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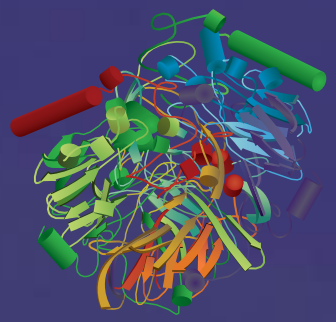

13TH ANNUAL

# 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

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**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 | |

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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.

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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., Vice President of Chemistry and Biochemistry, Bioptix*
*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*

**SC5: Introduction to Design of Experiments**
*Perceval Sondag, Senior Statistician, Non-Clinical Statistics, Arlenda*

**SC6: *In silico* Protein Docking**
*Vinodh B. Kurella, Ph.D., Ph.D., Senior Scientist, Molecular Engineering Unit, Intexon Corp.*

### 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*

**SC10: Bioanalysis of Biomarkers: ADCs, Multi-domain Biotherapeutics and New Modalities**
*Darshana Jani, M.S., Senior Manager, Pfizer, Inc.*

**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*

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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.*

## 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 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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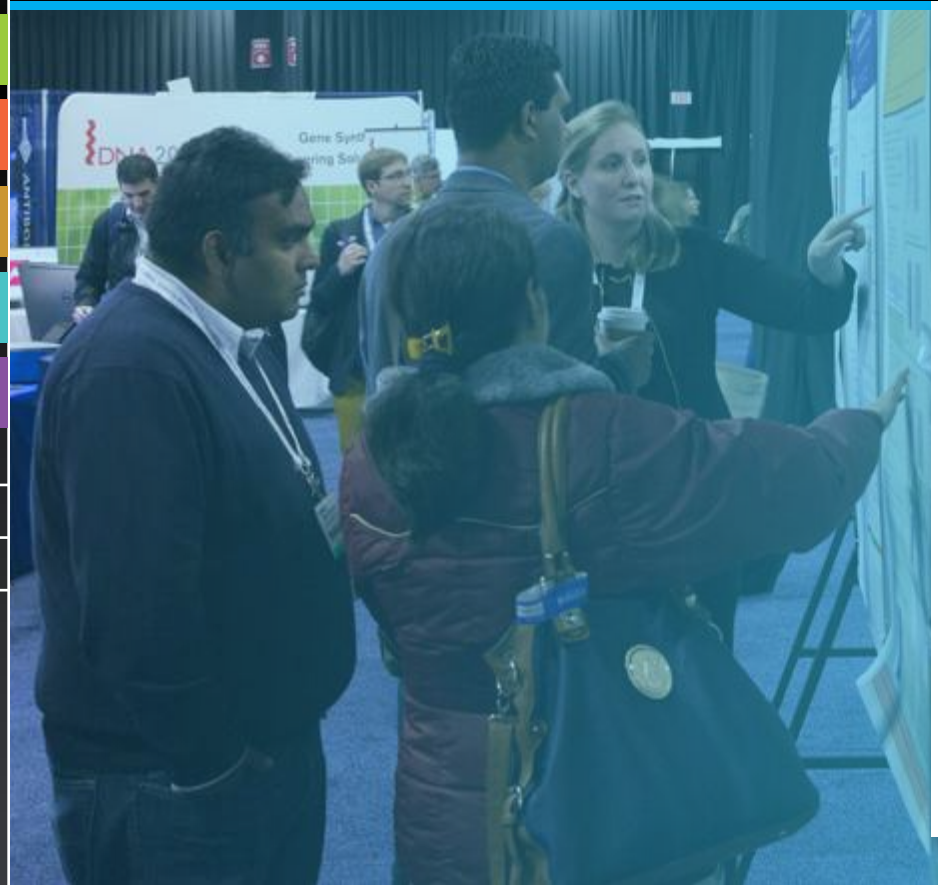
# STUDENT FELLOWSHIP

*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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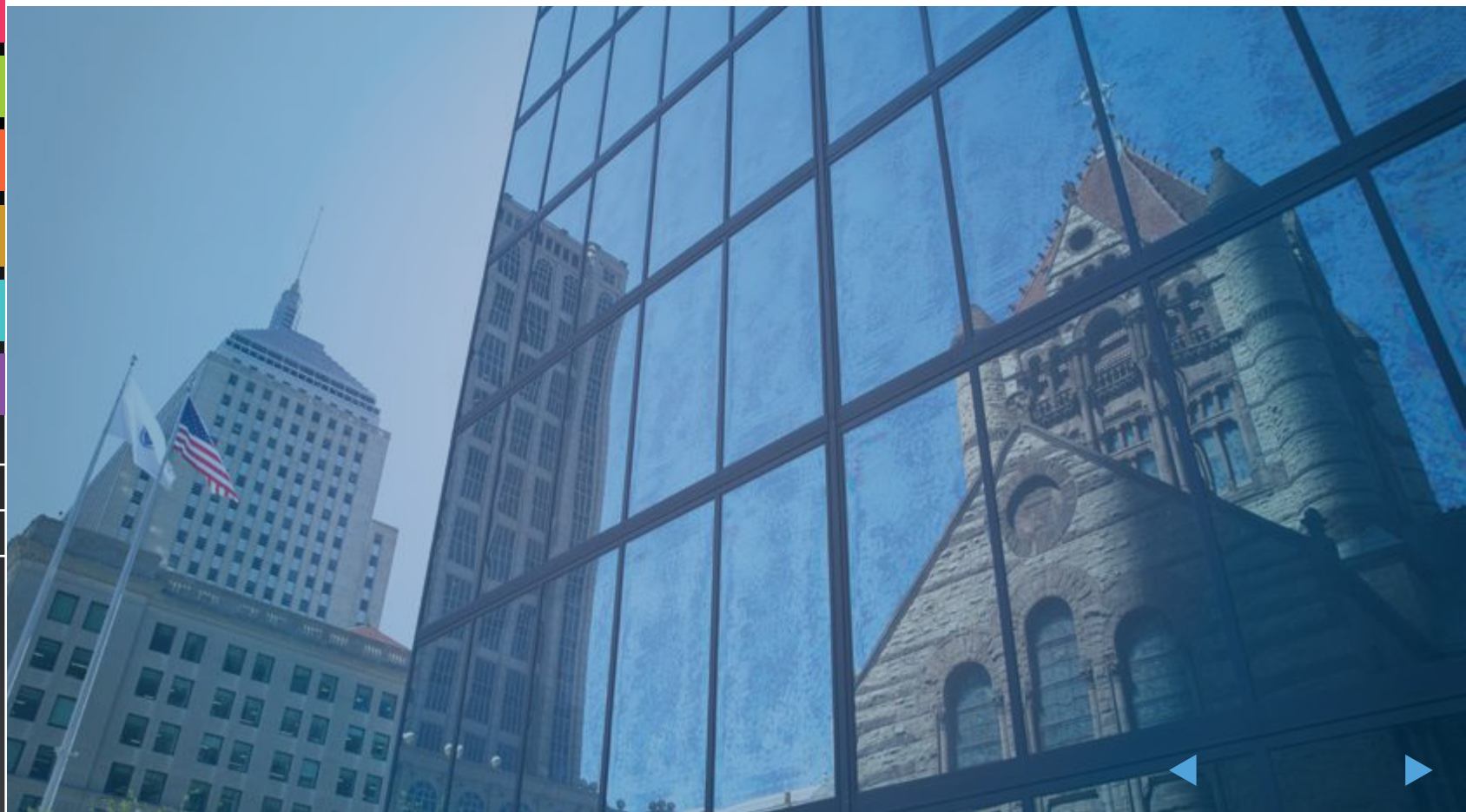
# ENGINEERING STREAM

