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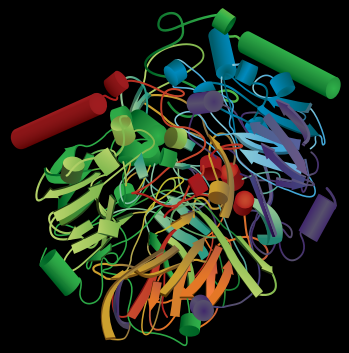

Cambridge Healthtech Institute's 12th Annual

PEGS BOSTON

the essential protein engineering summit

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PLENARY KEYNOTE SPEAKERS

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

Deborah Law, Ph.D., CSO, Jounce Therapeutics, Inc.

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CONFERENCE-AT-A-GLANCE

STREAMS	SUNDAY April 24	MONDAY April 25	TUESDAY April 26	WEDNESDAY April 27	THURSDAY April 28	FRIDAY April 29
ENGINEERING	PRE-CONFERENCE SHORT COURSES*	Phage and Yeast Display of Antibodies		Engineering Antibodies		Engineering Bispecific Antibodies
ONCOLOGY		Antibodies for Cancer Therapy		Advancing Bispecific Antibodies to the Clinic for Oncology		Antibody-Drug Conjugates II: Advancing toward the Clinic
IMMUNOTHERAPY		Preventing Toxicity in Immunotherapy		Adoptive T-Cell Therapy		Agonist Immunotherapy Targets
EXPRESSION		Difficult to Express Proteins		Optimizing Protein Expression		Protein Expression System Engineering
ANALYTICAL		Characterization of Biotherapeutics		Biophysical Analysis of Biotherapeutics		Protein Aggregation and Stability
IMMUNOGENICITY & BIOASSAYS		Immunogenicity: Regulatory and Clinical Case Studies		Strategies for Immunogenicity Assay Assessment		Optimizing Bioassays for Biologics
BIOCONJUGATES		Fusion Protein Therapeutics		Antibody-Drug Conjugates I: New Ligands, Payloads and Alternative Formats		Antibody-Drug Conjugates II: Advancing toward the Clinic
THERAPEUTICS		Biologics for Autoimmune Diseases		Biologics and Vaccines for Infectious Disease		Agonist Immunotherapy Targets
SHORT COURSES*			Dinner Short Courses*		Dinner Short Courses*	
TRAINING SEMINARS		Intro to Protein Engineering Intro to Formulation		Intro to Bioprocessing Regulatory Expectations for Analytical Elements of Biotechnology		

Separate Registration Required

"It is amazing how far the conference has evolved and grown since its early days. I really like the diversity of the topics and their relevance to the field of antibody engineering. Another attractive feature of the conference is a strong presence of the industry but at the same time a strong focus on the science."

- Senior Research Officer, National Research Council, Canada

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PLENARY KEYNOTE SESSION Monday, April 25 | 4:00 - 5:30 pm

Antibody Therapeutics: Past, Present and Future

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

Dr. Carter has ~30 years of biotechnology experience: Genentech (1986-2000 and 2010-present), Immunex/Amgen (2000-2003), Seattle Genetics (2003-2008) and VLST (2008-2009). His accomplishments in drug development include initiating the antibody humanization program at Genentech. He is a co-inventor of 5 antibodies that have entered clinical development including one that has become a commercial product - Herceptin® (trastuzumab). Additionally, Dr. Carter is a co-inventor of "knobs-into-holes" technology used to create the one-armed antibodies and bispecific antibodies. He also invented technology for high-level antibody fragment expression in *E. coli* used for Lucentis® (ranibizumab). He is an inventor or co-inventor on 41 issued US patents and 45 published patent applications.

Dr. Carter has authored or co-authored >100 scientific publications that together have been cited ~13,500 times. He has co-organized 12 international meetings on antibody engineering and antibody therapeutics. Dr. Carter has delivered >100 conference presentations and invited lectures including several keynote presentations. His professional experience includes heading the postdoctoral programs at Genentech (1998-2000), Immunex (2001-2002) and Amgen (2002-2003).

Dr. Carter received a BA in Natural Sciences from Cambridge University in 1982. He obtained a Ph.D. in 1986 under Sir Gregory Winter, Ph.D., FRS at the MRC Laboratory of Molecular Biology in Cambridge. From 1986-1989 Dr. Carter was a Postdoctoral Fellow with Dr. James A. Wells at Genentech.

The Promise of Cancer Immunotherapy: An Overview of Recent Advances and Jounce's Approach to Delivering the Right Therapy to the Right Patient

Deborah Law, D. Phil., CSO Jounce Therapeutics, Inc.

Deborah Law brings to Jounce nearly two decades of experience in biologics drug discovery and development, particularly in the fields of oncology and immunology. Dr. Law joined Jounce from Merck, where she most recently served as vice president of Therapy Area Biology for Immunology, Oncology and Immunomodulators. There, she was responsible for bringing cancer immunotherapy compounds from discovery to the clinic. Prior to Merck, Dr. Law served as the CSO for Ablynx n.v. and held various research positions in biotechnology companies including PDL Biopharma, EOS Biotechnology and Cor Therapeutics. Dr. Law holds a BSc in immunology from Glasgow University, a D. Phil. in immunology from Oxford University and pursued postdoctoral research at University of California, San Francisco.

Cambridge Healthtech Training SEMINARS

Comprehensive and Practical Training

MONDAY-TUESDAY, APRIL 25-26

Day 1: 8:30 - 5:30 Day 2: 8:30 - 12:30

TS1: Introduction to Protein Engineering

Instructor:
David Bramhill, Ph.D., Founder, Bramhill Biological Consulting, LLC and Research Corporation Technologies

The 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.

TS2: Introduction to Biologics Formulation and Delivery

Instructor:
Timothy Kelly, Ph.D., Vice President, Biopharmaceutical Development, KBI Biopharma, Inc.

The seminar focuses on strategies to plan and execute preformulation and formulation development studies for biologics, which require co-optimization of multiple physical, chemical and conformational stability attributes while operating under accelerated timelines to deliver the drug to the clinic. The course offers an overview of biophysical and biochemical properties of proteins, a typical development workflow and real-world examples.

WEDNESDAY-THURSDAY, APRIL 27-28

Day 1: 8:30 - 5:45 Day 2: 8:30 - 12:30

TS3: Introduction to Bioprocessing

Instructors:
Sheila G. Magil, Ph.D., Senior Consultant, BioProcess Technology Consultants, Inc.
Frank J. Riske, Ph.D., Senior Consultant, BioProcess Technology Consultants, Inc.

This seminar offers a comprehensive survey of the steps needed to produce today's complex biopharmaceuticals, from early development through commercial. The class steps through the stages of bioprocessing, beginning with the development of cell lines and ending at scaling up for commercial production – and explores emerging process technologies, facility design considerations and applicable regulatory and quality standards that govern our industry.

TS4: Current and Emerging Global Regulatory Expectations for Analytical Elements of Biotechnology/Biosimilar Products

Instructor:
Nadine M. Ritter, Ph.D., President & Senior Analytical Advisor, Global Biotech Experts LLC

This class presents the driving concepts that distinguish the regulatory approach to the production and testing of biologically derived molecules from chemical, small molecule pharmaceutical products. It provides a comprehensive overview of how analytical elements come together in global regulatory dossiers, and explains how regulatory dossier CMC sections are linked to analytical expectations in regulatory pre-approval inspections.

Each CHI Training Seminar offers 1.5 Days of instruction with start and stop times for each day shown 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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SHORT COURSES*

SUNDAY, APRIL 24 (10:00AM – 1:00PM)

SC1: Fluorescent Proteins in Protein Engineering
Andrew M. Bradbury, M.D., Ph.D., Staff Scientist, Biosciences, Los Alamos National Laboratory
Geoff Waldo, Ph.D., Research Scientist, Biosciences, Los Alamos National Laboratory

SC2: Bioanalytical Considerations of Multi-Domain Biotherapeutics: Preclinical and Clinical Development
Carol Gleason, MS, Principal Biostatistician, Bristol-Myers Squibb Co.
Yanchen Zhou, Ph.D., Scientist, Amgen Inc.
Darshana Jani, Ph.D., Senior Manager, Pfizer, Inc.
Priya Sriraman, Ph.D., Senior Principal Scientist, Nonclinical Safety, Celgene Corp
Heather A. Myler, Ph.D., Principal Investigator, Analytical and Bioanalytical Development, Bristol-Myers Squibb Co.

SC3: Antibody Humanization via One Hot Homology Model Workshop (Hands-On)
Vinodh B. Kurella, Ph.D., Senior Scientist, Molecular Engineering Unit, Intrexon Corp.

SC4: Translational Considerations for Development of Monoclonal Antibodies: Focus on Early Discovery (Part I)
Gadi Bornstein, Ph.D., Global Correlative Science Leader, Director, Novartis Pharmaceuticals
Randall Brezski, Ph.D., Scientist, Antibody Engineering, Genentech
Enrique Escandon, Ph.D., Senior Principal Scientist, DMPK and Disposition, Merck Research Laboratories
Vaishnavi Ganti, Ph.D., Senior Scientist, Biologics Discovery-DMPK, Merck Research Laboratories
Scott L. Klakamp, Ph.D., Vice President, Chemistry and Biochemistry, Bioptix
Mohammad Tabrizi, Ph.D., Head, Director & Senior Fellow, PKPD, Merck

SUNDAY, APRIL 24 (2:00 – 5:00PM)

SC5: Immunogenicity Risk Assessment and Regulatory Strategies
Bonnie Rup, Ph.D., Independent Consultant
Jim McNally, Associate Director, PDM Immunogenicity Expert, EMD Serono

SC6: *In silico* Immunogenicity Predictions (Hands-On) Workshop
Vinodh B. Kurella, Ph.D., Senior Scientist, Molecular Engineering Unit, Intrexon Corp.

SC7: Translational Considerations for Development of Monoclonal Antibodies: Focus on Nonclinical Development to Clinic (Part II)
Gadi Bornstein, Ph.D., Global Correlative Science Leader, Director, Novartis Pharmaceuticals
Randall Brezski, Ph.D., Scientist, Antibody Engineering, Genentech
Enrique Escandon, Ph.D., Senior Principal Scientist, DMPK and Disposition, Merck Research Laboratories
Vaishnavi Ganti, Ph.D., Senior Scientist, Biologics Discovery-DMPK, Merck Research Laboratories
Scott L. Klakamp, Ph.D., Vice President, Chemistry and Biochemistry, Bioptix
Mohammad Tabrizi, Ph.D., Head, Director & Senior Fellow, PKPD, Merck

TUESDAY, APRIL 26 (6:00PM-8:00PM)

DINNER

SC8: Next-Generation Sequencing of Antibody Libraries: Details on Experimental and Bioinformatic Methods
Sai Reddy, Ph.D., Assistant Professor, Biosystems Science and Engineering, ETH Zurich, Switzerland

SC9: Overcoming the Challenges of Immunogenicity Assessment
Jim McNally, Ph.D., Associate Director, PDM Immunogenicity Expert, EMD Serono
Valerie Theobald, Ph.D., Director, Bioanalytical Development, Shire

SC10: Analyzing and Rationalizing Protein-Protein Interactions
Nels Thorsteinson, Scientific Services Manager, Biologics, Chemical Computing Group
Alain Ajamian, Ph.D., Director, Chemical Computing Group

THURSDAY, APRIL 28 (5:45PM-7:45PM)

DINNER

SC11: Clinical Prospects of Cancer Immunotherapy
Gaurav Goel, M.D., Assistant Professor, Division of Medical Oncology, Medicine, University of Kentucky Markey Cancer Center
Weijing Sun, M.D., FACP, Professor, Medicine; Director, GI Cancers Section of Hematology-Oncology; Co-Director, GI Cancer Center of Excellence, Medicine/ Hematology-Oncology, University of Pittsburgh School of Medicine

SC12: Strategic Bioassay Design and Analysis
Liming Shi, MS, MA, Senior Research Scientist, Bioassay Development, Eli Lilly and Company

SC13: Critical Considerations for the Design and Development of Antibody-Drug Conjugates
Mohammad Tabrizi, Ph.D., Head, Director & Senior Fellow, PKPD, Merck
Isabel Figueroa, Ph.D., PTPK Scientist, Development Sciences, Genentech
Shawn Owen, Ph.D., Assistant Professor, Pharmaceutical Chemistry, University of Utah

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18th Annual | April 25 - 26

Phage and Yeast Display of Antibodies

Innovating Biologics

RECOMMENDED PRE-CONFERENCE SHORT COURSE*

SC1: Fluorescent Proteins in Protein Engineering

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

MONDAY, APRIL 25

7:00 am Registration and Morning Coffee

KEYNOTE SESSION

8:30 Chairperson's Remarks

Aaron K. Sato, Ph.D., Vice President, Research, Sutro Biopharma

8:40 KEYNOTE PRESENTATION: Serological Profiling of Antibody Targets Using a Synthetic Human Proteome

Stephen J. Elledge, Ph.D., Gregor Mendel Professor, Genetics, Harvard Medical School; Division of Genetics, Brigham and Women's Hospital; Investigator, Howard Hughes Medical Institute

I will present VirScan, a high-throughput method to comprehensively analyze antiviral antibodies using immunoprecipitation and massively parallel DNA sequencing of a bacteriophage library displaying proteome-wide peptides from all human viruses. We will show why the VirScan is a powerful approach for studying interactions between the virome and the immune system.

ADVANCES IN LIBRARY DESIGN

9:10 Preferential Germline Usage and VH/VL Pairing Observed in Human Antibodies Selected by mRNA Display

Lei Chen, Ph.D., Senior Scientist, Global Biologics, Abbvie, Inc.

We report here the development of an mRNA display technology and an accompanying HCDR3 size spectratyping monitor for human antibody discovery. We will show how we have identified trends and determined the productivity of each germline subgroup in the libraries that could serve as the knowledge base for constructing fully synthetic, next generation antibody libraries.

9:40 Fully Human Antibody Single Domains that Rival the Stability and Cleft Recognition of Camelid Antibodies

Daniel Christ, Ph.D., Associate Professor and Head, Antibody Therapeutics, Garvan Institute of Medical Research

Here we report the engineering and characterization of phage display libraries of stable human VH domains. Unlike 'camelized' human domains, the domains do not rely on potentially immunogenic framework mutations and maintain the structure of the VH/VL interface. Structure determination in complex with antigen revealed an extended VH binding interface, with CDR3 deeply penetrating into the active site cleft, highly reminiscent to what has been observed for camelid domains. Taken together, our results demonstrate that fully human VH domains can be constructed that are not only stable and well-expressed, but also rival the cleft binding properties of camelid antibodies.

10:10 Coffee Break

NEW USES OF PHAGE DISPLAY

Chairperson's Remarks

Aaron K. Sato, Ph.D., Vice President, Research, Sutro Biopharma

10:50 Matrix Guided Selection of Selective and Specific Affinity Ligands

Kimberly Kelly, Ph.D., Associate Professor, Biomedical Engineering, Robert M. Berne Cardiovascular Research Center, University of Virginia

Numerous applications such as targeted drug delivery and molecular imaging require the generation of high affinity targeted ligands. I will highlight a strategy that uses phage display as a starting point that utilizes quantitative and *in silico* methodologies as a means of rapidly generating high affinity targeted ligands for use in therapy and imaging. The discussion will be centered on pancreatic cancer as an example of the power of phage display derived peptide ligands.

11:20 Phage as a Surrogate for Counting miRNA Molecules in a Petri Dish

Chuanbin Mao, Ph.D., George Lynn Cross Research Professor, Chemistry & Biochemistry; Member, Peggy and Charles Stephenson Cancer Center, University of Oklahoma

T7 phage is used as a surrogate to establish a one-to-one correspondence between the macroscopic plaques and the target miRNAs. Target miRNAs crosslink a magnetic microparticle and one-to-one complexes of fluorescent phage and gold nanoparticles to form a sandwich complex. The phage is then released from the sandwich complex and developed into one fluorescent plaque in a Petri dish. Counting the plaques enables the multiplexed quantification of attomolar miRNAs.

11:50 Curing the Modern Dairy with Precision Microbiome Engineering

Nick Conley, Ph.D., CEO, EpiBiome

Bovine mastitis is an inflammation of the udder tissue, usually caused by bacterial infection, that results in annual losses of $35 billion and $2 billion to the global and US dairy industries, respectively. It is the #1 reason to treat a cow with small-molecule antibiotics. EpiBiome, an eleven-person, venture-backed precision microbiome engineering company based in South San Francisco, is using phage therapy as a replacement for small-molecule antibiotics to kill the bacteria that cause bovine mastitis.

Sponsored by Avacta LIFE SCIENCES

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

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

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

Sponsored by VACCINEX

12:50 Luncheon Presentation I: Antibody Library Display on a Mammalian Virus: Combining the Advantages of Panning and Cell Sorting in One Technology

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

We have developed an antibody discovery platform that enables efficient mammalian cell-based expression of a library of human antibodies in full length IgG format on the surface of a mammalian virus. Upon infection of mammalian cells, the antibody is not only incorporated into a newly produced virus, it is also displayed on the surface of the hosT Cell. This technology allows us to combine the advantages of virus panning and cell sorting into one technology.

Sponsored by aptaIT

1:20 Luncheon Presentation II: Improved Identification of Peptide and Antibody Ligands from Display Experiments by Analysis of Deep Sequencing Data

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

AptaIT's bioinformatic approach allows the exploitation of NGS data at very high resolution and therewith improves the identification of peptide and antibody ligands from display experiments. Besides quality control and optimization of libraries, early identification of rare but high quality ligands otherwise lost in the screening experiment as well as advanced screening strategies for difficult targets become possible. The wealth of comparative sequence data from

CONTINUED

18th Annual | April 25 - 26

Phage and Yeast Display of Antibodies

Innovating Biologics

the screening experiment is furthermore useful for subsequent lead optimization.

1:50 Session Break

2:20 Problem-Solving Breakout Discussions
See website for details.

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

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 The Promise of Cancer Immunotherapy: An Overview of Recent Advances and Jounce's Approach to Delivering the Right Therapy to the Right Patient
Deborah Law, D. Phil., CSO Jounce Therapeutics, Inc.
As immunotherapies become an increasingly important component of cancer treatment the challenge will be to identify ways to provide the best therapy(s) to the individual. This presentation will provide an overview of current cancer immunotherapies as well as highlight some of the challenges ahead including selection of optimal combinations, moving outside of T Cell-directed approaches, and will highlight how Jounce Therapeutics is using its Translational Science Platform as an approach to develop and deliver the right therapy to the right patient.

4:50 Antibody as Drugs: Then, Now and Tomorrow
Paul J. Carter, Ph.D., Senior Director and Staff Scientist, Antibody Engineering, Genentech
Antibodies have grown into a clinically and commercially important drug class with more than >45 antibodies marketed for imaging or therapy in the USA and/or Europe and with ~$63 billion in worldwide sales in 2013. This presentation will highlight progress in developing antibody drugs and consider opportunities for future innovation.

5:30 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 End of Day

TUESDAY, APRIL 26

8:00 am Morning Coffee

PHENOTYPIC SCREENING

8:25 Chairperson's Remarks
Andrew M. Bradbury, M.D., Ph.D., Staff Scientist, Biosciences, Los Alamos National Laboratory

8:30 Eukaryotic Virus and Cell Display for the Optimization of Antibodies
Mark J. Federspiel, Ph.D., Associate Professor, Molecular Medicine, Mayo Clinic
The availability of a robust, eukaryotic display technology comparable to phage display would improve the discovery and optimization of high affinity antibodies to important therapeutic targets by overcoming the protein translation limitations of microorganisms as well as more seamlessly transition into a large-scale mammalian expression system for clinical production. We will demonstrate that a eukaryotic retrovirus, Avian Leukosis Virus (ALV), offers such a robust, eukaryotic version of bacteriophage display.

9:00 Phenotypic Screening for Novel Antibody Targets in the Tumor Microenvironment
Ralph R. Minter, Ph.D., Fellow, Antibody Discovery and Protein Engineering, MedImmune Ltd.
The biopharmaceutical industry would benefit from better tools to discover and validate new antibody targets. Phenotypic antibody screening, which combines target-agnostic phage display with the early functional screening of antibodies, is an effective approach to target discovery and validation. Case studies will be presented to show that phenotypic screening has been successful in finding novel targets in the tumor microenvironment.

9:30 Generation of Antibodies Targeting Intracellular Oncogenic Mutations Presented by Common HLA Complexes
Andrew D. Skora, Ph.D., Postdoctoral Fellow, Ludwig Center for Cancer Genetics and Therapeutics, Johns Hopkins Kimmel Cancer Center
Genetics alterations of the KRAS oncogene are present in nearly all incidents of pancreatic cancer and half of colorectal cancer cases. We have devised a method to identify single chain variable fragments (scFvs) that target KRAS mutant epitopes present in the context of HLA-A2 on the cell surface. We demonstrate that scFvs identified through our technique can be successfully converted to full-length antibodies.

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

NEW APPLICATIONS AND TECHNOLOGIES FOR PHAGE AND YEAST DISPLAY

10:45 Chairperson's Remarks
Jennifer Cochran, Ph.D., Hitachi America Associate Professor, Bioengineering and Chemical Engineering, Stanford University

10:50 KEYNOTE PRESENTATION:
Phage-Assisted Continuous Evolution (PACE) of Proteins with Therapeutic and Industrial Potential
David R. Liu, Ph.D., Professor, Chemistry & Chemical Biology, Harvard University
Phage-assisted continuous evolution (PACE) enables proteins to evolve continuously in the laboratory. In this lecture I will describe the development and application of PACE to rapidly evolve a wide variety of proteins, several of which have potential to serve as novel therapeutic agents. In addition, I will describe a new effort that uses PACE to provide a solution to a major problem facing worldwide agricultural productivity: the rise of insects resistant to a widely used biological insecticide.

11:20 Shark-Derived Antibodies for Applications in Biotechnology and Medicine
Harald Kolmar, Ph.D., Professor & Head, Biochemistry, Technical University of Darmstadt
Due to their high affinity and specificity, physicochemical stability, small size and low-cost of production, single domain antibodies from sharks have evolved as promising target-binding scaffolds. We established a generic method for the isolation of shark-derived binding domains (sharkbodies) by yeast surface display obviating animal immunization. Tailor-made pH-selective as well as bispecific vNAR domains were generated for various applications in downstream processing and medicine.

11:50 Enhancing the Versatility of Yeast Display with Noncanonical Amino Acids
James A. Van Deventer, Ph.D., Assistant Professor, Chemical and Biological Engineering, Tufts University
The introduction of noncanonical amino acids into proteins offers attractive opportunities for engineering new classes of reagents, diagnostics, and therapeutics. We present here a noncanonical amino acid-compatible yeast display platform that enables the construction, evaluation, and screening of bioconjugates on the yeast surface.

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

PH DEPENDENT BINDING OF ANTIBODIES

CONTINUED

18th Annual | April 25 - 26

Phage and Yeast Display of Antibodies

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2:00 Chairperson's Remarks

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

2:05 Engineered Affibody Molecules Binding to the Neonatal Fc Receptor (FcRn) for Use in Medical Applications

Torbjorn Gräslund, Ph.D., Staff, Division of Protein Technology, School of Biotechnology, KTH Royal Institute of Technology and Affibody

The pH-dependent interaction of IgG (Fc) and serum albumin with FcRn results in extended serum circulation half-lives of these ligands and recombinant fusions including them. The talk will focus on alternative and much smaller affinity proteins (affibody molecules), capable of selectively interacting with FcRn in a pH-dependent manner. Examples of their potential use in different medical applications will be presented, including *in vivo* half-life extension and depletion of serum IgG.

2:35 The Creation of Potent Peptidic Inhibitors of Trypsin-Like Serine Proteases

Peter A. Andreasen, Ph.D., Professor, Molecular Biology and Genetics, Aarhus University

From phage-displayed peptide libraries, we isolated 10 – 12 amino acids long inhibitors of urokinase-type plasminogen activator, with Ki values around 0.5 mM. Through a maturation process involving additional library screenings, structure-based rational design, and the use of unnatural amino acids, we created highly specific urokinase inhibitors with Ki values down to 0.2 nM and retargeted the peptides from urokinase inhibitors to highly specific, high affinity inhibitors of plasma kallikrein.

3:05 Presentation to be Announced

Sponsored by

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

ANTIBODIES AGAINST ION CHANNELS AND DIFFICULT TARGETS

Chairperson's Remarks

K. Dane Wittrup, Ph.D., J.R. Mares Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

4:25 Identifying Antibodies Recognizing Plasma Membrane Targets

Eric V. Shusta, Ph.D., Howard Curler Distinguished Professor, Chemical and Biological Engineering, University of Wisconsin-Madison

Plasma membrane proteins represent key targets for many therapeutic applications. We have developed several different enabling platforms for the identification and engineering of antibodies against such targets. Here we will describe our recent efforts using phage and yeast display to increase the *in vivo* relevance of selected antibodies and to target specific molecular machinery present at the plasma membrane, such as that involved in endocytosis.

4:55 Ion Channel Topology Probed with Fibronectin-Domain Monobody Inhibitors

Randy B. Stockbridge, Ph.D., Assistant Professor, Biophysics and Molecular, Cell, and Developmental Biology, University of Michigan

The Fluc family of fluoride channels has an unusual and controversial architecture, with the subunits of the dimer arrayed in an antiparallel orientation. We established that topology using monobody inhibitors, based on a human fibronectic III domain scaffold, and selected using combinatorial phage- and yeast display libraries. In electrophysiological recordings, these monobodies block fluoride currents arising from single channels, allowing observation of single-molecule binding kinetics of the monobody applied sequentially to both sides of the membrane.

5:25 End of Phage and Yeast Display of Antibodies

5:30 Registration for Dinner Short Courses*

RECOMMENDED DINNER SHORT COURSE*

SC10: Analyzing and Rationalizing Protein-Protein Interactions

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

ALUMNI DISCOUNT

Cambridge Healthtech Institute (CHI) appreciates your past participation at our events. Through loyalty like yours, CHI has been able to build this event into a must-attend for senior-level decision makers. As a result of the great loyalty you have shown us, we are pleased to extend to you the exclusive opportunity to save an additional 20% off the registration rate. Just check off the box marked Alumni Discount on the registration form to receive the discount!

Please note: Our records must indicate you were an attendee at a past CHI event to qualify.

17th Annual | April 27 - 28

Engineering Antibodies

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

RECOMMENDED SHORT COURSES*

SC1: Fluorescent Proteins in Protein Engineering

SC8: Next-Generation Sequencing of Antibody Libraries: Details on Experimental and Bioinformatic Methods

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

WEDNESDAY, APRIL 27

7:00 am Registration and Morning Coffee

8:00 Chairperson's Remarks

James Ernst, Ph.D., Senior Scientist, Therapeutic Proteins, Protein Chemistry, Genentech

8:10 KEYNOTE PRESENTATION:
From Synthetic Antibodies to Synthetic Proteins

Sachdev Sidhu, Ph.D., Professor, Molecular Genetics, University of Toronto

We have used structure-based combinatorial design to build simple yet highly functional synthetic antibody libraries. The principles learned from antibody design have been applied to alternative natural scaffolds including ubiquitin and SH2 domains. Finally, we have developed highly optimized small scaffolds that are amenable to chemical synthesis to build D-amino acid binding proteins with traits favorable for therapeutic applications.

IMPROVING THE TARGETING OF ANTIBODY THERAPEUTICS

8:40 Retargeting T Cells in Hematologic Malignancies

Gerhard Zugmaier, M.D., Professor, Internal Medicine, Hematology/Oncology, Marburg University; Executive Medical Director, Global Development, Amgen Research Munich

Blinatumomab, the most advanced bispecific T Cell engager (BiTE), targets CD19 positive B cells. In patients with minimal residual disease (MRD) of B-precursor Acute Lymphoblastic Leukemia (ALL) blinatumomab induced molecular remissions resulting in an estimated relapse-free survival (RFS) of 60% at a follow-up of 31 months. In patients with relapsed/refractory B-precursor ALL blinatumomab induced remissions enabling successful allogeneic hematopoietic stem cell transplantation (HSCT). Blinatumomab induced durable responses in Non-Hodgkin Lymphoma.

9:10 Engineering Molecules for Cellular Uptake

Wouter Verdurmen, Ph.D., Postdoctoral Fellow, Biochemistry, University of Zurich

To accurately measure the delivery of proteins to the cytosol, the biotin ligase assay was developed that allows the objective quantification of cytosolic delivery. The method has been employed for comparing the cytosolic delivery of various engineered protein translocation mechanisms. This has enabled the identification of mechanisms that efficiently transport protein cargoes to the cytosol, as well as generated a detailed understanding of the characteristics that underlie efficient transport.

9:40 Blood-Brain Barrier Penetrating Dual Specific Binding Proteins for Treating Brain and Neurological Diseases

Denise Karaoglu Hanzatian, Ph.D., Principal Research Scientist, AbbVie Bioresearch Center

While naturally protective, the blood–brain barrier (BBB) provides a challenge for drug development as most of the small organic molecule drugs and nearly all biologics do not cross the BBB to reach therapeutically relevant concentrations. Here, we present the generation and expression of DVD-Ig proteins capable of binding specific disease targets in the brain. Uptake, retention and the elevated functional activity of DVD-Ig proteins in brain will be demonstrated.

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

10:55 An Fc Engineering Approach that Modulates Antibody-Dependent Cytokine Release Without Altering Cell-Killing Functions

Michelle Kinder, Ph.D., Scientist Immuno-Oncology Discovery, Janssen Research & Development, LLC

In addition to Fc-mediated targeT Cell-killing, therapeutic antibodies can elicit cytokine release from peripheral blood mononuclear cells and macrophages that can influence disease microenvironments and therapeutic outcomes. We describe an Fc engineering approach that results in macrophage-mediated phagocytosis and subsequenT Cell-killing without eliciting cytokine release from macrophages. When peripheral blood mononuclear cells are used as effectors, the resulting variants have similar cell-killing and cytokine release compared to IgG1.

OPTIMIZING ANTIBODY SELECTION AND SCREENING

11:25 Functional Antibody Screening Technology for Challenging Targets

Byeong Doo Song, Ph.D., President, Scripps Korea Antibody Institute

Current antibody screening technology is limited mostly to simple targets and has not been applied successfully to complex targets such as GPCRs, or ion channels. Scripps Korea Antibody Institute (SKAI) has developed functional antibody screening technology (FAST) that enables discovery of functional antibodies for targets of any structural complexity through individual & functional screening of spatially addressed antibody library using cell-based assays. Functional antibodies for GPCRs will be discussed.

11:55 *In vitro* Fab Display: A Next-Generation Antibody Discovery Platform

Ryan Stafford, Ph.D., Associate Director, Protein Engineering, Sutro Biopharma, Inc.

Once considered unviable, we have developed robust methods for discovering antibodies from large Fab libraries using ribosome display. Selected Fabs can be reformatted into full-length antibodies and directly expressed as IgGs in our cell-free platform for rapid screening. Lead IgGs usually have high affinity and excellent biophysical properties, but can also be easily affinity matured if necessary. Use of a common LC enables generation of IgG bispecifics.

12:25 pm Analysis of the Genomics and Transcriptomics of CHO-K1 to Accelerate and De-risk Biologics Development

Sponsored by SELEXIS

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

Detailed genomic and transcriptomic analysis of CHO-K1 can provide comprehensive data to supporT Cell line engineering and genomic characterization of research cell banks (RCB). We will present our CHO-K1 genome and transcriptome data and its use to enable the generation of RCBs for difficult-to-express proteins as well as support regulatory packages.

12:55 Luncheon Presentation I: Precisely Controlled, Highly Diverse Gene Mutant Libraries for Bioherapeutic Discovery and Development

Sponsored by TWIST BIOSCIENCE

Emily Leproust, Ph.D., CEO, Twist Bioscience

Critical to the success of bio-therapeutic discovery and development process is the availability of high quality libraries. By implementing a rational design approach and combining this with our expertise in synthetic DNA, Twist Bioscience delivers inexpensive, high diversity, high precision libraries with reduced turn-around time enabling optimization and acceleration of the design, build and test cycle.

1:25 Luncheon Presentation II: Uncovering Receptor Targets and Off-Targets Using Cell Microarray Technology

Sponsored by RETROGENIX

Jim Freeth, Ph.D., Managing Director, Retrogenix Ltd.

1:55 Session Break

EMERGING INDICATIONS FOR ANTIBODY THERAPEUTICS

2:10 Chairperson's Remarks

Carolyn Cuff, Ph.D., Leader, Translational Research & Investigation Unit, AbbVie Bioresearch Center, Inc.

2:15 A Novel Tissue-Specific Agonist of the FGF21 Pathway for the Treatment of Type 2 Diabetes

CONTINUED

17th Annual | April 27 - 28

Engineering Antibodies

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

James Ernst, Ph.D., Senior Scientist, Therapeutic Proteins, Protein Chemistry, Genentech

Activation of the FGF21 pathway has been shown to improve several features of type 2 diabetes in mice and humans. We have discovered a novel bispecific antibody that mimics the function and metabolic effects of FGF21. Treatment with this antibody improves glycemic and lipid profiles in mouse disease models. This talk will describe the discovery of an antibody that binds Klotho-Beta and FGFR1, thereby stimulating the cognate FGF21 co-receptor complex in adipose tissues.

2:45 Are PCSK9 Inhibitors the Next Breakthrough in the Cardiovascular Field?

Robert P. Giugliano, M.D., Senior Investigator, TIMI Study Group, Staff Physician, Cardiovascular Medicine, Brigham and Women's Hospital; Associate Professor, Medicine, Harvard Medical School

A potent new class of monoclonal antibodies directed again the PCSK9 protein represents the newest and most potent LDL-cholesterol lowering drugs currently available for clinical use. This talk will review their development, clinical efficacy and safety data, and the large phase III studies that are ongoing. The role of PCSK9 inhibition in the future management of patients with hypercholesterolemia will be explored.

Sponsored by CHEMICAL COMPUTING GROUP

3:15 Creating Focused Mutant Libraries for Protein Engineering

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

Protein engineering plays a pivotal role in modulating the function, activity and physical properties of biologics. However, the efficient search and evaluation of an excessively large sequence design space is challenging. Here we have developed a computational approach which predicts mutation probabilities for given residue sites in specified sequences. In assessing the probabilities at given residue sites, the sequence search space can be efficiently sampled to design and produce focused mutant libraries.

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

4:45 Problem-Solving Breakout Discussions

See website for details.

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

7:00 End of Day

THURSDAY, APRIL 28

8:00 am Morning Coffee

NEW TECHNOLOGIES FOR DISCOVERY AND ENGINEERING OF NOVEL ANTIBODIES

8:30 Chairperson's Remarks

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

8:35 High-Throughput Conformational Epitope Mapping to Guide Design of Structure-Based Vaccines

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

We have developed a novel method for rapid determination of fine conformational epitopes. This platform technology involves deep sequencing of yeast displayed antigen libraries. I will present determination of critical (and previously unknown) neutralizing epitopes for pertussis toxin and a breast cancer target. Further, I will discuss methodological improvements in throughput and cost needed to integrate epitope mapping upstream in candidate selection. Implications for structural vaccine design will be discussed.

9:05 Designer Libraries for Soluble, Membrane Anchored and Membrane Spanning Proteases for Monitoring Their Role in Disease

Charles S. Craik, Ph.D., Professor, Pharmaceutical Chemistry, University of California, San Francisco

Selective tools for studying an individual protease are important for characterizing its function and understanding its role in disease. Targeting specific proteases is challenging due to the high structural homology of enzymes in a given family. Our results highlight the value of biased Fab libraries and structure-guided design for efficient identification of protease inhibitors and development of selective antibody-based tools for determining the structure and function of serine proteases in disease and normal physiology.

9:35 Computational Advances in Antibody Design: Toward Improved Optimization and Selection

Sponsored by SCHRÖDINGER.

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

Recent computational advances hold significant promise both for improved prediction of antibody structure from sequence, and for the ability to precisely calculate physically relevant properties such as affinity and stability. When combined with additional theoretical approaches to identify liabilities, we can use these tools to variously optimize a lead antibody candidate and triage among multiple potential leads.

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

11:05 Unleashing the Structural Biology Toolbox to Facilitate Antibody Discovery

Jian Payandeh, Ph.D., Scientist, Structural Biology, Genentech

Structural biology can be leveraged in many ways to support therapeutic antibody discovery. Traditional applications at Genentech include facilitating structure-based antibody engineering efforts and understanding the mechanisms of antibody action. We have used insights from structural biology to engineer antigens and help guide our discovery campaigns, and we have implemented a high-throughput screening platform that streamlines the generation of challenging antigens, including ion channels, receptors, and GPCRs. Applications from our structural biology efforts will be described.

