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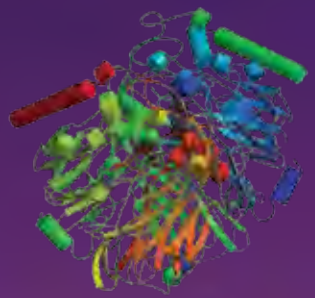

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PLENARY KEYNOTE SPEAKERS

Tillman Gerngross, Ph.D., CEO, Co-Founder, Adimab

Robert A. Weinberg, Ph.D., Founding Member, Whitehead Institute for Biomedical Research; Professor, Biology, Massachusetts Institute of Technology

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CONFERENCE-AT-A-GLANCE

STREAM	Monday-Tuesday (May 4-5)	Wednesday-Thursday (am) (May 6-7)	Thursday (pm) -Friday (May 7-8)
ENGINEERING	Phage and Yeast Display	Engineering Antibodies	Engineering Bispecific Antibodies
ONCOLOGY	Antibodies for Cancer Therapy	Advancing Bispecific Antibodies & Combination Therapy to the Clinic	ADCs: Preclinical and Clinical Updates
IMMUNOTHERAPY	Biologics for Autoimmune Diseases	Adoptive T Cell Therapy	Agonist Immunotherapy Targets
EXPRESSION	Difficult to Express Proteins	Optimizing Protein Expression	Cell Line and Cell Culture Development
ANALYTICAL	Characterization of Biotherapeutics	Biophysical Analysis of Biotherapeutics	Protein Aggregation and Stability
IMMUNOGENICITY & BIOASSAYS	Immunogenicity Prediction and Mitigation	Immunogenicity Assessment	Bioassays for Biologics
BIOCONJUGATES	Fusion Proteins	Engineering ADCs	ADCs: Preclinical and Clinical Updates
THERAPEUTICS	Fusion Proteins	Peptide Therapeutics	

PLENARY KEYNOTE SESSION

Monday, May 4 | 8:40 am

Robert A. Weinberg, Ph.D., Founding Member, Whitehead Institute for Biomedical Research; Professor, Biology, Massachusetts Institute of Technology

Dr. Robert A. Weinberg is a founding member of the Whitehead Institute for Biomedical Research and the Daniel K. Ludwig Professor for Cancer Research at the Massachusetts Institute of Technology (MIT). He is also the first Director of the Ludwig Cancer Center at MIT. He is an internationally recognized authority on the genetic basis of human cancer.

Dr. Weinberg and his colleagues isolated the first human cancer-causing gene, the ras oncogene, and the first known tumor suppressor gene, Rb, the retinoblastoma gene. The principal goal of his research program is to determine how oncogenes, their normal counterparts (proto-oncogenes), and tumor suppressor genes fit together in the complex circuitry that controls cell growth. More recently, his group has succeeded in creating the first genetically defined human cancer cells. He is particularly interested in applying this knowledge to improve the diagnosis and treatment of breast cancer.

Dr. Weinberg is the author or editor of six books and more than 420 articles. He has written a comprehensive cancer textbook entitled "The Biology of Cancer". His other books, intended for a lay audience, are "One Renegade Cell", "Racing to the Beginning of the Road: The Search for the Origin of Cancer" and "Genes and the Biology of Cancer," co-authored with Dr. Harold E. Varmus, former Director of the National Institutes of Health. He is an elected Member of the U.S. National Academy of Sciences and Fellow of the American Academy of Arts and Sciences. He is a Member of the American Philosophical Society and the Institute of Medicine.

Tillman Gerngross, Ph.D., CEO, Co-Founder, Adimab

Tillman Gerngross, Ph.D., is a Professor of Bioengineering at Dartmouth College and an active entrepreneur and innovator. He has founded several successful companies including GlycoFi, where he lead the effort to humanize the glycosylation machinery in yeast to produce fully human glycoproteins. For the past eight years Gerngross has served as a Venture Partner at SV Life Science where he advises on investment opportunities in the bio-therapeutics area. In 2007 he co-founded Adimab, which since has launched one of the most commercially successful antibody discovery technologies in the last few decades. In 2010 Adimab was awarded the Technology Pioneer award by the World Economic Forum. In 2010 Gerngross also co-founded Arsanis Inc. to develop antibody based therapies for the treatment of infectious diseases. In 2012 Gerngross co-founded Avitide to address a bottleneck in the purification of protein based therapeutics and in 2013 Gerngross co-founded Alector to develop new treatment strategies for dementia and Alzheimers related diseases. Since 2013 Gerngross has also served as the Associate Provost of Entrepreneurship and Technology Transfer at Dartmouth College.

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SHORT COURSES*

SUNDAY, MAY 3 (10:00 AM – 1:00 PM)

SC1: Phage and Yeast Display Libraries
Andrew M. Bradbury, Ph.D., MB, BS, Staff Scientist, Biosciences, Los Alamos National Laboratory
James D. Marks, M.D., Ph.D., Professor, Anesthesia & Pharmaceutical Chemistry, University of California, San Francisco; Chief, Anesthesia and Vice Chairman, Anesthesia & Perioperative Care, San Francisco General Hospital

SC2: Translational Considerations for Development of Monoclonal Antibodies Part 1: Focus on Early Discovery
Gadi Bornstein, Ph.D., Research Fellow, Centers for Therapeutic Innovation, Pfizer, Inc.
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 Klakamp, Ph.D., Vice President, Chemistry & Biochemistry, BiOptix
Mohammad Tabrizi, Ph.D., Head, Director & Senior Fellow, Merck Research Laboratories Palo Alto

SC3: Antibody Humanization via One Hot Homology Model (Hands-on Workshop)
Xavier Ambroggio, Ph.D., Director, Macromolcular Modeling, Rosetta Design Group, LLC

SUNDAY, MAY 3 (2:00 – 5:00 PM)

SC4: Translational Considerations for Development of Monoclonal Antibodies Part 2: Focus on Nonclinical Development to Clinic
Gadi Bornstein, Ph.D., Research Fellow, Centers for Therapeutic Innovation, Pfizer, Inc.
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 Klakamp, Ph.D., Vice President, Chemistry & Biochemistry, BiOptix
Mohammad Tabrizi, Ph.D., Head, Director & Senior Fellow, Merck Research Laboratories Palo Alto

SC5: Troubleshooting and Engineering of Antibody Constructs
Jonas Schaefer, Ph.D., Head, High-Throughput Laboratory, Biochemistry, University of Zurich, Switzerland
Christian Kunz, Ph.D., Associate Director, Discovery Alliances & Technologies, MorphoSys AG, Germany

SC6: *In Silico* Immunogenicity Predictions (Hands on Workshop)
Edita Karosiene, Ph.D. La Jolla Instute for Allergy & Immunology

SC7: Immunogenicity Risk Assessment and Regulatory Strategies
Shalini Gupta, Ph.D., Director, Clinical Immunology, Amgen, Inc.
Joao Pedras-Vasconcelos, Ph.D., Biotech Quality and Immunogenicity Reviewer, Office of Biotechnology Products, CDER-FDA

TUESDAY, MAY 5 (6:00 – 8:00 PM)

SC9: Tools for Analyzing Protein-Protein Interactions
Alain Ajamian, Ph.D., Director, Chemical Computing Group
Nels Thorsteinson, Scientific Services Manager, Biologics, Chemical Computing Group

SC10: Next-Generation Sequencing of Antibody Libraries: Bridging Experimental and Bioinformatic Methods
Sai Reddy, Ph.D., Assistant Professor, Biosystems Science and Engineering, ETH Zurich, Switzerland
Tarik Khan, Ph.D., Postdoctoral Researcher, Biosystems Science and Engineering, ETH Zurich, Switzerland

SC11: Overcoming the Challenges of Immunogenicity Assessment
Shalini Gupta, Ph.D., Director, Clinical Immunology, Amgen, Inc.
Jim McNally, Ph.D., Senior Principal Scientist, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

SC12: Production Challenges for Complex Biologics – ADCs, Bispecifics, & Fusion Proteins
Stefan R. Schmidt, Ph.D., MBA, Vice President, DSP, Rentschler Biotechnology
Christopher D. Thanos, Ph.D., Director, New Molecular Entities, Halozyme Therapeutics, Inc

THURSDAY, MAY 7 (5:45 – 7:45 PM)

SC13: Physicochemical and Biophysical Characterization of Antibody-Drug Conjugates
Janet Wolfe, Ph.D., President and Founder, Wolfe Laboratories, Inc.

SC14: Strategic Bioassay Design and Analysis
Liming Shi, MS, MA, Senior Research Scientist, Bioassay Development, Eli Lilly and Company

SC15: Clinical Prospects for Cancer Immunotherapy
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
Gaurav Goel, M.D., Clinical & Research Fellow, Medicine/Hematology-Oncology, University of Pittsburgh School of Medicine

*Separate Registration is Required

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17th Annual | May 4-5

Phage and Yeast Display of Antibodies

Innovating Molecular Evolution

Recommended Pre-Conference Short Courses*

SC1: Phage and Yeast Display Libraries

SC8: Designing Antibodies with Rosetta

**Separate registration required, please see page 4 for course details.*

MONDAY, MAY 4

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks

8:40 Cancer Stem Cells and Mechanisms of Malignant Progression

Robert A. Weinberg, Ph.D., Founding Member, Whitehead Institute for Biomedical Research; Professor, Biology, Massachusetts Institute of Technology

The cell-biological program termed the epithelial-mesenchymal transition (EMT) plays a role in conferring aggressive traits on carcinoma cells. In addition, it generates cancer stem cells (CSCs) that have the ability, following dissemination, to serve as founders of new metastatic colonies. The relationship between these CSCs and the SCs residing in normal tissues, and the participation of the CSCs in metastatic dissemination will be described.

9:25 Building an Antibody Discovery Company in a Crowded Field – the Adimab Story

Tillman Gerngross, Ph.D., CEO, Co-Founder, Adimab

The presentation will cover the evolution of Adimab from its founding in 2007 to becoming one of the few privately held profitable biotech companies in the last decade. Industry trends and specific strategic decisions along the way will be discussed and used to illustrate the importance of integrating finance and scientific information to build successful capital efficient biotech companies.

10:10 Coffee Break

KEYNOTE PRESENTATIONS

10:45 Chairperson's Remarks

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

» KEYNOTE PRESENTATIONS:

10 :50 Biophysical Properties of Antibody Drugs: Predicting and Engineering Developability

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

The field of antibody engineering has evolved from simply plucking binders out of libraries to engineering molecules with industrial-grade expression, stability, solubility, and specificity. For small molecules, the "Lipinski Rule of 5" provides a widely accepted rule of thumb for structural features consistent with successful drug development. Is there a similar pattern in the values for biophysical properties of developable antibody drugs? Analysis of a broad spectrum of features of a large sample of antibodies in commercial clinical development will be presented with an eye towards the emergence of such criteria for antibodies.

11:20 The Rise of Bispecific Antibodies as Therapeutics

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

Bispecific antibodies are coming of age as therapeutics with 1 bispecific antibody approved and over 20 more in clinical development. This presentation will discuss alternative technologies for the efficient production of bispecific antibodies including bispecific IgG plus potential therapeutic applications.

11:50 Novel Affinity and Targeting Tools for Life Sciences

Sponsored by Avacta Life Sciences

Paul Ko Ferrigno, Ph.D., CSO, Avacta Life Sciences

Affimers are engineered affinity proteins that are suitable for a range of applications. We will introduce Affimers in applications traditionally dominated by antibodies before focussing on two novel applications. First, inhibition of protein interactions in cells. And, secondly, development of a novel protein microarray. This has driven establishment of a HTP protein expression pipeline capable of producing > 4000 Affimers a week, allowing production of high complexity Affimer microarrays, which are being used for biomarker discovery.

12:20 pm Luncheon Presentation I: Antibody Library Display on a Mammalian Virus: Combining the Advantages of Panning and Cell Sorting in One Technology

Sponsored by Vaccinex

Ernest S. Smith, Ph.D., Senior Vice President, Research & Chief Scientific Officer, Vaccinex, Inc.

We have developed an antibody discovery platform that enables efficient 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 the 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.

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

1:20 Session Break

NOVEL LIBRARIES

1:50 Chairperson's Remarks

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

1:55 Construction and Use of Large Antibody Libraries in Mammalian Cells

UNPUBLISHED DATA

John McCafferty, Ph.D., CEO and Founder, IONTAS Ltd.

Using nuclease-directed integration of antibody genes we have constructed large libraries in mammalian cells containing a single antibody gene/cell. This allows surface display of antibodies, including IgG formatted antibodies, on the cell surface. This will permit the screening of millions of clones by flow sorting and provide information on both expression level and the extent of binding within the cell types used for antibody production.

2:25 Engineering Cow Ultra-Long CDR3 Antibodies

Vaughn Smider, M.D., Ph.D., Assistant Professor, Cell & Molecular Biology, Scripps Research Institute

Cows have ultralong CDR H3s which can have lengths of nearly 70 amino acids and form a novel b-ribbon "stalk" and disulfide-bonded "knob" structure that protrudes far from the canonical antibody paratope. We have engineered cow antibodies for binding and inhibiting an ion channel at high potency, and have humanized the scaffold for potential therapeutic use.

2:55 Phage Selection of Light-Responsive Ligands

UNPUBLISHED DATA

Christian Heinis, Ph.D., Professor, Institute of Chemical Sciences and Engineering (ISIC), Ecole Polytechnique Federale de Lausanne (EPFL)

Peptide libraries encoded by phage display can be modified in chemical reactions to extend their chemical and structural diversity. Well established is the method to cyclize peptides on phage to generate bicyclic peptide ligands. Recently, we have chemically modified phage peptide libraries with an azobenzene moiety in order to evolve light-responsive ligands. The approach and properties of the isolated photoswitchable peptides will be presented.

3:25 Towards a New Class of Bio-Therapeutics based on Synthetic Genetic Polymers

Philipp Holliger, Ph.D., MRC Laboratory of Molecular Biology, Cambridge Biomedical Campus

I'll present recent work on the discovery of novel aptamer ligands directed against a viral RNA and a protein target and composed entirely from an unnatural nucleic acid architecture that is completely resistant to degradation by serum nucleases and withstands prolonged exposure to acid without loss of structure or activity. I'll discuss the prospects of this technology to provide a new class of biotherapeutics based on an expanding range of evolvable synthetic genetic polymers.

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

CONTINUED

17th Annual | May 4-5

Phage and Yeast Display of Antibodies

Innovating Molecular Evolution

4:35 Human Antibody Phage Libraries with Elongated VH CDR3 Loops

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

Antibodies with longer (> 15 amino acids) VH CDR3 loops are naturally present in humans at low levels. Reports have suggested that they play a useful role in, for instance, viral neutralisation. Here we report on the design, construction and assessment of a novel phage display library of human antibodies with designed elongated VH CDR3 loops.

5:05 Optimizing Antibody Expression by Using the Naturally Occurring Framework Diversity in a Live Bacterial Antibody Display System

Christoph Spiess, Ph.D., Scientist, Antibody Engineering, Genentech

Rapid identification of residues that influence functional expression and stability of poorly behaved antibodies is often needed to move promising therapeutics into the clinic. To establish a method that can assess small expression differences, we developed a Bacterial Antibody Display system that overcomes previous limitations, enabling the use of full-length formats for antibody and antigen in a live cell setting. We designed a novel library of individual framework variants using natural diversity, and screened for increased expression. We successfully identify variants that dramatically improve yields and thermodynamic stability of two therapeutic antibodies in *E. coli* and mammalian cells. Our natural library design strategy could be applied during antibody humanization and library design for *in vitro* display methods to maintain expression and stability.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:50 End of Day

TUESDAY, MAY 5

8:00 am Morning Coffee

PHAGE VS.CELLS

8:25 Chairperson's Remarks

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

8:30 Amplified Signal Generation from Phage-Based Protein Sensors

Jennifer N. Cha, Ph.D., Norviel Associate Professor, Chemical and Biological Engineering, University of Colorado, Boulder

The first part of the talk will describe our use of a dually-modified version of filamentous bacteriophage that produces significantly higher colorimetric signals than what can be achieved using antibodies alone. The second half of the talk will highlight our recent efforts of using the genetic information of the M13 bacteriophage to generate highly amplifiable signals in a single solution isothermally.

9:00 Mining for Tumor Targeting Peptides: New Ligands for Molecular Imaging & Personalized Therapies

UNPUBLISHED DATA *Kathlynn C. Brown, Ph.D., Program Director, Center for Chemical Biology, SRI International*

Tumor targeting ligands are emerging components in cancer therapies. Widespread use of targeted therapies and molecular imaging depends on increasing the number of tumor-specific ligands. Biopanning of phage-displayed peptide libraries on a series of non-small cell lung cancer lines provided numerous ligands with affinities and cell-specificities that rival monoclonal antibodies. Selection and use of these ligands for diagnosis, molecular imaging, and therapies will be discussed.

9:30 Identify Macropinocytosing Antibodies by High Content Analysis of Phage Display Library Selection Output

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

The macropinocytosis pathway is capable of both rapid and bulk endocytosis, and recent studies have demonstrated that it is selectively upregulated by cancer cells. While phage antibody display libraries have been utilized to find antibodies that bind and internalize to target cells, no methods have been described to screen for antibodies that internalize specifically via macropinocytosis. We hereby describe a novel screening strategy based on High Content Analysis to identify novel human antibodies that enter tumor cells via macropinocytosis

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

INNOVATIVE SCAFFOLDS AND NEW TECHNOLOGIES

10:50 Engineering a Rationally-Identified 5 KDA Protein Scaffold for Molecular Imaging

UNPUBLISHED DATA *Benjamin J. Hackel, Ph.D., Assistant Professor, Chemical Engineering and Materials Science, University of Minnesota*

Using an algorithm to evaluate natural protein domains for their potential as scaffolds for molecular recognition, we developed a new 45 amino acid scaffold capable of picomolar affinity binding while retaining high thermal stability. Application to tumor targeting for molecular imaging will be discussed.

11:20 A New High-Throughput Platform that Enables Functional Screening of Diverse Protein Libraries

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

We developed a new screening platform that allows researchers to assay the functional activity of millions of protein variants, displayed on or secreted from bacteria or yeast. This transformative technology, which is essentially a 10 million well microtiter plate the size of a penny, has enabled a broad range of protein engineering applications, including antibody, enzyme, and biosensor engineering from bacteria or yeast libraries.

11:50 Zymogen Activator Peptides Selected by Phage Display

Robert A. Lazarus, Ph.D., Principal Scientist, Early Discovery Biochemistry, Genentech, Inc.

Serine proteases and serine protease-like domains undergo large conformational changes upon cleavage of single-chain inactive zymogens to two-chain fully active proteases. Using structure-guided peptide phage display combined with activity-based sorting, we engineered high affinity zymogen activator peptides (ZAPtides) that selectively bind to the 'activation pocket', trapping zymogens in their active protease conformations based on results from biochemical, biological and structural studies.

12:20 pm Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

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

ANTIBODIES AGAINST INFECTIOUS DISEASE

2:00 Chairperson's Remarks

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

2:05 Engineering Neutralizing Antibodies to Guide Vaccine Design

William R. Schief, Ph.D., Professor, Immunology & Microbial Science, Scripps Research Institute; Director, Vaccine Design, International AIDS Vaccine Initiative

Neutralizing antibodies isolated from natural infection can serve as guides for vaccine design and as leads for therapeutics, but there are limitations to those approaches. This talk will describe our efforts to employ computational design, yeast display directed evolution and other technologies to engineer antibodies to provide more detailed guidance for vaccine development, enabling a reductionist approach.

2:35 Synthetic Antibodies for Ebola virus Immunotherapy

Jonathan Lai, Ph.D., Associate Professor, Biochemistry, Albert Einstein College of Medicine

Synthetic antibody engineering is an emerging technology for the identification of highly specific antibodies from large molecular display libraries. Here, we will discuss our progress in application of this method to discover potential immunotherapies for Ebolavirus infections. The ebolaviruses and Marburg virus cause severe hemorrhagic fever with human case fatality rates of up to 90%. Cocktails of monoclonal antibodies have demonstrated post-exposure efficacy in non-human primate studies and therefore represent a promising therapeutic platform. We have identified novel synthetic antibodies against the glycoproteins of the Zaire (EBOV) and Sudan (SUDV) Ebolavirus species. These antibodies have neutralization potential and, in the case of SUDV, afford post-exposure protection of mice from lethal viral challenge. These antibodies have significant immunotherapeutic potential and demonstrate the applicability of synthetic antibody engineering to biomedical and public health challenges.

CONTINUED

17th Annual | May 4-5

Phage and Yeast Display of Antibodies

Innovating Molecular Evolution

Sponsored by AB SCIENCE

3:05 Combining Phage and Yeast-Display: Discovery and Optimization of Highly Developable Antibodies

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

An integrated discovery and optimization platform was established that selects for developable antibodies. Combining Phage and Yeast Display demonstrated as versatile to select dozens of IgG with good binding properties. The optimization platform AbAccel enables affinity maturation while simultaneously addressing stability, species cross-reactivity, specificity and humanness to generate highly developable antibodies from human and non-human leads. 10-100-fold affinity improvements have been achieved.

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

COMBINING IN SILICO ANALYSIS WITH DISPLAY

4:20 Chairperson's Remarks

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

4:25 Computer-Guided Design and Validation of Epitope-Specific Antibodies against Difficult Targets

UNPUBLISHED DATA

Yanay Ofran, Ph.D., Founder, Biolojic Design Ltd.

A major challenge in Ab discovery today is the development of biologically active Abs against difficult targets. We introduce a computer-guided platform that generates fully-human high affinity Abs against pre-selected epitopes on virtually any target. The platform allows efficient and rapid design of Abs against GPCRs and ion channel, species cross reactive Abs, bispecific Abs, and Abs against cryptic epitopes.

4:55 Design and Use of Hyperstable Synthetic Human Antibody Libraries

CASE STUDY UNPUBLISHED DATA

Pierre Martineau, Ph.D., Group Leader, IRCM, INSERM

The design of synthetic antibody libraries requires making choices: Choosing the right framework(s), where and how to introduce the diversity, best antibody format, optimizing expression levels. We will discuss the construction and the use of two generations of our hyperstable antibody library made in the group. We will exemplify particularly the links between design rules and the planed applications of the antibodies as intrabodies.

5:25 End of Conference

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC10: Next-Generation Sequencing of Antibody Libraries: Bridging Experimental and Bioinformatic Methods

Separate registration required, please see page 4 for course details.

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16th Annual | May 6-7

Engineering Antibodies

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

Recommended Pre-Conference Short Course*

SC10: Next-Generation Sequencing of Antibody Libraries: Bridging Experimental and Bioinformatic Methods

**Separate registration required, please see page 4 for course details.*

WEDNESDAY, MAY 6

7:00 am Registration and Morning Coffee

8:00 Chairperson's Remarks

Jonas V. Schaefer, Ph.D., Head, High-Throughput Laboratory, Department of Biochemistry, University of Zurich, Switzerland

» 8:10 KEYNOTE PRESENTATION:

NGS and Computational Motif Analysis to Identify the Antibody Epitope Specificities that Co-Associate with a Disease Phenotype

UNPUBLISHED DATA

Patrick Daugherty, Ph.D., Professor, Chemical Engineering, Biomolecular Science and Engineering, University of California, Santa Barbara

Autoimmune diseases frequently exhibit conserved antibody specificities in advance of clinical symptoms. The identification of the preferred and possibly environmental antigen targets of these antibodies has proven exceptionally challenging. Given this, we developed a method to characterize human antibody specificity repertoires in individual patients. Combining bacterial display peptide libraries with massively parallel sequencing and computational analysis we demonstrate the capability to discover disease associated antibodies and their environmental antigens.

ANTIBODY DISCOVERY FOR EMERGING TARGETS AND INDICATIONS

8:40 A Monoclonal Antibody that Targets a NaV1.7 Channel Voltage Sensor for Pain and Itch Relief

UNPUBLISHED DATA

Ru-Rong Ji, Ph.D., Professor, Anesthesiology and Neurobiology, Duke University Medical Center

Both loss-of-function and gain-of-function human mutations strongly suggest that the sodium channel subunit Nav1.7 is a key player in human pain sensation. However, a selective Nav1.7 blocker is lacking. I will present evidence showing a successful production of a Nav1.7 monoclonal antibody. This antibody not only blocks sodium currents in HEK cells, but also inhibits action potentials and synaptic transmission in native neurons and relives pain and itch in mice.

9:10 Rapid Development of Antibody Therapeutics for Infectious Disease Outbreaks

Wayne A. Marasco, M.D., Ph.D., Professor of Medicine, Harvard Medical School

Human mAbs may have a role in an outbreak setting for the prophylaxis and early treatment of emerging viral pathogens. However, obtaining timely access to B cells from infected patients for targeted selection is often challenging and can delay the discovery process. These restrictions have led us to use an ultra large non-immune human Ab-phage display library as a resource for the isolation of neutralizing mAbs to several emerging pathogens.