- Display of Antibodies
- Engineering Antibodies
- Engineering Bispecific Antibodies



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**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**
*Bradley L. Pentelute, Ph.D., Pfizer Laubach Career Development Assistant Professor, Chemistry, Massachusetts Institute of Technology*
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 & Chief Scientific Officer, 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**

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

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# Display of Antibodies

**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**

## Epitope Mapping Strategies

**10:45 Chairperson's Remarks**

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

**10:50 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.

## 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.

**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**

## 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.

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# Display of Antibodies

**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 Sponsored Presentation** *(Opportunity Available)*

**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.

## New Platform Development of Phage Display of Antibodies

**4:55 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.

**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.*

# Engineering Antibodies

New Science and Technologies for the Selection, Engineering and Targeting of the Next Generation of Antibody Therapeutics

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**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 Application of Negative Stain TEM and 2D Class Averaging to Development of a Novel Biopharmaceutical**
*Ramkrishna Sadhukhan, Ph.D., Principal Research Scientist, Global Protein Sciences, AbbVie*

**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 then used to screen and isolate antigen-specific antibodies.

# Engineering 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, 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 Luncheon Presentation II** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

**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 Talk Title to be Announced**

Sponsored By isogenica

*Guy Hermans, CSO, Isogenica Limited*

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

Sponsored By CHEMICAL COMPUTING GROUP

*Nels Thorsteinson, 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 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**

*Aaron Chevalier, Ph.D., CSO, Virvio, Inc.; Translational Investigator, Institute of Protein Design, University of Washington*

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

# Engineering Antibodies

viral infectivity. These computationally designed binders represent a new class of protein therapeutics for infectious diseases.

*Sponsored By* SCHRÖDINGER. BIOLOGICS

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

***David Pearlman, 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**

***Gai Ayalon, Ph.D., Scientist, Neuroscience, Genentech***

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**

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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.*

## 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 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**
*Annelise Vuidepot, Ph.D., Head, Protein Science, Immunocore*
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 Tumor-Localized Costimulatory T-Cell Engagement by the 4-1BB (CD137) Bispecific Agonists PRS-343 (4-1BB/HER2) & PRS-342 (4-1BB/GPC3)**
*Christine Rothe, Ph.D., Vice President, Discovery & Alliance Management, Pieris Pharmaceuticals GmbH*
We used the Anticalin® platform to generate the 4-1BB-based bispecifics PRS-343 (4-1BB/HER2) and PRS-342 (4-1BB/GPC3). Both bispecifics lead to efficient tumor target-dependent T-cell activation in *ex vivo* assays. In a humanized mouse model, PRS-343 dose-dependently leads to strong tumor growth inhibition accompanied by high tumor infiltration with human lymphocytes (hCD45+). The positive functional data of PRS-343 and an excellent developability profile support investigation of its anti-cancer activity in clinical trials.

**5:20 End of Day**

# Engineering Bispecific Antibodies

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.*

## 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 **Sponsored Presentation** *(Opportunity Available)*

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., Executive Vice President, Biologics, Kadmon Corporation, LLC*
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**

# Engineering Bispecific Antibodies

**1:05 Refreshment Break**

## Compartmental Targeting and Payload Delivery Strategies

**1:35 Chairperson's Remarks**

*Mahiuddin Ahmed, Ph.D., Assistant Attending, Immunotherapies, Pediatrics, 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**

*Björn Hock, Ph.D., Senior Director, Global Head ADCs and Targeted NBE Therapeutics, Merck KGaA (Darmstadt, Germany)*

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

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**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, 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 Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on your Own**

**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**

**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**

# Antibodies for Cancer Therapy

## 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**

### 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.

**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**

# Antibodies for Cancer Therapy

## 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 Sponsored Presentation** *(Opportunity Available)*

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

## 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 A. Weiskopf, Ph.D., Research Scientist, Institute for Stem Cell Biology and Regenerative Medicine, Stanford University School of Medicine*
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 Aberrant Bispecific Antibody Clearance**
*Amita Datta-Mannan, Ph.D., Research Advisor and Group Leader, Eli Lilly and Company*
The present work evaluated factors *in vivo* that result in the aberrant peripheral clearance of several bispecific antibody (BsAb) constructs. Results showed rapid clearance of all the BsAbs *in vivo* that was not attributable to target binding, reduced FcRn interactions or poor molecular/biochemical properties. Evaluation of the cellular distribution of all the constructs suggested that the major clearance mechanism was linked to binding/association with liver sinusoidal endothelial cells.