11:35 Human Antibody Transgenic Rabbits

Alain C. Tissot, Ph.D., Head, Immune Biology, Large Molecule Research, Roche Pharma Research & Early Development, Roche Innovation Center Penzberg, Roche Diagnostics GmbH, Switzerland

Antibodies generated in animal hosts represent the larger part of marketed therapeutic antibodies. Their generation undergoes positive and negative selection, delivering antibodies with robust therapeutic properties. Rabbits use a distinct diversity generation mechanism, which has long been exploited to achieve very high specificity. Humanization is, however, subsequently necessary. We report here on the generation of rabbits transgenic for human immunoglobulin genes, yielding therapeutic candidates of high affinity and specificity.

12:05 pm ABT-122, an Anti-TNF/IL-17 Dual Variable Domain Immunoglobulin (DVD-IgTM), Mechanisms of Translation: Bench to Bedside and Back Again

Carolyn Cuff, Ph.D., Leader, Translational Research & Investigation Unit, AbbVie Bioresearch Center, Inc.

ABT-122 is an anti-TNF/IL-17 dual variable domain immunoglobulin (DVD-Ig™) currently in Phase II clinical trials for Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA). As these chemokine receptors and cytokine responses have been suggested to play a role in disease pathology or its resolution, these data suggest that dual blockade of TNF and IL-17 by ABT-122 could provide a new therapeutic approach to patients with RA and immune mediated inflammatory diseases.

12:35 End of Engineering Antibodies

5:15 Registration for Dinner Short Courses*

RECOMMENDED DINNER SHORT COURSE*

SC13: Critical Considerations for the Design and Development of Antibody-Drug Conjugates

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

7th Annual | April 28 - 29

Engineering Bispecific Antibodies

The Future of Antibody Development

RECOMMENDED PRE-CONFERENCE SHORT COURSE*

SC2: Bioanalytical Considerations of Multi-Domain Biotherapeutics: Preclinical and Clinical Development

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

THURSDAY, APRIL 28

NOVEL APPROACHES TO ENGINEERING BISPECIFICS: ENHANCING FUNCTION

12:35 pm Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

G. Jonah Rainey, Ph.D., Senior Scientist, ADPE, MedImmune, LLC

» 1:50 KEYNOTE PRESENTATION:

Developing Dual-Specific and Bi-specific Antibodies for Cancer Treatment using Next Generation Maleimides (NGMs)

Kerry Chester, Ph.D., Professor, Molecular Medicine, University College London Cancer Institute

NGM conjugation technology can facilitate site specific labelling of the solvent accessible disulphide bonds in antibodies and their fragments. The versatility of this chemical approach also enables the construction of antibody fragment homo or hetero dimers and the incorporation of half-life extending technologies. The presentation will explore the potential of NGM technology to develop engineered antibodies for cancer therapy, both by site-specific attachment of warheads and as a flexible platform to create new bispecifics.

2:20 CrossMAb Vh-Vl and Fab

Jörg T. Regula, Ph.D., Head, Protein Analytics, Roche Diagnostics GmbH

The CrossMAb technology (Schäfer et al., 2011) can be used to generate a bispecific antibody from two independent parental antibodies by immunoglobulin domain exchange. The three different CrossMAb designs were named according to their exchanged domains: CH1-CL, Vh-Vl and Fab. The CrossMAb CH1-CL was used for the Ang2-VEGF CrossMAb (Kienast et al. 2013). The introduction of additional modifications renders the CrossMAb Vh-Vl and the CrossMAb Fab to suitable alternatives. The CrossMAb technology enables several bispecific molecules with 1+1, 2+1 or 2+2 binding sites.

2:50 Multimerization Strategy to Enhance Potency and Developability of Bispecific Antibodies

Mahiuddin Ahmed, Ph.D., Assistant Attending for Immunotherapies, Pediatrics, Memorial Sloan Kettering Cancer Center

Bispecific antibodies have proven to be highly efficient at re-directing T Cells for cancer immunotherapy. In order to enhance the anti-tumor potency and developability of tandem scFv bispecific antibodies (tsc-BsAbs or BITEs), we exploited the dimerization domain of the human transcription factor HNF1α to enhance the avidity of a tsc-BsAb to the tumor antigen disialoganglioside GD2 while maintaining functional monovalency to CD3 to limit potential toxicity.

3:20 Engineering Next-Generation Biotherapeutics: Developability & Manufacturability

Maria Wendt, Ph.D., Head , Science, Genedata

Next-gen biotherapeutics, specifically bi- and multi-specifics, alternative scaffolds and ADCs, provide significant advantages over traditional IgG-based molecules. As highly engineered molecules, they pose new design, cloning, expression, purification and analytics challenges. Our workflow platform automates the engineering, production, and testing of large panels of candidate therapeutic molecules. We demonstrate its capability to explore the huge combinatorial space of novel molecule-specific designs as well as its high-throughput capability and built-in tools for assessing developability and manufacturability.

3:50 Refreshment Break

4:20 Bispecific FynomAbs with Tailored Architecture and Novel Modes-of-Action

Simon Brack, Ph.D., Director, Discovery Research, Covagen (one of the Janssen pharmaceutical companies of Johnson & Johnson)

Covagen develops bispecific FynomAbs by fusing its human Fynomer binding protein to antibodies, resulting in bispecific protein therapeutics with novel modes-of-action and enhanced efficacy for the treatment of inflammatory diseases and cancer. We will present an update on COVA322, a clinical-stage bispecific TNF/IL-17A inhibitor that has the potential to improve currently existing anti-inflammatory therapies. Furthermore, we will present case studies demonstrating that FynomAbs with tailored architecture overcome limitations encountered with other therapeutic protein formats, such as suboptimal efficacy or lack of tumor selectivity.

4:50 How to Minimalize Antibodies: The Success of Antibodies as Pharmaceuticals has Triggered Interest in Crafting Much Smaller Mimics

Patrick J. McEnaney, Ph.D., Postdoctoral Researcher, Departments of Cancer Biology and Chemistry, The Scripps Research Institute Florida

In the past decade monoclonal antibodies have revolutionized the treatment of cancer. These antibodies possess excellent specificity and affinity for cell targets, and can perform their function through hijacking of native immune effector functions. However, the potential drawbacks are daunting, including immunogenicity, issues with scalability, storage and cost. This talk will look to leverage the specificity and efficacy seen with large biological agents through utilization of modular synthetic constructs, showing the development and optimization of a fully synthetic molecule capable of eliciting a targeted, specific immune response against prostate cancer.

5:20 End of Day

5:15 Registration for Dinner Short Courses*

RECOMMENDED DINNER SHORT COURSE*

SC11: Clinical Prospects of Cancer Immunotherapy

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

FRIDAY, APRIL 29

8:00 am Registration and Morning Coffee

TARGET COMBINATIONS FOR IMMUNOTHERAPY

8:30 Chairperson's Remarks

Robert Mabry, Ph.D., Director, Protein Sciences and Antibody Technology, Jounce Therapeutics

8:35 Arming of Effector T Cells or Tregs with BiTEs or CARs

Michael P. Bachmann, Ph.D., Director, Radio/Tumorimmunology, Institute of Radiopharmaceutical Cancer Research, Helmholtz Zentrum Dresden Rossendorf (HZDR)

In parallel to conventional BiTEs and CARs we established a modular platform technology (UniTARG) for retargeting of T Cells with complexes in either a BiTE (UniMAB) or CAR (UniCAR) format for simultaneous or subsequent application against different antigens, and, if requested, co-delivery of co-stimulatory or blocking signals. Armed effector T Cells were able to efficiently lyse targeT Cells while redirected Tregs failed but were fully functional in suppression of effector cells.

CONTINUED

7th Annual | April 28 - 29

Engineering Bispecific Antibodies

The Future of Antibody Development

9:05 Developing Full-Length CD3 Bispecific Antibodies: From Bench to NHP

Javier Chaparro-Riggers, Ph.D., Director, Antibody Technology, Rinat Pfizer, Inc.

The T Cell engaging antibody Blinatumumab against CD19 has been approved recently, but the short half-life makes continuous infusions necessary. We implemented a full-length IgG T Cell engaging platform, which increases the half-life and allows conventional dosing. Optimization of the platform from bench to NHP will be presented.

9:35 (scFab)2-Fc Type Bispecific Antibodies Engaging T Cells for Cancer Immunotherapy

Hyung-Kwon Lim, Ph.D., Senior Research Scientist, Antibody Engineering, MOGAM Biotechnology Institute

This presentation will describe a recent work for the (scFab)2-Fc format bispecific antibodies and its applications toward T Cell engagement for cancer immunotherapy. Using this platform, several bispecific antibodies targeting T Cell and tumor specific antigens were constructed. The challenges and opportunities of this format in terms of heterodimerization yield between two heavy chains, any modifications of Fc functions and mass analyses will be shared. In addition, performance of these antibodies such as T Cell activation and cytotoxic activities against several antigen specific tumor cells in the various experimental settings will be demonstrated.

10:05 Coffee Break

10:35 A Bispecific Antibody Targeting CD47 and CD20 Selectively Binds and Eliminates Dual Antigen Expressing Lymphoma Cells

Jie Liu, M.D., Ph.D., Senior Scientist, Institute for Stem Cell Biology and Regenerative Medicine, Stanford University

Anti-CD47 and CD20 BsAbs have been developed with reduced affinity for CD47, while retaining strong binding to CD20. These characteristics facilitate selective binding of BsAbs to tumor cells, leading to phagocytosis. BsAbs reduced tumor burden and extended survival in mouse xenograft lymphoma models, recapitulating the synergistic efficacy of anti-CD47 and anti-CD20 combination therapy. It may be broadly applied to cancer to add a CD47 blocking component to existing antibody therapies.

11:05 Engineering Bispecific Antibodies via Cell-Free and Conventional Mammalian Expression Systems

Jeonghoon Sun, Ph.D., Principal Scientist, Biotherapeutics, Celgene Corporation

Engineering asymmetric IgG-like bispecific antibodies via cell-free and conventional mammalian expression systems will be presented. Biophysical, biochemical and/or biological data sets will be compared between the two systems.

11:35 ADAPTIR Immunotherapeutics: A Unique Platform for Engaging T Cells

John W. Blankenship, Ph.D., Lead Scientist, Molecular Biology and Protein Engineering, BioSciences Division, Emergent BioSolutions

Emergent's ADAPTIRTM (modular protein technology) platform of bispecific protein therapeutics has unique and distinguishing properties, such as redirection of T Cell cytotoxicity with induction of minimal cytokine release compared to other formats. A pipeline of ADAPTIR therapeutics is currently under development from early discovery to clinical stage, targeting both solid and hematologic malignancies. Case studies will be presented for the development of two ADAPTIR therapeutics - MOR209/ES414 and ES425.

APPLICATIONS OUTSIDE ONCOLOGY

12:05 pm Chairperson's Remarks

Eric Smith, Ph.D., Associate Director, Bispecifics, Regeneron Pharmaceuticals

12:10 Case Study: Engineering of a Tetraspecific Anticalin Scaffold to Combat *Pseudomonas Aeruginosa* Infections

Carsten Corvey, Ph.D., Project Leader, Global Biotherapeutics, Sanofi-Aventis Deutschland GmbH

Highly specific Anticalin® binders were selected and further engineered against all iron-binding siderophores (Pvd I, Pvd II, Pvd III or Pch) of Pseudomonas aeruginosa. In this talk, we will show how siderophores-specific Anticalin proteins can possibly be used in the management of cystic fibrosis patients chronically infected by *P. aeruginosa* in order to improve lung health and safeguard the quality of life of patients.

12:40 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

1:10 Refreshment Break

1:40 A Tale of Two Bacteria: Developing Bispecific Antibody Drugs for *Pseudomonas aeruginosa and Clostridium difficile*

G. Jonah Rainey, Ph.D., Senior Scientist, ADPE, MedImmune, LLC

Pathogen-specific therapeutic strategies are gaining prominence as the antibiotic resistance crisis continues to grow. Ultra-narrow spectrum drugs provide unmet medical needs without contributing to broad antibiotic resistance. Given the adaptive nature of microbes to acquire resistance, two critical survival determinants often need to be targeted. A comprehensive strategic approach to select the most appropriate antibody technology platform given the target and pathogen will be described.

2:10 Bispecific Antibodies Perform a Disappearing Act

Katherine Cygnar, Ph.D., Staff Scientist, Genome Engineering Technologies, Regeneron Pharmaceuticals, Inc.

Herein we will present a novel method to block or destroy a target when the canonical blocking antibody approach has proved insufficient. We show that by using a bispecific antibody to couple a target to an internalizing 'effector' protein we are able to drive internalization and clearance of a target protein *in vitro* and *in vivo*. Several applications will be discussed.

2:40 Unique Application of Bispecific Antibody for Non-Oncology Disease Area

Shinya Ishii, Ph.D., Research Scientist, Discovery Research, Chugai Pharmaceutical Co., Ltd.

This talk will demonstrate two unique applications of bispecific antibody for non-oncology disease area. First application is a bispecific antibody against activated factor IXa and Factor X that mimics factor VIII function for the treatment of hemophilia A. Second application is biparatopic antibody against soluble antigen with pH dependent antigen property to accelerate the antigen clearance from plasma. Molecular design and *in vivo* data will be presented.

3:10 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.

3:40 End of Engineering Bispecific Antibodies

6th Annual | April 25 - 26

Antibodies for Cancer Therapy

Exploiting Successful Strategies

RECOMMENDED PRE-CONFERENCE SHORT COURSES*

SC4: Translational Considerations for Development of Monoclonal Antibodies: Focus on Early Discovery (Part I)

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

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

MONDAY, APRIL 25

7:00 am Registration and Morning Coffee

EMERGING TARGETS: KEYNOTE PRESENTATIONS

KEYNOTE PRESENTATIONS:

8:30 Chairperson's Remarks

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

8:40 IL-15 Augments Antibody-DependenT Cell-Mediated Cytotoxicity of Anticancer Monoclonal Antibodies

Thomas A. Waldmann, M.D., Co-Chief, Lymphoid Malignancies Branch; Senior Investigator, Head, Cytokine Immunology and Immunotherapy Section, Center for Cancer Research, National Cancer Institute

In clinical trials IL-15 increased the number of activated NK cells and monocytes in patients with metastatic malignancy. In a preclinical syngeneic tumor model IL-15 dramatically increased the ADCC efficacy of rituximab in the treatment of the human CD20 expressing murine EL4 leukemia model. IL-15 also augmented efficacy of the combination of anti-CTLA-4 and anti-PD-L1 anti-checkpoint antibodies. These studies support the use of IL-15 in combination with anticancer monoclonal antibodies.

9:10 Therapeutic Targeting of Breast Cancer Stem Cells

Max S. Wicha, M.D., Madeline and Sidney Forbes Professor, Oncology; Founding Director Emeritus, University of Michigan Comprehensive Cancer Center

Tumor heterogeneity represents the greatest challenge to the development of effective cancer therapies. In addition to genetic heterogeneity, tumors are hierarchically organized and driven by subpopulations of cells that display stem cell properties. These "cancer stem cells" also mediate tumor metastasis and contribute to treatment resistance. Both small molecule and antibody based therapies have been developed to target cancer stem cell populations. The assessment of clinical efficacy of cancer stem cell therapeutics will require innovative clinical trial design. Progress in developing cancer stem cell therapeutics will be reviewed.

9:40 Emerging Targets in Pediatric Cancers

Javed Khan, M.D., Deputy Chief, Genetics Branch; Senior Investigator, Head, Oncogenomics Section, National Cancer Institute

Despite improvement of survival rates in children with cancers over the past 20 years, patients with metastatic disease remain essentially incurable and novel therapies are required. I will describe strategies of using mRNA gene expression profiles to discover differentially expressed cell surface proteins in pediatric solid tumors. I will describe the Stand Up to Cancer St. Baldrick's Immunogenomics Dream Team's efforts to characterize the cell surfaceome of high risk pediatric solid cancers and to develop novel immunotherapeutic agents with a focus on targeting FGFR4.

10:10 Coffee Break

EMERGING TARGETS (CONT.)

Chairperson's Remarks

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

10:50 Targeting Sleeping Cancer Cells

Sridhar Ramaswamy, M.D., Associate Professor, Medicine, Massachusetts General Hospital Cancer Center, Broad Institute, Harvard University and MIT

We recently discovered a β1-integrin/FAK/mTORC2/AKT1/TTC3-associated signaling pathway that is triggered by rapidly proliferating cancer cells to undergo asymmetric division and produce slowly proliferating AKT1low daughter cells that are highly resistant to chemotherapy in patients with a variety of solid tumor types. These findings reveal that proliferative heterogeneity within cancer cell populations is produced through a potentially targetable signaling mechanism, with implications for understanding cancer progression, dormancy, and therapeutic resistance.

BISPECIFIC ANTIBODIES AND ADCs

11:20 Chairperson's Remarks

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

11:25 A Novel Auristatin-Based ADC that Targets PTK7

Marc Damelin, Ph.D., Associate Director, Oncology Research Unit, Pfizer, Inc.

PTK7 is a highly conserved, catalytically inactive kinase with oncogenic functions. We identified PTK7 by its enrichment on cancer stem cells, and we developed an auristatin-based anti-PTK7 ADC. The ADC induced sustained tumor regressions in preclinical tumor models and is currently in Phase I clinical testing. Two potential mechanisms that relate PTK7 to immuno-oncology will also be discussed.

11:55 Antibody-Drug Conjugates: Exploiting Differential Expression

Beverly A. Teicher, Ph.D., Chief, Molecular Pharmacology Branch, National Cancer Institute

Antibody-drug conjugates (ADCs) offer a unique therapeutic approach for treatment of solid and hematologic malignancies. ADCs deliver a potent cytotoxic agent on the backbone of an antibody specifically targeted to malignanT Cells. This two-pronged approach is predicted to provide a more efficient manner to destroy tumor cells while sparing normal tissues. The road of ADCs into clinical practice has not been an easy one; however, recent results have been positive.

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

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

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

See website for details.

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

CONTINUED

6th Annual | April 25 - 26

Antibodies for Cancer Therapy

Exploiting Successful Strategies

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 The Promise of Cancer Immunotherapy: An Overview of Recent Advances and Jounce's Approach to Delivering the Right Therapy to the Right Patient

Deborah Law, D. Phil. CSO Jounce Therapeutics, Inc.

As immunotherapies become an increasingly important component of cancer treatment the challenge will be to identify ways to provide the best therapy(s) to the individual. This presentation will provide an overview of current cancer immunotherapies as well as highlight some of the challenges ahead including selection of optimal combinations, moving outside of T Cell-directed approaches, and will highlight how Jounce Therapeutics is using its Translational Science Platform as an approach to develop and deliver the right therapy to the right patient.

4:50 Antibody as Drugs: Then, Now and Tomorrow

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

Antibodies have grown into a clinically and commercially important drug class with more than >45 antibodies marketed for imaging or therapy in the USA and/or Europe and with ~$63 billion in worldwide sales in 2013. This presentation will highlight progress in developing antibody drugs and consider opportunities for future innovation.

6:45 End of Day

TUESDAY, APRIL 26

8:00 am Morning Coffee

INTRACELLULAR ANTIGENS RECOGNIZED BY MONOCLONAL ANTIBODIES

8:25 Chairperson's Remarks

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

8:30 Intracellular Tumor Antigens as a Source of Targets for Antibody-Based Immunotherapy of Solid Tumors

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

It is generally assumed that to be recognized by an antibody in viable cells, the antigen has to be expressed on the plasma membrane of malignanT Cells. In this study we challenge this assumption and we show that the monoclonal antibody (mAb) W9, isolated from a phage human antibody library, recognizes an extracellular epitope of the chaperone molecule Grp94, which is located in the endoplasmic reticulum. mAb W9 recognizes many types of malignanT Cells, but does not stain normal cells. Because of the role of Grp94 in the biology of malignanT Cells, mAb W9 displays anti-tumor activity both *in vitro* and *in vivo*.

9:00 Targeting Intracellular Oncoproteins with Immunotherapies

*Qi Zeng, Ph.D., Research Director and Professor, Institute of Molecular and Cellular Biology, A*STAR*

Traditionally, antibody therapy has been limited to target extracellular oncoproteins, leaving large intracellular oncoproteins untapped. Professor Zeng will discuss a new concept of 'Targeting Intracellular Oncoproteins with Antibody Therapy or Vaccination' to vastly widen and usher a new era of cancer immunotherapies. The pioneer research works and views can be found in Cancer Biology & Therapy, 2008; Science Translational Medicine, 2011, Oncotarget, 2012; Cancer Research, 2013; FEBS, 2014.

9:30 Targeting Stress-Inducible Chaperone GRP78 in Cancer

Amy S. Lee, Ph.D., Professor, Biochemistry & Molecular Biology, Keck School of Medicine of University of Southern California, USC Norris Comprehensive Cancer Center

Glucose Regulated Protein GRP78 (HSPA5) is traditionally regarded as an endoplasmic reticulum chaperone protein critical for protein folding and control of the unfolded protein response. However, a subfraction of GRP78 can relocalize to the cell surface where it exerts regulation on signaling, proliferation, invasion and apoptosis. The preferential expression of GRP78 on the surface of tumor cells but not normal organs *in vivo* enables antibody-based tumor specific therapy.

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

FROM THE IMMUNO-ONCOLOGY TRENCHES: PRECLINICAL MONOTHERAPY, ANTIBODY COMBINATION AND BISPECIFIC ANTIBODY APPROACHES

Chairperson's Remarks

John Haurum, M.D., CEO, F-star GmbH & F-star Biotechnology Ltd.

10:50 Epacadostat (INCB024360): A Novel First-In-Class Inhibitor of IDO1 as Monotherapy and in Combination with other Checkpoint Inhibitors

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

Antibodies to CTLA-4 and PD1/PDL1 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) emerged as an immunotherapy target due to its role in regulating T Cell responses. The preclinical characterization and clinical activity of epacadostat, a first-in-class, potent, selective and orally bioavailable small molecule IDO1 inhibitor will be described.

11:20 Glypican-3 as a Liver Cancer Target for Antibody-Based Therapies

Mitchell Ho, Ph.D., Chief, Antibody Therapy Section, Laboratory of Molecular Biology, NIH NCI

Glypican-3 (GPC3) is expressed in hepatocellular carcinoma. We have developed human monoclonal antibodies that recognize functional sites in GPC3 and inactivate Wnt/Yap signaling pathways known to be important for liver cancer pathogenesis. HN3 is a human heavy-chain antibody that recognizes the core protein of GPC3. The HS20 human antibody recognizes the heparan sulfate chains on glypicans. Furthermore, we found that the HN3-based immunotoxin caused regression of liver cancer in mice. Its mechanism appears to involve both inhibition of cancer signaling (Wnt/Yap) and reduction in protein synthesis. Our recent work establishes GPC3 as a candidate for immunotoxin-based liver cancer therapy.

11:50 Antibodies Targeting Peptide/HLA Complexes for Cancer Therapy

Stefanie Urlinger, Ph.D., Director, R&D, MorphoSys AG

Tumor-specific peptide / HLA complexes make intracellular targets accessible to antibodies. However, the generation of therapeutic antibodies, which recognize a particular peptide / HLA complex specifically, is highly challenging. By identifying and applying appropriate counter-targets we generated fully human, high affinity antibodies against a WT1 peptide / HLA complex. These antibodies bind to target-positive cancer cell lines and outperform similar state-of-the-art antibodies regarding target specificity and binding affinity.

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

CONTINUED

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6th Annual | April 25 - 26

Antibodies for Cancer Therapy

Exploiting Successful Strategies

FROM THE IMMUNO-ONCOLOGY TRENCHES: PRECLINICAL MONOTHERAPY, ANTIBODY COMBINATION AND BISPECIFIC ANTIBODY APPROACHES (CONT.)

2:00 Chairperson's Remarks

John Haurum, M.D., CEO, F-star GmbH & F-star Biotechnology Ltd.

2:05 Combination Immunotherapy in Treating Advanced Cancer

Tara C. Gangadhar, M.D., Assistant Professor, Medicine, Hematology-Oncology Division, Abramson Cancer Center of the University of Pennsylvania

Novel immune therapies have demonstrated increasing efficacy in treating patients with advanced cancer. However, most patients remain resistant to these therapies. An overview of the current strategies to combine immune therapy approaches to improve outcomes and the ongoing research to develop predictive biomarkers of response.

2:35 Rapid Assessment of Bispecific mAb2 Molecules against Immuno-Modulatory Targets

John Haurum, M.D., CEO, F-star GmbH & F-star Biotechnology Ltd.

A bottleneck in the discovery of therapeutic bispecific antibodies is the lengthy process of generating stable molecules with sufficient quality and quantity to enable functional assessment and *in vivo* POC studies. F-star's proprietary Modular Antibody TechnologyTM addresses this through a robust "plug and play" process allowing the rapid testing of multiple target-specific combinations *in vivo*. Examples will be provided from the testing of several immuno-oncology products.

3:05 Sponsored Presentation *(Opportunity Available)*

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

ANTIBODIES IN THE CLINIC TO WATCH IN 2016

4:25 Cancer Antibodies to Watch in 2016

Janice M. Reichert, Ph.D., Managing Director, Reichert Biotechnology Consulting LLC

The success of novel antibody therapeutics for cancer has made them a primary focus of the biopharmaceutical industry, and antibody-drug conjugates (ADCs) and bispecifics are the most exciting of the antibody formats. This presentation will provide an update on ADCs and bispecifics in clinical development, and, for context, an overview of all antibodies in clinical studies for cancer. Recent approvals and antibodies in regulatory review will also be discussed.

5:25 End of Antibodies for Cancer Therapy

5:30 Registration for Dinner Short Courses*

RECOMMENDED DINNER SHORT COURSE*

SC11: Clinical Prospects of Cancer Immunotherapy

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

PEGS 2016 Student Fellowship Award Program

Present Your Poster to 1,800 Protein Engineering Researchers

Student Fellowship Award Winners will attend the 12th Annual PEGS the essential protein engineering summit for as low as $295*

Full time graduate students and Ph.D. candidates are encouraged to apply for the PEGS conference Student Fellowship. Twenty fellowship award winners will receive a poster presentation slot and a savings of over $900 on their registration fee. Applications are due by February 5, 2016.

STUDENT FELLOWSHIP DETAILS:

- Interested students must complete the application for the 2016 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 23, 2016 if they were accepted for the 2016 Student Fellowship
- Accepted 2016 Student Fellows will receive a discounted conference rate of $295*, which must be paid in full by March 11, 2016. 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, April 25-29, 2016. Excludes Short Courses.
- All accepted 2016 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 2016 Student Fellowship, can register at a discounted rate $595*, and will not be required to present a poster
- ADDED BONUS! Poster competition features cash prize winners (For all poster presenters).

Advancing Bispecific Antibodies & Combination Therapy to the Clinic

Novel Strategies for Oncology

ONCOLOGY STREAM

RECOMMENDED PRE-CONFERENCE SHORT COURSE*

SC2: Bioanalytical Considerations of Multi-Domain Biotherapeutics: Preclinical and Clinical Development

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

WEDNESDAY, APRIL 27

7:00 am Registration and Morning Coffee

CHANGING FUTURES WITH IMMUNOTHERAPY COMBINATIONS AND BISPECIFIC ANTIBODIES

8:00 Chairperson's Remarks

Rakesh Dixit, Ph.D., DABT, Vice President, R&D; Global Head, Biologics Safety Assessment, Translational Sciences, MedImmune

» 8:10 KEYNOTE PRESENTATION:

The Power of Combinations in Immuno-Oncology

Mohammed M. Dar, M.D., Vice President, Clinical Development Oncology, MedImmune

With the approval of several single agent checkpoint inhibitors for the treatment of multiple indications, what is becoming clear is that tumors have evolved to engage multiple mechanisms to evade the host anti-tumor immune response. As a result, only a proportion of patients are able to derive long-term benefit from single agent checkpoint inhibitor therapy, while the vast majority of patients will likely require a combinatorial approach for improved outcomes. Clinical validation for this concept recently came with the approval of the first combination of two checkpoint inhibitors for the treatment of metastatic melanoma. During the presentation, approaches to developing novel combinations with immunotherapy agents will be discussed along with some of the challenges.

8:40 Combination Bispecific and Immunotherapy Trials in the Clinic

Israel Lowy, M.D., Ph.D., Vice President and Head, Translational Science and Oncology, Regeneron

Does it make sense to combine bispecific antibodies with checkpoint blockade? Regeneron's approach to developing and testing bispecific antibodies and immunomodulatory antibodies will be reviewed, as well as our current progress in exploring novel combination approaches to augment the efficacy of immune therapy of tumors.

9:10 Enhancing Innate Immune Responses Augments Adaptive Immunity

Holbrook E.K. Kohrt, M.D., Ph.D., Assistant Professor, Medicine, Divisions of Hematology and Oncology, Center for Clinical Sciences Research, Stanford University Cancer Institute

Antibody-dependenT Cell-mediated cytotoxicity (ADCC), largely mediated by natural killer (NK) cells, is thought to play an important role in the efficacy of monoclonal antibodies (mAb)s including rituximab, trastuzumab, and cetuximab. CD137 is a costimulatory molecule expressed on a variety of immune cells following activation, including NK cells. We demonstrate that as the antitumor efficacy of mAbs is due, at least in part, to ADCC, the anti-cancer activity of these mAbs can be enhanced by stimulation of NK cells with an anti-CD137 agonistic mAb.

9:40 Novel T Cell Bispecific Antibodies for Cancer Immunotherapy

Peter Bruenker, Ph.D., Area Head, Molecular Biology and Cell Line Engineering; Large Molecule Research, Roche Pharma Research and Early Development (pRED), Roche Glycart AG

During the presentation, our IgG-based T Cell bispecific (TCB) antibody platform will be described. In particular, the design, generation and characterization of a novel, highly potent CEA targeted T Cell bispecific antibody for treatment of solid tumors, which is currently in Phase I trials, will be discussed.

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

10:55 Safe and Effective Inhibition of the Immune Checkpoint CD47 with Bispecific Antibodies

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

CD47 is an immune checkpoint that has emerged as an attractive target in oncology. As it is expressed on every cell anti-CD47 monoclonal antibodies face safety and pharmacology liabilities. We have developed bispecific κλ bodies, which selectively target CD47 on cancer cells and drive effective phagocytosis. Progress in the preclinical development of a CD47/CD19 κλ body will be reported, indicating that CD47 is a tractable target to increase the immune response against cancer.

11:25 Activated T Cells Armed with Bispecific Antibodies Kill Tumor Targets

Lawrence G. Lum, M.D., D.Sc., Professor, Oncology and Immunology & Microbiology; Scientific Director, BMT; Director, Immunotherapy, Karmanos Cancer Institute Wayne State University

Adoptive T Cell therapy has become one of the most exciting fields of cancer therapy in the past few years. In this article, we describe a method which combines adoptive T Cell therapy with antibody therapy by arming T Cells from cord blood, normal patients, and cancer patients with bispecific antibodies capable of binding to tumor-associated antigens on one side of the bispecific antibody construct and T Cells on another side of the construct. This approach redirects T Cells against tumor cells in a non-MHC-restricted manner. Activated T Cells armed with bispecific antibodies represent a promising treatment for cancer immunotherapy.

11:55 Combination Therapy

F. Stephen Hodi, M.D., Associate Professor, Medicine, Medical Oncology, Dana-Farber Cancer Institute

This presentation will include combinations of immune checkpoint blockade with cytokines and anti-angiogenesis treatment.

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

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

1:55 Session Break

MULTISPECIFIC ANTIBODIES IN CLINICAL DEVELOPMENT

2:10 Chairperson's Remarks

Steven Coats, Ph.D., Senior Director, R&D, MedImmune

2:15 Current and Future Applications of DART® and Trident™ Proteins

Syd Johnson, Ph.D., Vice President, Antibody Engineering, MacroGenics, Inc.

Bi- and trispecific antibodies represent a highly potent class of immunotherapeutic agents that may outperform or complement traditional chemotherapy, naked antibodies and ADCs. MacroGenics' Dual-Affinity Re-Targeting, or DART®, proteins are among the most stable and potent biologics in this therapeutic class. This talk will highlight several DART proteins currently in clinical studies, as well as new specificities and novel trispecific Trident™ formats that are under development for future drug candidates.

2:45 Development of Istiratumab (MM-141): A Tetravalent Bispecific Antibody Directed Against IGF-1R and ErbB3

Jason Baum, Ph.D., Director and Diagnostic Project Lead, Companion Diagnostics, Merrimack Pharmaceuticals

Despite recent approval of nab-paclitaxel/gemcitabine regimen, overall prognosis for pancreatic cancer patients remains poor. We demonstrated that istiratumab (MM-141) combines favorably with nab-paclitaxel/gemcitabine in preclinical models and has acceptable tolerability in the clinic. On these scientific bases, Phase II study was developed to evaluate istiratumab plus nab- paclitaxel/gemcitabine in metastatic pancreatic cancer patients positive

CONTINUED

Advancing Bispecific Antibodies & Combination Therapy to the Clinic

Novel Strategies for Oncology

for serum free IGF-1. We will provide study update and describe a preclinical experiments aimed at elucidation of mechanisms by which MM-141 can reactivate anti-tumor immunity.

3:15 Sponsored Presentation *(Opportunity Available)*

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

4:45 Problem-Solving Breakout Discussions
See website for details.

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

7:00 End of Day

THURSDAY, APRIL 28

8:00 am Morning Coffee

BISPECIFICS AND ADCs

8:30 Chairperson's Remarks
Robert Mabry, Ph.D., Director, Protein Sciences and Antibody Technology, Jounce Therapeutics

8:35 A Biparatopic HER2-Targeting Antibody-Drug Conjugate Demonstrates Potent Anti-Tumor Activity in Primary Tumor Models that are Refractory to or Ineligible for HER2-Targeted Therapies
John Li, Ph.D., Scientist, MedImmune
Current HER2-targeted therapeutics are ineffective in killing tumor cells lacking HER2 overexpression, therefore more than 60% of metastatic breast cancer patients are ineligible for HER2-targeted therapies. Furthermore, the vast majority of eligible patients who initially respond to the treatment will eventually relapse mainly due to intratumoral heterogeneity of HER2 expression. This presentation will discuss the development of a biparatopic HER2-targeting ADC and its potential in treating metastatic breast cancer patients that are refractory to or ineligible for current HER2-targeted therapies.

9:05 Antibody-Based Therapy of Acute Myeloid Leukemia (AML)
Roland B. Walter, M.D., Ph.D., MS, Assistant Member, Clinical Research Division, Fred Hutchinson Cancer Research Center; Associate Professor, Medicine, Medicine/Division of Hematology, University of Washington
The demonstration of improved survival with the CD33 antibody-drug conjugate gemtuzumab ozogamicin highlights the value of antibodies for AML. Current efforts are focused on several novel antibody formats and the exploration of other target antigens. Many important questions related to target antigen(s), disease situation in which to use these therapies, most suitable patient populations, exact treatment modalities, and details of supportive care needs remain to be addressed in upcoming studies.

9:35 Sponsored Presentation *(Opportunity Available)*

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

MULTISPECIFIC ANTIBODIES IN CLINICAL DEVELOPMENT (II)

11:00 Chairperson's Remarks
Robert Mabry, Ph.D., Director, Protein Sciences and Antibody Technology, Jounce Therapeutics

11:05 Engineering and Clinical Development of Fc-Containing Bispecific Antibodies
Matthew J. Bernett, Ph.D., Senior Scientist, Protein & Antibody Engineering, Xencor, Inc.
Xencor has developed various platforms to enable Fc-containing bispecific antibodies with long serum half-lives. These programs include CD32b bispecific antibodies targeting CD19 for autoimmune disease and IgE for allergy, as well as CD3 bispecific antibodies targeting CD123 and CD20 for oncology. The engineering and development process from the research stage to the clinic will be discussed for several of these programs.

11:35 Preclinical Development of MCLA-128 - A Bispecific Antibody Targeting HER2 and HER3
Mark Throsby, Ph.D., CSO, Merus
Proprietary platform technology was applied to generate the Biclonics® MCLA-128; a human common light chain bispecific antibody targeting HER2 and HER3. MCLA-128 specifically and potently inhibits ligand dependent HER2:HER3 signaling resulting in suppression of tumor growth *in vitro* and *in vivo*. This novel full-length bispecific antibody, that features ADCC enhancement, is undergoing clinical evaluation in a Phase I/II study of patients with HER2+ tumors.