9:40 Antibody Therapeutics for CNS Diseases and Delivery across the Blood-Brain Barrier

CASE STUDY

George Thom, Senior Scientist, Antibody Discovery and Protein Engineering, Medimmune

The blood-brain barrier (BBB) protects and regulates the homeostasis of the brain. However, this barrier also limits the transport of systemically administered drugs, including large molecule therapeutics, to the brain. This results in sub-therapeutic concentrations of drug reaching CNS targets. Therefore, we have developed a BBB targeting system, using receptor-mediated transport, which can deliver human IgGs across the BBB and elicit a pharmacodynamics response.

10:10 Phage Display Derived Calcium-Dependent Biparatopic Antibody for Eliminating High Plasma Concentration Target Antigen

UNPUBLISHED DATA

Shinya Ishii, Research Scientist, Research Division, Chugai Pharmaceutical Co., Ltd.

Enhancing soluble antigen clearance from plasma can be a novel approach to enhance the efficacy of antibody therapeutics. In our previous report, pH dependent antigen binding antibodies can reduce antigen concentration from plasma. Here we report a novel approach to further accelerate the antigen elimination from plasma. We will discuss multimeric antibody-antigen immune complex mediated approach using phage display derived calcium-dependent biparatopic antibody.

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

NEW RESEARCH TECHNOLOGIES FOR PROTEIN ENGINEERING

11:25 Antibody Discovery Using Single-Cell Technologies

UNPUBLISHED DATA

J. Christopher Love, Ph.D., Associate Professor, Chemical Engineering, Koch Institute, Massachusetts Institute of Technology

This talk will describe the use of microscale technologies to enable the identification of new antibodies from single B cells, and the recovery of the producing cells for single-cell sequencing. Applications of a platform based on arrays of nanowells to examine both specificity and function of antibodies, including neutralizing activity at the single-cell level, will be discussed. Integration of these data with next-generation sequencing will also be presented.

11:55 Multiplex Technologies to Improve Binder Generation and Characterization

UNPUBLISHED DATA

Jonas V. Schaefer, Ph.D., Head, High-Throughput Binder Selection Laboratory, Biochemistry, University of Zurich

Screening thousands of affinity reagent candidates and analyzing their specificity remains one of the major bottlenecks in binder generation. In my presentation, I will highlight our recent developments using a mixture of adapted and novel technologies to improve these steps and thus to increase the speed and efficiency of our binder generation pipeline. In addition, innovative applications of our selected binders will be presented.

12:25 pm Use of Engineered CHO Cell Libraries for Improves Protein Secretion

Sponsored by SELEXIS

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

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

1:55 Session Break

2:10 Chairperson's Remarks

George Thom, Ph.D., Senior Scientist, Antibody Discovery and Protein Engineering, Medimmune

2:15 A Pipeline for the Discovery of immunoPCR Reagents

UNPUBLISHED DATA

Andrew Ellington, Ph.D., Research Professor of Biochemistry, University of Texas at Austin

While antibodies are remarkable reagents for diagnostics, they are surprisingly underutilized for an older but powerful technology, immunoPCR. We will lay out a pipeline for mining immune repertoires for antibodies, conversion of antibodies to single chain or other formats, attachment of single oligonucleotide tags, and use in immunoPCR. I will also address methods for the high-throughput development of antibody libraries with unique nucleic acid tags that may be suitable for NextGen immunoPCR methods.

2:45 Enhanced IgG Hexamerization Mediates Efficient C1q Docking and More Rapid and Substantial Complement-Dependent Cytotoxicity (CDC): Preclinical Proof of Concept

UNPUBLISHED DATA

Janine Schuurman, Ph.D., Vice President, Research, Genmab

We revealed that IgG antibodies form hexamers on the cell surface following antigen binding. These hexamers are critical for optimal C1q binding and CDC. IgG hexamerization occurs through specific non-covalent interactions between Fc-segments. We now identified mutations that enhanced IgG clustering after antigen binding to cells which led to an increase in C1q binding and CDC. Our data represent a promising novel approach for improving the efficacy of therapeutic antibodies.

CONTINUED

16th Annual | May 6-7

Engineering Antibodies

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

3:15 CO-PRESENTATION: Creating Focused Mutant Libraries for Protein Engineering

Sponsored by CHEMICAL COMPUTING GROUP

Alain Ajamian, Ph.D., Director, Chemical Computing Group
Michael Drummond, Ph.D., Applications Scientist, Chemical Computing Group

Protein engineering plays a pivotal role in modulating the function, activity and physical properties of biologics. However, the efficient engineering of protein sequences with desirable properties can be challenging given the excessively large sequence space. 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

COMPUTATIONAL TOOLS IN ANTIBODY RESEARCH

4:45 Computational Design of Protein Antigens

CASE STUDY UNPUBLISHED DATA

William R. Schief, Ph.D., Professor, Immunology & Microbial Science, Scripps Research Institute; Director, Vaccine Design, International AIDS Vaccine Initiative

We have engaged in a variety of immunogen design projects aiming to induce antibodies against specific structural epitopes. These bring challenges such as stabilizing epitope conformation, influencing antibody angle of approach, enhancing affinity and specificity for particular germline precursors, presenting structural epitopes in a membrane context, and engineering glycoprotein epitopes. This talk will review a few case studies, highlighting lessons learned.

5:15 Structure-Guided Approaches to Antibody Development and Optimization

Matthew Robinson, Ph.D., Assistant Professor, Fox Chase Cancer Center

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

7:00 End of Day

THURSDAY, MAY 7

8:00 am Morning Coffee

8:30 Chairperson's Remarks

Janine Schuurman, Ph.D., Vice President, Research, Genmab, Denmark

SPECIAL PRESENTATION

8:35 Antibody Therapeutics: Charting a Course in Rough Seas of Intellectual Property

CASE STUDY

Konstantin M. Linnik, Ph.D., Partner, Intellectual Property, Nutter, McClennen & Fish, LLP

Antibody IP is crowded – the number of antibodies in development far exceeds the number of targets. The recent Federal Circuit case, Abbvie v. Centocor, related to anti-IL12, and the emerging battle in BMS v. Merck, related to anti-PD-1, are just two of several recent cases shaping up the future of antibody IP. How do these developments in patent law affect commercialization opportunities for antibody therapeutics?

CHARACTERIZATION AND EXPLOITATION OF NATURAL IMMUNE RESPONSES

9:05 NGS-Based Characterization of Antibody Responses Following Vaccination

CASE STUDY UNPUBLISHED DATA

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

Next-generation sequencing (NGS) of antibody repertoires offers the promise to aid existing immunological technologies such as serum antibody titers, which capture the functional phenotype of an immune response but does not provide quantitative information on molecular diversity and distribution. We have developed a systems vaccinology framework, which will facilitate the characterization of vaccine formulations by novel means, enabling a more complete evaluation of alterations to the landscape of antibody responses.

9:35 Ligand Discovery for T Cell Receptors Using Yeast Display

UNPUBLISHED DATA

Michael Birnbaum, Ph.D., Postdoctoral Fellow, Stanford University School of Medicine

A hallmark of T cell receptors and their MHC ligands is extreme diversity, which complicates their study. Recently, we have created a method to systematically determine the peptide-MHC binding specificities of immune receptors of interest. The method combines libraries of pMHC molecules displayed on yeast, binding-based receptor selections, deep sequencing, and computational predictions. Together, these methodologies allow highly accurate predictions of what peptide-MHCs will activate a given TCR.

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

11:05 An Antibody Discovery Platform for Efficient Mining of the B Cell Repertoire

CASE STUDY

Daniel Lightwood, Ph.D., Director, Antibody Discovery, UCB-Celltech

UCB's core antibody discovery technology enables extremely efficient interrogation of the natural antibody repertoire. The platform combines high-throughput B cell culture screening and a proprietary technique called the "fluorescent foci method" to identify and isolate single, antigen-specific, IgG-secreting B cells. The talk will provide case studies of the application of the platform to antibody discovery projects, including the use of bone marrow derived plasma cells as a source of mAbs.

11:35 Realizing the Therapeutic Potential of Antibodies Derived from a Human Immune Response – Case Studies in Indications of Oncology and Infectious Disease

CASE STUDY UNPUBLISHED DATA

Paul Algate,, Ph.D., Director, Molecular Biology, Theraclone Sciences

Theraclone discovers novel targets and antibodies and develops therapeutic monoclonal antibodies by using its proprietary B cell technology platform I-STAR to mine the immune system of patients who have mounted a disease impacting immune response. Our focus is to explore the memory B cell repertoire of cancer patients who demonstrate durable responses to immunotherapy including, e. g. checkpoint inhibitors, cancer vaccines and others. Case studies will be presented that illustrate this discovery approach.

12:05 pm Computational Approaches to Antibody Design: Improvements to the Predictions of Structure, Stability and Affinity

Sponsored by SCHRÖDINGER BIOLOGICS

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

We discuss computational advances demonstrating significant promise both for improved prediction of antibody structure from sequence, and for the ability to predict the changes in stability and affinity resulting from residue mutations. The Prime approach to *de novo* loop prediction is an appreciable improvement over previous methods for CDR loop prediction, while substantive improvements to free energy calculations (FEP) allow us to calculate stability and affinity changes with high precision.

12:35 End of Conference

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC12: Production Challenges for Complex Biologics – ADCs, Bispecifics, & Fusion Proteins

Separate registration required, please see page 4 for course details.

6th Annual | May 7-8

Engineering Bispecific Antibodies

Harnessing Complexity

Recommended Pre-Conference Short Courses*

SC1: Phage and Yeast Display Libraries
SC5: Troubleshooting and Engineering of Antibody Constructs
**Separate registration required, please see page 4 for course details.*

THURSDAY, MAY 7

CREATING THE NEXT WAVE OF BISPECIFICS

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Robert Mabry, Ph.D., Director, Protein Sciences and Antibody Technology, Jounce Therapeutics

» 1:50 KEYNOTE PRESENTATION:

Teaching Antibodies New Tricks: From Simulation to Clinical Benefit of Bispecific Antibodies
Alexey A. Lugovskoy, Ph.D., Vice President, Therapeutics, Merrimack Pharmaceuticals
Bispecific antibodies offer the potential to create highly specific therapeutics, with greater potency and even have the ability to inhibit multiple targets. This makes the therapeutic design process extremely complex because specificity, affinity and valency all need to be optimized in parallel. In our design process, we employ computational network models to engineer bispecific antibodies that embrace these complexities and address issues of tumor cell heterogeneity and network redundancies. We will present examples from three of Merrimack's bispecific antibodies that are currently in development.

2:20 Discovery, Characterization & Optimization of Bispecific Antibodies by Developing Structure/Activity Relationships Using an Engineered Cell-Free Expression System
Ryan Stafford, Ph.D., Associate Director, Protein Engineering, Sutro Biopharma, Inc.
Rapid transition of bispecific antibody candidates from initial discovery to development is enabled by selection of scFvs and Fabs from highly diverse libraries expressed using cell-free synthesis. Empirical selection of antigen-binding combinations enables selection of bispecific candidates that can be rapidly expressed for high-throughput characterization. Scaling to multiple gram quantities to support pharmacology and toxicological assessments can then be achieved within days.

2:50 Structurally Motivated Approach to Design Bispecific Antibodies with Improved Developability Properties
Srinath Kasturirangan, Ph.D., Scientist I, Antibody Discovery and Protein Engineering, MedImmune Inc.
While current scFv-based BiSAbs offer a variety of geometries between antigen binding sites, some spacing options are lacking. Using a structurally-motivated approach we designed additional variants with scFvs inserted into surface-exposed loops of an IgG1 Fc. The scFvs in these BiSAb variants are N- and C-terminally constrained, potentially preventing domain exchange and aggregate formation, thereby precluding the need for scFv engineering to stabilize the molecule.

3:20 High-Throughput Design, Production, and Evaluation of Bispecific Antibodies
Maria Wendt, Ph.D., Senior Scientific Consultant, Biologics, Genedata
Work on multispecific antibodies has exploded and more sophisticated engineering approaches are now used. Concurrently, increasing numbers of bispecific platforms (e.g. tandem-scFv-Fc, DVD-Ig, diabodies, KiH) and parametric variants (e.g. linkers, V-domain orientation, Fc) must be tested in higher throughputs. We present the latest advances in our workflow platform for in-format screening, fully automated molecule design, DNA synthesis and verification, and platform-specific expression processes (e.g. post-production exchange reactions). Integrated into a comprehensive data management system for samples, assays, and analytics results, the platform enables systematic evaluation of large panels of next-generation antibodies.

3:50 Refreshment Break

APPLICATIONS IN INFECTIOUS DISEASE

4:15 Chairperson's Remarks
G. Jonah Rainey, Ph.D., Senior Scientist, ADPE, MedImmune, LLC

4:20 Back to the Future: From Serum Therapy to Infectious Disease Monoclonal Antibodies
Eszter Nagy, M.D., Ph.D., Co-Founder, President and CSO, Arsanis, Inc; Managing Director, Arsanis Biosciences GmbH
The emergence of antibiotic resistance and the inability of antibiotics to counteract bacterial toxins implicated in severe bacterial infections call for novel approaches. Monoclonal antibody therapeutics are proven to be highly efficacious in many disease areas but rarely considered as anti-infectives. The complex pathogenesis of bacterial infections is considered as a formidable barrier for anti-bacterial antibody therapeutics. Therefore, multi-specific binding characteristics and cocktails of mAbs need to be considered.

4:50 Engineering Fully Human Anti-Infective Antibodies for Dengue Therapy
Paul MacAry, Ph.D., Associate Professor, Microbiology, National University of Singapore
In my talk, I will outline how we apply advanced antibody engineering approaches to make fully-human, therapeutic antibody candidates for acute viral infection with an emphasis on Dengue virus. I will also outline the thorough characterization of these antibodies and discuss the implications that these data have for our understanding of natural immunity plus future therapy for Dengue.

5:20 End of Day

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC10: Next-Generation Sequencing of Antibody Libraries: Bridging Experimental and Bioinformatic Methods
**Separate registration required, please see page 4 for course details.*

FRIDAY, MAY 8

8:00 am Morning Coffee

DELIVERY ACROSS THE BLOOD-BRAIN BARRIER

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

8:35 Engineering Blood-Brain Barrier-Crossing Bispecific Biologics
UNPUBLISHED DATA *Graham K. Farrington, Ph.D., Director, Chemical & Molecular Therapeutics, Antibody Discovery, Biogen Corporation*
The blood-brain barrier (BBB) serves to limit access of antibodies to the brain parenchymal space. There has been much effort by various groups to engineer antibodies that use receptor mediated transcytosis to enhance serum to parenchymal antibody transport and thereby increase parenchymal antibody concentration. This presentation will focus on engineering proteins to maximize cross BBB transport. The effects of mono- and bidentate molecules on cross BBB transport, the triage of molecules across a series of *in vitro* and *in vivo* assays and considerations around Fc functionality to select for the most effective transport molecule will be discussed.

CONTINUED

6th Annual | May 7-8

Engineering Bispecific Antibodies

Harnessing Complexity

9:05 Receptor-Mediated Delivery of a Bispecific Antibody into the Primate Brain: Challenges and Safety Findings

Mark S. Dennis, Ph.D., Principal Scientist, Antibody Engineering, Genentech, Inc.

We have previously demonstrated that the transfer in receptor transcytosis pathway at the BBB can deliver a therapeutically relevant dose of a bispecific antibody into the rodent brain. The therapeutic arm of the bispecific, directed against beta-secretase (BACE1), significantly lowered brain A-beta production. This approach has now been extended to non-human primate. The challenges and safety findings encountered will be discussed.

9:35 Functional Characterization of Blood-Brain Barrier-Crossing Antibodies

UNPUBLISHED DATA *Danica B. Stanimirovic, M.D., Ph.D., Director, R&D, Translational Bioscience, Human Health Therapeutics Portfolio, National Research Council of Canada*

The talk will cover workflows for functional characterization of engineered blood-brain barrier-crossing bi-specific biologics spanning *in vitro* and *in vivo* models. With recent advances in the development of molecular Trojan horses for brain delivery of large molecules, humanized *in vitro* BBB models and *in vivo* assessment allowing better PK/PD modeling, correlative and scale-up studies, will become critical to ensure clinical translation of CNS-targeting biologics.

10:05 Coffee Break

NEW METHODS FOR GENERATING BISPECIFIC ANTIBODIES: WHAT UNIQUE PROPERTIES DO THEY HAVE FOR SOLVING PROBLEMS?

10:30 Chairperson's Remarks

Martin Steegmaier, Ph.D., MBA, Head of Discovery, Large Molecule Research, Pharma Research & Early Development, Roche Innovation Center Penzberg

10:35 FIT-Ig: A Novel Bispecific Antibody Format Combining Any Two mAbs into One Bi-Functional Ig Molecule

UNPUBLISHED DATA *Robert Kamen, Ph.D., Epimab Biotherapeutics*

FIT-Ig is a new bispecific antibody format providing Ig-like, tetravalent, bispecific molecules with a standard Fc region. The heavy and light chains of FIT-Ig's are co-expressed in mammalian cells and secreted at high levels as single protein species, which can be readily purified. FIT-Ig's retain the full biological functions of the two parental mAbs, exhibit antibody-like pharmacokinetics as well as overall protein stability and solubility. This highly versatile bispecific design shows promise for next generation biotherapeutics.

11:05 Designing and Discovering Transformative Bispecific Antibody Therapeutics

Martin Steegmaier, Ph.D., MBA, Head of Discovery, Large Molecule Research, Pharma Research & Early Development, Roche Innovation Center Penzberg

The range of therapeutic uses for bispecific antibodies is expanding beyond oncology. This presentation will show the state of the art in bispecific heterodimeric IgG antibodies, with an emphasis on recent progress using CrossMAb technology to generate bispecific antibodies by IgG domain exchange. Examples given will include new bispecific molecules for ophthalmology indications and the use of Roche's Brain Shuttle technology to treat neurological disorders.

11:35 Bispecific Fynomabs: Novel Mode-of-Action through Tailored Architecture

UNPUBLISHED DATA *Simon Brack, Ph.D., Director, Discovery Research, Covagen AG*

We will present data to illustrate how FynomAbs with tailored architecture are generated to overcome limitations encountered with other therapeutic protein formats. As an example, we will present CD3 bispecific FynomAbs with strong anti-tumor activity but with virtually no toxicity on normal tissues expressing low but detectable levels of target antigen.

12:05 pm Facile Generation of Common Light Chain Bispecific Antibodies

CASE STUDY UNPUBLISHED DATA *Eric M. Krauland, Ph.D., Senior Director, Antibody Discovery and Optimization, Adimab LLC*

A variety of bispecific constructs benefit from the use of a single variable light region pairing with *multiple distinct variable heavy regions. This talk will demonstrate the facile e*ngineering of multiple VHs that pair with a single light chain. A panel of bispecific constructs are then generated that bind to each target with high affinity and exhibit favorable biophysical properties similar to traditional therapeutic antibodies.

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

1:05 Refreshment Break

1:35 Chairperson's Remarks

Martin Steegmaier, Ph.D., MBA, Head of Discovery, Large Molecule Research, Pharma Research & Early Development, Roche Innovation Center Penzberg

1:40 Bispecific Antibodies against HIV-1 and Cancer-Related Proteins

Dimiter S. Dimitrov, Ph.D., Senior Investigator, Experimental Immunology Laboratory, National Cancer Institute, NIH

We have designed, generated and characterized novel exceptionally potent bispecific fusion proteins of engineered antibody domains targeting the HIV-1 co-receptor binding site and one domain soluble CD4. They inhibited entry of all tested (more than 100) isolates *in vitro* and exhibited high potency in an animal model of HIV-1 infection. We have also developed bispecific antibodies targeting non-overlapping domains on IGF2. They form multimolecular complexes which through avidity effects bind to CD16a expressing cells much stronger than monomolecular antibodies and could lead to irreversible removal of IGF2 from the circulation.

2:10 Optimization and Application of an Fc-Containing Bispecific Platform

John R. Desjarlais, Ph.D., Chief Scientific Officer, Xencor, Inc.

Xencor has developed a novel bispecific platform that incorporates an antibody Fc domain in order to promote antibody-like half-life and convenient dosing. I will discuss optimization of the platform and its application to several therapeutic programs.

2:40 The Nanobody Platform: Opportunity for Next-Generation Multispecific Protein Therapeutics

UNPUBLISHED DATA *Catelijne Stortelers, Ph.D., Senior Scientist and Technology Project Leader, Discovery, Ablynx*

Nanobodies are clinically validated protein therapeutics based on the smallest functional fragments of naturally-occurring heavy-chain only antibodies. Ablynx has generated functional Nanobodies across a wide range of target classes enabling straight-forward multimeric drug targeting across several formats. The Nanobody platform provides excellent formatting flexibility allowing full control and tuning over valency, avidity and specificity. In combination with the excellent manufacturing and biophysical properties, Nanobodies are the ideal targeting agents for next-generation protein therapeutics. This will be exemplified by several of our drug pipeline candidates in clinical and preclinical development.

3:10 Bispecific Antibodies Targeting Tumor Antigens and Complement Regulators Increase The Efficacy of Antibody-Based Immunotherapy

Paolo Macor, Ph.D., Life Sciences, University of Trieste

The efficacy of antibody-based immunotherapy is often due to the activation of complement-dependent cytotoxicity but very few studies tried to enhance complement-mediated functions. We now report the generation of two bispecific antibodies that were designed to recognize tumor-associated antigens and to neutralize complement regulatory proteins, over-expressed on tumor cell surface. The bispecific antibodies targeting CD20 on B-lymphoma cells prevents tumor development and results in the survival of all tumor-bearing animals.

3:40 End of Conference

5th Annual | May 4-5

Antibodies for Cancer Therapy

Challenging the Current Treatment Paradigm

Recommended Pre-Conference Short Courses*

SC2: Translational Considerations for Development of mAbs Part 1: Focus on Early Discovery

SC4: Translational Considerations for Development of mAbs Part 2: Focus on Nonclinical Development to Clinic

**Separate registration required, please see page 4 for course details.*

MONDAY, MAY 4

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks

8:40 Cancer Stem Cells and Mechanisms of Malignant Progression

Robert A. Weinberg, Ph.D., Founding Member, Whitehead Institute for Biomedical Research; Professor, Biology, Massachusetts Institute of Technology

The cell-biological program termed the epithelial-mesenchymal transition (EMT) plays a role in conferring aggressive traits on carcinoma cells. In addition, it generates cancer stem cells (CSCs) that have the ability, following dissemination, to serve as founders of new metastatic colonies. The relationship between these CSCs and the SCs residing in normal tissues, and the participation of the CSCs in metastatic dissemination will be described.

9:25 Building an Antibody Discovery Company in a Crowded Field – the Adimab Story

Tillman Gerngross, Ph.D., CEO, Co-Founder, Adimab

The presentation will cover the evolution of Adimab from its founding in 2007 to becoming one of the few privately held profitable biotech companies in the last decade. Industry trends and specific strategic decisions along the way will be discussed and used to illustrate the importance of integrating finance and scientific information to build successful capital efficient biotech companies.

10:10 Coffee Break

ANTIBODIES FOR IMMUNOTHERAPY
WHAT ARE THE CHALLENGES AND HOW DO WE OVERCOME THEM?

10:45 Chairperson's Remarks

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

» 10:50 KEYNOTE PRESENTATION:

The Power of the Immune System: Paradigm Shift in the Treatment of Cancer

Bahija Jallal, Ph.D., Executive Vice President, MedImmune

This presentation will cover the latest trends and progress in using immune therapy to treat a variety of cancers. It will also provide a general overview on opportunities presented by various combination therapies.

11:20 Human Anti-CCR4 mAb Reverses Immunosuppression and Restores Anti-Tumor Immunity

Wayne A. Marasco, M.D., Ph.D., Professor, Medicine, Harvard Medical School

Regulatory T cells (Tregs) play an important role in tumor progression; they are recruited to the tumor site where they can suppress anti-tumor immunity. CCR4 is constitutively overexpressed on Tregs and represents a potential important target for cancer immunotherapy. We have reported that humanized anti-CCR4 mAb2-3 can reverse Treg-mediated immunosuppression and restore effector T cell proliferative responses. We will present an update on these findings and on mAb2-3's unique mode of action.

11:50 Using Multiple Antibody Discovery Platforms to Overcome the Challenges in Developing Antibody Drug against Immune Check Point Targets

Jing Li, MD, Ph.D., MBA, Vice President, WuXi Biologics, WuXi AppTec

The recent approvals of Pembrolizumab and Nivolumab, the two anti PD-1 antibodies, have attracted more attention to the immune check point targets. However the general protein sequence homology of those targets between human and mouse species is low, posing significant challenge on preclinical *in vivo* testing of such antibody drug candidates. We will show how to utilize different antibody discovery platforms to overcome the challenge and to expedite the drug discovery process.

