform technologies to investigate neoantigens as future targets for vaccines and adoptive T cell therapies exploring mutated targets in tumors with low mutational burden.

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

Targeting Solid Tumors

10:55 New Targets in Hematologic Malignancies and Solid Tumors
J. Joseph Melenhorst, Ph.D., Director, Product Development & Correlative Sciences Laboratories (PDCS); Adjunct Associate Professor, Center for Cellular Immunotherapies, University of Pennsylvania
Revamping a patient's own failed T cell repertoire with engineered tumor-targeting receptors has demonstrated efficacy with some chimeric antigen receptors (CAR). It has become clear that T cell-intrinsic and -extrinsic factors contribute to the clinical efficacy of this form of therapy. In my talk I will highlight several such mechanisms and novel ways in which we have turned our correlative sciences and product development studies in enhanced tumor targeting of CART cells.

11:25 Overcoming CAR T Cell Checkpoint Blockade in Solid Tumors
Prasad S. Adusumilli, M.D., F.A.C.S., Associate Attending and Deputy Chief, Thoracic Surgery, Memorial Sloan Kettering Cancer Center
CAR T-cell therapy for solid tumors is prone to the checkpoint blockade inhibition similar to innate tumor-infiltrating lymphocytes. Cell-intrinsic strategies to overcome this 'Adaptive Resistance' of infused CAR T cells can promote their functional persistence. Understanding solid tumor type-specific immune microenvironment can guide both cell-intrinsic and extrinsic strategies that can modulate the solid tumor microenvironment in addition to promoting CAR T-cell efficiency.

11:55 5 Enjoy Lunch on Your Own

12:25 pm Sponsored Presentation *(Opportunity Available)*

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

1:55 Session Break

Emerging Treatments and Targets

2:10 Chairperson's Remarks
Prasad S. Adusumilli, M.D., F.A.C.S., Associate Attending and Deputy Chief, Thoracic Surgery, Memorial Sloan Kettering Cancer Center

Adoptive T Cell Therapy

2:15 Exploiting Natural Killer Receptors for CAR T Cell Therapy

David Gilham, Ph.D., Vice President, Research & Development, Celyad S.A.

The effector functions of Natural killer (NK) cells are controlled by a series of activating and inhibitory receptors that provides target discrimination for the NK cell. NKG2D is an activating NK receptor that binds to 8 known stress ligands. These ligands are highly expressed on tumor cells while expression on healthy tissue is minimal and provides a potential route to target a broad range of hematological and solid tumors. Pre-clinical studies of a NKG2D-CD3z CAR (NKR2) show potent anti-tumor activity and also suggest that T cells bearing the NKR2 receptor modulate the immune component of the tumor microenvironment and also potentially target tumor neo-vasculature. These data have supported the translation of NKR2 technology into the early stage clinical trial setting.

2:45 New T Cell Targets by Dissection of Successful Tumor-Infiltrating Lymphocyte Therapy for Melanoma

Andrew Sewell, Ph.D., Distinguished Research Professor and Wellcome Trust Senior Investigator, Cardiff University School of Medicine

Over 20% of melanoma patients that have been refractory to other treatments undergo complete lasting remission after adoptive cell transfer of tumor-infiltrating lymphocytes (TILs). Dissection of these extraordinary successes by examining the dominant tumor-reactive T-cell clonotypes in the TIL infusion product and patient blood after 'cure' has revealed some surprising, exciting new HLA-restricted and non-HLA restricted targets that are expressed by many other tumour types.

3:15 Adoptive Cell Therapy for Cancer Using Tumour Infiltrating Lymphocytes

John S. Bridgeman, Ph.D., Director of Cell Therapy Research, Cellular Therapeutics, Ltd.

The prognosis for metastatic melanoma remains poor, and despite the success of novel immunotherapeutics, there exists an unmet need for new treatments. We have established a protocol to generate Tumour infiltrating lymphocytes (TIL) from surgically resected melanoma lesions. The results reported here support the success of melanoma TIL therapy seen in other centres worldwide and suggest that this is a viable means of treating a disease which has few effective options.

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 pm End of Day

THURSDAY, MAY 4

8:00 am Morning Coffee

Improved Techniques and Technologies for Immuno-Oncology

8:30 Chairperson's Remarks

Paul Beavis, Ph.D., Senior Postdoctoral Researcher, Cancer Immunotherapy, Peter MacCallum Cancer Centre

8:35 ImmunoMap: A Novel Bioinformatics Tool to Visualize and Analyze T-Cell Receptor Repertoire Sequence Data

Jonathan Schneck, M.D., Ph.D., Professor, Pathology Medicine and Oncology, Johns Hopkins University

We describe a novel method utilizing phylogenetic and sequencing analysis to visualize and quantify TCR repertoire diversity. To demonstrate the utility of the approach, we have applied it to understanding the shaping of the CD8 T Cell response to self (TRP2) and foreign (SIY) antigens in naïve and tumor-bearing B6 mice. We have developed and demonstrated a novel method to meaningfully parse and interpret TCR repertoire data and have applied it to yield a novel understanding of CD8 T Cell responses to different types of antigens.

9:05 Exploitation of T Cell Co-Stimulation for the Improvement of Adoptive T Cell Therapy

Abhishek Srivastava, Ph.D., Fellow, Surgery Branch, National Cancer Institute, NIH

Adoptive T cell therapy (ACT) involves the *ex vivo* stimulation and expansion of autologous tumor-infiltrating lymphocytes (TIL) and re-transfers into patients. However, current ACT strategy poses some limitations due to generation of sub-optimal TIL product for many patients which leads to poor survival, persistence and lack of effective anti-tumor efficacy of these cells after adoptive transfer. Therefore, utilization of a co-stimulatory signaling may play a critical role in restoring the survival, persistence and antitumor efficacy of these TILs in ACT.

9:35 First-in-Class Antibody Targeting Soluble NKG2D Ligand sMIC for Cancer Immunotherapy

Jennifer Wu, Ph.D., Professor, Hollings Cancer Center,Medical University of South Carolina; President and CSO, CanCure LLC

In response to oncogenic insult, human cells were induced to express a family of MHC I-chain related molecules A and B (MICA and MICB, generally termed MIC) on the surface which serve as the ligands for the activating immune receptor NKG2D expressed by all human NK, CD8 T, NKT, and subsets of ▯▯ T cells. Theoretically, engagement of NKG2D by tumor cell surface MIC is deemed to signal and provoke the immune system to eliminate transformed cells. Clinically, almost all advanced tumors in cancer patients produce soluble MIC through proteolytic shedding mediated by metalloproteases, or by release in exosomes derived from the cell membrane. Tumor-derived sMIC is known to be highly immune suppressive and profoundly insults the immune system by downregulating receptor NKG2D expression on effector NK and T cells, driving the expansion of tumor-favoring myeloid suppression cells, skewing macrophages into alternatively activated phenotypes, and perturbing NK cell peripheral maintenance. High levels of serum sMIC significantly correlate with advanced diseases of many types of cancer. These observations clearly endorse sMIC to be a cancer immune therapeutic target. However, due to mice lack homologues to human MIC, this concept was not proven until our recent studies. Using a "humanized" MIC-transgenic spontaneous mouse model which recapitulates the NKG2D-mediated onco-immune dynamics of human cancer patients, we show that neutralizing circulating sMIC with a first-in-field non-blocking antibody B10 that does not block the interaction of MIC with NKG2D revamps endogenous innate and antigen-specific CD8 T cell responses. We show that therapy with the non-blocking sMIC-neutralizing antibody results in effectively debulking of primary tumor and

Adoptive T Cell Therapy

elimination of metastasis, with no observed toxicity. Furthermore, we show that clearing sMIC with the first-in-class neutralizing antibody B10 also enhanced the efficacy of other cancer immunotherapeutic modalities, such as immune checkpoint blockade or adoptive cell-based therapy pre-clinically. Our study has launched a new avenue of cancer immunotherapy which can be readily translated into clinical trials.

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

Off-the-Shelf T Cells: From One for Many

11:05 ACTR (Antibody Coupled T Cell Receptor): A Universal Approach to T Cell Therapy

Seth Ettenberg, Ph.D., CSO, Unum Therapeutics, Inc.

Fusing the ectodomain of CD16 to the co-stimulatory and signaling domains of 41BB and CD3z generates an Antibody Coupled T cell Receptor (ACTR). T cells expressing this receptor show powerful anti-tumor cytotoxicity when co-administered with an appropriate tumor-targeting antibody. Such cells have potential utility as a therapy to treat a wide range of cancer indications. We will describe efforts specifically targeting B-cell malignancies using a combination of ACTR T cells with Rituximab.

11:35 Continuously Growing NK Cell Line as a Source for an Off-the-Shelf, Engineered NK Cell Therapeutic in Cancer and Infections

Hans Klingemann, M.D., Ph.D., Vice President, Research & Development, NantKwest, Inc.

NantKwest has developed the NK cell line NK-92 into an “off the shelf” activated NK (aNK) cell therapeutic. The cells can be expanded to 1010 within two weeks without feeder layer using FDA compliant medium. The safety of aNK as well as their activity against a broad range of cancers have been confirmed in several Phase I clinical trials in the U.S., Canada and Europe. The aNK cells can be administered in the outpatient setting and serve as a universal cell-based therapy without need for individualized patient matching. Moreover, the aNK cell platform has been bioengineered to incorporate a high-affinity antibody binding Fc-receptor (haNK). Both aNK and haNK cells can be equipped with chimeric antigen receptors (CARs) (called taNK) to further optimize targeting and potency in the therapeutic setting.

12:05 pm Off-the-Shelf Cancer Immunotherapy: Engineered Pluripotent Cell-Derived Natural Killer Cells

Bahram (Bob) Valamehr, Ph.D., MBA, Vice President, Cancer Immunotherapy, Fate Therapeutics, Inc.

Harnessing the power of 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 “off-the-shelf” source of cellular therapeutics. By coupling the unique capacity of our pluripotent cell platform to efficiently facilitate multiple genomic modifications at the single cell level with our ability to accurately recapitulate the stages of hematopoiesis, we demonstrate a viable method for the derivation of efficacious engineered natural killer cells, genomically-engineered with augmented potency, persistence, targeting and safety mechanisms.

12:35 End of Adoptive T Cell Therapy

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THURSDAY, MAY 4

Case Studies with Agonist Antibodies

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Peter Ellmark, Ph.D., Principal Scientist, Research & Development, Alligator Bioscience

1:50 KEYNOTE PRESENTATION: Engineering of an ICOS Agonist Antibody for Cancer Therapy
Patrick Mayes, Ph.D., Director, Early Development Leader, GlaxoSmithKline Pharmaceuticals, Inc

2:20 Tumor-Directed Immunotherapy – Tumor-Localized Immune Activation Using TNFR-SF Agonistic Antibodies
Peter Ellmark, Ph.D., Principal Scientist, R&D, Alligator Bioscience
Alligator Bioscience develops mono and bispecific agonistic antibodies, targeting TNFR-SF members, for tumor-directed immunotherapy of cancer. This approach provides new opportunities to generate an effective, immune-mediated, anti-tumor response. Alligators pipeline projects will be presented, including ADC-1013, a human monospecific agonistic IgG1 antibody in clinical development and ATOR-1015, a bispecific antibody targeting OX40 and CTLA-4 developed to deplete Tregs in the tumor microenvironment.

2:50 OX40: From Bench to Bedside and Back Again
Brendan Curti, Director, Genitourinary Oncology Research, Immunotherapy Clinical Program, Providence Medical Group
Cancer immunotherapy is an evolving treatment that boosts the immune system to recognize and destroy cancer cells. Head and neck squamous cell carcinomas (HNSCC) produce suppressive factors that impair the immune system, thus limiting effective antitumor immunity. OX40 is a member of the tumor necrosis factor (TNF) receptor family and a potent co-stimulatory pathway that when triggered can enhance T-cell memory, proliferation and anti-tumor activity in patients with metastatic cancer.

Sponsored By apogenix

3:20 Targeting Co-Stimulatory TNF Receptors with Hexavalent TNF Receptor Agonists (HERA)
Harald Fricke, M.D., COO/CMO, Apogenix AG
HERA compounds currently under development at Apogenix, including HERA -CD27L, -CD40L, -GITRL and -4-1BBL bind their cognate receptors by clustering six receptor chains in a spatially defined manner. This binding mode confers potent biological activity without requiring cross-linking and functional studies reveal differences in receptor signaling and anti-tumor efficacy compared to "agonistic" antibodies. These qualities, plus a short half-life, have been proven to eliminate immunogenicity and toxicity as well as to ensure optimal immunostimulatory activity.

3:50 Refreshment Break

4:20 Varlilumab, an Agonist Anti-CD27 Antibody, as Single Agent and in Combination
Tom Davis, M.D., Executive Vice President and CMO, Celldex Therapeutics Inc.
The CD27 co-stimulation pathway for immune cells has shown potent activity in pre-clinical models to eliminate tumors both as single agent and in combination with checkpoint inhibitors. Clinical trials to date using varlilumab, an agonist anti-CD-27 antibody, confirm this specific immune activation without significant immune toxicity. Single agent responses have been seen and multiple collaborative studies of varli in combination are ongoing.

4:50 JTX-2011: Development of an Agonist Antibody Targeting ICOS
Jennifer Michaelson, Ph.D., Executive Program Leader, Senior Director of Preclinical Development, Preclinical Development, Jounce Therapeutics Inc.
JTX-2011 is an agonist antibody to the co-stimulatory molecule ICOS. Preclinical studies demonstrated efficacy in syngeneic tumor models, with enhanced efficacy in combination with PD-1 inhibitors. JTX-2011 induces T effector cell activation and also preferentially reduces T regulatory cells in the tumors. This dual mechanism contributes to the significant anti-tumor response observed in preclinical models. A promising safety profile was revealed in preclinical studies. JTX-2011 is in clinical development as a monotherapy and in combination with anti-PD-1 therapy.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC18: Clinical Prospects of Cancer Immunotherapy
**Separate registration required, please see page 5-6 for course details.*

Agonist Immunotherapy Targets

FRIDAY, MAY 5

8:00 am Morning Coffee

Emerging Science

8:30 Chairperson's Remarks
Roland Kontermann, Ph.D., Professor of Biomedical Engineering, Institute of Cell Biology and Immunology, University of Stuttgart

8:35 Duokines: A New Class of Bifunctional Immunostimulatory Molecules
Roland Kontermann, Ph.D., Professor of Biomedical Engineering, Institute of Cell Biology and Immunology, University of Stuttgart
Duokines are bifunctional fusion proteins of TNF ligand superfamily members expressed either as homotrimer molecules or as single-chain derivatives. They act either in cis or in trans and are capable of amplifying immune responses, e.g., as shown for the antitumor activity of T-cell retargeting bispecific antibodies.

9:05 The Tetravalent, Bispecific CD30/CD16A TandAb AFM13 is a Prototype NK-Cell Engager with Unique CD16A-Binding Properties
Martin Treder, Ph.D., CSO, Affimed, NV.
AFM13 is currently in Phase II clinical development in Hodgkin lymphoma (HL) and other CD30+ malignancies. It engages NK-cells through CD16A with high affinity and specificity and confers significantly stronger NK-cell activation compared to other therapeutic antibodies. We have previously shown synergistic efficacy when NK-cell activation through AFM13 is combined with checkpoint modulation such as anti-PD-1 treatment, which is known to unleash T-cell and NK-cell activity. Mechanism of action as well as mono- and combination therapeutic approaches of an NK-cell engager will be discussed.

9:35 Activation of Myeloid IL-27 Production Initiates 4-1BB Agonist Hepatotoxicity
Michael A. Curran, Ph.D., Assistant Professor, Immunology, MD Anderson Cancer Center
The clinical progression of 4-1BB agonist antibodies has been stymied by limited understanding of their underlying mechanism of action and the resulting inability to separate off-target liver toxicity from on-target anti-tumor immunity. By analyzing the mechanisms underlying this toxicity, we have revealed novel insights into 4-1BB biology which can inform design of novel antibodies or combination strategies which favor tumor clearance over liver inflammation.

10:05 Coffee Break

10:35 Agonist Redirected Checkpoints for Cancer Immunotherapy
Taylor Schreiber, M.D., Ph.D., CSO, Shattuck Labs, Inc.
This presentation will outline the production, pre-clinical characterization and early GMP manufacturing for a lead ARC construct that simultaneously blocks signaling through PD-1 and activates signaling through OX40. This construct demonstrates significantly superior tumor rejection in multiple pre-clinical models as compared to either PD-1/L1 or OX40 specific antibody therapy.

11:05 Selection of Fc for Antibody Therapeutics to Achieve Optimal Antitumor Immunomodulating Activity
Jieyi Wang, Ph.D., CEO, Lyvgen Biopharma
Therapeutic antibodies have become important biologics for cancer immunotherapy. Their modes of action not only rely on variable domains responsible for specificity but also involve the constant domains that can interact with various Fc receptors. Blocking antibodies such as nivolumab and pembrolizumab were successfully developed in the clinic as IgG4 molecules. However, it is not clear what IgG isotypes would be optimal for agonist antibodies that are required to activate co-stimulatory targets such as CD40, OX40, CD27, CD137, GITR, ICOS and HVEM.

Combinatorial Therapies: Using Antagonists and Agonists to Maximize Response

11:35 Enhancing Checkpoint Inhibitor Efficacy via Combination with CMP-001, a VLP Packaged TLR9 Agonist
Aaron Morris, Senior Director, Research, Checkmate Pharmaceuticals, Inc.
Addition of TLR9 agonist CMP-001 to a standard checkpoint inhibitor regimen can induce a strong anti-tumor response when checkpoint inhibition alone has failed. CMP-001 is a formulation of a CpG-A oligonucleotide, G10, within a Qb virus-like particle (VLP). Preclinical studies and a phase Ib clinical trial have shown induction of robust anti-tumor immunity and tumor regression when CMP-001 is combined with anti-PD-1 therapy.

12:05 pm Novel Immunotherapy Combinations in Non-Small Cell Lung Cancer and Head and Neck Cancers
Erminia Massarelli, M.D., Ph.D., MS, Associate Clinical Professor, Medical Oncology and Therapeutics Research, City of Hope
Checkpoint inhibitors have become the standard second line treatment for patients with metastatic/incurable non-small cell lung cancer (NSCLC) and head and neck squamous cell carcinoma (HNSCC) with an overall survival advantage of 4-5 months compared to second line standard chemotherapy. I will review promising immunotherapy combinations that are currently under investigation with particular focus on T cell agonist targeting OX-40 and 41BB receptors in NSCLC and HNSCC.

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

1:05 Refreshment Break

Target Discovery Approaches in Immuno-Oncology

1:35 Chairperson's Remarks
Harpreet Singh, Ph.D., President & CEO, Immatics US, Inc.

1:40 Exploring the Intracellular Proteome for the Identification and Validation of Novel Targets for Cancer Immunotherapy
Yoram Reiter, Ph.D., Professor & Head, Laboratory of Molecular Immunology, Technion-Israel Institute of Technology
T-cell receptor-like (TCRL) antibodies bind HLA-peptide complexes on the surface

of cells and can bind specifically to the cell surface of diseased cells, thus, transforming intracellular disease-specific targets expressed inside malignant cells into targets that can be recognized on the cell surface by soluble TCRL antibodies. These antibodies can be armed with various modalities or they can be used as naked molecules to modulate responses or environments associated with immunity towards the target cells. This approach expands the pool of novel therapeutic targets and antibodies beyond the limits of currently available antibodies.

2:10 Novel Targets for Cancer Immunotherapies: The XPRESIDENT® Approach

Harpreet Singh, Ph.D., President & CEO, Immatics US, Inc.

Targeted adoptive cell therapies have been highly successful in achieving durable clinical responses in B-cell malignancies based on targeting CD19. Novel T-cell targets are required to expand this success to solid cancers. Here we present the outcome of the Human Immunopeptidome Program through applying our proprietary XPRESIDENT® target discovery strategy which employs systematic high-throughput and ultra-sensitive quantitative tandem mass spectrometry combined with next-generation sequencing and T-cell receptor discovery.

2:40 Development and Validation of a Phenotypic Screening Platform for the Identification of Novel Immuno-Oncology Targets

Christophe Quéva, Ph.D., CSO, iTeos Therapeutics SA

A co-culture assay combining immune suppressive cells and T-cells has been set up to allow the identification of novel immune-oncology targets by screening chemicogenomics, shRNA and cDNA libraries. Multi-parameter readouts are combined to assess both T cell activation and proliferation, through high content imaging, complemented with detection of IFNγ secretion, as well as tumor cell death, as assessed using a cytotoxicity assay. Application of this screening assay to the identification of rationale combinations will be described.

3:10 Emerging Innate Immune Targets for Enhancing Adaptive Anti-Tumor Responses

Gretchen Baltus, Associate Principal Scientist, Oncology Discovery, Merck Research Labs

Novel cancer immunotherapies targeting T cell checkpoint proteins have emerged as powerful tools to induce profound, durable regression and remission of many types of cancer. Despite these advances, multiple studies have demonstrated that not all patients respond to these therapies, and the ability to predict which patients may respond is limited. Harnessing the innate immune system to augment the adaptive anti-tumor response represents an attractive target for therapy, which has the potential to enhance both the percentage and rate of response to checkpoint blockade.

3:40 End of Conference

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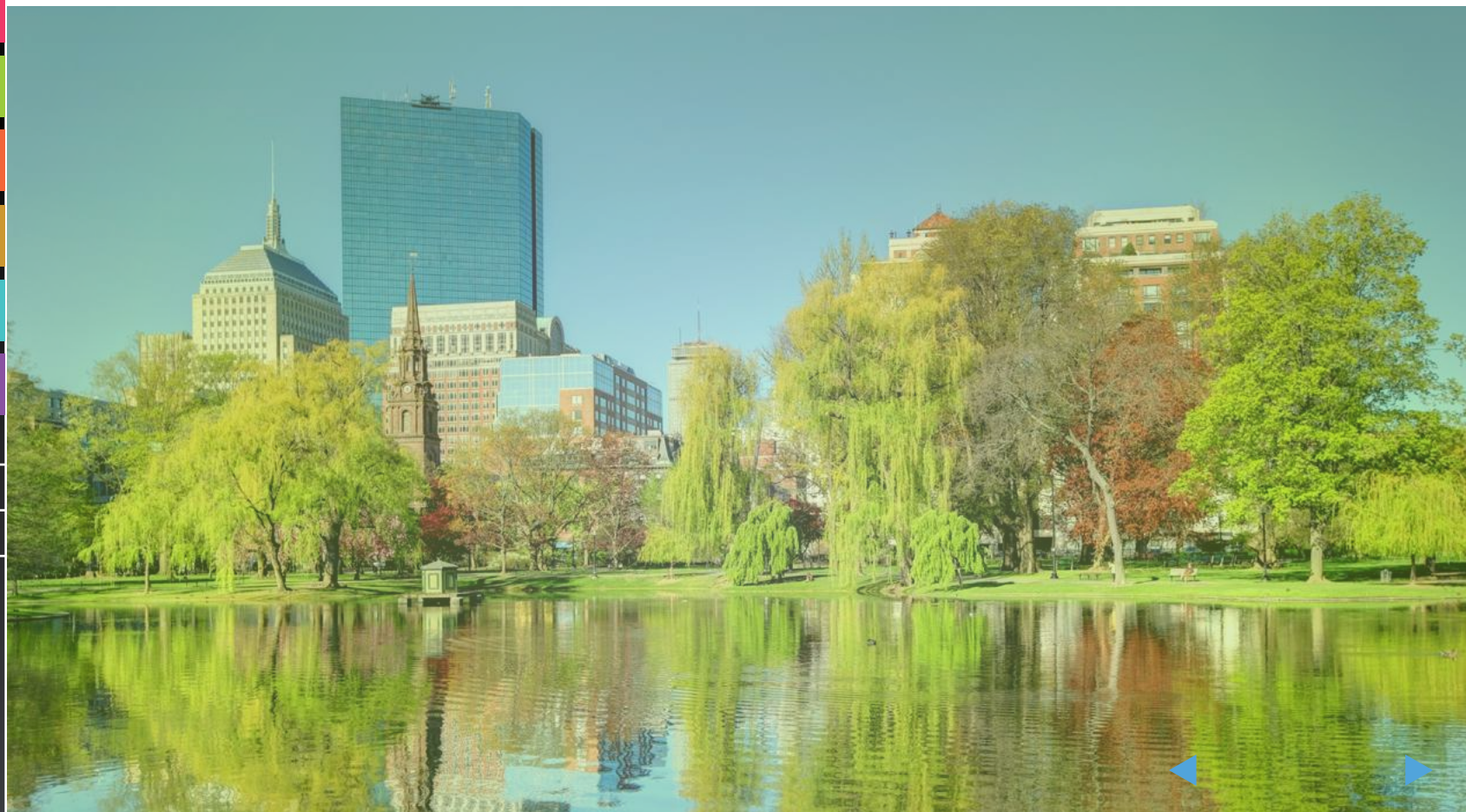
EXPRESSION STREAM

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



Difficult to Express Proteins

Strategies for Taming "Finicky" Proteins

Recommended Short Courses*

SC6: In-silico Protein Docking

SC8: *In silico* Immunogenicity Predictions (Hands-On) Workshop
**Separate registration required, please see page 5-6 for course details.*

MONDAY, MAY 1

7:00 am Registration and Morning Coffee

Solving Protein Expression Problems with Innovative Strategies

8:30 Chairperson's Remarks
Haruki Hasegawa, Ph.D., Principal Scientist, Therapeutic Discovery, Amgen, Inc.