12:05 pm First-in-Class T Cell-Redirecting Bispecific Antibody Targeting a Highly Tumor-Selective Antigen
Mika Kamata-Sakurai, Ph.D., Scientist, Biologics Discovery, Research Division, Chugai Pharmaceutical Co., Ltd.
T Cell-redirecting antibody may be a solution to the recent problems in immunotherapy. We have generated a T Cell-redirecting antibody with highly potent anti-tumor efficacy. This fully IgG antibody is asymmetric and bispecific, recognizing both CD3 and tumor-selective antigen, and its large scale production has been made possible by Chugai's ART-Ig technology. The findings observed in non-human primate toxicity studies were manageable and reversible. Optimization, pharmacology, and toxicity of this antibody will be presented.

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

RECOMMENDED DINNER SHORT COURSE*

SC11: Clinical Prospects of Cancer Immunotherapy
**Separate registration required, please see page 5 for course details*

6th Annual | April 28 - 29

Antibody-Drug Conjugates II: Advancing Toward the Clinic

THURSDAY, APRIL 28

12:35 pm Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Pamela Trail, Ph.D., Vice President, Oncology, Regeneron Pharmaceuticals

» 1:50 KEYNOTE PRESENTATION:

Building on Lessons Learned from Clinical Development in the Design and Development of the Next-Generation ADCs
John Lambert, Ph.D., Executive Vice President, Research, and Distinguished Research Fellow, ImmunoGen, Inc.
ADCs with potent tubulin-acting and DNA-acting agents can be effective anti-cancer agents with good therapeutic indices. However, not all cell-surface targets have proven susceptible to the development of effective ADCs utilizing the first generation ADC chemistries. Some of the lessons learned from the past 15 years of ADC preclinical and clinical experience, and how such lessons are being applied to current and future ADC developments, will be discussed.

» 2:20 KEYNOTE PRESENTATION:

Advances in Antibody-Based Conjugates for Cancer Therapy
Dennis Benjamin, Ph.D., Vice President, Translational Research, Seattle Genetics, Inc.
Insights into how ADCs can be effectively developed have been gained through studies on cancer antigen targets, drug potency and mechanism, and linker stability and conditional drug release. Adcetris is an example of an ADC designed with these parameters in mind. Since then, significant developments have been made in many areas of ADC technology, including the physicochemical properties of conjugates, biodistribution, and new high-potency drugs. An overview and progress surrounding new generation ADCs will be provided.

TRANSLATIONAL AND PKPD CHALLENGES

2:50 Antibody-Drug Conjugates: Translational Considerations
Mohammad Tabrizi, Ph.D., Senior Fellow and Head, PKPD, Merck
Targeted delivery of highly potent small molecule drugs to specific effecT Cells is intended to expand the therapeutic window for the payload in the clinical setting via curtailing the anticipated adverse effects. Here, we have attempted to address some of the key translational topics critical for early development of antibody-drug conjugates. As anticipated, a successful transition of ADCs into the clinic will be highly dependent on effective translation of critical attributes governing exposure-response relationships across species.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Refreshment Break

4:20 Ado-Trastuzumab Emtansine Targets Hepatocytes via Human Epidermal Growth Factor Receptor 2 to Induce Hepatotoxicity
Wen Jin Wu, Ph.D., Senior Investigator, Office of Biotechnology Products, CDER, US FDA
Hepatotoxicity is one of the serious adverse events associated with T-DM1 therapy; mechanisms underlying T-DM1–induced hepatotoxicity remain elusive. We find that T-DM1 is internalized upon binding to cell surface HER2 and is co-localized with LAMP1, resulting in DM1-associated cytotoxicity. We further demonstrate that T-DM1 treatment significantly increases the serum levels of AST, ALT, LDH, and induces inflammation and necrosis in hepatocytes. We propose that T-DM1-induced upregulation of TNFα enhances the liver injury that may be initially caused by DM1-mediated intracellular damage.

4:50 Evaluation of the Bi-Directional Interaction between the Mononuclear Phagocyte System (MPS) and the Pharmacokinetics and Pharmacodynamics of Carrier Mediated Agents and Antibody-Drug Conjugates
William C. Zamboni, Pharm.D., Ph.D., Associate Professor and Director, Translational Oncology and Nanoparticle Drug Development Initiative (TOND2I) Lab, The University of North Carolina
Carrier-mediated agents (CMA) and antibody-drug conjugates (ADCs) consist of the inactive-drug that remains encapsulated within or conjugated to the carrier and the active-drug that is released from the carrier. We will discuss: 1) pharmacologic methods to characterize CMAs and ADCs *in vivo* and *in vivo*; 2) animal models for pharmacologic and toxicology studies of CMAs and ADCs; 3) the development of phenotypic probes of the MPS to profile the interaction between CMAs and ADCs and the MPS; 4) bi-direction interaction between MPS and ADCs.

5:20 End of Day

5:15 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*
SC13: Critical Considerations for the Design and Development of Antibody-Drug Conjugates
**Separate registration required, please see page 5 for course details.*

FRIDAY, APRIL 29

8:00 am Registration and Morning Coffee

ADCs IN EARLY DEVELOPMENT

8:30 Chairperson's Remarks
Alan Rigby, Ph.D., CSO and Senior Vice President, Synta Pharmaceuticals

8:35 Regulatory Considerations during Early Development of ADCs
Bethany Rappoli, MA, MS, Director, Worldwide Regulatory Strategy, Pfizer
ADCs are complex molecules presenting unique development challenges. Given the highly competitive nature of drug development in oncology, teams need to be poised to accelerate early, but there is often confusion as to what this may entail from a regulatory perspective. The intent of this presentation is to touch on key regulatory considerations and strategies for the early stage development of ADCs.

9:05 Building on the Success of Trastuzumab Emtansine/Kadcyla®: Preclinical Development of New HER2-Directed Antibody-Drug Conjugates
Gail Lewis Phillips, Ph.D., Senior Scientist, Molecular Oncology, Genentech
Trastuzumab emtansine (Kadcyla®) is an antibody-drug conjugate (ADC) comprised of the therapeutically active HER2 antibody trastuzumab covalently linked to DM1, a microtubule inhibitor, through a non-cleavable linker. In patients with HER2-positive metastatic breast cancer (mBC) who were previously treated with HER2-directed therapies, trastuzumab emtansine is more active and better tolerated than standard of care treatment regimens. Recent studies are focused on developing new strategies for HER2-targeted ADCs by exploring different cytotoxic agents and linkers.

9:35 Update on MedImmune's Antibody-Drug Conjugate Platform: Developing Potent ADCs for Cancer Therapy
Ronald Herbst, Ph.D., Vice President and Head, Oncology Research, MedImmune

10:05 Coffee Break

CONTINUED

6th Annual | April 28 - 29

Antibody-Drug Conjugates II: Advancing Toward the Clinic

UPDATES FROM THE CLINIC

10:35 Development of ADCs Targeting Guanylyl Cyclase C (GCC) for the Treatment of Gastrointestinal Malignancies

Peter Veiby, Ph.D., Global Head, Biotherapeutics, Oncology Drug Discovery Unit, Takeda Pharmaceuticals International

MLN0264/TAK264 is a GCC targeting ADC in phase 2 clinical development in Gastric and pancreatic cancer patients. The target of MLN0264, GCC, is expressed in >95% of mCRC patient samples however the low response rate patients with mCRC treated MLN0264 led us to hypothesize that an ADC carrying a different cytotoxic payload could potentially provide an alternative for patients with GCC expressing mCRC. We will discuss our efforts to preclinically characterize next generation ADCs targeting GCC in patient derived xenografts refractory to MLN0264.

11:05 Celldex ADC Pipeline and Clinical Development Update

Christopher D. Turner, M.D., Vice President, Clinical Science, Celldex Therapeutics, Inc.

Celldex has developed a pipeline of proprietary antibodies and immunomodulators. Glembatumumab vedotin (CDX-011) is a novel ADC that delivers the potent cytotoxin, MMAE, to cancer cells expressing gpNMB. gpNMB is a transmembrane protein overexpressed in 20% of breast cancers (40% of TNBC) and 80% of melanomas. An overview of the clinical experience with glembatumumab vedotin and an update on the Phase 2 trials for TNBC ("METRIC") and melanoma will be presented.

11:35 Sacituzumab Govitecan (IMMU-132), a Next-Generation ADC in Advanced Clinical Trials for Solid Cancer Therapy

David M. Goldenberg, Sc.D., M.D., CSO and Chairman, Immunomedics, Inc.

IMMU-132 is an ADC involving the conjugation of 7.6 molecules of SN-38 to the IgG of the internalizing anti-Trop-2 humanized mAb, hRS7. Over 250 patients with diverse solid cancers have been treated, and the optimal dosing schedule has been determined to be 10 mg/kg on days 1 and 8 of 21-day cycles, permitting therapy over months without the induction of anti-antibody or anti-SN-38 antibodies. Objective durable responses have been achieved in a number of patients with advanced, metastatic cancers, after failing multiple prior therapies.

12:05 pm AGS67E, an Anti-CD37 Monomethyl Auristatin E (MMAE) Antibody-Drug Conjugate for NHL, CLL & AML

Leonard Reyno, M.D., Senior Vice President & CMO, Agensys

AGS67E is an antibody drug conjugate (ADC) composed of a fully human IgG2 antibody targeting CD37 that is conjugated to the anti-tubulin agent MMAE through a cleavable linker. A multicenter phase 1 dose-escalation study is currently evaluating the safety, PK, and anticancer activity of AGS67E given as monotherapy to patients with relapsed / refractory non-Hodgkin lymphoma. AGS67E is administered IV Q3 weeks until disease progression or unacceptable toxicity. Updated clinical results will be presented with implications for further development in hematological malignancies including Lymphoma and AML.

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

1:05 Refreshment Break

UPDATES FROM THE CLINIC (CONT.)

1:35 Chairperson's Remarks

Alan Rigby, Ph.D., CSO and Senior Vice President, Synta Pharmaceuticals

1:40 PRLR ADC: Development of a Novel Antibody Drug-Conjugate for the Treatment of PRLR Positive Breast Cancer

Pamela Trail, Ph.D., Vice President, Oncology, Regeneron Pharmaceuticals

Prolactin Receptor (PRLR) is a type I cytokine receptor that is overexpressed in approximately 25% of human breast tumors of various subtypes, including triple-negative cancers. Importantly, PRLR has limited normal tissue expression and is rapidly internalized following binding of anti-PRLR antibodies. We have explored the use of PRLR as a therapeutic target for development of anti-PRLR Antibody-Drug Conjugates. Results of those studies and the use of PRLR directed ADCs for treatment of breast cancer will be discussed.

2:10 Clinical Development of Mirvetuximab Soravtansine – A Maytansinoid ADC Targeting Folate Receptor Alpha

Charles Morris, MBChB, MRCP(UK), Chief Development Officer, ImmunoGen

Mirvetuximab soravtansine (IMGN853) is a maytansinoid ADC targeting folate receptor alpha (FRa) which is expressed in a number of solid tumors including ovarian, endometrial and non-small cell lung cancers. Early clinical data show encouraging activity in heavily pre-treated epithelial ovarian cancer with notably high response rates in patients whose tumors express high levels of FRa. This presentation will review the clinical data to date.

2:40 Seattle Genetics' Latest ADC Innovation: Increasing Potency to Maximize Activity

Elaina Gartner, M.D., Medical Director, Experimental Medicine, Seattle Genetics, Inc.

Through targeted delivery of potent cytotoxic agents, antibody-drug conjugates (ADCs) are revolutionizing cancer care. With the advent of more highly potent and stable drug linkers, such as pyrrolobenzodiazepine (PBD) dimers, the antitumor activity of ADCs may be enhanced while limiting off-target toxicity. The most recent, highly potent ADCs in development from Seattle Genetics' portfolio will be discussed, highlighting SGN-CD33A for acute myeloid leukemia.

3:10 Matching Technology Improvements with Biology to Enable Successful ADCs

Puja Sapra, Ph.D., Senior Director, Bioconjugates Discovery & Development, Pfizer, Inc.

This presentation will cover evolution of calicheamicin ADCs over last two decades. Learnings from several clinical programs including Mylotarg and Inotuzumab will be discussed. Improvements in technology and target selection strategies that can enable calicheamcin ADCs for solid tumors will be presented. Additionally, the presentation will disclose new technology improvements in development of tubulin inhibitor- based ADCs. Preclinical and clinical update from novel auristatin ADC programs will be covered. Preclinical data on combination strategies of ADCs and immune-oncology therapeutics will be presented.

3:40 End of Antibody-Drug Conjugates II: Advancing Toward the Clinic

Inaugural | April 25 - 26

Preventing Toxicity in Immunotherapy

Delivering Therapies to Patients Rapidly and Safely

MONDAY, APRIL 25

7:00 am Registration and Morning Coffee

BUILDING PRECLINICAL MODELS

8:30 Chairperson's Remarks

Michelle Krogsgaard, Ph.D., Assistant Professor, New York University School of Medicine

8:40 Biophysical Engineering of Tumor Specific TCRs to Carefully Balance Tumor Reactivity and Autoimmunity in Cancer Immunotherapy

Michelle Krogsgaard, Ph.D., Assistant Professor, New York University School of Medicine

We are taking a variety of biophysical and cellular imaging approaches to determine how specific thresholds for T Cell recognition of self (tumor)-antigens are set. Our recent results indicate that antitumor activity and autoimmunity are coupled and have a similar kinetic threshold; reducing autoimmunity cannot be accomplished without sacrificing efficacy of tumor killing. New strategies to overcome this issue include careful engineering of tumor-specific TCRs and T Cell signaling pathways to balance tumor-reactivity and autoimmunity.

9:10 A Mouse Model for Adoptive T Cell Therapies with Engineered T Cell Receptors

David M. Kranz, Ph.D., Phillip A. Sharp Professor, Biochemistry, University of Illinois

T Cell receptors engineered for higher affinity against class I-restricted cancer antigens allow recruitment of both CD4 and CD8 T Cells to the tumor. Adoptive T Cell therapies with such TCRs can mediate significant efficacy, but also run the risk of off-target toxicities against structurally-related self-peptides. Engineering and comprehensive mutagenic scanning of several human TCRs will be described, along with the use of HLA-A2 transgenic mice in assessing possible safety issues.

9:40 Tumor Models to Investigate CAR T Cell Potency, Acute and Chronic Toxicity

David Gilham, Ph.D., Senior Lecturer, Clinical and Experimental Immunotherapy Group; ICS PGR Director, Institute of Cancer Sciences, University of Manchester

Reports of objective clinical responses and tumor regression in patients receiving Chimeric Antigen Receptor (CAR) T Cell therapy are driving a major surge of interest in the field. CARs are artificial targeting proteins that exploit antibody-based approaches to re-direct the effector function of the T Cell to virtually any cell surface target. However, it remains unclear whether toxicity resulting from over-activity of the T Cell or lack of suitable target specificity is likely to be an issue. Models can provide some answer to this although the relevance of such models remains open to question.

10:10 Coffee Break

CYTOKINE STORM: PREDICTION, DIAGNOSIS, AND MANAGEMENT

10:45 Chairperson's Remarks

Simon Lacey, Ph.D., Director, Translational and Correlative Studies Laboratory, Product Development and Correlative Sciences, University of Pennsylvania

10:50 Cytokine Storm Following CAR-T Cell Therapy: An Interdisciplinary Approach to Diagnosis and Symptom Management

Chrystal Louis, Ph.D., Co-Director, Neuroblastoma Program, Texas Children's Hospital; Assistant Professor, Pediatrics, Section of Hematology-Oncology, Baylor College of Medicine

Chimeric antigen receptor (CARs) positive T Cells combines the specificity and anti-tumor effects of monoclonal antibodies with the direct cytotoxicity and long-term persistence of T Cells. However, modifications designed to improve the affinity and anti-tumor activity of CARs increases the likelihood of on- and off-target toxicity secondary to low level antigenic expression on normal tissues. Toxicity associated with cytokine storm and macrophage activation syndrome can be life-threatening if not quickly identified and requires interdisciplinary communication and teamwork to successfully manage the symptoms.

11:20 Biomarkers Accurately Predict Cytokine Release Syndrome (CRS) after Chimeric Antigen Receptor (CAR) T Cell Therapy for Acute Lymphoblastic Leukemia (ALL)

Simon Lacey, Ph.D., Director, Translational and Correlative Studies Laboratory, Product Development and Correlative Sciences, University of Pennsylvania

CAR T Cells with anti-CD19 specificity have demonstrated remission rates as high as 90% in ALL patients treated with CTL019 (Maude et al., NEJM 2014), but cytokine release syndrome (CRS) can be a complication. We studied 43 cytokines, chemokines, and soluble receptors in 51 ALL patients treated with anti-CD19 CAR T Cells. Biomarkers associated with severe CRS and predictive during the first 3 days after infusion of subsequent CRS4-5 compared to CRS0-3 were identified.

11:50 Managing Receptor-Engineered T Cell Cytokine Storms: Facts, Fabulations, Future Progress

Christopher A. Klebanoff, M.D., Assistant Clinical Investigator, Center for Cancer Research, National Cancer Institute

Adoptive transfer of receptor-engineered T Cells targeting tumor-associated antigens can mediate durable complete responses in patients with refractory solid and hematologic malignancies. In some cases, infusion of engineered T Cells is associated with a spectrum of toxicities attributed to an exuberant release of cytokines. Dissemination of this promising treatment modality beyond specialized academic medical centers will require detailed understanding of both the pathogenesis and medical management of cell-related toxicities.

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

See website for details.

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

CONTINUED

Inaugural | April 25 - 26

Preventing Toxicity in Immunotherapy

Delivering Therapies to Patients Rapidly and Safely

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 The Promise of Cancer Immunotherapy: An Overview of Recent Advances and Jounce's Approach to Delivering the Right Therapy to the Right Patient

Deborah Law, D. Phil. CSO Jounce Therapeutics, Inc.

As immunotherapies become an increasingly important component of cancer treatment the challenge will be to identify ways to provide the best therapy(s) to the individual. This presentation will provide an overview of current cancer immunotherapies as well as highlight some of the challenges ahead including selection of optimal combinations, moving outside of T Cell-directed approaches, and will highlight how Jounce Therapeutics is using its Translational Science Platform as an approach to develop and deliver the right therapy to the right patient.

4:50 Antibody as Drugs: Then, Now and Tomorrow

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

Antibodies have grown into a clinically and commercially important drug class with more than >45 antibodies marketed for imaging or therapy in the USA and/or Europe and with ~$63 billion in worldwide sales in 2013. This presentation will highlight progress in developing antibody drugs and consider opportunities for future innovation.

5:30 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 End of Day

TUESDAY, APRIL 26

8:00 am Morning Coffee

IN VITRO EXPERIMENTS FOR TESTING CROSS REACTIVITY

8:25 Chairperson's Remarks

Andrew K. Sewell, Ph.D., Distinguished Research Professor, Wellcome Trust Senior Investigator; Research Director, Institute of Infection and Immunity, Henry Wellcome Building, Cardiff University School of Medicine

8:30 ImmTACs: High Affinity T Cell Receptor-Based Bi-Functional Biologics for Redirected Tumor Killing

Joseph D. Dukes, Ph.D., Head, Preclinical Biology, Immunocore Ltd.

ImmTACs (Immune-mobilising monoclonal TCRs against cancer) are bi-specific reagents engineered to target tumor-specific antigens with high sensitivity and specificity, and then via an anti-CD3 antibody fragment redirect host T Cells to promote tumor killing. Careful selection of tumor antigens and TCR engineering overcome the natural low affinity of tumor-specific antigens. Preclinical testing of ImmTAC (e.g. IMCgp100) specificity, efficacy and safety are determined through a detailed molecular and cellular testing programme. Clinical observations from IMCgp100 Phase I trial support our pre-clinical approach.

9:00 Preventing Self Reactivity of Engineered TCRs

Andrew K. Sewell, Ph.D., Distinguished Research Professor, Wellcome Trust Senior Investigator; Research Director, Institute of Infection and Immunity, Henry Wellcome Building, 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.

9:30 Preclinical Models that Inform Development of Bispecific Antibodies

Paurene Duramad, Ph.D., MPH, DABT, Drug Safety & Pharmacometrics, Regeneron Pharmaceuticals, Inc.

Bispecific antibodies, while showing great therapeutic potential, pose formidable challenges with respect to their assembly, stability, immunogenicity, and pharmacodynamics. In this presentation, the preclinical mouse and non-human primate models used to inform development of a novel class of bispecific antibodies with native human immunoglobulin format will be described.

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

MONITORING THERAPIES IN REAL TIME

10:50 Next-Generation Immune Monitoring under ISO 17025 for Immuno-Oncology Trials and Biomarker Discovery

Thomas Oliver Kleen, Ph.D., Executive Vice President, Immune Monitoring, Epiontis GmbH

Novel, targeted therapies rendered immune monitoring in clinical trials obligatory. Epigenetic-based, quantitative real-time PCR assisted cell counting (qPACC) under ISO 17025 allows quantification of immune cells from only small amounts of blood or tissue. T Cells (Tregs), Th17 cells, Tfh cells, CD4+ and CD8+ cells, overall T Cells (CD3+), B cells, NK cells (CD56 dim), neutrophil granulocytes and monocytes are the first examples of a next-generation of immuno-oncology biomarker tools that can be used in these settings.

11:20 Monitoring the Balance between Effector and Regulatory Immune Responses in Tumor Immunotherapy Clinical Trials

Brian M Olson, Ph.D., Assistant Scientist, University of Wisconsin Carbone Cancer Center

Clinical trials evaluating tumor immunotherapies have focused on monitoring the generation of anti-tumor effector immune responses. However, the evaluation of concurrent regulatory responses (mediated by the immune system or the tumor itself) is often overlooked, despite the critical role they can play in the clinical efficacy of these immunotherapeutic interventions. Studying these regulatory responses, researchers can potentially uncover approaches targeting both effector and regulatory immunity to more effectively treat cancer.

11:50 Toxicities Associated with Checkpoint Inhibitor Immunotherapy

Alexander N. Shoushtari, M.D., Medical Oncologist, Memorial Sloan Kettering Cancer Center

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

DOSING CONSIDERATIONS AND SCALING UP

2:00 Chairperson's Remarks

Daniel W. "Trey" Lee, M.D., Assistant Clinical Investigator, St. Baldrick's Scholar, Pediatric Oncology Branch, National Cancer Institute

2:05 Paving the Road Ahead for CD19 CAR T Cell Therapy: Avoiding the Big Potholes

Daniel W. "Trey" Lee, M.D., Assistant Clinical Investigator, St. Baldrick's Scholar, Pediatric Oncology Branch, National Cancer Institute

CD19 CAR T Cell therapy has produced complete response rates of 70-90% in children and young adults with refractory pre-B acute lymphoblastic leukemia across multiple institutions. Neurotoxicities and severe cytokine release syndrome, which can be lethal without timely and appropriate intervention, represent the biggest challenges in exporting this therapy to non-CAR centers. This presentation will describe these toxicities and outline a management algorithm and other strategies for minimizing severe effects while maximizing response.

CONTINUED

Inaugural | April 25 - 26

Preventing Toxicity in Immunotherapy

Delivering Therapies to Patients Rapidly and Safely

2:35 Enhancing the Synthetic IQ of CAR T Cells

Michael C. Jensen, M.D., Professor, Pediatrics; Adjunct Professor, Bioengineering, University of Washington School of Medicine; Director, Ben Towne Center for Childhood Cancer Research, Seattle Children's Research Institute; Joint Member, Program in Immunology, Fred Hutchinson Cancer Research Center

The potential of immunotherapy to become a mainstream component of treatment for pediatric oncology patients is substantial. Emerging clinical data is depicting both the impressive potency as well as toxicities of CAR T Cell therapy for ALL. The Jensen lab is focused on developing next generation T Cells that are engineered with components that facilitate precise control of their function and fate. Our goal is to deliver on precision therapy that is controlled from the bedside to enhance both efficacy and safety of this therapeutic modality.

3:05 Sponsored Presentation *(Opportunity Available)*

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

4:25 PANEL DISCUSSION: The T Cell Therapy Race: How to Advance Safely

Moderator: Christopher A. Klebanoff, M.D., Assistant Clinical Investigator, Center for Cancer Research, National Cancer Institute

Panelists: Simon Lacey, Ph.D., Director, Translational and Correlative Studies Laboratory, Product Development and Correlative Sciences, University of Pennsylvania

Michael C. Jensen, M.D., Professor, Pediatrics; Adjunct Professor, Bioengineering, University of Washington School of Medicine; Director, Ben Towne Center for Childhood Cancer Research, Seattle Children's Research Institute; Joint Member, Program in Immunology, Fred Hutchinson Cancer Research Center

Daniel W. "Trey" Lee, M.D., Assistant Clinical Investigator, St. Baldrick's Scholar, Pediatric Oncology Branch, National Cancer Institute

- Who, what, where
- Location, location, location
- Cooling the flames
- Neurotoxicity associated with anti-CD19 targeted therapies
- Engineering safety

5:25 End of Preventing Toxicity in Immunotherapy

5:30 Registration for Dinner Short Courses*

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

3rd Annual | April 27 - 28

Adoptive T Cell Therapy

Current Challenges and Emerging Opportunities in Immunotherapy

WEDNESDAY, APRIL 27

7:00 am Registration and Morning Coffee

NEW UNDERSTANDINGS OF T CELL BIOLOGY

8:00 Chairperson's Remarks

Laszlo Radvanyi, Ph.D., Senior Vice President, Immuno-Oncology Translational Innovation Platform, EMD Serono Research and Development Institute

8:10 Viral and Non-Viral Gene Delivery for Adoptive Cell Therapy

Peter Emtage, Ph.D., Vice President, Synthetic Immunology, Intrexon

Harnessing the power of adoptive cell therapy (ACT) by leveraging current knowledge around T Cell biology using both viral and non-viral gene delivery technologies is important to the success of this immunotherapeutic approach. The ability to generate a potenT Cell moiety for ACT hinges not only on the survival, proliferation and activation of the delivery vehicle (T Cell, NK, etc.), but also on the microenvironment of the tumor. Modification of the ACT vehicle to address the challenges associated with environmental modification is crucial for success.

8:40 The State-of-the-Art with T Cell Receptor-Based Cancer Immunotherapies

Andrew K. Sewell, Ph.D., Distinguished Research Professor, Wellcome Trust Senior Investigator; Research Director, Institute of Infection and Immunity, Henry Wellcome Building, Cardiff University School of Medicine

The αβ TCR enables cytotoxic T Cells to scan the cellular proteome for anomalies from the cell surface. Tumor-specific TCRs can access a far greater range of targets than are available for antibodies. Engineered TCRs can be used in gene therapy and soluble molecule approaches. Next generation strategies allow circumvention of HLA-restriction. I will discuss future directions in the use of engineered T Cells and TCRs in cancer immunotherapy.

DEVELOPING CELL THERAPIES AGAINST SOLID TUMORS

9:10 Tumor Infiltrating Lymphocytes for Metastatic Cutaneous and Non-Cutaneous Melanoma: A UK Perspective

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

We have established the UK's only GMP-compliant and MHRA (Medicines and Healthcare Products Regulatory Agency) licensed unit capable of producing multiple T Cell product types (CAR or TCR-modified and natural T Cells (TIL)) using 'clean room free technology'. This unit has produced melanoma-derived TIL products which have been successfully returned to patients. This study supports the success of melanoma TIL therapy seen in other centers worldwide and suggests that this is a viable means of treating a disease which has few effective options.

9:40 Design of a Highly Efficacious, Mesothelin-Targeting CAR for Treatment of Solid Tumors

Boris Engels, Ph.D., Investigator, Exploratory Immuno-Oncology, Novartis Institutes for Biomedical Research

The treatment of solid tumors with CAR T Cells has shown to be challenging. We describe the design of a fully human CAR targeting mesothelin, a tumor associated antigen overexpressed in mesothelioma, pancreatic and ovarian cancer. The screen of a scFv pool has identified two scFvs, which show enhanced efficacy as CARs, superior to what is currently being used by several groups. We have performed in-depth characterization of the scFvs and CARs to gain insight into structure-activity relationships, which may influence CAR design and efficacy.

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

CAR, TCR, AND TIL

10:55 ACTR (Antibody Coupled T Cell Receptor): A Universal Approach to T Cell Therapy

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

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

11:25 Strategies to Optimize Tumor Infiltrating Lymphocytes (TIL) for Adoptive Cell Therapy

Shari Pilon-Thomas, Ph.D., Assistant Professor, Department of Immunology, Moffitt Cancer Center

Adoptive cell therapy (ACT) with tumor-infiltrating lymphocytes (TIL) has emerged as a powerful immunotherapy for cancer. TIL preparation involves surgical resection of tumors and *in vitro* expansion of TIL from tumor fragments. ACT depends upon the presence of TIL in tumors, successful expansion of TIL, and effective activation and persistence of T Cells after infusion. In this presentation, I will discuss optimization of TIL infiltration into tumors and TIL expansion for ACT in melanoma and other cancers.

11:55 Engineered T Cell Receptors for Adoptive T Cell Therapy in Solid Tumors

Jo Brewer, Ph.D., Director, Cell Research, Adaptimmune Ltd.

NY-ESO-1 is a cancer antigen that is expressed by a wide array of solid and hematological tumors. An enhanced affinity TCR that recognizes this antigen is currently in Phase I/II trials for synovial sarcoma, multiple myeloma, melanoma, ovarian and esophageal cancers. Early clinical data demonstrate encouraging responses and a promising benefit/risk profile.

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

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

1:55 Session Break

ARTIFICIAL ANTIGEN PRESENTING CELLS

2:10 Chairperson's Remarks

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

2:15 Artificial APCs: Enabling Adoptive T Cell Therapies

Marcela V. Maus, M.D., Ph.D., Director, Cellular Immunotherapy, Mass General Hospital Cancer Center

Adoptive T Cell therapies require *ex vivo* T Cell culture systems, which can include artificial antigen presenting cells. We will review several types of natural and artificial APCs and how they can be optimized to generate strong memory and effector T Cells usable for adoptive transfer.

2:45 Immunoengineering of Artificial Antigen Presenting Cells, aAPC: From Basic Principles to Translation

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

Artificial antigen presenting cells (aAPCs) are immuno-engineered platforms which advance adoptive immunotherapy by reducing the cost and complexity of generating tumor-specific T Cells. Our new approach, termed Enrichment and Expansion (E+E), utilizes paramagnetic nanoparticle-based aAPCs to rapidly expand both shared tumor antigen- and neoepitope-specific CTL. Streamlining the rapid generation of large numbers of T Cells in a cost-effective fashion can be a powerful tool for immunotherapy.

3:15 Sponsored Presentation *(Opportunity Available)*

CONTINUED

3rd Annual | April 27 - 28

Adoptive T Cell Therapy

Current Challenges and Emerging Opportunities in Immunotherapy

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

4:45 Problem-Solving Breakout Discussions
See website for details.

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

7:00 End of Day

THURSDAY, APRIL 28

8:00 am Morning Coffee

8:30 Chairperson's Remarks
Richard S. Kornbluth, M.D., Ph.D., President & CSO, Multimeric Biotherapeutics, Inc.

8:35 CD40 Ligand (CD40L) and 4-1BB Ligand (4-1BBL) as Keys to Anti-Tumor Immunity
Richard S. Kornbluth, M.D., Ph.D., President & CSO, Multimeric Biotherapeutics, Inc.
CD40 ligand (CD40L) and 4-1BB ligand (also called CD137L) activate immunity by binding to and clustering their receptors. We have solved the receptor clustering problem by creating fusion proteins that contain many TNFSF trimers. In this talk, we will discuss how soluble multi-trimer forms of TNFSFs such as CD40L and 4-1BBL have many important applications in cancer immunotherapy.

HARNESSING NK CELLS

9:05 Immunomodulation of NK Cells to Enhance Anti-Tumor Efficacy
Holbrook Kohrt, Ph.D., Assistant Professor, Medicine, Stanford University
We have recently demonstrated that ADCC function can be augmented by a second antibody against CD137, an NK/macrophage/T Cell activation molecule which is expressed following exposure to antibody-bound tumor cells. Agonistic anti-CD137 synergized with anti-CD20 in a syngeneic murine, CD20+ lymphoma model. Since anti-human CD137 antibodies are now becoming clinically available, this strategy can be applied to any tumor with a proven monoclonal treatment including lymphoma, breast, colorectal, and head and neck cancers.

9:35 Sponsored Presentation *(Opportunity Available)*

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

11:05 Late Breaking Presentation

GENE MODIFICATION STRATEGIES

11:35 Engineering Human T Cell Circuitry
Alex Marson, Ph.D., UCSF Sandler Fellow, University California, San Francisco
T Cell genome engineering holds great promise for cancer immunotherapies and for cell-based treatments for immune deficiencies, autoimmune diseases and HIV. We have overcome the poor efficiency of CRISPR/Cas9 genome engineering in primary human T Cells using Cas9:single-guide RNA ribonucleoproteins (Cas9 RNPs). Cas9 RNPs can promote targeted genome sequence replacement in primary T Cells by homology-directed repair (HDR), which was previously unattainable with CRISPR/Cas9. This provides technology for diverse experimental and therapeutic applications.

12:05 pm Engineering the Genome of CAR T Cells: From Therapeutic Procedures to Products
André Choulika, Ph.D., CEO and Chairman, Cellectis
Cellectis' therapeutics programs are focused on developing products using TALEN®-based gene editing platform to develop genetically modified T Cells that express a Chimeric Antigen Receptors (CAR) for cancer treatment. The first product, UCART19, T Cells has been gene-edited to suppress GvHD and enable resistance to an Alemtuzumab treatment. The objective of this first product is to convert the CART Cell therapy for an autologous approach to an off-the-shelve allogeneic CART product that can be produced in a cost effective fashion, stored, shipped anywhere in the world and immediately available to patient with an immediate unmet medical need.

12:35 End of Adoptive T Cell Therapy

5:15 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC11: Clinical Prospects of Cancer Immunotherapy
Separate registration required, please see page 5 for course details.

2nd Annual | April 28 - 29

Agonist Immunotherapy Targets

Moving Novel Targets from Discovery to Clinical Trials

THURSDAY, APRIL 28

CASE STUDIES WITH AGONIST BIOLOGICS

12:35 pm Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

Deborah Charych, Ph.D., Executive Director, Research Biology, Nektar Therapeutics

1:50 Hexavalent TNF-Superfamily Mimics for Cancer Treatment and Immune Modulation

Oliver Hill, Ph.D., Vice President, Molecular Biology, Apogenix, GmbH

Apogenix has developed a fusion protein technology to create hexavalent agonists targeting individual members of the TNFR-superfamily. Compared to conventional approaches using agonistic antibodies, Apogenix' compounds mimic the three-dimensional organization of the natural ligands (the TNFSF proteins). Consequently, their activity does not rely on secondary crosslinking events *in vitro* nor *in vivo*. We will present the molecular engineering concept and the current results obtained for the TRAIL-R-, CD40- and CD27-agonists.

2:20 NKTR-214: Harnessing the IL-2 Receptor Pathway for Cancer Immunotherapy

Deborah Charych, Ph.D., Executive Director, Research Biology, Nektar Therapeutics

Appropriate stimulation of the IL-2 pathway is a potent means of expanding tumor-killing CD8 T cells. However IL-2 also stimulates immune suppression through Tregs. NKTR-214 is a multi-PEGylated prodrug of IL-2 that significantly increases CD8 T cells over Tregs in the tumor. We will discuss the design of the molecule and its significant anti-tumor activity in multiple mouse models. The agent is currently in Phase 1 for the treatment of solid tumors.

2:50 OX40: From Bench to Bedside

Brendan D. Curti, M.D., Director, Genitourinary Oncology Research & Biotherapy Clinical Programs; Co-Director, Melanoma Program, Earle A. Chiles Research Institute, Providence Cancer Center

OX40 is a co-stimulatory pathway present in CD4 and CD8 T Cells. Engagement of OX40 on antigen-exposed T Cells results in enhanced memory and effector function. Numerous pre-clinical murine models show anti-tumor activity of OX40 agonists. The clinical development and immunologic changes induced by OX40 agonists in patients with cancer will be discussed along with pre-clinical work supporting the use of OX40 agonists with T Cell checkpoint inhibitors and other immune modulators.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Refreshment Break

4:20 Experimental Approaches for Cancer Immunotherapy Using Anti-CD40 Antibody

Alexander Rakhmilevich, M.D., Ph.D., Distinguished Senior Scientist, University of Wisconsin-Madison

CD40 ligation has been shown to induce antitumor effects in mice and cancer patients. We have demonstrated in several syngeneic mouse tumor models that anti-CD40 antibody, alone and in synergy with a toll-like receptor 9 agonist, CpG, activates macrophages and induces T Cell-independent antitumor effects. The antitumor efficacy of anti-CD40 and CpG can be further enhanced by chemotherapy or T Cell activation approaches involving checkpoint blockade.