12:20 pm Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

1:20 Session Break

1:50 Chairperson's Remarks

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

1:55 Intratumoral Gene-Therapy with IL-12 to Enhance Responses to Immune "Checkpoint" Therapy

UNPUBLISHED DATA

Robert H. Pierce, M.D., Chief Scientific Officer, OncoSec Medical, Inc.

The major mode of non-response to T cell checkpoint therapies like anti-PD1/PDL1 is the lack of CD8+PD-1+ TILs. IL-12 is a pro-inflammatory cytokine, critical to linking innate and adaptive immune responses, which is required for effective CTL development. The ability of intratumoral electroporation of IL-12 to augment immunogenicity, drive a TIL response and enhance responses to immune "checkpoint" therapy will be discussed.

2:25 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.

2:55 Biomarker Development in Immune Therapies for Oncology

Jennifer H. Yearley, D.V.M., Ph.D., DACVP, Senior Principal Scientist, Profiling and Expression, Merck Research Laboratories

The success of recent, immune-based cancer therapies in generating durable responses in patients across multiple indications has been groundbreaking. Nevertheless, not all patients respond to such therapies. Development of predictive biomarkers to assess the likelihood of patient response prior to initiation of therapy is of increasing importance to patients, payers, and regulators. Issues and examples of work in this domain will be provided.

3:25 Program on PDL1

Helen Sabzevari, Ph.D., Global Head, Oncology & Immunotherapy, EMD Serono Research Institute

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

CONTINUED

5th Annual | May 4-5

Antibodies for Cancer Therapy

Challenging the Current Treatment Paradigm

» 4:35 KEYNOTE PRESENTATION:

Antibody Targeted Cancer Immunotherapy

UNPUBLISHED DATA

Louis M. Weiner, M.D., Director, Oncology, Lombardi Comprehensive Cancer Center, Georgetown University Medical Center

Antibodies induce host protective immune responses that can be exploited to treat cancer. Recent studies that elucidate mechanisms of responsive and resistance to antibody therapy will be described.

5:05 Identification and Translation of Optimal Immunotherapy Combinations

UNPUBLISHED DATA

Michael A. Curran, Ph.D., Assistant Professor, Immunology, University of Texas MD Anderson Cancer Center

Although many co-stimulatory and co-inhibitory T cell receptors have now been described, we have shown that modulation of specific combinations of these pathways based on potentially synergistic underlying biology can promote immunologic rejection of established tumors in mice and in man.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:50 End of Day

TUESDAY, MAY 5

8:00 am Morning Coffee

ADCS FOR NOVEL TARGETS

8:25 Chairperson's Remarks

Horacio G. Nastri, Ph.D., Director, Biotherapeutics, Center for Therapeutic Innovation (CTI), Pfizer, Inc.

8:30 A Novel Calicheamicin-Based ADC for Solid Tumors

UNPUBLISHED DATA

Marc I. Damelin, Ph.D., Senior Principal Scientist, Oncology Research Unit, Pfizer, Inc.

I will describe a novel ADC based on the DNA-damaging agent calicheamicin, from the identification of the target, which is enriched on cancer stem cells, to the discovery and development of the ADC.

9:00 ADCs Targeting Embryonic and Pluripotent Stem Cell Markers as Novel Therapeutics for Metastatic Cancers

Michael Schopperle, Ph.D., CEO, CureMeta

Strong research data is emerging suggesting that metastatic and aggressive cancers are cause by cancer stem cells with embryonic and pluripotent characteristics. We have developed several antibodies which are specific for pluripotent stem cells markers and have made several ADCs as novel therapeutics for metastatic cancers. Our studies show that our new ADCs are specific for and highly efficient at killing pluripotent cancer stem cells.

9:30 Novel Anti-B Cell Maturation Antigen Antibody-Drug Conjugate Selectively Induces Killing of Multiple Myeloma

Yu-Tzu Tai, Ph.D., Senior Research Scientist, Dana Farber Cancer Institute

BCMA, a specific plasma cell antigen, may represent a more selective target for monoclonal antibody-based immunotherapy for multiple myeloma treatment. Generation of therapeutic BCMA monoclonal antibody-drug conjugates could be of significance in translational medicine using next-generation therapeutic antibodies linking with novel anti-tubulin drugs.

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

ANTIBODIES TO WATCH: PHASE III CLINICAL TRIALS

10:45 Chairperson's Remarks

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

10:50 Antibodies to Watch in 2015: Focus on Oncology

Janice M. Reichert, Ph.D., Managing Director, Reichert Biotechnology Consulting LLC; Editor-in-Chief, mAbs; President, The Antibody Society

Phase 3 clinical study results for a record number of antibody therapeutics are due in 2015. This presentation will provide an overview of the late-stage commercial pipeline, with a focus on oncology treatments. The prospects for antibodies for cancer that are poised to transition to Phase 3 in 2015 will also be discussed.

11:20 MM-302, Novel Antibody-Drug Conjugated Liposomal Doxorubicin that Specifically Targets Cancer Cells Overexpressing the HER2 Receptor

Thomas Wickham, Ph.D., MM-302 Project Leader and Vice President, Research & Development, Merrimack Pharmaceuticals, Inc.

Despite improvements in treatment with newly approved HER2-targeted therapies such as pertuzumab and ado-trastuzumab emtansine (T-DM1), HER2-positive metastatic breast cancer (MBC) remains a serious and life-threatening disease. The ongoing registration-directed trial of MM-302 in HER2-positive metastatic breast cancer will be discussed as well as future development pathways utilizing a liposomal PET imaging biomarker for predicting drug delivery and patient benefit.

11:50 Clinical Validation of a Predictive Biomarker for Clinical Benefit from Patritumab in Non-Small Cell Lung Cancer

Robert A. Beckman, M.D., Professor, Oncology and Biostatistics, Bioinformatics, and Biomathematics, Lombardi Cancer Center, Georgetown University Medical 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

EMERGING TARGETS AND TECHNOLOGIES

2:00 Chairperson's Remarks

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

» 2:05 KEYNOTE PRESENTATION:

Mesothelin as a Cancer Therapy Target

Ira Pastan, M.D., NIH Distinguished Investigator and Co-Chief, Laboratory of Molecular Biology, National Cancer Institute, National Institutes of Health

Mesothelin is a cell surface protein that is an excellent target for antibody based therapies, because it is expressed on many human cancers (mesothelioma, pancreas, ovary, lung, stomach, cholangiocarcinoma and triple negative breast), but only on normal mesothelial cells, which are not essential for survival. I will review the results of immunotoxin and other antibody-based therapies and discuss new agents now being developed.

2:35 Emerging Immune Checkpoint Targets for Cancer Immunotherapy

UNPUBLISHED DATA

Xingxing Zang, Ph.D., Associate Professor, Microbiology and Immunology Medicine, Albert Einstein College of Medicine

CTLA-4 and the PD-1/PD-L1 pathway are current focuses for cancer immunotherapy. This presentation will discuss other new immune checkpoints for future human cancer immunotherapy.

CONTINUED

5th Annual | May 4-5

Antibodies for Cancer Therapy

Challenging the Current Treatment Paradigm

3:05 Cancer Systems Immunology: Harvesting the Conditions of Remission from Single Cells

Jacob Glanville, CSO, Distributed Bio Inc

Advancements in immune checkpoint inhibitors have greatly facilitated the analysis of immune-mediated tumor remission. Here we review new algorithms in deep T-cell and B-cell repertoire analysis, describe advances in single cell TCR & phenotype analysis from tumor infiltrating lymphocytes in human tumors, and present an effort to harvest vast immune libraries from the blood of cancer survivors.

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

4:25 Targeted Depletion of Metastasis-Initiating Tumor Cells with ARGX-111, a Novel, MET-Specific Human Antibody

Anna Hultberg, Ph.D., Senior Scientist, Research, Argen-X Nv

To extend the clinical impact of modulating the function of MET in cancer, we have developed a potent antagonistic anti-MET antibody, ARGX-111, that inhibits both HGF dependent and independent signaling and has enhanced Antibody-Dependent Cell-mediated Cytotoxicity (ADCC) to selectively deplete MET-expressing tumor cells. In studies of its effects on MET positive patient biopsies, we have shown targeted depletion of MET-expressing stem cells – the known precursors of metastasis arising from primary solid tumors.

4:55 Shark Heavy Chain-Only Antibodies: Basic Science and Applications

Martin Flajnik, Ph.D., Professor, Microbiology and Immunology, University of Maryland at Baltimore

Antigen-specific IgNARs have been used to study affinty maturation of the elasmobranch immune response, and are of potential use for diagnosic and therapeutic applications. The IgNAR V is ancient (over 400 million years old) and is used not only as an immunoglobulin but as a T cell receptor as well. This talk will review the data which suggests that as early in evolution as heterodimeric Igs and TCRs and found that the monomeric single-V antigen receptors existed as well.

5:25 End of Conference

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Courses*

SC9: Tools for Analyzing Protein-Protein Interactions

SC15: Clinical Prospects for Cancer Immunotherapy

**Separate registration required, please see page 4 for course details.*

ONCOLOGY STREAM

Advancing Bispecific Antibodies & Combination Therapy to the Clinic

Novel Strategies for Oncology

Recommended Pre-Conference Short Course*

SC8: Designing Antibodies with Rosetta

**Separate registration required, please see page 4 for course details.*

WEDNESDAY, MAY 6

7:00 am Registration and Morning Coffee

ACTIVATING THE IMMUNE SYSTEM

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:

Clinical Progress in the Development of Immunotherapy for Advanced Cancer: Focus on Targeted Therapy Combinations

Jason J. Luke, M.D., FACP, Assistant Professor, Medicine, Hematology/Oncology, University of Chicago

Immunotherapy is a centerpiece of melanoma treatment and early results in lung, kidney and bladder cancers suggest robust activity. Prior to immune-checkpoint blocking antibodies, standard of care in most tumors included targeted and chemotherapies. A clear imperative is to understand which treatments are rational partners for immunotherapy and which may be combined safely. Immunotherapy combinations completed and in development in multiple tumors will be discussed.

8:40 Improving Cancer Treatment through Combination Immunotherapy

UNPUBLISHED DATA

Ashok K. Gupta, M.D., Ph.D., Vice President, Clinical Oncology, MedImmune

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 (mAbs) 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.

9:10 GBR1302-BEAT® Bispecific Antibody for the Treatment of HER2 Positive Cancers

Jonathan Back, Ph.D., Head, In Vivo Pharmacology, Biologics Research, Glenmark Pharmaceuticals

Glenmark Pharmaceutical's BEAT® platform is a novel bispecific heavy chain hetero-dimerization platform based on a unique concept of bio-mimicry. We have produced a bispecific antibody, GBR1302, designed to effectively recruit cytotoxic T cells against HER2 positive breast cancer cells. GBR1302 potently re-directs T cells to HER2 positive cancer cells demonstrating strong tumor cell lysis activity and possessing an excellent safety-efficacy margin.

9:40 Activating the Immune System with Bispecific Technologies

Justin M. Scheer, Ph.D., Senior Scientist, Protein Chemistry, Genentech

Bispecific antibody technologies are validated for their ability to selectively activate immune effector cells in the presence of a tumor cell target. This presentation will describe recent advances in targeting B-cells for hematological malignancies using bispecific technologies. Further, we will explore conformational and geometrical considerations that may influence the design of more effective bispecifics.

10:10 Lightning Poster Round

Poster Presenters to be Announced

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

11:25 Controlled Fab-Arm Exchange for the Generation of Stable Bispecific IgG1

UNPUBLISHED DATA

Joost Neijssen, Ph.D., Senior Scientist, Antibody Science, Genmab B.V.

The DuoBody platform represents a novel and elegant post-production technology for the generation of stable bispecific antibodies. This platform is based on the easy-to-use method of controlled Fab-arm exchange and is used to generate bispecific antibodies that retain the biochemical characteristics and quality attributes of regular IgGs. The process has shown to be robust and scalable from bench (µg-mg) to mini bioreactor (mg-g) and manufacturing (kg) production. The presentation will highlight recent progress in terms of DuoBody discovery, proof-of-concepts, characterization and development.

11:25 PANEL DISCUSSION

Moderator:

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

Panelists:

Jason J. Luke, M.D., FACP, Assistant Professor, Medicine, Hematology/Oncology, University of Chicago

Ashok K. Gupta, M.D., Ph.D., Vice President, Clinical Oncology, MedImmune

Jonathan Back, Ph.D., Head, In Vivo Pharmacology, Biologics Research, Glenmark Pharmaceuticals

Justin M. Scheer, Ph.D., Senior Scientist, Protein Chemistry, Genentech

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

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

1:55 Session Break

2:10 Chairperson's Remarks

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

2:15 Identification and Optimization of T Cell-redirecting Asymmetric Bispecific Fully IgG Antibody

Takahiro Ishiguro, Ph.D., Researcher, Discovery Research, Chugai Pharmaceutical Co., Ltd.

T cell engaging bispecific antibody currently tested in clinical trial is BiTE molecules which are different from most popular IgG antibodies. We have generated T cell engaging antibody which is asymmetric bispecific fully IgG antibody recognizing CD3 and tumor specific antigen. Validated proprietary antibody engineering technologies were applied to enable large scale manufacturing of the bispecific antibody. Identification, optimization and pharmacology of this bispecific antibody will be presented.

2:45 Re-Envisioning "Classical" Cancer Therapy through the Lens of the Immune System to Develop Optimal Combination Immune Therapies

Israel Lowy, M.D., Ph.D., Vice-President, Clinical Sciences; Head, Translational Science and of Oncology, Regeneron Pharmaceuticals, Inc.

Regeneron is conducting new clinical trials with REGN1979, an anti-CD20xCD3 bispecific antibody, to treat CD20+ NHL or CLL, and REGN2810, an anti-PD-1 mAb for multiple tumor types. Each is being developed as an immunologic foundation for therapeutic regimens capable of eliciting durable responses. Further augmentation of anti-tumor activity by combination with classical agents will not rely on standard of care dosing, but instead seek to optimize their immune enhancing effects.

3:15 IMCgp100 ImmTAC: A Bispecific TCR Anti-CD3 Fusion for the Treatment of Malignant Melanoma

Annelise Vuidepot, Ph.D., Head, Protein Science, Immunocore Ltd.

ImmTACs are soluble bispecific-TCR-antiCD3 fusions suitable for the treatment of several tumor types. Unlike antibodies, TCRs target MHC-bound peptide antigens derived from endogenously processed proteins, providing a large pool of intracellular antigens from which to select appropriate target molecules. Our most advanced program, IMCgp100, is currently in a phase IIa clinical trial for the treatment of malignant melanoma.

CONTINUED

ONCOLOGY STREAM

Advancing Bispecific Antibodies & Combination Therapy to the Clinic

Novel Strategies for Oncology

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

THURSDAY, MAY 7

8:00 am Morning Coffee

ADC MULTISPECIFICS

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

8:35 Multifunctional ADCs Unleash the Limitations of Conventional ADCs
Zhenwei (David) Miao, Ph.D., CTO, Sorrento Therapeutics
Our multifunctional ADC platform is able to expand the scope of the conventional ADC format that is limited by one target and one class of payloads. In this presentation, we will talk about the design and conjugation process of multifunctional ADCs from the regular IgG antibodies. The newest *in vitro* and *in vivo* results of multifunctional ADCs with improved potency and safety profiles will be discussed as well in the case studies.

9:05 Bi-Specific Redirected T Cell Killing Using Site Specific Incorporation of Tumor Cell Ligands
Marco Gymnopoulos, Ph.D., Group Leader and Project Leader, Ambrx, Inc.

9:35 Dual-Targeting Triplebodies for the Elimination of Leukemic Blasts and Leukemia Stem Cells
Georg H. Fey, Ph.D., Professor Emeritus, Biology, University of Erlangen-Nuremberg
Triplebodies carry 3 single-chain Fv (scFv) binding domains in a single polypetide chain. The 2 distal modules bind 2 different targets on the same cancer cell, the central one a trigger on a cytolytic effector (NK- or T-) cell. Triplebody 33-16-123 binds CD33 and CD123 on acute mye¬loid leukemia (AML) cells, and recruits NK cells through CD16 (Fc gamma RIII). This pair allows us to target both AML blasts and AML Leukemia Stem Cells (LSCs), the presumed culprits responsible for Minimal Residual Disease (MRD) and frequently life-limiting relapses.

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

11:05 Harnessing Effector and Regulatory Pathways for Immunotherapy with DARTs
Scott Koenig, M.D., Ph.D., President & CEO & Director, Macrogenics, Inc.
Monoclonal antibodies (mAbs) are a mainstay of therapy for treating or preventing malignancies, autoimmune disorders, and infectious diseases. Engineering modifications in the primary structure of certain domains of mAbs or combining them with small molecules or toxins has enhanced their therapeutic potency in some cases and has led to recent regulatory approvals of the next-generation of biologicals. In this presentation, promising approaches to modulate physiological mechanisms with Dual Affinity Re-Targeting molecules or DARTs will be discussed with illustrations of their utility to treat leukemias and solid tumors, autoimmune diseases, or viral infections with our clinical and preclinical candidates.

11:35 Development of a Novel HER2-Targeting ADC to Address Unmet Medical Needs
John Li, Ph.D., Senior Scientist, Biosuperiors, MedImmune
Only 20-25% of the breast cancer patients are eligible for currently approved anti-HER2 therapies. Not all eligible patients respond to the therapies; moreover the vast majority of patients who initially respond to the treatment will eventually relapse. To date metastatic breast cancer remains an incurable disease. This presentation will discuss the development of a novel HER2-specific biparatopic antibody-drug conjugate and its potential in treating metastatic breast cancer patients that are refractory to or ineligible for current HER2-targeted therapies.

12:05 pm Sponsored Presentation *(Opportunity Available)*

12:35 End of Conference

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Courses*

SC12: Production Challenges for Complex Biologics – ADCs, Bispecifics & Fusion Proteins

SC15: Clinical Prospects for Cancer Immunotherapy

Separate registration required, please see page 4 for course details.

5th Annual | May 7-8

ADCs: Preclinical and Clinical Updates

Leveraging Lessons Learned in Preclinical and Early Clinical to Strategize for the Future

THURSDAY, MAY 7

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

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

» 1:50 KEYNOTE PRESENTATION:

ADCs: Building on the Past, Delivering on the Present and Optimizing for the Future
Clay B. Siegall, Ph.D., President, CEO and Chairman of the Board, Seattle Genetics, Inc.
Antibody-drug conjugates represent an increasingly important therapeutic approach for the treatment of cancer, with two ADCs currently approved by the FDA and dozens of other programs progressing through clinical trials and preclinical development. This presentation will highlight ADCETRIS® (brentuximab vedotin) and other ADCs in development. In addition, advances in ADC technology will be discussed.

TRANSLATIONAL CONSIDERATIONS

2:20 Optimizing ADC-Based Therapies in Cancer
John Lambert, Ph.D., Executive Vice President and Distinguished Research Fellow, ImmunoGen, Inc.
Our growing clinical experience with antibody-maytansinoid conjugates is leading to an enhanced understanding regarding critical attributes for their success. This presentation will highlight a recent clinical/translational R&D effort leading to a change in the treatment paradigm of an ADC.

2:50 Antibody-Drug Conjugates: Translational Considerations
CASE STUDY *Isabel Figueroa, Ph.D., Principal Scientist, DMPK and Disposition, Biologics Discovery Operations, MRL Biologics*
Antibody-Drug Conjugates (ADCs) are increasingly employed as novel targeted therapies. ADCs combine the exquisite selectivity of targeted antibodies and high potency of small molecule drugs with the aim in achieving the desired therapeutic objectives. Successful strategies for the development of the lead ADC candidates will require comparative investigations and integration of knowledge with respect to target- and modality-related considerations across species. Here, we have attempted to address some of the key translational considerations critical for early development of ADCs in an integrated fashion.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Refreshment Break

4:20 Problem-Solving Breakout Discussions

5:20 End of Day

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC13: Physicochemical and Biophysical Characterization of Antibody-Drug Conjugates
Separate registration required, please see page 4 for course details.

FRIDAY, MAY 8

8:00 am Morning Coffee

TRANSITIONING TO THE CLINIC

8:30 Chairperson's Remarks
Alan Rigby, Ph.D., Vice President, Antibody-Drug Conjugate Biology, Eli Lilly and Company

8:35 Preclinical Development of IGN786: A Homogeneous Antibody-Drug Conjugate Directed Against C16orf54 for the Treatment of Hematological Malignancies
Jason Damiano, Ph.D., Director, Discovery Research, Igenica Biotherapeutics
Using Igenica's proprietary proteomics-based target discovery technology, C16orf54 was identified as a novel cell-surface antibody target. C16orf54 is overexpressed with high prevalence in primary CLL and AML tumor specimens and has restricted expression in normal tissues. Using Igenica's proprietary SNAP technology, a homogeneous ADC directed against C16orf54 was developed. The IGN786 clinical candidate is highly efficacious in C16orf54-expressing xenograft models.

9:05 Advances in ADC Development at Pfizer Oncology
Puja Sapra, Ph.D., Senior Director, Oncology Research Unit, Pfizer, Inc.
This presentation will highlight the innovations made in Pfizer in terms of development of novel linker-payloads, conjugation chemistries and target identification for ADC development. Case studies will be used to elaborate on the multifaceted optimization required to yield a viable clinical candidate. Highlights from late stage preclinical and clinical ADCs will be discussed including candidates targeting tumor-initiating cells and Notch pathway. Finally, translational biology and combination strategies to enable clinical development of ADCs will be discussed.

9:35 Molecular Integrity of Antibody-Drug Conjugates: Applying Preclinical Learnings to the Clinic
Brooke Rock, Ph.D., Senior Scientist, Pharmacokinetics and Drug Metabolism, Amgen, Inc.
Characterizing the mechanisms of ADC instability and release of free cytotoxin are germane in the design of ADCs. Understanding the mechanism behind release of the cytotoxin is important in both the efficacy of the ADC as well as toxicity profile. Factors affecting the ADC stability will be reviewed and the subsequent impact on ADC disposition will be considered in the context of clinical monitoring.

10:05 Coffee Break

10:35 mAbXcite: A Novel Immunotherapy Platform that Initiates a Robust Anti-Cancer Immune Response by Recruiting and Activating Neutrophils
UNPUBLISHED DATA *Ifat Rubin-Bejerano, Ph.D., Co-Founder and CSO, ImmuneXcite, Inc.*
mAbXcite is a platform that exhibits a lasting immune response that is initiated by neutrophils. mAbXcite constructs of two validated antibodies, trastuzumab and cetuximab, as well as a syngeneic antibody demonstrate significantly greater efficacy in resistant tumor models. Mice that show complete regression or stasis do not grow tumors upon rechallenge, suggesting a memory response that is initiated by neutrophils.

11:05 Engineering and Clinical Development of Antibody-Targeted Nanotherapeutics
Daryl C. Drummond, Ph.D., Vice President, Discovery, Merrimack Pharmaceuticals
The use of nanotherapeutics provides a novel and highly effective platform for developing next generation antibody-drug conjugates. These novel immunotargeted nanotherapeutics are engineered with the antibody indirectly conjugated through the lipidic carrier, and with a wide range of possible payloads. An ErbB2-targeted pegylated liposomal doxorubicin is currently showing promising preclinical and early clinical activity, and is currently being evaluated in a Phase II trial in metastatic breast cancer.

CONTINUED

5th Annual | May 7-8

ADCs: Preclinical and Clinical Updates

Leveraging Lessons Learned in Preclinical and Early Clinical to Strategize for the Future

11:35 Toward Clinical Development of the Novel HER2-Targeting Antibody-Drug Conjugate SYD985

UNPUBLISHED DATA

Patrick Groothuis, Ph.D., Principal Scientist, Preclinical Pharmacology, Synthon Biopharmaceuticals B.V.

SYD985 is a novel anti-HER2 antibody-drug conjugate (ADC) based on the monoclonal antibody trastuzumab, a cathepsin B-sensitive dipeptide linker (valine-citrulline (vc) motif) and a unique prodrug seco-duocarmycin-hydroxybenzamide-azaindole. *In vitro* and *in vivo* studies exemplify that SYD985 is a promising therapeutic modality for cancer patients with moderate or even low HER2 levels in tumors.

12:05 Anti-Tumor Activity of the Antibody-Drug Conjugate (ADC), BT-062, Against CD138-Positive Solid Tumors

Kurt Schönfeld, Ph.D., Manager, Research Immunology, Global Research, Biotest AG

BT-062 is an ADC comprising a chimeric anti-CD138 antibody conjugated to the maytansinoid DM4. CD138 has long been recognized as being highly expressed on multiple myeloma (MM), and findings previously reported include BT-062's highly selective cytotoxic activity against CD138-positive MM cells. Here, we show the potential of BT-062 as a treatment for CD138-positive solid tumors.