8:40 Investigation of GPR34 Topogenesis and Cell Surface Trafficking by Monitoring a Unique Epitope That Is Simultaneously Sensitive to Topology, Conformation, and Redox Status
Haruki Hasegawa, Ph.D., Principal Scientist, Therapeutic Discovery, Amgen, Inc.
We identified and characterized an epitope that reports correct protein conformation, membrane topology, and cell surface trafficking competency of a GPCR family member GPR34. The epitope formation required the oxidation of four cysteine residues located individually in the four separate extracellular regions of GPR34. The underlying biochemical properties of the conformational epitope not only illustrated the challenges of raising mAbs against GPCRs, but also suggested preferred strategies for GPCR antigen design.

9:10 Glycoengineering of Chinese Hamster Ovary Cells for Enhanced Erythropoietin N-Glycan Branching and Sialylation
Bojiao Yin, Ph.D., Researcher, Protein Technologies, Amgen
In order to examine the impact of glycosyltransferase expression on the N-glycosylation of recombinant erythropoietin (rEPO), a human α2,6-sialyltransferase (ST6Gal1) was expressed in Chinese hamster ovary (CHO-K1) cells. In this way, coordinated overexpression of these three glycosyltransferases for the first time in model CHO-K1 cell lines provides a means for enhancing both N-glycan branching complexity and sialylation with opportunities to generate tailored complex N-glycan structures on therapeutic glycoproteins in the future.

9:40 KEYNOTE PRESENTATION: Design of Water-Soluble Variants of Membrane Proteins to Facilitate "Soluble Expression"
Jeffrey G. Saven, Ph.D., Professor, Chemistry, University of Pennsylvania
Here we present the first study involving the computational design, expression and characterization of a water-soluble variant of a human GPCR, the human mu opioid receptor (MUR), which is involved in pain and addiction. This study exemplifies the potential of the computational approach to produce water-soluble variants of GPCRs amenable for structural and functionally related characterization in aqueous solution.

10:10 Coffee Break

Engineering for Successful Expression

10:45 Chairperson's Remarks
Haruki Hasegawa, Ph.D., Principal Scientist, Therapeutic Discovery, Amgen, Inc.

10:50 High-Throughput Baculovirus Expression System for Membrane Protein Production
Ravi C. Kalathur, Ph.D., New York Structural Biology Center, New York Consortium on Membrane Protein Structure (NYCOMPS)
The ease of use, robustness, cost-effectiveness, and post-translational machinery make the baculovirus expression system a popular choice for production of eukaryotic membrane proteins. This system can be readily adapted for high-throughput operations. The modified pFastBac vector with mammalian promoter called BacMam can be used to transduce mammalian cells like HEK, CHO and BHK and this is an attractive alternative for glycosylation and biosafety concerns.

11:20 Engineering High-Titer Heterologous Protein Secretion in Bacteria
Lisa Burdette, Tullman-Ercek Laboratory, Chemical and Biological Engineering, Northwestern University
Biomaterial production in bacteria would benefit greatly from a high-titer secretion strategy. We engineered the type III secretion system in *Salmonella enterica* for this purpose because it is non-essential for bacterial metabolism and allows for target proteins to cross both bacterial membranes in one step. Our platform enables the high-titer production of a variety of challenging biomaterial-forming proteins at titers >100 mg/l and >85% purity.

Difficult to Express Proteins

11:50 Improving Membrane Protein Overexpression in Mammalian Cells by Flow Cytometric Sorting
Juni Andréll, Ph.D., Researcher, Biochemistry and Biophysics, University of Stockholm
Many membrane proteins from higher eukaryotic organisms cannot be expressed in bacterial or yeast systems, but are favourably expressed in a functional state in mammalian cells. However, the expression levels can often be too low for protein structural studies requirements. Using an optimised protocol of flow cytometric sorting to generate stable-cell lines can significantly and sufficiently improve the inducible expression of different membrane proteins in mammalian cells.

12:20 pm New Solutions for Production of Difficult-to-Express Proteins
Sponsored By WACKER
Martina Huber, Ph.D., Local Site Head, Bioprocess Development, Wacker Biotech GmbH
Wacker Biotech will present highly competitive solutions for production of difficult-to-express proteins based on its proprietary *E. coli* expression systems ESETEC® and FOLDTEC®. Recent case studies will include secretion of functional antibody fragments and enzymes to the fermentation broth with up to 14 g/L. Together with its *E. coli* refolding platform FOLDTEC®, Wacker Biotech offers a novel and comprehensive approach to rapidly assess manufacturability of therapeutic proteins.

12:50 Luncheon Presentation I: Building Better Protein Pharmaceuticals at the Intersection of Machine Learning and Quantitative Biology
Sponsored By ATUM
Claes Gustafsson, Ph.D., Co-Founder and Chief Commercial Officer, ATUM (formerly DNA2.0)
Gene synthesis and current molecular biology tools allow unprecedented ability to create any biology imaginable. Due to the high cost of commercially relevant functional measurements and the vast size of available sequence space it is not feasible to randomly search the space. However, utilizing Artificial Intelligence (AI) and systematic variance of the sequence space data we will describe how we engineer efficient optimization of genes, proteins, pathways, organisms without any mechanistic understanding of the system.

1:20 Vmax™ – a Next-generation Microbial Workhorse for the Biotech Industry
Sponsored By SGIDNA
Matthew Weinstock, Ph.D., Scientist II, DNA Technology, Synthetic Genomics, Inc.
This presentation will focus on Vmax™, a novel prokaryotic host with a rapid growth rate that promises to accelerate biotech R&D efforts on multiple fronts. We will describe the development of the platform, the advantages of using it in molecular cloning and protein expression applications, and ongoing large-scale genome engineering efforts to further enhance performance.

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

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

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks
Gregory A. Weiss, Ph.D., Professor, Chemistry, Molecular Biology & Biochemistry, University of California, Irvine

4:10 Bicycles and Bicycle Drug Conjugates: Next Generation Therapeutics
Sir Gregory Winter, Ph.D., FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics
Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles' unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs); a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. This presentation will describe both the Bicycle® and BDC platforms.

4:55 Young Scientist Keynote: Programming Proteins by Deep Sequencing and Design
Tim Whitehead, Ph.D., Assistant Professor, Chemical Engineering and Materials Science, Michigan State University
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 group leverages this unprecedented wealth of sequence-function information to design and engineer protein affinity, specificity, and function and to infer structural complexes of proteins. My talk will present an overview of the above and detail methodological improvements that enable the engineering work.

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

6:55 End of Day

TUESDAY, MAY 2

8:00 am Registration and Morning Coffee

Scaffolds and Synthetic Biology

8:25 Chairperson's Remarks
Alexei Yeliseev, Ph.D., Staff Scientist, LMBB, NIH/ NIAAA

8:30 Utilizing Selenocysteine for Expressed Protein Ligation and Bioconjugations
Sharon Rosovsky, Ph.D., Assistant Professor, Chemistry and Biochemistry, University of Delaware
Selenoproteins are enzymes that contain the rare amino acid selenocysteine. They play a cardinal role in the management and regulation of reactive oxygen species. Selenoproteins remain understudied because of the technical challenges associated with their production since the selenocysteine codon UGA also encodes a stop codon. We have developed a new method to prepare

Difficult to Express Proteins

selenoproteins using expressed chemical ligation. Selenocysteine high reactivity can be used to introduce site-specific chemistry into the protein scaffold.

9:00 The All *E. coli* TX-TL Toolbox 2.0: A Platform for Cell-Free Synthetic Biology

Vincent Noireaux, Ph.D., School of Physics and Astronomy, University of Minnesota

In vitro transcription-translation (TX-TL) is becoming a highly versatile technology for applications in synthetic biology and quantitative biology. I will present a unique TXTL system that my laboratory has developed. We implemented novel metabolisms to stimulate reporter protein synthesis up to 2 mg/ml in batch mode reactions and 6 mg/ml in semi-continuous mode. We use this experimental platform for synthetic biology, from gene circuit prototyping to the cell-free synthesis of entire bacteriophages.

9:30 Applications of panARS-Based Vectors for High Throughput Screens and Structural Studies in *Pichia pastoris*

Damien B. Wilburn, Ph.D. Post-Doctoral Senior Researcher, Genome Sciences, University of Washington

Pichia pastoris is widely considered an industrial workhorse for expression of recombinant proteins, but a limitation of the system has been the requirement for stable integration of heterologous genes that can result in high clonal variability and limit high throughput screening. Here we describe expression of multiple protein constructs using episomal vectors that include panARS: an autonomous replicating sequence that enables stable plasmid maintenance and excellent protein yield in Pichia expression systems.

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

Designing Expression to Facilitate Purification

10:50 High Yield, Large-Scale Affinity Purification of the Functional G Protein-Coupled Receptors

Alexei Yeliseev, Ph.D., Staff Scientist, LMBB, NIH/ NIAAA

We purified the recombinant CB2 expressed in *E. coli* cells as a fusion with maltose-binding protein and small affinity tags, with yields up to 2-3 mg/ L. We demonstrate an efficient isolation of functional CB2 receptor labeled with stable isotopes in minimal medium. The protocols developed in our laboratory can be applied to expression and purification of other membrane receptors for structural and functional studies.

11:20 A Systematic Approach to Improve the Expression and Purification of Membrane Proteins in *E. coli*

Luis G. Cuello, Ph.D., Associate Professor, Cell Physiology and Molecular Biophysics and Center for Membrane Protein Research, Texas Tech University Health Sciences Center

We developed a method for the production of membrane proteins in *E. coli*. The method consists in the systematic pipeline evaluation of different: *E. coli* strains, chemical chaperones, growth media, blockers or inhibitors, temperature, inexpensive detergents for solubilizing the target membrane protein alongside optimizing the ionic strength, pH, and temperature.

11:50 Lessons from an α-Helical Membrane Enzyme: Expression, Purification, and Detergent Optimization for Biophysical and Structural Characterization

Raquel Lieberman, Ph.D., School of Chemistry & Biochemistry, Georgia Institute of Technology

We outline the protocol developed in our lab to produce a multipass α-helical membrane protein. We present our work flow, from ortholog selection to protein purification, including molecular biology for plasmid construction, protein expression in *E. coli*, membrane isolation and detergent solubilization, protein purification and tag removal, biophysical assessment of protein stability in different detergents, and detergent concentration determination using thin-layer chromatography. We focus on results from our ongoing work with intramembrane aspartyl proteases from archaeal organisms.

12:20 pm High-Resolution Epitope Mapping and Specificity Profiling of mAbs Targeting Complex Proteins

Sponsored By integral molecular

Duncan Huston-Paterson, D.Phil., Project Leader, Integral Molecular

Integral Molecular specializes in characterizing antibodies against complex targets, including GPCRs, ion channels, and transporters. Our Shotgun Mutagenesis technology rapidly maps conformational antibody epitopes at single-amino acid resolution using comprehensive mutagenesis and cellular-expression with >95% success, generating critical IP and detailed mechanistic insights. Our Membrane Proteome Array enables safety analysis of antibodies by testing each antibody against an expression array of 5,304 structurally-intact membrane proteins, providing a comprehensive assessment of off-target antibody interactions.

12:50 Talk Title to be Announced

Sponsored By FUJIFILM Diosynth biotechnologies

Ian Hodgson, Ph.D., Head, Molecular Biology, FUJIFILM Diosynth Biotechnologies

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

Building on Successful Expression Experience

2:00 Chairperson's Remarks

Vinodh Kurella, Ph.D., Senior Scientist, Protein Engineering, ImmunoOncology Division, Intrexon Corporation

2:05 Making Spider Silk: How Hard Can It Be, Spiders Do It?

Randolph P. Lewis, Ph.D., USTAR Professor, Biology / Synthetic Bio-Manufacturing, Utah State University

Spider silk proteins are unique in being highly repetitive, very large and composed of very few amino acids. These each lead to complications when trying to express these proteins in quantities needed to develop commercial products. With a major focus on expression in E.coli solutions to some of these unique problems will be discussed as well as identifying difficulties still to be overcome. Brief discussions of other expression systems will be presented.

Difficult to Express Proteins

2:35 Development of a Dual Fluorescent Protein Reporter System for Detection of Unfolded Protein Response Pathway Activation in Mammalian (CHO) Cells and its Application in Therapeutic Proteins Production

Gargi Roy, Ph.D., Scientist, MedImmune

We developed a reporter system that detects IRE1α mediated XBP1 splicing for monitoring the UPR activation in IgG expressing cells. Using this reporter we show ER stress activation in stable IgG expressing cells during fed-batch. We demonstrate that it can be used to isolate high expresser clonal hosts. This reporter system with its ability to monitor the stress has a potential for devising strategies for the selection of high expressers and improved yields of bio-therapeutics.

Sponsored By

3:05 Oral Insulin: Challenges, Learnings and Pitfalls: Premas Biotech

Prabuddha Kundu, Ph.D., Executive Director & Co-Founder, Premas Biotech Pvt Ltd

The ability to Translate scientific concepts created at research scale to a viable commercial scale, is of significant importance to clinical medicine; an area of specialization for Premas over a decade. Oral Insulin, a revolutionizing concept for Diabetics, conceptualized by Oramed, where Premas has partnered actively in the journey to make it a success through Clinical trials from lab scale, technology development, scale up, to manufacturing (grams to kilograms per batch) and into Phase III.

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

Expression Success Stories

4:25 IQGAP1 Protein Purification and X-Ray Crystallography

Vinodh Kurella, Ph.D., Senior Scientist, Protein Engineering, ImmunoOncology Division, Intrexon Corporation

Protein purification process is a prelude to X-ray crystallography for certain studies. A case study will be presented on a scaffold protein - IQGAP1, overexpressed in colon cancer. IQGAP1- Calponin Homology domain was purified but precipitated before crystallization trials. Construct redesign lead to stabilization and also yielded high-quality crystals. However, in-house diffraction pattern revealed a fragile crystal. Finally, a synchrotron beam was utilized to solve the structure to 2.4 Å.

4:55 Stable Drosophila Cell Lines: An Alternative Approach to Exogenous Protein Expression

Thomas Krey, Ph.D., Institute of Virology, Structural Virology Group, Hannover Medical School

Among numerous expression systems, insect cells provide the possibility to produce complex target proteins that require posttranslational modifications. Stable expression in Drosophila S2 cells represents an attractive alternative to the widely used baculovirus expression system, offering important advantages in particular for difficult-to-express proteins, e.g., membrane proteins or heavily glycosylated multi-domain proteins that are stabilized by a complex disulfide pattern. Here we present the methodology that is required for the generation of stable Drosophila S2 cell transfectants and for production of recombinant proteins using those transfectants.

5:25 End of Difficult to Express Proteins

5:30 Registration for Dinner Short Courses

Optimizing Protein Expression

Enhancing Expression Systems

Recommended Short Courses*

SC13: Phenotypic Screening Applications and Technologies

SC17: Transient Protein Production in Mammalian Cells
*Separate registration required, please see page 5-6 for course details.

WEDNESDAY, MAY 3

7:30 am Registration and Morning Coffee

Protein Expression Strategies

8:30 Chairperson's Remarks
Oliver Spadiut, Ph.D., Principal Investigator, Biochemical Engineering, Vienna University of Technology

8:40 KEYNOTE PRESENTATION: Protein Expression Demands and Demanding Protein Expressions: Protein Sciences the BioPharma Way
David Humphreys, Ph.D., Director and Head, Protein Sciences, UCB NewMedicines
Protein expression in BioPharma can span from small quantity bespoke expression of antigenic proteins for immunisations and assays, large numbers of antibodies to support project discovery needs through proteins for structural studies to therapeutic antibody manufacturing systems. UCB uses a whole range of expression and purification systems from *E. coli* to mammalian cells to meet project and manufacturing demands. These will be highlighted in a general protein expression context.

9:10 Early Development Strategies for Innovative Therapeutic Molecules Now and Then
Nicola Beaucamp, Ph.D., Head, Process Research, Pharma Research and Early Development, Roche Innovation Center
A number of novel antibody formats have been advanced into clinics by Roche pRED. In order to discover and develop differentiated monoclonal antibodies, Roche's strategy is based on engineering technologies that bear several challenges for technical development. Examples on innovative therapeutic molecules for multi-pathway-inhibition or specific tumor-targeting will be given.

9:40 Alexion's Protein Production Process and Platforms: Comparison of Expi293 and ExpiCHO Expression Systems
Tadas Panavas, Ph.D., Associate Director, Discovery Research, Alexion Pharmaceuticals, Inc.
This presentation will showcase how Alexion has implemented streamlined processes across multiple sites to automate our engineering and production of enzyme replacement therapeutics (ERTs) as well as single and multi-domain antibodies. The selection of expression system for antibody therapeutics and ERTs will be discussed, and thorough comparison between Expi293 and ExpiCHO will be presented.

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

CHO Expression

10:55 Deletion of a Telomeric Region on Chromosome 8 Correlates with Higher Productivity and Stability of CHO Cell Lines
Corinne Ueberschlag, M.Sc., Fellow, Functional Lead Cell Line Development, Biologics Technical Development and Manufacturing, Novartis AG
A new parental CHO cell line lacking a telomeric region of the chromosome 8 was generated, resulting in significantly improved productivity of the cells after gene transfer, as well overall improved production stability of these cells. Combining this cell line with new vector technologies, we have implemented a high-performing platform for therapeutic protein production.

11:25 Prediction and Mitigation of Production Instability of Recombinant CHO Cell Lines
Ulrich Göpfert, Ph.D., Principal Scientist, Cell Line & Molecular Development, Roche Innovation Center
During expansion and maintenance, CHO cell lines are prone to production instability, which may be caused by promoter silencing, loss of transgene copies, or post-transcriptional effects. Silencing of recombinant genes may be accompanied by DNA methylation and histone modification. We examined a variety of epigenetic modifications and identified molecular indicators which provide the opportunity to enrich stable producers.

11:55 Signal Peptide Processing of Material Produced in CHO Stable Cell Lines
Barry A. Morse, Ph.D., Principal Research Scientist, Janssen Research and Development

Sponsored By sartorius stedim

12:25 pm Applying QbD Principles in Discovery and Early Stage Process Development Facilitates the Scale-Up of Robust Processes
Remi Laliberte, Process Development Manager, Sartorius Stedim North America
There is substantial potential for the research and development space to increase its impact on today's industry goals through a more integrated approach between discovery and process science. New technologies and services are becoming available that allow for a more seamless integration of discovery work, CQA's, design spaces, process development and process/product quality control. The integration of those technologies across the biopharma drug development cycle will allow for substantial efficiency gains and time savings getting molecules to the clinic.

Optimizing Protein Expression

12:55 New Tools for Screening & Harvesting Solutions for CHO & HEK293 Cells, for Both Transient and Stable Cell

Sponsored By THOMSON Instrument Company

Sam Ellis, Vice President & Biochemist, 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.

1:25 Difficult to Express Proteins: Novel Plasmid Technology Results in Significant Yield Increase in CHO

Sponsored By BATAVIA biosciences

Marco Cacciuttolo, Ph.D., Director Operations, Batavia Biosciences

Yield is still an area that requires significant improvement for many promising recombinant protein and antibodies. Especially in the field of biosimilars and orphan diseases, the ability to manufacture products cost-effectively could have a profound impact on the interest of the industry to develop safe, affordable and efficacious products. Novel plasmid technology enables rapid generation of stable, CHO cell lines able to provide at least 10-fold more product per cell.

1:55 Session Break

Escherichia coli

2:10 Chairperson's Remarks

Tadas Panavas, Ph.D., Associate Director, Discovery Research, Alexion Pharmaceuticals, Inc.

2:15 Codon Influence on Protein Expression in *E. coli* Correlates with mRNA Levels

John Hunt, Ph.D., Professor, Biological Sciences, Columbia University

We have developed new computational gene-design algorithms based on multiparameter modeling of results from 6,348 experiments employing bacteriophage T7 polymerase to drive protein overexpression *E. coli*. Our analyses define the relative influence of mRNA sequence parameters including predicted folding energy, base composition, and codon usage. Our new codon-influence metric differs significantly from prior expectations and permits generation of diverse synonymous gene sequences that consistently drive high level protein overexpression.

2:45 How Induction Impacts Inclusion Body Properties and Inclusion Body Processing in *E. coli*

Oliver Spadiut, Ph.D., Principal Investigator, Biochemical Engineering, Vienna University of Technology

I will show our ongoing work, where we 1) understand the effect of lactose/IPTG induction on *E. coli* physiology and productivity, 2) demonstrate the effects of induction on inclusion body properties (size, amount, density, purity), and 3) finally show how induction and consequent inclusion body properties affect the subsequent inclusion body processing (wash, solubilization, refolding).

3:15 Expression Flexibility at the 2-12L scale: SB10 Orbital-Shaken SUB for High Density Cultivation in Multiple Cell Types

Sponsored By Kuhner shaker

David Laidlaw, MSc, CEO, Kuhner Shaker, Inc.

Batch, fed-batch and perfusion protein production may be accomplished using a number of platforms. Production simplicity is achieved when small scale results predict those of the bench scale bioreactor. Here we present data from users of the orbital-shaken SB10 bioreactor with CHO, Sf9, AGE1.CR and moss cells (P. Patens).

3:30 The 3rd Generation Strep-tag® System – Superior Performance in Protein Purification and Assays with Strep-Tactin®XT

Sponsored By iba Solutions For Life Sciences

Uwe Carl, Ph.D., Head, Protein Production, Strep-Tag Products and Proteins, IBA Lifesciences

IBA is focused on building a comprehensive product portfolio around its proprietary Strep-tag® technology to provide solutions for protein production and assays, including cloning, expression, purification and immobilization. Especially our 3rd generation Strep-tag® system is superior to other systems due to its extreme high affinity and still reversible binding.

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, MAY 4

8:00 am Morning Coffee

Improving Production

8:30 Chairperson's Remarks

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

8:35 Pathway Engineering for Customizing Eukaryotic Protein Glycosylation

Nico Callewaert, Ph.D., Director, VIB Medical Biotechnology Center, Ghent University

Glycosylation is the most common post-translational modification on biopharmaceuticals produced in eukaryotic hosts. Developments over the past decade have enabled to achieve higher levels of control over the glycan structures on biopharmaceuticals, allowing to customize these structures for particular therapeutic functionality. In this talk, I will discuss *Pichia pastoris* GlycoSwitch (TM) and mammalian cell/yeast/plant GlycoDelete technologies, as well as position these novel systems within the available range of biopharmaceutical expression hosts.

9:05 Implement High Temperature Short Time (HTST) Viral Control Strategy in Large Scale Biotherapeutics Manufacturing

Optimizing Protein Expression

Min Zhang, Ph.D., Director, Manufacturing Sciences and Technology, AstraZeneca/ MedImmune

9:35 Accelerating Development Timelines Using Scalable Delivery Platform for Transient and Stable Protein Expression

Sponsored By MaxCyte FLOW TRANSFECTION

James Brady, Ph.D., Vice President, Technical Applications and Customer Support, MaxCyte, Inc.

Transitioning early stage discovery with later stage development is critical for efficiently moving therapies into the clinic.MaxCyte's electroporation-based delivery platform enables high titer expression of antibodies and other proteins in cells that are relevant to biomanufacturing. We present data using MaxCyte electroporation for gram scale transient antibody production followed by rapid and streamlined migration to stable cell lines. Finally, we discuss means for targeted genomemodification for generation of cells engineered for maximum productivity.

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

Alternative Expression Systems

11:05 Application of a Baculovirus Platform for the Production of Vaccines

Indresh K. Srivastava, Ph.D., Vice President, Product Realization, Senior Project Manager, Protein Sciences Corp.

In this talk, I will present the data on the production, characterization and immunogenicity of our FDA-approved Trivalent and Quadrivalent Influenza Vaccines, and strategy to perform process improvements for yield improvement. Will also present the data on ZIKV vaccine development program.

11:35 Production of Recombinant Proteins in Eukaryotic Green Algae: Growth of a New Green Sector

Miller Tran, Ph.D., Associate Director, Triton Algae Innovations, Inc.

At Triton Algae Innovations, we focus specifically on the chloroplast of eukaryotic green algae. Chloroplasts house complex molecular chaperones and protein disulfide isomerases that allow them to efficiently and economically produce a large class of proteins. Another interesting facet of algae is their ability to be consumed. This trait effectively eliminates the costly process of protein purification. However, moving algae from a system used for biofuels to one used to produce recombinant protein required a shift in production strategies and a development of a novel suite of expression tools to facilitate a new growth and production strategies. At Triton, Dr. Tran has pioneered the development of these expression vectors and the production of a large class of proteins for use in the gut health industry.

12:05 pm *Pichia*-Based Recombinant Proteins: From Difficulty to Development

Chandrasekhar Gurramkonda, Ph.D., Research Assistant Professor, Chemical, Biochemical and Environmental Engineering, University of Maryland

Pichia pastoris emerged as a next door expression organism for many scientists and engineers. Because of its ability to reach high-cell densities, it can grow in simple buffer and GRAS host for the expression of recombinant proteins such as disulphide bonded proteins, oligomeric forms and proteins with its cognate partners in very high quantities by multicopy integration.