4:40 Generation of an Optimal Anti-Tumor Immune Response as Prime for Checkpoint Inhibition

Thomas Davis, M.D., CMO & Executive Vice President, Clinical Development, Celldex Therapeutics

Combinations of immune modulators have shown marked synergy in preclinical studies and a range of combination studies are in progress. The combination of antigen specific vaccines with immune actuators, such as flt3L and agonist anti-CD27 antibodies, may offer improved responses to checkpoint as well as independent activity.

5:00 Reprograming the Tumor Microenvironment from Support to Fight

David Urech, Ph.D., CSO and Co-CEO, Numab AG

Numab's bispecific anti-IL23RxCD3 antibody fragment NM7-389 exclusively eliminates IL23R+ lymphocytes via CD8 T Cell mediated cytotoxicity. The bispecific anti-IL23RxCD3 molecule ameliorates symptoms in models for psoriasis, multiple sclerosis and colitis. In solid tumors, it depletes tumor supporting IL23R+ cells, stimulates CD8 T Cells to release factors including IFNγ and granzyme, and inhibits infiltration of regulatory T Cells, thereby generating a microenvironment, which effectively boosts specific anti-tumor immune cell responses. We propose NM7-389 as a new immune-modulatory agent for the therapy of autoimmune diseases and cancer.

5:20 End of Day

5:15 Registration for Dinner Short Courses*

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

RECOMMENDED DINNER SHORT COURSE*

SC11: Clinical Prospects of Cancer Immunotherapy

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

FRIDAY, APRIL 29

8:00 am Registration and Morning Coffee

EMERGING AGONIST AND ANTAGONIST TARGETS

8:30 Chairperson's Remarks

Adam J. Adler, Ph.D., Professor, Immunology, School of Medicine, UConn Health

8:35 Unlocking the Full Potential of Agonist Antibodies: A Multi-Faceted Challenge

Robert B. Stein, M.D., Ph.D., CSO, Agenus

Recent work on activating checkpoint targets such as GITR and OX40 has revealed that in addition to their co-stimulatory potential to enhance T Cell responsiveness to tumor associated antigens, they are also highly expressed by activated intratumoral regulatory T Cells. A more complete picture of the anti-tumor potential of GITR or OX40 agonist antibodies emerges when their regulatory T Cell depleting capacity is considered. A review of selected findings supporting this picture will be presented.

9:05 Preclinical Evaluation of JTX-2011, an Anti-ICOS Agonist Antibody

Deborah Law, D. Phil. CSO Jounce Therapeutics, Inc.

ICOS (inducible co-stimulator molecule), a member of the CD28 superfamily, is a co-stimulatory molecule expressed on T lymphocytes. We have generated agonistic anti-ICOS antibodies which are efficacious as monotherapies and in combination with anti-PD1 in multiple syngeneic tumor models. Mechanistic studies demonstrate enhanced cytotoxic CD8:T-regulatory cell ratios and preferential reduction in T-regulatory cells in the tumor microenvironment. JTX-2011, a species cross-reactive humanized antibody, has been selected for development. Evaluation of JTX-2011 in nonhuman primate models, including safety and PK parameters, will be presented. Our preclinical data provides rational for clinical development of JTX-2011 in solid tumor indications.

9:35 Immunoregulation by VISTA in the Tumor Microenvironment

J. Louise Lines, Research Scientist, Microbiology & Immunology, Dartmouth College

VISTA is a recently identified PDL1/PD1-like ligand/receptor that is being developed as a target for cancer immunotherapy. VISTA blockade is therapeutic in CT26 cancer and synergizes with PD1 blockade. VISTA is highly expressed on tumor infiltrating myeloid cells, and impacts on myeloid function. Tumors from anti-VISTA treated mice show increased myeloid cells overall, but decreased granulocytic-MDSCs. This unique feature of anti-VISTA treatment may explain why it works well in combination with anti-PD1.

CONTINUED

2nd Annual | April 28 - 29

Agonist Immunotherapy Targets

Moving Novel Targets from Discovery to Clinical Trials

10:05 Coffee Break

AGONISTS IN COMBINATION WITH OTHER MODALITIES

10:35 Exploiting Unexpected Properties of Combination OX40 Plus 4-1BB Agonist Costimulated T Cells for Tumor Immunotherapy

Adam J. Adler, Ph.D., Professor, Immunology, School of Medicine, UConn Health

Combining agonists to the costimulatory receptors CD134 and CD137 (dual costimulation) elicits potent T Cell-mediated tumor immunity. Two approaches have been explored to further enhance therapeutic potency. First, engaging tumor-unrelated CD4 T Cells that provide help to CD8 T Cells in both antigen-linked and non-linked manners. Second, treatment with particular cytokine combinations (IL-12 or IL-2 plus IL-33 or IL-36) that trigger dual costimulated effector T Cells via a TCR-independent mechanism.

11:05 Presentation to be Announced

11:35 Combinatorial Immunotherapy in Mouse Syngeneic Tumor Models

Hua Long, Senior Principal Scientist, Pfizer

Immunotherapies targeting the programmed death 1 (PD-1) coinhibitory receptor have shown great promise in the clinic. However, robust and safe combination therapies are still needed. We have investigated the antitumor activity of the anti-4-1BB/anti-PD-1 combination in the poorly immunogenic B16F10 melanoma model which resulted in pronounced tumor inhibition. The activity of the anti-4-1BB/anti-PD-1 combination was dependent on IFNγ and CD8(+) T Cells and elicited a robust antitumor effector/memory T Cell response. Combinatorial treatment with other agents will also be discussed.

12:05 pm Co-Stimulatory Agonists for the Immunotherapy of Cancer

Alan L. Epstein, M.D., Ph.D., Professor, Pathology, USC Keck School of Medicine

Co-stimulation is a key step in the development of an effective immune response to tumors. RT-PCR and IHC show that the tumor microenvironment lacks these key agonists to hinder the immune destruction of tumors. Our data demonstrate that providing missing co-stimulation using intravenously administered Fc-fusion proteins can be synergistic with methods to reduce immune suppression to provide effective and lasting treatment of cancer as a new direction of cancer immunotherapy.

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

1:05 Refreshment Break

STRATEGIES FOR TARGET DISCOVERY

1:35 Chairperson's Remarks

Yoram Reiter, Ph.D., Professor & Head, Laboratory of Molecular Immunology, Technion-Israel Institute of Technology

1:40 FivePrime's Approaches to New IO Target Discovery

Art Brace, Ph.D., Executive Director, Immuno-Oncology Research, Five Prime Therapeutics

2:10 Discovery of Novel Targets for Cancer Immunotherapy

Kai W. Wucherpfennig, M.D., Ph.D., Professor, Dana-Farber Cancer Institute and Harvard Medical School

We have developed novel *in vivo* screens for discovery of key negative regulators of T Cell function in the tumor microenvironment. A pooled shRNA (or gRNA) library is introduced into tumor-specific T Cells which are then transferred into mice bearing a subcutaneous melanoma (B16-Ova). Most transferred T Cells are inhibited in the immunosuppressive microenvironment of the tumor and therefore fail to proliferate in response to tumor antigen recognition. However, if a shRNA alleviates a significant block, T Cells can accumulate substantially in tumors. In our screen such shRNA (gRNAs) are identified by Illumina sequencing of the shRNA/gRNA cassette. This analysis is done across different tissues, enabling discovery of genes that control T Cell function in tumors. I will discuss novel targets we have identified and how they can be used to advance the treatment of cancer patients.

2:40 Discovering New Immunotherapy Targets by Dissecting Subsets of Human Tumor Infiltrating Lymphocytes

Andrew D. Weinberg, Ph.D., Chief, Laboratory of Basic Immunology, Providence Cancer Center; Agonox, Inc.

Our group has been interrogating CD8 and CD4 T Cell phenotypes within several different human tumor types. We have found common phenotypic themes that are selectively expressed within the tumor and not in the blood. Gene arrays have been performed within these subsets of TIL and we will discuss new immunotherapy approaches based on targeting these T Cell specific subsets within the tumor.

3:10 Discovery and Validation of Novel Targets for Cancer Immunotherapy: Exploring the Untapped Intracellular Proteome for Antibody-Based Novel Therapeutics

Yoram Reiter, Ph.D., Professor & Head, Laboratory of Molecular Immunology, Technion-Israel Institute of Technology

The ability to generate T Cell receptor like (TCRL) antibodies which bind HLA-peptide complexes on the surface of cells and are derived from intracellular-derived targets opens new possibilities for developing new therapeutic modalities. These antibodies can bind specifically to, and kill, the diseased cells. Thus, it transforms disease-specific targets that are expressed inside malignanT Cells into targets that can be recognized on the cell surface by soluble TCRL antibodies. This approach expands the pool of novel therapeutic antibodies beyond the limits of currently available antibodies.

3:40 End of Agonist Immunotherapy Targets

11th Annual | April 25 - 26

Difficult to Express Proteins

Strategies for Taming "Finicky" Proteins

RECOMMENDED PRE-CONFERENCE SHORT COURSES*

SC3: Antibody Humanization via One Hot Homology Model (Hands-On Workshop)

SC6: *In Silico* Immunogenicity Predictions (Hands-On) Workshop

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

MONDAY, APRIL 25

7:00 am Registration and Morning Coffee

NEW RESEARCH THAT CHANGES THE FIELD

8:30 Chairperson's Remarks

Haruki Hasegawa, Ph.D., Principal Scientist, Therapeutic Discovery, Amgen, Inc.

» 8:40 KEYNOTE PRESENTATION

The Human Secretome Project - Making and Functional Testing of All Secreted Human Proteins

Rick Davies, Ph.D., Associate Director, Reagents & Assay Development, AstraZeneca

Through a collaboration between The Royal Institute of Technology (KTH) in Stockholm and AstraZeneca, a project has been initiated to produce the entire 'Secretome' using state-of-the-art recombinant expression technology in mammalian cells. In this presentation, I will explain the concept and describe an initial pilot project in which a subset of the 'Secretome' consisting of 500 proteins was produced and tested in several different phenotypic assays

9:10 Discovery and Manipulation of Genes that Regulate ER Export and ER to Golgi Transport: Critical Implications for Protein Expression

Jesse C. Hay, Ph.D., Professor, Division of Biological Sciences, University of Montana

ER to Golgi transport is the first and rate-limiting step in the secretory pathway. We identified a calcium signaling pathway that regulates ER to Golgi protein trafficking that can be modified to increase ER export and ER to Golgi flux. This discovery will allow increased secretion into the medium or transport to the cell surface of soluble and membrane proteins, respectively, during manufacturing and research processes.

9:40 Is Endoplasmic Reticulum a Friend or a Foe to the Biopharmaceutical Industry? Lessons We Learned from 12 Angry mAbs

Haruki Hasegawa, Ph.D., Principal Scientist, Therapeutic Discovery, Amgen, Inc.

The stringency of protein quality control mechanisms in the endoplasmic reticulum (ER) is known for many years. This is something you experience firsthand when your proteins of interest are synthesized but not secreted. Is the ER just giving us the hard time or does this common phenomenon have larger implications? I will discuss how we can take advantage of what the ER is programed to do during protein expression in a mAb-specific manner and why it offers new approach to identifying high quality biotherapeutic lead candidates, fast.

10:10 Coffee Break

MEMBRANE PROTEINS AND OTHER "BEASTLY" EXPRESSION PROBLEMS

10:45 Chairperson's Remarks

Haruki Hasegawa, Ph.D., Principal Scientist, Therapeutic Discovery, Amgen, Inc.

10:50 Integrated Cell and Process Development for a Difficult to Express Protein

Christine Alves, Ph.D., Cell Culture Development, Biogen

New approaches in cell line and culture process development were utilized to increase expression of a difficult to express, positively charged protein by greater than 10-fold while maintaining product quality similar to early clinical material. A combination of multiple CHO hosts, optimization of media additives, and use of 15mL automated bioreactors resulted in evaluation of over 100 cell lines.

11:20 Dealing with Difficult Proteins via Molecular Design and Advanced Process Platforms

Randal Bass, Ph.D., Vice President, Process Design, Just Biotherapeutics

Proteins destined for clinical and commercial manufacturing require considerable work to establish robust manufacturing with molecular attributes that lead to a successful therapeutic. Difficult proteins require even larger, sometimes herculean efforts to make it through development. We apply an integrated approach from molecule design, process design, and even the manufacturing plant design to optimize the sequence, structure and production of therapeutic proteins.

11:50 Purification of Stabilized GPCRs for Structural and Biophysical Analyses

James C. Errey, Ph.D., Associate Director, Protein Biochemistry, Heptares Therapeutics, Ltd.

Integral membrane proteins are generally unstable when removed from their membrane environment, precluding them from the wide range of structural and biophysical techniques which can be applied to soluble proteins. Example protocols for the purification of StaR proteins for analysis, ligand screening with the thiol-specific fluorochrome N-[4-(7-diethylamino-4-methyl-3-coumarinyl)phenyl]maleimide (CPM), surface plasmon resonance (SPR), and crystallization for structural studies are presented.

Sponsored by

12:20 pm Development of an Eukaryotic Expression System for Expression of Complex Difficult-to-Express Proteins, Including Ion Channels

Prabuddha K. Kundu, Ph.D., Executive Director, Premas Biotech Pvt Ltd.

Premas Biotech has developed an eukaryotic expression system that enables high fidelity expression of difficult to express proteins, including ion channels, etc. The yeast, S cerevisae system includes the modified strain, vectors, and expression conditions to express the membrane proteins in their correct confirmation and activity. This has been demonstrated for a number of GPCRs, Ion Channels, and difficult to express proteins. The strain has demonstrated high levels of expression and high yields.

Sponsored by

12:50 Luncheon Presntation I: Engineering Genes, Vector Elements and Strain Properties for Optimized mAb Production in Mammalian Cell Lines

Claes Gustafsson, Chief Commercial Officer, DNA2.0, Inc.

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

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

See website for details.

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

CONTINUED

11th Annual | April 25 - 26

Difficult to Express Proteins

Strategies for Taming "Finicky" Proteins

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 The Promise of Cancer Immunotherapy: An Overview of Recent Advances and Jounce's Approach to Delivering the Right Therapy to the Right Patient

Deborah Law, D. Phil. CSO Jounce Therapeutics, Inc.

As immunotherapies become an increasingly important component of cancer treatment the challenge will be to identify ways to provide the best therapy(s) to the individual. This presentation will provide an overview of current cancer immunotherapies as well as highlight some of the challenges ahead including selection of optimal combinations, moving outside of T Cell-directed approaches, and will highlight how Jounce Therapeutics is using its Translational Science Platform as an approach to develop and deliver the right therapy to the right patient.

4:50 Antibody as Drugs: Then, Now and Tomorrow

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

Antibodies have grown into a clinically and commercially important drug class with more than >45 antibodies marketed for imaging or therapy in the USA and/or Europe and with ~$63 billion in worldwide sales in 2013. This presentation will highlight progress in developing antibody drugs and consider opportunities for future innovation.

5:30 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 End of Day

TUESDAY, APRIL 26

8:00am Morning Coffee

CELL-FREE AND OTHER CUTTING-EDGE STRATEGIES FOR SUCCESS

8:25 Chairperson's Remarks

Matthew Coleman, Ph.D., Senior Scientist, Physics and Life Sciences, Lawrence Livermore National Laboratory

8:30 Harmonization of Transient CHO and Stable CHO Expression Platforms for Early Phase Drug Discovery

Gavin Barnard, Ph.D., Group Leader, Eli Lilly & Co.

We describe the development of a transient CHO system capable of generating high titers, currently scalable to 6L. Additionally, we describe the use of stable CHO bulk pools (instead of master wells or clones) for generation of gram quantities of therapeutic protein. Using the same CHO cell line and media package for both platforms streamlines expression during early phase drug discovery.

9:00 Enhancing Protein Expression in HEK-293 Cells by Lowering Culture Temperature

Li Niu, Ph.D., Chemistry Department, Center for Neuroscience Research, University at Albany, SUNY

Animal cells and cell lines are commonly cultured and used to express recombinant proteins at 37 °C. We show dropping culture temperature to 33 °C, but not lower, 24 hours after transient transfection with HEK-293 cells will yield ~1.5-fold higher expression of a recombinant protein, such as green fluorescent protein. A mild hypothermia reduces the HEK-293 cell growth rate, while increasing cellular productivity of a protein without affecting the protein function. We demonstrate that this method may be also useful when a recombinant protein is difficult to express, such as in PC-12 cells, using a chemical-based, transient transfection method.

9:30 BacMam Production of Active Recombinant Lecithin-Cholesterol Acyltransferase: Expression, Purification and Characterization

William G. Romanow, Senior Associate Scientist, Protein Technologies, Amgen, Inc.

We recently reported a high-resolution crystal structure for lecithin-cholesterol acyl transferase (LCAT). Here we discuss the methods used to produce recombinant LCAT, and other glycoproteins suitable for X-ray crystallography. This will include the use of BacMam as a transient system for the production of secreted proteins, the use of cell lines and reagents to inhibit glycosylation and the bioprocessing of conditioned media and purification.

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

10:50 Cell-Free Co-Translation Systems for Biophysical and Biochemical Characterization of Proteins and Protein Complexes

Matthew Coleman, Ph.D., Senior Scientist, Physics and Life Sciences, Lawrence Livermore National Laboratory

Here we discuss how our laboratory has incorporated cell-free technologies to produce labeled proteins, protein complexes and trans-membrane proteins in yields that are more than sufficient for biophysical and biochemical characterization. Because cell-free translation is an open process, we have adapted commercial systems for multiple high-throughput screening techniques dependent on the suspected proteins function. For example, labels and co-factors can easily be added to synthesis reactions, such as fluorescent protein tags, peptides, SNAP-tags, small molecule co-factors, nanolipoproteins, lipids and fluorescently-labeled lipids.

11:20 Combining a PagP Fusion Protein System with Nickel Ion-Catalyzed Cleavage to Produce Intrinsically Disordered Proteins in *E. coli*

Peter Hwang, Ph.D., Assistant Professor, Biochemistry, University of Alberta

Intrinsically disordered regions (IDRs) are solvent-exposed and unstructured, making them susceptible to post-translational modifications. They are thus important for regulation, though they can be difficult to produce. Unfolded PagP membrane protein is an effective fusion partner for producing IDRs. Using a nickel cleavage-sensitive linker, SRHW, allows for removal of PagP under denaturing conditions, leaving behind a target protein with its native C-terminus.

11:50 Improved Protein Quality through Moss-Based Manufacturing

Andreas Schaaf, Ph.D., CSO, R&D, Greenovation Biotech GmbH

BryoTechnology is a plant-based cGMP expression platform using the moss Physcomitrella patens. As a plant production system it comes with an excellent safety profile, free of human pathogens, antibiotics and animal derived components. Moss genetic engineering is straightforward, time-effective and results in stable strains. From a technical perspective, the system is comparable to mammalian cell processes. Suspension cultures of stable, fully regenerated moss plantlets produce in well-established, single use fermenters from best-known suppliers in a fully controllable, cell-bank based process.

12:20pm New Approaches for MAb Discovery Against GPCRs, Ion Channels, and Transporters

Ross Chambers, Ph.D., Director, Antibody Discovery, Integral Molecular

Integral Molecular has developed new approaches to elicit, characterize, and engineer MAbs against challenging membrane proteins using its MPS Discovery Engine®. Robust immune responses are generated against native antigens using Lipoparticles (high-concentration membrane proteins) and DNA immunization. Chickens are used because most membrane proteins are highly conserved, while both phage display and B-cell cloning are used for isolation. MAbs are engineered using high-throughput Shotgun Mutagenesis and profiled for specificity using a comprehensive membrane proteome array.

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

CONTINUED

11th Annual | April 25 - 26

Difficult to Express Proteins

Strategies for Taming "Finicky" Proteins

CASE STUDIES: MAKING THE DIFFICULT EASY

2:00 Chairperson's Remarks

Arjan Snijder, Ph.D., Associate Principal Scientist, AstraZeneca Discovery R&D

2:05 Efficient Production of Aggregation-Prone Proteins Inspired by How Spiders Store Silk Proteins

Janne Johansson, Ph.D., Professor, Neurobiology, Care Sciences and Society, Karolinska Institutet Center for Alzheimer Research, Novum

Spiders are able to store silk proteins (spidroins) at huge concentrations by sequestering the spridroins' aggregation-prone regions into micellar structures, in which the very soluble spidroin N-terminal domain (NT) contributes to the shell. We found that yields of soluble NT-transmembrane protein (TM) fusions after expression in *E. coli* are two to eight times higher compared to conventional tags like thioredoxin and PGB1. Furthermore, NT enables production of non-TM aggregation prone proteins that have previously been refractory to recombinant production.

2:35 Development of an Alternative Purification Method for Difficult to Express Proteins

Arjan Snijder, Ph.D., Associate Principal Scientist, AstraZeneca Discovery R&D

We present a purification method where affinity resin is contained in a porous-walled container, which supports clarification, capture and purification, in a single step thus reducing hands-on and processing time without significant investments in equipment. The process will be illustrated with a number of challenging pharmaceutically relevant protein targets, including secreted proteins, membrane proteins, enzymes and kinases.

Sponsored by WACKER

3:05 Manufacturing of Recombinant Biopharmaceuticals by FOLDTEC® - A Novel Toolbox of Expression Hosts, Plasmids and Refolding Expertise

Andreas Anton, Ph.D., Director, BioProcess Development, Wacker Biotech GmbH

Wacker Biotech is showcasing its novel refolding technology for bioengineered pharmaceutical proteins. With the new technology biopharmaceuticals that tend to aggregate can be efficiently produced in their soluble-active form in high yields. The proprietary process utilizes optimized bacterial strains and a patented, antibiotic-free expression system. WACKER can now cost-efficiently and reliably produce pharmaceutical proteins that are prone to aggregation, and thus difficult to manufacture, in high yields and utmost purity for its customers.

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

TRANS-SPLICING AND PROTEIN SYNTHESIS

4:25 Assembling Correctly Folded and Functional Heptahelical Membrane Protein by Protein Trans-Splicing

Michaela Mehler, Doctoral Researcher, Biophysical Chemistry, JW Goethe University

Protein trans-splicing using split inteins is established as a tool for protein engineering. We show that this method can be applied to a membrane protein under native conditions *in vivo*. Our data show that the ligation product is identical to its non-ligated counterpart demonstrating that a correctly folded and functional protein can be produced in this artificial way. Our findings are of high relevance for a general understanding of the assembly of membrane proteins and they support the development of novel labeling options.

4:55 Eukaryotic *in vitro* Translation Systems: Cell-Free Synthesis of Post-Translationally Modified Membrane Proteins

Lena Thoring, Bioanalytics and Bioprocesses, Fraunhofer Institute for Cell Therapy and Immunology (IZI)

In vivo expression systems currently used for protein production processes have often shown issues during synthesis of so called "difficult-to-express" proteins. To circumvent the disadvantages of *in vivo* protein expression systems novel cell-free systems for the synthesis of proteins were developed based on translationally active extracts of eukaryotic cells. Endogenous microsomal structures present in these platforms enable the direct production of correctly folded, membrane embedded and post-translationally modified proteins.

5:25 End of Difficult to Express Proteins

5:30 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC8: Next-Generation Sequencing of Antibody Libraries: Bridging Experimental and Bioinformatic Methods

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

6th Annual | April 27 - 28

Optimizing Protein Expression

Enhancing Expression Systems

RECOMMENDED PRE-CONFERENCE SHORT COURSE*

SC9: Overcoming the Challenges of Immunogenicity Assessment

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

WEDNESDAY, APRIL 27

7:00 am Registration and Morning Coffee

OPTIMIZING EXPRESSION SYSTEMS

8:00 Chairperson's Remarks

Donald L. Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming

» 8:10 KEYNOTE PRESENTATION:

Expression and Purification of Proteins for Drug Discovery – Challenges and Trends

Ian Hunt, Ph.D., Group Leader, Protein Sciences, Novartis

8:40 Multiple Approaches to Optimize Protein Production for Shortening the Discovery Process of Non-Antibody Protein Therapeutics

Liang Tang, Ph.D., Senior Scientist and Group Head, Molecular Biology and Protein Expression, Global Biologic Research, Global Drug Discovery, Bayer HealthCare

During therapeutic drug discovery, we need to produce non-antibody proteins. Expression of these proteins with proper post translation modifications within a limited time is challenging. At Bayer, we established systems of multiple approaches to optimize the process of non-antibody protein expression starting from expression vector design, evaluation and selection of cell types for protein expression, purification and efficient QC process for shortening the discovery process of new protein therapeutics.

9:10 Reducing Manufacturing Costs from the Start: Optimization of COGs at the Early Cell Line Development Stage

Irene Liu, Senior Associate Scientist, Cell Line Development, Pre-Pivotal Drug Substance-PD, Amgen, Inc.

A major focus in mammalian biopharmaceutical process development is lowering the manufacturing cost of goods (COGs). One major COG is the high cost of medium supplements used throughout the upstream cell culture process. We focus on the production cell line requirements for these additives. A gradual directed evolution strategy was applied to several existing production CHO cell lines and non-expressing host cell lines. These studies illustrate that significant COG savings can be achieved when applied during early cell line development.

9:40 Enhanced Synthesis of Recombinant Phosphoproteins in *E. coli* is Enabled by a New Genetic Code

Jesse Rinehart, Ph.D., Assistant Professor, Cellular & Molecular Physiology, Systems Biology Institute, Yale University School of Medicine

We have recently created a technology that enables site-specific incorporation of phosphoserine into proteins by expanding the genetic code of Escherichia coli. We are now applying this technology to understand the properties of phosphoserine in human kinases. Our current research aims have benefitted tremendously from our recent improvements to our phosphoserine technology. Advances on all fronts will be discussed with attention to the broad application of recombinant phosphoprotein production.

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

CONTINUED

6th Annual | April 27 - 28

Optimizing Protein Expression

Enhancing Expression Systems

EXPRESSING PROTEIN WITH CHO

10:55 Stable Glycoengineering of CHO Cells for Production of Diverse, Homogeneous Glycoproteins

Malene Bech Vester-Christensen, Ph.D., Senior Scientist, Recombinant Expression Technologies, Novo Nordisk A/S

Production of glycoprotein therapeutics in Chinese hamster ovary (CHO) cells is limited by the cells' generic capacity for N-glycosylation, and production of glycoproteins with desirable homogeneous glycoforms remains a challenge. We conducted a comprehensive knockout screen of glycosyltransferase genes controlling N-glycosylation in CHO cells and constructed a design matrix that facilitates the generation of glycoproteins with a desired homogeneous N-glycosylation.

11:25 Direct PCR Methods for Quantification of Residual Host DNA in Monoclonal Antibody Drugs Manufactured in CHO Cells

Musaddeq Hussain, Ph.D., Principal Scientist, BioProcess Development, Biologics and Vaccines Research, Merck Research Laboratories

Chinese hamster ovary (CHO) cells are the host of choice for manufacturing monoclonal antibody (mAb) drugs. HosT Cell DNA is an impurity of such manufacturing process and must be monitored. Conventional methods require extraction of DNA from the mAb drug before quantification by PCR. Since femtogram amount DNA extraction is typically inefficient, we have developed 'direct PCR' methods eliminating extraction step. The method is usable for both qPCR and dPCR.

11:55 To Fucosylate or Not: Utilizing FX Knockout CHO Lines to Express WT or Afycosylated Antibodies on Command

Shahram Misaghi, Ph.D., Scientist, Early Stage Cell Culture, Genentech, a member of the Roche Group

Here we introduce generation and use of a FX-KO CHO hosT Cell line that is capable of expressing antibody molecules with either afucosylated or WT glycan profiles. This host not only obviates the need for undertaking two separate CLD efforts, but it can also be used to generate WT or afucosylated antibody molecules with similar product quality attributes, since both versions of the antibody are made by the same cell-line.

12:25 pm A 2L-12L Orbital-Shaken SUB as an Alternative to Stirred and Wave Reactors for Protein Expression Experiments

Sponsored by Kuhner shaker

David Laidlaw, CEO, Kuhner Shaker, Inc

Ina Dittler, Ph.D., Zurich University of Applied Sciences

A technically conserved, low-shear and low foaming 2L-12L orbital shaken SUB, the Kühner SB10-X, is presented here as an alternative to stirred and wave reactors for batch protein production. This presentation will describe the bioreactor technical specifications and provide Sf9 and CHOK1 cultivation data for the SB10-X compared to flasks and stirred reactors.

12:40 Automated Cell Culture and Cell Line Development to Optimize Expression

Sponsored by Beckman Coulter Life Sciences

Speaker to be Announced

12:55 Luncheon Presentation I: Maximizing Soluble Expression of Complex Multimeric Proteins in the *E. coli* Cytoplasm Using Tightly Regulated Expression

Sponsored by AbSci

Sean McClain, CEO and Founder, AbSci

Cytoplasmic expression of large complex proteins in *E. coli* is limited primarily due to protein aggregation, which results from poorly controlled expression. AbSci has developed a tightly regulated, dual titratable expression system, SoluPro, that is able to homogenously induce high levels of these proteins, without modification, in a form that is soluble and active. SoluPro is an all-in-one platform that accelerates drug discovery, eliminates extended cell line development, and achieves multi g/L yields in 24-48 hours.

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

1:55 Session Break

EXPRESSING PROTEIN WITH CHO (CONT.)

2:10 Chairperson's Remarks

Robert Roth, Ph.D., Associate Principle Scientist, Reagents and Assay Development, Discovery Sciences iMed, AstraZeneca

2:15 miRNA Engineering of CHO Cells

Vaibhav Jadhav, Ph.D., Scientist, Austrian Centre of Industrial Biotechnology, ACIB

In this presentation, I will give an overview of miRNAs and a detailed study of miR-17 overexpression, which resulted in a two-fold increase in specific productivity without loss in growth rate. Dissection of the effects of miR-17 overexpression on the transcriptome and proteome of CHO cells contributes to understanding the molecular mechanisms that control the interaction of growth and productivity, the two most important process-relevant parameters in CHO.

2:45 Designed to be Scaled Up: *Pichia pastoris, E. coli, S. cerevisiae* and CHO

Anton Glieder, Ph.D., Professor, Molecular Biotechnology, Graz University of Technology

Employing *Pichia pastoris* as a host strain, we emphasized vector design, development of new chassis strains, and alternative biosynthetic pathway assembly strategies in order to obtain robust microbial strains with stable maintenance of multiple gene copies, opportunities for stepwise increase in bioreactors, and enhanced reliability in larger volumes. The methodology is generic and can be transferred to other hosts, as demonstrated by examples using *E. coli*, S. cerevisiae and CHO.

3:15 Automated Transient Transfection for High-Throughput Protein Production

Sponsored by PhyNexus

Chris Suh, Ph.D., Business Development Manager, PhyNexus, Inc.

Transient transfection of mammalian cell lines is being implemented by the pharmaceutical industry to produce the therapeutic protein candidates very rapidly compared to previous technology thus allowing large numbers of drug candidates to be screened and studied. However, high throughput automated transient transfection is required for increased sample load. Here we describe the integration, implementation and validation of different robotic platforms for automated transient transfection of mammalian cells.

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

4:45 Problem-Solving Breakout Discussions

See website for details.

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

7:00 End of Day

CONTINUED

6th Annual | April 27 - 28

Optimizing Protein Expression

Enhancing Expression Systems

THURSDAY, APRIL 28

8:00 am Morning Coffee

ENGINEERING ALTERNATIVE SYSTEMS

8:30 Chairperson's Remarks

Vaibhav Jadhav, Ph.D., Scientist, Austrian Centre of Industrial Biotechnology, ACIB

8:35 Improving InsecT Cells as Hosts for the Baculovirus System

Donald L. Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming

InsecT Cell lines have several limitations as hosts for recombinant protein production. These limitations can and should be addressed to optimize the baculovirus system as a recombinant protein manufacturing platform. For the past 20 years, we have focused on optimizing protein glycosylation in the baculovirus system. This presentation will focus on those efforts, on the new systems emerging from these efforts, and on their major biomedical applications.

9:05 Next-Generation Biotherapeutic Production System: The Filamentous Fungus Trichoderma Reesei

Christopher Landowski, Ph.D., Senior Research Scientist, Industrial Biotechnology, VTT Technical Research Centre of Finland, Ltd.

The filamentous fungus Trichoderma reesei is an important production organism used by industrial enzyme companies worldwide. It secretes its native enzymes at levels exceeding 100 g/L of culture medium and is amenable to large-scale fermentation processes. We have adapted the fungus to become more suitable for biotherapeutic production by reducing secreted protease activity and in some cases altering glycosylation pathways needed for adding mammalian glycoforms.

9:35 Strep-Tactin XT– A Superior Next Generation System for Purification of Proteins, Isolation of Cells and Assay Development

Uwe Carl, Ph.D., Head, Protein Production, Strep-tag Products and Proteins, IBA GmbH

Sponsored by

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Solutions For Life Sciences

9:50 Sponsored Presentation *(Opportunity Available)*

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

NEXT-GENERATION TECHNOLOGIES FOR PROTEIN EXPRESSION

11:05 Genomically Encoded Analog Memory with Precise *in vivo* DNA Writing in Living Cell Populations

Timothy K. Lu, M.D., Ph.D., Assistant Professor, Biological & Electrical Engineering, Massachusetts Institute of Technology (MIT)

The conversion of transient information into long-lasting responses is a common aspect of many biological processes and is crucial for the design of sophisticated synthetic circuits. Genomic DNA provides a rich medium for the storage of information in living cells. However, currenT Cellular memory technologies are limited in their storage capacity and scalability. We converted genomic DNA into a "tape recorder" for memorizing information in living cell populations.

11:35 Expression and Characterization of the Human Cytomegalovirus (HCMV) Pentamer Complex for Vaccine Use

Andrea Carfi, Ph.D., U.S. Head, Protein Biochemistry, GlaxoSmithKline Vaccines

Human cytomegalovirus (HCMV) causes significant disease worldwide. The HCMV gH/gL/UL128/UL130/UL131A complex (Pentamer) is the main target of neutralizing antibodies (Nabs) in HCMV seropositive individuals and raises high titers of Nabs in small animals and non-human primates . We describe here the development of a mammalian expression system for large scale Pentamer production. We also present initial biochemical, antigenic and structural characterization of this promising vaccine candidate.

12:05 pm Identification of Novel Regulators of Recombinant Protein Expression Using Phenotypic Screening Followed by Target Validation using CRISPR/Cas9

Robert Roth, Ph.D., Associate Principle Scientist, Reagents and Assay Development, Discovery Sciences iMed, AstraZeneca

By creating isogenic cell lines with a defined copy number of the gene encoding the expressed recombinant protein of interest, we minimized genetic locus effects. Using phenotypic screening, we identified positive and negative regulators of recombinant protein secretion, which was then confirmed using precise genome editing. Our findings show that utilising model isogenic reporter cell lines in orthogonal screening assays is a powerful method to rapidly identify novel regulators critical to enhanced protein expression.

12:35 End of Optimizing Protein Expression

5:15 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC12: Strategic Bioassay Design and Analysis

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

2nd Annual | April 28 - 29

Protein Expression System Engineering

Gene to Structure

RECOMMENDED PRE-CONFERENCE SHORT COURSE*

SC9: Overcoming the Challenges of Immunogenicity Assessment

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

THURSDAY, APRIL 28

GAINING GREATER INSIGHTS

12:35 pm Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

Jagroop Pandhal, Ph.D., Lecturer, Biological Engineering, Chemical and Biological Engineering, The University of Sheffield

» 1:50 KEYNOTE PRESENTATION:

Protein Microarrays for Studies in Biomarkers and Post Translational Modification

Joshua LaBaer, M.D., Ph.D., Director, Virginia G. Piper Center for Personalized Diagnostics, The Biodesign Institute, Arizona State University

Self-assembling protein microarrays arrays can be used to study protein-protein interactions, protein-drug interactions, search for enzyme substrates, and as tools to search for disease biomarkers. In particular, recent experiments have focused on using these protein microarrays to search for autoantibody responses in cancer patients. These experiments show promise in finding antibody responses that appear in only cancer patients. New methods using click chemistry-based reagents also allow the application of these arrays for discovering new substrates of post translational modification.