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

1:05 Refreshment Break

CLINICAL UPDATES ON ADCs

1:35 Chairperson's Remarks

Alan Rigby, Ph.D., Vice President, Antibody-Drug Conjugate Biology, Eli Lilly and Company

1:40 pm Clinical Results with SN-38-Conjugated Antibody-Drug Conjugates in Patients with Metastatic Solid Cancers

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

2:10 Clinical Perspective of ADC Development

Michael K. Bauer, Ph.D., Senior Vice President, Clinical Development, Genmab

- Mechanism of action of HuMax-Tissue Factor-ADC
- Translation of preclinical research into the clinic
- Striking the right balance between patient safety and charting unknown clinical territory
- Beyond dose-escalation
- Patient selection - why, when and how

2:40 Clinical Development of Auristatin-Based ADCs at Seattle Genetics

Nancy Whiting, Pharm.D., BCOP, Executive Director & Head, Medical Affairs, Seattle Genetics

In addition to a broad clinical development program with Seattle Genetics' approved ADC ADCETRIS® (brentuximab vedotin), the company has multiple other auristatin-based ADC programs as well as novel pyrolobenzodiazepine dimer-based ADCs in its pipeline. This talk will highlight novel auristatin-based ADCs in development with a focus on recent clinical data.

3:10 Tumor Selective Anti-EGFR Antibody-Drug Conjugates for Multiple Indications

Ed Reilly, Ph.D., Senior Research Fellow, Project Director, Oncology Discovery, Abbvie

Most approved EGFR antibodies are unsuitable for use as antibody-drug conjugates (ADCs) because of on target toxicities. We have developed EGFR-directed ADCs that bind to a tumor selective epitope thereby limiting the effects of the toxin on normal cells while maintaining a high degree of activity on EGFR-overexpressing tumor cells. Early promising clinical data, including durable objective responses, in subjects with EGFR-positive tumors will be presented.

3:40 AGS67E, An Anti-CD37 Monomethyl Auristatin E (MMAE) Antibody-Drug Conjugate for NHL, CLL & AML

Leonard M. Reyno, M.D., Senior Vice President and Chief Medical Officer, Agensys, Inc.

Our growing clinical experience with antibody-maytansinoid conjugates is leading to an enhanced understanding regarding critical attributes for their success. This presentation will highlight some recent efforts to incorporate this translational knowledge into the future development of these compounds.

4:10 End of Conference

2nd Annual | May 4-5

Biologics for Autoimmune Diseases

Emerging Targets, Therapeutic Strategies and Product Formats for a Growing Market

Recommended Pre-Conference Short Course*

SC5: Troubleshooting and Engineering of Antibody Constructs

**Separate registration required, please see page 4 for course details.*

MONDAY, MAY 4

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks

8:40 Cancer Stem Cells and Mechanisms of Malignant Progression

Robert A. Weinberg, Ph.D., Founding Member, Whitehead Institute for Biomedical Research; Professor, Biology, Massachusetts Institute of Technology

The cell-biological program termed the epithelial-mesenchymal transition (EMT) plays a role in conferring aggressive traits on carcinoma cells. In addition, it generates cancer stem cells (CSCs) that have the ability, following dissemination, to serve as founders of new metastatic colonies. The relationship between these CSCs and the SCs residing in normal tissues, and the participation of the CSCs in metastatic dissemination will be described.

9:25 Building an Antibody Discovery Company in a Crowded Field – the Adimab Story

Tillman Gerngross, Ph.D., CEO, Co-Founder, Adimab

The presentation will cover the evolution of Adimab from its founding in 2007 to becoming one of the few privately held profitable biotech companies in the last decade. Industry trends and specific strategic decisions along the way will be discussed and used to illustrate the importance of integrating finance and scientific information to build successful capital efficient biotech companies.

10:10 Coffee Break

10:45 Chairperson's Remarks

Paul D. Rennert, Founder & Principal, SugarCone Biotech Consultants LLC

» 10:50 KEYNOTE PRESENTATION:

The Impact of the Accelerated Medicines Program (AMP) on the Development of Biologics for Autoimmune Diseases

Michael B. Brenner, M.D., Theodore B. Bayles Professor of Medicine, Harvard Medical School; Chief, Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital

A consortium of clinical, molecular and computational teams sponsored by the NIH, industry and non-profit partners are working to deconstruct inflammatory diseases (RA and SLE). To identify new biomarkers and therapeutic targets, the approach will focus on molecular analyses in single cells and subsets from involved tissues with systems level bioinformatic analyses to reveal networks, nodes and regulators of pathways in specific cell types responsible for end organ pathology.

11:20 Unmet Medical Need in Autoimmune Diseases: Opportunities for Biotherapeutics

Roland Kolbeck, Ph.D., Senior Director, Research, Respiratory, Inflammation & Autoimmunity, MedImmune

The approval of mAbs for the treatment of autoimmune diseases has provided patients with additional options to manage their illnesses. However, a large medical need remains for additional therapies. Two examples of mAbs at various stages of clinical testing, exemplifying potentially new therapeutic options, are discussed: sifalimumab, a monoclonal antibody inhibiting INF-α for the management of SLE and mavrilimumab, a antagonistic antibody directed against GMCSF-R for the management of RA.

11:50 Sponsored Presentation *(Opportunity Available)*

12:20 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

1:20 Session Break

EMERGING TARGETS (1)

1:50 Chairperson's Remarks

Paul D. Rennert, Founder & Principal, SugarCone Biotech Consultants LLC

1:55 CSF1 and IL34 Cytokines as Therapeutic Targets in Macrophage Driven Inflammation

UNPUBLISHED DATA

Ali Zarrin, Ph.D., Scientist, Immunology, Genentech

We describe how neutralizing both CSF-1 and IL-34 versus single blockade affects the outcome of a variety of inflammatory diseases such as collagen-induced arthritis compared to TNF blockade. In addition, we provide mechanistic insights on how CSF1 and/or IL34 specifically contribute to the inflammation, bone remodeling and macrophages subsets throughout the study. We propose that single and dual blockade of IL34 and CSF1 provides new therapeutic opportunities in disease indications that involve macrophages.

2:25 Cell-Penetrating Bacterial Effector Proteins as a Novel Class of Biologic Autoimmune Therapeutics

UNPUBLISHED DATA

M. Alexander Schmidt, Ph.D., Director & Head, Institute of Infectiology - ZMBE, University of Münster

Bacterial pathogens have developed intriguing molecular machines for injecting effector proteins into host cells to exploit, inhibit or modulate signaling pathways. We discovered that some effector proteins are cell-penetrating proteins (CPP) that enter cells autonomously. In a paradigm change, these effectors are seen no longer as targets but rather as tools for manipulating signaling pathways for the benefit of the host (e.g. in autoimmune disorders).

2:55 Activated Invariant NKT Cells Control Central Nervous System Autoimmunity in a Mechanism that Involves Myeloid-Derived Suppressor Cells

UNPUBLISHED DATA

Vrajesh Parekh, Ph.D., Research Assistant Professor, Pathology, Microbiology and Immunology, Vanderbilt University School of Medicine

Activation of invariant natural killer T (iNKT) cells with a canonical glycolipid antigen confers protection against central nervous system autoimmunity in mice. Mechanistically, we demonstrate that their cooperation with myeloid-derived suppressor cells (MDSCs) in this process is critical. We propose that these immunosuppressive interactions between iNKT cells and MDSCs could be exploited for the development of improved immunotherapies for multiple sclerosis and other autoimmune diseases.

3:25 Modulation of TLRs for Potential Treatment of Rare Autoimmune Diseases

CASE STUDY

Timothy M. Sullivan, Ph.D., Vice President, Development Programs and Alliance Management, Idera Pharmaceuticals, Inc.

Toll-like receptors (TLRs) play a crucial role in autoimmune diseases through the detection of damage-associated molecular patterns (DAMPs) and the induction of pro-inflammatory cytokines. Blocking the activation of TLRs may provide a novel treatment approach for rare autoimmune disease such as myositis, by preventing activation of the pro-inflammatory response, thereby cutting off the disease cycle that propagates inflammation. Clinical proof of concept of TLR antagonism has been established in psoriasis.

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

4:35 Problem-Solving Breakout Discussions

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:50 End of Day

CONTINUED

2nd Annual | May 4-5

Biologics for Autoimmune Diseases

Emerging Targets, Therapeutic Strategies and Product Formats for a Growing Market

TUESDAY, MAY 5

8:00 am Morning Coffee

EMERGING TARGETS (2)

8:25 Chairperson's Remarks
Tony Manning, Ph.D., Vice President, Research, Momenta Pharmaceuticals

8:30 Targeting Mechanisms at Sites of Complement Activation for Therapeutic Applications
V. Michael Holers, M.D., Head, Division of Rheumatology, University of Colorado, Denver
Complement therapeutics are being successfully applied to a number of human orphan diseases, and these efforts will be briefly discussed. In order to optimally broaden the use of therapeutics directed to the complement system, though, it is likely that strategies to identify novel activation mechanisms and target inhibitors to sites of complement activation must be developed. Ongoing studies addressing these strategies will be reviewed.

9:00 Dampening Pathological Immune Responses via Targeting OX40 with GBR 830, an Antagonist Monoclonal Antibody
UNPUBLISHED DATA *Jonathan Back, Ph.D., Head, In Vivo Pharmacology, Biologics Research, Glenmark Pharmaceuticals*
GBR 830 is a humanized anti-human OX40 monoclonal antibody that demonstrates antagonistic activity. Preclinical data have revealed that targeting OX40 with GBR 830 can potently suppress pathological T cell mediated immune responses such as graft versus host reactions and psoriasis. These data have supported and lead to the testing of GBR 830 in the clinic.

9:30 Selective Modulation of Fc Receptors for Improved Therapy of Orphan Autoimmune Diseases: Lessons from IVIg
UNPUBLISHED DATA *Tony Manning, Ph.D., Vice President, Research, Momenta Pharmaceuticals*
Based on extensive characterization of the mechanism of action of IVIg, both in animal models and in humans, we rationally designed a series of recombinant drug candidates with the potential to deliver improved therapeutic benefit compared to IVIg. These agents are termed Selective Immunodulators of Fc Receptors (SIF's), and they selectively modulate the activity of members of the Fcg receptor family. In cell and animal models of immune-complex-mediated autoimmunity, SIF's display up to 500-fold greater potency than IVIg.

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

INFLAMMATORY CYTOKINES

10:50 Clinical Update for Secukinumab, an anti-IL-17 Antibody for Treatment of Psoriasis
CASE STUDY *Franco Di Padova, Ph.D., Director, Novartis Institutes for Biomedical Research*
Secukinumab was effective for psoriasis in two randomized phase III clinical trials, validating interleukin-17A as a therapeutic target. In the 300 mg sc dose groups, about 90% of the patients achieved a PASI 75 response at Week 16, with sustained response rates through Week 52. Around 40% of the patients achieved complete clearance (PASI 100 response). Adverse events were comparable between dose and placebo groups.

11:20 Generation of Novel Bispecific Antibodies against TNFα and IL-17 with Different Binding Properties
CASE STUDY UNPUBLISHED DATA *Stefan Seeber, Ph.D., Principal Scientist, Large Molecule Research, Roche Pharma Research & Early Development, Roche Innovation Center Penzberg*
Combined inhibition of TNFα and IL-17 show additive effects in RA-models: suppression of mesenchymal cell activation *in vitro* and inflammation and tissue destruction in arthritis *in vivo*. We further showed that combined blockade of TNFα and IL-17 is more effective in *in vitro* and *in vivo* arthritis models. Bi-specific crossMab antibodies with 1+1 and 2+2 valences were generated and compared *in vitro* towards their potency for the treatment of arthritis.

11:50 ORgt Regulation of Inflammatory Cytokines in Autoimmunity
Daniel Cua, Ph.D., Senior Principal Scientist, Autoimmunity and Inflammation Merck Research Labs
The orphan nuclear receptor transcription factor RORgt is essential for TGF-b- and IL-6-dependent lineage commitment of Th17 cells. Using RORgt, IL-23R, and IL-17-eGFP reporter mice, we tracked the fate of multiple innate cell subsets critical for maintenance of mucosal integrity and immune surveillance. We will discuss how innate lymphoid cells influence and shape the adaptive T cell responses. The significance of these findings will be discussed in the context of targeting the IL-17 pathway for treatment of auto-inflammatory diseases.

12:20 Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

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

BIOMARKERS AND CLINICAL ENDPOINTS

2:00 Chairperson's Remarks
Jonathan Back, Ph.D., Head, In Vivo Pharmacology, Biologics, Glenmark Pharmaceuticals

2:05 Predictive Biomarker Discovery in Proof-of-Concept Clinical Studies in Inflammatory Diseases: 3 Case Studies
CASE STUDY UNPUBLISHED DATA *Joseph R. Arron, M.D., Ph.D., Associate Director & Senior Scientist, Biomarker Discovery, Genentech*
Asthma, inflammatory bowel disease, and age-related macular degeneration are heterogeneous, which is a challenge for developing new molecularly targeted therapies. We have discovered mechanism-related predictive biomarkers identifying subsets of patients with increased benefit in phase II proof-of-concept studies for targeted experimental therapies in each indication. Peripheral blood proteins, tissue biopsy gene expression, and genetic polymorphisms can each be used as predictive diagnostics for inflammatory diseases.

2:35 Endpoints and Clinical Trial Design for Biologics in Autoimmune Diseases
Matthew Linnik, Ph.D., Senior Research Fellow, Autoimmunity, Eli Lilly and Company
Clinical strategies are readily available for autoimmune diseases with multiple approved treatment options. In contrast, endpoints and trial designs are less well-defined in autoimmune diseases with few approved treatment options and uncertain regulatory requirements. This talk will critically evaluate the evolution of trial designs and endpoints in diseases like SLE, where past experience is teaching us the critical design elements and feasibility assessments needed for future trials.

3:05 Clinical Biomarker Profile of AVX-470, an Orally Administered Gut-Targeted Anti-TNF Antibody, in Ulcerative Colitis Patients
Deborah S. Hartman, Ph.D., Vice President, Research, Avaxia Biologics, Inc.
AVX-470 is a bovine-derived, polyclonal anti-TNF antibody with local activity in the gastrointestinal tract. Effects of AVX-470 on tissue and serum biomarkers of inflammatory activity were profiled in patients with active ulcerative colitis in a first-in-human, double-blind, placebo-controlled clinical trial. The findings provide evidence for AVX-470 mediated reduction of inflammatory disease activity by local TNF neutralization, and support further evaluation of AVX-470 in induction and maintenance of remission of IBD.

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

CONTINUED

2nd Annual | May 4-5

Biologics for Autoimmune Diseases

Emerging Targets, Therapeutic Strategies and Product Formats for a Growing Market

NEW BIOLOGICS PLATFORMS FOR AUTOIMMUNE DISEASES

4:25 COVA322, a Bispecific TNF/IL-17A Inhibitor: A Next-Generation Treatment for Patients with Inflammatory Diseases

CASE STUDY UNPUBLISHED DATA

Mathias Locher, Ph.D., Chief Development Officer, Covagen AG

TNF inhibitors are well established as treatment opportunities for patients with RA, PsA and other inflammatory diseases. Anti-IL17 antibodies are in development or in the approval process and have shown considerable efficacy in almost the same indications. There is strong evidence from animal models as well as from clinical observations that the dual inhibition of TNF and IL17 leads to a strong synergistic therapeutic effect. COVA322 is an antibody-Fynomer-fusion (FynomAb) currently in clinical development. First safety, tolerability and efficacy data will be presented.

4:55 ARGX-113, A Novel Fc-Based Therapeutic Approach for Antibody-Induced Pathologies

UNPUBLISHED DATA

Peter Ulrichts, Ph.D., Senior Scientist, arGEN-X BV

ARGX-113 is a proprietary antibody fragment based on arGEN-X' ABDEG™ technology. ARGX-113 works by preventing pathogenic autoantibodies from being recycled, promoting their degradation and thereby clearing them from circulation. Preclinical data in cynomolgus monkeys proved ARGX-113 to be highly effective in rapidly eliminating pathogenic antibodies, while sparing the broader immune response. The data support further clinical development of this novel therapeutic approach in autoimmune disease management.

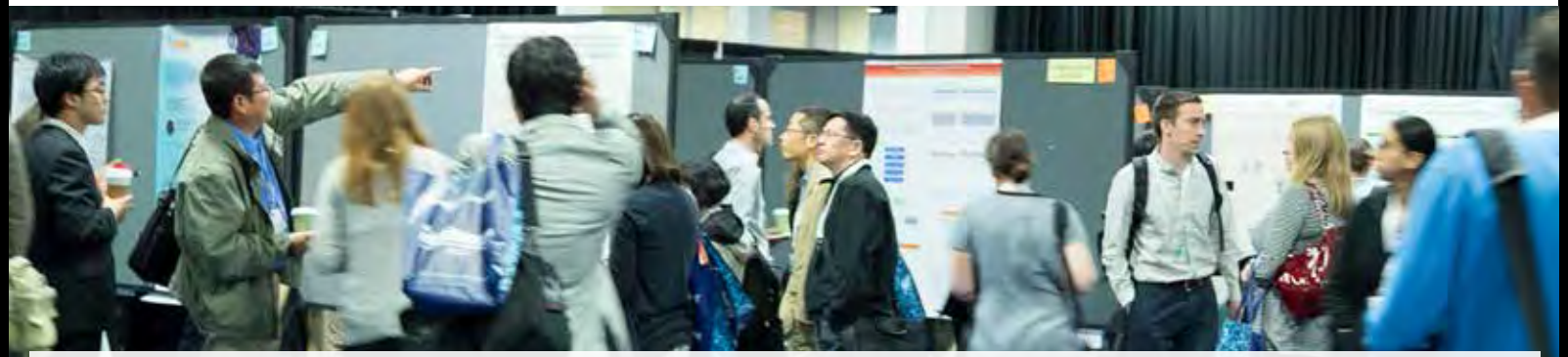
5:25 End of Conference

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC10: Next-Generation Sequencing of Antibody Libraries: Bridging Experimental and Bioinformatic Methods

**Separate registration required, please see page 4 for course details.*



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

Reasons you should present your research poster at this conference:

- Your poster will be presented to our international delegation
- Receive $50 off your registration
- Your poster abstract will be published in our conference materials
- You will automatically be entered into the poster competition
- Your research will be seen by leaders from top pharmaceutical, biotech, academic and government institutes

To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by March 27, 2015.

2nd Annual | May 6-7

Adoptive T Cell Therapy

Techniques and Strategies for Cell Therapy Discovery and Development

WEDNESDAY, MAY 6

7:00 am Registration and Morning Coffee

CAR, TCR, AND TIL

8:00 Chairperson's Remarks
Adrian Bot, M.D., Ph.D., Vice President, Translational Medicine, Kite Pharma, Inc.

8:10 CAR T Cell Therapy; The CD19 Paradigm and Beyond
Michel Sadelain, M.D., Ph.D., Director, Center for Cell Engineering, Memorial Sloan Kettering Cancer Center
T cell engineering provides a powerful means to rapidly generate large supplies of tumor-targeted T cells for cancer immunotherapy. CARs are recombinant receptors that retarget and reprogram T cell function to destroy tumor cells, sustain T cell persistence and enhance T cell function within the tumor microenvironment. The CD19 model has emerged as the paradigm for CAR therapy, paving the way for tackling other cancers.

8:40 Presentation to be Announced

9:10 Clinical Development of Tumor-Infiltrating Lymphocyte Therapy for Solid Tumors: The Myths and the Reality
Laszlo G. Radvanyi, Ph.D., Chief Scientific Officer, Lion Biotechnologies
Many of the patients treated with TILs have progressed after multiple therapies, including checkpoint blockade with anti-CTLA-4 and anti-PD-1/PD-L1, making TIL also an ultimate salvage therapy option. In this presentation, we will discuss common misconceptions about TIL therapy and current efforts that can realistically bring TIL therapy into the mainstream as an approved product for melanoma care as well as its promise as a cellular therapy for other solid cancers.

9:40 PANEL DISCUSSION: CAR vs. TCR vs. TIL
Moderator: Adrian Bot, M.D., Ph.D., Vice President, Translational Medicine, Kite Pharma, Inc.
Panelists: Laszlo G. Radvanyi, Ph.D., Chief Scientific Officer, Lion Biotechnologies
Gwendolyn K. Binder-Scholl, Ph.D., Executive Vice President & Head, Clinical and Regulatory Affairs, Adaptimmune, LLC
Michel Sadelain, M.D., Ph.D., Director, Center for Cell Engineering & Gene Transfer and Gene Expression Laboratory; Stephen and Barbara Friedman Chair, Memorial Sloan-Kettering Cancer Center

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

PREDICTING AND PREVENTING TOXICITY

11:25 Ensuring the Safety of Cellular Therapy
UNPUBLISHED DATA
Malcolm K. Brenner, MB, Ph.D., Founding Director, Professor, Center for Cell and Gene Therapy, Baylor College of Medicine
Unlike toxicities from small molecule therapeutics, cell therapies may cause harm that persists and worsens over time. Genetic modification of transplanted cells to incorporate a suicide or safety system that can be activated as required should ameliorate this problem. We developed an inducible caspase 9 molecule that can kill cells with the desired properties of speed, effectiveness and titratability and will describe its clinical application.

11:55 Clinical Manufacturing of Chimeric Antigen Receptor (CAR) T Cells Targeted to Carcinoembryonic Antigen (CEA)
Pranay Khare, Ph.D., Director, Cancer Immunotherapy and Gene Therapy cGMP Facility, Roger Williams Medical Center
We recently completed phase I Hepatic Immunotherapy for Metastases (HITM) trial with CEA targeted CAR-T cells. We tested the safety of CEA specific CAR-T cells by hepatic artery infusions (HAI) for unresectable CEA+ liver metastases (LM). We successfully produced and infused 18 doses of CEA CAR-T cells under good manufacturing practice (GMP) facility. The safety of CEA targeted CAR-T cells and further advancement in the CAR-T cell production process will be discussed.

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

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

1:55 Session Break

PREDICTING AND PREVENTING TOXICITY CONT.

2:10 Chairperson's Remarks
Michelle Krogsgaard, Ph.D., Assistant Professor, New York University Perlmutter Cancer Center, New York University School of Medicine

2:15 Mechanisms of Efficacy and Acute Toxicity after Adoptive CAR T Cell Treatment
Charles Sentman, Ph.D., Professor, Microbiology & Immunology, Geisel School of Medicine
Chimeric antigen receptors based on NK cell receptors have shown efficacy in tumor models of lymphoma, ovarian cancer, and multiple myeloma. Extensive testing has been done to evaluate the mechanisms for how these CAR T cells interact with host cells and the tumor microenvironment. At very high cell doses, an acute toxicity response similar to cytokine release syndrome has been observed. Both the CAR T cell and host contribute to this toxicity through specific mechanisms. This presentation will describe the mechanisms involved in anti-tumor efficacy and acute toxicity after adoptive therapy with these CAR T cells.

2:45 *In vivo* Functionality of Immune Cells Engineered via Vector Free Intracellular Delivery
Armon Sharei, Ph.D., CEO, SQZ Biotech
In this presentation we describe a novel method for the ex vivo delivery of materials directly to the cytoplasm of primary immune cells and the subsequent minimal effect on immunological function of the adoptively transferred cells. To demonstrate the immunological capabilities of the engineered cells, protein antigen was delivered to antigen presenting cells and the *in vivo* T cell activation was measured. In a murine model we show that compared to incubation with the antigen, intracellular delivery causes a 10-100x increase in antigen specific T-cell proliferation for a robust immune response.

3:15 Sponsored Presentation *(Opportunity Available)*

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

THURSDAY, MAY 7

8:00 am Morning Coffee

CONTINUED

2nd Annual | May 6-7

Adoptive T Cell Therapy

Techniques and Strategies for Cell Therapy Discovery and Development

TARGET DISCOVERY AND ANTIGEN SELECTION

8:30 Chairperson's Remarks
Armon Sharei, Ph.D., Founder, SQZ Biotech

8:35 Novel Cancer Targets for Adoptive Cellular Therapy
Harpreet Singh, Ph.D., CSO and Managing Director, immatics biotechnologies GmbH

9:05 Durable Clinical Responses without Persisting CAR T Cells in Circulation or Protracted On-Target Toxicity
Adrian Bot, M.D., Ph.D., Vice President, Translational Medicine, Kite Pharma, Inc.
It is believed that long lasting CAR-T cells are a prerequisite for durable clinical responses, leading to protracted on-target off-tumor toxicities in cases of targets shared by normal tissues such as CD19. Based on this paradigm, some efforts have been directed mainly at optimizing CAR technologies for CAR-T cell persistence in peripheral blood as a surrogate biomarker. However, emerging clinical evidence especially in aggressive and indolent lymphomas, challenges the paradigm that long lasting CAR T cells accompanied by on target toxicity, are needed for durable clinical responses.

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

ENHANCING EFFICACY OF IMMUNOTHERAPIES

11:05 Engineering the Immune Response to "Self" for Effective Adoptive T Cell Therapy
Michelle Krogsgaard, Ph.D., Assistant Professor, New York University Perlmutter Cancer Center, 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 includes careful engineering of tumor-specific TCRs and T cell signaling pathways to carefully balance tumor-reactivity and autoimmunity.