**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.

**11:25 OMP-305B83: A Novel, Potent DLL4 & VEGF Targeting Bispecific Antibody for the Treatment of Solid Tumors**
*Jakob Dupont, Ph.D., Senior Vice President, Oncomed Pharmaceutical*
OMP-305B83 is a novel bispecific antibody that targets both Delta-like Ligand 4 (DLL4) ligand in the Notch pathway as well vascular endothelial growth factor (VEGF). This drug candidate has broad, potent anti-tumor activity in a wide variety of minimally passaged patients-derived tumor xenografts. This drug candidate also combines well with anti-programmed death receptor-1 (anti-PD1) therapy in preclinical models. OMP-305B83 is in clinical development in Oncology both as a single agent and in combination with several standards of care. Updated data will be presented.

**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.

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

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

# Advancing Bispecific Antibodies and Combination Therapy to the Clinic

**1:55 Session Break**

## 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 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 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**
*Chloé Ackaert, Ph.D., Post-Doctoral Researcher, Bioengineering Sciences, Camel Antibodies Lab, Cellular and Molecular Immunology, Vrije Universiteit Brussel (VUB)*
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 Sponsored Presentation** *(Opportunity Available)*

**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 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 Antibody Engineering & CMC, Affinita Biotech*
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**
*Scott J. Dylla, Ph.D., Vice President, Research & Development, CSO, AbbVie Stemcentrx, LLC*

- Tumor-initiating cells (TICs) remain controversial and will remain so until findings in the lab translate into drugs providing clear clinical benefit to patients
- Antibody-drug conjugates are a promising class of drugs able to target and specifically reduce the frequency of TICs

## Modeling and Simulation Approaches

**2:20 Novel Approaches for Modeling Pre-Clinical Activity of ADCs and Informing Biomarker Strategy**
*Carl Uli Bialucha, Ph.D., Director, Oncology Biotherapeutics, Novartis Institutes for Biomedical Research, Inc.*

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 Sponsored Presentation** *(Opportunity Available)*

**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 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.*

# Antibody-Drug Conjugates II: Advancing Toward the Clinic

## 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**
*Dario Neri, Ph.D., Professor, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology (ETH Zurich), and Co-Founder, Philogen*
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 Sponsored Presentation** *(Opportunity Available)*

**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 a Tumor-Specific ADC: From Discovery to Clinical Trials**
*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

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**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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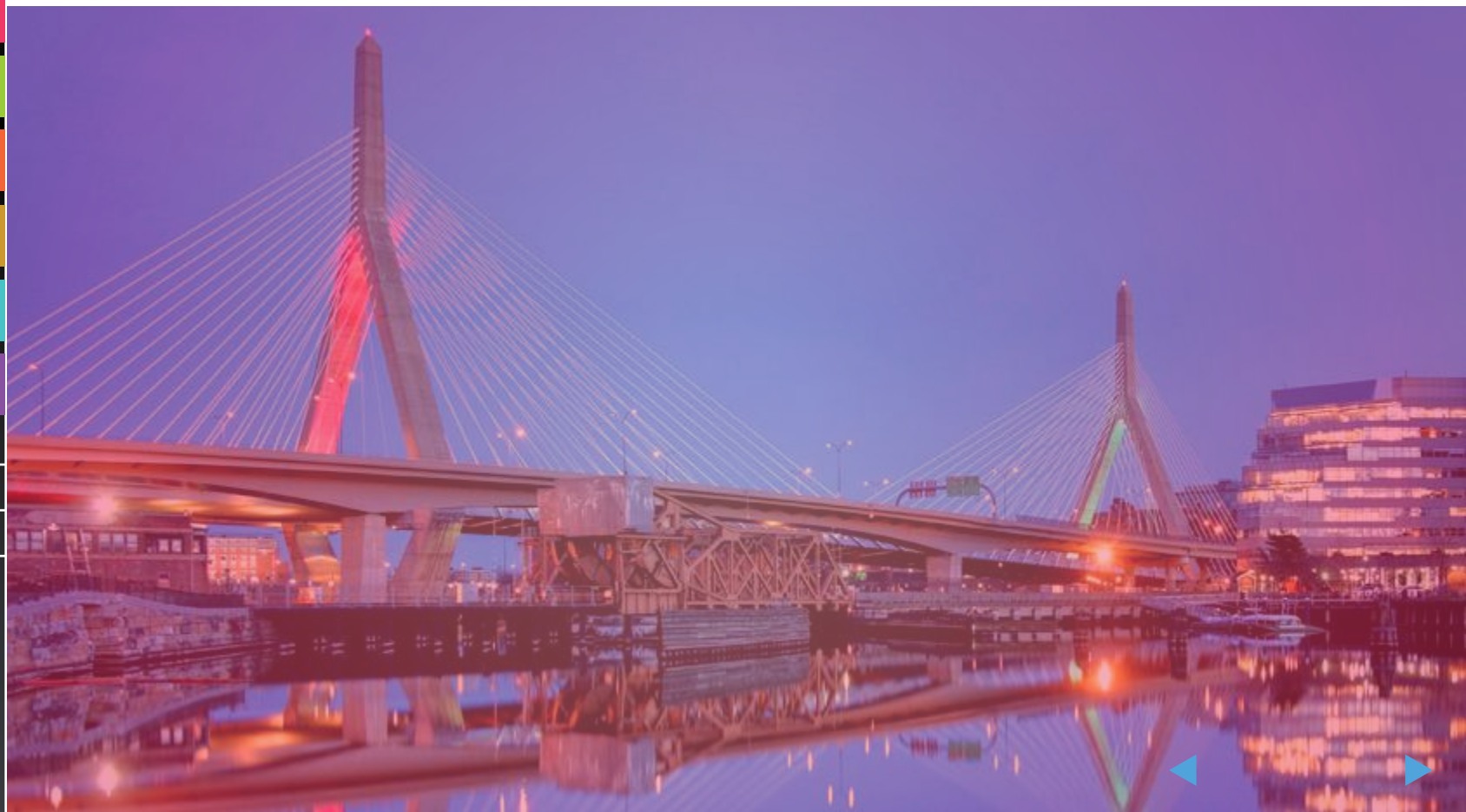
# IMMUNOTHERAPY STREAM

- 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 KEYNOTE PRESENTATION: Ensuring Safety of ImmTACTM Therapy: Development of a Preclinical Package**
*Bent Jakobsen, Ph.D., CSO, Immunocore Ltd.*
Immune Mobilising Monoclonal TCRs Against Cancer (ImmTAC) molecules are highly efficient and specific at targeting tumor cells. Essential to the development of ImmTAC molecules is a robust pre-clinical testing package, of which cross-reactivity is central. We have developed an extended safety package which includes not only normal cell screens but also specialised cell type cultures. Potential off-target toxicity is also identified through molecular analyses and further explored through pre-clinical testing.