2:20 Application of GFP Micro Domain Tagging for Protein Detection and Directed Evolution

Geoffrey Waldo, Ph.D., Research Scientist Level 4, HRL, Los Alamos National Labs

We have developed a new suite of genetically encoded tags that do not perturb protein function or folding. These tags are comprised of single beta strands of GFP. They bind to the rest of the GFP to restore fluorescence. We describe the application of these systems to evaluate protein expression, engineer proteins for soluble expression, and monitor protein complex formation. Our most recent work now includes the challenging class of membrane proteins.

2:50 GlycoExpress: A Toolbox for High Yield Production of Glycooptimized Fully Human Biopharmaceuticals in Perfusion Bioreactors at Different Scales

Rainer Stahn, Ph.D., Head, Clone Development, Upstream Process Development and PTM Analytics, Glycotope GmbH

With the GlycoExpress toolbox, we have generated a set of glycoengineered human cell lines for high yield production and for improvement of the clinical efficacy and side effects of fully human biopharmaceuticals. Independent of the applied cell retention mechanism and production scale, GlycoExpress cells show robust growth and consistent glycosylation along with no measurable differences in product quality between batches, batch sizes, reactor sizes, process control strategies, DSP scales and production site.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Refreshment Break

ENGINEERING EXPRESSION SYSTEMS FOR GREATER PRODUCTIVITY

4:20 Tiny but Mighty: Harnessing microRNAs for Pathway Engineering of CHO Cell Factories

Simon Fischer, Ph.D., Scientist, BP Process Development Germany, Boehringer Ingelheim Pharma GmbH & Co. KG

The biopharmaceutical industry is currently facing increasing numbers of new biological entities that often turn out to be difficult to express. These molecules can substantially challenge cell line development in order to establish high-yielding production clones. microRNAs were recently demonstrated as exciting new modulators of cell phenotypes in CHO cells. This presentation provides insights into successful exploitation of microRNAs as next-generation cell engineering tool for CHO production cells.

4:50 Role of Codon Optimization and Signal Peptide towards High Titer in Antibody Production

Saurabh Sen, Ph.D., Principal Scientist, Immune Modulation and Biotherapeutics Discovery, Boehringer Ingelheim Pharmaceuticals, Inc.

Multitudes of factors play an integral role towards generation of high antibody titers in a transient expression system. The increasing demands in volume and speed have driven us to explore the need for optimization of the codon bias and use of proper signal peptides during transient expression. The presentation will describe our recent efforts towards this end.

5:20 End of Day

5:15 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC12: Strategic Bioassay Design and Analysis

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

FRIDAY, APRIL 29

8:00 am Registration and Morning Coffee

ENGINEERING *E. COLI* FOR GREATER PRODUCTIVITY

8:30 Chairperson's Remarks

Krista Alvin, MS, Associate Principal Scientist, Bioprocess Technology & Expression, Merck, Inc.

8:35 Maximizing the Output from an RBS

Daniel Daley, Ph.D., Associate Professor, Biochemistry & Biophysics, Stockholm University

High-level production of recombinant proteins in *E. coli* is usually obtained with plasmids containing optimised genetic elements (i.e. promoter / RBS / ori). Despite this, some proteins are still difficult to produce. Our data indicate that incompatibly between the RBS and the CDS is a common cause of poor production. We will present a simple and inexpensive PCR-based method for harmonizing these two elements that boosts production levels considerably.

CONTINUED

2nd Annual | April 28 - 29

Protein Expression System Engineering

Gene to Structure

9:05 A New, Growth Decoupled *E. coli* Expression System

Gerald Striedner, Ph.D., Assistant Professor, Biotechnology, University of Natural Resources and Life Sciences, Vienna

Our *E. coli* expression system design is strongly focused on making them fit for production conditions. One strategy to improve the capabilities of cells for production of finicky or toxic proteins by decoupling cell growth and product formation. In such decoupled systems cells allocate full protein synthesis capacity to recombinant protein production.

9:35 Expanding the *E. coli* Toolbox: Metabolic Engineering to Improve Protein Glycosylation Efficiency

Jagroop Pandhal, Ph.D., Lecturer, Biological Engineering, Chemical and Biological Engineering, The University of Sheffield

E. coli is a relatively simple cell chassis with no native glyco-machinery and could therefore make uniform homogenous glycoforms. Although attention has been afforded to the different glycans that can be produced, the efficiency of the system is poor (~1-13% of recombinant protein is glycosylated). We work to improve this efficiency, using systematic metabolic engineering, omics-based forward engineering, and inverse metabolic engineering, together with improving quantitative analysis of the proteins using high accuracy mass spectrometry.

10:05 Coffee Break

SYSTEMS BIOLOGY & GENE EDITING

10:35 CRISPR-Cas9 Mediated Efficient and Complete Knock-In of Destabilization Domain-Tags Allows for Reversible and Regulated Knock-Out of Protein Function

Benhur Lee, M.D., Professor and Ward-Coleman Chair, Microbiology, Icahn School of Medicine, Mount Sinai

We present a CRISPR-Cas9 mediated strategy for efficient and complete knock-in of in-frame degron-domain (DD) tags for interrogating the function of genes that are critical for cell growth and viability. Protein levels can be regulated by different small molecules that control the activity of the various degron-domains. CRISPR/Cas9-mediated knock-in of DD tags represents a generalizable and efficient strategy to achieve rapid modulation of protein levels in mammalian cells.

11:05 Overcoming Obstacles to Recombinant Production of Human Homologs of Bacterial Asparaginases Used as Approved Antileukemic Enzymes

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

As an alternative to currently used therapeutic enzymes of bacterial origin, we pursue molecular engineering of human asparaginase homologs. We developed expression strategies to efficiently produce two human enzymes that require posttranslational processing to gain catalytic activity. We show that transient translational pausing due to rare codons may be essential to overcoming protein misfolding and that strong complexation with the chaperonin complex GroEL/ES can be suppressed in order to achieve efficient protein production.

11:35 Chromatin Function Modifying Elements in an Industrial Antibody Production Platform

Mark Ellis, Principal Scientist, UCB-New Medicines

The isolation of stably transfected cell lines for the manufacture of biotherapeutic protein products can be an arduous process. This frequently involves transgene amplification and maintenance over many generations. We assessed four chromatin function modifying elements for their ability to negate chromatin insertion site position effects and their ability to maintain antibody expression. Stability analysis demonstrated that the reduction in expression was mitigated in the clones containing A2UCOE-augmented transgenes.

12:05 pm Empowering VHH Single-Domain Antibodies with Protein A Binding Activity

Mehdi Arbabi Ghahroudi, Ph.D., Research Officer/Adjunct Professor, Human Health Therapeutics, National Research Council Canada

Here we present a rapid engineering approach to confer SpA binding upon camelid single-domain antibodies, based on mutagenesis studies and a comparison with a protein A:Fab crystal structure, with no adverse effect on antigen binding. Next-generation sequencing of llama, alpaca and dromedary sdAb repertoires revealed sequence hallmarks that may underlie species-specific SpA binding patterns. This approach may be applicable to IGHV domains of other species, or non-IGHV3 human domains (scFvs or Fabs).

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

1:05 Refreshment Break

VECTOR, CODON & CLONE ENGINEERING

1:35 Chairperson's Remarks

Geoffrey Waldo, Ph.D., Research Scientist Level 4, HRL, Los Alamos National Labs

1:40 Expression of Multiple Antibody Formats in Mammalian Cells from a Single Phage Display Clone Mediated by RNA Trans-Splicing

Isidro Hotzel, Ph.D., Senior Scientist, Antibody Engineering, Genentech, a member of the Roche Group

Antibody discovery and optimization campaigns usually need different antibody formats such as IgG and Fab fragments for screening, requiring the transfer of inserts in large panels of phage display clones to multiple specialized mammalian expression vectors. We developed a modular protein expression system based on pre-mRNA trans-splicing that bypasses clone reformatting steps and enables the expression of multiple antibody formats in mammalian cells directly from a single phage display clone.

2:10 Optimizing Assembly and Production of Bispecific Antibodies by Codon De-Optimization

Giovanni Magistrelli, Ph.D., Head, Protein Engineering, NovImmune SA

We have developed a native human bispecific antibody format, the kλ body , which relies on the co-expression of three polypeptides, one heavy chain and two light chains. Maximal bispecific antibody production is achieved when expression of the two light chains is relatively equivalent. Of particular significance was the finding that codon de-optimization - instead of optimization - of the chain that is over expressed led to significant improvements in bispecific antibody yield.

2:40 Systematic Approaches to Engineering Antibody and Integral Membrane Protein Expression

James Love, Ph.D., Director, Technology Development, Biochemistry, Albert Einstein College of Medicine

We describe a systematic engineering approach that combined machine learning methods with gene synthesis to explore vector element and codon optimization determinants of protein/antibody expression. Combinations of vector components were designed so that elements are varied systematically and independently; this Design-of-Experiment approach allowed us to sample a large sequence-space without exhaustive testing. We then used advanced machine learning algorithms to assess the contribution of each element to vector performance.

3:10 Cell Engineering to Improve Productivity through High-Throughput Screening Technologies

Krista Alvin, MS, Associate Principal Scientist, Bioprocess Technology & Expression, Merck, Inc.

Recombinant protein productivity has increased at an exponential rate over the past 10 years, making the task of further improving mammalian cell production increasingly challenging. Here, we will present the identification of new intracellular targets and the corresponding signaling pathways that affect recombinant protein secretion through high-throughput approaches. It provides a basis for the rational design of both cellular and process engineering strategies to further improve protein production.

3:40 End of Protein Expression System Engineering

6th Annual | April 25 - 26

Characterization of Biotherapeutics

Optimizing the Analytical Function in an Era of New Product Formats

RECOMMENDED PRE-CONFERENCE SHORT COURSES*

SC2: Bioanalytical Considerations of Multi-Domain Biotherapeutics: Preclinical and Clinical Development

SC6: *In Silico* Immunogenicity Predictions (Hands-On) Workshop

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

MONDAY, APRIL 25

7:00 am Registration and Morning Coffee

8:30 Chairperson's Remarks

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

» 8:40 KEYNOTE PRESENTATION

Analytics: A View to the Horizon and Applications Advancing Attribute Control

Janet Cheetham, Ph.D., Executive Director, Attribute Sciences Core Technologies, Amgen Inc.

Concurrently, advances in analytical technologies have delivered significant improvements in sensitivity, resolution, speed and precision, as well as increased deployment flexibility through reduced footprints. With a view to the horizon, a strategic roadmap can be shaped and scientific and technology advances and transformation accelerated through a commitment to collaboration between industry peers and vendors leveraging established pre-competitive models, together with a continuing partnership and engagement with the international regulatory agencies.

ANALYTICAL DEVELOPMENT FOR EMERGING BIOTHERAPEUTICS

9:10 Analytics by Design: Tailored Approaches to Detect Product-Related Impurities in Next-Generation Biotherapeutics

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

Generic analytical methods for the characterization of biotherapeutics save time and resources during early stages of development. However, generic methods may not provide enough information about critical quality attributes for next-generation biotherapeutics such as bispecific antibodies and fusion proteins. Here, we describe tailored approaches for the rapid analytical method development for such proteins. We combine theoretical considerations with analytical data collected during cell line development and developability assessments to draft a control strategy.

9:40 Biophysical and Functional Characterization of an Anti-TNF Polymer

Ivan Correia, Ph.D., Research Fellow; Head, Global Protein Sciences, AbbVie Bioresearch Center

We engineered repeats of the hydrophobic polypeptide "VPGXG" from the ECM protein elastin onto an anti-TNF monoclonal antibody. The engineered molecule retained properties of its parent and in addition showed a temperature driven phase transition (Tt). Insoluble aggregates were formed above the Tt and upon lowering the temperature the molecule re-dissolved and retained properties of the parent molecule. We exploit features of this engineered anti-TNF molecule for novel therapeutic applications.

10:10 Coffee Break

10:50 Selective, Non-Covalent Conjugation of Peptides with Proteins Using Host-Guest Chemistry

Christopher van der Walle, Ph.D., Fellow, MedImmune

In a host-guest chemistry approach, the macrocycle cucurbit[8]uril host is shown to selectively conjugate two guests: a recombinant protein with a synthetic peptide. This non-covalent approach does not require chemical modification of the protein and maintains the biological activity of the conjugated peptide. Calorimetry, fluorescence and light scattering data are used to fully characterize the heteroternary complex. The strategy represents a powerful approach for the development of novel therapeutic biologics.

11:20 A High Throughput Functional Assay Screening Platform for Cancer Immunotherapies

Ying-Kai Wang, Ph.D., Senior Research Investigator, Lead Discovery and Optimization, Bristol-Myers Squibb

In light of the success of monoclonal antibodies as biotherapeutics, there is a critical need for establishing a high throughput functional assay screening platform for biotherapeutics, with fully integrated automation process and informatics support. However, biotherapeutics are aqueous, protein-containing samples that are liable to many factors, for example, contamination, and degradation, thus requiring different working conditions and processes in high throughput environments.

11:50 High Throughput Assays for the Determination of the Potency and Comparability of Biosimilars and Innovator Products

Michael G. Tovey, Ph.D., INSERM Director, Research, Laboratory of Biotechnology & Applied Pharmacology, Ecole Normale Supérieure de Cachan

Biosimilar development is dependent upon establishment of validated and standardized assays that allow comparisons of innovator molecules and biosimilars. A validated standardized high throughput assay platform will be described that is applicable to most biopharmaceuticals and that allows direct comparison of drug potency and comparability of innovator molecules and biosimilars in the same assay. Case studies will be presented for biopharmaceuticals ranging from novel forms of human insulin and FGF-21 to structurally diverse TNF-(INSERT SYMBOL) antagonists.

Sponsored by UNCHAINED LABS

12:20 pm Stop Losing Your Mind Over Biologic Stability, Break Free!

Speaker to be Announced

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

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

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

See website for details.

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

CONTINUED

6th Annual | April 25 - 26

Characterization of Biotherapeutics

Optimizing the Analytical Function in an Era of New Product Formats

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 The Promise of Cancer Immunotherapy: An Overview of Recent Advances and Jounce's Approach to Delivering the Right Therapy to the Right Patient

Deborah Law, D. Phil. CSO Jounce Therapeutics, Inc.

As immunotherapies become an increasingly important component of cancer treatment the challenge will be to identify ways to provide the best therapy(s) to the individual. This presentation will provide an overview of current cancer immunotherapies as well as highlight some of the challenges ahead including selection of optimal combinations, moving outside of T Cell-directed approaches, and will highlight how Jounce Therapeutics is using its Translational Science Platform as an approach to develop and deliver the right therapy to the right patient.

4:50 Antibody as Drugs: Then, Now and Tomorrow

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

Antibodies have grown into a clinically and commercially important drug class with more than >45 antibodies marketed for imaging or therapy in the USA and/or Europe and with ~$63 billion in worldwide sales in 2013. This presentation will highlight progress in developing antibody drugs and consider opportunities for future innovation.

5:30 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 End of Day

TUESDAY, APRIL 26

8:00 am Morning Coffee

AUTOMATION AND EMERGING ANALYTICAL METHODS

8:25 Chairperson's Remarks

Ivan Correia, Ph.D., Senior Principal Research Scientist; Head, Global Protein Sciences, AbbVie Bioresearch Center

8:30 Use of Molecular Dynamics to Predict Chemical Degradation

Trevor Swartz, Ph.D., Senior Scientist, Early Stage Pharmaceutical Development, Genentech

Liquid formulation of therapeutic monoclonal antibodies requires the protein to be chemically stable during long-term storage. This presentation describes in-silico tools to predict potential for chemical modification. These tools involve building three-dimensional structures using homology modeling and then running molecular dynamics simulations. The potential for both Trp oxidation and Asp isomerization was predicted by extracting structural parameters from molecular dynamics simulations. The *in silico* tools described allow for rapid screening for mAb candidates during early discovery, enabling selection of molecules with optimal behavior.

9:00 The Role of Analytical Automation in Transforming Drug Product Development

Rahul Rajan, Ph.D., Director and Functional Area Head, Drug Product Formulation, Amgen, Inc.

The industry needs to develop drug products faster, in the face of new modalities that challenge the development status quo. We present case studies where assays and workflows critical to robust drug product development were miniaturized and/or automated. These include attributes such as viscosity and particulate level measurement, as well aspects such as sample preparation and labeling. These advances accelerate product development and create the capability to measure a larger design space.

9:30 Biochemical Analysis and Its Correlation with Functional Assays

Babita Parekh, Ph.D., Director, Bioanalytical Science, Eli Lilly and Company

Therapeutic monoclonal antibodies typically exist as a heterogeneous mixture of product variants. Furthermore proper protein folding is critical to an antibodies biological activity and efficacy. Post translational modifications that impart heterogeneity may change the biological functions of an antibody. Structural characterization helps in pinpointing the change and in establishing structure function correlation. Analytical work performed to understand the molecule and to support product safety, quality and efficacy will be discussed.

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

10:50 Applications of an Automated and Quantitative CE-Based Size and Charge Western Blot for Therapeutic Proteins and Vaccines

Richard Rustandi, Ph.D., Principal Scientist, Vaccine Analytical Development, Merck Research Labs

Labor intensive SDS-PAGE and IEF slab gels have been replaced with CE-SDS and CE-IEF methods, respectively, in the biopharmaceutical industry. Another traditional slab gel technique is the western blot, which detects proteins using immuno-specific reagents after SDS-PAGE separation. This technique is very laborious, manual, time consuming and only semi-quantitative. Here, we describe the applications of a relatively new CE-based western blot technology that is automated, fast and quantitative.

11:20 The Neonatal Fc Receptor (FcRn) Binds Independently to Both Sites of the IgG Homodimer with Identical Affinity mAbs

Yasmina Abdiche, Ph.D., Research Fellow; Head, Bioanalytical Group, Rinat-Pfizer

FcRn plays a central role in extending an antibody's half-life, yet published studies on the molecular binding mechanism of the FcRn/IgG interaction have been confounded by avidity, often due to an earlier hypothesis of disparate FcRn-binding sites. We demonstrate that two FcRn molecules bind an IgG homodimer with identical affinities at independent sites. Our *in vivo* studies highlight the biological importance of avidity in extending an IgG's serum half-life.

11:50 Deciphering Factors that Have Impacts on Glycosylation of mAb and its Biophysical Properties

Zhimei Du, Ph.D., Senior Principal Scientist, Merck

Consistent and reproducible generation of mAb glycoform profiles still remains a considerable challenge in biopharmaceutical industry. To assess the mechanism of immature glycan process, and to minimize the environment-mediated lot-to-lot variations, we identified a broad range of factors that impact on the glycosylation maturation of mAbs. Our results indicate that high mannose may lead to changes in biophysical properties including protein conformation, thermal stability, colloidal stability, and aggregation propensity.

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

CONTINUED

6th Annual | April 25 - 26

Characterization of Biotherapeutics

Optimizing the Analytical Function in an Era of New Product Formats

AUTOMATION AND EMERGING ANALYTICAL METHODS (CONT.)

2:00 Chairperson's Remarks
Babita Parekh, Ph.D., Director, Eli Lilly and Company

2:05 Molecular Interaction Analysis of a Non-Equivalent Two-Site Protein-Protein Interaction with Multiple Biophysical Methods
Michael Doyle, Ph.D., Senior Principal Scientist, Protein Science, Bristol-Myers Squibb
Quantitative analysis of protein interactions with biophysical methods plays a key role in discovery of drug candidates. The accuracies of different biophysical methods is influenced by different caveats and assumptions. We used a bivalent form of barnase and barstar as a model system to test the abilities of ITC, SPR and AUC to resolve both binding equilibrium constants. The strengths, weaknesses, and synergies of these technologies will be discussed.

2:35 Optimization of the Sensitivity and Selectivity of an Immunoassay for an ADC mAb in Cancer Patients
Molly Karlinsey, Ph.D., Investigator, Bioanalysis, GlaxoSmithKline
Therapeutic target receptor up-regulation and shedding in disease populations can be problematic for adequate immunoassay sensitivity and selectivity. Competition between the up-regulated/shed target and immunoassay capture mechanisms require careful optimization to ensure the most robust tolerance to circulating target concentrations. Strategies for proper optimization of the capture reagent, sample diluent and wash steps to allow suitable clinical support will be discussed in detail.

3:05 Sponsored Presentation *(Opportunity Available)*

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

ADVANCED APPLICATIONS OF MASS SPECTROMETRY

4:25 Hydrogen Exchange Mass Spectrometry to Address Questions of Higher Order Structure for Biotherapeutics
Roxana Iacob, Ph.D., Research Assistant Professor, Northeastern University
The higher-order structure of proteins is responsible for their uniqueness and dictates their function. Higher-order structure can be interrogated with mass spectrometry and in particular by hydrogen exchange mass spectrometry (HDX MS). HDX MS is a widely used tool for the structural characterization of biotherapeutics and plays an important role in the biopharmaceutical industry. Here, recent advances in HDX MS and its applicability in biotherapeutics characterization will be presented.

4:55 A Customized HDX Workflow for Locating Protein Binding Interactions and Conformational Differences
Kristopher Truncali, Scientist, Mass Spectrometry, Boehringer Ingelheim Pharmaceuticals
Through changes in deuterium uptake, Hydrogen-Deuterium Exchange (HDX) mass spectrometry can identify differences in solvent accessibility. A customized HDX workflow was developed utilizing a Leap H/D-X PAL, an Orbitrap Fusion, and an in-house software platform. This lecture will provide an overview of the implementation, optimization, and limitations of this customized HDX workflow. Case studies will then be presented where protein binding interactions and conformational differences were identified by the HDX workflow.

5:25 End of Characterization of Biotherapeutics

5:30 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC9: Overcoming the Challenges of Immunogenicity Assessment
**Separate registration required, please see page 5 for course details.*

4th Annual | April 27 - 28

Biophysical Analysis of Biotherapeutics

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

RECOMMENDED PRE-CONFERENCE SHORT COURSE*

SC9: Overcoming the Challenges of Immunogenicity Assessment

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

WEDNESDAY, APRIL 27

7:00 am Registration and Morning Coffee

8:00 Chairperson's Remarks

Joel Bard, Ph.D., Principal Research Scientist, Global Biotherapeutic Technologies, Pfizer

» 8:10 KEYNOTE PRESENTATION:

Designing and Evolving Antibodies with Improved Biophysical Properties

Peter M. Tessier, Ph.D., Associate Professor, Chemical & Biological Engineering, Rensselaer Polytechnic Institute

Methods for rapidly generating and optimizing the properties of monoclonal antibodies are important for a wide range of applications. I will discuss our progress in improving methods for designing, evolving and selecting of single- and multidomain antibodies with stability and solubility in addition to high affinity.

AUTOMATION AND COMPUTATIONAL TOOLS IN BIOPHYSICAL ANALYSIS

8:40 *In Silico* Tools for Predicting PK (Clearance) and Viscosity

Vikas Sharma, Ph.D., Senior Group Leader and Senior Scientist, Late Stage Pharmaceutical Development, Genentech

Delivery of high doses of monoclonal antibodies (mAbs) into the subcutaneous space necessitates that mAb solutions exhibit low viscosity and concomitantly demonstrate normal *in vivo* clearance to enable less frequent dosing. Herein, novel *in silico* tools are discussed that provide rapid assessment of atypical behavior with respect to high viscosity and faster *in vivo* clearance. Strikingly, these behaviors are predicted from simple sequence-derived parameters of hydrophobicity, charge dipole distribution and net charge.

9:10 Database Systems for Consolidation and Analysis of Biotherapeutic Molecular Assessment Results

Joel Bard, Ph.D., Principal Research Scientist, Global Biotherapeutic Technologies, Pfizer

Global Biotherapeutic Technologies at Pfizer uses a number of biophysical and biochemical assays to predict the developability of early stage biotherapeutics. Data from these assays is used to remove sequence liabilities before they can cause problems in production. To improve access to this data and allow analysis across multiple projects, we have recently implemented a database to store these results and provided web applications to simplify its deposition and analysis.

9:40 Understanding Protein Dynamics from Empirical Modeling and Fast Screening

Donald Jacobs, Ph.D., Professor, Physics and Optical Science, University of North Carolina

A critical factor to successful rational drug discovery is the use of representative conformational ensembles to capture the role protein dynamics has on function, kinetics and stability through conformational entropy. To overcome computational challenges in constructing and utilizing conformational ensembles for *in silico* screening applications, the costly molecular dynamics paradigm is replaced with a fast all-atom empirical interfacial thermodynamic model. The link between protein dynamics and thermodynamics is then elucidated.

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

ANALYSIS OF COMPLEX BIOPHYSICAL DATA

10:55 Application of Differential Scanning Calorimetry in Biotherapeutic Comparability

William M. Matousek, Ph.D., Staff Scientist, Protein Biochemistry Preclinical Development, Regeneron Pharmaceuticals, Inc.

Differential Scanning Calorimetry (DSC) is a sensitive technique commonly used to define protein thermal unfolding transitions, assess relative thermal stability, and compare high order structural content. Multiple characteristic unfolding transitions are often observed, making the method amenable for both establishing identity and the estimation of impurities. Thermodynamic properties such as Tm, enthalpy, and heat capacity were evaluated as indicators of structural similarity and purity.

11:25 A Showcase of the Application of Biophysical Analysis in Formulation and Process Development: Interpretation and Misinterpretation of Biophysical Data

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

Enthalpy-entropy compensation causes protein structure to be marginally stable. Therefore, in order to reduce both physical and chemical degradation of a protein, the primary objective is to maximize both its conformational and colloidal stabilities. This presentation will discuss case studies that evaluate (i) the relationship among apparent solubility, conformational stability and protein-protein interactions, (ii) concentration dependent inverse correlation of aggregation, (iii) heat-induced viral inactivation, and (iv) chemical and cold denaturation.

11:55 Supporting Development of Biologic Drugs with Biopharmaceutical Informatics

Satish Singh, Ph.D., Research Fellow and Group Leader, Pfizer

Proactive elimination or mitigation of product development challenges can assure efficient translation of biologic drug candidates into innovative products. Application of computational tools such as informatics, data analyses, modeling and simulations at the earliest stages of product development (i.e., during molecular screening and discovery) helps ensure selection of well-behaved biologic drug candidates. Application of *in silico* tools will be illustrated with the objective of addressing chemical degradation and viscosity.

12:25 pm Next-Generation Microarrays

Sponsored by biametrics biomolecular interaction analysis

Julia Schuette, Head, Marketing and Sales, Biametrics GmbH

Biametrics provides a label-free read out and screening technology for microarrays in standard microscope-slide format. This technology enables the determination of accurate kinetic and thermodynamic constants of almost any kind of biomolecular interaction, ranging from small peptides and antigen/antibody interactions up to virus detection and cell-based assays.

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

1:55 Session Break

EMERGING BIOPHYSICAL ANALYTICAL METHODS

2:10 Chairperson's Remarks

Robert Walters, Ph.D., Senior Scientist, Pfizer

2:15 Developing Protein-Polymer Conjugates for Ocular Therapeutics

Whitney Shatz, MS, Senior Scientific Researcher, Genentech

Studies with intact antibodies and antibody fragments have suggested a size dependence of vitreal clearance and ocular tissue distribution. Protein PEGylation offers an attractive avenue for potentially increasing size and decreasing vitreal clearance. However, protein- polymers are complex molecules and analytical characterization is often challenging. The work here describes the development of a biophysical toolbox that has enabled systematic characterization of a range of potential therapeutic agent-polymer (TAP) conjugates.

CONTINUED

4th Annual | April 27 - 28

Biophysical Analysis of Biotherapeutics

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

2:45 Case Study: Novel Biophysical Approaches to High Concentration Formulation Development

Robert Walters, Ph.D., Senior Scientist, Pfizer

High concentration formulations of therapeutic proteins are desirable as they may enable the delivery of an efficacious dose through subcutaneous injection, which is preferable to intravenous administration. Unfortunately, high concentration formulations often suffer from elevated viscosity that may make subcutaneous injection infeasible. This case study will highlight biophysical and computational approaches to creating novel viscosity reducing agents to facilitate high concentration formulation development.

Smaller, Faster, Deeper: Advanced Light Scattering Tools for Biophysical Characterization

Sponsored by WYATT TECHNOLOGY

3:15 Smaller, Faster, Deeper: Advanced Light Scattering Tools for Biophysical Characterization

John Champagne, Senior Applications Scientist, Northeast Regional Manager, Wyatt Technology Corp.

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

4:45 Problem-Solving Breakout Discussions

See website for details.

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

7:00 End of Day

THURSDAY, APRIL 28

8:00 am Morning Coffee

NEW DEVELOPMENTS IN PARTICLE ANALYSIS

8:30 Chairperson's Remarks

William M. Matousek, Ph.D., Staff Scientist, Protein Biochemistry, Regeneron Pharmaceuticals, Inc.

8:35 Biases between Different Particle Counting Instruments in the 1 µm to 100 µm Range

Dean Ripple, Ph.D., Group Leader, NIST

Particle counting instruments may give particle concentrations that differ by a factor of ten or more, especially for proteinaceous particles. This talk presents experimental data and models that describe these biases for light obscuration, flow imaging, and electrical sensing zone techniques. Prospects and challenges on applying reference materials and instrument models to the correction of these biases will also be discussed.

9:05 The Known Unknowns in Subvisible Particle Characterization – Factors Governing the Analytical Performance of Subvisible Particle Measurement Methods

Atanas Koulov, Ph.D., Group Head, Senior Principal Scientist, Pharma Technical Development Europe (Biologics) Analytics, F. Hoffmann-La Roche Ltd., Switzerland

Although the biopharmaceutical community is actively using a number of techniques for subvisible particle characterization, the current knowledge of the analytical performance of these tools is inadequate to support their routine use in the development of biopharmaceuticals. This talk will outline some recent efforts to increase this knowledge by systematic evaluation of the analytical performance of the principal subvisible particle characterization techniques and also will provide analysis of the fundamental factors governing it.

9:35 Sponsored Presentation *(Opportunity Available)*

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

ANALYSIS OF HIGHER ORDER STRUCTURES FOR FINGERPRINTING AND COMPARABILITY ANALYSIS

11:05 A New Method for Oxidative Mapping of Molecular Interfaces

Michael D. Brenowitz, Ph.D., Professor, Biochemistry, Albert Einstein School of Medicine

New tools are needed for the development of protein therapeutics. Indirect structure mapping ('footprinting') can define solvent accessible surface with as fine as single residue resolution. We have developed a new approach, Pyrite Shrink-Wrap Laminate that supports hydroxyl radical generation via Fenton chemistry for quantitative protein oxidation. Our protocol is inexpensive to conduct, parsimonious with precious material, easy to implement with a laboratory pipet, and scalable to high-throughput implementation.

11:35 High Order Structures (HOS) Elucidation Using Orthoganol Technologies with Case Studies

Jihong Yang, Ph.D., Senior Scientist, Bioanalytical Sciences, Genentech

Higher Order Structure (HOS) is important to ensure the biological functions of protein and antibody therapeutics. Sensitive and robust technologies that can accurately reveal HOS information and subtle changes are therefore valuable for fingerprinting and comparability analysis, and for drug product stability and process control. Emerging technologies that can be used to elucidate HOS were evaluated using a mAb therapeutic case study, and results from orthogonal methods will be discussed.

12:05 pm Critical Review of HOS Fingerprinting Methods

Tapan Das, Ph.D., Director, Biologics Molecular and Analytical Development, Bristol-Myers Squibb

Structural characterization is an integral part of biotherapeutic development. However, appropriate scrutiny of structural methods is key to ensure the chosen methods serve the intended purpose – based on sensitivity of a method and phase-appropriateness. This talk is intended to provide a critical review of selected higher order structure fingerprinting methods along with examples for utility of such data.

12:35 End of Biophysical Analysis of Biotherapeutics

5:15 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC12: Strategic Bioassay Design and Analysis

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

9th Annual | April 28 - 29

Protein Aggregation & Stability

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

RECOMMENDED PRE-CONFERENCE SHORT COURSE*

SC10: Analyzing and Rationalizing Protein-Protein Interactions

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

THURSDAY, APRIL 28

12:35 pm Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

Shantanu Sule, Ph.D., Senior Engineer, Parenteral Drug Product Development, Biogen

» 1:50 KEYNOTE PRESENTATION:

Subvisible Particle and Cell-Based Immunogenicity Characterization of Antibody Therapeutics Pumped Through Clinical Intravenous Infusion Systems: Current In-line Filters are not Adequate

John F. Carpenter, Ph.D., Professor, Pharmaceutical Sciences; Co-Director, Center for Pharmaceutical Biotechnology, University of Colorado Anschutz Medical Center

Numerous therapeutic proteins are administered by intravenous (IV) infusion and can cause immunogenicity and infusion reactions in patients. We found that IV saline contains > 20 million nano- and > 20,000 microparticles per ml; particle levels increased upon addition of therapeutic protein solution. The particles, even in solutions passed through in-line IV filters, stimulated several *in vitro* cellular functions associated with immunogenicity and/or infusion reactions including T Cell proliferation, dendritic cell activation and cytokine secretion.

PREDICTION OF AGGREGATION AND STABILITY

2:20 Predicting High-Concentration Protein-Protein Interactions, Aggregation, and Phase Behavior

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

Proteins are increasingly formulated and delivered at high concentrations (~ 100 mg/mL or higher). This poses a number of challenges, including increased propensity for reversible and irreversible aggregation, elevated viscosity, and phase separation. This talk focuses on combined experimental and modeling approaches to predict the behavior of proteins at high concentrations using different levels of molecular and thermodynamic modeling. Examples include monoclonal antibodies and globular proteins.

2:50 Impact of Linker-Payload on the Physical Stability of Cysteine-Based Antibody-Drug Conjugates

Jianxin Guo, Ph.D., Principal Scientist, Pfizer

The impact of linker-payload on the physical stability of cysteine-based Antibody-Drug Conjugates (ADC) will be addressed with case studies. The application of biophysical techniques on the evaluation of structural stability and aggregation propensity will be elaborated. The implication of higher order structural characterization for process and formulation development will be illustrated.

Sponsored by

3:20 Counting and Sizing Protein Aggregates Down to 0.15 um in sub-mL Volumes by New Focused-Beam Light Scattering Technology

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

A new single-particle optical sizing (SPOS) technique uses light scattering from a focused laser beam to count and size protein aggregates down to 0.15 um at high concentrations, inaccessible by conventional light obscuration and scattering. Addition of a hybrid light obscuration/scattering sensor extends the upper size limit to 150 um. Analysis can be made on sub-mL samples of high viscosity resulting from high protein concentrations, with conservation of the sample.

3:50 Refreshment Break

4:20 Protein Aggregation Kinetics; Monitoring and Mechanisms Under Applied Stressors

Wayne F. Reed, Ph.D., Professor, Physics; Founding Director, PolyRMC, Tulane University

Time dependent light scattering signatures are used to measure aggregation rates and to make deductions about aggregation mechanisms. Simultaneous Multiple Sample Light Scattering (SMSLS) allows many samples under different stressors to be measured independently. Results focus on thermal and mechanical stressors and differentiating kinetics and mechanisms. Real time SMSLS data allow rational scheduling of complementary analyses, such as GPC and DSC. Relations between scattering and fluorescence based kinetics are also compared.

4:50 Characterization of Higher Molecular Weight Species in New Monoclonal Antibody Formats

Michael Leiss, Ph.D., Lab Manager, Development Analytics Roche Diagnostics GmbH

In most protein-based biotherapeutics higher molecular weight species represent a critical quality attribute due to the potential impact on immunogenicity and safety. Here, we show a case study of a bispecific antibody. Interestingly, different species of dimers are formed, one at bioprocess and one during a stability study at 5°C. Biochemical and biophysical methods such as SEC-MALLS and mass spectrometry are applied to characterize the observed HMW forms.

5:20 End of Day

5:15 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC12: Strategic Bioassay Design and Analysis

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

FRIDAY, APRIL 29

8:00 am Registration and Morning Coffee

UNDERSTANDING AGGREGATION

8:30 Chairperson's Remarks

Dana Filoti, Ph.D., Senior Scientist, Protein Analytics, AbbVie

8:35 Understanding the Role of Aggregation in the Immunogenicity of Biotherapeutic Proteins

Jeremy Derrick, Ph.D., Professor, Molecular Microbiology, University of Manchester

We have compared the immunological responses to immunization with an scFv fragment in monomeric and aggregated forms in a mouse model; the results were indicative of a Th1-type response. In addition, our data also indicate that the heat shock protein DnaK, a common HCP, could play a role in modulating the immune response; the implications for our understanding of the immunogenicity of biotherapeutic proteins will be discussed.