11:35 Targeting Tumor-Induced Immunosuppression Leads to Potent Anti-Tumor Responses by CAR T Cells
Phil Darcy, Ph.D., Group Leader, Cancer Immunotherapy, Peter MacCallum Cancer Centre
A major problem inhibiting Adoptive Immunotherapy is the immunosuppressive mechanisms utilized by tumors to suppress immune clearance and thus facilitate tumor cell survival. One of these immunosuppressive pathways which has largely been ignored is the generation of adenosine by CD73 expressed on tumor cells. We demonstrated that blocking the A2A receptor with the small molecule antagonist SCH58621 could enhance the ability of chimeric antigen receptor (CAR) transduced T cells targeting the Her-2 antigen to produce cytokines and reject established tumors *in vivo*. This study shows that specifically blocking tumor induced immunosuppression can potently enhance CAR T-cell therapy and this has significant implications for potentially improving therapeutic outcomes of CAR T cell therapy for patients.

12:05 pm Sponsored Presentation *(Opportunity Available)*

12:35 End of Conference

"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

Inaugural | May 7-8

Agonist Immunotherapy Targets

Impacting the Future of Antibody-Based Immune Therapy

THURSDAY, MAY 7

AGONISTIC RECEPTORS: CASE STUDIES

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

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

1:50 CDX-1127: An Agonist Antibody against CD27 for Safe and Specific Immune Activation

Thomas Davis, M.D., CMO, Clinical and Regulatory, Celldex Therapeutics

CDX-1127 has completed phase 1 and shown no toxicity and clear immunologic activation with objective tumor regressions. Preclinical data show marked synergy from multiple combinations with immune targeted agents. A range of combination studies are in progress.

2:20 Anti-Tumor Effects and Preclinical Development of the Human Agonistic CD40 Antibody ADC-1013

Peter Ellmark, Ph.D., Principal Scientist, Alligator Bioscience AB

Alligator Bioscience has developed a fully human agonistic CD40 antibody (IgG1), ADC-1013, optimized for tumor-directed immunotherapy by increasing potency and tumor retention. The design and anti-tumor effect in human CD40 transgenic mice using different syngeneic tumor models will be presented. Further, the toxicokinetics and pharmacodynamics markers identified in cynomolgus monkey will be discussed. To our knowledge, ADC-1013 represents the first CD40 antibody optimized for tumor directed immunotherapy of cancer, and it is currently in late preclinical development for clinical trials.

2:50 Pre-Clinical Evaluation of an Agonist Antibody Targeting ICOS

Jennifer S. Michaelson, Ph.D., Director, Research, Tumor Biology, Jounce Therapeutics

Jounce is developing an agonistic antibody to the co-stimulatory molecule ICOS. Preclinical studies demonstrate that anti-ICOS agonistic antibodies are efficacious in syngeneic tumor models, with enhanced efficacy observed in combination with PD-1 inhibition.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Refreshment Break

4:20 Problem-Solving Breakout Discussions

5:20 End of Day

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC15: Clinical Prospects for Cancer Immunotherapy

**Separate registration required, please see page 4 for course details.*

FRIDAY, MAY 8

8:00 am Morning Coffee

AGONIST RECEPTORS: CASE STUDIES (CONT.)

8:30 Chairperson's Remarks

Thomas Davis, M.D., CMO, Clinical and Regulatory, Celldex Therapeutics

8:35 Breakout Discussion Report-Outs

Moderators from the previous day's problem-solving breakout discussions will each give a 10 minute briefing on the topics covered and solutions presented as well as outline future directions for the topic discussed.

9:05 Humanized Monoclonal Antibodies as Agonists for GITR or OX40 Signaling

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

We now know that there are many checkpoints in addition to CTLA-4 and PD-1. A new category of CPMs includes agonist antibodies targeting other checkpoint proteins, such as the receptors on T-lymphocytes called GITR and OX40. They stimulate anti-tumor immune responses and may play major roles in treating patients with a broad range of cancers. They can be developed as single agents and in optimized combinations, possibly including combinations with anti-cancer vaccines and other agents.

9:35 Presentation to be Announced

10:05 Coffee Break

STRATEGIES FOR COMBINATION CANCER IMMUNOTHERAPY

10:35 OX40 Agonist Combined with PD-1 and TGFb Receptor Blockade

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

11:05 Enhanced Combination Immunotherapy Using Anti-PD-1 Antibodies and in Conjunction with Tumor Targeting Therapies

Cary Opel, Graduate Researcher, Koch Institute, Massachusetts Institute of Technology

Cancer vaccine treatment, cytokine therapy, checkpoint blockade, and tumor-targeting antibody dosing allowed various immunological mechanisms to be activated in a syngenetic mouse model. The most aggressive combinations cured large, established, subcutaneous tumors without the need for adoptive cell transfer. Extensive characterization of the immune system response to the tumor created by the combination therapy revealed a complex interplay of various cell types to mount a durable rejection of the primary tumor, as well as subsequent rechallenge. Finally, cytokine therapy was shown to be essential for the enhancement of the other targeted therapies.

11:35 Improving Cancer Immunotherapy by Combining Costimulatory Agonists

UNPUBLISHED DATA

Adam J. Adler, Ph.D., Professor, Immunology, University of Connecticut Health Center

Costimulatory receptor agonists can elicit T cell-mediated tumor immunity. Further, combining different agonists can enhance therapeutic impact. In particular, dual costimulation through CD134 plus CD137 elicits potent cytotoxic CD8+ T cells and, surprisingly, cytotoxic CD4 Th1 cells. In addition to directly targeting tumors, these cytotoxic CD4 Th1 cells appear to maximize the overall anti-tumor T cell response by providing both antigen-linked and non-linked help.

12:05 pm Combining Novel Immunotherapies for Enhanced Clinical Efficacy

Speaker to be Announced, EMD Serono

The iONC innovation platform was launched in 2013 with a pipeline specifically built to deliver novel immunotherapy combinations that can enhance treatment efficacy. We will present a strategic overview of the iONC portfolio that demonstrates the potentially enhanced anti-tumor efficacy of various combinations, including anti-cancer stem cells combined with anti-CD-20, vaccines combined with targeted cytokines, and checkpoint inhibitors combined with targeted cytokines.

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

1:05 Refreshment Break

CONTINUED

Inaugural | May 7-8

Agonist Immunotherapy Targets

Impacting the Future of Antibody-Based Immune Therapy

OVERCOMING CHALLENGES WITH THE TNF SUPER FAMILY/ IMMUNOMODULATORS

1:35 Chairperson's Remarks

Denise L. Faustman, M.D., Ph.D. Director, Immunobiology, Massachusetts General Hospital; Associate Professor, Medicine, Harvard Medical School

1:40 IL-12: A Safe Bet for Combination Immunotherapy

Chris Lawrence, Ph.D., Senior Director, Research, Neumedicines Inc.

We have safely advanced HemaMax™, a subcutaneously administered recombinant human IL-12, to Phase 1B clinical trials and have developed a new clinical paradigm for its combined use with either chemotherapy, radiotherapy or immunotherapy. We present evidence that HemaMax is expected to provide a durable anti-tumor response through immunoactivation, and anti-angiogenic effects in various cancer types, while mitigating blood toxicity, and is safe, well tolerated and non-immunogenic.

2:10 Using the TNF Superfamily Ligands (TNFSF) as Many-Trimer Multimers for Vaccines and Cancer Immunotherapy

Richard S. Kornbluth, M.D., Ph.D., President & CSO, Multimeric Biotherapeutics, Inc.

TNF superfamily ligands (TNFSF) are trimeric, Type II membrane proteins that can be released from the cell surface by proteolysis as soluble trimeric proteins. While the soluble trimer of TNF itself has some activities, most TNFSFs act by clustering their respective receptors on responding cells, which necessitates a multi-trimer arrangement for the TNFSF ligands. To mimic the natural cell surface array of TNFSFs, we have developed fusion proteins consisting of TNFSF extracellular domains joined to self-assembling multimerizing scaffolds based on Acrp30 or surfactant protein D (SPD). The resulting 2- and 4-trimer soluble TNFSFs have high activity both *in vitro* and *in vivo*. Four immunologically active, multi-trimer TNFSFs will be highlighted: CD40L, 4-1BBL, OX40L, and GITRL.

2:40 Suppression of Human Regulatory T Cells for Oncology Indications Using TNFR2 Antagonism

UNPUBLISHED DATA

Denise L. Faustman, M.D., Ph.D., Director, Immunobiology, Massachusetts General Hospital; Associate Professor, Medicine, Harvard Medical School

Human regulatory T cells (Tregs) are a subpopulation of T lymphocytes that play a critical role in regulation of the immune response. In cancer, these cells are considered the greatest barrier to successful immunotherapy because of their ability to powerfully inhibit the body's antitumor immune response when recruited or induced by growing tumors. Selective Treg inactivation using a TNFR2 antagonist antibodies has enabled the development of new therapeutic regimens for oncology indications. Major near-term market opportunities in cancer include both hematologic and non-hematologic malignancies.

3:10 PANEL DISCUSSION: EMERGING IMMUNOTHERAPY TARGETS

Moderator: Denise L. Faustman, M.D., Ph.D., Director, Immunobiology, Massachusetts General Hospital; Associate Professor, Medicine, Harvard Medical School

Panelists to be Announced

4:10 End of Conference

PEGS 2015 Student Fellowship Award Program

Present Your Poster to 1,600+ Protein Engineering Researchers

Student Fellowship Award Winners will attend the 11th Annual PEGS the essential protein engineering summit for as low as $295*

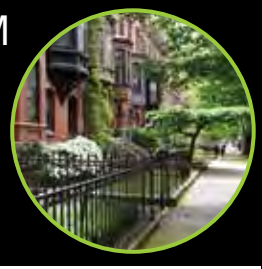
Full time graduate students and Ph.D. candidates are encouraged to apply for the PEGS conference Student Fellowship. Twenty fellowship award winners will receive a poster presentation slot and a savings of over $900 on their registration fee. Applications are due by February 20, 2015.

STUDENT FELLOWSHIP DETAILS:

- Interested students must complete the below application for the 2015 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 March 6, 2015 if they were accepted for the 2015 Student Fellowship
- Accepted 2015 Student Fellows will receive a discounted conference rate of $295*, which must be paid in full by March 27, 2015. Credit card information is requested at the time of the application and will be charged upon application approval.
- This fellowship is limited to 20 students and is for the Premium Conference Package, May 4-8, 2015. Excludes Short Courses.
- All accepted 2015 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 2015 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.

** This discounted rate cannot be combined with any other discounts for this event. Your discounted registration does not grant access to any of the short courses or preconference events. It also does not include hotel, travel or meals.*



10th Annual | May 4-5

Difficult to Express Proteins

Taming "Finicky" Proteins through Innovation

Recommended Pre-Conference Short Courses*

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

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

**Separate registration required, please see page 4 for course details.*

MONDAY, MAY 4

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks

8:40 Cancer Stem Cells and Mechanisms of Malignant Progression

Robert A. Weinberg, Ph.D., Founding Member, Whitehead Institute for Biomedical Research; Professor, Biology, Massachusetts Institute of Technology

The cell-biological program termed the epithelial-mesenchymal transition (EMT) plays a role in conferring aggressive traits on carcinoma cells. In addition, it generates cancer stem cells (CSCs) that have the ability, following dissemination, to serve as founders of new metastatic colonies. The relationship between these CSCs and the SCs residing in normal tissues, and the participation of the CSCs in metastatic dissemination will be described.

9:25 Building an Antibody Discovery Company in a Crowded Field – the Adimab Story

Tillman Gerngross, Ph.D., CEO, Co-Founder, Adimab

The presentation will cover the evolution of Adimab from its founding in 2007 to becoming one of the few privately held profitable biotech companies in the last decade. Industry trends and specific strategic decisions along the way will be discussed and used to illustrate the importance of integrating finance and scientific information to build successful capital efficient biotech companies.

10:10 Coffee Break

EMERGING STRATEGIES FOR FINICKY PROTEINS

10:45 Chairperson's Remarks

Shahram Misaghi, Ph.D., Scientist, Early Stage Cell Culture, Genentech, Inc.

» 10:50 KEYNOTE PRESENTATION:

Exploring Codon Optimization Strategies for Production of Membrane Proteins

CASE STUDY

Morton Nørholm, Ph.D., Center for Biomembrane Research, Biochemistry and Biophysics, Stockholm University

Using a library of GFP-tagged membrane proteins, we have compared different codon optimisation strategies including synonymous mutations in the 5´end, complete re-coding using multiparameter optimisation algorithms and complementing rare codon usage with additional copies of the corresponding low-concentration tRNAs.

11:20 It's Time to Regulate: Coping with Product-Induced Nongenetic Clonal Instability in CHO Cell Lines via Regulated Protein Expression

Shahram Misaghi, Ph.D., Scientist, Early Stage Cell Culture, Genentech, Inc.

In some cases, clonal instability is due to the toxicity of the therapeutic protein(s) that clones express. To circumvent such product-induced clonal instability, we have developed a vector construct that utilizes a regulated protein expression system in which the constitutive expression of the target protein(s) is prevented unless doxycycline is added to the culture. Our findings suggest that a regulated expression system could be suitable for production of difficult proteins that trigger instability.

11:50 Expression of Difficult-to-Express Proteins via Novel *in silico* Software Coupled with Multi-Modal Expression Screen

Sponsored by

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

Expression of difficult-to-express proteins is rigorous, fraught with failures and frequent delays. We have developed a multi-modal expression tool coupled with an *in silico* guidance software. We are able to express successfully multi-membrane pass proteins, immuno-modulatory proteins, rCRM197, viral vaccine candidates, etc in less than 8 weeks to generate the data.

12:05 pm New Tools for Protein Solubility

Sponsored by Lucigen® Simplifying Genomics

David Mead, Ph.D., Founder & CSO, Lucigen Corp

A panel of 24 solubility and expression enhancing fusion partners has been developed to simultaneously test multiple tags within the context of a single promoter, vector and host system. In addition, a novel yellow fluorescent protein significantly enhances solubility and expression while providing an instant visual report of the amount of soluble, active protein. This system permits rapid, simultaneous screening of multiple factors demonstrated to improve solubility and/or expression in a high-throughput format using a robust enzyme-free cloning platform. The utility of the panel was proven in expressing soluble, active LRRK2, a very challenging biomarker for Parkinson's disease.

12:20ESETEC® 2.0: New Generation of *E. Coli* Secretion Technology for the High-Yield Production of Fabs

Sponsored by WACKER

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

WACKER has profoundly refined its patented ESETEC® *E. coli* based system for the manufacture of biopharmaceuticals. Targeted genetic modifications and process optimization measures led to the development of new, extremely productive cell lines and fermentation procedures. ESETEC® 2.0 is now able to produce several grams per liter of secreted Fabs.

1:20 Session Break

TAGS, DETERGENTS, SOLUBILITY & PURIFICATION

1:50 Chairperson's Remarks

Sotirios Koutsopoulos, Ph.D., Research Scientist, Center for Biomedical Engineering, Massachusetts Institute of Technology

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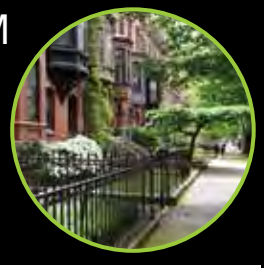

10th Annual | May 4-5

Difficult to Express Proteins

Taming "Finicky" Proteins through Innovation

1:55 Optimized *E. coli* Expression Strain LOBSTR Eliminates Common Contaminants from His-Tag Purification

Thomas U. Schwartz, Ph.D., Principal Investigator, Department of Biology, Massachusetts Institute of Technology

We engineered a new *E. coli* expression strain, LOBSTR (low background strain), which eliminates the most abundant contaminants. LOBSTR is derived from the *E. coli* BL21(DE3) strain and carries genomically modified copies of arnA and slyD, whose protein products exhibit reduced affinities to Ni and Co resins, resulting in a much higher purity of the target protein. The use of LOBSTR enables the pursuit of challenging low-expressing protein targets by reducing background contamination with no additional purification steps, materials, or costs, and thus pushes the limits of standard His-tag purifications.

2:25 Expression, Purification, and Micelle Reconstitution of Antimicrobial Piscidin 1 and Piscidin 3 for NMR Studies

CASE STUDY

Wen Chen, Ph.D., Biological Chemistry & Molecular Pharmacology, Harvard Medical School

The piscidin 1 and 3 genes were cloned into the TrpLE vector. The corresponding TrpLE-piscidin fusion partners were expressed in *E. coli* and recovered from inclusion bodies. Following steps that included Ni-NTA chromatography, cyanogen bromide cleavage of the fusion proteins, & reverse-phase HPLC, purified piscidins 1 & 3 were recovered in very good yield & characterized by NMR. High quality (15)N-(1)H HSQC spectra of piscidins 1 and 3 bound to SDS micelles were collected, demonstrating the feasibility of producing and purifying the isotopically-labeled piscidin peptides required to determine their full structures by multidimensional NMR spectroscopy.

2:55 Designer Surfactant-Like Peptides for Membrane Protein Purification and Stabilization

Sotirios Koutsopoulos, Ph.D., Research Scientist, Center for Biomedical Engineering, Massachusetts Institute of Technology

Membrane proteins are integral proteins of the cell membrane and are directly involved in the regulation of many biological functions and in drug targeting. However, our knowledge of membrane proteins is limited due to difficulties in producing sufficient quantities of soluble, functional, and stable receptors. Designer, surfactant-like peptides may be used to extract the protein from the cell membrane and stabilize the protein outside the membrane bilayer for further studies.

3:25 The Saga of T3SS Translocator Protein Purification

Wendy L. Picking, Ph.D., Associate Director, Kansas Vaccine Institute; Professor, Pharmaceutical Chemistry, University of Kansas

The type III secretion apparatus (T3SA) resembles a syringe embedded in the bacterial membranes with an external needle and needle tip complex that senses target cell contact. The translocators associate with host cell membranes. The adventures of the purification of these proteins and their vaccine formulations with various detergents will be discussed.

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

4:35 Problem-Solving Breakout Discussions

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:50 End of Day

TUESDAY, MAY 5

8:00 am Morning Coffee

MAMMALIAN EXPRESSION SOLUTIONS

8:25 Chairperson's Remarks

Michael R. Dyson, Ph.D., Group Leader, IONTAS Ltd.

8:30 Protein Expression Screening in Mammalian Suspension Cells

CASE STUDY

Michael R. Dyson, Ph.D., Group Leader, IONTAS Ltd.

Multi-domain and membrane proteins can often be expressed by a combination of domain truncation and screening in mammalian suspension cells. However proteins can exist in different conformations when in their natural environment, in complex with binding partners. Here methods are presented to identify antibodies binding to components of the EGFR and FGFR signalling pathways by traditional and phenotypic screening.

9:00 Enhanced Transient Recombinant Protein Production in CHO Cells through the Co-Transfection of the Product Gene with Bcl-xL

Matthew Zustiak, Ph.D., Researcher, Gallus Biopharmaceuticals

We examine an alternative method of using the benefits of anti-apoptotic gene expression to enhance the transient expression of biotherapeutics, namely, through the co-transfection of Bcl-xL and the product-coding gene. Cells co-transfected with Bcl-xL showed reduced levels of apoptosis, increased specific productivity, and an overall increase in product yield of approximately 100%. This work provides an alternative method for increasing yields of therapeutic proteins in TGE applications without generating a stable cell line and subsequent screening, which are both time- and resource-consuming.

9:30 TAPBOOST Technology: Enhanced Production for Hard-to-Produce Proteins

Akinori Hishiya, Ph.D., Director, Biology, Boston Strategics Corporation

Therapeutic recombinant proteins produced in mammalian expression systems might have folding issues and are confined in the endoplasmic reticulum by cellular quality control system, resulting in poor expression and yields. We have developed a novel technology called TAPBOOST technology, which controls protein folding and cellular quality control systems specifically for a targeted protein. A proprietary protein (TAPBOOSTER) is expressed together with a therapeutic protein (targeted protein), followed by the interaction between TAPBOOOSTER and the targeted protein, resulting in enhanced production of the targeted protein.

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

SOLVING EXPRESSION PROBLEMS FOR STRUCTURAL STUDIES

10:50 Overproduction and Biophysical Characterization of Human HSP70 Proteins

Rebba Boswell-Casteel, Ph.D., Biochemistry and Molecular Biology, University of Oklahoma Health Sciences Center

Functional characterization of human HSP70s has been stymied by difficulties in obtaining large quantities of purified protein. Within this work, we present optimized protocols for the heterologous overexpression and purification of either the nucleotide binding domain (NBD) or the nucleotide and substrate binding domains of human HSPA9, HSPA8, and HSPA5in either *E. coli* or S. cerevisiae. This work provides the basis for future biochemical studies of human HSP70 protein function and structure.

11:20 Overcoming Barriers to Expression, Purification and Sample Preparation for Structural Characterization of GPCRs using NMR Spectroscopy

Aditya Pandey, Ph.D., Biochemistry & Molecular Biology, Dalhousie University

G-protein coupled receptors are inherently dynamic membrane proteins that have remained elusive to structural characterization using NMR spectroscopy. Due to the challenges involved in production of large quantities of isotope enriched GPCRs, we have employed a "divide and conquer" approach. Here, we discuss various strategies that we have used to express, purify and biophysically characterize large fragments of the apelin receptor.

11:50 Recombinant Expression, Purification, and Biophysical Characterization of the Transmembrane and Membrane Proximal Domains of HIV-1 gp41

Tsafrir Mor, Ph.D., Associate Professor, The Biodesign Institute, Infectious Diseases and Vaccinology, Arizona State University

While high-resolution X-ray structures of some segments of the MPR were solved in the past, they represent the post-fusion forms. Structural information on the TM domain of gp41 is scant and at low resolution. Here we describe the design, expression and purification of a protein construct that includes MPR and the transmembrane domain of gp41 (MPR-TMTEV-6His), which reacts with the broadly neutralizing antibodies 2F5 and 4E10 and thereby may represent an immunologically relevant conformation mimicking a prehairpin intermediate of gp41.

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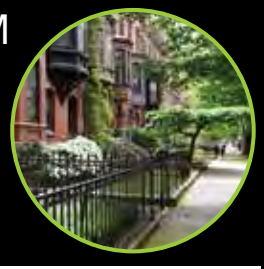

10th Annual | May 4-5

Difficult to Express Proteins

Taming "Finicky" Proteins through Innovation

12:20 pm Luncheon Presentation: Overcoming the Challenges Associated with the Production of Bone Morphogenetic Proteins in CHO Cells

Sponsored by ARAGEN

Christopher T. Brown, Program Manager – Early Stage Protein Manufacturing, Research & Development, Bioventus LLC

BMP production for preclinical/clinical studies offers unique challenges not present with more conventional biologics. BMPs, expressed as large precursor proteins, undergo proteolytic processing by furin-like proteases to remove the N-terminal propeptide which releases the mature cytokine. CHO cells produce low amounts of endogenous furin which leads to N-terminal heterogeneity and the presence of unprocessed/partially processed forms that must be removed during purification. This presentation will focus on process development and implementation to overcome BMP production challenges in mammalian systems.

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

CONQUERING OVEREXPRESSION

2:00 Chairperson's Remarks

2:05 Development of an Improved Mammalian Overexpression Method for Human CD62L

Peter D. Sun, Ph.D., Structural Immunology Section, Lab of Immunogenetics, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Like other stable mammalian over-expression systems, a major shortcoming of the GS-based expression system is its lengthy turn-around time, typically taking 4-6 months to produce. To shorten the time, we replaced the multi-round target gene amplifications with single-round *in situ* amplifications, thereby shortening the cell line construction to 2 months. In addition, we developed a MSX resistance assay as an alternative to utilizing ELISA for evaluating the expression level of stable recombinant CHO cell lines.

2:35 Engineering Strategies for Improving Yeast Production of Brain-derived Neurotrophic Factor

Eric V. Shusta, Ph.D., Professor, Department of Chemical and Biological Engineering, University of Wisconsin, Madison

Brain-derived neurotrophic factor (BDNF) is one of a family of difficult-to-produce cysteine knot proteins. Here we describe protein and cellular engineering approaches to optimize the display and secretion of BDNF from yeast. Engineered proteins exhibit better per molecule folding as demonstrated by improved receptor binding in addition to elevated display and secretion levels.

3:05 Discovery of MAbs Against Difficult GPCRs, Ion Channels, and Transporters

Sponsored by integral

Benjamin Doranz, Ph.D., MBA, President & CEO, Integral Molecular

To enable the isolation, characterization, and engineering of MAbs against challenging membrane protein targets, Integral Molecular has developed the MPS Discovery Engine™ platform, encompassing Lipoparticles for concentrating native membrane proteins and Shotgun Mutagenesis for membrane protein engineering and epitope mapping. Using the MPS platform, we have generated inhibitory MAbs against the ion channel P2X3 for treating neuropathic and inflammatory pain, and have ongoing discovery programs against additional GPCR, ion channel, and transporter targets.