**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.

### 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.

# Preventing Toxicity in Immunotherapy

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

**12:50 Luncheon Presentation I: Identifying Critical Receptor Targets and Off-Target Profiling Using Plasma Membrane Protein Array Technology**

*Sponsored By* RETROGENIX

***Jim Freeth, 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**

**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**

***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 with a small molecule definable mechanism in the case of THROTTLE-Switch™ and a logic gated decision paradigm in the case of synNotch™. 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**

# Preventing Toxicity in Immunotherapy

## 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.

**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 Immunogenises, Diagnoses and Management of Immune-Related Adverse Events**
*Adi Diab, M.D., Assistant Professor, MD Anderson Cancer Center*

**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 Sponsored Presentation** *(Opportunity Available)*

**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.*

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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**

### 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?**
*Dolores Schendel, Ph.D., CEO and CSO, 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 Enhancing Chimeric Antigen Receptor T Cell Therapy by Targeting Adenosine Mediated Immunosuppression**
*Paul Beavis, Ph.D., Senior Postdoctoral Researcher, Cancer Immunotherapy, Peter MacCallum Cancer Centre*
Recent evidence indicates that targeting adenosine-mediated immunosuppression enhances endogenous anti-tumor T cell responses and has resulted in several clinical trials targeting this pathway. We hypothesized that targeting adenosine may also enhance Chimeric Antigen Receptor (CAR) T cell function, thus making them more efficacious in solid cancers. Our studies have revealed that targeting A2A at either the genetic or pharmacological level significantly enhanced CAR T cell in immunocompetent mouse models.

**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*

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 **Sponsored Presentation** *(Opportunity Available)*

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.


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# Adoptive T Cell Therapy

**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**

# Agonist Immunotherapy Targets

Clinical Progress with CAR, TCR, and TIL

## 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 Sponsored Presentation** *(Opportunity Available)*

**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 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.

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# Agonist Immunotherapy Targets

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 **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.

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**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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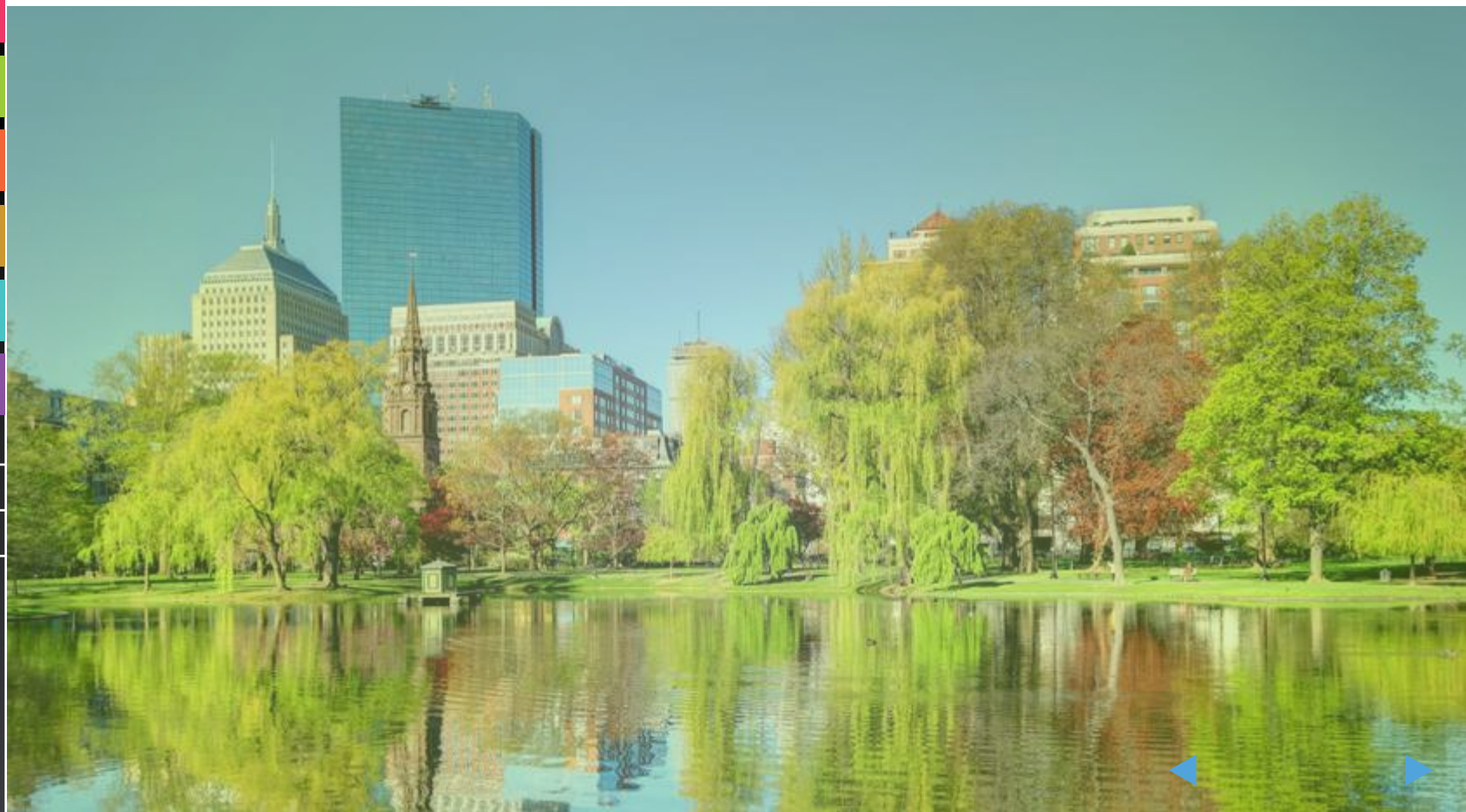
# EXPRESSION STREAM

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



# Difficult to Express Proteins

Strategies for Taming "Finicky" Proteins

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**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**
*Michael J. Betenbaugh, Ph.D., Department of Chemical and Biomolecular Engineering, Johns Hopkins University*
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**
*Danielle Tullman-Ercek, Ph.D., Associate Professor, Laboratory for the Engineering of Membrane Proteins and Protein Membranes, Department of Chemical and Biomolecular 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.