9:05 Functional and Structural Characterization of Process-Related Aggregate Species of an IgG4 Monoclonal Antibody

Flaviu Gruia, Ph.D., Scientist, Analytical Biotechnology, MedImmune

This study details the characterization of aggregate species of an IgG4 monoclonal antibody. Monomer, dimer and

CONTINUED

9th Annual | April 28 - 29

Protein Aggregation & Stability

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

high-molecular-weight (HMW) species were chromatographically separated. A comparative analysis of the three species was performed. Progressive oxidation and conformational differences were detected for aggregate species. The activity of the HMW species was higher than dimer but lower than monomer species. Further characterization determined that non-covalent mechanisms provided the main path for protein aggregation.

9:35 The Role of Surfactants in Managing Protein Aggregation

Sponsored by Lonza

Hanns-Christian Mahler, Ph.D., Head, Drug Product Services, Lonza AG

Non-Ionic surfactants are commonly used in protein formulations to protect the protein from aggregation and particle formation. Polysorbates can undergo autooxidation, cleavage at ethylene oxide subunits and hydrolysis of fatty acid ester bonds. Possibly, the cascade of degradation may impact product quality, e.g., formation of hydroperoxides and degradation products that may impact protein stability. This talk aims to discuss benefits and concerns related to the use of surfactants in formulations.

10:05 Coffee Break

10:35 New Insight into the Stability of Concentrated Protein Solutions from a Combination of Light, Neutron and X-Ray Scattering, Viscometry and Computer Simulations

Anna Stradner, Ph.D., Associate Professor, Physical Chemistry, Lund University

Many biopharmaceuticals require a single dose delivery at high concentration, where the stability and the resulting viscosity are very difficult to control. We show how we can use a combination of advanced characterization techniques such as small-angle neutron (SANS) and x-ray scattering (SAXS) or 3D cross correlation light scattering (3DDLS), combined with state-of-the-art computer simulations to assess and predict interparticle interactions, stability and flow behavior of concentrated solutions of biopharmaceuticals.

11:05 Aggregate Recursors and Aggregation Kinetics

Dana Filoti, Ph.D., Senior Scientist, Drug Product Preformulations, AbbVie

Due to the complex nature of protein aggregation kinetics, the underline mechanistic truths and physiological consequences of the solubility of proteins are not always well understood. In this presentation, we will discuss the time-dependent protein aggregation mechanism, particle formation and the nature of electrostatic intermolecular interactions governing protein aggregation kinetics at low and high concentrations for a monoclonal antibody.

UPSTREAM AND DOWNSTREAM PROCESS CONTROL OF AGGREGATION

11:35 Profiling Product Quality & Stability for Process Development

Christine P. Chan, Ph.D., Principal Scientist and Technical Lead, Global Manufacturing Science and Technology, Genzyme - a SANOFI Company

Protein therapeutics encounters many external factors that influence aggregation and stability during the manufacturing process stages. Due to the complexity of biopharmaceuticals, a combination of orthogonal analytical methods is often required to facilitate evaluation of process impact and define relevant operational controls. This presentation will discuss strategies in product testing and review case studies on characterization of different proteins in support of process development.

12:05 pm A Novel Screening Method to Assess Developability of Antibody-Like Molecules

Melissa Geddie, Ph.D., Principal Scientist, Merrimack Pharmaceuticals

The discovery of antibodies that bind to particular targets with high affinity is now a routine exercise. However, it is still challenging to identify antibodies that in addition to having the desired biological effect also express well, remain soluble at different pH levels, remain stable at high concentrations, can withstand high shear stress, and have minimal non-specific interactions. Here, we present a simple HPLC based screening method to assess these developability factors earlier in discovery process.

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

1:05 Refreshment Break

UPSTREAM AND DOWNSTREAM PROCESS CONTROL OF AGGREGATION (CONT.)

1:35 Chairperson's Remarks

Camellia Zamiri, Ph.D., Scientist, Late Stage Pharmaceutical Development, Genentech

1:40 Polysorbate 20 Hydrolysis and Exploring Options for Mitigating Particulate Formation

Camellia Zamiri, Ph.D., Scientist, Late Stage Pharmaceutical Development, Genentech

Visible particles in mAb Drug Products have been identified upon storage at 2-8°C. Studies indicated hydrolytic (enzymatic) polysorbate 20 degradation in mAb formulations resulted in accumulation of fatty acids. At low temperatures (e.g. 2-8°C), fatty acids can exceed their solubility limit and form visible particles. Effect of polysorbate 20 source on particle formation will be presented. In addition, for screening studies selection of enzyme and method conditions that mimic polysorbate 20 degradation profile in mAb products will be discussed.

2:10 Efficient Membrane Chromatography Devices for Monoclonal Antibody Separation

Raja Ghosh, Ph.D., Professor, Chemical Engineering, McMaster University

Column chromatography, which is widely used for monoclonal antibody aggregate separation is slow and poorly scalable. Membrane chromatography is a fast alternative that is increasingly being used in the biopharmaceutical industry. However, resolution of separation obtained with currently available devices tends to be poor. Novel membrane chromatography devices suitable for high-resolution protein purification, and their used for monoclonal antibody aggregate separation will be discussed in this presentation.

2:40 Impact of Uncontrolled Drug Substance Attributes on Downstream Biologic Product Quality

Shantanu Sule, Ph.D., Senior Engineer, Parenteral Drug Product Development, Biogen

This presentation will discuss how uncontrolled chemical modifications and impurities during upstream drug substance process influence protein stability in the downstream drug product. Formulation and process control strategies will be presented to address such challenges along with opportunities to improve drug product quality by impurity removal during purification. Further, novel stability study design approaches will be examined specific to high titer concentrated biopharmaceuticals where such situations can commonly arise.

3:10 Stabilization of Antibody Solutions Using a Novel Excipient

Iris Batalha, Ph.D., Postdoctoral Research Associate, Chemical Engineering and Biotechnology, University of Cambridge

We report a novel excipient that at concentrations of only 10 mM can reduce the viscosity of high concentration protein liquid formulations (150 mg/mL). The excipient also reduced the phase separation of the same antibody formulations during heating from 4 to 40° C. A salt screen identified various counterions to improve the solubility of excipient, which did not cause protein conformational instability as measured by differential scanning calorimetry.

3:40 End of Protein Aggregation & Stability

Immunogenicity: Regulatory and Clinical Case Studies

Preclinical & Clinical Immunogenicity Assessment for Successful Product Registration

RECOMMENDED PRE-CONFERENCE SHORT COURSES*

SC2: Bioanalytical Considerations of Multi-Domain Biotherapeutics: Preclinical and Clinical Development

SC5: Immunogenicity Risk Assessment and Regulatory Strategies

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

MONDAY, APRIL 25

7:00 am Registration and Morning Coffee

REGULATORY PERSPECTIVE

8:30 Chairperson's Remarks

Narendra Chirmule, Owner & Principal, 7immune Consulting

» 8:40 KEYNOTE PRESENTATION

Talk Title to be Announced

Amy Rosenberg, Ph.D., Director, Therapeutic Proteins, FDA/CDER

9:10 Update on EU Regulatory Environment for Immunogenicity Assessment of Therapeutic Proteins

Paul Chamberlain, NDA Advisory Board

The EU regulatory environment for assessment of immunogenicity-related risks for therapeutic proteins continues to evolve, broadly in parallel to that in USA, but with some differences in detail. This presentation will summarize: 1) Main changes introduced by September 2015 draft revision of main EU immunogenicity guideline, including feedback from stakeholder discussion. 2) Learnings for recent product reviews.

9:40 Immunogenicity of Biologics and Biosimilars: Clinical Impact of Aggregates, Glycosylation and Other Post-Translational Modifications

Narenda Chirmule, Ph.D., Owner & Principal, 7immune Consulting

Assessment of clinical immunogenicity is a critical step in establishing biosimilarity. We will present our experience in development, validation and implementation of the immunogenicity assessment strategy for Biologics and Biosimilars. The presentation will discuss the unique challenges involved immunogenicity assessment, which in the final step towards demonstrating the similarity to the reference licensed product, with "totality of evidence".

10:10 Coffee Break

PRECLINICAL STUDIES

10:45 Chairperson's Remarks

Theo Rispens, Ph.D., Senior Scientist, Immunopathology, Sanquin

10:50 Humanized Mice as a Tool to Measure Immunogenicity

Michael Brehm, Ph.D., Professor, Program in Molecular Medicine, University of Massachusetts Medical School

The development of severely immunodeficient IL2rgnull mice that support engraftment of functional human immune systems has enabled the *in vivo* study of human immunity. This presentation will include a general overview of these humanized mouse models, describing currently available strains, the protocols to generate humanized mice, the strengths of each system and a discussion of the application of these models to study immunogenicity.

11:20 Immunogenicity Assessment In Toxicology Studies

Mark Milton, Ph.D., Executive Director, DMPK-Biologics PKPD, Novartis Institutes for Biomedical Research Inc.

Analysis of samples for the presence of anti-drug antibodies in Toxicology studies is a common practice. However, there is no standard for the interpretation of these data. This presentation will describe the different ways in which the data can be interpreted and will discuss the value of generating such data.

11:50 Clinical Implications of Immunogenicity of TNF Inhibitors

Theo Rispens, Ph.D., Senior Scientist, Immunopathology, Sanquin

Many patients treated with adalimumab or infliximab develop anti-drug antibodies (ADA) to these TNF inhibitors. However, there remains controversy about the clinical consequences of ADA formation, which is in part due to different assay methodologies and testing strategies. This presentation will address the characteristics of ADA responses to TNF inhibitors and the relationship between drug concentration, ADA, and clinical outcome.

12:20 pm How to Develop a "Fit-for-Purpose" Development Pathway that is Associated with "Faster to Market" Options for Clinical Development

Sponsored by NDA

Niamh Kinsella, Principal Consultant, Vice President, Early Stage Product Development, NDA Regulatory Science Ltd.

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

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

See website for details.

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

» PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 The Promise of Cancer Immunotherapy: An Overview of Recent Advances and Jounce's Approach to Delivering the Right Therapy to the Right Patient

Deborah Law, D. Phil. CSO Jounce Therapeutics, Inc.

As immunotherapies become an increasingly important component of cancer treatment the challenge will be to identify ways to provide the best therapy(s) to the individual. This presentation will provide an overview of current cancer immunotherapies as well as highlight some of the challenges ahead including selection of optimal combinations, moving outside of T Cell-directed approaches, and will highlight how Jounce Therapeutics is using its Translational Science Platform as an approach to develop and deliver the right therapy to the right patient.

4:50 Antibody as Drugs: Then, Now and Tomorrow

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

Antibodies have grown into a clinically and commercially important drug class with more than >45 antibodies marketed for imaging or therapy in the USA and/or Europe and with ~$63 billion in worldwide sales in 2013. This presentation will highlight progress in developing antibody drugs and consider opportunities for future innovation.

5:30 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 End of Day

CONTINUED

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Immunogenicity: Regulatory and Clinical Case Studies

Preclinical & Clinical Immunogenicity Assessment for Successful Product Registration

TUESDAY, APRIL 26

8:00 am Morning Coffee

DETERMINING CLINICAL RELEVANCE

8:25 Chairperson's Remarks
Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.

8:30 Statistical Considerations in Design of Multi-Tiered Methods to Detect and Confirm the Presence of ADAs in Clinical Studies
Harry Yang, Ph.D., Senior Director R&D, Medimmune, LLC
Biopharmaceuticals have an inherent propensity to elicit immunogenic responses. Key to successful evaluation of immunogenicity is to have well developed and validated assays. This talk will focus on statistical strategies related to ADA assay validation, sample size determination, cut point estimation in the presence of outliers and skewed distributions. In addition, we will explore ways to combine information from screening and confirmatory assays, so as to derive optimal cut point.

9:00 Talk Title to be Announced
Florian Deisenhammer, Ph.D., Clinical Department of Neurology, Innsbruck Medical University

9:30 Measures of a Clinically Relevant Immune Response: Weighing between the Sensitivity and Impactful Response
Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.
The immunoassays currently employed for the immunogenicity assessment are highly sensitive and can detect low signals of anti- therapeutic immune responses. However, the impact of such responses on exposure and efficacy requires further evaluation. The relevance of ADA impact on PK depends on the study design and impact on PD. The onset and magnitude of the ADA response on PK and PD will also be discussed in the context of clinical relevance.

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

DETERMINING CLINICAL RELEVANCE (CONT.)

10:50 De-Immunizing Immunotoxins
Ira Pastan, M.D., Co-Chief, Molecular Biology, National Cancer Institute, National Institutes of Health
Many non-human proteins have beneficial therapeutic properties, but cannot be administered repeatedly to humans, because of their immunogenicity. We have developed an immunotoxin targeting mesothelin-expressing malignancies (SS1P) that contains a portion of Pseudomonas exotoxin A. The protein has shown activity against mesothelioma in human and we have been improving its usefulness by identifying and removing T Cell and B cell epitopes.

11:20 Impact of Target Interference in PK and ADA Assays and Potential Mitigation Strategies
Manoj Rajadhyaska, Ph.D., Director, Bioanalytical Sciences, Regeneron Pharmaceuticals Inc.
Ligand binding assays are susceptible to interfering target molecules that can distort assay results by generating false positive or negative signals or blocking desired assay interactions. If not properly characterized and mitigated, these artefactual results can impact the result interpretation. With the help of some case studies, the mechanistic aspects of the variety of ways by which target interference can occur will be discussed with potential mitigation strategies for each case.

11:50 PANEL DISCUSSION: Determining a ClinicalRelevantResponse
Moderator: Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.
This panel will discuss:
-What determines a clinically relevant response?
-Are assays too sensitive?
-The relevance of ADA impact on PK

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

CLINICAL CASE STUDIES

2:00 Chairperson's Remarks
Sally Fischer, Ph.D., Principal Scientist, Development Sciences, Genentech

2:05 Robust Immune Response to a Product Related Impurity and Impact on Immunogenicity Rate of an Antibody Therapeutic
Sally Fischer, Ph.D., Principal Scientist, Development Sciences, Genentech
A product related impurity was identified in the material used in clinical study. To assess the potential ability of patients to develop an immune response to the impurity and impact on immunogenicity of the therapeutic two bridging ELISA were developed and validated. Samples from treated subjects were evaluated in both assays. This presentation will discuss the results of the immunogenicity assessment to the impurity and observed immunogenicity rate of the antibody therapeutic.

2:35 Immunogenicity: Why and How
Michel Awwad, Ph.D., former Director, Pharmacokinetics & Dynamics & Metabolism, Merrimack Pharmaceuticals

3:05 Sponsored Presentation *(Opportunity Available)*

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

CLINICAL CASE STUDIES (CONT.)

4:25 Positive Effects in Reducing Immunogenicity Target Interference
Erik Meyer, Ph.D., Senior Scientist, GlaxoSmithKline
During Phase II clinical studies, a high incidence of immunogenicity did not correlate with decreased PK profiles or loss of drug efficacy. Drug target analysis revealed its accumulation during treatment, with target interference possibly impacting immunogenicity analysis. Subsequent immunogenicity assay modifications reduced the ADA positive rate and supported clinical observations for additional clinical studies.

4:55 ERT Immunogenicity and Experimental Immune Tolerance Induction: Results of a BioMarin Sponsored Advisory
Brian Long, Ph.D., Senior Scientist, Immunology Assessment, BioMarin
Enzyme replacement therapies (ERT) for the treatment of lysosomal storage diseases (LSD) have demonstrated great success in attenuating the disease phenotype for many rare and debilitating disorders. We convened an advisory board of treating physicians and key opinion leaders where we reviewed the current data regarding immunogenicity with ERTs and contemporary immune tolerance inducing regimens; the results of which are presented.

5:25 End of Immunogenicity: Regulatory and Clinical Case Studies

5:30 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC9: Overcoming the Challenges of Immunogenicity Assessment
**Separate registration required, please see page 5 for course details.*

Strategies for Immunogenicity Assay Assessment

Mitigating Immunogenicity through Proactive Evaluation and Testing

RECOMMENDED PRECONFERENCE SHORT COURSES*

SC2: Bioanalytical Considerations of Multi-Domain Biotherapeutics: Preclinical and Clinical Development

SC5: Immunogenicity Risk Assessment and Regulatory Strategies

SC9: Overcoming the Challenges of Immunogenicity Assessment

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

WEDNESDAY, APRIL 27

7:00 am Registration and Morning Coffee

NEUTRALIZING ANTIBODY ASSAYS

8:00 Chairperson's Remarks

Yao Zhuang, Ph.D., Principal Scientist, PKDM Bioanalytical Sciences, Amgen

8:10 Strategies to Determine Assay Format for the Assessment of Neutralizing Antibody Responses to Biotherapeutics

Bonnie Wu, Ph.D., Principal Scientist, Bioanalytical Sciences, Janssen R&D, LLC

A white paper has currently been developed that provides recommendations on how to select a suitable NAb assay format (cell-based or non cell-based) to detect clinically relevant NAbs for biotherapeutics with varying MoAs and diverse complexity. This talk will provide an overview of the white paper and discuss the practical considerations for NAb assay format selection strategies. The utility of correlating NAb response with pharmacodynamic data will also be presented.

8:40 Cell-Based Assays for the Detection of Neutralizing Antibodies against BiTe Molecules and ADCC-Based Therapeutic Monoclonal Antibodies

Yao Zhuang, Ph.D., Principal Scientist, PKDM Bioanalytical Sciences, Amgen

Recruiting effector cells for targeT Cell destruction is an important strategy to provide the therapeutic interventions in the oncology or auto-immune diseases. Molecules like Rituxan leverage on the mechanism of (ADCC), others like Blincyto® are Bispecific T Cell Engager (BiTE®) molecules. Due to their complex mechanisms, developing assays for detecting neutralizing antibodies (NAbs) poses significant challenges. Successful approaches in developing robusT Cell-based assays for NAb detection will be described.

9:10 A Neutralizing Antibody Assay Based on a Reporter of Antibody DependenT Cell-Mediated Cytotoxicity

Yuling Wu, Ph.D., Principal Scientist, Clinical Pharmacology & DMPK, Translational Sciences, MedImmune

Immunogenicity assessment is an essential component of safety evaluation in biopharmaceuticals clinical development. Benralizumab is a humanized afucosylated mAb against IL5Rα with enhanced effector function. It potently induces ADCC (antibody-dependenT Cell-mediated cytotoxicity) of eosinophils and basophils. To support benrulizumab clinical development, we developed an ADCC cell-based neutralizing antibody (NAb) assays to detect NAb against benrulizumab in human serum. This study presents the development, optimization and characterization of an ADCC cell-based NAb assay.

9:40 Optimizing Reporter-Gene Assays for the Quantification of Neutralizing Anti-Drug Antibodies

Michael Tovey, Ph.D., INSERM Director, Research, Laboratory of Biotechnology & Applied Pharmacology, Ecole Normale Supérieure de Cachan

Regulatory authorities recommend cell-based assays for the detection of neutralizing anti-drug antibodies (NADAs). Fully validated reporter-gene assays for numerous biopharmaceuticals including novel insulins, FGF21 peptides, Herceptin, and Avastatin based on innovative engineered reporter-gene cell lines will be described that quantify both functional drug levels and NADAs with a high degree of precision within 2 to 4 hours in the same sample without drug interference or serum matrix effects.

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

ANTI-DRUG ANTIBODY ASSAYS

10:55 Anatomy of an Anti-Drug Antibody Assay

Dharmesh Desai, Ph.D., Group Leader, Bristol-Myers Squibb

Protein therapeutics can come in various sizes and shapes ranging from small hormones to monoclonal antibodies to even larger antibody fusion proteins. All of these biologic therapeutics have the potential to generate an immune response against the drug. I will discuss current strategies for designing a robust method for detecting anti-drug antibody. I will cover selection and characterization of the positive control, assay formats and assay optimization (e.g., improving drug tolerance) using design of experiments.

11:25 PandA: A Novel Method Effective at Reducing or Eliminating the Drug and Target Interferences in Immunogenicity Assays

Jad Zoghbi, Senior Scientist, Sanofi (Genzyme)

Biological matrix interference in immunoassays remains a major challenge in the field of bioanalysis. Circulating drug may interfere with the detection of anti-drug antibodies (ADA) and drug target, or ADA may interfere in drug quantitation assays. Various approaches have been used to improve drug tolerance in ADA analysis but limited success was observed. Our novel method uses Precipitation and Acid (PandA) to overcome drug or target interference in immunogenicity assays.

11:55 PANEL DISCUSSION: Immunogenicity Testing Strategy: Assay Format Selection, Validation Challenges and Data Impact

Moderator: Jim McNally, Ph.D., Associate Director, QPD Program Representative and Immunogenicity Expert at EMD Serono, Inc.

Panelists: Dharmesh Desai, Ph.D., Group Leader, Bristol-Myers Squibb

Yuling Wu, Ph.D., Principal Scientist, Clinical Pharmacology & DMPK, Translational Sciences, MedImmune

Jad Zoghbi, Senior Scientist, Sanofi (Genzyme)

- New technologies
- How you deal with poor drug tolerance, lack of sensitivity and matrix interference
- Challenges for validation
- Interpretation of the results and implications for risk assessment

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PRECISION FOR MEDICINE

12:25 pm Presentation to be Announced

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

1:55 Session Break

2:10 Chairperson's Remarks

Michael Tovey, Ph.D., INSERM Director, Research, Laboratory of Biotechnology & Applied Pharmacology, Ecole Normale Supérieure de Cachan

CONTINUED

Strategies for Immunogenicity Assay Assessment

Mitigating Immunogenicity through Proactive Evaluation and Testing

2:15 Method to Improve the Recovery of pH Labile Anti-Drug Antibodies during Acid Dissociation and Extraction

Weifeng Xu, Ph.D., Senior Research Investigator, BAS-Biologics, Bristol-Myers Squibb

When large amount of biotherapeutics drug is present in the clinical samples, these drugs has to be dissociated and removed from anti-drug antibodies (ADA) so that ADAs can be detected by either ligand-binding assay or cell-based bioassay. By screening a panel of more than 20 ADA positive control mAbs, we found that current widely used acid dissociation followed by biotinylated-drug extraction led to low recovery of more than 40% of these ADA PCs, due to sensitivity to low pH and denaturation. Here we discuss the alternative methods for ADA extraction so that both pH labile and pH resistant species can be maximally recovered.

2:45 Case Studies and Methods for Limiting Target Interference in Anti-Drug Antibody Assays

Jim McNally, Ph.D., Associate Director, QPD Program Representative and Immunogenicity Expert, EMD Serono, Inc.

The presence of soluble target in study samples can present significant issues for anti-drug antibody (ADA) assays. In particular, multimers of the target create multiple binding sites for the biotherapeutic and may result in false positives in ADA assays using the bridging format. This presentation will focus on identifying these false positives and methods to either block or remove circulating target from samples to minimize false positives that occur due to this problem.

3:15 Sponsored Presentation *(Opportunity Available)*

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

4:45 Problem-Solving Breakout Discussions

See website for details.

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

7:00 End of Day

THURSDAY, APRIL 28

8:00 am Morning Coffee

CONSIDERATIONS FOR MULTI-SPECIFIC ANTIBODIES

8:30 Chairperson's Remarks

Wenfeng Xu, Ph.D., Associate Director, BioAnalytical Sciences, Genentech Inc

8:35 Immunogenicity Assessment of Bi-Specific Antibodies

Laura I. Salazar-Fontana, Ph.D., Strategic Advisor for Immunology and Biomarkers, Sanofi R&D

Bi-specific antibodies represent a new class of biologics aimed to treat conditions such as cancer and autoimmunity. As for any other therapeutic protein, these molecules can elicit an immune response once administered into patients. An adequate immunogenicity risk assessment is extremely useful in guiding assay development and testing strategies since it is tailored to the associated risks identified for the bi-specific antibody therapy. The goal of this talk is to illustrate how this approach helps predict, collect, report and mitigate anti-drug antibody (ADA) data during the clinical development of this class of biologics.

9:05 Bioanalytical Strategy for a Bispecific Antibody in Cancer Immunotherapy

Wenfeng Xu, Ph.D., Associate Director, BioAnalytical Sciences, Genentech Inc

Designing appropriate bioanalytical strategies and approaches for new multi-domain protein therapeutic molecules requires specific considerations. This includes not only the selection of suitable nonclinical and clinical pharmacokinetic (PK) formats, but also the corresponding immunogenicity risk assessments and anti-therapeutic (ATA) assay formats for characterization. This presentation will provide the bioanalytical strategy for a new bispecific cancer immunotherapy molecule. The difference between this and a bioanalytical strategy for a typical IgG is summarized.

9:35 Sponsored Presentation *(Opportunity Available)*

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

11:05 PANEL DISCUSSION: Assays for Novel Products

Moderator: Jack A. Ragheb, M.D., Ph.D.,Chief Medical Research Officer, Office of Biological Products, CDER/FDA; Attending Physician, Warren Grant Magnuson Clinical Center, NIH

Panelists: Wenfeng Xu, Ph.D., Associate Director, BioAnalytical Sciences, Genentech Inc

Laura I. Salazar-Fontana, Strategic Advisor for Immunology and Biomarkers, Sanofi R&D

- Applying risk factors and systems immunology
- Designing bioanalytical strategies
- Selecting PK formats

IMMUNOGENICITY FROM ANIMAL MODELS AND BEYOND

11:35 Humanized Mouse Models: Applicability and Potential Use in Immunogenicity Studies

Jack A. Ragheb, M.D., Ph.D., Chief Medical Research Officer, Office of Biological Products, CDER/FDA; Attending Physician, Warren Grant Magnuson Clinical Center, NIH

Various efforts have been made to generate "humanized" mouse models that would more accurately reflect the human experience. We have focused on the humanized BLT mouse model. We hope to address whether biologic drug product attributes that are thought to be immunogenic *in vivo* can be predicted utilizing this novel humanized mouse model. The qualification of an animal model that will accurately predict the clinical immunogenicity of therapeutic proteins would be expected to result in safer and more efficacious therapeutic biologicals.

12:05 pm Historical Perspective on Immunogenicity: What Have We Learned and Where are We Headed

Melissa Wojcik, Sr. Associate Scientist, Analytical Development, Histogenics Corp. (Contractor)

In 1985, the FDA approved the organ transplant rejection therapy, Muromonab-CD3, the first monoclonal antibody. Patients responded well; however, some experienced serious adverse events. The immunogenic hybridoma structure forced scrutiny on dosing strategy. Unlike small molecules, biologics don't have the luxury of *in vitro* toxicity ADME modeling. In spite of these challenges, biologics improved to predict immune responses. This presentation walks through industry's lessons learned and future path.

12:35 End of Strategies for Immunogenicity Assay Assessment

5:15 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC12: Strategic Bioassay Design and Analysis

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

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Optimizing Bioassays for Biologics

Strategies and Statistics for Increasingly Complex Antibodies

RECOMMENDED DINNER SHORT COURSE*

SC9: Overcoming the Challenges of Immunogenicity Assessment

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

THURSDAY, APRIL 28

INNOVATIVE ASSAY FORMATS AND TECHNOLOGIES

12:35 pm Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

Tilman Schlothauer, Ph.D., Principal Scientist, Large Molecule Research, Roche Innovation Center

1:50 Potency Assay Development and Associated Extended Characterization Strategy of Therapeutic mAb

Tilman Schlothauer, Ph.D., Principal Scientist, Large Molecule Research, Roche Innovation Center

During the past years we have collected several examples of profound structure function correlations for IgG-based therapeutic modality development. These insights have been used as the basis for the following Potency Assay strategy. Applying a set of orthogonal cell-based and cell free functional assays always provides a deep understanding of the molecule and related critical quality attributes.

2:20 Our Bioassay Approach to Meet the Immuno-Oncology Biologics Surge: Building the Bioassay Core Team and the Platform Assays

Han Li, Ph.D., Principal Scientist, Leads Discovery and Optimization, Bristol-Myers Squibb

To address the bioassay backlog due to immuno-oncology surge and to meet the QA requirements for assay robustness, we took a strategic approach by developing master cell lines and platform assays for the target super families. We also used the knowledge we learned through discovery support on target and molecule specific primary immune cells signaling to guide our MOA-based cellular bioassay selections. Our science driven, QA minded and technology enabled bioassay strategy not only allowed us to accelerate the assay development with limited resource but also helped to harmonize the assay detection format.

2:50 Development of Luminex as a Platform for the Detection of Anti-Drug Antibody IgE Isotypes in Human Serum

LiNa Loo, Ph.D., Associate Principal Scientist, Bioanalytical Development, Merck

Since biotherapeutic drugs such as monoclonal antibodies (mAbs) have the potential to induce immunogenicity, it is critical to perform an immunogenicity assessment to ensure drug efficacy and patient safety. Here, Luminex and Mesoscale were evaluated as platforms for detection of anti-drug antibody IgE isotype in human serum. By using a mouse-human chimeric drug-specific monoclonal IgE antibody as the positive control, the assay characteristics were compared for the two platforms.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Refreshment Break

BIOASSAYS FOR ADCs AND BISPECIFICS

4:20 Potency Assay Selection for Antibody-Drug Conjugates: Challenges and Considerations

Shelley Elvington, Ph.D., Technical Development Scientist, Genentech

Antibody-drug conjugates combine the target specificity of a monoclonal antibody with the activity of a potent therapeutic compound. This unique format leads to special considerations when developing potency assays. Here, I will present our strategy for ADC assay development, including selection of appropriate formats and cell lines that take into account the unique properties of the ADC (including impact of drug-antibody ratio).

4:50 Bioassay Strategy and Challenges for a κλ Body - A Next Generation Bispecific

Anaëlle Dos Santos, Head, Bioanalytics Unit, NovImmune SA

κλ bodies are a novel bispecific format with proprieties indistinguishable from an IgG. The strategy will be presented for development of a potency assay for a κλ body which has a carefully selected affinity for CD47 in order to selectively block this receptor in B cell malignancies. A comprehensive suite of highly sensitive binding and reporter gene assays have been developed and qualified to assess the potency of the product in batch release, stability and characterization studies. The advantages and limitations of each of these assays will be discussed.

5:20 End of Day

5:15 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC12: Strategic Bioassay Design and Analysis

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

FRIDAY, APRIL 29

8:00 am Registration and Morning Coffee

8:30 Chairperson's Remarks

Shelley Elvington, Ph.D., Technical Development Scientist, Genentech

8:35 PANEL DISCUSSION: Bioassays for the Changing Biologics Landscape

Moderator: Shelley Elvington, Ph.D., Technical Development Scientist, Genentech

Panelists: Tilman Schlothauer, Ph.D., Principal Scientist, Large Molecule Research, Roche Innovation Center

Han Li, Ph.D., Principal Scientist, Leads Discovery and Optimization, Bristol-Myers Squibb

- Immuno-oncology bioassays
- Antibody-drug conjugates
- Bispecific antibodies

ASSAY BRIDGING, TRANSFER AND VALIDATION

9:35 Successful Assay Validation – The Role of Sample Size Calculations to Ensure Regulatory Acceptance

Walter Hoyer, Ph.D., Principal Statistician, CMC Statistics, GSK Vaccines GmbH

In recent years regulatory authorities have strongly increased demand for (bio-)analytical method validations. Two recurring themes are "variance component analysis" to assess intermediate precision and more generally the preference for equivalence tests over the classical nullhypothesis testing approach, as outlined in USP. The presentation combines both aspects and presents a pragmatic way of performing power and sample-size calculations for the total variance of general multi-factor mixed models. The approach allows to enter an assay validation with confidence to pass and yet satisfy the stringent requirements of regulatory authorities.

10:05 Coffee Break

10:35 Presentation to be Announced

CONTINUED

2nd Annual | April 28 - 29

Optimizing Bioassays for Biologics

Strategies and Statistics for Increasingly Complex Antibodies

USING DOE TO OPTIMIZE PERFORMANCE

11:05 Improved Consistency and Efficiency by Applying Ready-to-Plate Cells in Immunogenicity Testing

Linda Collins, Senior Associate Scientist, Functional Biocharacterization, Amgen

A cell-based bioassay, often used in detecting neutralizing antibodies (NAb) against protein therapeutics, not only can produce inconsistent response due to cell age and culture conditions, but also is labor intensive in maintaining a continuous culture. Here we described using ready-to-plate cryopreserve cells as a reagent to develop and optimize a NAb assay. A comparison of assay performance overtime with regard to the continuous culture was also provided.

11:35 Optimization of a Potency Assay Using DoE in Support of Monoclonal Antibody Product Development

Arden Bond, Staff Scientist, Analytical Development, Genzyme

This presentation describes the use of Design of Experiment (DoE) to evaluate the method performance of a cell-based potency assay. DoE is a technique for designing and analyzing experiments, using a minimum number of assays by systematically varying several parameters simultaneously. After initial development of a cell-based potency assay, DoE was used to confirm method accuracy, range, sensitivity and robustness. Once appropriate method performance was demonstrated, the cell-based potency assay was used to support product development. The potency assay method design and optimization will be discussed.

12:05 pm Optimization and Robustness Study of a Potency Assay Using DoE

Jan Amstrup, Ph.D., Principal Scientist, CMC Bioassay, Novo Nordisk A/S

Optimization of a potency assay by use of DoE in the optimization process will be shown. Nine assay factors and four factor interactions based on time consumption and complexity of buffers were evaluated. Results obtained from the DoE provided improved assay conditions and settings that were successfully evaluated in a proof-of-concept assay. Furthermore, how to implement the optimizations will be discussed with regard to validation status of the assay.

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

1:05 Refreshment Break

1:35 Chairperson's Remarks

Gaël Debauve, Ph.D., Analytical Sciences for Biologicals - Bioassay Development Laboratory, UCB Pharma S.A., Braine-L'Alleud

1:40 PANEL DISCUSSION: DoE for Biological Assays

Moderator: Gaël Debauve, Ph.D., Analytical Sciences for Biologicals - Bioassay Development Laboratory, UCB Pharma S.A., Braine-L'Alleud

Panelists: Vineetha Jayasena, Principal Scientist, Functional Biocharacterization, Amgen

Arden Bond, Staff Scientist, Analytical Development, Genzyme

Jan Amstrup, Ph.D., Principal Scientist, CMC Bioassay, Novo Nordisk A/S

- Why? Business and regulatory expectations
- How? Pro/cons, limitations and challenges
- When/What? DoE integration into method lifecycle: When is it implemented?

STATISTICAL TOOLS FOR BIOASSAY MONITORING

2:40 Bioassay Lifecycle: From Development to Continuous Verification

Gaël Debauve, Ph.D. Analytical Sciences for Biologicals - Bioassay Development Laboratory, UCB Pharma S.A., Braine-L'Alleud

Biological activity is a critical quality attribute for biopharmaceutical products and cell-based bioassays are generally used to accurately determine this activity. Classical proliferation assay presents a lot of drawbacks that could be overcome by the gene reporter technology (e.g. in terms of method simplicity, reduced variability and improved lead time). This presentation will go through a case study illustrating the gene reporter journey: from the decision to switch to a gene reporter assay to the tools implemented to monitor the method performance.

3:10 Determination of the Limit of Detection and the Limit of Quantitation during Assay Development in the Biopharmaceutical Industry

Eloi P. Kpamegan, Ph.D., MSF, Executive Director, Clinical & Nonclinical Biostatistics, Novavax, Inc.

The usefulness and optimal throughput of an assay may depend on the appropriate determination of the LOD and the LOQ. The experiment design and statistical analysis method used for the determination of LOD and LOQ are dependent on the assay type (e.g., ELISA, Functional or PCR). This presentation describes the design, testing and statistical procedures required to determine the LOD and LOQ during assay development. The procedures to be used to confirm the LOD and the LOQ during assay validation are discussed.

3:40 End of Optimizing Bioassays for Biologics

2nd Annual | April 25 - 26

Fusion Protein Therapeutics

Engineering Next-Generation Biologics

RECOMMENDED PRE-CONFERENCE SHORT COURSES*

SC2: Bioanalytical Considerations of Multi-Domain Biotherapeutics: Preclinical and Clinical Development

SC6: *In Silico* Immunogenicity Predictions (Hands-On) Workshop

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

MONDAY, APRIL 25

7:00 am Registration and Morning Coffee

THE PROMISE OF FUSION PROTEINS

8:30 Chairperson's Remarks

Eric Furfine, Ph.D., CSO, Eleven Biotherapeutics, Inc.