12:35 End of Optimizing Protein Expression

THURSDAY, MAY 4

Enhancing *Escherichia coli*

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Donald Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming

1:50 FEATURED PRESENTATION:

How Far Can We Go? Towards Automated Quality Analysis and Mechanistic Model Supported Process Development for Recombinant Inclusion Body-Based Processes
Peter Neubauer, Ph.D., Professor, Bioprocess Engineering, Biotechnology, Technische Universität Berlin (TU Berlin)
Although inclusion bodies (IBs) are beneficial from the side of production, still the downstream refolding process is variable by a low process robustness and varying quality of IBs. Therefore, strategies for fast detection of inclusion bodies are of great interest as well as methods for a computer-based evaluation of how process changes affect the amount and quality of IBs. Here we present our approaches including a fluorescence-based quantitative detection of inclusion bodies and a mechanistic model-based analysis of process robustness.

2:20 Design, Synthesis, and Testing toward a 57-Codon Genome
Nili Ostrov, Ph.D., Research Fellow, Genetics, Harvard Medical School
Recoding—the repurposing of genetic codons—is a powerful strategy for enhancing genomes with functions not commonly found in nature. The talk will describe design, synthesis, and progress toward assembly of a 3.97-megabase, 57-codon *E. coli* genome in which seven codons were replaced with synonymous alternatives across all protein-coding genes. This work underscores the feasibility of rewriting genomes and establishes a framework for design, assembly, and phenotypic analysis of synthetic organisms.

2:50 Engineering *Escherichia coli* into a Protein Delivery System for Mammalian Cells
Cammie Lesser, M.D., Ph.D., Associate Professor, Medicine, Microbiology and Immunobiology, Infectious Diseases, Massachusetts General Hospital
Many Gram-negative pathogens encode type III secretion systems, sophisticated nanomachines that deliver proteins directly into the cytosol of mammalian cells. Here we report our advances in outfitting non-pathogenic strains of *E. coli* with a tunable type III secretion system capable of secreting therapeutic payloads directly into to mammalian cells as well as the extracellular milieu. This work illustrates a potential new paradigm for the treatment of a variety of human diseases.

Sponsored By OXFORD GENETICS

3:20 Rapid Vector Development and Bioinformatics Tools to Enable Biopharmaceutical Discovery and Development
Tom Payne, Ph.D., CTO, Oxford Genetics
Oxford Genetics offers a wide variety of 'best-in-class' solutions for synthetic biology and bioproduction applications. In particular we will focus on offerings around DNA vector development for rapid expression optimisation, bioinformatics services, and stable cell line development for recombinant protein expression.

Sponsored By DYADIC

3:35 C1 – The Journey of a More Productive Cell Expression Technology System
Ronen, Tchelet, Ph.D., Research & Development, Dyadic
The C1 platform technology is a hyper-productive fungal expression system used to develop & manufacture large quantities of desired proteins at industrial scale at significantly lower CapEx and OpEx costs.

3:50 Refreshment Break

Engineering CHO Systems

4:20 POSTER SPOTLIGHT: Synthetic Promoters from CHO Endogenous Elements for High-Level Recombinant Protein Production
Yusuf Johari, Ph.D., Postdoctoral Research Associate, Chemical and Biological Engineering, The University of Sheffield

4:50 Engineering the CHO Cell
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark
Using high-throughput (HT) technologies, the CHO Cell Line Engineering project at the Center for Biosustainability is genetically modifying CHO cells based on experimental and *in silico* generated data, to engineer CHO cell lines optimised for the production of therapeutic proteins. The HT cell line engineering pipeline, as well as examples of the engineered improved cell lines, will be described.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Courses*

SC16: New USP Initiatives for Characterization and Release of Biologics

SC17: Transient Protein Production in Mammalian Cells
**Separate registration required, please see page 5-6 for course details.*

Protein Expression System Engineering

FRIDAY, MAY 5

8:00 am Morning Coffee

Baculovirus/Insect Cells &CHO

8:30 Chairperson's Remarks
Chava Kimchi-Sarfaty, Ph.D., Research Chemist, Principal Investigator, Division of Hematology Research and Review, FDA/CBER/OBRR

8:35 Doxycycline Regulated Protein Expression in the Baculovirus Insect Cell Expression System
Ricarda Friebe, MSc, Scientific Assistant, Institute of Bioprocess Engineering, Friedrich-Alexander-University Erlangen-Nürnberg
This is the first time the Tet-Off system was fully introduced in a baculovirus genome and used for regulated protein expression in Sf21 insect cells. Regulation of transgene expression will be crucial for a plethora of industrial applications. One important issue to reach maximum protein yield will be the induction of synthesis at the correct time-point of cultivation. Toxic proteins or proteins interfering with the metabolism of the expression organism will gain more and more importance in developing biotechnology.

9:05 New Insect Cell Systems for Enhanced Structural Biology of Recombinant Glycoproteins
Donald Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming
We produced new insect cell lines designed to enhance the utility of the baculovirus-insect cell system for use in studies on the structural biology of recombinant glycoproteins. We used two diametrically opposed approaches, both directed at simplifying glycosylation patterns. One results in production of immature glycans that can be easily removed and the other results in production of homogeneous insect-type paucimannosidic N-glycans more amenable to protein crystallization.

9:35 Presentation Cancelled

10:05 Coffee Break

Improving Production for Antibodies and Mutant Proteins

10:35 Best Practices towards High Titers for Antibody Expression
Saurabh Sen, Ph.D., Principal Scientist, Boehringer Ingelheim Pharmaceuticals, Inc.
Demand for expression of high-quality therapeutic antibodies and recombinant proteins is on a spiral rise, yet the production process is laborious, time consuming and expensive. Transient Gene Expression (TGE) using mammalian cells has been the most extensively used technology for production of antibodies and recombinant proteins and has been widely adapted by both academia and industrial labs. A lot of variable factors, including clone design, vector backbone, codon usage, clone/host selection and process parameters operate in a matrix setting for the optimized production and yield of a functional therapeutic molecule. CHO cells have become one of the major work horses for transient expression of recombinant biologics due to its attractive features: post-translation modification, adaptation to high-cell densities, use of serum-free media etc. There is always an ongoing challenge and need for optimization of the entire process for fulfilling the demands of higher levels of expressed proteins and antibodies. We describe here an intermix of different parameters for TGE towards developing an improved process with significant cost and time savings.

11:05 Cell Line Development of Complex Therapeutic Antibodies
Stella Tournaviti, Ph.D., Senior Scientist, Cell Line and Molecular Development, Roche Innovation Center
We have established a platform for production of complex format CrossMab bispecific antibodies in stable CHO cell lines. CH1-CL exchange in one of the Fab domains, together with the knob into hole principle, significantly improves correct assembly by preventing undesirable side products. We continuously optimize our process in order to yield the maximal fraction of the main product. Case studies showing the importance of the interplay of large clone statistics and high quality assays will be the focus of this presentation.

11:35 Construction and Usage of Large IgG Antibody Libraries in Mammalian Cells
Michael Dyson, Ph.D., CTO, IONTAS, Ltd.
The availability of large libraries of binders expressed within mammalian cells allows direct screening for function through simultaneous expression and functional reporting within the same cell. The main limitation in achieving this has been the inability to construct sufficiently large libraries containing a single antibody gene/cell. We have solved this problem by directing the integration of antibody genes into a single genomic locus through the use of site-specific nucleases. IgG antibody libraries consisting of many millions of clones have been constructed and binders selected.

12:05 pm Rapid Production in Milligram Quantities of a Hundred Kinds of Newly Generated Mutant Proteins
Takanori Kigawa, Ph.D., Team Leader, Quantitative Biology Center (QBiC), RIKEN
We have established a system to produce milligram quantities of a hundred kinds of mutant proteins within a day without using recombinant DNA. The system is composed of 1) newly developed PCR-based method for site-directed mutagenesis with high efficiency and robustness, and 2) fully automated protein preparation (expression and purification) using PCR-generated linear DNA-driven cell-free protein synthesis. Our system is highly useful for protein engineering with rational design approaches because protein preparation steps can be dramatically accelerated without recombinant DNA technology.

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

1:05 Refreshment Break

Codon Optimization and Innovative Processes

1:35 Chairperson's Remarks
Michael Dyson, Ph.D., CTO, IONTAS, Ltd.

1:40 Codon Optimization: Lessons Learned from Recombinant Factor IX
Chava Kimchi-Sarfaty, Ph.D., Research Chemist, Principal Investigator, Division of Hematology Research and Review, FDA/CBER/OBRR
We followed up on a large body of work showing that synonymous mutations can

Protein Expression System Engineering

and do affect protein structure and function by studying codon optimized version of recombinant Factor IX (FIX). Our results suggest that codon optimization may alter mRNA structure/stability and translation kinetics, offering an insight into the mechanisms that may lead to altered protein structure. Knowledge gained from these studies may be used to develop an optimization system that can increase protein production without altering safety and efficacy.

2:10 Codon Usage Tables at the Peak of the Sequencing Era

Aikaterini Alexaki, Ph.D., Staff Fellow, Hematology Research and Review, FDA/CBER/OBRR

We have developed a new database to analyze and present codon usage tables for every organism available, taking advantage of the exponential growth of GenBank and the creation of NCBI's RefSeq database. Our database is more comprehensive than existing tools, addresses concerns that limited the accuracy of earlier databases, and provides several new functionalities, such as the ability to view and compare codon usage across taxonomical clades as well as individual organisms.

2:40 Discovering Novel Enzyme Function through Computational Protein Design and Genomic Mining

Justin B. Siegel, Ph.D., Assistant Professor, Chemistry, Biochemistry & Molecular Medicine, University of California, Davis

The ability to biosynthetically produce chemicals beyond what is commonly found in Nature requires the discovery of novel enzyme function. Here, we utilize two approaches to discover enzymes. The first approach combines bioinformatics and molecular modelling to mine sequence databases, resulting in a diverse panel of enzymes capable of performing the targeted reaction. This integrative genomic mining approach establishes a unique avenue for enzyme function discovery in the rapidly expanding sequence databases. The second approach uses computational enzyme design to reprogram specificity.

3:10 The Biomolecule Copier

Günter Roth, Ph.D., Group Head, Center for Biological Systems Analysis (ZBSA), University of Freiburg

We invented and developed a device capable to take DNA in a PCR mix and generate a DNA microarray. This device can furthermore then copy a DNA microarray into additional DNA, RNA or protein microarrays. We call this the device the biomolecule copier. This technology can be used in many applications including DNA in solution in and on demand DNA, RNA or protein microarrays; and everything can be analysed directly label-free in real-time.

3:40 End of Conference

FINAL DAYS TO REGISTER

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Cambridge 25 YEARS HEALTHTECH Institute
A Division of Cambridge Innovation Institute

ANALYTICAL STREAM

- Characterization of Biotherapeutics
- Biophysical Analysis of Biotherapeutics
- Protein Aggregation and Stability in Biopharmaceuticals

Characterization of Biotherapeutics

Optimizing the Analytical Function in an Era of New Product Formats

Recommended Short Courses*

SC1: Preclinical and Clinical Immunogenicity Bioanalysis: ADCs, Multi-Domain Biotherapeutics and New Modalities

SC10: Bioanalysis of Biomarkers: ADCs, Multi-domain Biotherapeutics and New Modalities

**Separate registration required, please see page 5-6 for course details.*

MONDAY, MAY 1

7:00 am Registration and Morning Coffee

8:30 Chairperson's Remarks

Zhimei Du, Ph.D., Senior Principal Scientist, Merck & Company, Inc.

8:40 KEYNOTE PRESENTATION: Development and Characterization Challenges for New Immuno-Oncology Therapeutics and Combinations

Tom Spitznagel, Ph.D., Senior Vice President, BioPharmaceutical Development and Manufacturing, MacroGenics, Inc.

Immuno-Oncology therapeutics and combinations are revolutionizing the way cancer patients are treated. Development strategies to accommodate these novel molecular entities and the speed at which clinical development often occurs will be presented.

Characterization of Novel Modalities

9:10 Characterization of Process-Related High Molecular Weight Species Observed in a Randomly Conjugated Antibody-Drug Conjugate

Wendy Lan, Ph.D., Senior Investigator, Bristol-Myers Squibb

During the development of a randomly conjugated antibody-drug conjugate (ADC), two high molecular weight (HMW) species were observed by CE-SDS analysis under reducing conditions. Multiple analytical techniques were used to demonstrate that these HMW species were not method induced impurities and likely were generated from the ADC conjugation process. Mass spectrometry methods were used to characterize structures of the HMW species.

9:40 Bioanalytical Strategies and Workstreams for Different Modalities during Early Drug Development

Zhimei Du, Ph.D., Senior Principal Scientist, Merck & Company, Inc.

There are many design formats for non-conventional biologics modalities, such as nanobodies and bispecific antibodies, and the best design choice is not only dependent on the final application but also their manufacturability. Here we will show some new observations in product quality characterization that directly impact bioactivity and manufacturability. It improves our understanding for some of these new modalities and might shed some light on protein engineering and selection at early stage.

10:10 Coffee Break

10:50 Biophysical Characterization of Structure and Interactions in Fab-PEG Conjugates

Jonathan Zarzar, Engineer, Genentech

Addition of polyethylene glycol (PEG) is an attractive strategy for the modification of proteins. More recently, novel PEG geometries have become available. However, little is known about the impact of polymer conjugation geometry on protein interactions. In this study, we demonstrate the utility of a variety of biophysical measurements to understand both polymer and protein behavior in conjugated systems, and the importance of polymer geometry on the conjugate's solution behavior.

11:20 Mitigating Developability Risks by Application of Affinity-Capture Self-Interaction Nanoparticle Spectroscopy (AC-SINS)

Craig D. Dickinson, Ph.D., Senior Research Advisor, AME, Eli Lilly and Company

High concentration reversible self-association of biologics can result in significant viscosity and solubility issues in development. AC-SINS is a remarkably sensitive high-throughput screening tool that we show can be applied to any Fc containing protein to rank self-association propensity. Examples will be provided that demonstrate its utility in antibody discovery and engineering processes.

11:50 Physicochemical and Immunological Comparison of CRM197 from Different Manufacturers and Expression Systems

John Hickey, Ph.D., Assistant Director, Macromolecule and Vaccine Stabilization Center, University of Kansas

CRM197, an inactive and non-toxic variant of diphtheria toxin, is a carrier protein in many polysaccharide-conjugate vaccines on the market and in clinical development. In attempts to develop efficient, low-cost processes for manufacturing vaccines, researchers and manufacturers have produced CRM197 that varies in cost, availability, purity, post-translational modifications, and stability. CRM197's physicochemical and immunochemical profiles from five different sources were comprehensively examined and compared in an analytical biosimilarity assessment.

12:20 pm Pyrogen Detection by Monocyte Activation Test in Antibody Formulations

Sponsored By solvias

Anja Fritsch, Ph.D., CSO, Solvias

The Monocyte Activation Test was developed for cases where potential contaminants other than endotoxin might be present in the antibody formulation. This test monitors the release of cytokines induced by pyrogens present in the sample using human cells. MAT provides a sensitive, reliable alternative to the rabbit pyrogen test.

Characterization of Biotherapeutics

Sponsored By RAPID NOVOR

12:35 Antibody Protein *De Novo* Sequencing with LC-MS/MS
Mingjie Xie, MSc, MBA, Co-Founder and 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.

Sponsored By charles river

12:50 Profiling and Characterization of O-Linked Glycans from Therapeutic Glycoporteins using Porous Graphitized Carbon HPLC
Andrew Hanneman, Ph.D., Associate Director, Mass Spectrometry, Charles River
O-linked glycosylation is a feature of complex therapeutic glycoproteins including hormones, receptor-Fc fusions and mucin-like proteins. The range of O-glycan structures present is dependent on the nature of the recombinant protein, the expression system and the process conditions used. Unlike N-linked glycans, O-linked glycans cannot be enzymatically released intact and are instead released chemically, however, the exact reaction conditions employed can sometimes lead to degradation and losses.

Sponsored By BSi

1:20 Software Platform for Therapeutic Protein Characterization with LC-MS
Lin He, Ph.D., Senior Application Scientist, Bioinformatics Solutions, Inc.
Mass spectrometry with a multi-attribute method has a proven ability to well-characterize therapeutic proteins. This application needs a tool developed to process the data to maximize the amount of information and report it efficiently. In this study, a software platform, PEAKS AB, is presented with the following protein characterization functions: Antibody *de novo* sequencing with multiple-enzyme digestion; Sequence validation bottom-up and middle-down approaches; PTM quantification, glycan profiling, disulfide linkage; and Sequence variance analysis.

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

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

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks
Gregory A. Weiss, Ph.D., Professor, Chemistry, Molecular Biology & Biochemistry, University of California, Irvine

4:10 Bicycles and Bicycle Drug Conjugates: Next Generation Therapeutics
Sir Gregory Winter, Ph.D., FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics
Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles' unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs); a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. This presentation will describe both the Bicycle® and BDC platforms.

4:55 Young Scientist Keynote: Programming Proteins by Deep Sequencing and Design
Tim Whitehead, Ph.D., Assistant Professor, Chemical Engineering and Materials Science, Michigan State University
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 group leverages this unprecedented wealth of sequence-function information to design and engineer protein affinity, specificity, and function and to infer structural complexes of proteins. My talk will present an overview of the above and detail methodological improvements that enable the engineering work.

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

6:55 End of Day

TUESDAY, MAY 2

8:00 am Registration and Morning Coffee

Characterization Issues in Immuno-Oncology Drug Development

8:25 Chairperson's Remarks
Randal Ketchem, Ph.D., Vice President, Molecular Design, Just Biotherapeutics

8:30 Characterizing Submicron Protein Particles with Resistive Pulse Sensing and Light Scattering Based Approaches
Gregory Barnett, Scientist, Bristol-Myers Squibb

9:00 Targeting B Cell Maturation Antigen (BCMA) Positive Multiple Myeloma Cells with CAR T Cell Therapy
Kathy Seidl, Ph.D., Director, Immunotherapy, bluebird bio
We developed chimeric antigen receptors (CARs) targeting B cell maturation antigen (BCMA), an antigen expressed on most multiple myeloma (MM) cells. Lentivectors containing anti-BCMA single chain variable fragment (scFv), 4-1BB, and CD3zeta signaling domains were generated. A lead CAR (bb2121) was selected for clinical development (NCT02658929). Approaches for next-generation CAR T cell products, such as *ex vivo* culture with a PI3K inhibitor that enhances *in vivo* efficacy, will be discussed.

Characterization of Biotherapeutics

Characterizing *in vivo* Quality Attributes

9:30 Characterizing *in vitro* and *in vivo* Stability of Bispecifics, Fusions, and Immunocytokines

Josh T. Pearson, Ph.D., Principal Scientist, Pharmacokinetics & Drug Metabolism, Amgen

The presentation will cover strategies and workflows for characterizing potential instabilities of dual targeting protein therapeutics during their *in vivo* trafficking. Combined with *in vivo* studies, *in vitro* assays to elucidate whether degradative events occur during systemic circulation versus at the site of action are necessary for understanding factors contributing to the observed *in vivo* PK/PD relationship. This information is essential to guide engineering and for preclinical to clinical translation.

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

10:50 Assays for PK Prediction to Support Design and Selection of Next-Generation Biotherapeutics

Hubert Kettenberger, Ph.D., Senior Principal Scientist, Protein Analytics, Roche Pharma Research & Early Development, Roche Innovation Center Penzberg

For most biotherapeutics, long *in vivo* half-life and thus long durability is desired. Comparing many different monoclonal antibodies, we and several other authors observed large differences in their pharmacokinetics which cannot be explained by different Fc:FcRn interactions. Unspecific, low-affinity interactions with highly abundant targets may, however, negatively impact PK. We present predictive assays to identify mAbs with fast clearance during the lead selection and protein engineering phase.

11:20 Testing for *in vivo* Fitness for the Development and Selection of Novel Biotherapeutics

Torsten Kuiper, Principal Scientist, BTDM Integrated Biologics Profiling, Novartis Pharma AG

This presentation will describe our integrated approach of assessing the *in vivo* fitness of novel biotherapeutics. Various parameters such as pharmacokinetics and stability with the respective methods will be discussed. A case study will illustrate how the individual parameters create a holistic picture of the *in vivo* fitness that contributes to the developability risk assessment and lead selection during the pre-clinical development phase.

11:50 Tools in Formulation Development to Understand Biological Performance of Biotherapeutics Following s.c. Injection

Sabine Eichling, Senior Scientist, Abbvie

Expectations of regulatory authorities are rising towards the demonstration of a thorough understanding of the mechanisms and interactions taking place following subcutaneous injection. Screening models generate knowledge about the distribution and transport of biotherapeutics following these injections. *In vitro, ex vivo* and *in vivo* methods were evaluated regarding the effect of molecule and formulation properties on systemic bioavailability. This information complements current decisions which to date are focusing on optimizing physicochemical properties.

12:20 pm Luncheon Presentation I: Comprehensive PTM Characterizations of the NIST mAb Reference Standard using an IMS QTOF Mass Spectrometry

Sponsored By Waters

Ying Qing Yu, Ph.D., Senior Science Manager, Scientific Operations, Waters Corporation

12:50 Cyto-Mine® – An Enabling Platform for Biologic Discovery and Development

Sponsored By Sphere Fluidics

Frank Craig, Ph.D., MBA, CEO, Sphere Fluidics Ltd.

Picodroplet technology can be used to rapidly screen, identify and isolate rare and valuable variants within large heterogeneous cell populations. We are launching the Cyto-Mine® Single Cell Analysis and Monoclonality Assurance System, a new industrially robust system which leverages this cutting-edge approach for the discovery, development and characterization of novel biotherapeu¬tics. It will deliver dramatic time, cost and labor savings and integrate into established workflows.

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

Spectroscopic Methods

2:00 Chairperson's Remarks

Elsa Wagner-Rousset, Ph.D., Senior Scientist, Analytical Chemistry & Mass Spectrometry, Pierre Fabre

2:05 Harness the Benefits of LC-MS and CE-MS for Multilevel mAb and ADC Structural Characterization

Elsa Wagner-Rousset, Ph.D., Senior Scientist, Mass Spectrometry, Pierre Fabre

The development and optimization of mAbs and ADCs rely on improving their analytical and bioanalytical characterization by assessing several critical quality attributes (CQAs). Progresses of multi-level state-of-the-art mass spectrometry methods combined with chromatographic and electrophoretic techniques (2D-LC-MS, CESI-MS, Native MS, Ion Mobility-MS, Top-Down Sequencing) will be presented. They will be illustrated by extensive structural characterization of reference FDA and EMA approved therapeutic mAbs and ADCs.

2:35 Rapid Identification of Biotherapeutics with Label-Free Raman Spectroscopy

Ishan Barman, Ph.D., Assistant Professor, Mechanical Engineering, Johns Hopkins University

Biotherapeutics represent a challenging cohort for testing product identity because of their similarity in chemical structure. Traditional techniques employed for product identification are time and labor intensive leading to an unmet need for rapid, facile tools. Exploiting subtle differences in vibrational modes of the biologics, we demonstrate that label-free Raman spectroscopy provides a powerful method and offers excellent differentiation capability when used along with partial least-squares-discriminant analysis derived decision algorithms.

3:05 Let UNcle Tell You the Whole Stability Story

Sponsored By UNCHAINED LABS

Dina Finan, Ph.D., Product Manager, Unchained Labs

Biologic stability characterization traditionally requires juggling disjointed data from multiple instruments. UNcle reduces these complications and conserves

Characterization of Biotherapeutics

samples by combining fluorescence, SLS, and DLS detection modes in one instrument. This enables 10 different protein characterization applications, and allows for sizing, polydispersity, thermal melting, and aggregation data to be obtained at the same time from the same sample. We will demonstrate how UNcle can thoroughly characterize more biologics and formulations quickly and easily.

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

4:25 Implementing QC-Level Mass Spectrometers

Tatyana Mezhebovsky, Ph.D., Principal Scientist, BioFormulations Development, Sanofi

Mass Spectrometry has become the major tool in protein biotherapeutics development. Currently, new generation of Mass Spectrometers (MS), targeted for Mass Detection in routine application by non Mass Spectrometrists, is being introduced. These MS instruments rely on peak identification based on the methods transferred from the specialized MS laboratories. The UPLC-MS/UV/FLR setup in our laboratory as well as the challenges we had to overcome to launch the system will be presented.

4:55 Implementation of Open-Access & Automated Analysis Mass Spectrometry within Discovery Protein Generation Workflows

David Winarta, Research Scientist, Global Protein Sciences, AbbVie

Sample hand-offs, information recapitulation, and manual data analysis are hallmarks of workflow bottlenecks. In line with efforts to build a world-class biologics generation platform, we have implemented open-access software solutions to facilitate placing powerful mass spectroscopic techniques in the hands of a diverse user base. Furthermore, we have developed an automated web script to intelligently analyze and annotate generated data. The observed benefits are presented with an eye on future improvements.