**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.

# Difficult to Express Proteins

**12:20 pm New Solutions for Production of Difficult-to-Express Proteins**

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***Guido Seidel, Managing Director, Operations, 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: Engineering of Antibodies for Humanization and Developability using Machine Learning**

*Sponsored By* DNA 2.0

***Speaker to be Announced***

**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**

**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 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**

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# Difficult to Express Proteins

***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 Luncheon Presentation I to be Announced**

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

**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.

**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.

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**3:05 Presentation to be Announced**

**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*

**12:25 pm 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.

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

# Optimizing Protein Expression

**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).

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**3:15 Presentation to be Announced**

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**3:30 The 3rd Generation Strep-tag® System – Superior Performance in Protein Purification and Assays with Strep-Tactin®XT**
*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**
*Min Zhang, Ph.D., Director, Manufacturing Sciences and Technology, AstraZeneca/MedImmune*

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

**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 Optimizing Genetic Tools and Production Strategies to Increase Protein Titers in Green Algae**
*Miller Tran, Ph.D., Associate Director, Triton Algae Innovations, Inc.*

**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**

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## 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.

**3:20 Sponsored Presentation** *(Opportunity Available)*

**3:50 Refreshment Break**

### Engineering Breakthroughs

**4:20 KEYNOTE PRESENTATION: Enhanced Protein Production in Mammalian and Insect Cells by Precise Genome Editing with the Cas9/CRISPR Technology**
*Lorenz M. Mayr, Ph.D., Vice President & Global Head, Biological Reagents & Assay Development, AstraZeneca R&D*
- Overview of established protein expression technologies at AstraZeneca
- Optimization of transient gene expression (TGE) technologies
- Precise genome editing (PGE) with the Cas9/CRISPR technology
- Use of PGE for the engineering of mammalian and insect cell lines
- Case studies for difficult-to-express proteins and protein complexes
- Summary and outlook

**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

**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 Sponsored Presentation** *(Opportunity Available)*

**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.*

**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 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.

# Protein Expression System Engineering

**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**

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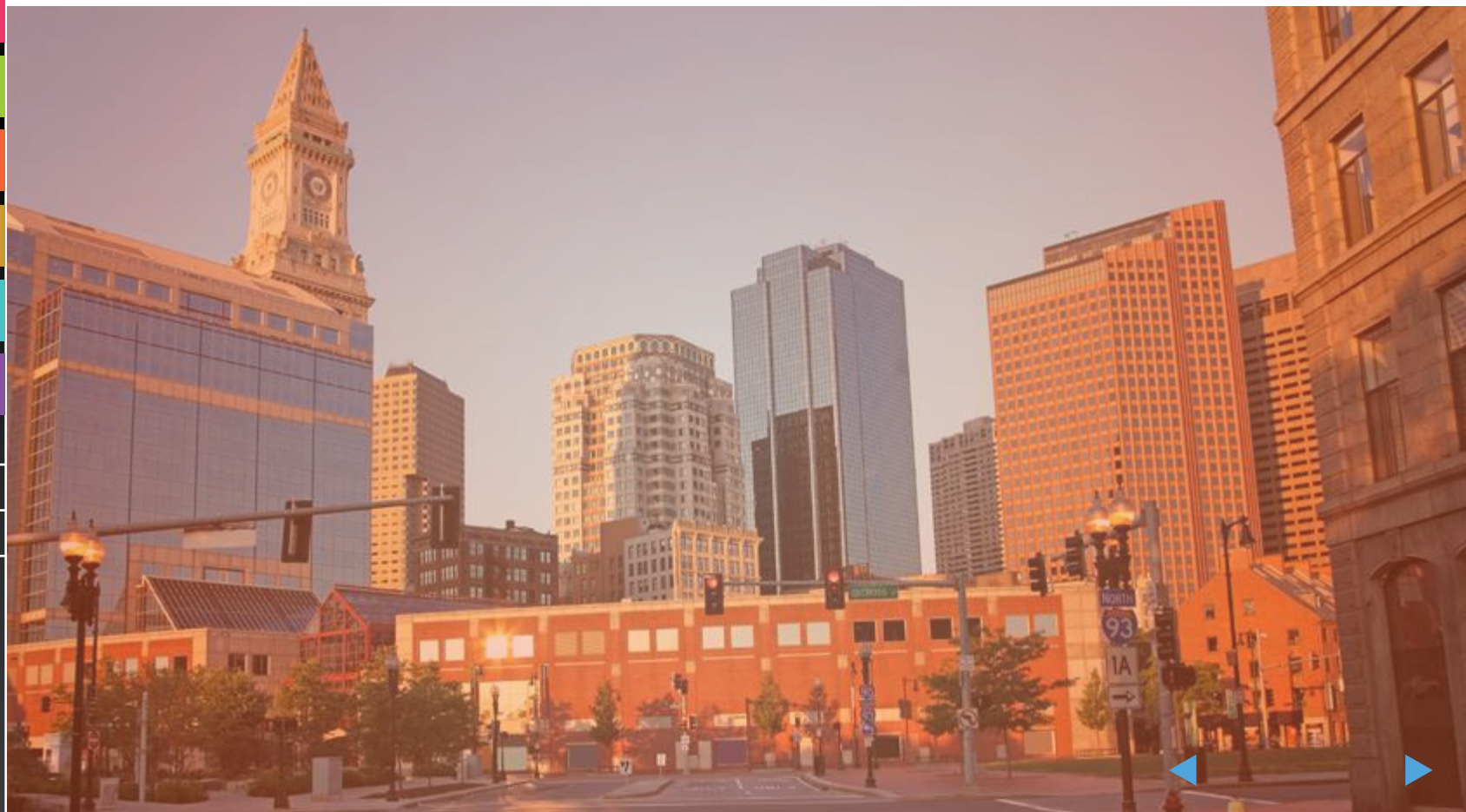
# ANALYTICAL STREAM