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

LOOKING TOWARDS A THERAPEUTIC

4:25 Overexpression of Pseudomonas aeruginosa LpxC with Its Inhibitors in an acrB-Deficient Escherichia coli Strain

Ning Gao, Associate Principal Scientist, Discovery Sciences Innovative Medicine Unit, AstraZeneca R&D

LpxCprotein when overexpressed in *Escherichia coli* has limited the availability of high quality protein for X-ray crystallography. Expression of LpxCin the presence of an inhibitor dramatically increased protein solubility, shortened crystallization time and led to a high-resolution crystal structure of LpxC bound to the inhibitor. However, this approach required large amounts of compound, restricting its use. To reduce the amount of compound needed, an overexpression strain of *E. coli* was created lacking acrB, a critical component of the major efflux pump.

4:55 Rapid Production of High-Quality, Functional Membrane Proteins using ACM technology

Sourabh Banerjee, Ph.D., Director of Technology, ACM Biolabs, Singapore

Artificial Cell Membrane (ACM) technology dramatically simplifies the production of different classes of challenging membrane proteins using a combination of cell-free synthesis and specialized block copolymer membranes. We discuss how ACMs allow rapid access to 'hard targets', and demonstrate flexibility and scalability for downstream assay development, finding broad applicability for the discovery of new therapeutics.

5:25 End of Conference

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC12: Production Challenges for Complex Biologics – ADCs, Bispecifics, & Fusion Proteins

Separate registration required, please see page 4 for course details.

5th Annual | May 6-7

Optimizing Protein Expression

Enhancing Expression Systems

Recommended Pre-Conference Short Course*

SC12: Production Challenges for Complex Biologics: ADCs, Bispecifics and Fusion Proteins

**Separate registration required, please see page 4 for course details.*

WEDNESDAY, MAY 6

7:00 am Registration and Morning Coffee

OPTIMIZING PROCESSES FOR GREATER PRODUCTIVITY & CHO EXPRESSION

8:00 Chairperson's Remarks

Christopher W. Kemp, Ph.D., President, Kempbio, Inc.

» 8:10 KEYNOTE PRESENTATION:

Innovations in Protein Expression Technologies to Deliver New Biotherapeutics

CASE STUDY *Pranhitha Reddy, Ph.D., Director, BioProcess & Analytical Sciences, Seattle Genetics, Inc.*

Advances in protein expression and related technologies have enabled the establishment of expression platforms and flexible manufacturing to help deliver high yield, rapid development timelines and desired product quality profile. In addition, protein and process engineering efforts have led to development of new bio therapeutic modalities, including high potency molecules. Examples of different antibody therapeutics, their development challenges, and innovations to meet these challenges will be reviewed. The evolving use of new information on genome structure and cell metabolism for expression optimization will be discussed.

8:40 FEATURED PRESENTATION:

Enhanced Protein Production in Mammalian and Insect Cells by Precise Genome Editing with the Cas9/CRISPR Technology

Lovisa Holmberg-Schiavone, Ph.D., Team Leader, Reagents and Assay Development, AstraZeneca R&D

We will describe recent developments for transient gene expression (TGE) and precise genome editing (PGE) in mammalian and insect cells. We predict that PGE with the novel Cas9/CRISPR technology will change the way how recombinant proteins will be produced in the future.

9:10 Using the Endoplasmic Reticulum as a Physiological Test Tube: Predicting Poor Solution Behaviors of mAb Clones during Transient Expression *in cellulo*

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

Have you picked a lead candidate mAb clone that looked very promising until tested in formulation? How can we avoid selecting physicochemically unfavorable mAb clones unknowingly? In this talk, I will discuss the predictive values of overexpression-induced cellular phenotypes in assessing the solution behavior properties of individual mAb clones. Our approach paves the way for a preemptive elimination of unfavorable mAb clones from the lead panel from the very beginning.

9:40 FEATURED PRESENTATION:

MicroRNAs: Targets for Improving CHO Cells as Protein Factories

Colin Clarke, Ph.D., Bioinformatics Research Fellow, National Institute for Cellular Biotechnology (NICB), Dublin City University

MicroRNAs (miRNAs) have emerged as an exciting means of engineering the expression of multiple proteins or even entire pathways to build better CHO cells. A number of studies have reported the association of miRNAs with desirable industrial phenotypes and demonstrated how the manipulation of miRNA expression levels can improve CHO cell culture performance. This presentation will give an overview of the current state-of-the-art in the field.

10:10 GeneOptimizer Program-Assisted cDNA Reengineering Enhances sRAGE Autologous Expression in Chinese Hamster Ovary Cells

CASE STUDY *Li Lin, Ph.D., Senior Research Fellow, Laboratory of Cardiovascular Science, National Institute on Aging, National Institutes of Health (NIH)*

Soluble receptor for advanced glycation end products (sRAGE) functions as a decoy to counter-react RAGE signaling-resultant pathological conditions, and has high therapeutic potential. Our studies showed that recombinant human sRAGE expressed in CHO cells is modified by specific N-glycosylation, and exhibits higher bioactivity than that expressed in other host systems. We reengineered sRAGE cDNA using the GeneOptimizer program and the resultant cDNA augmented sRAGE expression over 2 fold and maintained bioactivity.

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

BACTERIA/*ESCHERICHIA COLI*

11:25 Hijacking *E. coli*'s Heat-Shock Response Enhances Recombinant Protein Production

Xin Zhang, Ph.D., Burroughs Wellcome–CASI Fellow, Scripps Research Institute

The production of high-yield and high-quality recombinant proteins from *Escherichia coli* is highly desirable for both academic and industrial settings. In this talk, I will describe a generally applicable method for this purpose, using a transcriptionally reprogrammed *E. coli* by overexpressing a heat-shock response transcription factor. Similar strategies of hijacking stress-responsive pathways should be useful to enhance cellular protein folding capacity and improve recombinant protein production in other cell types.

11:55 Using Chromosomal Engineering for Enhanced Protein Expression in Bacteria

UNPUBLISHED DATA *Joseph D. Kittle, Jr., Ph.D., Assistant Professor, Chemistry and Biochemistry, Ohio University; Founder, Molecular Technologies Laboratories LLC*

Traditional protein expression systems rely on the use of plasmids for production of proteins from cloned genes. We present data showing the advantages of using synthetic DNA to rapidly engineer bacterial chromosomes to produce commercially important levels of high value proteins. The improved stability and lack of antibiotics in the fermentation media provide for impressive overall improvements in gene-to-commercial scale production.

12:25 pm Optimizing CHO Expression for Rapid Identification of Relevant Drug Candidates with Flow Electroporation

Sponsored by CARBION

James Brady, Ph.D., MBA, Director, Technical Applications, MaxCyte, Inc

When preclinical research is done in a cell line other than the manufacturing cell line, promising candidates are overlooked while irrelevant candidates are put forward. Flow electroporation, a universal means of fully scalable TGE capable of producing multiple grams of antibodies, bispecifics, and non-antibody like recombinant proteins, enables R&D with CHO cells for rapid clinical-grade biotherapeutics. Using this technology and optimizing cell culture and transfection variables to further increase the amount of antibody produced will be discussed.

12:55 Luncheon Presentation I: Novel Fungal Ultra-High Performance Protein Production Platform for Therapeutic Proteins and Its Application to Site Specific Antibody Drug Conjugationor Enjoy Lunch on Your Own

Juhani Saarinen, CEO, Carbion Ltd

Novel protein production platform for therapeutic proteins is presented. Current strains are optimized for antibodies, antibody fragments and certain non-glycoproteins. The host yields from several grams/liter to double digit titers in short process times in simple microbial bioreactors. All production strains are glycoengineered and are devoid of fungal type O-glycosylation. N-glycosylation engineered strains offer humanized N-glycans as well as novel opportunities in efficient site specific coupling of payloads to antibodies. An ADC candidate is presented.

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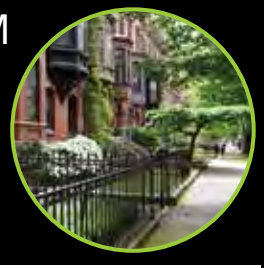

5th Annual | May 6-7

Optimizing Protein Expression

Enhancing Expression Systems

1:25 Luncheon Presentation II: Superior Protein Yields in CHO and HEK-293 Cells Using a Novel, Highly Efficient Transfection Reagent – FectoPRO

Sponsored by Polyplus transfection

Jelena Vjetrovic, Ph.D., Bioproduction Technical Support Specialist, Polyplus-transfection

Low transfection efficiency of CHO cells is a major bottleneck hampering Transient Gene Expression (TGE). Polyplus-transfection®, with its 10+ year expertise in transfection, has developed a novel technologically advanced transfection solution specifically designed for bioproduction. FectoPRO™ outperforms currently available PEI-based and lipid-based transfection reagents. We will present data and protocols leading to unmatched protein and antibody yields in CHO and HEK-293 cells.

1:55 Session Break

BACULOVIRUS AND ALGAE

2:10 Chairperson's Remarks

Sam Ellis, Vice President, Thomson Instrument Company

2:15 Baculovirus Expression of HSV-2 Vaccine Antigens: Challenges and Solutions

UNPUBLISHED DATA

Rajiv Gangurde, Ph.D., Associate Director, Protein Production, Genocea Biosciences, Inc.

GEN-003 is a therapeutic HSV-2 subunit vaccine containing two antigens expressed independently in insect cells. The antigens were expressed as Histidine-tagged proteins as part of a successful Phase 1 campaign. For Phase 2 and beyond, we eliminated Histidine-tags and revised the expression parameters to significantly improve protein titer and control antigen-specific proteolysis. The approaches employed and resulting outcomes will be discussed.

2:45 Production of Antibody Toxin Fusions as a Next-Generation Targeted Therapy Using Algae Chloroplast

Miller Tran, Ph.D., Senior Scientist, Lead Discovery, Verdant Therapeutics, Inc.

Over the last decades, targeted antibody therapies including antibody-drug conjugates and recombinant immuntoxins have garnered increasing attention. However, their production has become increasingly complicated and expensive. To overcome the challenges associated with the production of targeted therapies, eukaryotic algae are being used to produce recombinant antibody toxin fusions that overcome the shortcomings of established technologies. With media cost in the cents per liter, the potential of algae are now being realized.

3:15 Cell Line Development Tool Box for Expression: *E.coli*, HEK293, CHO, Insect Cells

Sponsored by THOMSON Solutions at Work INSTRUMENT COMPANY

Sam Ellis, Vice President, Thomson Instrument Company

The conditions for *E.coli*, HEK293, CHO and Insect Cell lines need to be maintained at small scale and within fermentation. Data will be presented on techniques and technology that allow for mimicking large scale fermentation with non-controlled devices from 1mL-3L. All of these techniques are proven technologies for protein production, structural biology, and can lead to successful transfer from different protein groups.

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

THURSDAY, MAY 7

8:00 am Morning Coffee

COMPARE/CONTRAST EXPRESSION SYSTEMS

8:30 Chairperson's Remarks

Lorenz Mayr, Ph.D., Vice President, Reagents & Assay Development, AstraZeneca

8:35 *E. coli* and CHO Protein Expression Technology at Genentech

CASE STUDY

Dorothea E. Reilly, Ph.D., Associate Director, Early Stage Cell Culture, Genentech, Inc. – A Member of the Roche Group

Genentech uses both CHO and *E. coli* to manufacture therapeutic proteins. This talk will provide an overview of cell culture process development at Genentech and some of our more recent work to make complex proteins in *E. coli*.

9:05 Differences in Clearance of Recombinant Proteins Expressed in HEK and CHO Cells

Mengmeng Wang, Ph.D., Principal Scientist, PDM, Pfizer, Inc.

This investigation used *in vitro* cell-based uptake assay and *in vivo* PK studies to study the relationship between glycosylation and clearance of two monomeric versions of antibody that was produced either transiently by HEK293 cells or stably by CHO cells. We demonstrated that higher clearance of the HEK derived protein was likely due to its higher mannose receptor mediated clearance and co-administration of mannose receptor inhibitor, Mannan, can reduce the clearance.

9:35 A Comparison of Two Methods for the Transient Expression and Purification of Ebola Glycoprotein from HEK-293 and CHO Cells

UNPUBLISHED DATA

Christopher W. Kemp, Ph.D., President, Kempbio, Inc.

Advances in transient mammalian expression protocols allow proteins to be expressed at levels supportive of large-scale applications. The ability to rapidly produce diagnostic antigens is of particular interest in the area of emerging viral diseases. This presentation focuses on the comparison of PEI-mediated transient transfection and BacMam transduction for the expression of Ebola glycoprotein. The gene-to-protein approach illustrates the utility of these methods for the rapid production of diagnostic antigens.

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

YEAST

11:05 Optimizing the Quality of IgGs Produced in Yeast – Removal of Glycans at a Non-Consensus Asparagine Residue

Juergen Nett, Ph.D., Senior Principal Scientist, Adimab, LLC

Yeast cells offer a facile way to produce milligram quantities of IgGs for screening in high-throughput workflows. In order to avoid the addition of large, high-mannose glycans the consensus asparagine at position N297 is often removed by site directed mutagenesis. Despite this modification, IgGs produced in yeast often are decorated with additional, high molecular weight glycan structures. This talk will provide an overview on how sequence optimization and purification are able to remove these unusual post-translational modifications.

11:35 Double Digit-Titers and High Product Quality of Nanobodies® Using *Pichia pastoris*

UNPUBLISHED DATA

Peter Schotte, Ph.D., Section Head, CMC - Host Creation, Ablynx nv

Pichia pastoris is currently Ablynx' preferred production host for Nanobodies, a novel class of therapeutic proteins based on single-domain antibody fragments, mainly because of its high expression yields and low amount of secreted host cell proteins, resulting in short process development timelines. This presentation will address the different aspects of *Pichia* process development for Nanobody production, from host creation to fermentation and downstream processing, with the main focus on the optimization of product yield and quality.

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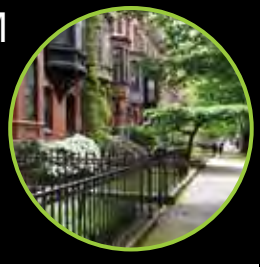


5th Annual | May 6-7

Optimizing Protein Expression

Enhancing Expression Systems

12:05 pm Meeting the Need for Rapid Protein Expression and Development with a Cloud-Based Informatics System

Sponsored by CORE INFORMATICS

Diane Retallack, Ph.D., Director, Molecular Biology, Pfenex, Inc.

Pfenex Expression Technology™ has been developed as a protein production platform to rapidly identify strains that express high titers of soluble, active protein. Employing a combinatorial approach to strain engineering, thousands of unique expression strains are evaluated in parallel. Core LIMS™ enables tracking results from strain construction/ screening through fermentation and protein purification.

12:20 Best of Both Worlds: Innovative Microbial System Leverages the Advantages of Both Bacterial and Mammalian Manufacturing

Sponsored by ALTHEA

Kristin DeFife, Ph.D., Vice President, Biologics, Ajinomoto Althea Inc.

Reach high expression using a microbial system and overcome challenges associated with *E. coli* including lengthy purification, protein aggregation and inefficient refolding processes. The Corynex® system secretes properly folded, biologically active proteins into the extracellular fermentation broth like mammalian cells, which eliminates multiple recovery and purification steps, lowering cost and speeding time to market.

12:35 End of Conference

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC14: Strategic Bioassay Design and Analysis

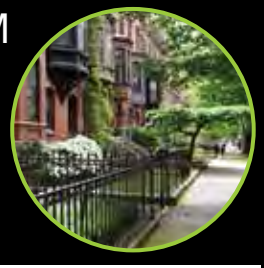
**Separate registration required, please see page 4 for course details.*

Inaugural | May 7-8

Accelerating Cell Line & Cell Culture Development

Advancing Protein Expression

EXPRESSION STREAM



Recommended Pre-Conference Short Course*

SC12: Production Challenges for Complex Biologics: ADCs, Bispecific & Fusion Proteins

**Separate registration required, please see page 4 for course details.*

THURSDAY, MAY 7

THE BIG PICTURE OF PROTEIN EXPRESSION

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

Susan Sharfstein, Ph.D., Associate Professor, NanoBioscience, College of Nanoscale Science and Engineering, SUNY Polytechnic Institute

» 1:50 KEYNOTE PRESENTATION:

Speed to Clinic and Cell Line Stability: How Do We Reconcile These Competing Requirements?

James P. Fandl, Ph.D., Senior Vice President, Protein Expression Sciences, Regeneron Pharmaceuticals, Inc.

Clonality and stability, both of which are fundamental to a robust therapeutic protein production process, should be the sole key drivers in cell line development. However, the pressure to quickly deliver novel protein therapeutics to the clinic, and the economic demand for high productivity, may at times be in conflict with assuring clonality and stability. Regeneron's approach for harmonizing these seemingly disparate drivers of cell line development will be discussed.

2:20 Bioreactor Process Improvements in a Legacy Perfusion-Based Process

Lada Ivana Laenen Horvat, Ph.D., Senior Director and Head, Allston MSAT, Genzyme, A Sanofi Company

2:50 Development of Next-Generation of Therapeutic Proteins

Nicola Beaucamp, Ph.D., Head, Cell Culture Research, Innovation Center Penzberg, Large Molecule Research, Pharma Research and Early Development, Roche Diagnostics GmbH

We present an integrated approach to CHO cell line selection, USP, DSP and analytics that enabled us to deliver high quality drug substance. Supported by this approach, this presentation demonstrates that expression titer is not the primary selection criterion for the best suited clone. In summary, we have succeeded in designing and developing complex protein-based therapeutics for clinical use enabled by a sophisticated integrative technical program to select the best clone.

3:20 Efficient Manufacture of Autologous Therapeutics: Automated Hollow-Fiber Bioreactors as a Key Enabling Technology

Sponsored by BIOVEST INTERNATIONAL

Scott Waniger, Director, Cell Culture, Biovest International

Production demand for protein therapeutics ranges from large scale commercial batches to small, unique lots required for patient-specific applications. To accommodate these diverse needs, a novel, fully automated system was developed for high density cell culture and collection of concentrated proteins. More specifically, this novel platform technology allows for concurrent production of numerous proteins and addresses regulatory concerns associated with multi-product facilities. Through feedback control and minimal operator interaction, this closed system results in a more safe and cost effective method for autologous or heterologous therapeutic protein production.

3:35 Sponsored Presentation *(Opportunity Available)*

3:50 Refreshment Break

4:20 Problem-Solving Breakout Discussions

5:20 End of Day

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC14: Strategic Bioassay Design and Analysis

**Separate registration required, please see page 4 for course details.*

FRIDAY, MAY 8

8:00 am Morning Coffee

SYNTHETIC BIOLOGY & OMICS TECHNOLOGIES

8:30 Chairperson's Remarks

Patrick Hossler, Ph.D., Senior Scientist III, Process Sciences, AbbVie Bioresearch Center

8:35 FEATURED PRESENTATION:

Mammalian Synthetic Biology: From Parts to Modules to Therapeutic Systems

UNPUBLISHED DATA

Ron Weiss, Ph.D., Professor, Biological Engineering, MIT

Synthetic biology is revolutionizing how we conceptualize and approach the engineering of biological systems. In this talk, we will discuss the creation of foundational elements for mammalian synthetic biology, including genetically encoded cellular sensors, information processing, and actuation. These genetic devices enable us to implement precise control over gene expression and other cellular behaviors. We will also briefly discuss applications that are uniquely enabled by genetically encoded programs, including cancer therapy, programmable organoids, and vaccination.

9:05 Next Generation Bioprocess: How the 'Omics' Era will Affect Future Biotherapeutic Development

Chapman M. Wright, Ph.D., Scientist II, Cell Culture Development, Biogen Idec, Inc.

The Next-Generation Sequencing (NGS) and Omics revolution has had a profound effect on the manner in which we approach the study of biology and medicine, but these effects are not limited to these fields alone. With the process of collecting and analyzing large datasets becoming more seamless, a growing number of disciplines are incorporating these techniques into their workflow. In this presentation, I will highlight areas of interest in which NGS and Omics could guide changes to current biotherapeutic development and lead us into the 'next generation of bioprocess.'

9:35 Omics Meets Process Science: From Marker Discovery to Application

Sohye Kang, Ph.D., Senior Scientist, Amgen, Inc.

Omics technology allows integration of powerful analytical and computational tools to identify predictive markers associated with various phenotypes exhibited by different cell lines. Moreover, omics evaluations reveal mechanism of action associated with phenotypic changes induced by process or raw material alterations. Examining both intrinsic and external factors at the systems level using multi-omics approach could enable us to develop effective application strategies to improve recombinant protein production with desired product quality.

10:05 Coffee Break

QUALITY & BIOPROCESSING

10:35 Expression of Monoclonal Antibody Variants in Transient and Stable Cultures, the Effects of Sequence and Culture Temperature on Stability and Expression Level

Susan Sharfstein, Ph.D., Associate Professor, NanoBioscience, College of Nanoscale Science and Engineering, SUNY Polytechnic Institute

We examined the effects of protein sequence on expression level for two monoclonal antibodies with a single amino acid difference. The change in sequence altered the expression level more than ten-fold and significantly changed the protein stability. We found that reducing the culture temperature improved the expression of the lower productivity variant, but not the higher producing variant. Biophysical analysis suggested that lower culture temperatures improved the folding and stability of the lower productivity variant.

11:05 Quantification of Cytosolic Plasmid DNA Degradation Using High-Throughput Sequencing

CONTINUED

Accelerating Cell Line & Cell Culture Development

Advancing Protein Expression

Mark M. Banaszak Holl, Ph.D., Professor, Chemistry and Biomedical Engineering, University of Michigan

Cytosolic DNA degradation plays an important role in decreasing transgene expression; however, the cleavage locations remain largely unexplored. High-throughput sequence mapping of cytosolic nuclease cleavage sites for Luciferase plasmid in HeLa cells revealed the following most common cut sites: the poly(A) region between the β-lactamase gene and the cytomegalovirus promoter, the 5′ end of the β-lactamase gene, the OriC region, the SV40/poly(A) region, the luciferase gene, and the CMV promoter.

11:35 High-Throughput Automation Solutions in Bioprocess Development

UNPUBLISHED DATA

Gregory Keil, MS, Senior Scientist, Merck

Within Merck's Bioprocess Development organization we have implemented a fully automated approach to cell line development involving multiple automation systems designed to streamline many of the activities involved in cell line development, characterization, and process development. Here we will demonstrate how a modular approach to automation allows for increased functionality, flexibility, and overall throughput. With these automation solutions in place bioprocess development has observed both increased efficiency and productivity across the entire the platform.

12:05 pm Integrated Continuous Bioprocessing: A Bench-Top Factory Framework for Production of Complex Recombinant Proteins

Mats Åkesson, Ph.D., Principal Scientist, Cell Culture Technology, Novo Nordisk A/S

We have developed an integrated continuous framework for end-to-end production of complex recombinant proteins based on perfusion cultivation and automated multi-step purification. The integrated set-up employs standard laboratory equipment, and it enables compact automated bench-top factories converting cell culture media to purified protein without intermediate storage. Examples from production of complex recombinant proteins for preclinical supply will be presented.

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

1:05 Refreshment Break

OPTIMIZING PROCESS DEVELOPMENT

1:35 Chairperson's Remarks

Mark M. Banaszak Holl, Ph.D., Professor, Chemistry and Biomedical Engineering, University of Michigan

1:40 Expansion of the Genetic Alphabet

Floyd Romesberg, Ph.D., Associate Professor, Chemistry, The Scripps Research Institute

Expansion of the genetic alphabet to include a third base pair would be a fundamental accomplishment that would not only have immediate utility for a number of applications, but would also lay the foundation for a semi-synthetic organism. We have developed an unnatural base pair, d5SICS-dNaM, that forms based on packing and hydrophobic interactions rather than complementary H-bonding. Structural studies, as well as several applications, including ongoing selections for unnatural DNAzymes will be discussed.

2:10 Fast Early Development of a Complex Novel IL2-Based Immunocytokine

Ingo Gorr, Ph.D., Senior Scientist, Roche Diagnostics GmbH

We present a fast and elegant strategy for cell line selection and development of a manufacturing process for IL2 fusion proteins. Here, only cell line development (CLD), upstream processing (USP) and downstream processing (DSP) together were capable of reducing critical impurities and producing the molecule in high amount with high quality. Intriguing tricks to achieve a high quality therapeutic protein in combination with accelerated timelines are highlighted.

2:40 Cell Culture Media Supplementation of Uncommonly Used Sugars Sucrose and Tagatose for the Targeted Shifting of Protein Glycosylation Profiles of Recombinant Protein Therapeutics

CASE STUDY

Patrick Hossler, Ph.D., Senior Scientist III, Process Sciences, AbbVie Bioresearch Center

Protein glycosylation is an important post-translational modification towards the structure & function of recombinant therapeutics. In this presentation we highlight a series of studies utilizing the uncommonly used sugars sucrose & tagatose for the targeted shifting of protein glycosylation profiles on recombinant glycoproteins. Both sugars were found to significantly increase the levels of high mannose N-glycans, and reduce fucosylation. Structure/function studies, as well as potential bioprocessing implications will be discussed.