5:25 End of Characterization of Biotherapeutics

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Courses*

SC12: Study Design and Statistical Data Analysis of Flow Cytometry Assays

SC16: New USP Initiatives for Characterization and Release of Biologics

**Separate registration required, please see page 5-6 for course details.*

Biophysical Analysis of Biotherapeutics

Characterizing and Fine-Tuning the Physical Properties of Proteins in the Research and Development of Next Generation Protein Therapeutics

Recommended Short Courses*

SC12: Study Design and Statistical Data Analysis of Flow Cytometry Assays

SC14: Overcoming the Challenges of Immunogenicity Assays, Risk Assessment and Regulatory Requirements

**Separate registration required, please see page 5-6 for course details.*

WEDNESDAY, MAY 3

7:30 am Registration and Morning Coffee

8:30 Chairperson's Remarks

David D. Weis, Ph.D., Associate Professor, Pharmaceutical Chemistry, University of Kansas

8:40 KEYNOTE PRESENTATION: Criticality of Biologics Quality Attributes and Integrated Analytical Control

Tapan Das, Ph.D., Director, Biologics Characterization & Analytical Development, Bristol-Myers Squibb

Increasing emphasis is placed for in-depth understanding of critical quality attribute and associated control strategy in biologics development and production. Link of CQAs to robust development, manufacturing, and pre-clinical and clinical outcomes is paramount to modern biologics development strategies. This session will cover phase-appropriate CQA assessments and establishing advanced analytical control.

Methods and Instruments

9:10 Understanding and Overcoming Trade-Offs between Antibody Affinity, Specificity, Solubility and Stability

Peter M. Tessier, Ph.D., Richard Baruch M.D. Career Development Professor, Chemical & Biological Engineering, Rensselaer Polytechnic Institute

Antibodies initially identified via immunization or *in vitro* display methods are often further engineered for therapeutic applications. The process of engineering antibodies for improved properties – such as increased affinity, effector functions and/or bispecificity – often involves trade-offs between improvements in some properties and defects in other ones. We will discuss our work in identifying the causes for these trade-offs as well as our development of new methods for overcoming such trade-offs.

9:40 Forced Degradation Strategies for Biotherapeutics Development

Yite Robert Chou, Ph.D., Principal Scientist, Merck

Forced degradation studies are often used in biotherapeutics development to determine possible biologic product degradation pathways under various stress conditions. Forced degradation also plays an important role in the development of analytical methods, setting specifications, and design of formulations under the quality by design (QbD) paradigm. Different strategies on applying force degradation at different stages and on increasing the workflow of biotherapeutics development will be presented. 10:10 Coffee Break in the Exhibit Hall with Poster Viewing

10:55 Stable Formulation Development of Peptides - Interpretation of Ordered Peptide Aggregation

Adrian Podmore, Ph.D., Formulation Scientist, Medimmune

The current understanding of ordered peptide aggregation will be discussed with respect to formulation development strategies. The presentation will review the application of techniques such as field flow fractionation with light scattering, batch method dynamic light scattering, and nanoparticle tracking analysis to investigate ordered aggregation in the context of defining a 'stable' formulation. A new suggested strategy of stable peptide formulation development will be provided.

11:25 Biophysical Mechanism of Captisol-Induced Solubility of Protein Biologicals

Murali Bilikallahalli, Ph.D., Senior Director, Ultragenyx Pharmaceuticals

Captisol has been historically used to solubilize small hydrophobic drug molecules. This study for the first time establishes the mechanism of Captisol as a protein solubilizer at high concentrations. Results illustrate why and why not this works with all kinds of proteins that differ in their physic-chemical properties.

11:55 An Innovative Method That Provides Direct Molecular Evidence Used to Decipher the Mechanism and Extent of Aggregation under Stress Conditions

Belinda Pastrana, Ph.D., Professor, Chemistry, University of Puerto Rico Mayaguez, Puerto Rico

The technology presented is transformative for the biopharma industry, because it is capable of determining mechanism and extent of aggregation, as well as the stability of the candidate in one experiment. The method is a label free method, and is independent of the protein therapeutic molecular weight or modification. Because the results are based on first principle, they can be analyzed in a quantitative manner providing the much needed information to decision makers.

Biophysical Analysis of Biotherapeutics

12:25 pm An Automated Platform to Predict and Characterize the Colloidal and Conformational Stability of Biologics

Sponsored By NanoTemper Technologies

Dennis Breitspecher, Ph.D., Head, Research and Development – Biochemistry, NanoTemper Technologies, GmbH

Biopharmaceutical development projects become increasingly complex, which calls for straightforward and precise analytical tools to increase research efficiency. Automated stability prediction and characterization by nanoDSF can help to significantly streamline development processes from early discovery to formulation development, resulting in better informed decisions and eventually reduced time to market.

12:55 Luncheon Presentation: Optimizing the Speed and Efficiency of Vaccine Analytical Development Using Automated Simple Western Technology

Sponsored By protein simple

John Loughney, MSc, Senior Scientist, Vaccine Analytical Development, Merck & Co.

Simple Western is a technology that separates, immunoprobes and detects proteins, all steps taking place in a capillary. We have used the size based assay to replace both traditional qualitative and quantitative Westerns. Traditionally, theses assays are performed using either an ELISA or manual Westerns, which are tedious, laborious, and they can be difficult to transfer. We illustrate how Simple Western allows for reproducible and quantitative results that are also fully automated.

12:40 Sponsored Presentation *(Opportunity Available)*

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

1:55 Session Break

Methods and Instruments (Cont.)

2:10 Chairperson's Remarks

Anacelia Ríos Quiroz, Ph.D., Group Leader, Particle Lab, Pharma Technical Development Europe (Biologics) Analytics, F. Hoffmann-La Roche Ltd.

2:15 Enabling Structural Biology In Situ – Ribosome Biogenesis in C. Reinhardtii

Philipp S. Stawski, Ph.D., Scientist, Molecular Structural Biology, Max Planck Institute of Biochemistry, Germany

Cryo focused ion beam (FIB) milling has opened new avenues to explore the biology of cells in their native state. Here we showcase the process of sample preparation and data processing in the green alga C. Reinhardtii by following its path of ribosome biogenesis. Specifically, we focus on the role of the nucleolus and the precursor of the small ribosomal subunit, the pre 90s particle.

2:45 New USP Initiatives for Biophysical Characterization of Biologics

Maura Kibbey, Ph.D., Director, Science & Standards, Global Biologics, United States Pharmacopeial Convention

The USP is an independent scientific organization that protects public health through standards for medicines and their ingredients. As biological science contributes to more advanced therapies, standards continue to play a critical role in drug development and manufacturing. This talk will preview a USP Stimuli Article resulting from USP's recently convened roundtable of recognized experts on higher order structure characterization of biologics. These best practices may lead to a new USP General Chapter.

3:15 Recent Advancements in Differential Scanning Calorimetry for Stability Profiling of Biotherapeutics

Sponsored By Malvern

Verna Frasca, Ph.D., Product Marketing Manager, Sales and Marketing, Malvern Instruments

Microcalorimetry is the gold standard technique for thermal stability characterization of protein drugs. DSC measures the protein's thermal transition temperature (TM), and heat (ΔH) of unfolding. DSC data are used to optimize formulations, choose "developable" candidates, and comparability and biosimilarity studies. The new MicroCal PEAQ-DSC introduces advancements in DSC function, speed, and accessibility, including tools to support regulatory requirements. Protein stability characterization by DSC complements data from Dynamic Light Scattering and Taylor Dispersion Analysis.

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, MAY 4

8:00 am Morning Coffee

Applications of Mass Spectrometry in Biophysical Analysis

8:30 Chairperson's Remarks

Murali Bilikallahalli, Ph.D., Senior Director, Ultragenyx Pharmaceuticals

8:35 HX-MS in Formulation Development and Similarity Assessment

David D. Weis, Ph.D., Associate Professor, Pharmaceutical Chemistry, University of Kansas

Hydrogen exchange mass spectrometry (HX-MS) is gaining acceptance for its ability to monitor higher order structure in proteins. This talk highlights two areas of recent work. First, developing a molecular-level understanding of how protein-excipient interactions alter physical stability. Second, exploring the limits of HX-MS to detect small changes in higher-order structure in similarity contexts.

9:05 Mass Spec Based Techniques for the Characterization of Protein Biopharmaceuticals

George Bou-Assaf, Ph.D., Scientist, Technical Development, Biogen

Characterization of PTMs is essential to understanding the structure-function relationship in a protein and in the successful development of biopharmaceuticals. Here, we elucidate the impact of methionine versus methionine and cysteine oxidation on the HOS and structural dynamics of IFNβ-1a. We selectively oxidize IFNβ-1a and characterize the products of each oxidation condition with various

Biophysical Analysis of Biotherapeutics

methods. MS-based techniques, especially HDX-MS, play a dominant role in revealing the differential oxidation effects.

9:35 Identification and Quantitation of DuoBody® Bispecific IgG1 Using Mass Spectrometry and Automated Data Processing and Analysis Workflow

Ewald Van den Bremer, Ph.D., Senior Scientist, Genmab

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

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

Computational Methods

11:05 Computationally-Guided Protein and Formulation Engineering

Paul Dalby, Ph.D., Professor of Biochemical Engineering and Biotechnology, University College London

Protein stability is a critical factor for the successful development of non-aggregating biopharmaceuticals. Routes to predictably engineer protein stability are therefore crucial. We have used a wide range of biophysical analyses to characterize the aggregation landscape of proteins, and used this understanding to inform better formulation design strategies. The use of molecular dynamics to guide protein engineering and formulation for improved shelf-life will be discussed.

11:35 Interfacing Simulation and Experiment for Protein-Protein Interactions

Christopher J. Roberts, Ph.D., Professor, Chemical & Biomolecular Engineering, University of Delaware

This presentation will show an example of combining "minimal" experimental data with molecular models to predict non-ideal interactions of monoclonal antibodies at high concentrations. It will illustrate examples where "simple" models can reasonably capture the high-concentration behavior if one uses low-concentration behavior to adjust the model, as well as challenges for systems with strong attractions and phase separation.

12:05 pm Computational Design and High-Throughput Characterization to Predict and Repair Molecular Attributes

Randal Ketchem, Ph.D., Vice President, Molecular Design, Just Biotherapeutics

Antibodies undergo somatic hypermutation to obtain their high levels of both antigen specificity and affinity. Hypermutation also leads to molecular issues as therapeutic candidates. Early molecular analysis enables an integrated approach to therapeutic design encompassing *in silico* tools, high-throughput screening, and development of predictive tools coupled with large scale data capture. Pushing molecular design earlier in the therapeutic pathway increases the success and lowers the cost of therapeutics.

12:35 End of Biophysical Analysis of Biotherapeutics

10th Annual | May 4-5, 2017

Protein Aggregation and Stability in Biopharmaceuticals

Understanding and Controlling Protein Aggregation from Early Development to Manufacturing and Clinical Us

Recommended Short Course*

SC14: Overcoming the Challenges of Immunogenicity Assays, Risk Assessment and Regulatory Requirements
**Separate registration required, please see page 5-6 for course details.*

THURSDAY, MAY 4

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Gayatri Ganeshan, Scientist, Biologics and Vaccines, Merck

1:50 KEYNOTE PRESENTATION: Measuring Changes in Protein Structure in Lyophilized Solids and Impacts on Aggregation
Elizabeth M. Topp, Ph.D., Dane O. Kildsig Chair and Department Head, Department of Industrial and Physical Pharmacy, Perdue University
The lack of adequate methods to measure protein structure in the solid state has slowed the development of protein drug products. Here, we present solid-state hydrogen deuterium exchange with mass spectrometric analysis (ssHDX-MS) as a high resolution method to assess protein structure in lyophilized solids. We also show that ssHDX-MS results are highly correlated with the aggregation of a MAb and of myoglobin during storage.

Understanding Aggregation Phenomena

2:20 Chaperonin-Based Biolayer Interferometry to Assess the Kinetic Stability of Metastable, Aggregation-Prone Proteins
Mark T. Fisher, Ph.D., Professor, Biochemistry and Molecular Biology, University of Kansas Medical School
Stabilizing the folded state of metastable and/or aggregation-prone proteins through exogenous ligand binding is an appealing strategy to decrease disease pathologies brought on by protein folding defects or deleterious kinetic transitions. This presentation describes an automated method for assessing the kinetic stability of folded proteins and monitoring the effects of ligand stabilization for metastable proteins using a GroEL chaperonin-based biolayer interferometry (BLI) denaturant-pulse platform.

2:50 Understanding the Causes of Immunogenicity in Biotherapeutic Proteins
Jeremy Derrick, Ph.D., Professor, Molecular Microbiology, University of Manchester
Understanding the origins and factors contributing to the immunogenicity of biotherapeutic proteins remains a challenge. Here I will discuss our recent work in which we seek to investigate the roles of aggregation, chemical modification and host cell protein impurities on the immune response to selected proteins. I will also show how aggregation, in particular, affects the quality as well as the amplitude of the immune response.

Sponsored By Albumedix

3:20 Reviving Otherwise Hard-to-Stabilize Biopharmaceuticals through Protein Co-Formulation
Eleonora Cerasoli, Ph.D., Senior Research Scientist, Bioprocessing and Characterisation, Albumedix Ltd.
Aggregation and depletion of biopharmaceuticals is a source of both dosage form and storage instability, compromising safety and efficacy. Human serum albumin is well known to stabilize proteins preventing adsorption, aggregation and oxidation due to its natural roles and inherent properties. Recombinant human albumin is therefore a promising stabilizer for hard-to-formulate biopharmaceuticals. We will present data on the use of Albumedix™ Recombumin® as a stabilizing agent for model biopharmaceuticals and elucidate on potential mechanisms.

3:50 Refreshment Break

4:20 Understanding What Could Make Subvisible Protein Particles Immunogenic
Anacelia Ríos Quiroz, Ph.D., Group Leader, Particle Lab, Pharma Technical Development Europe (Biologics) Analytics, F. Hoffmann-La Roche Ltd.
The likely immunogenic reactions that have been attributed to subvisible protein particles constitute a safety concern around the use of biotherapeutic proteins. The talk will give a comprehensive overview of the current status of the related literature together with the results of a study which evaluated the particle characteristics needed to break immune tolerance in an IgG1 transgenic mouse. This talk will help increase our understanding on the biological consequences of particulate matter.

4:50 Speaker has cancelled - delegates may attend concurrent sessions.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC15: Critical Considerations for the Design and Development of

Protein Aggregation and Stability in Biopharmaceuticals

Antibody-Drug Conjugates
**Separate registration required, please see page 5-6 for course details.*

FRIDAY, MAY 5

8:00 am Morning Coffee

Particle Characterization

8:30 Chairperson's Remarks
Reema Raghavendra, Scientist, AbbVie

8:35 Protein Particle Standards: Use and Guidelines for Analyses
Dean Ripple, Ph.D., Leader, Bioprocess Measurements Group, National Institute of Standards and Technology
New particle standards, spanning the subvisible and visible size range, are being developed using ethylene tetrafluoroethylene (ETFE) polymer and a photoresist because they have desirable properties that make them better than currently available standards. These particles can be used to 1) standardize subvisible particle measurements, primarily through correcting instrument bias and 2) develop a semi-quantitative method for monitoring visible proteinaceous particles.

9:05 Flow Cytometry: A Promising Tool for Sub-Visible Particle Characterization
Reema Raghavendra, Scientist, AbbVie
Immunogenicity concerns of therapeutic protein aggregates have necessitated detailed particle characterization not only in the sub-visible range, but also into the sub-micron range. Flow cytometry has potential to bridge particle characterization across these regimes. Here, we present quantitative particle measurements of novel protein-like standards and therapeutic proteins by flow cytometry. Particle responses were compared to micro-flow imaging and corrected for refractive index biasing, allowing accurate particle quantitation.

Sponsored By

9:35 Counting and Sizing Protein Aggregates down to 0.15um by Focused-Beam Light Scattering Technology
David Nicoli, Ph.D., Vice President, Research & Development, Particle Sizing Systems LLC
A novel single-particle optical sizing (SPOS) technique using a focused laser beam collects scattered light from individual particles in a flowing suspension, allowing protein aggregates to be counted/sized down to 0.15 um, at concentrations much higher than possible using normal light scattering technology. Combining this "FX-Nano" sensor with a second conventional sensor extends the upper size limit.

10:05 Coffee Break

Formulation and Process Control

10:35 Improvements in Downstream Processes to Minimize and Mitigate Aggregation
Steven Cramer, Ph.D., Professor, Rensselaer Polytechnic Institute
The propensity of downstream processing conditions for forming aggregates will be discussed along with strategies for avoiding these scenarios via high throughput screening, protein property analyses and appropriate use of mobile phase modifiers. Techniques for removal of aggregates will then be discussed including how best to operate various chromatographic resin systems for these separations and how to properly screen and develop optimal modes of column operation using various strategies and modeling approaches.

11:05 The Role of Surfactants in Phase I Vaccine Formulations
Sashikanth Banappagari, Ph.D., Scientist, Formulation Development, Vaccine Research Center, National Institutes of Health
Non-ionic surfactants are commonly used in vaccine/protein formulations to minimize instability induced by self-interaction and/or interfacial interactions occurring during manufacturing and long term storage. These interactions may result in conformational changes leading to aggregation or material loss via container adsorption, which may be further enhanced by the low doses common to vaccine formulations. Two case studies, involving Chikungunya Virus Virus-Like Particles and Hemagglutinin-Ferritin Nanoparticles, will be discussed.

11:35 Novel Biophysical Tools for the Study of Insulin Aggregates and Their Ability to Distinguish between Fibrillar and Amorphous Aggregates
Gayatri Ganeshan, Scientist, Biologics and Vaccines, Merck
Fluorescent dyes including Thioflavin-T are typically used to measure fibrils in insulins. However, some of the newer unfibrillated insulin analogs (Tresiba®, Levemir®, etc.) show high background ThT fluorescence making it difficult to screen for fibrils. We have developed a Flow Cytometry method using ThT that can distinguish between amorphous aggregates and fibrils in different stressed commercial insulins. Its sensitivity and turnover time are valuable as a design tool to de-risk key attributes.

12:05 pm Optimization Strategy to Generate Antibody with Low Viscosity for High Concentration Subcutaneous Formulation
Masaru Muraoka, Ph.D., Research Scientist, Chugai Pharmabody Research PTE. LTD.
Developing high concentration formulations brings forth several challenges due to solubility limitations and increased viscosity. High solubility and low viscosity are desired. However, in some cases, protein engineering has adverse effects on physicochemical properties of antibody, even with a single mutation. This presentation will provide case studies covering these issues and discuss the optimization strategies for protein engineering.

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

1:05 Refreshment Break

Controlling Stability in High Concentration Protein Formulations

1:35 Chairperson's Remarks
Shantanu Sule, Ph.D., Senior Research Scientist, Eli Lilly & Company

1:40 Profiling Molecular Feasibility for High Dose Biological

Protein Aggregation and Stability in Biopharmaceuticals

Therapeutics
Shantanu Sule, Ph.D., Senior Research Scientist, Eli Lilly & Company

2:10 Affinity Capture Self-Interaction Nanoparticle Spectroscopy (AC-SINS) Measurements of Weak Interactions in Dilute Solution Support Early Assessment of Antibody Manufacturability
Marissa Mock, Ph.D., Senior Scientist, Therapeutic Discovery; Biologics, Amgen
Methods to identify molecules with potential manufacturability liabilities are desired during the preclinical selection of large molecule therapeutics. Current techniques are often impractical in early pipelines because they require large amounts of highly pure material. We evaluated and implemented the high-throughput AC-SINS assay, developed by Prof. Peter Tessier at RPI, and will present a test case demonstrating that AC-SINS successfully predicted high viscosity variants from an antibody engineering panel.

Long Term Stability Prediction

2:40 Evaluation of Early Stage Formulation Development Strategies for Monoclonal Antibodies
Hardeep Samra, Ph.D., Senior Scientist, Formulation Sciences, MedImmune
Selection of optimal formulation conditions for monoclonal antibodies can be challenging due to short timelines and reliance on predictive assays to ensure product quality and adequate long term stability. High-throughput screening (HTS) techniques can be used to screen solution conditions for early formulation development. The utility of using accelerated stability, differential scanning light scattering (DSLS), and differential scanning fluorescence (DSF) were evaluated as early formulation screening techniques. This talk highlights the correlation between data from these techniques and predictability to real time stability.

3:10 Using Viscosity-Derived Parameters and Thermal Analysis to Evaluate the Solution Properties of Bispecific Dual Variable Domain Antibodies
Ralf Joe Carrillo, Ph.D., Senior Scientist, Physical Chemistry, AbbVie
Changes in Simha shape, maximum packing fraction, intrinsic viscosity and DSC thermal stability for mAbs and bi-specific Dual Variable Domain Immunoglobulins DVD-Ig proteins have been studied and analyzed to ascertain how the viscoelastic properties for mAbs and DVD-Igs differ and how these properties can predict long term stability.

3:40 End of Conference

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A Division of Cambridge Innovation Institute

IMMUNOGENICITY & BIOASSAY STREAM

- Immunogenicity: Regulatory and Clinical Relevance
- Strategies for Immunogenicity Assay Assessment
- Optimizing Bioassays for Biologics

Immunogenicity: Regulatory and Clinical Relevance

Pre-Clinical and Clinical Risk Assessment to Ensure Product Safety

Recommended Short Course*

SC8: *In silico* Immunogenicity Predictions – A Hands-On Workshop
**Separate registration required, please see page 5-6 for course details.*

MONDAY, MAY 1

7:00 am Registration and Morning Coffee

Immunogenicity for Immuno-Oncology and Complex Biologics

8:30 Chairperson's Remarks
LiNa Loo, Ph.D., Principal Scientist, Non-Clinical Safety, Celgene

8:40 Current Regulatory Updates and Expectations
Bonnie Rup, Ph.D., Independent Consultant

9:10 KEYNOTE PRESENTATION: Immunogenicity of Avelumab - An Immune Checkpoint Inhibitor for Oncology
Theresa J. Goletz, Ph.D., Global Head, NBE Drug Disposition, QPD, EMD Serono
Avelumab binds PD-L1, blocking the interaction with PD-1 to subsequently potentiate T-cell cytotoxicity against tumor cells. Avelumab is in clinical development for the treatment of metastatic Merkel cell carcinoma, a rare form of skin cancer. The incidence of immunogenicity with avelumab was found to be low with no apparent impact on clinical pharmacokinetics, safety, or efficacy. Progress towards obtaining neutralizing antibody data will also be presented.

9:40 Preclinical Testing Strategies in IO and Complex Biologics
Sofie Pattijn, Ph.D., Member, European Immunogenicity Platform, CTO at ImmunXperts
During the last decade, the field of early immunogenicity assessment has significantly matured and progressed. With the new wave of immuno-oncology drugs and new modalities, new approaches and assays will be required to deal with the complex mechanisms and mode of actions of this class of therapeutics.

10:10 Coffee Break

Predictive Models and De-Risking Strategies

10:45 Chairperson's Remarks
Priya Sriraman, Ph.D., Principal Investigator, Non-Clinical Safety, Celgene

10:50 Developing Tools for De-Risking Immune Mediated Drug Hypersensitivity: Humanized Mice
Michael Oropallo, Ph.D., Associate Scientist, Postdoctoral Fellow, Safety Assessment & Laboratory Animal Resources, Merck
Drug induced hypersensitivity reactions pose a significant safety risk, yet pre-clinical animal models often fail to detect the potential of drugs to cause these reactions. This discussion will summarize current first and second generation humanized mouse models and their potential to predict clinically relevant immunogenicity. It will share methods to determine if these mice recapitulate human physiology, as well as data comparing various commercially available 1st and 2nd generation models. It will also discuss the potential of humanized mice to be combined with other techniques in the pre-clinical pipeline.

11:20 Latest Advances in T Cell and B Cell Epitope Prediction
Paolo Marcatili, Ph.D., Assistant Professor, Bio and Health Informatics, Technical University of Denmark
The prediction of B and T cell epitopes has substantially improved in the last few years, thanks to novel machine learning algorithms and larger datasets. We will go through the latest advances in the field, see the strengths and limitations of the available computational tools, and describe the latest developments concerning the inclusion of antibody and TCR information in epitope prediction.

11:50 Broad Mapping of the Immunome with Peptide Phage Display and NGS
Michael Szardenings, Ph.D., Group Head, Ligand Development, Fraunhofer Institute for Cell Therapy and Immunology
A new way to analyse the NGS data from peptide phage display experiments in combination with a proprietary library allows the identification of multiple potential epitopes from a single selection experiment. This is allowing to efficiently map and compare antibodies from different patient sera by *in silico* data analyses.

12:20 pm An Integrated Approach to Managing Immunogenicity Risk and Drug Immune Modulation
Sponsored By PROIMMUNE
Emilee Knowlton, Ph.D., Immunology Sales Specialist, ProImmune

12:50 Luncheon Presentation: Predicting, Avoiding and Mitigating Risk of Failure when Developing Biotherapeutics
Sponsored By Lonza
Yvette Stallwood, Ph.D., Head, Applied Protein Services, Lonza Biologics
In silico methods can be used to evaluate protein sequence and structure to assess the likelihood of immunogenic responses and potential critical quality attributes. Ex vivo T and B-Cell responses enable the assessment of overall immunogenicity risks and to identify processed and presented epitopes. This presentation will discuss how such methodologies are employed to perform a manufacturability and immunogenicity risk assessment in order to highlight potential risks of failure early in the development of biotherapeutics.