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



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**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 Insights in the Mode of Action of Angiopoietin 2 and VEGF Binding CrossMAbs**

*Joerg Regula, Ph.D., Head of Functional Characterization, Roche*

The CrossMAb technology enabled the design and manufacturing of bispecific antibodies. The CrossMAb targeting Ang2 and VEGF was the first project that was initiated and is currently in clinical trials. Initial experiments compared the *in vivo* efficacy of these CrossMAbs to the originating antibodies. This data set is aligned with the *in vitro* functional characterization data to gain novel insights in the interaction of the CrossMAb with its two ligands.

**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*

**12:35 Antibody Protein *De Novo* Sequencing with LC-MS/MS**
*Mingjie Xie, 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.

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

**1:50 Session Break**

**2:20 Problem-Solving Breakout Discussions**

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

## PLENARY KEYNOTE SESSION

**4:00 Chairperson's Remarks**

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

**8:30 Proteomics Characterization of Antibody-Nanoparticle Conjugates for Tumor Therapy**
*Raghuraman Kannan, Ph.D., Associate Professor, Radiology and Biological Engineering, School of Medicine, University of Missouri*
We hypothesized that by covalently attaching these two antibodies to a single nanoparticle would accelerate the cancer cell death in lower concentrations of antibodies. We will show covalent conjugation of two different antibodies to gold nanoparticle (AuNP) and characterization of the conjugates using Proteomics. We confirmed both the presence and the structural identity of antibodies covalently attached to AuNP using proteomics. The efficacy of this dual-antibody nanoconjugate and the mechanism of interaction with tumor cells will be presented.

**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.

### 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**

# Characterization of Biotherapeutics

**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 THE SCIENCE OF WHAT'S POSSIBLE.

***Ying Qing Yu, Senior Science Manager, Scientific Operations, Waters Corporation***

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

**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 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.

# Characterization of Biotherapeutics

**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

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**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 High-Throughput Screening Platform for the Formulation of Vaccines**

*Vanessa Jully, Ph.D., Scientist, Research & Development, GlaxoSmithKline*

A robust and rapid high-throughput screening (HTS) platform was developed for vaccine formulation. This platform brings together different applications into one unit: the automated handling of reagents and characterization. Data management was fully integrated using an IT application to collect and process raw data by creating an output file that can be used in data analysis software. This platform has the potential to accelerate significantly the development of new vaccines.

**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

Sponsored By NanoTemper technologies

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

*Dennis Breitspecher, Ph.D., Head of 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.

**12:40 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 and Doing Structural Biology *in situ***

*Juergen M. Plitzko, Ph.D., Head, TEM, Molecular Structural Biology, Max Planck Institute of Biochemistry*

To visualize and analyse molecular structures in their native state and in their cellular context is the overarching aim of *in situ* structural biology. We have seen stunning results of isolated molecular structures at atomic or near-atomic resolution obtained by single-particle cryo-EM. However, many supra- and macromolecular assemblies involved in key cellular processes cannot be studied in isolation. The challenge for us is to apply cryo-EM to protein complexes and other biological objects within their native environment within cells.

**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 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 End of Day**

## THURSDAY, MAY 4

**8:00 am Morning Coffee**

## Applications of Mass Spectrometry in Biophysical Analysis

**8:30 Chairperson's Remarks**

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

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

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

**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.

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**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**

# Protein Aggregation and Stability in Biopharmaceuticals

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

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**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**
*Ramil Latypov, Ph.D., Associate Director, Research & Development, Sanofi Genzyme*

**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.

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**3:20 Presentation to be Announced**

**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 Precipitation Methods to Assess Colloidal Stability**
*Ramil Latypov, Ph.D., Associate Director, Research & Development, Sanofi Genzyme*
The use of precipitation methods to assess colloidal stability of antibodies has become widespread. Concentrated antibodies can lose their colloidal stability through various phase transitions, including aggregation, gelation and crystallization. Colloidal stability assessments are done to characterize the propensity of antibodies and their formulations to undergo such phase transformations. PEG-induced liquid-liquid phase separation method has evolved into a fast and convenient way to quantitatively evaluate colloidal stability of antibody solutions.

**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.*

# Protein Aggregation and Stability in Biopharmaceuticals

## 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**
*Srivalli Telikepalli, Ph.D., Research Chemist, 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.

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

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

# Protein Aggregation and Stability in Biopharmaceuticals

**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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# 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

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**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**
*Priya Sriraman, Ph.D., Principal Investigator, Non-Clinical Safety, Celgene*

**8:40 Immunogenicity Assessment of Immunotherapies**
*Shefali Kakar, Ph.D., Executive Director, Head, Oncology, Clinical Pharmacology, Novartis*
As the number of Immuno-Oncology (IO) therapies in development continues to grow, it is important for immunogenicity scientists and related departments to prepare themselves for the unique challenges ahead. Using examples, this presentation will review the key challenges in IO immunogenicity assessment, risk mitigation and combination therapies.

**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 Risk Based Immunogenicity Strategy for mRNA Programs**
*Mark Ma, Ph.D., Senior Director, Bioanalytical Development, Alexion Pharmaceuticals*
An immunogenicity strategy is proposed based on the regulatory perspectives and scientific considerations on utilization of mRNA product for a broad range of protein-replacement applications. The risk-based approach is used in the development of Alexion immunogenicity strategy for mRNA programs.