3:10 Rapid Generation of Recombinant Baculoviruses for GMP Production of Recombinant Hemagglutinins, Components of Influenza Vaccine Flublok

Nikolai Khramtsov, Ph.D., Associate Director, Upstream Development, Product Realization, Protein Sciences Corp.

We developed universal process for the GMP production of influenza recombinant hemagglutinins (rHAs), components of seasonal influenza vaccine Flublok®. The GMP manufacture of drug substances in BEVS (baculovirus expression vector system) begins in less than two months from FDA announcement vaccine composition for new flu season (in February of each year). The rapid generation of recombinant baculoviruses containing rHA genes is completed within 25 days that allowed producing and delivering vaccine to the users on time.

3:40 End of Conference

5th Annual | May 4-5

Characterization of Biotherapeutics

The Changing Analytical Function in an Era of New Product Formats

Recommended Pre-Conference Short Course*

SC7: Immunogenicity Risk Assessment and Regulatory Strategies

**Separate registration required, please see page 4 for course details.*

MONDAY, MAY 4

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks

8:40 Cancer Stem Cells and Mechanisms of Malignant Progression

Robert A. Weinberg, Ph.D., Founding Member, Whitehead Institute for Biomedical Research; Professor, Biology, Massachusetts Institute of Technology

The cell-biological program termed the epithelial-mesenchymal transition (EMT) plays a role in conferring aggressive traits on carcinoma cells. In addition, it generates cancer stem cells (CSCs) that have the ability, following dissemination, to serve as founders of new metastatic colonies. The relationship between these CSCs and the SCs residing in normal tissues, and the participation of the CSCs in metastatic dissemination will be described.

9:25 Building an Antibody Discovery Company in a Crowded Field – the Adimab Story

Tillman Gerngross, Ph.D., CEO, Co-Founder, Adimab

The presentation will cover the evolution of Adimab from its founding in 2007 to becoming one of the few privately held profitable biotech companies in the last decade. Industry trends and specific strategic decisions along the way will be discussed and used to illustrate the importance of integrating finance and scientific information to build successful capital efficient biotech companies.

10:10 Coffee Break

10:45 Chairperson's Remarks

John F. Kellie, Ph.D., Investigator, Bioanalytical Sciences and Toxicokinetics, GlaxoSmithKline

» 10:50 KEYNOTE PRESENTATION:

Native and Subunit Analysis of Antibody-Drug Conjugates

UNPUBLISHED DATA

Alain Beck, Ph.D., Senior Director, Antibody and ADC Physico-Chemistry, Center of Immunology, Pierre Fabre; Associate Editor, mAbs

Most of the current ADCs in clinical trials are controlled, but heterogeneous, mixtures of isomers and isoforms. Drug loading and distribution, amount of naked antibody and average drug to antibody ratio (DAR) are Critical Quality Attributes for ADCs. At the top level, the advantages of cutting-edge mass spectrometry (MS) techniques such as native MS and Ion-Mobility MS will be compared to Hydrophobic Interaction Chromatography (HIC). In addition, optimization of middle up and bottom up strategies will be presented allowing structural assessment of positional isomers.

CHARACTERIZATION FOR BIOCONJUGATES

11:20 Novel FRET Assay for the Evaluation of Intracellular Activation of ADC Linkers

UNPUBLISHED DATA

Byoung-Chul Lee, Ph.D., Scientist, Protein Chemistry, Genentech, Inc.

Despite the recent success of ADCs, their mechanisms of action are not fully understood. In order to gain further understanding of the ADC intracellular uptake and payload release, we developed a novel fluorescence resonance energy transfer (FRET) ADC. This FRET assay will provide a facile and robust assessment of the intracellular processing and have significant implications for the future development and clinical use of ADCs.

11:50 Ten Lessons for the Formulation Development of Monoclonal Antibodies from Multimodal Thermal Unfolding Case Studies

Sponsored by UNCHAINED LABS

Mark Brader, Ph.D., Principle Scientist, Protein Pharmaceutical Development, Biogen Idec

The recent availability of technologies enabling simultaneous monitoring of spectroscopic and light scattering readouts creates new opportunities for high throughput analysis and expanded protein formulation parameter space. Importantly, a better understanding of how formulation conditions affect domain stability and thermal unfolding becomes more readily accessible. This presentation will describe a series of case studies of multimodal thermal unfolding that provide insights into various aspects of monoclonal antibody formulation design.

12:20 pm Luncheon Presentation I: Uncovering Receptor Targets and Off-Targets of Antibodies and Protein Ligands Using Human Cell Microarray Technology

Sponsored by RETROGENIX

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

12:50 Luncheon Presentation II: Advanced Characterization of Antibody Drug Conjugates (ADC's) by Liquid Chromatography and Mass Spectrometry (LC/MS)

Sponsored by Waters

John C. Gebler, Ph.D., Director, Biopharmaceuticals, Waters Corporation

Antibody drug conjugates (ADC's) are a complex the amalgamation of monoclonal antibodies (mAb) and low molecular weight toxins. The combination is often a mAb targeted to cancer to deliver a potent cytotoxin to a specific site or cell. The resulting conjugate is complex and typically heterogeneous making physical chemical characterization challenging. Liquid chromatography coupled to mass spectrometry (LC/MS) is a powerful tool for the characterization of proteins including mAb. At Waters we have placed a focus on the LC/MS for ADC's based on cysteine, lysine, and engineered conjugates. An ADC specific work flow will be shown for intact, sub-unit, peptide level, and glycan characterization by LC/MS.

1:20 Session Break

1:50 Chairperson's Remarks

John F. Kellie, Ph.D., Investigator, Bioanalytical Sciences and Toxicokinetics, GlaxoSmithKline

1:55 FTiH Support of an ADC: Stability, Assay Development, and Clinical Experiences

UNPUBLISHED DATA

John Kellie, Ph.D., Investigator, Bioanalytical Sciences and Toxicokinetics, GlaxoSmithKline

Characterization of circulating ADC species (conjugated antibody, total antibody, and payload) is critical to understanding the safety and efficacy of ADC therapeutics. Current methodology requires development and validation of immunoassays and liquid chromatography-mass spectrometry assays. This presentation will share experiences from assay validation through first time in human bioanalytical study support along with an update and outlook for state-of-the-art technologies set to drive ADC method development in the future.

2:25 Comparative Clinical Pharmacokinetics of Antibody-Drug Conjugates in First-in-Human Phase 1 Studies

CASE STUDY

Céline Amara, Senior Pharmacokineticist, Sanofi

Comparison of the clinical pharmacokinetics (PK) for ADCs now in development is challenging because of the large number of targets, ADC constructs, dosing regimens, and patient populations. This presentation presents an evaluation of ADC clinical PK properties, dosing regimens, determination of doses ranges and associated maximum tolerated doses. The effect of structural characteristics and target types (hematological vs. solid tumors) on PK will also be discussed.

2:55 Bioanalytical Strategy for Development and Validation of Ligand Binding Assays for ADCs

CASE STUDY UNPUBLISHED DATA

Seema Kumar, Ph.D., Principal Scientist, Pfizer, Inc.

The dynamic and heterogeneous mixture of ADCs containing various drug-to-antibody ratios (DAR) species and different conjugation sites may have different binding affinities for the capture and detection reagents typically used in ligand binding assays (LBA). These differences in binding affinity may translate into a variation in the ability of the LBA to accurately detect various DAR species. The case studies presented will evaluate various bioanalytical strategies employed for the development and validation of DAR independent LBAs for ADC bioanalysis.

3:25 Characterization of Fusion Proteins

CONTINUED

5th Annual | May 4-5

Characterization of Biotherapeutics

The Changing Analytical Function in an Era of New Product Formats

CASE STUDY *Wilma Lau, Ph.D., Senior Scientist, Large Molecule Research, Roche Pharma Research & Early Development, Roche Innovation Center Penzberg*

The engineering of multi-domain proteins such as Fab-Cytokine or Fab-Toxin fusion proteins promises the advancement of superior biotherapeutics. Their development requires design and characterization strategies tailored to the properties and the critical quality attributes of the combined domains. Here, we present examples for early design testing using Hapten and Sortase coupling technologies, for adaption of developability concepts for fusion proteins and for equitable evaluation of fusion protein characteristics.

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

4:35 Problem-Solving Breakout Discussions

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:50 End of Day

TUESDAY, MAY 5

8:00 am Morning Coffee

ANALYZING THE *IN VIVO* BEHAVIOR OF BIOTHERAPEUTICS

8:25 Chairperson's Remarks

Yelena Lyubarskaya, Ph.D., Senior Principal Scientist, Biogen Idec

8:30 Application of *in vitro* Models to Understand and Optimize Pharmacokinetic Properties of Biologic-Based Molecules

CASE STUDY UNPUBLISHED DATA *Tim Carlson, Scientific Director, Pharmacokinetics & Drug Metabolism, Amgen, Inc.*

Proteins and peptides are attractive drug candidates due to their biological activity, but they often have suboptimal pharmacokinetic properties. These molecules are prone to high clearance and low bioavailability, limiting their duration of action and systemic exposure. We are developing and applying *in vitro* approaches to predict the *in vivo* stability of peptides and proteins. The goal is to characterize pharmacokinetic liabilities and ultimately to design molecules with more optimal properties.

9:00 *In vitro* Biological Characterization of IFN-β-1a Major Glycoforms

CASE STUDY *Horst Bierau, Ph.D., Scientific Advisor and Relation Manager, Merck Serono S.p.A.*

Interferon β-1a glycoforms were subjected to physico-chemical and biological characterization by means of mass spectrometry, sialic acid content, thermal denaturation and various *in vitro* bioassays. The *in vitro* bioassay responses revealed a correlation mainly with the glycan antennarity. It is therefore suggested that all glycoforms are having biological activity and play a role in modulating the overall IFN-β biological activity with higher-antennarity glycoforms being able to better sustain IFN-β-1a bioactivity over time.

ANALYTICAL STUDIES IN SUPPORT OF PROCESS DEVELOPMENT AND PRODUCT QUALITY

9:30 Characterization and Control of Product Variants Applying QbD Principles

CASE STUDY *Jochen Felix Kepert, Ph.D., Senior Manager, Pharma Technical Development Europe, Roche Diagnostics GmbH*

The application of quality by design principles on characterizing and controlling product variants for a recently approved therapeutic monoclonal antibody is illustrated. During development several product variants and process related impurities were characterized and categorized into critical and non-critical quality attributes (CQAs) applying a risk ranking and filtering tool. The identified CQAs were further monitored in process development studies and an attribute testing strategy was developed encountering process capability and CQA impact.

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

10:50 Protein Characterization for APC: Monitoring Product Quality Attributes for Process Development and Manufacturing

CASE STUDY *Yelena Lyubarskaya, Ph.D., Senior Principal Scientist, Biogen Idec*

Advanced process control can provide flexibility and efficiency in biopharmaceutical manufacturing. Understanding of the effect of manufacturing process variables on product quality attributes is required in support of APC development. The use of mass spectrometry for monitoring glycan distribution of a glycoprotein during cell culture process will be demonstrated. The measurements are performed to obtain early readout of product quality to enhance process understanding and explore potential process analytical tools.

11:20 Novel Method for Assessing Host Cell Protein Assays

Susan Flor, Senior Research Associate, Analytical Operations, Genentech

Immunoassays are typically used to monitor residual host cell protein (HCP) clearance from biopharmaceuticals. Antibodies to a complex mixture of total HCPs are generated for this purpose. Health authorities often request a quantitative assessment of HCP coverage with the antibody used in the immunoassay. 2D gels and Westerns have inherent limitations that prevent accurate quantification of coverage. We explore a new method for HCP reagent coverage characterization.

11:50 High-Throughput Analytics in Support of Process Development and Identification of Critical Quality Attributes

UNPUBLISHED DATA *Hui Cai, Ph.D., Research Investigator, Process Development Analytics, Bristol Myers Squibb*

The Quality by Design (QbD) initiative aims to thoroughly understand the product and the manufacturing process for better product quality and faster product development. One of the first steps in the QbD approach consists in identification of the critical quality attributes (CQA). At BMS, we use automation for both process development and process analytics. Here we present data that show the use of automation in the facilitation of CQA establishment.

12:20 pm Assessing IgG Fc Variant Cross-Reactivity between Human and Rhesus Macaque Fc-gamma Receptors using Array-Based SPR

Sponsored by

Austin Boesch, Ph.D., Candidate, Dartmouth College

A number of antibody therapies rely on Fc receptor (FcR)-mediated effector functions for optimal activity, prompting the need to understand how IgG scaffolds engineered to differentially bind to the human receptors translate in non-human primate (NHP) models. Use of a high-throughput array-based surface plasmon resonance (SPR) platform enabled efficient characterization of the affinity between an IgG Fc variant panel (including subclass, Fc mutants and glycosylation) and major human and rhesus FcR allotypic variants.

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

CHARACTERIZATION OF BISPECIFIC ANTIBODIES AND NOVEL BIOLOGICS

2:00 Chairperson's Remarks

Timothy Fenn, Ph.D., Principal Scientist, Boehringer Ingelheim

2:05 Analytical Development for Bispecific Antibodies

UNPUBLISHED DATA *Matthew Bunce, Ph.D., Principal Research Scientist, Janssen*

2:35 Pharmacology of Blood–Brain Barrier-Permeable Bispecific Antibodies

Sue Twine, Ph.D., Team Leader, Human Health Therapeutics Portfolio, National Research Council Canada

This talk will focus on the development of targeted SRM-ILIS and 2D-LC-SRM methods with improved sensitivity for quantification of BBB-crossing bi-specific antibodies in small samples of cerebrospinal fluid (less than 2 µl) and in complex protein matrices of brain tissue. These analytical techniques can be multiplexed to allow quantification of several antibodies in the same sample and is well suited for serum-CSF-brain PK analyses of co-injected antibodies as well as for simultaneous measurements of target-engagement biomarkers.

CONTINUED

5th Annual | May 4-5

Characterization of Biotherapeutics

The Changing Analytical Function in an Era of New Product Formats

3:05 Biologics Developability Assessment and Formulations Optimization Using Isothermal Chemical Denaturation (ICD)

Sponsored by AVIA BIOSYSTEMS

Richard K. Brown, Ph.D., President, AVIA Biosystems

Stability optimization and aggregation minimization are two of the most important hurdles in the development of biologics. ICD provides the most accurate way of measuring protein stability under different formulation conditions. Additionally, ICD experiments performed at different protein concentrations provide a quantitative assessment of protein aggregation in the native and denatured states. ICD is ideally suited to optimize the formulation of highly concentrated formulations, bispecific antibodies and antibody drug conjugates. In this presentation, the fundamentals of ICD and its application to the evaluation of protein stability and optimization of formulation conditions will be discussed.

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

4:25 Development and Characterization of Novel Antibody Formats

UNPUBLISHED DATA

Melissa Geddie, Ph.D., Principal Scientist, Merrimack Pharmaceuticals

Multispecific antibodies and antibody-like molecules broaden the therapeutic application of IgGs, but can be challenging to engineer and manufacture. Using a network biology approach to identify key design parameters, we have engineered novel formats for specific biological targeting. We then use rapid design cycles followed by high-throughput characterization of these formats to select for potential therapeutic candidates with robust pharmaceutical properties.

4:55 FDA/Sponsor Interaction on the Development of a Control Strategy for the Albumin Domain of an Albumin-fusion Protein

Weijie Wang, Ph.D., Senior Scientist, Teva Biopharmaceutical USA, Inc.

Fully recombinant Albumin fusion proteins are an established platform for extending the serum half-life of therapeutic proteins. While control strategies for the therapeutically active domain are common, including a cell-based potency assay, the control of the albumin portion of the product needed to be developed. This talk will present a case study where a comprehensive control strategy was designed with FDA input based on a fundamental structure/function assessment of the criticality of Quality Attributes.

5:25 End of Conference

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC11: Overcoming the Challenges of Immunogenicity Assessment

**Separate registration required, please see page 4 for course details.*

3rd Annual | May 6-7

Biophysical Analysis of Biotherapeutics

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

Recommended Pre-Conference Short Course*

SC11: Overcoming the Challenges of Immunogenicity Assessment

**Separate registration required, please see page 4 for course details.*

WEDNESDAY, MAY 6

7:00 am Registration and Morning Coffee

8:00 Chairperson's Remarks

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

» 8:10 KEYNOTE PRESENTATION:

Competing Effects for Optimizing Protein Behavior at Low and High Concentrations

UNPUBLISHED DATA

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

Multiple factors are considered when selecting protein product formulation and manufacturing conditions, as there may be competing effects that require optimization. This presentation focuses on examples from therapeutic proteins and model proteins that highlight the balance between different behaviors (e.g., aggregation, solubility, viscosity) and how to reasonably account for or predict these in at least a semi-quantitative manner based on biophysical measurements.

PREDICTIVE MODELING OF BIOPHYSICAL CHARACTERISTICS

8:40 Beauty or Beast? *In Silico* Molecule Assessment to Support Lead Selection

CASE STUDY

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

Successful new biotherapeutics should possess – besides the desired biological activity – high biochemical and biophysical stability. *In silico* prediction of chemical degradation "hotspots", charge distribution, molecular dynamics and other features can support the lead selection and protein engineering process.

9:10 Engineering Developability Using Computational Tools

Bojana Popovic, Ph.D., Senior Research Scientist, Protein Sciences, MedImmune

Structural data of antibodies and other biotherapeutics provide key knowledge for understanding their biophysical characteristics which impacts both research and development of these molecules. Predictive tools using structures complement experimental analyses and can enable rational engineering of biotherapeutics. In this talk examples of these tools and their applications in engineering favourable biophysical properties of biotherapeutics will be highlighted.

9:40 Structural Flexibility and Allosteric Responses are Widely Redistributed Within Antibody Fragments Upon Mutation

UNPUBLISHED DATA

Dennis Livesay, Ph.D., Professor, Bioinformatics and Genomics, University of North Carolina

Recombinant antibody fragments have emerged as credible alternatives to full therapeutic antibodies. Unfortunately, reduced thermostability is frequently observed, limiting their broad utility. In response, screening for mutants that increase stability without compromising affinity is commonly employed. Little is known about how the uncovered mutations affect dynamical properties. In this talk, I will discuss the frequency and scale of changes in structural flexibility and allostery across a number of different antibody fragment systems.

10:10 Analyzing Varying Biochemical and Biophysical Data in Discovery Biologics

UNPUBLISHED DATA

Timothy Fenn, Ph.D., Principal Scientist, Boehringer Ingelheim

In discovery biologics, simple and information rich biochemical/biophysical methods are required to provide the wide variety of information necessary to evaluate antigens, multispecifics, and potential antibody leads. This talk will focus on some common analytical methods and how the information derived from each can be used in a complementary manner. Examples will be provided in a variety of contexts, including bispecific scaffold selection, antibody purification and protein reagent analysis.

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

11:25 Combining Biophysical Tools and Transgenic Mouse Models to Understand the Immunogenic Potential of Subvisible Particles

UNPUBLISHED DATA

Emilien Folzer, Scientist, Pharma Technical Development Europe (Biologics) Analytics, Roche

Theoretical concerns regarding the potential immunogenicity of proteinaceous sub-visible particles in protein therapeutics have being widely debated in literature with very limited experimental data available to date. This talk will focus on describing two methods for particle fractionation that have been developed to isolate defined particle species, as well as the detailed physicochemical and biological characterization of these species.

11:55 Biophysical Tools for Molecular Assessment of mAbs

UNPUBLISHED DATA

Arun Alphonse Ignatius, Ph.D., Principal Scientist, Biotherapeutics Pharmaceutical Science, Pfizer, Inc.

Molecular assessment is a key component of the candidate selection process. Previously, candidate selection has focused mainly on the biological properties of the protein and developability/manufacturability aspects were not considered. Many programs required additional resources and non-platform approaches during development due to lack of early developability assessment data. In this presentation, biophysical characterization tools optimized to probe into the conformational and colloidal stability of mAbs will be used on a set of Pfizer candidates to enable de-selection of risky candidates and ranking during molecular assessment stages.

12:25 pm Molar Mass, Size, Charge and Conformation: Light Scattering Tools for Biophysical Characterization of Macromolecules

Sponsored by WYATT TECHNOLOGY

John Champagne, Ph.D., Senior Applications Scientist & Northeast Regional Manager, Wyatt Technology Corporation

This seminar describes a comprehensive suite of characterization tools based on static and dynamic light scattering, which work together with size-based separation, to provide first principles biophysical characterization of macromolecules. Some of the key applications of the light scattering toolbox include analyses of molar mass and size distributions, aggregation, branching and other measures of conformation, and the composition of complex protein systems and other conjugated macromolecules.

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

1:55 Session Break

NOVEL BIOPHYSICAL ANALYTICAL METHODS

2:10 Chairperson's Remarks

Bojana Popovic, Ph.D., Senior Research Scientist, Protein Sciences, MedImmune

2:15 Optimizing Selection of Aggregation-Resistant Antibodies Using Self-Interaction Nanoparticle Spectroscopy

UNPUBLISHED DATA

Jiemin (Jimmie) Wu, Research Associate, Chemical and Biological Engineering, Rensselaer Polytechnic Institute

Conventional methods of measuring mAb self-association are difficult to employ during antibody discovery due to the low purities, limited quantities, and large numbers of mAb candidates. To address this challenge, we are developing a robust method (affinity-capture self-interaction nanoparticle spectroscopy, AC-SINS) capable of identifying mAbs with low self-association propensity at extremely low antibody concentrations and in the presence of contaminants.

CONTINUED

3rd Annual | May 6-7

Biophysical Analysis of Biotherapeutics

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

2:45 Catching the Seeds of Destruction: Probing Structurally Altered and Aggregated States of Therapeutically Relevant Proteins Using GroEL Coupled to Bio-Layer Interferometry

UNPUBLISHED DATA *Mark T. Fisher, Ph.D., Professor, Biochemistry and Molecular Biology, University of Kansas Medical School*

Nature employs a wide array of chaperone proteins to prevent large scale aggregation *in vivo* by interacting with partially folded protein species. This chaperone network actively or passively reverses misfolding to prevent and/or reverse the accumulation of aggregation prone species. Taking this tact, we demonstrate that a GroEL chaperonin-based biolayer interferometry platform can successfully detect initial "seed" preaggregate species in therapeutic protein formulations prior to large aggregate formation *in vitro*.

3:15 Simple Approaches to Monitoring Bio Pharmaceutical Purification with Flow Imaging

Sponsored by proteinsimple

Aaron Noyes, Process Engineer, Purification Process Development, Pfizer

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

4:45 Microspectroscopic Analysis of Free Fatty Acid Particles in Protein Formulations

CASE STUDY *Xiaolin Cao, Ph.D., Principal Scientist, Amgen*

Free fatty acid particles were identified in a number of protein formulations containing the surfactant polysorbate 20 using multiple microspectroscopic methods. These fatty acid particles were numerous in number, granular or sand-like in morphology and were several microns in size. In addition, protein particles and particles containing a mixture of protein and fatty acids were also identified. The techniques and observations described in this case study will be useful for the identification of microparticles in pharmaceutical products.

5:15 HELM: Setting the Standard for Biomolecular Data Exchange

CASE STUDY *Sergio Rotstein, Ph.D., Director, Research Business Technology, Pfizer, Inc.*

The Hierarchical Editing Language for Macromolecules (HELM) enables the representation of complex biologic entities such as oligonucleotides, peptides, proteins, antibodies and bioconjugates in a flexible and compact fashion. The technology, originally developed at Pfizer Incorporated, was released into the public domain through the Pistoia Alliance and is well on its way to becoming the industry standard for the exchange and manipulation of complex biomolecule structures and their associated data.

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

7:00 End of Day

THURSDAY, MAY 7

8:00 am Morning Coffee

SPECTROSCOPIC METHODS FOR BIOPHYSICAL ANALYSIS

8:30 Chairperson's Remarks

Wim Jiskoot, Ph.D., Professor of Drug Delivery Technology, Leiden University, The Netherlands

8:35 Leveraging the Power of Mass Spectrometry to Study ADME Properties of Therapeutic Biologics

CASE STUDY UNPUBLISHED DATA *Ji Ma, Ph.D., Principal Scientist, Amgen*

Benefiting from rapid advances in protein engineering field, discovery of therapeutic biologics has evolved from primarily monoclonal antibodies to different molecular types, e.g. ADCs, huFc and HSA fusions. Using several case studies, cutting edge mass spectroscopic technologies have been applied to understand ADME properties of therapeutic biologics in discovery stage.

9:05 Using Hydrogen-Deuterium Exchange Mass Spectrometry to Characterize Protein Higher-Order Structure and Dynamics

UNPUBLISHED DATA *George Bou-Assaf, Ph.D., Scientist, Biogen Idec*

Hydrogen/Deuterium exchange mass spectrometry provides superior assessment of protein higher-order structure. Here, we discuss the applications of HDX-MS in various aspects of drug discovery and development. We showcase how its use in comparability and biosimilarity studies enables stronger regulatory filings. We discuss how the technique has been instrumental for epitope mapping and in characterizing protein-protein or protein-ligand interactions. Finally, we explore how it could be used in protein formulation development.