Immunogenicity: Regulatory and Clinical Relevance

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

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

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks
Gregory A. Weiss, Ph.D., Professor, Chemistry, Molecular Biology & Biochemistry, University of California, Irvine

4:10 Bicycles and Bicycle Drug Conjugates: Next Generation Therapeutics
Sir Gregory Winter, Ph.D., FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics
Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles' unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs); a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. This presentation will describe both the Bicycle® and BDC platforms.

4:55 Young Scientist Keynote: Programming Proteins by Deep Sequencing and Design
Tim Whitehead, Ph.D., Assistant Professor, Chemical Engineering and Materials Science, Michigan State University
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 group leverages this unprecedented wealth of sequence-function information to design and engineer protein affinity, specificity, and function and to infer structural complexes of proteins. My talk will present an overview of the above and detail methodological improvements that enable the engineering work.

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

6:55 End of Day

TUESDAY, MAY 2

8:00 am Registration and Morning Coffee

Preclinical and Clinical Immunogenicity Monitoring

8:25 Chairperson's Remarks
Darshana Jani, Ph.D., Senior Manager, Global Assay Lead, Pfizer

8:30 Preclinical Immunogenicity Assessment of Engineered Lysins: Next-Gen Antibiotics
Chris Bailey-Kellogg, Ph.D., Professor, Computer Science, Dartmouth
Lysostaphin is a highly potent antibacterial lysin and a promising lead in the search for next generation therapies to treat infections by MRSA superbugs. Like most lysins, however, lysostaphin has proven to be immunogenic due to its microbial origins. Using advanced biotherapeutic design algorithms, we have reengineered lysostaphin to evade T cell mediated immune recognition in human subjects. Here we describe preclinical efficacy and immunogenicity analysis of one high-performance variant.

9:00 Preclinical Assessments of Immunogenicity
Zuben Sauna, Ph.D., Principal Investigator, Division of Plasma Protein Therapeutics and Office of Tissues and Advances Therapies, FDA/CBER (invited)

9:30 Immunogenicity Assessment of Tumor Necrosis Factor Antagonists in the Clinical Laboratory
Julio Delgado, Ph.D., Medical Director and Section Chief, Immunology Division, ARUP Laboratories; Associate Professor, Pathology, University of Utah School of Medicine
TNF antagonists are used for the treatment of inflammatory diseases. Development of antibodies against these drugs is a major impediment that contributes to therapeutic failure. Rational and cost-effective evaluation of therapeutic failure includes measurement of drug levels, and detection of drugspecific antibodies. A functional, cell-based reporter gene assay (RGA) was developed in the clinical laboratory for measuring the biological activity and neutralizing antibody response to TNF antagonists.

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

Immunogenicity in Haemophilia Patients

10:50 Implementation of Therapeutic Drug Monitoring in Clinical Practice as a Reactive or Proactive Tool to Optimize Treatment Outcomes of Biologics
Niels Vande Casteele, Pharm.D., Ph.D., Postdoctoral Fellow, Gastroenterology, University of California, San Diego
Anti-drug antibodies (ADA) can impair the treatment effect of biologics and have been associated with adverse events. However, it is important to distinguish transient from persistent ADA and how this covariate (continuous or categorical) is included in pharmacological models. ADA are typically used in a reactive setting to support treatment decisions, whereas drug concentrations can be used in a proactive setting to guide dosing based on exposure.

11:20 Immunogenicity in Haemophilia Patients
Pedro Paz., Ph.D., BR US Lead Discovery, Immunoassay/Immunoprofiling Group, Bayer HealthCare

11:50 Engineering Less Immunogenic and Antigenic FVIII Proteins
Kathleen Pratt, Ph.D., Associate Professor, Department of Medicine, Uniformed Services University
Development of antibodies that interfere with factor VIII (FVIII) pro-coagulant activity ("inhibitors") can complicate the treatment of hemophilia A. Our laboratory has identified an immunodominant epitope in FVIII, tested its potential promiscuity, and generated amino acid substitutions in FVIII peptides and proteins to abrogate or reduce its immunogenicity. This proof-of-principle study presents a strategy for designing less immunogenic FVIII proteins targeted to specific

Immunogenicity: Regulatory and Clinical Relevance

hemophilia A subpopulations.

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

Immunotoxins

2:00 Chairperson's Remarks
Darshana Jani, Ph.D., Senior Manager, Global Assay Lead, Pfizer

2:05 Strategies to Reduce the ADA Response to Immunotoxin Therapy of Cancer
Ira Pastan, Co-Chief, Molecular Biology, National Cancer Institute, NIH
Recombinant immunotoxins are anti-cancer agents composed of an Fv targeting a protein on a cancer cell fused to a bacterial toxin. They have good anti-cancer activity in hematologic malignancies, where the immune system is suppressed and neutralizing antibodies do not develop. SS1P is an immunotoxin targeting mesothelin expressing tumors. We have pursued several strategies to reduce the immunogenicity of SS1P, which include identification and removal of B and T cell epitopes and the induction of tolerance using novel approaches.

2:35 Challenges and Solutions in Immunogenicity Assessment of Moxetumomab Pasudotox, a Recombinant Immunotoxin with Two Functional Domains
Inna Vainshtein, Ph.D., Principal Scientist, Clinical Pharmacology & DMP, MedImmune LLC
Immunogenicity is an important part of clinical development for biologics as it impacts drug PK, efficacy and safety. Immunogenicity assessment of moxetumomab pasudotox, an anti-CD22 recombinant immunotoxin, was challenging because of pre-existing anti-toxin antibodies of high prevalence. In addition, two domain structure of the drug required characterization of anti-drug antibodies for domain specificity. This talk will present challenges and solutions to obtain the most accurate assessment of drug immunogenicity.

Sponsored By NDA

3:05 Considerations for Development Projects: Combination Therapy
Josefin-Beate Holz, Ph.D., part of NDA Group Network
Considerations of an integrated development plan for a product as part of a combination regimen impact on candidate selection impact on non-clinical development impact on translational research impact on first-in-human strategy impact on assessment of "clinical Proof-of-Concept".

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

Defining ADA Clinical Relevance

4:25 Development and Early Clinical Development of Synthetic Vaccine Particles (SVP) to Prevent the Formation of Anti-Drug Antibodies
hi Kei Kishimoto, Ph.D., CSO, Selecta Biosciences
The development of ADAs is a common cause for treatment failure and adverse events, such as hypersensitivity reactions, associated with biologic therapies. We have recently engineered nanoparticles to provide a tolerogenic signal to antigen-presenting cells to induce antigen-specific immune tolerance. We have demonstrated the ability to mitigate immunogenicity against a broad array of biologic therapies, including coagulation factor VIII in a model of hemophilia A, anti-TNF monoclonal antibody in a model of spontaneous arthritis, immunotoxins in tumor models, pegylated uricase in uricase deficient mice and in nonhuman primates, and adeno-associated vectors used in gene therapy. Tolerogenic nanoparticle therapy for the prevention of ADAs against pegylated uricase in the treatment of gout is currently being evaluated in Phase 2 clinical trials.

4:55 Are ADA Results Reflecting the Impact on Pharmacokinetic Exposure?
Niklas Czeloth, Ph.D., Head, Biosciences, Biosimilars, Boehringer Ingelheim GmbH

5:25 End of Immunogenicity: Regulatory and Clinical Relevance

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC14: Overcoming the Challenges of Immunogenicity Assays, Risk Assessment and Regulatory Requirements
**Separate registration required, please see page 5-6 for course details.*

10th Annual | May 3-4, 2017

Strategies for Immunogenicity Assay Assessment

Improving Assay Detection Performance, Sensitivity and Relevance

Recommended Conference Short Course*

SC14: Overcoming the Challenges of Immunogenicity Assays, Risk Assessment and Regulatory Requirements
**Separate registration required, please see page 5-6 for course details.*

WEDNESDAY, MAY 3

7:30 am Registration and Morning Coffee

Immunogenicity Assessment of Multi-Domain Therapies

8:30 Chairperson's Remarks
Wendy White, Ph.D., Fellow and Scientific Director, Translational Sciences, MedImmune, LLC

8:40 Immunogenicity Assay Strategies for Multi-Domain Products
Seema Kumar, Ph.D., Associate Director, EMD Serono
Many biotherapeutics currently in development have complex mechanisms of action and contain more than one domain, each with a specific role or function. In general, the presence of a domain with high immunogenicity risk or presence of a domain with high endogenous protein homology may result in an overall high immunogenicity risk level for the entire multi-domain biotherapeutic. Depending on the specific risk factors, the tiered immunogenicity assay strategy may benefit from additional characterization such as domain specificity of immune response, as discussed in this presentation.

9:10 Development and Characterization of Neutralizing Anti-Idiotype Antibodies Directed against Mirvetuximab Soravtansine
Sven Loebrich, Ph.D., Development Scientist III, Immunogen
The antibody-drug conjugate Mirvetuximab soravtansine represents a potential new treatment for ovarian cancer patients. Anti-idiotypic antibodies are powerful tools in the development of sensitive and specific bioassays for monitoring patient immune responses. Here, we report the generation and characterization of highly specific anti-idiotypic antibodies against Mirvetuximab soravtansine, and assess their utility in proof-of-concept studies of a simulated anti-drug-antibody (ADA) assay.

9:40 Assays for Multi-Domain Immunogenicity Assessment
Cheikh Kane, Ph.D., Principal Scientist, DMPK, Boehringer Ingelheim

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

Interpreting ADA Data

10:55 Setting Targets for Relative ADA Assay Performance
Theo Rispens, Ph.D., Senior Scientist, Department of Immunopathology, Sanquin
One factor that hampers our understanding of immunogenicity is the difficulty in unambiguously generating and interpreting ADA data. This presentation will address comparability of ADA assays, the use of standards in determining assay performance and pitfalls in doing so, as well as the relationship between technical and clinical performance.

11:25 KEYNOTE PRESENTATION: The Use of Population Specific ADA Assay Cut Points
Albert Torri, Ph.D., Executive Director, Bioanalytical Sciences, Regeneron
In various disease populations, patient background responses in an ADA assay can vary significantly. This variability in the background response may require the establishment of population specific assay cut points. This presentation will discuss case studies where baseline samples from different clinical studies were evaluated to determine the appropriateness of the established assay cut points, and when necessary, how alternative cut points were established.

11:55 Strategies for Mitigating the Impact of Pre-Existing Antibodies and Interfering Substances on Anti-Drug Antibody Screening Assay Cutpoints
Jason DelCarpini, Ph.D., Manager, Clinical Assays, Celldex Therapeutics
Pre-existing antibodies and other interfering matrix components can confound anti-drug antibody screening assay cutpoint calculations and increase the risk of false negative results for patients. Strategies for mitigating the impact of these factors on the assay cutpoint are dependent on both the nature and prevalence of the interfering substance. A variety of approaches exist that can be employed pre-study to reduce the risk of false-negative responses in-study.

12:25 pm Sponsored Presentation *(Opportunity Available)*

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

1:55 Session Break

Interpreting ADA Data (Cont.)

2:10 Chairperson's Remarks
Wendy White, Ph.D., Fellow and Scientific Director, Translational Sciences, MedImmune, LLC

Strategies for Immunogenicity Assay Assessment

2:15 Storage Conditions of Conjugated Reagents Can Impact Results of Immunogenicity Assays: Lessons Learned
Robert Kubiak, Ph.D., Senior Manager, Clinical Immunology and Bioanalytics Group, MedImmune LLC
Integrity of conjugated reagents used for measurement of anti-drug antibody (ADA) in study samples is critical for generation of reliable immunogenicity data. Small amounts of aggregates present in preparations of conjugated reagents may lead to a spurious increase of ADA positive classifications creating an appearance of immune response developing in certain individuals. Methods for maintenance of critical reagents and ensuring consistent long-term performance of ADA methods will be discussed.

2:45 New Technology on Multiplex ADA Isotyping
Shuangping Shi, Ph.D., Director, Biologics and Vaccines Bioanalytics, Merck Research Laboratories
Biotherapeutic drugs such as monoclonal antibodies (mAbs) have the potential to induce immunogenicity; therefore, it is critical to perform an immunogenicity assessment to ensure drug efficacy and patient safety. In general, an immunogenicity assessment is performed in a multi-tiered approach: screening of anti-drug antibodies (ADA), confirmatory test, titer assessment, characterization of ADA for neutralizing drug activity and isotyping. The goal of our work is to develop multiplex approaches on various platforms including Meso Scale Discovery (MSD), Luminex and Delfia for ADA characterization.

3:15 Sponsored Presentation *(Opportunity Available)*

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 pm End of Day

THURSDAY, MAY 4

8:00 am Morning Coffee

Effect of ADA on PK Assays

8:30 Chairperson's Remarks
Zhandong Zhong, Ph.D., Senior Scientist, Amgen

8:35 Evolving Methodologies for Measuring Immunogenicity: A Novel Automated all in one Cell-Based Ligand Binding Assay
Michael Tovey, Ph.D.Michael Tovey, Ph.D., INSERM Director, Research, Laboratory of Biotechnology & Applied Pharmacology, Ecole Normale Supérieure de Cachan
Immunogenicity is a constant point of concern in the development in biotherapeutics both in terms of safety and efficacy. Understanding the potential impact on a project early in the life cycle is preferred. Thus we developed a method to better characterize the circulating immune complexes in preclinical species in terms of their size. The method can be applied to any humanized antibody or derivatives of such.

9:05 Predicting Clinical Immunogenicity for Biotherapeutics Using a Systems Model of the Immune Response
Abhinav Tiwari, Ph.D., Clinical Pharmacologist, Pfizer

9:35 Sponsored Presentation *(Opportunity Available)*

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

Managing Drug and Target Interference

11:05 Innovative Approaches to Overcome Matrix Interference for Anti-Drug Antibody Detection
Meina Liang, Ph.D., Director, Clinical Pharmacology and DMPK, Translational Sciences, MedImmune
Immunogenicity assessment is a requirement for biopharmaceutics registration. It is often evaluated in clinical studies as a secondary endpoint. Matrix interference is a common challenge for immunogenicity testing. If not addressed during method development, the interference could lead to inaccuracy in immunogenicity reporting. In this presentation, we will use case examples to discuss innovative approaches to overcome various matrix interferences to ensure accurate immunogenicity assessment.

11:35 Elimination of Drug Interference in Detection of Neutralizing Anti-Drug Antibodies in Samples Containing High Levels of Therapeutic Protein
Sheng Dai, Ph.D., Associate Director, Immunogenicity Biologics Assays and Technology, Teva
Neutralizing antibodies against therapeutic proteins can potentially impact patient safety and directly mediate loss of drug efficacy. In detection of the neutralizing anti-drug antibodies (ADA), the remaining therapeutic protein drug can inhibit the neutralizing activity of the antibody and prevent the detection. We developed a procedure that used magnetic beads to specifically remove therapeutic drug from assay samples. With this procedure, we can detect the neutralizing ADA in the presence of high levels of drug.

12:05 pm Drug Target Interference in Immunogenicity Assays
Zhandong Zhong, Ph.D., Senior Scientist, Amgen

12:35 End of Strategies for Immunogenicity Assay Assessment

Optimizing Bioassays for Biologics

Improving the Speed, Development and Validation of Biological Assays

Recommended Short Course*

SC16: New USP Initiatives for Characterization and Release of Biologics
**Separate registration required, please see page 5-6 for course details.*

THURSDAY, MAY 4

Bioassay Strategies for Cancer Therapies

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Natko Nuber, Ph.D., Laboratory Head, BTDM-BPD, Novartis Biologics R&D, Novartis

1:50 KEYNOTE PRESENTATION: Potency Methods for Combination Therapies and Points to Consider for Regulatory Compliance
Isam Qahwash, Ph.D., Manager, Bioassay Development, Molecular and Analytical Development, Bristol-Myers Squibb
Combination therapies are currently under consideration for cancer therapy. Independent and synergistic mechanisms of action contribute to feasibility of combination therapies but also to control strategy complexity. This is further compounded by a variety of ratio and formulation presentations.

2:20 Development and Optimization of Cell-Based Bioassays for Novel Cancer Immunotherapy
Natko Nuber, Ph.D., Laboratory Head, BTDM-BPD, Novartis Biologics R&D, Novartis
An ideal bioassay should mimic the MoA and be able to detect changes in the integrity of the drug. Results obtained development and optimization of commercially available bioassays for cancer immunotherapy drugs will be presented. Ability of these, cell based, bioassays to detect stressed material was assessed in comparison to standard binding assays.

2:50 Design, Develop and Optimize MOA Reflective Potency Assays for Immunomodulatory Biologics
Shihua Lin, Ph.D., Senior Scientist, Analytical Biotechnology Development, MedImmune LLC
Immunotherapy is now a promising approach for the treatment of cancer and autoimmune diseases. Bioassay plays an important role in the development of product and manufacture process. This presentation will highlight general consideration on the design, development and optimization of mechanism of action (MOA) reflective and QC-suitable bioassays for potency determination of immunomodulatory biologics.

3:20 Bioassay Design, Development and Validation
John A. Garza, Ph.D., Development Scientist II, Analytical Sciences, Alexion Pharmaceuticals
Several aspects of bioassay design should be taken into consideration during assay development and through validation. Quality Control laboratories and practices as should be considered during the fundamental bioassay design. Additionally, understanding and interpretation of regulatory guidance expectations is key.

3:50 Refreshment Break

4:20 Bioassay Development and Validation Strategies for Antibody-Drug Conjugates
Adrienne Wildt, Ph.D., Senior Scientist III, Bioanalytical Sciences, ImmunoGen
Antibody-drug conjugates (ADCs) represent an increasingly important approach to cancer treatment by targeting the delivery of cytotoxic agent to tumor cell type of interest. ADCs are generally complex heterogeneous mixtures of multiple *in vivo* drug species and present unique challenges to bioassay development. We will present some examples from our experience in the development of bioassays for the measurement of a new class of payloads from biological matrices.

4:50 Implementing Bioassays for a kλ-Body
Marie Kosco-Vilbois, Ph.D., CSO, Novimmune SA
A comprehensive suite of highly sensitive and complementary binding and reporter gene assays have been implemented to assess the potency of a kλ-Body as part of product quality analysis and characterization studies. Results obtained using the different assays were correlated to demonstrate the assays' stability indicating properties, locate degradations and initiate the identification of critical quality attributes.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC19: Strategic Bioassay Design and Analysis
**Separate registration required, please see page 5-6 for course details.*

Optimizing Bioassays for Biologics

FRIDAY, MAY 5

8:00 am Morning Coffee

Bioassay Strategies for Bispecifics

8:30 Chairperson's Remarks
Michael Tovey, Ph.D., INSERM Director, Research, Laboratory of Biotechnology & Applied Pharmacology, Ecole Normale Supérieure de Cachan

8:35 SPR-Based Assays Enable the Full Functional Analysis of Bispecific Molecules
Joerg Moelleken, Ph.D., Senior Scientist, Roche Pharmaceutical Research and Early Development, Large Molecule Research, Roche Innovation
We have developed an alternative SPR-based assay principle, which allows the individual assessment of both targets in solution. Comparison of data between the assays showed that simultaneous binding can be calculated based on both individual readouts, and revealed a good correlation. Hence, both SPR-based assay principles allow a "full" functional analysis of a bispecific CrossMab in only one assay. The assay principles can be qualified and enable an efficient drug development.

9:05 Development of Synergistic Cell-Based Assay for Bispecifics
Piyush M. Vyas, Ph.D., Senior Research Scientist, Bioassay Development, Eli Lilly and Company
We developed a synergy cell-based assay for one of our bispecific antibodies as we have seen *in vivo* synergy with this molecule in our preclinical animal model. We were able to identify the optimum conditions to achieve our goal where we were able to determine the response from both the targets in a single cell-based assay. Data analyses of such efficacy data was challenging as the traditional model cannot fit such data. Novel mathematical approach is used to determine the synergy of such bispecific antibodies.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Coffee Break

Optimizing Assay Development and Determining Potency

10:35 FEATURED PRESENTATION: Conformationally Selective Biophysical Assay for Influenza Vaccine Potency Determination
Yingxia Wen, Ph.D., Director, Head, Protein Chemistry, Seqirus
Influenza vaccines are the primary intervention for reducing the health burden from influenza. HA is the most important influenza vaccine antigen. Inactivated influenza vaccines are formulated, released for clinical use, and tested for stability based on an *in vitro* potency assay, SRID. We demonstrate that trypsin digestion, to pre-select immunologically active HA, followed by quantification by RP-HPLC is a promising alternative *in vitro* potency assay for influenza vaccines.

11:05 Development and Automation of Cell-Based Assays for Biologics
Natalia Kozhemyakina, Ph.D., Head, Bioassay Laboratory, Analytical Development Department, BIOCAD
Main problems of cell-based potency assays are variability and complexity. Classical potency assay presents a lot of drawbacks that could be overcome by automation. The use of automatic station for cell-based assays allows reduction of procedure time and implementation of complex designs. It significantly reduces variability and facilitates assay development and validation. This talk will present case studies of potency assays for bispecific and monoclonal antibodies with the use of automation.

11:35 A Novel System for Improved Quantification of ADCC Activity
Michael Tovey, Ph.D., INSERM Director, Research, Laboratory of Biotechnology & Applied Pharmacology, Ecole Normale Supérieure de Cachan
Novel target cells, together with homologous control cells, have been developed for the quantification of the ADCC activity of rituximab, trastuzumab. cetuximab and TNFα antagonists. The ADCC activity of the TNF antagonist infliximab has been quantified in serum samples from patients with Crohn's disease and that of adalimumab and etanercept in patients with rheumatoid arthritis with a high degree of precision and with minimal interference from human serum.

12:05 pm Strategic Design and Analysis for Bioassays
David Lansky Ph.D., Precision Bioassay, Inc.
While combining data from replicate assays is a simple way to improve the properties of reportable values, there are other methods to consider. A review of what is known about bioassays (including how they are both inherently robust and non-robust) leads to suggested targets to focus on to improve assays, strategies for design and analysis of bioassays, wise choices for assay acceptance criteria, and good choices among measures to use to monitor assays. Modular design of bioassays and appropriate analyses support efficient and flexible procedures for development and validation. Further, if validation is focused on documenting the performance properties of the core modules of the bioassay, a single validation experiment and analysis can then support a variety of ways to use these modules to produce reported values with properties appropriate for each of many different intended uses.

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

1:05 Refreshment Break

Lifecycle Management and Statistical Analysis

1:35 Chairperson's Remarks
Gael Debauve, Ph.D., Associate Director, Bioassays, UCB

1:40 Challenges When Transferring NAb Assays to CROs
Linlin Luo, Ph.D., Senior Research Investigator, BMS
Cell-based neutralizing antibody (NAb) assay posts many challenges in assay development, validation and execution. Extra considerations need to be given during a NAb assay transfer to contract research organization (CRO) labs, including but not limited to work cell bank preparation and qualification, sample pretreatment to increase drug tolerance, proper analyst training, and prompt communication. I will discuss the lessons learned and pitfalls to avoid from our

Optimizing Bioassays for Biologics

NAb assay transfer experience.

2:10 Lifecycle Management for Bioassay Development and Validation
Steven Walfish, Ph.D., Principal Science & Standards Liaison, USP
Lifecycle management for bioassay development starts with procedure design and continues through validation based on QbD. The concept of QbD is understood as a systematic approach that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management (ICH Q8). An overview of variability and measurement uncertainty to align decisions with results generated by a procedure.

2:40 Tips and Tricks to Develop and Validate a Bioassay According to the USP Approach
Gael Debauve, Ph.D., Associate Director, Bioassays, UCB
Biological activity is a critical quality attribute for biopharmaceutical products, and relative potency bioassays are generally used to accurately determine this activity. Case study will go through the method development journey: from the development itself to the tools implemented to monitor the method performance using the latest recommendations from the USP.

3:10 Statistical Considerations regarding Assay Robustness Studies
Ryan Yamagata, Principal Statistician, Tech R&D, GlaxoSmithKline Vaccines
Robustness is an important aspect for analytical methods. Guidelines have always encouraged assessing robustness before method validation. In practice, however, robustness studies have often been included in a not-too-rigorous manner during assay validation. With an increased focus on QbD, we have revisited the concept of method robustness, spread across different stages of method development. We will present different ways how robustness can be assessed and which statistical methods are employed.

3:40 End of Conference

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- Antibody Drug Conjugates II: Advancing Toward the Clinic

Fusion Protein Therapeutics

Engineering Next-Generation Biologics

Recommended Short Courses*

SC4:The Multi-Attribute Method (MAM) for Improving Product and Process Development

SC9: Target Selection for Biologics

**Separate registration required, please see page 5-6 for course details.*

MONDAY, MAY 1

7:00 am Registration and Morning Coffee

Next-Generation Therapeutic Fusion Proteins

8:30 Chairperson's Remarks

Fredrik Frejd, Ph.D., CSO, Affibody AB

8:40 KEYNOTE PRESENTATION: From Cytokine Traps to Antibody-Based Protein Therapeutics: A Scientific Journey

Aris N. Economides, Ph.D., Executive Director; Genome Engineering Technologies, and Skeletal Diseases TFA, Co-Founder & Head of Functional Modeling; Regeneron Genetics Center, Regeneron Pharmaceuticals, Inc.