**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 Sponsored Presentation** *(Opportunity Available)*

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

**1:50 Session Break**

**2:20 Problem-Solving Breakout Discussions**

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

# Immunogenicity: Regulatory and Clinical Relevance

## PLENARY KEYNOTE SESSION

**4:00 Chairperson's Remarks**

**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**
*Karl E. Griswold, Ph.D., Associate Professor, Thayer School of Engineering, 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 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**

# Immunogenicity: Regulatory and Clinical Relevance

## 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.

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**3:05 Considerations for Development Projects: Combination Therapy**
*Josefin-Beate Holz, Ph.D., Bioneer-Consulting, 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 Conduct of Clinically Meaningful Immunogenicity Assessment for Defining ADA Clinical Relevance**
*Linglong Zou, Ph.D., Director of Experimental Immunology, Biologics Assays and Technology, Teva*
Unwanted immunogenicity of a biologic may result in decreased drug concentrations, impaired clinical efficacy and/or lead to severe adverse events such as hypersensitivity reactions. Clinical impact assessment of anti-drug antibody requires well-designed immunogenicity assays, adequate sampling schedule, and parallel measurement of clinical efficacy, adverse events, and/or drug concentrations. In this presentation, a strategy and case studies will be illustrated for conducting clinically meaningful immunogenicity assessment to define ADA clinical relevance.

**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.*

# Strategies for Immunogenicity Assay Assessment

Improving Assay Detection Performance, Sensitivity and Relevance

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**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**

# Strategies for Immunogenicity Assay Assessment

## Interpreting ADA Data (Cont.)

**2:10 Chairperson's Remarks**
*Wendy White, Ph.D., Fellow and Scientific Director, Translational Sciences, MedImmune, LLC*

**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 Effect of ADA on PK Assays**
*Pérez Tosar Luis, Ph.D., Principle Scientist, Bioanalytical Scientist, UCB*

**9:05 SEC Based Method for Size Determination of Immune Complexes of Therapeutic Antibodies in Animal Matrix**
*Mario Richter, Ph.D., Principal Scientist, DMPK-BA, AbbVie, Inc.*
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.

**9:35 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**

3rd Annual | May 4-5, 2017

# 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 Sponsored Presentation** *(Opportunity Available)*

**3:50 Refreshment Break**

**4:20 Bioassay Development and Validation Strategies for Antibody-Drug Conjugates**
*Michelle Palmer, Ph.D., Director, Bioanalytical Science, 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.*

## 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

# Optimizing Bioassays for Biologics

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 Bioassays Design, Development and Validation**
***John Garza, Ph.D., Development Scientist II, Analytical Sciences, Alexion Pharmaceuticals***

**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 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**
***Walter Hoyer, Ph.D., Manager, Statistics, GSK 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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# BIOCONJUGATES STREAM

- Fusion Protein Therapeutics
- Antibody Drug Conjugates I : New Targets, Payloads and Alternative Formats
- 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**

**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 Synergistic Inhibition of R5 HIV-1 by the Fusion Protein (FLSC) IgG1 Fc and Maraviroc in Primary Cells: Implications for Prevention and Treatment**

*Olga S. Latinovic, Ph.D., Assistant Professor, Microbiology and Immunology, Institute of Human Virology, School of Medicine, University of Maryland*

We have previously shown that (FLSC) IgG1, a fusion protein containing gp120BAL and CD4, specifically binds cellular coreceptor CCR5, inhibiting R5 HIV entry in primary cells. We reported that treatment with the CCR5 antagonist Maraviroc increased exposure of the (FLSC) IgG1 binding sites on CCR5. We demonstrate that (FLSC) IgG1, strongly synergizes with Maraviroc inhibiting R5 HIV. This finding suggests that this combinatorial treatment has potential merit. Future *in vivo* studies are warranted.

**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 Luspatercept (ACE-536) Increases Hemoglobin and Reduces Transfusion Burden in Patients with Low or Intermediate-1 Risk Myelodysplastic Syndromes (MDS)**

*Asya Grinberg, Ph.D., Senior Director, Cell Biology and Protein Chemistry, Acceleron Pharma, Inc.*

**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 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

# Fusion Protein Therapeutics

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

**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 to a Highly Stable Consensus Albumin Binding Domain Allows for Tunable Pharmacokinetics**
***Karyn O'Neil, Ph.D., Senior Director and Venture Leader, Centyrex, Janssen R&D***
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 Presentation to be Announced**

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**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

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**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, Global Head of 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**

## KEYNOTE PRESENTATIONS

**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 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 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 Sponsored Presentation** *(Opportunity Available)*

**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.

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# ADCs I: New Targets, Payloads & Alternative Formats

**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 Explore Novel ADC Avenues through PDT and Bispecifics**

*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**
*Scott J. Dylla, Ph.D., Vice President, Research & Development, CSO, AbbVie Stemcentrx, LLC*

- Tumor-initiating cells (TICs) remain controversial and will remain so until findings in the lab translate into drugs providing clear clinical benefit to patients
- Antibody-drug conjugates are a promising class of drugs able to target and specifically reduce the frequency of TICs

## Modeling and Simulation Approaches

**2:20 Novel Approaches for Modeling Pre-Clinical Activity of ADCs and Informing Biomarker Strategy**
*Carl Uli Bialucha, Ph.D., Director, Oncology Biotherapeutics, Novartis Institutes for Biomedical Research, Inc.*

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 Sponsored Presentation** *(Opportunity Available)*

**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 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.*

# ADCs II: Advancing Toward the Clinic

## 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**
*Dario Neri, Ph.D., Professor, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology (ETH Zurich), and Co-Founder, Philogen*
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 Sponsored Presentation** *(Opportunity Available)*