» 8:40 KEYNOTE PRESENTATION

Fusion Proteins: Introduction to the Field and 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 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. In this presentation, I will describe Roche's strategies to discover and design such molecules, give examples but will also address challenges for technical development.

9:10 Fc Fusion Coagulation Factors for Improved Hemophilia Therapies: Clinical Development of rFVIIIFc and rFIXFc

Baisong Mei, M.D., Ph.D., Senior Director, Global Clinical Development, Biogen

Longer-acting coagulation factors FVIII and FIX would represent a key advancement in the management of hemophilia A and B. Biogen has developed a novel monomeric recombinant Fc fusion technology to extend the half-life of coagulation factors. The safety, efficacy, and prolonged half-life of rFVIIIFc and rFIXFc were demonstrated in clinical studies. rFVIIIFc and rFIXFc have been approved in US and other countries.

9:40 Fusion Protein Design: Consequences for Manufacturability

Stefan Schmidt, Ph.D., MBA, Vice President, Process Science and Production, Rentschler Biotechnologie GmbH

Fusion proteins are generated by artificially combining unrelated domains not connected in nature, resulting in novel properties and promise for therapeutic success. The specific design of these engineered proteins requires highly specific process development strategies and adaptations during manufacturing that differ from traditional platform approaches. Here I demonstrate in a number of examples what general principles to follow to meet critical manufacturing parameters.

10:10 Coffee Break

ENGINEERING IMPROVED PROPERTIES

10:50 Overcoming AAT Deficiency with Recombinant AAT-Fc: An Optimized Therapeutic for Improved Efficacy

John Timmer, Ph.D., Research Director, InhibRx LLC

AAT deficient patients are treated with serum derived AAT at high doses weekly. However, sdAAT is rapidly cleared leaving patients susceptible to lung degradation by neutrophil elastase. Inhibrx has developed a recombinant AAT-Fc with improved properties (extended half-life, and oxidation resistance) that is highly protective in a model of acute lung injury. Bi-weekly or monthly dosing with Inhibrx's AAT-Fc is expected to be more efficacious than sdAAT.

11:20 Epsi-gam: A Novel Fusion Protein for the Treatment of Asthma and Other Allergic Diseases

Nolan Sigal, M.D., Ph.D., President and CEO, Tunitas Therapeutics, Inc.

Epsi-gam is a genetically engineered and expressed bifunctional human fusion protein that is comprised of the Fc portions of human IgE and IgG1. This platform was designed to link the receptors for IgE on basophils, masT Cells and B cells with the inhibitory FcγRIIb receptor on these cells and thereby inhibit their function. This intervention is designed as a therapeutic agent for the treatment of asthma and other serious allergic diseases.

11:50 Engineering Proteins to Treat Ocular Disorders

Eric Furfine, Ph.D., CSO, Eleven Biotherapeutics, Inc.

Our lead product, the IL-1 receptor inhibitor EBI-005, was designed and engineered for the topical treatment of dry eye disease and was biologically active in subjects with dry eye disease. In addition, we engineered an IL-6 inhibitor for local (intravitreal) treatment diabetic macular edema and posterior uveitis. The drug has a long residence time in the vitreous of rabbits and monkeys and potently inhibits cis and trans IL-6 signaling.

12:20 pm Optimized Serum Half-Life Extension with Veltis® Engineered Albumins

Karen Bunting, Ph.D., Science Director, Molecular Biology & Fermentation, Albumedix Ltd

Short circulatory half-life represents a major obstacle for many protein and peptide-based therapeutics. This can be significantly improved by conjugation or fusion to albumin, due to increased size and recycling via the neonatal Fc receptor (FcRn). The increased FcRn affinity of the Veltis® engineered albumins translates to more than doubling of the already long half-life of native albumin. We will describe rationally engineered albumins and their application to improve the pharmacokinetic properties of therapeutic candidates.

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

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

See website for details.

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

» PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 The Promise of Cancer Immunotherapy: An Overview of Recent Advances and Jounce's Approach to Delivering the Right Therapy to the Right Patient

Deborah Law, D. Phil. CSO Jounce Therapeutics, Inc.

As immunotherapies become an increasingly important component of cancer treatment the challenge will be to identify ways to provide the best therapy(s) to the individual. This presentation will provide an overview of current cancer immunotherapies as well as highlight some of the challenges ahead including selection of optimal combinations, moving outside of T Cell-directed approaches, and will highlight how Jounce Therapeutics is using its Translational Science Platform as an approach to develop and deliver the right therapy to the right patient.

4:50 Antibody as Drugs: Then, Now and Tomorrow

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

Antibodies have grown into a clinically and commercially important drug class with more than >45 antibodies marketed for imaging or therapy in the USA and/or Europe and with ~$63 billion in worldwide sales in 2013. This presentation will highlight progress in developing antibody drugs and consider opportunities for future innovation.

5:30 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 End of Day

CONTINUED

2nd Annual | April 25 - 26

Fusion Protein Therapeutics

Engineering Next-Generation Biologics

TUESDAY, APRIL 26

8:00 am Morning Coffee

NEXT-GENERATION IMMUNOTHERAPIES

8:25 Chairperson's Remarks

Stefan Schmidt, Ph.D., MBA, Vice President, Process Science and Production, Rentschler Biotechnologie GmbH

8:30 Immunocytokines for the Therapy of Cancer and of Chronic Inflammation: From the Bench to Phase II Clinical Trials

Dario Neri, Ph.D., Professor, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology, ETH Zürich

Certain monoclonal antibodies can be used as vehicles for the selective pharmacodelivery of potent immunomodulatory payloads, including cytokines. In this lecture, I will review our work in the field and present the most recent clinical data, originating from on-going Phase II clinical trials.

9:00 Combination Immunotherapy Enabled by a Tumor-Targeting Peptide-Fc Fusion

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

I will discuss an engineered peptide-Fc fusion protein that we have adapted for targeted delivery of chemotherapeutic agents, as well as recruitment of 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 melanoma and colon carcinoma models, which is further enhanced by combination with checkpoint blockade inhibitors.

9:30 Diphtheria-Toxin Based Anti-Human CCR4 Immunotoxin for Targeting Human CCR4+ Tumors and Tregs

Zhirui Wang, Ph.D., Assistant Professor, Center for Transplantation Sciences, Massachusetts General Hospital and Harvard Medical School

We have successfully developed an anti-human CCR4 immunotoxin using yeast *Pichia Pastoris* expression system. *In vivo* efficacy for targeting CCR4+ tumors was assessed using human CCR4+ tumor-bearing NSG mouse model. *In vivo* efficacy for depleting CCR4+ Tregs was characterized in two naïve cyno monkeys. This immunotoxin is a promising drug candidate for targeting human CCR4+ tumors and Tregs.

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

PEPTIDE FUSIONS

10:50 Engineering of a GLP-1 Analogue Peptide in Fusion with a PCSK9 Antibody for Type 2 Diabetes Patients at High Cardiovascular Risk

Matthieu Chodorge, Ph.D., Senior Scientist, Antibody Discovery and Protein Engineering, MedImmune, Ltd.

In addition to high blood glycose, Type 2 diabetic patients often have an impaired cholesterol balance and are at greater risk of cardiovascular disease. We have developed a GLP-1 receptor agonist peptide in fusion with a PCSK9 antibody to provide glucose control and LDL cholesterol reduction in one molecule. Here we will present how the fusion has been exquisitely engineered to deliver optimum pharmacology on both axis and adequate manufacturability.

11:20 Apolipoprotein A-I as a Novel Scaffold for Protein Delivery

Pedro Berraondo, Ph.D., Researcher, Program of Immunology & Immunotherapy, University of Navarra

Clinical use of therapeutic proteins and peptides is limited by the short half-life in circulation and the absence of a specific targeting. Fusion to apolipoprotein A-I is a strategy to improve the pharmacokinetic and pharmacodynamics properties: the half-life in circulation is improved, the fusion proteins are targeted to the liver and tumors, the blood brain passage is modified and the activity of the fused protein is modulated by the interaction with the scavenger receptor class B type I.

11:50 Human Serum Albumin and p53-Derived Peptide Fusion Protein Promotes Cytotoxicity Irrespective of p53 Status in Cancer Cells

Zhiyu Li, Ph.D., Associate Professor, Pharmaceutical Sciences, Philadelphia College of Pharmacy

Human serum albumin (HSA) fusion protein is a feasible and effective approach to target and inhibit essential intracellular pathways. HSA and p53-derived peptide fusion protein (rHSA-p53i) binds to 4 intracellular proteins, including MDM2, MDMX, BCL-XL, and Mcl-1. Therefore, rHSA-p53i is capable of promoting cytotoxicity irrespective of p53 status (wild type, mutation, and deficiency). Moreover, rHSA-p53i can carry fatty acid-modified chemotherapeutics for synergistic therapeutic efficacy.

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

ENGINEERING ENZYMES

2:00 Chairperson's Remarks

Zhirui Wang, Ph.D., Assistant Professor, Center for Transplantation Sciences, Massachusetts General Hospital and Harvard Medical School

2:05 Modifying a Lysosomal Enzyme to Facilitate Distribution to the Brain via the Intravenous Route

Stefan Svensson Gelius, Ph.D., Senior Scientist, Biochemistry, Swedish Orphan Biovitrum (SOBI)

In an attempt to increase the distribution of the lysosomal enzyme sulfamidase to the brain, several protein engineering approaches were evaluated. Studies on passive uptake as well as targeted receptor mediated uptake, e.g., via LRP-1 led to the finding of a sulfamidase that reduces heparan sulfate storage in the brain of the mucopolysaccharidosis IIIA mouse model after repeated intravenous administration. In this talk structural and functional attributes will be discussed.

2:35 A Novel Protease Enzyme-Based Fusion Protein Platform with Utility across a Range of Disease Areas

Nathaniel Gordon, Ph.D., Senior Scientist, MedImmune, Ltd.

Proteases have a unique mechanism of action and could offer a number of therapeutic advantages relative to neutralizing monoclonal antibodies, however their practical realization is impeded by the difficulty in engineering protease specificity. We have bypassed limitations in protease engineering by designing protease-fusion proteins with a modular, multi-domain architecture, in which specificity and hydrolytic activity are conferred by complementary domains. Further engineering principles and therapeutic implications of our platform will be discussed.

3:05 Sponsored Presentation *(Opportunity Available)*

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

CONTINUED

2nd Annual | April 25 - 26

Fusion Protein Therapeutics

Engineering Next-Generation Biologics

INNOVATING TECHNOLOGIES

4:25 Target-Engaged Complementation: Replacing ELISA and Resurrecting ADEPT

Shawn Owen, Ph.D., Assistant Professor, Pharmaceutics and Pharmaceutical Chemistry, University of Utah

We are developing a technology, termed Target Engaged Complementation (TEC), which utilizes enzymes split into inactive components. Each fragment is fused to an individual antibody Fab; the binding of the Fabs forces the split enzyme fragments into proximity where they refold to the active form. The activity of the split enzyme is used to activate luminescence for diagnostic applications or activate prodrug for therapeutic applications.

4:55 Therapeutic Strategies Combining Specificities on the Outside and Inside: Ligands Sneaking into Cells

Stefan Dübel, Ph.D., Director, Biotechnology, Technical University of Braunschweig

Our "Sneaking Ligand" fusion proteins provided a cell-specific delivery of an intracellular regulator of immune activation. The E-selectin–specific "Sneaking Ligand" fusion protein inhibited NF-κB by interfering with endothelial IκB kinase 2 activity inside the cells *in vitro* and *in vivo*. The treatment drastically reduced the extravasation of inflammatory cells murine experimental peritonitis and significantly ameliorated the disease course in murine models of rheumatoid arthritis.

5:25 End of Fusion Protein Therapeutics

"A GREAT MEETING FOR GAINING INSIGHT INTO UNPUBLISHED DATA AND CLINICAL FINDINGS, AND A SIGNIFICANT OPPORTUNITY TO NETWORK AND PROBLEM-SOLVE WITH COLLEAGUES"

-Senior Scientist, ADPE, MedImmune, LLC

Antibody-Drug Conjugates I: New Ligands, Payloads and Alternative Formats

Challenging the Convention in Next-Generation ADC Engineering

WEDNESDAY, APRIL 27

7:00 am Registration and Morning Coffee

8:00 Chairperson's Remarks

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

» 8:10 KEYNOTE PRESENTATION:

Determination of Cellular Processing Rates Points to Key Parameters for Antibody-Drug Conjugate Design

K. Dane Wittrup, Ph.D., C.P. Dubbs Professor, Chemical Engineering & Biological Engineering, Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

Numerous processing steps occur before the active drug component of an ADC can reach its intracellular target. Increased understanding of ADC cellular processing may facilitate more rational design of ADCs. In this work, we present a generalizable method to determine kinetic parameters, which can be used in a basic model for cellular processing of ADCs and can be incorporated into larger scale pharmacokinetic/pharmacodynamic models.

» 8:40 KEYNOTE PRESENTATION:

Combining Antibody-Drug Conjugates and Immune-Mediated Cancer Therapy: What to Expect?

Hans-Peter Gerber, Ph.D., Vice President, CSO, Bioconjugates Discovery & Development, Oncology Research Unit East, Pfizer Worldwide Research & Development

Toxins targeting DNA like anthracyclines or tubulin poisons like vinblastine can stimulate the innate immune system. When combined immuno-oncology (IO) compounds, both classes of toxins further enhanced the adaptive immune response and improved the anti-tumor responses. Therefore, identification of optimal combination regimens between ADCs employing different classes of toxins and IO compounds holds strong promise to overcome the key limitations of current immune checkpoint inhibitors, by increasing the recruitment and infiltration of CD8+ effector T Cells to the tumor.

ALTERNATIVE FORMATS AND NEW TARGETING LIGANDS

9:10 Small Ligand-Targeted Drug Conjugates: An Alternative to ADCs

Philip S. Low, Ph.D., Director of the Purdue Center for Drug Discovery, Ralph C. Corley Distinguished Professor, Department of Chemistry, Purdue University

We have developed small molecule ligands for use in targeting attached drugs to pathologic cells, thereby avoiding collateral toxicity to healthy cells. We have also developed low molecular weight targeting ligands to deliver attached drugs selectively to cancers that over-express PSMA, CCK2 receptor, neurokinin 1 receptor, carbonic anhydrase IX , and several other tumor-specific receptors. Finally, ligand-targeted imaging and therapeutic agents for autoimmune, inflammatory, and infectious diseases (e.g. malaria, rheumatoid arthritis, multiple sclerosis, psoriasis, atherosclerosis, osteoarthritis, etc.) will also be described.

9:40 Targeted Protein Therapeutics (TPTs) for the Treatment of Cancer

Greg Adams, Ph.D., Chief Development Officer, Viventia Biotech

TPTs are fully biologic constructs containing antibody fragments and protein toxin payloads in a single engineered molecule. The preclinical/clinical development of TPTs employing fully deimmunized payloads for the treatment of systemic disease and non-deimmunized payloads for use in the treatment of loco regional disease will be discussed.

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

10:55 Development of Probody-Drug Conjugates Targeting Highly Expressed Tumor Antigens

Jon Terrett, Ph.D., Vice President, Oncology CytomX

PDCs are antibody prodrugs that are designed to be activated in tumors while avoiding binding to normal tissues. PDCs can safely enable targeting of antigens with broad, persistent & very high expression in cancer that are also expressed in normal tissues, and therefore cannot be approached with traditional Antibody-Drug Conjugates. Such targets can show >70% prevalence at 3+ expression in many cancer types. Preclinical proof of concept for safety, efficacy & developability of PDCs to high expression targets will be shown.

11:25 Immunomodulation by CO Delivered from Artificial Metalloproteins

Goncalo J.L. Bernardes, Ph.D., Chemistry, University of Cambridge

A new class of therapeutic metalloproteins allows for the controlled and targeted delivery of carbon monoxide (CO) into tumors. When administered into tumor bearing mice, the CO-releasing metalloproteins result in strong tumor growth retardation. The CO-mediated effect is due to the combined downregulation of important angiogenic factors as well as activation of CD8 cytotoxic T Cells. Finally, when used in combination with current standard of care chemotherapeutic drugs, the novel CO immune-modulation treatment results in cancer cures in mice.

11:55 Drug Conjugation and Delivery Enabled by a Tumor-Targeting Peptide-Fc Fusion

Jennifer Cochran, Ph.D., Associate Professor, Bioengineering, Stanford University

We are creating novel peptide-drug conjugates for targeted delivery of chemotherapeutic agents to tumors. As an example, an integrin targeted peptide-Fc fusion, conjugated to an auristatin derivative, was effective as a single agent at inducing regression and prolonged survival in tumor xenograft models. These studies provide proof-of-concept for further development of peptide-drug conjugates as attractive alternatives to ADCs for tumor targeting and drug delivery applications.

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

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

1:55 Session Break

NOVEL APPLICATIONS OF ADCs

2:10 Chairperson's Remarks

Hans-Peter Gerber, Ph.D., Vice President and CSO, Bioconjugates Discovery & Development, Oncology Research Unit East, Pfizer Worldwide R&D

2:15 Development of a Novel Protease Cleavable Linker for Anti-Staphylococcus Aureus Antibody-Antibiotic Conjugates

Martine Darwish, MSc, Senior Scientific Researcher, Protein Chemistry, Genentech

Antibody-Antibiotic Conjugates (AACs) employ an antibody specific for cell wall components of *Staphylococcus aureus* conjugated with a potent antibiotic. We describe the development of a peptide linker that is cleaved by staphopain B, a secreted endopeptidase of S. aureus. The resultant AAC has demonstrated efficacy in *in vitro* and *in vivo* models of MRSA infection, providing a novel mechanism by which to target MRSA infections and release payload in a disease specific manner.

2:45 Tau-Specific Single Domain Antibody-Nanoparticle Complex as Biomarker for Traumatic Brain Injury

Mehdi Arbabi Ghahroudi, Ph.D., Research Officer/Research Scientist, Human Health Therapeutics, National Research Council Canada

Tau, a microtubule-associated protein, accumulates in the brain following traumatic brain injury and neurodegenerative diseases. We identified a single-domain antibody, specific for tau and its hyper-phosphorylated

CONTINUED

Antibody-Drug Conjugates I: New Ligands, Payloads and Alternative Formats

Challenging the Convention in Next-Generation ADC Engineering

form. Here we demonstrate that this antibody fragment, conjugated to an MR visible nanoparticle, can cross the primary hippocampal neuronal membrane *in vitro* and bind to intracellular tau. This is the first step towards a new, non-invasive method of detecting tau deposition in patients.

3:15 Developing Site-Specifically Modified ADCs Using a Chemoenzymatic Approach

Sponsored by Catalent BIOLOGICS

David Rabuka, Global Head, Research & Development, Chemical Biology, Catalent Pharma Solutions

Antibody-drug conjugates (ADCs) have become de rigueur for pharmaceutical oncology drug development pipelines. We have developed the SMARTagTM technology platform, which enables precise, programmable, site-selective chemical protein modification. We will highlight progress in developing these SMARTagTM ADCs with a focus on preclinical studies as well as highlight our progress in cell line development and manufacturing of bioconjugates using this chemoenzymatic approach.

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

4:45 Problem-Solving Breakout Discussions

See website for details.

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

7:00 End of Day

THURSDAY, APRIL 28

8:00 am Morning Coffee

ENGINEERING AND CONJUGATION CHEMISTRY TO IMPROVE PROPERTIES OF ADCs

8:30 Chairperson's Remarks

Greg Adams, Ph.D., Chief Development Officer, Viventia Biotech

8:35 Engineering a Tumor-Specific, Next-Generation Anti-EGFR ADC Development Candidate

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

9:05 HSP90 Inhibitor Drug Conjugates (HDCs): A Novel Conjugation Platform

Alan Rigby, Ph.D., CSO and Senior Vice President, Synta Pharmaceuticals

I will discuss an innovative strategy that utilizes HSP90 inhibitor-drug conjugates (HDC) for the purpose of directed intratumoral targeting of chemotherapeutic agents. STA-12-8666 is a first in class HDC that is comprised of an HSP90 inhibitor fused to SN-38, the active metabolite of irinotecan. We have observed intratumoral payload release by STA-12-8666 that contributed to a broad therapeutic window, sustained biomarker activity, and remarkable degree of efficacy and durability of response in multiple *in vivo* cell line and patient-derived xenograft models.

9:35 Sponsored Presentation *(Opportunity Available)*

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

11:05 A Plug-and-Play Approach to Antibody-Based Therapeutics via a Chemoselective "Dual Click" Strategy

Vijay Chudasama, Ph.D., MSc, Lecturer, Chemistry, University College London

There is a clear demand for the construction of novel antibody-drug conjugate (ADC) platforms that offer greater stability, homogeneity and flexibility. A significant step towards the ideal platform for next generation antibody-based therapeutics is presented. Our technology provides decorated antibody constructs that are highly stable, with complete retention of antibody binding/structure post-modification. It combines site-specific functionalisation with exceptional versatility via the functional re-bridging of interchain disulfide bonds native to antibodies.

11:35 Improving the Therapeutic Window of an Antibody-Drug Conjugate by a New Stable Conjugation Method

Sang Hoon Lee, Ph.D., CEO and Founder, ABL BIO

To overcome the limitation of ADC due to off-target toxicity and narrow therapeutic window, we have developed s new conjugation technique that attaches drugs to N-terminal of an antibody through amine bond by reductive alkylation reaction (NTERM). NTERM ADC showed superior *in vitro* and *in vivo* stability as well as tolerability than commonly used thiol-conjugate and lysine conjugate. Therefore, NTERM can be a novel conjugation method to improve therapeutic window.

12:05 pm A Non-Genetic Approach to ADCs with Improved Therapeutic Index with GlycoConnect™ and HydraSpace™ Technology

Floris van Delft, Ph.D., Co-Founder and CSO, Synaffix

GlycoConnect™ is a highly efficient technology to obtain, without protein engineering, antibody-drug conjugates (ADCs) in a two-stage process involving (a) enzymatic N-glycan remodeling and (b) copper-free click attachment of payload. Conjugation of highly hydrophobic payloads is accommodated with polar HydraSpace™ technology. Excellent *in vivo* efficacy and high tolerability is demonstrated, thus paving the way for the next generation of ADCs with an improved therapeutic index.

12:35 End of Antibody-Drug Conjugates I: New Ligands, Payloads and Alternative Formats

5:15 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC13: Critical Considerations for the Design and Development of Antibody-Drug Conjugates

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

Antibody-Drug Conjugates II: Advancing Toward the Clinic

Learning from Preclinical and Clinical Data to Inform Next-Generation ADC Design

THURSDAY, APRIL 28

12:35 pm Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

Pamela Trail, Ph.D., Vice President, Oncology, Regeneron Pharmaceuticals

» 1:50 KEYNOTE PRESENTATION:

Building on Lessons Learned from Clinical Development in the Design and Development of the Next-Generation ADCs

John Lambert, Ph.D., Executive Vice President, Research, and Distinguished Research Fellow, ImmunoGen, Inc.

ADCs with potent tubulin-acting and DNA-acting agents can be effective anti-cancer agents with good therapeutic indices. However, not all cell-surface targets have proven susceptible to the development of effective ADCs utilizing the first generation ADC chemistries. Some of the lessons learned from the past 15 years of ADC preclinical and clinical experience, and how such lessons are being applied to current and future ADC developments, will be discussed.

» 2:20 KEYNOTE PRESENTATION:

Advances in Antibody-Based Conjugates for Cancer Therapy

Dennis Benjamin, Ph.D., Vice President, Translational Research, Seattle Genetics, Inc.

Insights into how ADCs can be effectively developed have been gained through studies on cancer antigen targets, drug potency and mechanism, and linker stability and conditional drug release. Adcetris is an example of an ADC designed with these parameters in mind. Since then, significant developments have been made in many areas of ADC technology, including the physicochemical properties of conjugates, biodistribution, and new high-potency drugs. An overview and progress surrounding new generation ADCs will be provided.

TRANSLATIONAL AND PKPD CHALLENGES

2:50 Antibody-Drug Conjugates: Translational Considerations

Mohammad Tabrizi, Ph.D., Director Biologics Discovery, Merck Research Laboratories

Targeted delivery of highly potent small molecule drugs to specific effecT Cells is intended to expand the therapeutic window for the payload in the clinical setting via curtailing the anticipated adverse effects. Here, we have attempted to address some of the key translational topics critical for early development of antibody-drug conjugates. As anticipated, a successful transition of ADCs into the clinic will be highly dependent on effective translation of critical attributes governing exposure-response relationships across species.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Refreshment Break

4:20 Ado-Trastuzumab Emtansine Targets Hepatocytes via Human Epidermal Growth Factor Receptor 2 to Induce Hepatotoxicity

Wen Jin Wu, Ph.D., Senior Investigator, Office of Biotechnology Products, CDER, US FDA

Hepatotoxicity is one of the serious adverse events associated with T-DM1 therapy; mechanisms underlying T-DM1–induced hepatotoxicity remain elusive. We find that T-DM1 is internalized upon binding to cell surface HER2 and is co-localized with LAMP1, resulting in DM1-associated cytotoxicity. We further demonstrate that T-DM1 treatment significantly increases the serum levels of AST, ALT, LDH, and induces inflammation and necrosis in hepatocytes. We propose that T-DM1-induced upregulation of TNFα enhances the liver injury that may be initially caused by DM1-mediated intracellular damage.

4:50 Evaluation of the Bi-Directional Interaction between the Mononuclear Phagocyte System (MPS) and the Pharmacokinetics and Pharmacodynamics of Carrier Mediated Agents and Antibody-Drug Conjugates

William C. Zamboni, PharmD, Ph.D., Associate Professor, Director of the UNC Translational Oncology and Nanoparticle Drug Development Initiative (TOND2I) Lab, The University of North Carolina

Carrier-mediated agents (CMA) and Antibody-Drug Conjugates (ADCs) consist of the inactive-drug that remains encapsulated within or conjugated to the carrier and the active-drug that is released from the carrier. We will discuss: 1) pharmacologic methods to characterize CMAs and ADCs *in vivo* and *in vivo*; 2) animal models for pharmacologic and toxicology studies of CMAs and ADCs; 3) the development of phenotypic probes of the MPS to profile the interaction between CMAs and ADCs and the MPS; 4) bi-direction interaction between MPS and ADCs.

5:20 End of Day

5:15 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC13: Critical Considerations for the Design and Development of Antibody-Drug Conjugates

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

FRIDAY, APRIL 29

8:00 am Registration and Morning Coffee

ADCs IN EARLY DEVELOPMENT

8:30 Chairperson's Remarks

Alan Rigby, Ph.D., CSO and Senior Vice President, Synta Pharmaceuticals

8:35 Regulatory Considerations during Early Development of ADCs

Bethany Rappoli, MA, MS, Director, Worldwide Regulatory Strategy, Pfizer

ADCs are complex molecules presenting unique development challenges. Given the highly competitive nature of drug development in oncology, teams need to be poised to accelerate early, but there is often confusion as to what this may entail from a regulatory perspective. The intent of this presentation is to touch on key regulatory considerations and strategies for the early stage development of ADCs.

9:05 Building on the Success of Trastuzumab Emtansine/Kadcyla®: Preclinical Development of New HER2-Directed Antibody-Drug Conjugates

Gail Lewis Phillips, Ph.D., Senior Scientist, Molecular Oncology, Genentech

Trastuzumab emtansine (Kadcyla®) is an antibody-drug conjugate (ADC) comprised of the therapeutically active HER2 antibody trastuzumab covalently linked to DM1, a microtubule inhibitor, through a non-cleavable linker. In patients with HER2-positive metastatic breast cancer (mBC) who were previously treated with HER2-directed therapies, trastuzumab emtansine is more active and better tolerated than standard of care treatment regimens. Recent studies are focused on developing new strategies for HER2-targeted ADCs by exploring different cytotoxic agents and linkers.

9:35 Update on MedImmune's Antibody-Drug Conjugate Platform: Developing Potent ADCs for Cancer Therapy

Ronald Herbst, Ph.D., Vice President and Head, Oncology Research, MedImmune

10:05 Coffee Break

CONTINUED

Antibody-Drug Conjugates II: Advancing Toward the Clinic

Learning from Preclinical and Clinical Data to Inform Next-Generation ADC Design

UPDATES FROM THE CLINIC

10:35 Development of ADCs Targeting Guanylyl Cyclase C (GCC) for the Treatment of Gastrointestinal Malignancies

Peter Veiby, Ph.D., Global Head, Biotherapeutics, Oncology Drug Discovery Unit, Takeda Pharmaceuticals International

MLN0264/TAK264 is a GCC targeting ADC in phase 2 clinical development in Gastric and pancreatic cancer patients. The target of MLN0264, GCC, is expressed in >95% of mCRC patient samples however the low response rate patients with mCRC treated MLN0264 led us to hypothesize that an ADC carrying a different cytotoxic payload could potentially provide an alternative for patients with GCC expressing mCRC. We will discuss our efforts to preclinically characterize next generation ADCs targeting GCC in patient derived xenografts refractory to MLN0264.

11:05 Celldex ADC Pipeline and Clinical Development Update

Christopher D. Turner, M.D., Vice President, Clinical Science, Celldex Therapeutics, Inc.

Celldex has developed a pipeline of proprietary antibodies and immunomodulators. Glembatumumab vedotin (CDX-011) is a novel ADC that delivers the potent cytotoxin, MMAE, to cancer cells expressing gpNMB. gpNMB is a transmembrane protein overexpressed in 20% of breast cancers (40% of TNBC) and 80% of melanomas. An overview of the clinical experience with glembatumumab vedotin and an update on the Phase 2 trials for TNBC ("METRIC") and melanoma will be presented.

11:35 Sacituzumab Govitecan (IMMU-132), a Next-Generation ADC in Advanced Clinical Trials for Solid Cancer Therapy

David M. Goldenberg, Sc.D., M.D., CSO and Chairman, Immunomedics, Inc.

IMMU-132 is an ADC involving the conjugation of 7.6 molecules of SN-38 to the IgG of the internalizing anti-Trop-2 humanized mAb, hRS7. Over 250 patients with diverse solid cancers have been treated, and the optimal dosing schedule has been determined to be 10 mg/kg on days 1 and 8 of 21-day cycles, permitting therapy over months without the induction of anti-antibody or anti-SN-38 antibodies. Objective durable responses have been achieved in a number of patients with advanced, metastatic cancers, after failing multiple prior therapies.

12:05 pm AGS67E, an Anti-CD37 Monomethyl Auristatin E (MMAE) Antibody-Drug Conjugate for NHL, CLL & AML

Leonard Reyno, M.D., Senior Vice President & CMO, Agensys

AGS67E is an antibody drug conjugate (ADC) composed of a fully human IgG2 antibody targeting CD37 that is conjugated to the anti-tubulin agent MMAE through a cleavable linker. A multicenter phase 1 dose-escalation study is currently evaluating the safety, PK, and anticancer activity of AGS67E given as monotherapy to patients with relapsed / refractory non-Hodgkin lymphoma. AGS67E is administered IV Q3 weeks until disease progression or unacceptable toxicity. Updated clinical results will be presented with implications for further development in hematological malignancies including Lymphoma and AML.

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

1:05 Refreshment Break

UPDATES FROM THE CLINIC (CONT.)

1:35 Chairperson's Remarks

Alan Rigby, Ph.D., CSO and Senior Vice President, Synta Pharmaceuticals

1:40 PRLR ADC: Development of a Novel Antibody Drug-Conjugate for the Treatment of PRLR Positive Breast Cancer

Pamela Trail, Ph.D., Vice President, Oncology, Regeneron Pharmaceuticals

Prolactin Receptor (PRLR) is a type I cytokine receptor that is overexpressed in approximately 25% of human breast tumors of various subtypes, including triple-negative cancers. Importantly, PRLR has limited normal tissue expression and is rapidly internalized following binding of anti-PRLR antibodies. We have explored the use of PRLR as a therapeutic target for development of anti-PRLR Antibody-Drug Conjugates. Results of those studies and the use of PRLR directed ADCs for treatment of breast cancer will be discussed.

2:10 Clinical Development of Mirvetuximab Soravtansine – A Maytansinoid ADC Targeting Folate Receptor Alpha

Charles Morris, MBChB, MRCP(UK), Chief Development Officer, ImmunoGen

Mirvetuximab soravtansine (IMGN853) is a maytansinoid ADC targeting folate receptor alpha (FRa) which is expressed in a number of solid tumors including ovarian, endometrial and non-small cell lung cancers. Early clinical data show encouraging activity in heavily pre-treated epithelial ovarian cancer with notably high response rates in patients whose tumors express high levels of FRa. This presentation will review the clinical data to date.

2:40 Seattle Genetics' Latest ADC Innovation: Increasing Potency to Maximize Activity

Elaina Gartner, M.D., Medical Director, Experimental Medicine, Seattle Genetics, Inc.

Through targeted delivery of potent cytotoxic agents, Antibody-Drug Conjugates (ADCs) are revolutionizing cancer care. With the advent of more highly potent and stable drug linkers, such as pyrrolobenzodiazepine (PBD) dimers, the antitumor activity of ADCs may be enhanced while limiting off-target toxicity. The most recent, highly potent ADCs in development from Seattle Genetics' portfolio will be discussed, highlighting SGN-CD33A for acute myeloid leukemia.

3:10 Matching Technology Improvements with Biology to Enable Successful ADCs

Puja Sapra, Ph.D., Senior Director, Bioconjugates Discovery & Development, Pfizer, Inc.

This presentation will cover evolution of calicheamicin ADCs over last two decades. Learnings from several clinical programs including Mylotarg and Inotuzumab will be discussed. Improvements in technology and target selection strategies that can enable calicheamcin ADCs for solid tumors will be presented. Additionally, the presentation will disclose new technology improvements in development of tubulin inhibitor- based ADCs. Preclinical and clinical update from novel auristatin ADC programs will be covered. Preclinical data on combination strategies of ADCs and immune-oncology therapeutics will be presented.

3:40 End of Antibody-Drug Conjugates II: Advancing Toward the Clinic

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Biologics for Autoimmune Diseases

Emerging Targets, Therapeutic Strategies and Product Formats for a Growing Market

RECOMMENDED PRE-CONFERENCE SHORT COURSES*

SC4: Translational Considerations for Development of Monoclonal Antibodies: Focus on Early Discovery (Part I)

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

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

MONDAY, APRIL 25

7:00 am Registration and Morning Coffee

8:30 Chairperson's Remarks

Ali Zarrin, Ph.D., Scientist, Immunology, Genentech

8:40 KEYNOTE PRESENTATION:

Complement in Tolerance and Autoimmunity: Opportunities for Biotherapeutics Targeting Complement

Uday Kishore, Ph.D., Director, Center for Infection, Immunity and Disease Mechanisms, Brunel University

Complement system is a potent link between innate and adaptive immunity. Complement is a double-edged sword whose central role in immune tolerance as well as development and aggravation of inflammatory disorders including autoimmune diseases is well established. A number of antibody-dependent and independent strategies have been devised to manipulate and contain the complement activators and regulators. The lecture will give a holistic view of the field with a state-of-the-art critique.

EMERGING TARGETS AND MECHANISMS OF ACTION

9:10 Merging New and Old Paradigms to Understand Immunopathology of Smoker's Lung Disease

Farrah Kheradmand, M.D., Professor, Pathology and Immunology, Baylor College of Medicine

The basis for cigarette smoke-induced autoimmune-mediated inflammation stems from our discovery that memory T Cell responses directed against lung elastin peptides can be detected in smokers with emphysema. We have embarked on investigating the pathophysiology of chronic obstructive pulmonary disease using preclinical models that share common features with human emphysema. Our studies have elucidated the function of several upstream activators of autoimmune inflammation that could be harnessed for novel therapy.

9:40 "Accelerating" Discoveries in Autoimmunity

PJ Utz, M.D., Professor, Immunology and Rheumatology, Stanford University School of Medicine

Autoimmune diseases as a group share features including genetics, pathogenesis, and treatment choices. The field is now moving from murine studies and experiments using blood toward single cell methodologies for characterizing tissues. The speaker will describe NIH's new Accelerating Medicines Partnership (AMP) program in rheumatoid arthritis and systemic lupus erythematosus in which synovium, bone marrow, skin, kidney and blood are being studied using RNA-Seq, ATAc-Seq, repertoire analysis, and CyTOF.