Engineered proteins such as receptor ectodomain-Fc fusions and cytokine traps are complex fusion proteins comprised of two different receptor ectodomains fused to human Fc, and in as much as they are potent and highly specific, they also present engineering and production challenges. Technological advances in monoclonal antibody generation and production have largely supplanted cytokine trap technology and have also enabled the engineering of antibody-based therapeutics with novel properties. Examples of these technologies and their applications for the generation of therapeutics will be discussed.

9:10 FEATURED PRESENTATION: Fusion Proteins: Case Studies from Roche's Research & Early Development Pipeline

Stefan Weigand, Ph.D., Head, Large Molecule Research, Roche Pharma Research and Early Development (pRED), F. Hoffmann-La Roche, Ltd.

This talk will briefly introduce the concept of fusion proteins and provide examples from Roche's pipeline how to discover, design, develop and deliver differentiated, multi-functional therapeutics that allow for tailored solutions for the biological problem at hand. Lastly, I will raise challenges and opportunities for future applications of fusion proteins.

9:40 Fusion Protein Approaches to Generate Biobetters – Current Status and Future Outlook

Stefan Schmidt, Ph.D., M.B.A., Vice President, Process Science and Production, Rentschler Biotechnology

Next-generation biologics with enhanced properties are one of the fastest growing protein classes. These biobetters typically demonstrate improved pharmacokinetics or more selective targeting. In many cases, this is achieved by fusing the therapeutic entity to other protein modules influencing plasma half-life or reducing off-target toxicity. Here I highlight the current strategies to generate biobetters with these superior properties while describing their benefits and limits in examples from the present development pipeline.

10:10 Coffee Break

Engineering to Improve Properties

10:50 PASylation: The Biological Alternative to PEGylation for Plasma Half-Life Extension and Beyond

Arne Skerra, Ph.D., Professor, Technische Universität Munich; and Chairman & Founder, XL-protein GmbH

Fusion of proteins or peptides with conformationally disordered polypeptides comprising the L-amino acids Pro, Ala, and/or Ser (PAS) is a beneficial way to enlarge the hydrodynamic volume and retard kidney clearance, a common drawback during biological drug development. PAS sequences are strongly hydrophilic, uncharged biological polymers with biophysical properties surprisingly similar to PEG while, in contrast, allowing traceless metabolization. Case studies on the route to clinical development will be presented.

11:20 Hexavalent Agonists Targeting Co-Stimulatory Receptors of the TNFR-Superfamily

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

TNFRSF targeting compounds with a solely agonistic activity on immune cells are still rare. Apogenix's single-chain-based fusion proteins mimic the three-dimensional organization of the natural ligands (the TNFSF-proteins). In contrast to antibodies, their agonistic activity does not rely on secondary crosslinking events *in vitro* nor *in vivo*. We will present the modular engineering concept and the current results obtained for the hexavalent CD40-, 4-1BB-, GITR-, HVEM- and CD27-agonists.

11:50 Monomeric Fc Platform for Monomeric Fusion Proteins

Lu Shan, Ph.D., Scientist II, Antibody Discovery & Protein Engineering, MedImmune/AstraZeneca

Monomeric Fc or Fc halfmer is a versatile format for generating monovalent fusion proteins. We present a strategy that generated a stable Fc monomer using rational design combined with *in vitro* evolution methodologies, resulting in monomeric Fc fusion proteins with FcRn binding and serum half-life comparable to wildtype IgG.

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

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

Fusion Protein Therapeutics

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

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

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks
Gregory A. Weiss, Ph.D., Professor, Chemistry, Molecular Biology & Biochemistry, University of California, Irvine

4:10 Bicycles and Bicycle Drug Conjugates: Next Generation Therapeutics
Sir Gregory Winter, Ph.D., FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics
Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles' unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs); a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. This presentation will describe both the Bicycle® and BDC platforms.

4:55 Young Scientist Keynote: Programming Proteins by Deep Sequencing and Design
Tim Whitehead, Ph.D., Assistant Professor, Chemical Engineering and Materials Science, Michigan State University
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 group leverages this unprecedented wealth of sequence-function information to design and engineer protein affinity, specificity, and function and to infer structural complexes of proteins. My talk will present an overview of the above and detail methodological improvements that enable the engineering work.

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

6:55 End of Day

TUESDAY, MAY 2

8:00 am Registration and Morning Coffee

Conquering Disease

8:25 Chairperson's Remarks
Stefan Weigand, Ph.D., Head, Large Molecule Research, Roche Pharma Research and Early Development (pRED), F. Hoffmann-La Roche, Ltd.

8:30 Engineering an Affibody Fusion Protein Trap towards Therapeutic Blocking of IL-17 in Humans
Fredrik Frejd, Ph.D., CSO, Affibody AB
Psoriasis is an IL-17 driven disease. An Affibody® based 18.6 kDa ligand trap was engineered to block IL-17 with femtomolar affinity. The trivalent bispecific fusion protein blocks IL-17 with unparalleled affinity and display long plasma half-life as shown in man. Early development and data from Phase I/II will be presented.

9:00 PolyXen: A Polysialylation Technology for Enhancing Therapeutic Proteins and Its Clinical Application
Curtis Lockshin, Ph.D., Chief Scientific Officer, Xenetic Biosciences, Inc.
PolyXen™ is a proprietary platform for conjugating polysialic acid (PSA) to protein or peptide therapeutics, which can improve their pharmacological properties. Preclinical and human clinical data has been generated with a number of compounds, including recombinant Factor VIII, rhEPO, and oxyntomodulin. Therapeutic proteins polysialylated with the PolyXen platform have displayed extended circulating half-life, improved thermodynamic stability and protease resistance, while retaining pharmacological activity. We have seen no evidence to date of PSA- induced immunogenicity, an issue commonly associated with PEG.

9:30 A New Fab-Fusion Protein Therapeutic for Enzymatic Targeting
Michiel E. Ultee, Ph.D., Principal, Ulteemit BioConsulting, LLC
We describe the design, development and manufacture of a unique antibody-fusion protein consisting of a Fab-linked enzyme rather than the more typical Fc-linked fusion protein. VAL-1221, a preclinical product candidate for glycogen-storage diseases, contains a humanized anti-dsDNA Fab genetically linked to the acid alpha glucosidase enzyme (GAA). CHO-cell production was straightforward, but purification was challenging. The final process overcame these challenges for production of clinical material at the 500L scale.

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

10:50 Development of Luspatercept: A Receptor Fusion Protein Engineered to Treat Anemia caused by Ineffective Erythropoiesis
Rajasekhar Suragani, Ph.D., Associate Director, Acceleron Pharma, Inc.
Soluble receptor-Fc fusion proteins, also known as ligand TRAPs, are often used as high-affinity decoys to block signaling through their cognate receptors. Transforming Growth Factor-Beta (TGF-beta) superfamily member activin receptor type IIB (ActRIIB) binds to multiple ligands driving Smad 2/3 and Smad1/5/8 signaling pathways that affect multiple cellular processes. We successfully utilized protein engineering to fine-tune the selectivity of the ActRIIB receptor. In this talk, we will discuss engineering and development of Luspatercept – a modified activin receptor type IIB Fc-fusion protein that acts as a TRAP for selective ligands of the TGF-beta superfamily involved in the late stages of erythropoiesis. We show that Luspatercept regulates late-stage erythrocyte precursor cell differentiation and maturation. This mechanism of action is distinct from that of erythropoietin (EPO), which stimulates the proliferation of early-stage erythrocyte precursor cells.

11:20 Engineering Novel General Amyloid Interaction Motif (GAIM)-Immunoglobulin Fusions for Targeting Misfolded Protein Aggregates in Neurodegenerative Diseases
Ming Proschitsky, Ph.D., Senior Scientist, Research, Proclara Biosciences
The tip protein g3p of the filamentous bacteriophage M13 was previously identified as a General Amyloid Interaction Motif (GAIM) that binds and remodels a variety of fibrillar, amyloidogenic aggregates in a conformation-dependent

Fusion Protein Therapeutics

manner. To prolong the half-life of this molecule in the blood, we genetically fused GAIM with a human immunoglobulin (hIgG1Fc). The fusion protein, currently in a Phase Ib clinical trial, displays 2 copies of GAIM, retains binding and remodeling activities towards amyloid fibrils *in vitro* and *ex vivo*.

11:50 New Strategies for Immunotherapy

Steven Almo, Ph.D., Chairman, Biochemistry, and Professor, Biochemistry and Physiology & Biophysics, Montefiore Medical Center, Albert Einstein College of Medicine

We describe a novel platform for the clonal specific expansion of disease-relevant T cells. Our approach manipulates antigen-specific (i.e., clonal) lymphocyte populations by covalently linking single chain peptide-MHC (sc-pMHC) and costimulatory molecules in a manner that recapitulates the proximity, orientation and overall organization experienced at the immunological synapse. These constructs are generated as Fc-fusion proteins (i.e. IgG) for enhanced avidity and stability. This combined targeting modulation construct is referred to as synTac (artificial immunological Synapse for T-cell Activation).

12:20 pm Tailor Made Sortases for Site Specific Bioconjugation

Sponsored By Roche

Mara Boenitz-Dulat, Ph.D., Head, Enzyme Development, Roche Diagnostics

We present a new type of sortase assay applicable as a high throughput screening tool and a very sensitive analytical method. Screening alternatives to generate new sortase variants by protein engineering and molecular dynamics simulations of engineered Sa-SrtA variant with substrate binding interactions will be discussed.

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

Harnessing Albumin

2:00 Chairperson's Remarks

Stefan Schmidt, Ph.D., M.B.A., Vice President, Process Science and Production, Rentschler Biotechnology

2:05 Fusion of Centyrin Scaffold Proteins to Engineered Albumin Binding Domains Allows for Tunable Pharmacokinetics

Shalom Goldberg, Ph.D., Senior Scientist, Johnson & Johnson

Targeted delivery of therapeutic payloads to specific tissues is an important component of modern pharmaceutical development. Antibodies or other scaffold proteins can provide the cellular address for delivering a covalently linked payload. Optimization of bioconjugate properties and exposure profile are important components on the path to developing a therapeutic candidate. This presentation will focus on current efforts to optimize Centyrins for payload delivery.

2:35 A Human Serum Albumin Domain I Fusion Protein for Antibody Conjugation

James Patterson, Ph.D., Senior Scientist, Project Leader, Antibody Technologies and Chemical Biology, Sorrento Therapeutics, Inc.

Bioorthogonal labeling of antibodies enables the conjugation of compounds to expand targeting capacity or enhance cytotoxicity. Taking advantage of a cyclohexene sulfonamide compound that site-selectively labels Lys64 in human serum albumin (HSA), we demonstrate that domain I of HSA can be used as a fusion protein for the preparation of serum-stable antibody conjugates. Conjugation via HSA domain I fusion should therefore have broad utility for making antibody conjugates.

3:05 The Potential of Veltis® Engineered Albumins for Optimized Drug Dosing

Sponsored By Albumedix

Joanna Hay, Ph.D., Science Manager, Customer Solution, Albumedix Ltd.

Albumin has been used for decades to enhance the pharmacokinetic and pharmacodynamic properties of drug candidates. We will describe rationally engineered albumins that further enhance these properties; variants with modified affinity to FcRn offer more than double the half-life extension to a drug candidate compared to that achieved with native albumin. We also present new engineered albumin variants with additional free thiol groups that allow multi-valent site specific drug loading.

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

TRAIL: Tumor Necrosis Factor-Related Apoptosis-Inducing Ligand

4:25 Multivalent Antibody-TRAIL Fusion Proteins for Cancer Therapy

Oliver Seifert, Ph.D., Post-Doc, Institute of Cell Biology and Immunology, University of Stuttgart

Engineering of multivalent antibody-scTRAIL (single-chain derivatives of TRAIL) by introducing different homodimerization modules leads to a novel platform of therapeutic molecules for cancer therapy. Our results show that both tumor targeting and enhancing the valency of scTRAIL fusion protein provides enforced apoptosis induction together with good anti-tumoral activity and tolerance *in vivo*. Due to the modular composition of this novel platform, exchanging the specificity of the antibody moiety facilitates the treatment of a broad spectrum of different cancer entities.

4:55 Functional Characterization of Mesothelin-Targeted TR3 Connects Translational Cancer Research with Fundamental Concepts of Native TRAIL Biology

Dirk Spitzer, Ph.D., Assistant Professor, Surgery, Washington University School of Medicine

The newly designed, genetically stabilized and constitutively trimerized TRAIL-based fusion protein TR3 has tremendous potential as a cancer therapeutic due to the possibility of creating biomarker-targeted variants under strict stoichiometric control. A detailed characterization of the improved activity profile of mesothelin-targeted scFv-TR3 revealed unexpected drug properties, which resulted in a better understanding of targeted drug design but also offered new insight into the ligand/receptor biology of the native TRAIL cytokine.

5:25 End of Fusion Protein Therapeutics

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*
SC14: Overcoming the Challenges of Immunogenicity Assays, Risk Assessment and Meeting Regulatory Requirements
****Separate registration required, please see page 5-6 for course details.***

Antibody-Drug Conjugates I: New Targets, Payloads & Alternative Formats

Innovative Engineering and Creative Chemistry to Optimize Therapeutic Impact

Recommended Short Courses*

SC9: Target Selection for Biologics

SC15: Critical Considerations for the Design and Development of Antibody-Drug Conjugates
**Separate registration required, please see page 5-6 for course details.*

WEDNESDAY, MAY 3

7:30 am Registration and Morning Coffee

Alternative Formats and Effector Moieties

8:30 Chairperson's Remarks
Ravi Chari, Ph.D., Vice President, Chemistry & Biochemistry, ImmunoGen, Inc.

8:40 BT1718, A Bicycle Drug Conjugate (BDC) Targeting MT1-MMP for Treatment of Solid Tumors
Peter Park, Ph.D., Vice President, Oncology Research, Bicycle Therapeutics
The Bicycle® platform allows hugely diverse libraries of constrained, bicyclic peptides (Bicycles®), generated with a chemical scaffold, to be displayed on the surface of viable bacteriophage. Their relatively small size (1.5-2 kDa) delivers advantages in tumor penetration and extravasation and the fast, renal clearance avoids liver and GI toxicity often associated with other drug modalities. This presentation will exemplify the Bicycle platform and describe the discovery and development of BT1718, a potent Bicycle Drug Conjugate targeting MT1-MMP.

9:10 Abdurin-Drug Conjugates: A New Generation of Targeted Therapeutics
Kurt Gehlsen, Ph.D., Vice President and CSO, Therapeutics, Research Corporation Technologies, Inc.
Abdurins are a small antibody-like scaffold that retains a long circulating half-life. Abdurins are amenable to high-throughput screening to isolate binders to targets of interest. Abdurins have demonstrated improved tumor penetration compared to a monoclonal antibody and have been conjugated to MMAE and a deimmunized ribotoxin, SarcinDI. The smaller size and longer half-life of Abdurins may facilitate enhanced payload delivery to solid tumors compared to standard antibody-drug conjugates.

9:40 Small is Beautiful – Humabodies Drug Conjugates, HDCs a Real Alternative to ADCs
Thomas Sandal, Ph.D., Vice President, Preclinical Development and Protein Engineering, Crescendo Biologics Ltd.
- HDCs demonstrate exceptionally fast tumour penetration
- HDCs facilitate low systemic exposure
- Humabodies enable plug and play engineering allowing simple exploration of limitless format options
- The versatility of the Humabody™ platform enables creation of optimal HDC format and half-life with improved Therapeutic Index

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

Novel Payloads

10:55 HDP-101 – A BCMA-Targeted Amanitin-Based ADC
Andreas Pahl, Ph.D., CSO, Heidelberg Pharma
Antigen-Targeted Amanitin-Conjugates (ATACs) represent a new class of ADCs using the payload Amanitin. This payload introduces a novel mode of action into oncology therapy, the inhibition of RNA polymerase II. The technology platform around ATACs includes Amanitin supply, site-specific conjugation, demonstrated safety profile and biomarker. A BCMA-ATAC has been selected based on favorable preclinical data to start the clinical development of the first ATAC.

11:25 Development of Potent and Selective Antibody-Drug Conjugates Targeting Different Antigens with Pyrrole-Based KSP Inhibitors as Novel Payload Class
Hans-Georg Lerchen, Ph.D., Principal Scientist, Drug Discovery, MedChem, Bayer AG
The identification of ADC payload classes with a novel mode of action will increase therapeutic options and potentially help to overcome resistance. Small molecule inhibitors of kinesin spindle protein (KSP/Eg5) have generated interest due to their high antitumor potency. A new pyrrole subclass of KSP inhibitors with sub-nanomolar potency against a large panel of tumor cell lines has been established as a versatile new payload class for the generation of potent and selective ADCs against different targets.

11:55 Expanding the Therapeutic Window of ADCs with Zymelink™ Novel Linkers and Payloads
John Babcook, Ph.D., Senior Vice President, Discovery Research, Zymeworks Inc.
Zymelink™ is a novel drug-conjugate platform consisting of a modular suite of proprietary payloads, linkers and site-specific conjugation technologies designed for the targeted delivery of therapeutics with optimal efficacy and safety profiles. It is compatible with traditional monoclonal antibodies, Azymetric™ (bispecific) and AlbuCORE™ (multispecific) platforms for the development of next-generation biotherapeutics.

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ADCs I: New Targets, Payloads & Alternative Formats

Sponsored By Catalent BIOLOGICS

12:25 pm Latest Advances Developing ADCs using SMARTag™ Technology

David Rabuka, Ph.D., Global Head, Research & Development, Chemical Biology, Biologics Research & Development, Catalent Pharma Solutions

We have developed the SMARTag™ technology platform, which enables precise, programmable, site-selective chemical protein modification. Leveraging the target sequence of Formylglycine Generating Enzyme (FGE) we chemoenzymatically modify proteins to generate a precisely placed aldehyde functionality that can be chemically elaborated. We will present our novel protein modification platform and its application to generating ADCs, including our new conjugation chemistries and linkers.

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

1:55 Session Break

Novel Payloads (Cont.)

2:10 Chairperson's Remarks

Peter Park, Ph.D., Vice President, Oncology Research, Bicycle Therapeutics

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2:15 KEYNOTE PRESENTATION: Antibody Drug Conjugates with Novel DNA Alkylating Agents: Design and Preclinical Evaluation

Ravi J. Chari, Ph.D., Vice President, Chemistry & Biochemistry, ImmunoGen, Inc.

There are currently over 50 Antibody-Drug Conjugates (ADCs) in clinical development, reflecting the growing interest in ADCs for the treatment of cancer. As part of our effort to expand the available toolbox of cytotoxic payloads, we have designed a new class of potent DNA-alkylating agents, "indolino-benzodiazepine dimers" (termed IGNs). The chemical design and preclinical data for representative IGN ADCs will be discussed.

2:45 KEYNOTE PRESENTATION: Novel DNA-Targeting Payloads for ADCs

Puja Sapra, Ph.D., Vice President and CSO, Target Therapeutics Unit, Oncology Research & Development, Pfizer, Inc.

We will review the development of Mylotarg & Inotozumab Ozogamicin. This talk will explore the next generation of Pfizer DNA-damaging ADCs

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3:15 Poster Spotlight I: Fully Synthetic Trioxacarcin Analogs for Use in Antibody-Drug Conjugates

Ethan Magno, Sc.B, Graduate Student, Chemistry and Chemical Biology, The Myers Lab, Harvard University

The Myers lab has developed a highly efficient total synthesis of the antineoplastic compound trioxacarcin A using a modular, convergent, and scalable route. Trioxacarcin A is a bacterial metabolite exhibiting sub-nanomolar 50% growth inhibition in a number of human cancer cell lines. This presentation details the preparation of fully synthetic analogs of trioxacarcin A with comparable activity to the natural product. In addition, we describe the conjugation of these novel analogs to the anti-HER2 antibody, trastuzumab, through a series of enzyme-cleavable linker systems.

3:30 Poster Spotlight II: Stable and Potent Selenomab-Drug Conjugates

Xiuling Li, Ph.D., Research Associate, Immunology and Microbiology, The Scripps Research Institute

Selenomabs are engineered monoclonal antibodies with one or more translationally incorporated selenocysteine residues, the 21st natural amino acid. The unique reactivity of the selenol group of selenocysteine permits rapid, single step, and efficient site-specific conjugation of drugs to selenomabs. Using a tailored conjugation chemistry, we generated site-specific selenomab-drug conjugates which demonstrated excellent stability, potency, and selectivity *in vitro* and *in vivo*. Our data from breast cancer and multiple myeloma xenograft models revealed broad therapeutic utility of these antibody-drug conjugates.

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, MAY 4

8:00 am Morning Coffee

Overcoming Drug Resistance

8:30 Chairperson's Remarks

Vijay Chudasama, Ph.D., Lecturer, Organic Chemistry and Chemical Biology, University College London

8:35 Elimination of Multidrug-Resistant Melanoma by Humax-AXL MMAE

David Satijn, Ph.D., Director, New Antibody Products, Genmab

- AXL is overexpressed in many types of cancer, including melanoma, and is associated with EMT and increased invasiveness of tumors.
- AXL is also upregulated upon resistance to a variety of therapies including the oft-used BRAF and MEK inhibitors in melanoma
- HuMax-AXL-MMAE shows efficacy in AXL-expressing melanoma CDX and PDX models

9:05 Herceptin® (Trastuzumab, Tz) with Covalent Attached Redox Selenium is More Cytotoxic to Tz Resistant JIMT-1 Breast Cancer Cells than Tz Alone by Generating Intracellular Superoxide and H2O2

Julian Spallholz, Ph.D., Professor, Nutritional Biochemistry, Nutritional Sciences, Texas Tech University

Herceptin® (Trastuzumab, Tz) treated women with Her/2 + breast cancer (BC) often relapse with their cancer becoming Herceptin resistant. To overcome resistance, an ADC, antibody-drug conjugate, Kadcyla® (ado-trastuzumab emtansine) was developed by Genentech. We replace Emtansine with a small redox selenium moiety (Mab-SeCN) that redox cycles and increases intracellular BC oxidative stress. The Se-Herceptin® ADC is more cytotoxic to Herceptin® resistant and Kadcyla® treated Herceptin® resistant JIMT-1 BC cells.

9:35 RESPECT (REsidue-SPEcific Conjugation Technology): A Platform Technology Utilizing Native Cysteine and Lysine Residues for the Generation of Homogeneous Antibody-Drug Conjugates

ADCs I: New Targets, Payloads & Alternative Formats

Jared Spidel, Ph.D., Principal Scientist, Antibody Core, Morphotek, Inc.

Our cysteine-specific conjugation method exploits a unique intrachain disulfide bond in the light chain of rabbit antibodies between residues 80 and 171 of the variable and constant domains, respectively. Our humanization strategy allows retention of the cysteine at position 80 with a free thiol group that is both amenable for residue-specific conjugation and compatible with optimal antibody biophysical properties. Our C-terminal lysine-specific linkage method employs the transglutaminase enzyme that catalyzes the formation of a stable isopeptide bond between the γ-carboxyamide group (acyl donor) of a glutamine and the ε-amino group (acyl acceptor) of a lysine. BlAntibody-drug conjugates prepared using our RESPECT technology targeting the tumor associated-mesothelin protein produced uniform drug-to-antibody ratios and were shown to be highly potent and specific *in vitro* and effective *in vivo* in reduction of tumor growth in a highly aggressive mesothelin-expressing xenograft tumor model.

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

Optimizing Linker and Conjugation Chemistry

11:05 Site Selective Antibody Drug Conjugates Enabled by Cysteine Arylation

Bradley L. Pentelute, Ph.D., Professor, Chemistry, Massachusetts Institute of Technology

Here we report a robust bioconjugation method using cysteine arylation. This chemistry enables site-specific conjugation at cysteine residues within peptides, proteins, and antibodies. Our two developed approaches use either perfluoroaryl-cysteine SNAr chemistry or organometallic palladium reagents. Recently, we discovered a self-labeling four-residue sequence that enables regioselective conjugation at only one cysteine residue within an intact antibody containing natural amino acids.

11:35 Novel Lysosoma Cleavage Linker Leads to Potent and Stable Duocarmycin Conjugates

Ying Sun, Ph.D., Associate Director of Chemistry, Ambrx

Duocarmycin is very potent DNA alkylating agent. Duocarmycin as small molecule in the clinical trial was not successful due to the toxicity. Duocarmycin as payload for antibody drug conjugates has been explored by several companies. But the linker design for duocarmycin has been challenging. Here, we report a new linker design with novel lysosomal cleavage mechanism, which leads to potent and stable duocarmycin conjugates.

12:05 pm Fine-Tuning Functional Disulfide Re-Bridging to Enable the Formation of Homogeneous Antibody Conjugates and Exploring Novel ADC Avenues

Vijay Chudasama, Ph.D., Lecturer, Organic Chemistry and Chemical Biology, University College London

Our latest data on next generation maleimide and pyridazinedione reagents for the site-selective modification of antibodies will be detailed (robust serum stability, *in vitro* selectivity, *in vivo* efficacy, and an update our first-in-class reagents that effect both disulfide reduction and functional re-bridging). Also presented, will be how we have been able to use our platforms to create bispecifics, and a novel strategy for making DAR 2 constructs from a native antibody scaffold.