**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 a Tumor-Specific ADC: From Discovery to Clinical Trials**
*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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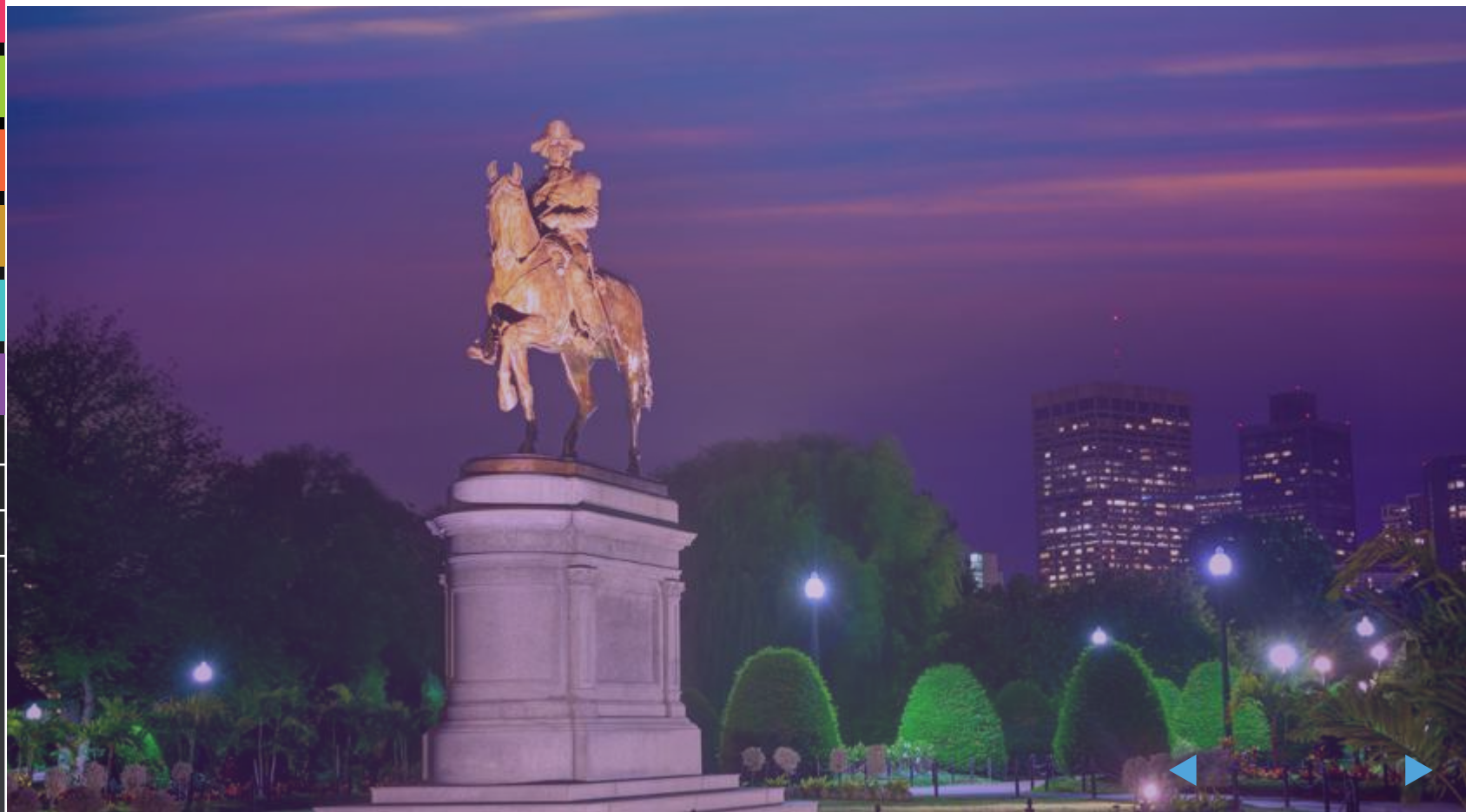
# THERAPEUTICS STREAM

- Drug Discovery for Autoimmunity and Inflammation
- Biologics and Vaccines for Infectious Diseases
- Agonist Immunotherapy Targets



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**
*Tony Manning, Ph.D., Vice President, Research, Momenta Pharmaceuticals*

**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**

**1:50 Session Break**

**2:20 Problem-Solving Breakout Discussions**

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

# Drug Discovery for Autoimmunity and Inflammation

## PLENARY KEYNOTE SESSION

**4:00 Chairperson's Remarks**

**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**

*Rudi Beyaert, Ph.D., Vice Department Director, Inflammation Research Center, 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 disease will be presented.

# Drug Discovery for Autoimmunity and Inflammation

**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 Sponsored Presentation** *(Opportunity Available)*

**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.*

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**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**
**Sean Gray, Ph.D., Vice President, PAI Life Sciences**

**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 Translational Activities to Enable Neglected Tropical Disease (NTD) Vaccines**
*Sean Gray, Ph.D., Vice President, PAI Life Sciences*

Despite significant promise to address global health needs, candidate vaccines for many NTDs proceed towards deployment slowly, and often fail to enter human clinical trials. PAI Life Sciences, Inc., located in Seattle, Washington, aims to bridge the gap between research and clinical testing by performing translational research on NTDs. By partnering with research organizations, we are working to move promising vaccine candidates for Schistosomiasis, Onchocerciasis, and Leishmaniasis to clinical trials with the goal of protecting people in the poorest countries from these debilitating NTDs.

# Biologics & Vaccines for Infectious Diseases

**11:55 Vaccine Vectors for Zika and Other Viruses**
*David M. Knipe, Ph.D., Department of Microbiology and Immunobiology, Harvard Medical School*
We have utilized herpes simplex virus recombinant viruses as vectors for expression of various microbial antigens as vaccine candidates, including HIV, influenza, SARS, anthrax protective antigen, and West Nile virus. This study highlights the flavivirus coding sequences needed for efficient assembly of virus-like particles. This information will facilitate generation of additional vaccine vectors against other flaviviruses including the recently emerged Zika virus.

**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 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 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*
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.

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**11:35 Human Antibody Cocktails for Universal Immunotherapy against Ebolaviruses**

*Kartik Chandran, Ph.D., Principal Investigator, Professor, 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**

# Agonist Immunotherapy Targets

Stepping on the Gas with Costimulatory Agents

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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**

*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 Sponsored Presentation** *(Opportunity Available)*

**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 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.

# Agonist Immunotherapy Targets

**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.

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**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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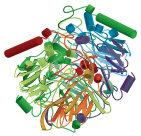


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