10:10 Coffee Break

10:45 Chairperson's Remarks

10:50 Novel Mechanisms of Action for Inhibitory Receptors as Targets for Autoimmune Indications

Ali Zarrin, Ph.D., Scientist, Immunology, Genentech

Paired Ig-like type 2 receptor α (PILRα) inhibitory receptor and its counter-part PILRβ activating receptor, are both co-expressed on myeloid cells. PILRα is elevated in various inflammatory diseases such as rheumatoid arthritis. Pilrα–/– mice produce more pathogenic cytokines during inflammation and are prone to enhanced autoimmune arthritis. We report how modulation of this pathway has utility in inflammatory diseases.

11:20 Venom-Derived Peptides for the Treatment of Autoimmune Disease

Christine Beeton, Ph.D., Associate Professor, Molecular Physiology and Biophysics, Baylor College of Medicine

CCR7- effector memory T lymphocytes are involved in autoimmune diseases and up-regulate Kv1.3 channels upon activation. We have used ShK, a peptide isolated from a sea anemone venom, to design dalazatide (formerly ShK-186) as a selective and potent Kv1.3 blocker. Dalazatide has undergone preclinical testing *in vitro* and animal models. It was well tolerated in clinical trials with healthy volunteers and is currently being evaluated in patients with autoimmune diseases.

11:50 Investigation of Antibody-Drug Conjugates to Target Glucocorticoids to Immune Cells

Philip E. Brandish, Ph.D., Principal Scientist, Immunology & Oncology, Merck Research Laboratories

The magic bullet idea of using antibodies to target cytotoxic agents to tumor cells has proven feasible and we sought to build on those successes to enable dose-limited therapeutics beyond oncology. Using glucocorticoids as an example, we have used site-specific incorporation at a genetically encoded non-natural amino acid, novel linker chemistry, and a potent glucocorticoid receptor agonist to assess the feasibility of the general approach.

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

See website for details.

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

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Biologics for Autoimmune Diseases

Emerging Targets, Therapeutic Strategies and Product Formats for a Growing Market

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 The Promise of Cancer Immunotherapy: An Overview of Recent Advances and Jounce's Approach to Delivering the Right Therapy to the Right Patient

Deborah Law, D. Phil. CSO Jounce Therapeutics, Inc.

As immunotherapies become an increasingly important component of cancer treatment the challenge will be to identify ways to provide the best therapy(s) to the individual. This presentation will provide an overview of current cancer immunotherapies as well as highlight some of the challenges ahead including selection of optimal combinations, moving outside of T Cell-directed approaches, and will highlight how Jounce Therapeutics is using its Translational Science Platform as an approach to develop and deliver the right therapy to the right patient.

4:50 Antibody as Drugs: Then, Now and Tomorrow

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

Antibodies have grown into a clinically and commercially important drug class with more than >45 antibodies marketed for imaging or therapy in the USA and/or Europe and with ~$63 billion in worldwide sales in 2013. This presentation will highlight progress in developing antibody drugs and consider opportunities for future innovation.

5:30 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 End of Day

TUESDAY, APRIL 26

8:00am Morning Coffee

BIOLOGICS FOR SMALL AND ORPHAN AUTOIMMUNE INDICATIONS

8:25 Chairperson's Remarks

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

8:30 New Diseases for Old Tools, Different Approaches to Known Targets: Expanding Indications for Approved Biologics into Rare Diseases

John H. Stone, M.D., MPH, The Edward Fox Chair in Medicine, Massachusetts General Hospital; Professor, Medicine, Harvard Medical School

Expanding indications into less common diseases requires the clinical insight to identify unmet need. This is facilitated by knowing the natural history of treated disease, but even more so by the ability to evaluate patients before they begin any treatment at all (not all conditions permit this). I will review the background to pivotal trials in vasculitis and the identification of a novel therapeutic for fibroinflammatory disease that grew out of studies in IgG4-related disease. The latter experience has broad implications for other fibrosing diseases.

9:00 Biologics for Orphan Autoimmune Indications

Jeffrey Siegel, M.D., Senior Group Medical Director, Product Development Immunology, Genentech

Orphan diseases represent an area of high unmet medical need. Though once a neglected area of drug development, legislation passed in the US and in other regions has provided incentives that have dramatically accelerated clinical development. In this talk I will explore opportunities and challenges in the development of targeted biologic therapies for orphan autoimmune conditions.

9:30 Deep Biocharacterization of Autoimmune Disease Patients Yields Unique Insights into Unmet Medical Need

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

Development of novel therapeutics is confounded by our inability to understand the complex basis of disease, resulting in a high failure rate in development and unclear benefit for patients. We developed high-resolution analytics to identify novel drug targets and patient stratification markers that address unmet medical need in autoimmune disease. This presentation will describe the application of this technology to four different disease settings, and the actionable results it yielded.

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

10:50 TH17 Targets for Multiple Autoimmune Diseases

Andrea Itano, Ph.D., Vice President, Head of Tempero Discovery Performance Unit, Immuno-Inflammation, GlaxoSmithKline

The pathogenic role of the TH17/IL-23 axis in autoimmune and inflammatory diseases has been validated by recent the successes reported in late-stage clinical trials for the treatment of diseases including psoriasis, ankylosing spondylitis, and Crohn's disease by antibodies targeting the IL-17, IL-17R, and IL-23. This talk will review the current status of TH17/IL-23-targeting therapeutics in clinical studies, and discuss the implications for new targets and new disease areas.

11:20 Regulatory T Cells-Based Cellular Immunotherapy of Inflammation and Autoimmunity

Arnaud Foussat, Ph.D., CSO, TxCell

Due to their natural function in inhibiting inflammation, Regulatory T (Treg) cells are seen as a promising therapeutic tool for patients with refractory chronic inflammatory and autoimmune diseases. As of today, several clinical trials have demonstrated the safety of Treg cell administration into patients and interesting signs of efficacy. Specific challenges of Treg cell therapy development have been described and new approaches to target Treg cells in specific diseases are in development.

11:50 Tolerogenic Nanoparticles for the Treatment of Autoimmune Diseases

Kei Kishimoto, Ph.D., CSO, Selecta Biosciences

We have developed novel nanoparticles carrying a tolerogenic immunomodulator to induce durable and antigen-specific immune tolerance. We illustrate two potential applications of tolerogenic nanoparticles for the treatment of autoimmune disease: 1) immune tolerance induction directed against a pathogenic autoantigen in a model of experimental autoimmune encephalomyelitis, and 2) tolerance to prevent the formation of anti-drug antibodies directed against an immunogenic biologic therapy, adalimumab, in a spontaneous mouse model of arthritis.

12:20pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on your Own**

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

PRECLINICAL AND CLINICAL STUDIES

2:00 Chairperson's Remarks

Rachel Ettinger, Ph.D. Senior Scientist Respiratory, Inflammatory, and Autoimmune Diseases, MedImmune

2:05 Investigation and Mitigation of Safety Issues in Autoimmune Disease Biologics

Meena Subramanyam, Ph.D., Vice President, Global Biomarker Product Safety, Biogen

A number of biological therapeutics have been approved for treating a diverse group of autoimmune diseases. The immune modulating properties of biological therapeutics for autoimmune diseases has prompted scrutiny and careful evaluation in post-marketing surveillance for increased incidence of cancer, central nervous system related events, and other opportunistic infections. This talk will discuss the safety events observed with the use of these agents in autoimmune disorders and strategies in consideration to manage the risk.

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Emerging Targets, Therapeutic Strategies and Product Formats for a Growing Market

2:35 Early and Transient Blockade of CD40/CD40L Interactions Abolishes Sjögren's Manifestations in Aged Autoimmune Mice

Rachel Ettinger, Ph.D. Senior Scientist Respiratory, Inflammatory, and Autoimmune Diseases, MedImmune

Autoantibodies can be present decades before the onset of autoimmune disease manifestations. This suggests that the initial trigger involves a peripheral component that drives disease in local tissue later in life. In an autoimmune mouse model of Sjögren's we show that "pre-diseased" autoantibodies arise from early-life germinal centers; removal of which reverses disease pathology. These data suggest that early prophylactic intervention may prove efficacious for those diseases pre-dated by autoantibodies.

3:05 Sponsored Presentation *(Opportunity Available)*

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

4:25 Potent Neutralizing Anti-CD1d Antibody Reduces Lung Cytokine Release in Primate Asthma Model

Adam Clarke, Ph.D., Director, Lead Generation, Biologics, Teva Pharmaceuticals Australia

CD1d is a receptor on APCs that activate NKT Cells. Targeting the CD1d/NKT pathway may have therapeutic potential in asthma. We developed a high affinity CD1d antibody (NIB.2) that has strong neutralizing activity in human primary cell-based assays. We characterize the epitope and specificity of NIB.2 for CD1d in complex with lipids. Anti-CD1d antibody blockade of the CD1d/NKT pathway modulates inflammatory parameters *in vivo* in an A.suum primate inflammation model.

4:55 Dissecting the Properties of Anti-CXCL10 Antibodies Having Anti-Inflammatory Activity *In Vivo*

Marie Kosco-Vilbois, Ph.D., CSO, Novimmune

We characterized three anti-murine CXCL10 mAbs targeting different epitopes, having different potencies and capacities to bind chemokines in the context of glycosaminoglycans (GAG). Binding to CXCL10 on GAG lead to rapid serum clearance and lower efficacy in mouse models of inflammation. In contrast, antibodies binding only to soluble chemokine persisted in circulation and showed superior efficacy. These results indicate mAb characteristics required for therapeutic intervention and suggest a revised model for chemokines function.

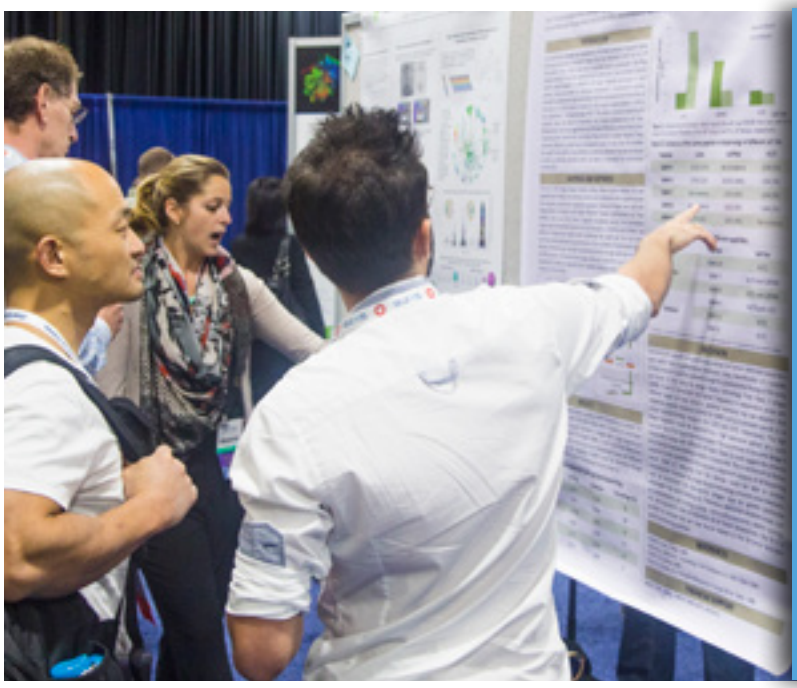
5:25 End of Biologics for Autoimmune Diseases

5:30 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC8: Next-Generation Sequencing of Antibody Libraries: Details on Experimental and Bioinformatic Methods

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



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Biologics and Vaccines for Infectious Diseases

Novel & Emerging Strategies for Clinical Success

RECOMMENDED PRE-CONFERENCE SHORT COURSE*

SC10: Analyzing and Rationalizing Protein-Protein Interactions

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

WEDNESDAY, APRIL 27

7:00 am Registration and Morning Coffee

IMPORTANT IMPLICATIONS IN BASIC SCIENCE AND MOA

8:00 Chairperson's Remarks

Galit Alter, Ph.D., Associate Professor, Medicine; Kristine and Bob Higgins MGH Research Scholar; Director, Ragon Institute Imaging Core; Director, Harvard Center for Aids Research Immunology Core, Ragon Institute of MGH, MIT and Harvard

» 8:10 KEYNOTE PRESENTATION:

Progress Towards an HIV Vaccine

Dennis R. Burton, Ph.D., Professor, Immunology and Microbial Science, Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery, and IAVI Neutralizing Antibody Center, The Scripps Research Institute; Ragon Institute of MGH, MIT & Harvard

Highly antigenically variable viruses such as HIV present major problems for vaccine design. Broadly neutralizing antibodies to HIV generated during natural infection can identify weaknesses in the surface structures of the virus. These weaknesses can help guide vaccine and drug design and reveal fascinating aspects of the interplay between two highly mutable systems-the virus and antibody.

8:40 Solving Structures of Macromolecular Complexes Involved in Viral and Bacterial Pathogenesis

David Veesler, Ph.D., Assistant Professor, Department of Biochemistry, University of Washington

Recent developments have revolutionized single particle cryo-electron microscopy (cryoEM) and led to a wave of near-atomic resolution reconstructions. During my presentation, I will illustrate how my lab harnesses these advances in molecular imaging to study macromolecular complexes involved in viral and bacterial pathogenesis at high-resolution. Our aim is to provide a structural framework that can be used to expedite structure-guided drug and vaccine design.

9:10 Unbiased NGS Analysis of B-Cell Responses in HIV-1 Infection and Vaccination

Jiang Zhu, Ph.D., Assistant Professor, Immunology & Microbial Science, Scripps Research Institute

Next-generation sequencing (NGS) has become a transformative technology in antibody and vaccine research. By combining 5'-RACE PCR, a single reverse primer, and long-read NGS platform, we can now capture B-cell repertoires in an unbiased manner. This technology has been applied to study the emergence of broadly neutralizing antibodies (bNAbs) during HIV-1 infection and HIV-1 vaccine-induced B-cell responses in nonhuman primates.

9:40 Tailoring Vaccines to Induce Innate Immune Cell-Recruiting Antibodies

Galit Alter, Ph.D., Associate Professor, Medicine, Kristine and Bob Higgins MGH Research Scholar; Director, Ragon Institute Imaging Core; Director, Harvard Center for Aids Research Immunology Core, Ragon Institute of MGH, MIT and Harvard

Following vaccination, waves of polyclonal antibodies are generated forming immune complexes poised to eliminate pathogens via innate immunity. With mounting evidence pointing to a role for extra-neutralizing-antibody functions in protection from HIV and other pathogens, a "systems serology" profiling approach captures the interactions between antibodies at unprecedented depths, revealing unique "vaccine-fingerprints" and providing mechanistic insights for the development of novel monoclonal therapeutics or next generation vaccine design.

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

ENABLING DISCOVERY

10:55 Rapid Development and Testing of Fully Human Antibodies against Emerging Viruses

Christos Kyratsous, Ph.D., Senior Staff Scientist, Infectious Diseases, Regeneron Pharmaceuticals, Inc.

Traditional approaches for development of antibodies are poorly suited to combating emerging pathogens, as they require laborious optimization and process adaptation for clinical development. We used state-of-the-art technologies to rapidly generate and validate antibodies against two emerging viruses, MERS-CoV and Ebolavirus, following an optimized process that links immunization to production of clinical grade antibodies and developed promising clinical candidates. Generation of the antibodies, testing and future development will be discussed.

11:25 Targeting HIV Latent Reservoir by DART and Trident Proteins

Chia-Ying K. Lam, Ph.D., Scientist II, Antibody Engineering, MacroGenics, Inc.

We will discuss the latest breakthroughs and usage of DART and Trident proteins in targeting latent HIV reservoirs in humans.

11:55 Novel Monoclonal Antibodies for the Prevention and Treatment of Bacterial Infections

Antonio DiGiadomenico, Ph.D., Scientist II, Infectious Diseases, MedImmune

To date, there has been some modest biologics drug discovery efforts to discover novel antibacterial agents for the prevention and/or treatment of Staphylococcal, Pseudomonal and Clostridium difficile infections but these efforts now appear to be picking up speed and are progressing in the clinic. Is there hope?

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

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

1:55 Session Break

FEATURED PRESENTATIONS- REGULATORY & PRODUCTION ISSUES

2:10 Chairperson's Remarks

Michael Wittekind, Ph.D., Senior Vice President of Research and CSO, ContraFect Corp.

2:15 Early Planning to Prevent Vaccine Production Problems

Richard Schwartz, Ph.D., Chief, Vaccine Production Program Lab, NIAID, NIH

Taking the opportunity to plan early for production can save considerable time and prevent problems downstream in the production process. This presentation will discuss the whys and hows that will make the transition from development to production run more smoothly.

2:45 Bringing New Vaccines from the Bench to Bedside: Regulatory Considerations for Initiation of Clinical Development

Bharat Khurana, DVM, Ph.D, MBA, Microbiologist, Division of Vaccines, FDA/CBER/OVRR/DVRPA

Only those vaccines that are demonstrated to be safe and effective, and that can be manufactured in a consistent manner are licensed by the U.S. FDA. Submission of an Investigational New Drug (IND) application to FDA prior to initiating a clinical investigation during the product development of a new vaccine is required to ensure the safety of subjects participating in the trial. In this presentation, the regulatory requirements for a first-in-human study will be discussed.

CONTINUED

Biologics and Vaccines for Infectious Diseases

Novel & Emerging Strategies for Clinical Success

3:15 Sponsored Presentation *(Opportunity Available)*

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

4:45 Problem-Solving Breakout Discussions
See website for details.

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

7:00 End of Day

THURSDAY, APRIL 28

8:00 am Morning Coffee

GETTING IT TO THE CLINIC PART 1

8:30 Chairperson's Remarks
Yin Luo, Ph.D., Associate Research Fellow, Analytical Research & Development, BTxPS, Pfizer

8:35 Structure and Function of the Bacterial Lipoproteins in Trumenba, A Prophylactic Vaccine against Invasive Meningococcal Meningitis B Disease
Yin Luo, Ph.D., Associate Research Fellow, Analytical Research & Development, BTxPS, Pfizer
Trumenba is a bivalent vaccine comprising two recombinant bacterial lipoproteins, which were demonstrated in pre-clinical and clinical studies to contain immunogenic epitopes that elicit potent bactericidal antibodies against diseases caused by Neisseria meningitidis bacteria serogroup B. The thorough understanding of the structure and function of each part of the lipoproteins, as well as their relationship, not only demonstrates that Trumenba is a well-characterized vaccine, but also lays the foundation for identifying critical parameters to guide the control of the vaccine manufacture.

9:05 Discovery and Clinical Development of Bacteriophage Lysin CF-301 for Treating Staphylococcal Infections
Michael Wittekind, Ph.D., SVP, Research; CSO, ContraFect Corp.
Because recombinant lysins kill quickly, have narrow spectrum activities across species, possess low resistance profiles while remaining effective against strains that have become resistant to antibiotics, quickly remove bacterial biofilms, and synergize strongly with standard-of-care antibiotics, lysins have unique therapeutic profiles compared to conventional antibiotics. In this talk, data for anti-staphylococcal lysin CF-301 will be presented, including *in vitro* characterizations, activity in animal infection models, and other preclinical analyses as well as an update on the ongoing clinical trials.

9:35 Sponsored Presentation *(Opportunity Available)*

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

LOOKING TO THE FUTURE OF THE FIELD

11:05 Whole Genome Functional Display Accesses a Novel Subset of Pathogen Biomarkers
Michael Hust, Ph.D., Group Leader, Institut für Biochemie, Biotechnologie und Bioinformatik, Technische Universität Braunschweig
Proteomes of cultivated pathogens significantly differ from those inside a patient. Our novel method allows to functionally identify biomarkers from the genome, as it is completely independent from cDNA generation from cultivated pathogens. We use genomic open reading frame selection by phage display to identify all possible immunogenic proteins (biomarker). Examples for the identification of novel biomarkers of Mycoplasma species and Salmonella Typhimurium as well as the identification of immunogenic proteins of ticks (Ixodes scapularis) will be given.

11:35 Immunogen-Design Approaches to Activate and Mature the Germline Forms of Broadly Neutralizing HIV-1 Antibodies
Leonidas Stamatatos, Ph.D., Member, Vaccine and Infectious Disease Division, Immunology and Vaccine Development Program, Fred Hutchinson Cancer Research Center
HIV-1 escapes detection by various components of the immune system by diverse mechanisms. One such mechanism is based on a stealth approach the virus adopted to avoid detection by the progenitors of B cells that give rise to broadly neutralizing antibodies. New immunogen-design approaches to bypass this obstacle are being developed and tested.

12:05 pm Intrabodies: Potent Molecules for *in Vivo* Knockdown of Proteins
Thomas Böldicke, Ph.D., Recombinant Protein Expression/Intrabody Unit, Helmholtz-Centre for Infection Research
The number of intracellular antibodies targeted to the ER or cytoplasm is increasing. Until now most intrabodies have been tested *in vitro*. *In vivo* application of ER intrabodies, which are easier to select than cytoplasmic intrabodies have also been reported. ER intrabodies have been applied in appropriate mouse models and in transgenic intrabody mice. Moreover intrabodies have been selected against toll-like receptors and viral antigens which might have therapeutic potential.

12:35 End of Biologics and Vaccines for Infectious Diseases

5:15 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE*

SC12: Strategic Bioassay Design and Analysis
**Separate registration required, please see page 5 for course details.*

2nd Annual | April 28 - 29

Agonist Immunotherapy Targets

Moving Novel Targets from Discovery to Clinical Trials

THURSDAY, APRIL 28

CASE STUDIES WITH AGONIST BIOLOGICS

12:35 pm Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Deborah Charych, Ph.D., Executive Director, Research Biology, Nektar Therapeutics

1:50 Hexavalent TNF-Superfamily Mimics for Cancer Treatment and Immune Modulation
Oliver Hill, Ph.D., Vice President, Molecular Biology, Apogenix, GmbH

Apogenix has developed a fusion protein technology to create hexavalent agonists targeting individual members of the TNFR-superfamily. Compared to conventional approaches using agonistic antibodies, Apogenix' compounds mimic the three-dimensional organization of the natural ligands (the TNFSF proteins). Consequently, their activity does not rely on secondary crosslinking events *in vitro* nor *in vivo*. We will present the molecular engineering concept and the current results obtained for the TRAIL-R-, CD40- and CD27-agonists.

2:20 NKTR-214: Harnessing the IL-2 Receptor Pathway for Cancer Immunotherapy
Deborah Charych, Ph.D., Executive Director, Research Biology, Nektar Therapeutics

NKTR-214 is a protein prodrug that consists of recombinant human interleukin-2 (IL-2) chemically conjugated with multiple releasable chains of polyethylene glycol (PEG). NKTR-214 provides significant anti-tumor activity in multiple mouse models. NKTR-214 harnesses the robust immune modulatory properties of a cytokine but with controlled anti-tumor activity, and with dosing schedules similar to that of an antibody.

2:50 OX40: From Bench to Bedside
Brendan D. Curti, M.D., Director, Genitourinary Oncology Research & Biotherapy Clinical Programs; Co-Director, Melanoma Program, Earle A. Chiles Research Institute, Providence Cancer Center

OX40 is a co-stimulatory pathway present in CD4 and CD8 T Cells. Engagement of OX40 on antigen-exposed T Cells results in enhanced memory and effector function. Numerous pre-clinical murine models show anti-tumor activity of OX40 agonists. The clinical development and immunologic changes induced by OX40 agonists in patients with cancer will be discussed along with pre-clinical work supporting the use of OX40 agonists with T Cell checkpoint inhibitors and other immune modulators.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Refreshment Break

4:20 Experimental Approaches for Cancer Immunotherapy Using Anti-CD40 Antibody
Alexander Rakhmilevich, M.D., Ph.D., Distinguished Senior Scientist, University of Wisconsin-Madison

CD40 ligation has been shown to induce antitumor effects in mice and cancer patients. We have demonstrated in several syngeneic mouse tumor models that anti-CD40 antibody, alone and in synergy with a toll-like receptor 9 agonist, CpG, activates macrophages and induces T Cell-independent antitumor effects. The antitumor efficacy of anti-CD40 and CpG can be further enhanced by chemotherapy or T Cell activation approaches involving checkpoint blockade.

4:40 Generation of an Optimal Anti-Tumor Immune Response as Prime for Checkpoint Inhibition
Thomas Davis, M.D., CMO & Executive Vice President, Clinical Development, Celldex Therapeutics

Combinations of immune modulators have shown marked synergy in preclinical studies and a range of combination studies are in progress. The combination of antigen specific vaccines with immune actuators, such as flt3L and agonist anti-CD27 antibodies, may offer improved responses to checkpoint as well as independent activity.

5:00 Reprograming the Tumor Microenvironment from Support to Fight
David Urech, Ph.D., CSO and Co-CEO, Numab AG

Numab's bispecific anti-IL23RxCD3 antibody fragment NM7-389 exclusively eliminates IL23R+ lymphocytes via CD8 T Cell mediated cytotoxicity. The bispecific anti-IL23RxCD3 molecule ameliorates symptoms in models for psoriasis, multiple sclerosis and colitis. In solid tumors, it depletes tumor supporting IL23R+ cells, stimulates CD8 T Cells to release factors including IFNγ and granzyme, and inhibits infiltration of regulatory T Cells, thereby generating a microenvironment, which effectively boosts specific anti-tumor immune cell responses. We propose NM7-389 as a new immune-modulatory agent for the therapy of autoimmune diseases and cancer.

5:20 End of Day

5:15 Registration for Dinner Short Courses*

RECOMMENDED DINNER SHORT COURSE*

SC11: Clinical Prospects of Cancer Immunotherapy
**Separate registration required, please see page 5 for course details.*

FRIDAY, APRIL 29

8:00 am Registration and Morning Coffee

EMERGING AGONIST AND ANTAGONIST TARGETS

8:30 Chairperson's Remarks
Adam J. Adler, Ph.D., Professor, Immunology, School of Medicine, UConn Health

8:35 Unlocking the Full Potential of Agonist Antibodies: A Multi-Faceted Challenge
Robert B. Stein, M.D., Ph.D., CSO, Agenus

Recent work on activating checkpoint targets such as GITR and OX40 has revealed that in addition to their co-stimulatory potential to enhance T Cell responsiveness to tumor associated antigens, they are also highly expressed by activated intratumoral regulatory T Cells. A more complete picture of the anti-tumor potential of GITR or OX40 agonist antibodies emerges when their regulatory T Cell depleting capacity is considered. A review of selected findings supporting this picture will be presented.

9:05 Preclinical Evaluation of JTX-2011, an Anti-ICOS Agonist Antibody
Deborah Law, D. Phil. CSO Jounce Therapeutics, Inc.

ICOS (inducible co-stimulator molecule), a member of the CD28 superfamily, is a co-stimulatory molecule expressed on T lymphocytes. We have generated agonistic anti-ICOS antibodies which are efficacious as monotherapies and in combination with anti-PD1 in multiple syngeneic tumor models. Mechanistic studies demonstrate enhanced cytotoxic CD8:T-regulatory cell ratios and preferential reduction in T-regulatory cells in the tumor microenvironment. JTX-2011, a species cross-reactive humanized antibody, has been selected for development. Evaluation of JTX-2011 in nonhuman primate models, including safety and PK parameters, will be presented. Our preclinical data provides rational for clinical development of JTX-2011 in solid tumor indications.

9:35 Immunoregulation by VISTA in the Tumor Microenvironment
J. Louise Lines, Research Scientist, Microbiology & Immunology, Dartmouth College

VISTA is a recently identified PDL1/PD1-like ligand/receptor that is being developed as a target for cancer immunotherapy. VISTA blockade is therapeutic in CT26 cancer and synergizes with PD1 blockade. VISTA is highly expressed on tumor infiltrating myeloid cells, and impacts on myeloid function. Tumors from anti-VISTA treated mice show increased myeloid cells overall, but decreased granulocytic-MDSCs. This unique feature of anti-VISTA treatment may explain why it works well in combination with anti-PD1.

CONTINUED

2nd Annual | April 28 - 29

Agonist Immunotherapy Targets

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10:05 Coffee Break

AGONISTS IN COMBINATION WITH OTHER MODALITIES

10:35 Exploiting Unexpected Properties of Combination OX40 Plus 4-1BB Agonist Costimulated T Cells for Tumor Immunotherapy

Adam J. Adler, Ph.D., Professor, Immunology, School of Medicine, UConn Health

Combining agonists to the costimulatory receptors CD134 and CD137 (dual costimulation) elicits potent T Cell-mediated tumor immunity. Two approaches have been explored to further enhance therapeutic potency. First, engaging tumor-unrelated CD4 T Cells that provide help to CD8 T Cells in both antigen-linked and non-linked manners. Second, treatment with particular cytokine combinations (IL-12 or IL-2 plus IL-33 or IL-36) that trigger dual costimulated effector T Cells via a TCR-independent mechanism.

11:05 Presentation to be Announced

11:35 Combinatorial Immunotherapy in Mouse Syngeneic Tumor Models

Hua Long, Senior Principal Scientist, Pfizer

Immunotherapies targeting the programmed death 1 (PD-1) coinhibitory receptor have shown great promise in the clinic. However, robust and safe combination therapies are still needed. We have investigated the antitumor activity of the anti-4-1BB/anti-PD-1 combination in the poorly immunogenic B16F10 melanoma model which resulted in pronounced tumor inhibition. The activity of the anti-4-1BB/anti-PD-1 combination was dependent on IFNγ and CD8(+) T Cells and elicited a robust antitumor effector/memory T Cell response. Combinatorial treatment with other agents will also be discussed.

12:05 pm Co-Stimulatory Agonists for the Immunotherapy of Cancer

Alan L. Epstein, M.D., Ph.D., Professor, Pathology, USC Keck School of Medicine

Co-stimulation is a key step in the development of an effective immune response to tumors. RT-PCR and IHC show that the tumor microenvironment lacks these key agonists to hinder the immune destruction of tumors. Our data demonstrate that providing missing co-stimulation using intravenously administered Fc-fusion proteins can be synergistic with methods to reduce immune suppression to provide effective and lasting treatment of cancer as a new direction of cancer immunotherapy.

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

1:05 Refreshment Break

STRATEGIES FOR TARGET DISCOVERY

1:35 Chairperson's Remarks

Yoram Reiter, Ph.D., Professor & Head, Laboratory of Molecular Immunology, Technion-Israel Institute of Technology

1:40 FivePrime's Approaches to New IO Target Discovery

Art Brace, Ph.D., Executive Director, Immuno-Oncology Research, Five Prime Therapeutics

2:10 Discovery of Novel Targets for Cancer Immunotherapy

Kai W. Wucherpfennig, M.D., Ph.D., Professor, Dana-Farber Cancer Institute and Harvard Medical School

We have developed novel *in vivo* screens for discovery of key negative regulators of T Cell function in the tumor microenvironment. A pooled shRNA (or gRNA) library is introduced into tumor-specific T Cells which are then transferred into mice bearing a subcutaneous melanoma (B16-Ova). Most transferred T Cells are inhibited in the immunosuppressive microenvironment of the tumor and therefore fail to proliferate in response to tumor antigen recognition. However, if a shRNA alleviates a significant block, T Cells can accumulate substantially in tumors. In our screen such shRNA (gRNAs) are identified by Illumina sequencing of the shRNA/gRNA cassette. This analysis is done across different tissues, enabling discovery of genes that control T Cell function in tumors. I will discuss novel targets we have identified and how they can be used to advance the treatment of cancer patients.

2:40 Discovering New Immunotherapy Targets by Dissecting Subsets of Human Tumor Infiltrating Lymphocytes

Andrew D. Weinberg, Ph.D., Chief, Laboratory of Basic Immunology, Providence Cancer Center; Agonox, Inc.

Our group has been interrogating CD8 and CD4 T Cell phenotypes within several different human tumor types. We have found common phenotypic themes that are selectively expressed within the tumor and not in the blood. Gene arrays have been performed within these subsets of TIL and we will discuss new immunotherapy approaches based on targeting these T Cell specific subsets within the tumor.

3:10 Discovery and Validation of Novel Targets for Cancer Immunotherapy: Exploring the Untapped Intracellular Proteome for Antibody-Based Novel Therapeutics

Yoram Reiter, Ph.D., Professor & Head, Laboratory of Molecular Immunology, Technion-Israel Institute of Technology

The ability to generate T Cell receptor like (TCRL) antibodies which bind HLA-peptide complexes on the surface of cells and are derived from intracellular-derived targets opens new possibilities for developing new therapeutic modalities. These antibodies can bind specifically to, and kill, the diseased cells. Thus, it transforms disease-specific targets that are expressed inside malignanT Cells into targets that can be recognized on the cell surface by soluble TCRL antibodies. This approach expands the pool of novel therapeutic antibodies beyond the limits of currently available antibodies.

3:40 End of Agonist Immunotherapy Targets

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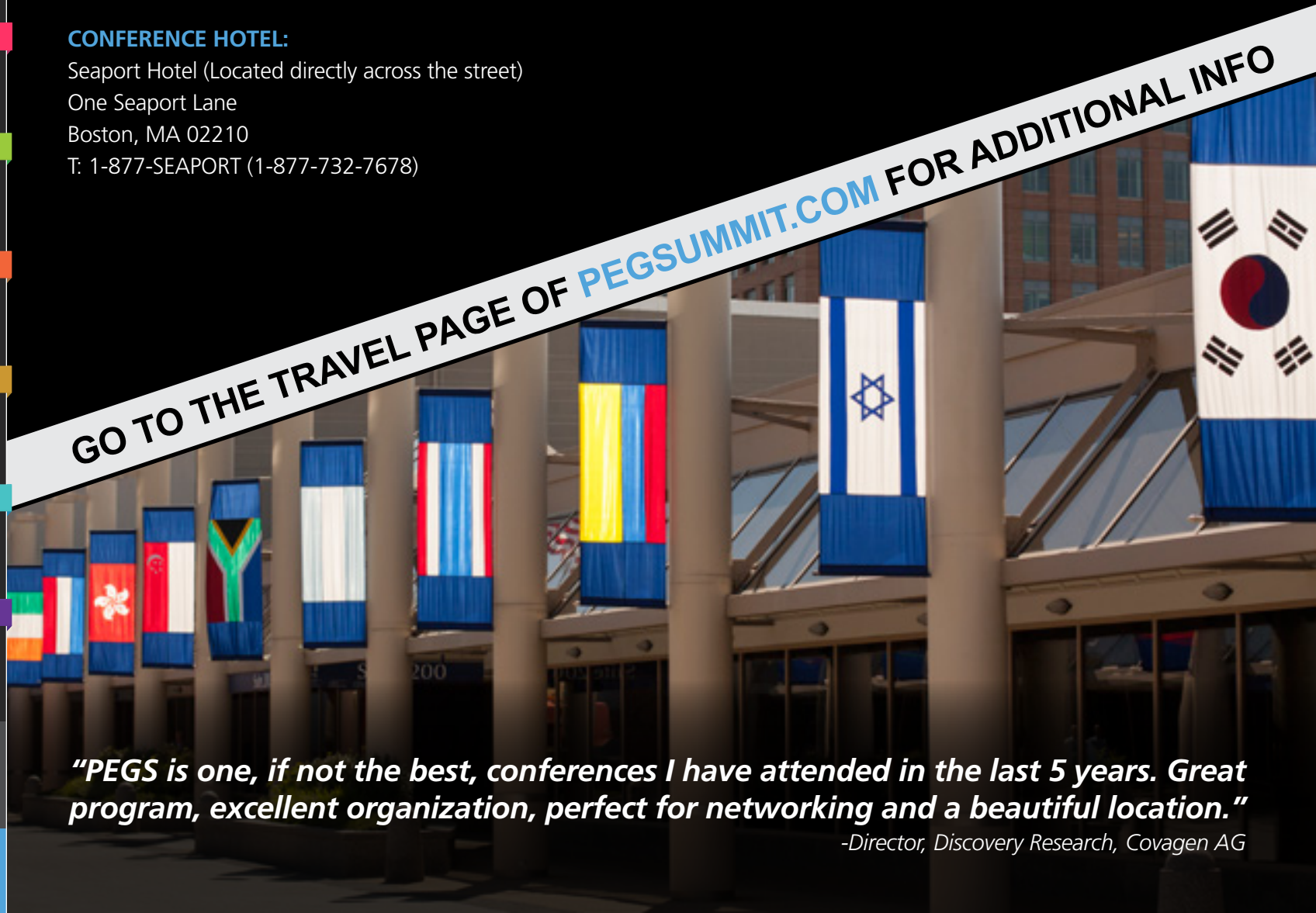

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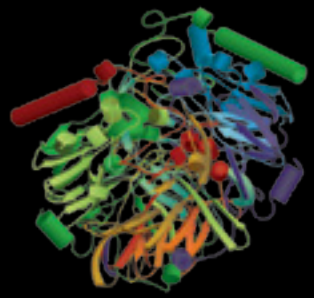

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