12:35 End of Antibody-Drug Conjugates I: New Targets, Payloads and Alternative Formats

7th Annual | May 4-5, 2017

Antibody-Drug Conjugates II: Advancing Toward the Clinic

Lessons Learned from Preclinical and Early Trials to Drive Clinical Success

Recommended Short Course*

SC9: Target Selection for Biologics
**Separate registration required, please see page 5-6 for course details.*

THURSDAY, MAY 4

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
John Lambert, Ph.D., Executive Vice President and Distinguished Research Fellow, ImmunoGen

1:50 KEYNOTE PRESENTATION: Leveraging Antibody-Drug Conjugates to Eradicate Tumor-Initiating Cells
Alex Bankovich, Ph.D., Senior Director, Head of Late Stage Research, AbbVie Stemcentrx, LLC

Tumor-initiating cells (TICs) will remain controversial until findings in the lab translate into drugs providing clear clinical benefit to patients. Antibody drug conjugates (ADCs) are a promising class of drugs able to target and reduce the frequency of TICs in patient-derived xenografts. My company has worked to discover TIC phenotypes and to utilize methods well-suited to specifically identify cell surface proteins targetable by specific ADCs. My talk will explain the drug development path that we followed to some of our current clinical programs.

Modeling and Simulation Approaches

2:20 Novel Approaches for Modeling Pre-Clinical Activity of ADCs and Informing Biomarker Strategy
Tony D'Alessio, Ph.D., Research Investigator, Oncology Biotherapeutics, Novartis Institutes for Biomedical Research

Using PTX mouse clinical trials, we have begun to generate population-based *in vivo* activity datasets on several emerging ADC programs. By integrating response data with molecular features across these models, we are building a rich dataset for biomarker analysis. Additionally, we are employing fully syngeneic murine tumor models to profile ADC activity in immune-competent settings and characterized pharmacodynamic changes in the tumor microenvironment to inform rational combination approaches.

2:50 Predicting Clinical Success of ADCs using a Mechanistic Modeling & Simulation Approach
Alison Betts, Ph.D., Associate Research Fellow, Biomedicine Design, Pfizer

Quantitative modeling and simulation was used to analyze data on 10 ADCs in patient trials or approved for oncology indications. Clinical efficacious dose was predicted from preclinical PK/PD studies and compared with clinical MTD, recommended Phase II and clinically approved doses. Monte Carlo clinical trial simulations were performed to predict objective response rate. This information can be used to select the best ADC, to optimize clinical trial design and determine likelihood of success versus clinical standard of care.

3:20 Poster Spotlight: Glypican-3 Specific Antibody Drug Conjugate for Hepatocellular Carcinoma
Ying Fu, Ph.D., Postdoctoral Fellow, National Cancer Institute, National Institutes of Health

Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related death. Glypican-3 (GPC3) is a potential target for HCC. The hypothesis of using anti-GPC3 antibody drug conjugate to treat HCC patients has not been tested in clinical trials. Here we report the development of hYP7-PC, a humanized anti-GPC3 antibody conjugated to a highly potent DNA damaging agent through cysteine via protease-cleavable linker. hYP7-PC caused tumor remission in HCC Hep3B xenograft model.

3:50 Refreshment Break

PKPD and Bioanalytics of ADCs in Support of Clinical Development

4:20 Relationship between the Mononuclear Phagocyte System and the Pharmacokinetics and Pharmacodynamics of Antibody Drug Conjugates in Patients
William C. Zamboni, Pharm.D., Ph.D., Associate Professor; Director, TOND2I Lab, University of North Carolina at Chapel Hill

The PKPD of carrier-mediated agents (CMA) and ADC agents are dependent on their recognition and interaction with the mononuclear phagocyte system (MPS) where the conjugated drug is cleared via interactions with the MPS. It is important to evaluate how mediators, characteristics and function of the MPS affect the PK and PD of ADCs. We will discuss: 1) pharmacologic methods to characterize ADCs *ex vivo* and *in vivo*; 2) MPS variability across patient populations; and 3) relationship between mediators, characteristics and function of the MPS and the PK and PD of ADCs in patients.

4:50 Challenges and Solutions Associated with Bioanalysis of Antibody Drug Conjugates in Support of Clinical Studies
Rafiq Islam, Ph.D., Senior Director, Bioanalytical Services, Celerion, Inc.

Since ADCs are generally complex heterogeneous mixtures of multiple species, these novel therapeutic products present unique bioanalytical challenges. Novel bioanalytical approaches and strategies including a combination of ligand-binding

ADCs II: Advancing Toward the Clinic

assays (LBA) and LC–MS-based platforms are needed to overcome challenges unique to ADCs. This presentation will examine the different methodologies such as LBAs and LC-MS/MS methods for the bioanalysis of ADCs using Kadcyla® (ado-trastuzumab emtansine) as a case study.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC15: Critical Considerations for the Design and Development of Antibody-Drug Conjugates
**Separate registration required, please see page 5-6 for course details.*

FRIDAY, MAY 5

8:00 am Morning Coffee

Preclinical and Clinical Updates

8:30 Chairperson's Remarks
Christopher D. Thanos, Ph.D., Senior Director, Biotherapeutics Discovery, Halozyme Therapeutics

8:35 Clinical Development of ADCs: From Bench to Clinic and Back Again
Jonathan Drachman, M.D., CMO and Executive Vice President, Research and Development, Seattle Genetics
Antibody-drug conjugates are emerging as an important therapeutic option for both hematologic malignancies and solid tumors. As more clinical trials are completed, it may be possible to identify patterns that will help guide future technological advances. Lessons learned from different antigens, payloads, and early trial design will be discussed.

9:05 Antibody-Cytokine Fusion Proteins for the Therapy of Cancer and of Chronic Inflammation
Francesca Pretto, Ph.D., Head, Preclinical Research, Philogen, Inc.
Antibodies represent ideal vehicles for the delivery of cytokines to the site of disease and for the selective modulation of the immune system in pathological conditions. In this lecture, I will present preclinical and clinical data on antibody-cytokine fusion proteins that we have moved to advanced controlled clinical trials in patients with cancer or with chronic inflammatory conditions.

9:35 9:35 Pre-Clinical Development of a Novel FLT3 Targeting Antibody-Drug Conjugate Employing Site-Specific Conjugate for the Treatment of Acute Myeloid Leukemia Regardless of FLT3 Status
Nandini Rudra-Ganguly, Ph.D., Principal Scientist, Discovery Research, Agensys

10:05 Coffee Break

10:35 ImmunoGen's ADC Platform Technologies: Current Progress and Future Prospects
John Lambert, Ph.D., Executive Vice President and Distinguished Research Fellow, ImmunoGen

11:05 Update on Mersana's Antibody-Drug Conjugates: Progress into the Clinic
Donald A. Bergstrom, M.D., Ph.D., CMO, Mersana Therapeutics
XMT-1522 is a HER2-targeting ADC that induces complete regressions in models of heavily-pretreated HER2-positive breast tumors, as well as breast and non-small cell lung cancer (NSCLC) without HER2 gene amplification and lower HER2 expression. XMT-1522 entered clinical development in October 2016. XMT-1536 is a Dolaflexin ADC targeting NaPi2b that is highly active in models of NSCLC adenocarcinoma and epithelial ovarian cancer. XMT-1536 has significantly improved efficacy and tolerability compared to a monomethyl auristatin E ADC against the same target. XMT-1536 will enter clinical development in late 2017.

11:35 Treatment of Non-Hodgkin Lymphoma with the Beta-Emitting Anti-CD37 Antibody Radionuclide Conjugate Betalutin®
Jostein Dahle, Ph.D., CSO, Nordic Nanovector ASAc
177Lu-satetraxetan-lilotomab (Betalutin®) is a novel CD37-binding antibody radionuclide conjugate (ARC). CD37 is an internalizing transmembrane antigen highly expressed on most B-cell malignancies. Betalutin is currently in Phase I/II clinical development for the treatment of Non-Hodgkin lymphoma. Updated clinical and pre-clinical data will be presented.

12:05 pm Development of Novel EGFR Antibody Drug Conjugates for Solid Tumor Indications
Ed Reilly, Ph.D., Senior Research Fellow, Oncology Discovery, AbbVie
Abbvie has multiple antibody drug conjugate (ADC) programs encompassing various linker payload combinations. Several of these ADCs have advanced to clinical trials where objective responses in patients with different solid tumors have been observed. Appropriate patient selection biomarker strategies have been developed including protein, RNA and gene amplification detection methods. This presentation will focus on the development of a tumor-target specific ADC from discovery to clinical trials.

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

1:05 Refreshment Break

Novel ADC Concepts with Promising Preclinical Results

1:35 Chairperson's Remarks
Ed Reilly, Ph.D., Senior Research Fellow, Oncology Discovery, AbbVie

1:40 Synergistic Potential of Combining Antibody-Drug Conjugate and Immunotherapy for Cancer Treatment
Herren Wu, Ph.D., Senior Vice President, CTO, MedImmune, LLC.
- Race to develop combinatory cancer therapy of ADC and IO
- Promising preclinical results
- Opportunities and challenges

ADCs II: Advancing Toward the Clinic

2:10 HTI-1511, A Novel Anti-EGFR-ADC, Demonstrates Significant Activity against KRAS- or BRAF-Mutated Tumors of Various Types In Preclinical Studies

Christopher D. Thanos, Ph.D., Senior Director, Biotherapeutics Discovery, Halozyme Therapeutics

We have previously described HTI-1511, an ADC in pre-clinical development that targets EGFR. Here we screened a panel of over 70 tumor cell lines derived from various solid tumor malignancies. Evaluations in several human xenograft tumor models and patient derived tumor models in mice demonstrated potent tumor regression. These results support further development of HTI-1511 as a possible treatment for EGFR overexpressing tumors, including those with downstream activating mutations in the KRAS/BRAF pathway.

2:40 Novel Medicines that Exploit Extracellular Protein-Protein Interactions

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

The talk will review the development of EDCs to multiple cancer-related targets and describe their extracellular mechanism which resembles necrosis. In addition, data using cynomolgus monkey models will be discussed, where a CD20-specific EDC was able to eliminate all CD20+ B-cells while having no effect on other cells or tissues. This talk will therefore describe a new level of therapeutic precision that depends on protein-protein proximity and not simply expression.

3:10 Probody Drug Conjugates for the Treatment of Cancer

Jason Sagert, Ph.D., Senior Scientist II, Oncology, CytomX Therapeutics

Probody™ Drug Conjugates (PDCs) are a class of antibody-based therapeutics that remain in a substantially inert, masked form until activated proteolytically in the tumor microenvironment. This platform allows the targeting of antigens that are highly expressed on tumor cells with high prevalence across multiple types of cancer regardless of normal tissue expression. Preclinical data supporting the development of PDCs will be presented.

3:40 End of Conference

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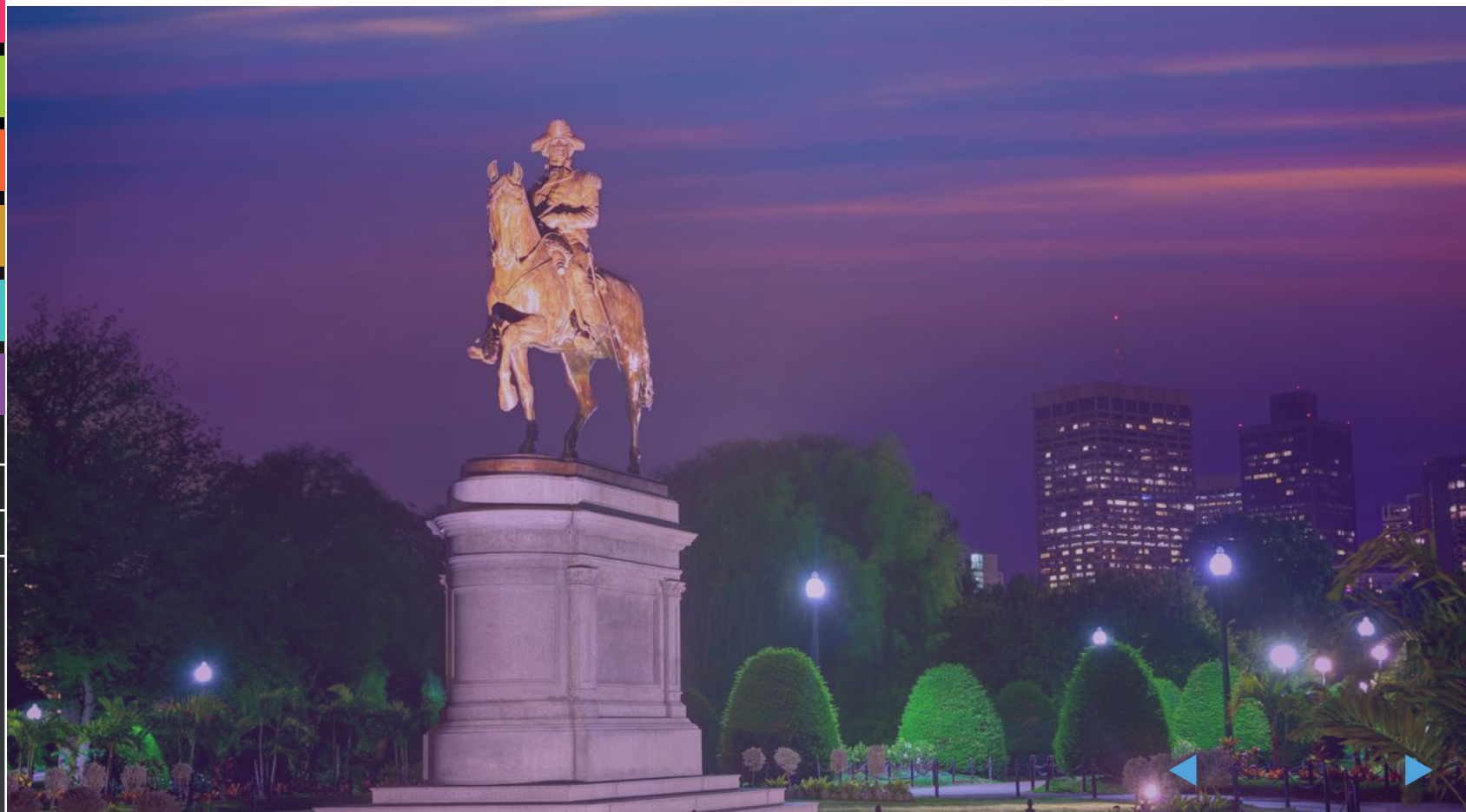

4th Annual | May 1-2, 2017

Drug Discovery for Autoimmunity and Inflammation

Emerging Targets, Therapeutic Strategies and Product Formats for a Growing Market

Recommended Short Courses*

SC2: Translational Considerations for Development of Monoclonal Antibodies Part I: Focus on Early Discovery

SC7: Translational Considerations for Development of Monoclonal Antibodies Part II: Focus on Nonclinical Development to the Clinic
**Separate registration required, please see page 5-6 for course details.*

MONDAY, MAY 1

7:00 am Registration and Morning Coffee

Emerging Targets and Pathways

8:30 Chairperson's Remarks
Rajita Pappu, Ph.D., Senior Scientist, Genentech

8:40 Targets and Pathways for Airway Diseases
Matthew Sleeman, Ph.D., Executive Director, Immunology & Inflammation, Regeneron Pharmaceuticals, Inc.
In this talk I will present an overview of pathways and the new targets that are being considered in respiratory disease and the underlying data that supports these mechanisms; in addition I will discuss how translational medicine is being used to find biomarkers to improve response rates and how newly described phenotypes of airway disease such as ACOS (asthma COPD overlap syndrome) are being used to develop new biological therapies.

9:10 IL33 in Lung Inflammation
Rajita Pappu, Ph.D., Senior Scientist, Genentech
Dysregulated Type-2 inflammation is associated with a number of allergic and atopic diseases. The significance of Type-2 cytokines, IgE and eosinophils in disease pathophysiology is most appreciated in asthma, where many trials have demonstrated clinical benefit from blocking Type-2 cytokines. We demonstrate IL33 regulates multiple pathogenic pathways including IL5 and IL13. These data suggest blocking IL33 signaling in asthma may provide clinical benefit due to inhibition of multiple pathogenic pathways.

9:40 KEYNOTE PRESENTATION: Opportunities and Challenges for Biotherapeutics in Autoimmunity and Inflammation
Christian Antoni, Ph.D., Vice President, Immunology & Inflammation, Sanofi
Biotherapeutics have revolutionized the treatment outcome for major autoimmune diseases and greatly enhanced our understanding of the underlying immune-pathology but rarely achieved complete disease control. We have now the opportunity to apply the knowledge gained to further improve treatment outcomes by tackling efficacy ceilings and to expand into underserved smaller indications while facing challenges of biosimilar entry, high CMC costs and the need to demonstrate added value for new drugs.

10:10 Coffee Break

10:45 Chairperson's Remarks

10:50 New Targets and Pathways to Treat Unmet Medical Need in Scleroderma and Fibrotic Diseases
Elma Kurtagic, Ph.D., Principal Scientist, Momenta Pharmaceuticals
Development of novel therapeutics is confounded by our inability to understand the complex basis of disease, resulting in a high failure rate in development and unclear benefit for patients. We developed high-resolution analytics to identify drug targets and patient stratification markers that address unmet medical need in autoimmune disease. This presentation will describe the application of this technology to RA and Scleroderma.

11:20 Antibodies Specific to Damaged Arthritic Cartilage as Imaging Probes and for Targeting Payload Drugs to Joint with Rheumatoid Arthritis and Osteoarthritis
Ahuva Nissim, Ph.D., Associate Professor, Antibody and Therapeutic Engineering, William Harvey Research Institute, Queen Mary University of London
We have developed a panel of human scFvs that bind specifically to collagen type II post-translationally modified by oxidants present in arthritic joints, anti-ROS-CII: a) bind specifically to human rheumatoid arthritic and osteoarthritic cartilage and to cartilage from murine models of inflammatory arthritis and osteoarthritis; b) enhance resolution of inflammation by targeting payload drugs specifically to inflamed arthritic joints; and c) detect disease activity in osteoarthritic joints before any overt cartilage damage.

11:50 Old Target Revives: Potential Novel Therapeutic Strategy for Rheumatoid Arthritis
Yoshi Itoh, Ph.D., Associate Professor and Principal Investigator, Cell Migration Group, Kennedy Institute of Rheumatology, University of Oxford
Rheumatoid arthritis (RA) is characterized by destruction of joint tissues by metalloproteinases (MPs). MPs were considered to be therapeutic targets, but clinical trials of broad spectrum MP inhibitors were all failed due to lack of efficacy and side effects. However, recent studies have indicated that highly selective inhibition of some MPs may provide significant benefits in RA. Potential novel therapeutic strategies for RA will be discussed.

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

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

Drug Discovery for Autoimmunity and Inflammation

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

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

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks
Gregory A. Weiss, Ph.D., Professor, Chemistry, Molecular Biology & Biochemistry, University of California, Irvine

4:10 Bicycles and Bicycle Drug Conjugates: Next Generation Therapeutics
Sir Gregory Winter, Ph.D., FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics
Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles' unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs); a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. This presentation will describe both the Bicycle® and BDC platforms.

4:55 Young Scientist Keynote: Programming Proteins by Deep Sequencing and Design
Tim Whitehead, Ph.D., Assistant Professor, Chemical Engineering and Materials Science, Michigan State University
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 group leverages this unprecedented wealth of sequence-function information to design and engineer protein affinity, specificity, and function and to infer structural complexes of proteins. My talk will present an overview of the above and detail methodological improvements that enable the engineering work.

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

6:55 End of Day

TUESDAY, MAY 2

8:00 am Registration and Morning Coffee

Controlling Immune Response

8:25 Chairperson's Remarks
Kris F. Sachsenmeier, Ph.D., Associate Director, Translational Sciences, AstraZeneca

8:30 Modulating T Cell and Myeloid Cell Functions for Treatment of Autoimmune Diseases and Cancer
Tariq Ghayur, Ph.D., Distinguished Research Fellow, AbbVie Bioresearch Center
Advances in T cell and myeloid cell biology coupled with advances in protein engineering provides novels ways to modulate immune functions for treatment of a variety of disease states. The challenges now will be to identify the right target and/or target combinations and to design the right therapeutic modalities to modulate immune functions to achieve the desired outcome.

9:00 XmAb5871, A Non-Depleting B Cell Inhibitor for the Treatment of Autoimmune Diseases
John Desjarlais, Ph.D., CSO, Xencor
FcγRIIb is an inhibitory receptor that regulates B cell responses through a negative feedback loop that requires co-localization of FcγRIIb to the BCR complex. XmAb5871 is an anti-CD19 antibody whose Fc domain was engineered to increase affinity for FcγRIIb dramatically. *In vitro* and *in vivo* studies show potent B cell suppression. Early clinical data demonstrate B cell inhibition in patients and promising activity in rheumatoid arthritis and IgG4 related disease (IgG4-RD).

9:30 Parallel Aspects of the Microenvironment in Cancer and Autoimmune Disease: Possible New Therapeutic Targets?
Miki Rahat, D.Sc., Assistant Professor, Immunology, Technion; Director, Research Laboratories, Carmel Medical Center
Cancer and autoimmune diseases are fundamentally opposite pathological conditions, as the immune response is suppressed and unable to eradicate tumor cells in the former, while it is hyper-activated against self-antigens in the latter. Nevertheless, some intriguing similarities, particularly in aspects relating to the microenvironments exist between the two. Understanding these parallels may help identify new therapeutic targets that might skew the microenvironment in the right direction to regain balance and homeostasis.

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

Talk Protein Engineering and Emerging Product Formats

10:50 Adenosine and the Inflammatory Microenvironment: Turning the Heat Off or On?
Kris F. Sachsenmeier, Ph.D., Associate Director, Translational Sciences, AstraZeneca
We have identified that co-blockade of the ectonucleotidase that generates adenosine CD73 and the A2A adenosine receptor (A2AR) that mediates adenosine signaling in leukocytes, by using compound gene-targeted mice or therapeutics that target these molecules, limits tumor initiation, growth, and metastasis. This tumor control requires effector lymphocytes and interferon-gamma. These data are presented in light of experiments showing that adenosine also plays a role in shaping inflammation associated with autoimmunity.

11:20 Non-Antibody Based Cytokine Trapping Molecules for the Treatment of Asthma and Atopic Dermatitis
Erik Depla, Ph.D. Expert, Discovery Biology, VIB
IL-33 and TSLP are two cytokines that are released from epithelial surfaces and which control the fate of downstream allergic immune responses in asthma and atopic dermatitis. We have developed a new type of biologics that function as high affinity decoy receptors for IL-33 and TSLP. The underlying principle and data showing their potent antagonistic activity *in vitro* and in murine models of allergic

Drug Discovery for Autoimmunity and Inflammation

disease will be presented.

11:50 When Is It Right, and When Is It Not Right, for Therapeutic Antibodies to Engage Fc Receptors?

Anthony Shock, Ph.D., Director, Immunology Portfolio, UCB

Direct targeting of Fc receptors (activating and inhibitory FcγRs and FcRn) is considered an attractive concept to treat autoimmune diseases and how the pharmaceutical industry is approaching this will be discussed by focusing on specific examples of biotherapeutics in clinical development. In contrast, other drugs are being developed which have been designed to avoid FcR engagement and this will also be discussed by reference to specific examples in the clinic.

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

Tolerance Induction

2:00 Chairperson's Remarks

Rachel Ettinger, Ph.D. Senior Scientist Respiratory, Inflammatory, and Autoimmune Diseases, MedImmune

2:05 Nanoparticles for the Therapeutic Induction of Antigen-Specific Tolerance in Autoimmune Diseases

Francisco Quintana, Ph.D. Associate Scientist, Brigham and Women's Hospital; Associate Professor, Neurology, Harvard Medical School

Here we describe nanoparticles (NPs) that co-administer the aryl hydrocarbon receptor (AhR) agonist ITE and T-cell epitopes to dendritic cells (DCs) *in vivo* to reestablish immune tolerance in autoimmune disorders. These NPs induce tolerogenic DCs through the AhR-dependent induction of Socs2, inhibiting nuclear factor kB (NF-kB) activation. Consequently, NP-induced tolerogenic DCs induced antigen-specific Tregs, suppressed pathogenic T cells and arrested the development of experimental autoimmunity.

2:35 Tolerogenic Immunotherapy for Autoimmune Disease Using Antigen-Encapsulating PLG Nanoparticles

Stephen D. Miller, Ph.D., Professor, Microbiology-Immunology and Dermatology, Northwestern University

We have demonstrated the utility of i.v infusion of antigen-encapsulating PLG nanoparticles (Ag-NP) for therapy of Th1/Th17-mediated autoimmune disease models of MS, T1D, and celiac disease. Ag-NP-induced tolerance is mediated by both PD-L1/PD1 anergy and Treg activation and dependent on particle uptake and antigen re-presentation by splenic marginal zone and liver APCs via the MARCO scavenger receptor. This approach is being tested in a phase 1 trial in celiac disease.

3:05 Featured Poster Presentation: Antibodies Against Ion Channel Targets for Autoimmune Disorders

Yelena Bisharyan, Ph.D., Director, External Alliances, Tetragenetics Inc.

Ion channels have been historically difficult to raise antibodies against due to sequence conservation, paucity of cell surface epitopes, and poor expression levels in heterologous systems. Tetragenetics addresses these issues by combining a technology for membrane protein expression in Tetrahymena thermophila with antibody generation in phylogenetically diverse animals to develop therapeutic antibodies against a range of ion channel targets including Kv1.3, a voltage-dependent channel produced by effector memory T-cells implicated in certain autoimmune disorders.

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

Biomarkers and Patient Stratification

4:25 Disease Heterogeneity and Drug Response Subsets in Rheumatoid Arthritis

Michael Townsend, Ph.D., Associate Director, Biomarker Discovery OMNI, Genentech

Rheumatoid arthritis (RA) is a heterogeneous autoimmune disease and the relationship between drivers of disease in RA and therapeutic outcome is incompletely understood. Advances are needed if improved drugs are to be developed. I will discuss our work using genomics, histologic phenotyping, and cellular analysis of RA synovial samples that have revealed different pathological phenotypes of RA with differential association with disease activity, clinical progression, and response to drug therapy.

4:55 Altered B Cell Subsets in SLE

Rachel Ettinger, Ph.D. Senior Scientist Respiratory, Inflammatory, and Autoimmune Diseases, MedImmune

Here, we describe an unusual subset of B cells highly expanded in a large cohort of systemic lupus erythematosus (SLE) patients. These B cells displayed a unique phenotype not noted on other B cell populations, including high densities of CD11c, FcRL5, and T-bet. These CD11chi B cells significantly correlate with SLEDAI, autoantibodies and IL-21. CD11chi B cells may serve as an important pharmacodynamic marker in clinical trials that target inflammatory processes.

5:25 End of Drug Discovery for Autoimmunity and Inflammation

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Courses*

SC13: Phenotypic Screening Applications and Technologies

SC14: Overcoming the Challenges of Immunogenicity Assays

**Separate registration required, please see page 5-6 for course details.*

Recommended Short Courses*

SC14: Overcoming the Challenges of Immunogenicity Assays, Risk Assessment and Meeting Regulatory Requirements

SC17: Transient Protein Production in Mammalian Cells
**Separate registration required, please see page 5-6 for course details.*

WEDNESDAY, MAY 3

7:30 am Registration and Morning Coffee

Breaking News in Vaccine Design & Science

8:30 Chairperson's Remarks

8:40 New Research Uncovers Why Hepatitis C Virus Vaccine Has Been Difficult to Make
Mansun Law, Ph.D., Associate Professor, Immunology & Microbial Science, Scripps Research Institute
Prior studies have shown that HCV's receptor binding site adopts a narrow range of conformations (shapes) when bound by virus-neutralizing antibodies. A vaccine that elicited high levels of antibodies against only these key conformations would, in principle, provide effective protection. But this study suggests that the E2 protein used in candidate vaccines displays far too many other binding-site conformations--and thus elicits antibodies that mostly do nothing to stop the actual virus.

9:10 Recombinant Expression of *Chlamydia trachomatis* Major Outer Membrane Protein in *E. coli* Outer Membrane as a Substrate for Vaccine Research
Lan Zhang, Ph.D., Principal Scientist, Vaccine Discovery, Merck & Co Inc.
A safe and efficacious vaccine against *Chlamydia trachomatis* infection remains an unmet medical need. *C. trachomatis* major outer membrane protein (MOMP), a β-barrel integral outer membrane (OM) protein, is the most abundant antigen in the OM of the bacterium. We targeted the recombinant expression of MOMP to the *E. coli* OM. The OM expressed and purified recombinant MOMP is immunogenic in mice and elicits antibodies that react to the native antigen, Chlamydia elementary body (EB).

9:40 KEYNOTE PRESENTATION: Structures of HIV-1 Env V1V2 with Broadly Neutralizing Antibodies Reveal Commonalities that Enable Vaccine Design
Jon R. McDaniel, Ph.D., Georgiou Laboratory, Chemical Engineering, Biomedical Engineering, Molecular Biosciences; Institute for Cellular and Molecular Biology, University of Texas at Austin
Here we report the cocrystal structure of V1V2 with antibody CH03 from a second donor and model Env interactions of antibody CAP256-VRC26 from a third donor. These V1V2-directed bNAbs used strand-strand interactions between a protruding antibody loop and a V1V2 strand but differed in their N-glycan recognition. Ontogeny analysis indicated that protruding loops develop early, and glycan interactions mature over time. The ontogeny-based design of vaccine antigens described here may provide a general means for eliciting antibodies of a desired class.

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

Novel Approaches for Vaccine Success

10:55 Physicochemical and Preclinical Evaluation of a Novel Buccal Measles Vaccine
Rikhav P. Gala, Ph.D. Candidate, Pharmaceutics, Mercer University
The measles vaccine microparticles were made with biocompatible and biodegradable bovine serum albumin (BSA) and processed by spray drying. There was significant induction of innate immune response by vaccine microparticles which was observed *in vitro* when compared to blank microparticles. The microparticles also significantly increased the antigen presentation and co-stimulatory molecules expression on antigen presenting cells, which is a prerequisite for Th1 and Th2 immune responses. The results suggest that the ODF measles vaccine formulation is a viable dosage form alternative to noninvasive immunization.

11:25 Presentation to be Announced

Biologics & Vaccines for Infectious Diseases

11:55 Antibody-Based Therapies against New World Arenavirus Hemorrhagic Fevers

Jonathan Abraham, M.D., Ph.D., Instructor, Biological Chemistry and Molecular Pharmacology, Harvard Medical School; Laboratory of Molecular Medicine, Boston Children's Hospital

The spillover of hemorrhagic fever viruses from their animal reservoirs into human populations continuously threatens public health. While most viral hemorrhagic fevers have limited treatment options, transfusions of immune plasma containing neutralizing antibodies are highly effective in treating hemorrhagic fever caused by the New World arenavirus Junín. This presentation will discuss the role of viral receptor-binding site directed monoclonal antibodies in the neutralization of New World arenaviruses and their potential roles as therapeutics.

12:25 pm Sponsored Presentation *(Opportunity Available)*

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

1:55 Session Break

Emerging Therapeutics

2:10 Chairperson's Remarks

Robert F. Garry, Ph.D., Professor, Microbiology & Immunology, Tulane Medical School; Co-Founder, Zalgen Labs

2:15 Human Monoclonal Antibodies for Immunotherapy of Ebola and Lassa Fever

Robert F. Garry, Ph.D., Professor, Microbiology & Immunology, Tulane Medical School; Co-Founder, Zalgen Labs

Combinations of potent broadly neutralizing monoclonal antibodies (mAbs) isolated from survivors of Lassa fever or Ebola protect in animal models even if treatment is delayed until after clinical signs of these diseases manifest. These results point to the potential utility of human mAbs against hemorrhagic fever viruses as improved immunotherapeutic drugs that can reduce costs of production with lower potential for adverse events than chimeric mouse-human mAbs.

2:45 The Impact of Adjuvants on Antibody Sequence Diversity and Protective Capacity in an Arboviral Disease Vaccine

Neal Van Hoeven, Ph.D., Senior Scientist, Infectious Disease Research Institute

Effective vaccine development for emerging and pre-pandemic diseases often requires the use of complex adjuvant formulations. Understanding the impact that these adjuvants have on the development of a complex anti-pathogen polyclonal antibody response is important to both refine and accelerate vaccine development. We have developed methods for analysis of antibody repertoire sequence data, and have applied these to investigate the mechanism by which vaccine adjuvants generate an effective antibody response.

3:15 High-Throughput Discovery of Natural Human Antibodies against Clinically Important Bacterial Pathogens

Ester Falconer, Ph.D., Senior Research Scientist. AbCellera

Natural immune repertoires from patients are a potential resource for fully human antibodies against diverse antigens, including "priority" pathogens that threaten global health. AbCellera's microfluidic platform combines flexible and robust assays with fast, ultra-deep screening of millions of B-cells from patients, to deeply mine natural immune repertoires for lead antibodies.

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, MAY 4

8:00 am Morning Coffee

Breakthroughs in Biologics

8:30 Chairperson's Remarks

Galit Alter, Ph.D., Associate Professor, Medicine; Kristine & Bob Higgins MGH Research Scholar; Director, Ragon Institute Imaging Core; Director, Harvard Center for Aids Research Immunology Core

8:35 Natural Infection-Inspired Monoclonal Antibody Design

Galit Alter, Ph.D., Associate Professor, Medicine; Kristine & Bob Higgins MGH Research Scholar; Director, Ragon Institute Imaging Core; Director, Harvard Center for Aids Research Immunology Core

The presentation will discuss new methods that utilize natural infection-inspired antibody design, as well as our current outcomes using this technique.

9:05 Exploiting Large Sized Cow Antibodies for Developing Novel Therapeutics and Vaccines

Azad Kaushik, DVM, D.Sc., Associate Professor, College of Biological Science, Department of Molecular and Cellular Biology, University of Guelph

Our laboratory discovered that bovine antibodies are the largest known to exist in a species because of an exceptionally long CDR3H (~61 amino acids). These 'Megabodies' offer an opportunity to develop new therapeutics and vaccines. An evidence for structural optimization of bovine scFvs to enhance viral neutralization potency will be presented. In addition, a 'proof of concept' for developing novel vaccines, via antigenization of bovine scFv with an exceptionally long CDR3H, will be presented.

9:35 Sponsored Presentation *(Opportunity Available)*

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

Promising & Emerging Biologics

11:05 Human Monoclonal Antibodies for Viral Diseases

James E. Crowe, Jr., M.D., Professor, Pathology, Microbiology & Immunology, Vanderbilt University

Biologics & Vaccines for Infectious Diseases

Viral pathogens already cause a significant proportion of human diseases, and emerging pathogens now regularly cause major unexpected outbreaks. Human monoclonal antibodies increasingly hold promise as the most rapid mode of therapy that can be developed and deployed for such outbreaks. We will review general principles of molecular recognition of viral pathogens by human antibodies, and illustrate these concepts with specific examples of therapeutic antibodies derived from the B cells of survivors of virus infections.

11:35 Human Antibody Cocktails for Universal Immunotherapy against Ebolaviruses

Anna Z. Wec, Microbiology & Immunology, Albert Einstein School of Medicine

Three ebolaviruses cause outbreaks of a lethal viral disease for which no approved treatments are available. Current-generation immunotherapeutics like the ZMapp™ mAb cocktail show promise, but suffer from lack of breadth, targeting only one of five known ebolaviruses. Here, we describe pan-neutralizing mAbs isolated from a human survivor of the 2014–16 Ebola epidemic in West Africa, and evaluate cocktails derived from them as immunotherapeutics potentially capable of combating outbreaks caused by any known ebolavirus.

12:05 pm Bioinspired Peptide Engineering to Combat Infectious Diseases

Cesar de la Fuente, Ph.D., Postdoctoral Associate, Biological Engineering, MIT/ Broad Institute of MIT and Harvard

Antibiotic resistance will kill 10 million people annually by 2050, costing the global economy $100 trillion. I will discuss our ongoing work engineering peptide therapeutics to counter biofilms and other difficult-to-treat infections.

12:35 End of Biologics and Vaccines for Infectious Diseases

3rd Annual | May 4-5, 2017

Agonist Immunotherapy Targets

Stepping on the Gas with Costimulatory Agents

THURSDAY, MAY 4

Case Studies with Agonist Antibodies

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Peter Ellmark, Ph.D., Principal Scientist, Research & Development, Alligator Bioscience

1:50 KEYNOTE PRESENTATION: Engineering of an ICOS Agonist Antibody for Cancer Therapy
Axel Hoos, M.D., Ph.D., Senior Vice President, Therapeutic Area Head for Oncology R&D, GlaxoSmithKline Pharmaceuticals, Inc.

2:20 Tumor-Directed Immunotherapy – Tumor-Localized Immune Activation Using TNFR-SF Agonistic Antibodies
Peter Ellmark, Ph.D., Principal Scientist, R&D, Alligator Bioscience
Alligator Bioscience develops mono and bispecific agonistic antibodies, targeting TNFR-SF members, for tumor-directed immunotherapy of cancer. This approach provides new opportunities to generate an effective, immune-mediated, anti-tumor response. Alligators pipeline projects will be presented, including ADC-1013, a human monospecific agonistic IgG1 antibody in clinical development and ATOR-1015, a bispecific antibody targeting OX40 and CTLA-4 developed to deplete Tregs in the tumor microenvironment.

2:50 OX40: From Bench to Bedside and Back Again
Brendan Curti, Director, Genitourinary Oncology Research, Immunotherapy Clinical Program, Providence Medical Group
Cancer immunotherapy is an evolving treatment that boosts the immune system to recognize and destroy cancer cells. Head and neck squamous cell carcinomas (HNSCC) produce suppressive factors that impair the immune system, thus limiting effective antitumor immunity. OX40 is a member of the tumor necrosis factor (TNF) receptor family and a potent co-stimulatory pathway that when triggered can enhance T-cell memory, proliferation and anti-tumor activity in patients with metastatic cancer.

3:20 Targeting Co-Stimulatory TNF Receptors with Hexavalent TNF Receptor Agonists (HERA)
Harald Fricke, M.D., COO/CMO, Apogenix AG

Sponsored By apogenix

3:50 Refreshment Break

4:20 Varlilumab, an Agonist Anti-CD27 Antibody, as Single Agent and in Combination
Tom Davis, M.D., Executive Vice President and CMO, Celldex Therapeutics Inc.
The CD27 co-stimulation pathway for immune cells has shown potent activity in pre-clinical models to eliminate tumors both as single agent and in combination with checkpoint inhibitors. Clinical trials to date using varlilumab, an agonist anti-CD-27 antibody, confirm this specific immune activation without significant immune toxicity. Single agent responses have been seen and multiple collaborative studies of varli in combination are ongoing.

4:50 JTX-2011: Development of an Agonist Antibody Targeting ICOS
Jennifer Michaelson, Ph.D., Executive Program Leader, Senior Director of Preclinical Development, Preclinical Development, Jounce Therapeutics Inc.
JTX-2011 is an agonist antibody to the co-stimulatory molecule ICOS. Preclinical studies demonstrated efficacy in syngeneic tumor models, with enhanced efficacy in combination with PD-1 inhibitors. JTX-2011 induces T effector cell activation and also preferentially reduces T regulatory cells in the tumors. This dual mechanism contributes to the significant anti-tumor response observed in preclinical models. A promising safety profile was revealed in preclinical studies. JTX-2011 is in clinical development as a monotherapy and in combination with anti-PD-1 therapy.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC18: Clinical Prospects of Cancer Immunotherapy
**Separate registration required, please see page 5-6 for course details.*

FRIDAY, MAY 5

8:00 am Morning Coffee

Emerging Science

8:30 Chairperson's Remarks
Roland Kontermann, Ph.D., Professor of Biomedical Engineering, Institute of Cell Biology and Immunology, University of Stuttgart

8:35 Duokines: A New Class of Bifunctional Immunostimulatory Molecules
Roland Kontermann, Ph.D., Professor of Biomedical Engineering, Institute of Cell Biology and Immunology, University of Stuttgart
Duokines are bifunctional fusion proteins of TNF ligand superfamily members expressed either as homotrimer molecules or as single-chain derivatives. They act

Agonist Immunotherapy Targets

either in cis or in trans and are capable of amplifying immune responses, e.g., as shown for the antitumor activity of T-cell retargeting bispecific antibodies.

9:05 The Tetravalent, Bispecific CD30/CD16A TandAb AFM13 is a Prototype NK-Cell Engager with Unique CD16A-Binding Properties
Martin Treder, Ph.D., CSO, Affimed, NV.
AFM13 is currently in Phase II clinical development in Hodgkin lymphoma (HL) and other CD30+ malignancies. It engages NK-cells through CD16A with high affinity and specificity and confers significantly stronger NK-cell activation compared to other therapeutic antibodies. We have previously shown synergistic efficacy when NK-cell activation through AFM13 is combined with checkpoint modulation such as anti-PD-1 treatment, which is known to unleash T-cell and NK-cell activity. Mechanism of action as well as mono- and combination therapeutic approaches of an NK-cell engager will be discussed.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Coffee Break

10:35 Agonist Redirected Checkpoints for Cancer Immunotherapy
Taylor Schreiber, M.D., Ph.D., Scientific Founder, R&D, Shattuck Labs, Inc.
This presentation will outline the production, pre-clinical characterization and early GMP manufacturing for a lead ARC construct that simultaneously blocks signaling through PD-1 and activates signaling through OX40. This construct demonstrates significantly superior tumor rejection in multiple pre-clinical models as compared to either PD-1/L1 or OX40 specific antibody therapy.

11:05 Selection of Fc for Antibody Therapeutics to Achieve Optimal Antitumor Immunomodulating Activity
Jieyi Wang, Ph.D., CEO, Lyvgen Biopharma
Therapeutic antibodies have become important biologics for cancer immunotherapy. Their modes of action not only rely on variable domains responsible for specificity but also involve the constant domains that can interact with various Fc receptors. Blocking antibodies such as nivolumab and pembrolizumab were successfully developed in the clinic as IgG4 molecules. However, it is not clear what IgG isotypes would be optimal for agonist antibodies that are required to activate co-stimulatory targets such as CD40, OX40, CD27, CD137, GITR, ICOS and HVEM.

Combinatorial Therapies: Using Antagonists and Agonists to Maximize Response

11:35 Enhancing Checkpoint Inhibitor Efficacy via Combination with CMP-001, a VLP Packaged TLR9 Agonist
Aaron Morris, Senior Director, Research, Checkmate Pharmaceuticals, Inc.
Addition of TLR9 agonist CMP-001 to a standard checkpoint inhibitor regimen can induce a strong anti-tumor response when checkpoint inhibition alone has failed. CMP-001 is a formulation of a CpG-A oligonucleotide, G10, within a Qb virus-like particle (VLP). Preclinical studies and a phase Ib clinical trial have shown induction of robust anti-tumor immunity and tumor regression when CMP-001 is combined with anti-PD-1 therapy.

12:05 pm Clinical Safety and Efficacy Assessment of CD137 in Combination with Nivolumab
Erminia Massarelli, M.D., Ph.D., MS, Associate Clinical Professor, Medical Oncology and Therapeutics Research, City of Hope

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

1:05 Refreshment Break

Target Discovery Approaches in Immuno-Oncology

1:35 Chairperson's Remarks
Harpreet Singh, Ph.D., President & CEO, Immatics US, Inc.

1:40 Exploring the Intracellular Proteome for the Identification and Validation of Novel Targets for Cancer Immunotherapy
Yoram Reiter, Ph.D., Professor & Head, Laboratory of Molecular Immunology, Technion-Israel Institute of Technology
T-cell receptor-like (TCRL) antibodies bind HLA-peptide complexes on the surface of cells and can bind specifically to the cell surface of diseased cells, thus, transforming intracellular disease-specific targets expressed inside malignant cells into targets that can be recognized on the cell surface by soluble TCRL antibodies. These antibodies can be armed with various modalities or they can be used as naked molecules to modulate responses or environments associated with immunity towards the target cells. This approach expands the pool of novel therapeutic targets and antibodies beyond the limits of currently available antibodies.

2:10 Novel Targets for Cancer Immunotherapies: The XPRESIDENT® Approach
Harpreet Singh, Ph.D., President & CEO, Immatics US, Inc.
Targeted adoptive cell therapies have been highly successful in achieving durable clinical responses in B-cell malignancies based on targeting CD19. Novel T-cell targets are required to expand this success to solid cancers. Here we present the outcome of the Human Immunopeptidome Program through applying our proprietary XPRESIDENT® target discovery strategy which employs systematic high-throughput and ultra-sensitive quantitative tandem mass spectrometry combined with next-generation sequencing and T-cell receptor discovery.

2:40 Development and Validation of a Phenotypic Screening Platform for the Identification of Novel Immuno-Oncology Targets
Christophe Quéva, Ph.D., CSO, iTeos Therapeutics SA
A co-culture assay combining immune suppressive cells and T-cells has been set up to allow the identification of novel immune-oncology targets by screening chemicogenomics, shRNA and cDNA libraries. Multi-parameter readouts are combined to assess both T cell activation and proliferation, through high content imaging, complemented with detection of IFNγ secretion, as well as tumor cell death, as assessed using a cytotoxicity assay. Application of this screening assay to the identification of rationale combinations will be described.

3:10 Emerging Innate Immune Targets for Enhancing Adaptive Anti-Tumor Responses

Michael Rosenzweig, Ph.D., Executive Director, Oncology Discovery, Merck Research Labs

Novel cancer immunotherapies targeting T cell checkpoint proteins have emerged as powerful tools to induce profound, durable regression and remission of many types of cancer. Despite these advances, multiple studies have demonstrated that not all patients respond to these therapies, and the ability to predict which patients may respond is limited. Harnessing the innate immune system to augment the adaptive anti-tumor response represents an attractive target for therapy, which has the potential to enhance both the percentage and rate of response to checkpoint blockade.

3:40 End of Conference

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Reach your target audience by presenting in the main session room as part of the conference program in your track of choice. Whether over lunch or part of the main agenda, conferences attendees will be seated and ready to listen to your talk. Presentations will sell out quickly! Sign on early to secure your talk.

Invitation-Only Dinner/Hospitality Suite

Sponsors will select their top prospects from the conference pre-registration list for an evening of networking at the hotel or choice local venue. CHI will extend invitations, conduct follow-up and confirm attendees. The evening will be customized to meet with your specific objectives.

Mobile App Sponsorship

PEGS provides all 2,100+ conference participants with a mobile app to facilitate communication and navigation of various event features.

Exhibit

Exhibitors will enjoy facilitated networking opportunities with qualified delegates. Speak face-to-face with prospective clients and showcase your latest product, service, or solution.

One-on-One Meetings

Sponsors will select their top prospects from the conference pre-registration list, and CHI will organize a guaranteed minimum number of face-to-face meetings.

Additional Opportunities Available for Sponsorship Include:

- Poster Awards
- Focus Groups
- User Group Meetings
- Conference Tote Bags
- Badge Lanyards - SOLD
- Hotel Room Keys
- Conference Notebook
- Footprints
- Program Guide Advertisement
- …and More!

Looking for additional ways to drive leads to your sales team?

CHI Lead Generation Programs will help you obtain more targeted, quality leads throughout the year. We will mine our database of over 800,000 life science professionals to your specific needs. We guarantee a minimum of 100 leads per program! Opportunities include:

- White Papers
- Web Symposia
- Custom Market Research Survey
- Podcasts

For sponsorship, exhibit & lead generation information, please contact:

Companies A-K
Jason Gerardi
Business Development Manager
781-972-5452 | jgerardi@healthtech.com

Companies L-Z
Carol Dinerstein
Senior Manager, Business Development
781-972-5471 | dinerstein@healthtech.com

FINAL DAYS TO REGISTER

Register Online!
PEGSummit.com

Cambridge HEALTHTECH Institute
25 YEARS
A Division of Cambridge Innovation Institute

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

Discounted Room Rate:
$280 s/d

Discounted Room Cut-off Date:
March 23, 2017

RESERVATIONS:
Please note that PEGS Boston is utilizing a trusted third party hotel booking service called Conference Technology Enhancements USA (CTE USA). CTE USA will work with you directly regarding hotel accommodations.

Go to the travel page of PEGSummit.com for additional information.

PEGS is one, if not the best, conferences I have attended in the last 5 years. Great program, excellent organization, perfect for networking and a beautiful location.
-Director, Discovery Research, Covagen AG

FINAL DAYS TO REGISTER

Register Online!
PEGSummit.com

Cambridge 25 YEARS HEALTHTECH Institute
A Division of Cambridge Innovation Institute

Pricing and Registration Information

	Commercial	Academic, Government, Hospital-affiliated
SHORT COURSE PRICING		
Choose 1 Short Course	$699	$349
Choose 2 Short Courses	$999	$599
Choose 3 Short Courses	$1199	$699
CONFERENCE PRICING		
Premium Package (Includes access to all conferences and Training Seminars Monday-Friday. Excludes short courses.)		
Early Registration until February 17, 2017	$2999	$1499
Advance Registration until March 17, 2017	$3149	$1699
Registration after March 17, 2017	$3349	$1799
Standard Package (Includes access to 2 conferences and/or Training Seminars. Excludes short courses.)		
Early Registration until February 17, 2017	$2549	$1229
Advance Registration until March 17, 2017	$2699	$1349
Registration after March 17, 2017	$2849	$1399
Basic Package (Includes access to 1 conference or Training Seminar. Excludes short courses.)		
Early Registration until February 17, 2017	$1649	$849
Advance Registration until March 17, 2017	$1799	$899
Registration after March 17, 2017	$1999	$1049

CONFERENCE DISCOUNTS

Poster Submission - Discount: ($50 off) Poster abstracts are due by March 17, 2017. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. *CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

The Antibody Society Members: (20% off) CHI is pleased to offer all Antibody Society Members a 20% discount to attend. Records must indicate you are a member at time of registration.

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: (20% off) CHI appreciates your participation at its events. Through loyalty like yours, CHI has been able to build this event into a must-attend for senior-level decision makers. 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. Just check off the box marked Alumni Discount on the registration form to receive the discount!

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

**Alumni, Protein Society, Twitter, LinkedIn, Facebook or any other promotional discounts cannot be combined. Discounts not applicable on Event Short Courses.*

How to Register: **PEGSummit.com**

reg@healthtech.com • P: 781.972.5400 or Toll-free in the U.S. 888.999.6288

Please use keycode PEGS F when registering

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.