9:35 Terahertz Spectroscopy of mAb Formulations

UNPUBLISHED DATA *Christopher van der Walle, Ph.D., Principal Scientist, Development, MedImmune*

Terahertz time domain spectroscopy (THz-TDS) provides insight into the interaction between proteins and water, or 'hydration shell', by analyzing the nonlinear relationship between protein concentration and THz absorption. Distinct changes in THz absorption were observed for mAbs formulated up to 150 mg/ml in different excipients: NaCl, sucrose, proline and arginine. Relating these changes to key formulation parameters such as viscosity will improve our understanding of mAb behavior at high concentrations.

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

BIOPHYSICAL ANALYSIS OF HIGH CONCENTRATION PROTEINS

11:05 Light Obscuration Measurements of Highly Viscous Solutions: Sample Pressurization Overcomes Underestimation of Subvisible Particle Counts

CASE STUDY *Wim Jiskoot, Ph.D., Professor of Drug Delivery Technology, Leiden University*

Light obscuration (LO) is a standard technique for subvisible particle analysis of therapeutic protein products. Some of those, however, exhibit high viscosities, which can lead to an underestimation of subvisible particle concentrations. To solve this problem, we evaluated the application of sample pressurization during analysis, which turned out to be an elegant way to restore the reliability of LO analysis of highly viscous products without the need for dilution.

11:35 Protein Intermolecular Organization within Clusters in High Concentration Solutions Effectively Differentiates Crystallization, Liquid-Liquid Phase Separation, Gelation and Viscous Rheology Processes

UNPUBLISHED DATA *Wenhua Wang, Ph.D., Postdoctoral Fellow, Late Stage Pharmaceutical Development Department, Genentech, Inc.*

Protein self-association, particularly at high concentrations, often leads to manufacturing and administration problems such as aggregation, high viscosity, opalescence, and liquid-liquid phase separation (LLPS). Here, the physical nature of phase behavior in concentrated monoclonal antibody solutions is addressed by characterizing protein interactions and cluster structures. A molecular-level understanding of protein self-assembly of different high concentration phase behaviors helps to control opalescence/LLPS and mitigate viscosities in drug product formulations.

12:05 pm Adopting Imaging and Other Analytical Techniques to Better Characterize and Study Novel Therapeutic Modes Such As the DVD-IgTM Molecule

Ivan Correia, MBA, Ph.D.,Senior Principal Research Scientist,cHead, Global Protein Sciences, AbbVie Bioresearch Center (ABC)

12:35 End of Conference

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC13: Physicochemical and Biophysical Characterization of Antibody- Drug Conjugates

Separate registration required, please see page 4 for course details.

ANALYTICAL STREAM

Protein Aggregation & Stability in Biopharmaceuticals

Analytic, Formulation, Manufacturing and Regulatory Challenges

Recommended Pre-Conference Short Course*

SC11: Overcoming the Challenges of Immunogenicity Assessment

**Separate registration required, please see page 4 for course details.*

THURSDAY, MAY 7

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

Ankit Patel, Ph.D., Scientist, Genentech

» 1:50 KEYNOTE PRESENTATION:

New Aggregation Properties of Therapeutic Proteins Revealed by New Analytical Methods

CASE STUDY UNPUBLISHED DATA

Tudor Arvinte, Ph.D., Professor, Biopharmaceutics, University of Geneva; CEO, Therapeomic, Inc.

Proof and understanding of protein aggregation phenomena can be achieved only through a convergence of evidence from numerous lines of inquiry using classical and orthogonal analytical methods. Based on case studies, different orthogonal methods will be presented. No single result form these methods denotes a general, absolute proof of the aggregation state, but together they point to unmistakable conclusions and reveal a broad picture on the protein aggregation states.

PREDICTING AND CHARACTERIZING THE MECHANISMS OF AGGREGATION

2:20 Understanding Agitation-Induced Aggregation and Predicting Aggregation Propensity of Monoclonal Antibodies

Ankit Patel, Ph.D., Scientist, Genentech

While surfactants are commonly used to prevent agitation-induced aggregation, they are typically not present at earlier stages in the monoclonal antibody production process and may be significantly diluted during dose preparation in infusion systems. Several interfacial analytical techniques have been utilized to evaluate the dynamics of adsorption to the air-water interface and evaluate interfacial protein-protein interactions leading to aggregation. In addition, a simple method to predict the aggregation propensity of monoclonal antibodies will be presented.

2:50 Predicting Aggregation-Prone Sequences in Proteins

CASE STUDY

Joost Schymkowitz, Ph.D., Principal Investigator, VIB Switch Lab, KULeuven, University of Leuven

As proteins have only evolved to be soluble at the concentration at which they naturally occur, they often tend to aggregate when employed in applications that require much higher concentrations. The propensity of proteins to aggregate is determined by their primary sequence and can be predicted with reasonable accuracy. Although computational assessment of protein quality is still in its infancy, it holds great promise to help shape the protein therapeutics of the future. I will discuss a number of key determinants and how to employ them to engineer polypeptide sequences to obtain superior proteins, with a particular focus on antibodies.

3:20 Fully Automated Antibody Structure Prediction from Sequence

Sponsored by BIOVIA

Ken Butenhof, Ph.D., Advisory Field Applications Scientist, BIOVIA

We have captured the best practices developed during the Second Antibody Modeling Assessment in a single fully automated antibody structure prediction method implemented in Discovery Studio through a Pipeline Pilot protocol. In this assessment we predicted the structure of eleven unpublished antibody Fv fragments. The prediction method utilizes fully automated multiple framework and antibody CDR Loop template selection, alignment and modeling. The resulting models are compared to the revealed X-Ray crystal structures and manually derived models. The comparison demonstrates that Biovia Antibody Modeling Cascade is capable of generating quite accurate models without manual intervention for the framework and the canonical CDR regions, with RMSDs to the X-ray structure on average below 1 A° for most of these regions. Furthermore, local geometry assessment scores are similar to that of the target X-ray structures. This method is applicable to Fv, Fab, and scFv sequences and is suitable for submission of multiple antibody sequences.

3:50 Refreshment Break

4:20 Problem-Solving Breakout Discussions

5:20 End of Day

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC13: Physicochemical and Biophysical Characterization of Antibody- Drug Conjugates

**Separate registration required, please see page 4 for course details.*

FRIDAY, MAY 8

8:00 am Morning Coffee

FORMULATION AND PROCESS STRATEGIES TO CONTROL PROTEIN AGGREGATION

8:30 Chairperson's Remarks

Jifeng Zhang, Ph.D., Head, Drug Product Analytics and Characterization, Drug Delivery and Delivery Development, MedImmune

8:35 Predicting Protein Aggregation in Lyophilized Solids Using Hydrogen Deuterium Exchange with Mass Spectrometric Analysis

CASE STUDY

Elizabeth M. Topp, Ph.D., Dane O. Kildsig Chair and Head, Industrial and Physical Pharmacy, Purdue University

Our group has developed solid-state hydrogen deuterium exchange (ssHDX-MS) with mass spectrometric analysis to probe protein conformation and matrix interactions in lyophilized solids with peptide-level resolution. This case study presents ssHDX-MS results for equine myoglobin (Mb), demonstrating a strong correlation between Mb aggregation during one year of storage in the solid state and ssHDX-MS results immediately following lyophilization.

9:05 Thermal Unfolding and Aggregation of Human IgG1 Fc Fragment: the Relevance of Solution Composition

CASE STUDY

Jifeng Zhang, Ph.D., Head, Drug Product Analytics and Characterization, Drug Delivery and Delivery Development, MedImmune

This presentation highlights the importance of understanding the specific ion effect on the protein behavior with respect to the biophysical properties of proteins during formulation development.

CONTINUED

Protein Aggregation & Stability in Biopharmaceuticals

Analytic, Formulation, Manufacturing and Regulatory Challenges

9:35 Combined *In Silico* and Biophysical Approaches to Enhance Aggregation Resistance of Biologics

UNPUBLISHED DATA

Michaela Blech, Ph.D., Scientist, Structural Biology, Boehringer Ingelheim Pharma GmbH & Co.,

To meet the requirements of current clinical indications with respect to drug delivery, highly concentrated therapeutic protein drugs up to 100-200 mg/ml are necessary. In order to achieve such concentrations, a number of protein properties like solubility, self-association, solution viscosity, and protein aggregation have to be controlled. Our current strategy uses a combination of *in silico* modeling approaches to identify critical amino acids or sequences, as well as biophysical tools to understand conformational and colloidal properties of the protein candidate at the molecular level and the impact on macroscopic solution properties.

10:05 Coffee Break

10:35 The Effect of Resin Porflore Size, Particle Diameter, and Ionic Capacity on the Resolution of Monoclonal Antibody Monomer from Aggregate During Preparative Cation Exchange Chromatography

UNPUBLISHED DATA

Benjamin Guzman, Senior Associate Scientist, Purification Process Development, Amgen

This work focuses on understanding the effect of resin properties on the removal of aggregates from a mAb feed stream utilizing a DOE approach. We will present results examining nine GE Healthcare Capto™ S Impact CEX prototype resins with variations in pore size, particle diameter, and ionic capacity within a designed space. In addition to the effect on resolution of aggregate and monomer, implications for other quality attributes and process integration will be discussed.

11:05 High-Throughput Methods to Assess Solution Behavior of Biologics

UNPUBLISHED DATA

Patricia Lowden, Scientist, Protein Production and Analytics Department, Eleven Biotherapeutics

11:35 Targeted Mutagenesis of a Therapeutic Human Monoclonal IgG1 Antibody Prevents Gelation at High Concentrations

Paul Casaz, Ph.D., Research Scientist, University of Massachusetts Medical School

A human monoclonal antibody was found that forms an opaque white gel at concentrations >30 mg/mL and temperature <6°C. Gelation was prevented by a low pH or high sodium chloride concentrations but a protein engineering solution was also sought. The substitution of a glutamic acid residue in the heavy chain variable region framework with lysine was found to prevent gelation.

12:05 pm Detection, Analysis, Purification and Processing of Monoclonal Antibody Aggregates

CASE STUDY UNPUBLISHED DATA

Raja Ghosh, Ph.D., Professor, Canada Research Chair in Bioseparations Engineering, McMaster University

Monoclonal antibodies (mAbs) which are an important category of biopharmaceuticals are particularly prone to aggregation. The presence of aggregates in formulations is undesirable. Recent studies have shown that the hydrophobicity of a mAb increases with the degree of aggregation and aggregates can be fractionated using hydrophobic interaction membrane chromatography (HIMC). Different case studies where HIMC is used to detect, analyse, separate and process mAb aggregates will be discussed in this presentation.

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

1:05 Refreshment Break

DEVELOPABILITY EVALUATION AND OPTIMIZATION

1:35 Chairperson's Remarks

Peter Ihnat, Ph.D., Principal Research Scientist, Drug Product Development Pre-Formulation, AbbVie

1:40 Defining Antibody Developability Rule of Thumb by It's Self- and Cross-Interactions

UNPUBLISHED DATA

Yingda Xu, Ph.D., Associate Director, Protein Analytics, Adimab

Developability issues, such as aggregation, low solubility, high viscosity and poor pK can usually be linked to antibody self- or cross-interactions. Ideally, high-throughput screening assays can be applied to catch candidates possessing these undesirable properties to minimize downstream risks early in the process. Here we report the application of such assays on a large panel of clinical stage mAbs to develop a simple model for antibody developability rule of thumb.

2:10 Anion-Protein Interactions and Relevance to Solution Properties and Stability

UNPUBLISHED DATA

Peter Ihnat, Ph.D., Principal Research Scientist, Drug Product Development Pre-Formulation, AbbVie

Cosolutes stabilize thermodynamic and colloidal properties of the protein to prevent aggregation in solution and improve hydration of the protein. We used light scattering techniques, thermal analysis and viscometry to probe the interactions between a series of anions and model proteins in solution. This information supports better insight into the stabilizing roles of common excipients and an improved rational approach to developing stable protein solution formulations.

2:40 Mutational Approaches to Improve the Biophysical Properties of Human Single-Domain Antibodies

CASE STUDY

Jamshid Tanha, Ph.D., Senior Research Officer, National Research Council, Canada

Various mutational approaches for improving the biophysical properties of VH and VL single-domain antibodies have been described. Here we zoom in on one particular approach, namely disulfide engineering approach, which improves the stability VHs and VLs. The approach appears to be universally applicable across all VHs and VLs.

3:10 Concentration Dependent Viscosity of Monoclonal Antibody Solutions: Explaining Experimental Behavior in Terms of Molecular Properties

Li Li, Ph.D., Senior Principal Scientist, Pfizer

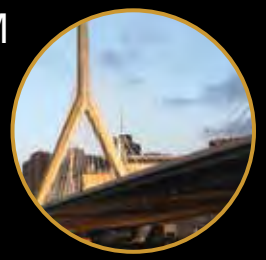
Antibody variable regions (Fv) were analyzed to explain concentration dependent viscosity behaviors of 11 mAbs. Net charge, x-potential and pI of the Fv regions correlate with viscosities of the mAbs at high concentrations. Coarse-grained molecular dynamics simulations of two problematic mAbs suggest that negative net charge on their Fv regions facilitates attractive inter-molecular interactions, leading to formation of transient antibody networks. These networks cause the problematic mAbs to diffuse slowly.

3:40 PEG-Induced Liquid-Liquid Phase Separation in Protein Solutions

Ying Wang, Ph.D., Research Associate, Physics and Biological Physics, Massachusetts Institute of Technology

Globular proteins, e.g. antibodies, can lose their solubility without unfolding, both in-vivo and in pharmaceutical formulations. Proteins with low colloidal stability are associated with some diseases and can cause problems in the development of protein drugs. In this talk, I will present a universal method for quantifying colloidal stability of protein solutions using PEG-induced liquid-liquid phase separation. The physical basis of liquid-liquid phase separation and depletion interaction will be discussed.

4:10 End of Conference



3rd Annual | May 4-5

Immunogenicity Prediction & Mitigation

Understanding and Control from Pioneers in the Field

Recommended Pre-Conference Short Course*

SC7: Immunogenicity Risk Assessment and Regulatory Strategies

**Separate registration required, please see page 4 for course details.*

MONDAY, MAY 4

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks

8:40 Cancer Stem Cells and Mechanisms of Malignant Progression

Robert A. Weinberg, Ph.D., Founding Member, Whitehead Institute for Biomedical Research; Professor, Biology, Massachusetts Institute of Technology

The cell-biological program termed the epithelial-mesenchymal transition (EMT) plays a role in conferring aggressive traits on carcinoma cells. In addition, it generates cancer stem cells (CSCs) that have the ability, following dissemination, to serve as founders of new metastatic colonies. The relationship between these CSCs and the SCs residing in normal tissues, and the participation of the CSCs in metastatic dissemination will be described.

9:25 Building an Antibody Discovery Company in a Crowded Field – the Adimab Story

Tillman Gerngross, Ph.D., CEO, Co-Founder, Adimab

The presentation will cover the evolution of Adimab from its founding in 2007 to becoming one of the few privately held profitable biotech companies in the last decade. Industry trends and specific strategic decisions along the way will be discussed and used to illustrate the importance of integrating finance and scientific information to build successful capital efficient biotech companies.

10:10 Coffee Break

RISK ASSESSMENT AND PREDICTIVE STRATEGIES

10:45 Chairperson's Remarks

Ronit Mazor, Ph.D., Post Doctoral Fellow, Molecular Biology, National Cancer Institute (NCI)

» 10:50 KEYNOTE PRESENTATION:

Immunogenicity Risk Assessment

Steven J. Swanson, Ph.D., Immunogenicity Consultant, Steven J Swanson Consulting

An important consideration when developing a new protein therapeutic is the potential and consequences of the therapeutic inducing an immune response. A careful analysis of the amino acid sequence can identify the presence of regions that are associated with higher rates of immunogenicity. Other tools are available to further help predict if a therapeutic will induce an immune response. Risk assessment includes deciding if any of the available prediction tools should be utilized. The possible consequences of an immune response are also evaluated when completing a risk assessment.

11:20 Case Studies on Immunogenicity Prediction Strategies for Early Decision-Making in Therapeutic Protein Development

CASE STUDY *Tim Hickling, Ph.D., Associate Research Fellow, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.*

Identification of immunogenicity risk is performed for all therapeutic proteins. However, not all proteins undergo a complete investigation of risk potential through the suite of assays available. I will present case studies of risk assessment, including application of *in silico* and *in vitro* methods to contribute to protein engineering and the selection of clinical candidates. Strategies for low immunogenicity risk and de-immunization will be discussed.

11:50 Human *in silico* and *in vitro* tools for Immunogenicity and Developability Risk Assessment and Risk Mitigation

Sponsored by Lonza

Yvette Stallwood, Ph.D., Head, Applied Protein Services, Lonza Biologics

Incorporating immunogenicity and developability risk assessment into the early stages of development is important for optimal lead selection. This presentation will focus on the human immunogenicity risk assessment platforms and other developability assessment tools at Lonza to aid the selection and optimization of lead candidates. Platforms include Epibase™ *In Silico* for the prediction of T cell epitopes and Epibase™ *In Vitro* for the assessment of T cell and B cell responses in human donor PBMC.

12:20 pm Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on Your Own

1:20 Session Break

RISK FACTORS THAT CONTRIBUTE TO IMMUNOGENICITY

1:50 Chairperson's Remarks

Tim Hickling, Ph.D., Associate Research Fellow, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

1:55 The Role of the Target in Antibody Biodisposition

Enrique Escandon, Ph.D., Principal Scientist, DMPK and Disposition, Merck Research Laboratories

For therapeutic antibodies, proximal target engagement is equivalent to immune complex formation; therefore, depending on the nature of the target (valence, abundance, location, metabolism, and its intrinsic biology), antibody-target and off-target mediated mechanisms of disposition and clearance will be affected by interactions with the Fc Gamma family of receptors. Here we present specific experimental examples where dramatic changes in exposure and biodisposition relate to target engagement.

2:25 Impact of Different Types of Aggregate on Immunogenicity

Narendra Chirmule, Ph.D., 7immune Consulting

Aggregation of proteins presents a significant safety concern in the development of this class of therapeutics. In recent years, there have been several elegant studies on delineating potential mechanism of action of aggregate induced immune activation. This presentation will focus on comparing the impact of different types of aggregates on immune activation. These observations may inform the monitoring approaches of these aggregates during process development.

2:55 Particulate Matter in Injectable Drug Products-A Regulatory Perspective and Reflections from the Draft Immunogenicity Guidance

Jack Ragheb, Ph.D., Principal Investigator, Laboratory of Immunology, Division of Therapeutic Proteins, CDER/FDA

3:25 Predictive Studies with Factors VII and VIII based on Genetic Analyses of Patients

Zuben E. Sauna, Ph.D., Principal Investigator, Department of Haematology, Research and Review, CDER/FDA

Based on genetic analyses of individual hemophilia A patients, we developed a predictive algorithm for immunogenicity (Receiver-operator-characteristic curve analysis, AUC, 0.890, P=0.001). The algorithm can be applied to determine the putative immunogenicity-risk of neo-epitopes introduced in bioengineered protein-therapeutics. A poof-of-principle study will be presented using a bio-engineered analog of Factor VIIa as an example. The development of this molecule was discontinued due to the development of ADAs in some patients in a phase 3 clinical trial.

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

4:35 Problem-Solving Breakout Discussions

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:50 End of Day

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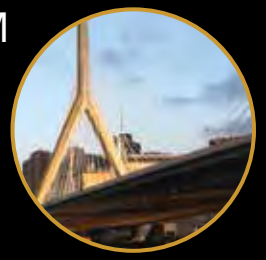

3rd Annual | May 4-5

Immunogenicity Prediction & Mitigation

Understanding and Control from Pioneers in the Field

TUESDAY, MAY 5

8:00 am Morning Coffee

TOOLS FOR IMMUNOGENICITY RISK PREDICTION

8:25 Chairperson's Remarks

Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.

8:30 Development of Humanized Mouse Models for the Study of Immunogenicity

UNPUBLISHED DATA *Michael A. Brehm, Ph.D., Assistant Professor, Diabetes Center of Excellence, Program in Molecular Medicine, University of Massachusetts Medical School*

The development of severely immunodeficient IL2rγ^{null} 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.

9:00 A Systems Pharmacology Approach to Immunogenicity – A Multi-Scale, Mechanistic Mathematical Model and Its Applications

Xiaoying Chen, Ph.D., Principal Scientist Pharmacokinetics, Dynamics, and Metabolism (PDM) Pfizer, Inc.

We have developed a mechanistic, multi-scale mathematical model by recapitulating fundamental biological mechanisms. The key strength of this model lies in its capacity to integrate various risk factors, e.g., T- and B- epitopes, patients' HLA background, and naïve T and B cell numbers into the underlying biology. The model can provide many clinical-relevant predictions. An example to illustrate potential applications in drug development will be provided.

9:30 Studies on Immunogenicity of Subvisible Particles using an IgG1 Transgenic Mouse

Björn Boll, Ph.D., Pharma Technical Development Europe, F. Hoffmann-La Roche Ltd.

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

CONTROLLING IMMUNOGENICITY/IMMUNOSUPPRESSIVE MECHANISMS

10:50 Anti-Drug Antibody – A Challenge in the Field of Therapeutic Proteins, Lessons Learned from Pompe Disease

CASE STUDY *Priya Kishnani, M.D., C.L. and Su Chen Professor of Pediatrics, Division Chief, Medical Genetics, Pediatrics, Duke University Medical Center*

Cross-Reactive Immunological Material (CRIM)-negative (CN) and a subset of CRIM-positive (CP) Infantile Pompe disease (IPD) mount an immune response against enzyme replacement therapy (ERT) resulting in clinical decline. Prophylactic immune tolerance induction (ITI) protocol has prevented immune response in CN patients treated with ERT. We will present data on the safety and efficacy of ITI approaches for CP and CN IPD receiving ERT.

11:20 Modulation of Immunogenicity by T Regulatory Cells

Ethan M. Shevach, M.D., Chief, Cellular Immunology Section, Laboratory of Immunology, NIAID/NIH

Foxp3+ T regulatory cells (Treg) are essential for immunological tolerance and immune homeostasis. T follicular helper (T_{FH}) cells provide help to B cells, while a new Treg subset (T_{FR}) has been shown to suppress germinal center B cell responses. Both T_{FH} and T_{FR} express the follicular homing receptor CXCR5, PD-1, and the transcription factors Bcl6. Enhancement of T_{FR} function represents an attractive target for decreasing immunogenicity.

11:50 Design of Immunotoxins with Reduced Immunogenicity

UNPUBLISHED DATA *Ronit Mazor, Ph.D., Postdoctoral Fellow, Molecular Biology, National Cancer Institute (NCI)*

Immunotoxins are highly immunogenic recombinant proteins designed to treat cancer. We identified and removed the T cell epitopes in immunotoxins in order to reduce its immunogenicity. In this talk we will discuss the methods we used to identify and eliminate the T cell epitopes, show a comparison of *in silico* predicted and experimental T cell epitopes in PE38 and lastly show a proof of concept using a mouse model that shares the immune-dominant epitopes.

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

IMMUNE SUPPRESSION AND DEIMMUNIZATION

2:00 Chairperson's Remarks

Michael A. Brehm, Ph.D., Assistant Professor, Diabetes Center of Excellence, Program in Molecular Medicine, University of Massachusetts Medical School

2:05 Biotherapeutic Deimmunization Using Computationally Designed, Combinatorial Libraries

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

Biotherapeutic deimmunization via T cell epitope deletion can enable therapeutic applications for otherwise highly immunogenic proteins. Here, we demonstrate the use of computationally designed, combinatorial libraries for aggressive epitope deletion in challenging biotherapeutic candidates. Highly engineered variants of exogenous therapeutic enzymes were evaluated in humanized murine models where they mitigated immune cell responses, suppressed development of anti-biotherapeutic antibodies, and enhanced efficacy in repeat dosing therapeutic regimes.

2:35 Immune Suppression of Humanized Antibodies

CASE STUDY *Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.*

Fully human biotherapeutics such as mAbs may be potentially immunogenic when administered to preclinical animal models and in the clinic and are associated with the formation of anti-drug antibodies (ADA). In this work we assessed the impact of various immunosuppressive regimens on ADA formation and the consequent impact on the PK profile of a fully human mAb in a rodent study . A better understanding of the mechanisms behind induction of tolerance with chronic dosing of a biotherapeutic and the impact of different immune suppressive regimens will also be discussed.

3:05 Tools and Technologies for Comprehensive Immunogenicity Risk Management

Sponsored by PROIMMUNE

Jeremy Fry, D.Phil., Director, Sales, ProImmune

Immunogenicity is one of the most complex issues to address in drug design and development. I will provide an overview of the best tools for immunogenicity risk mitigation, including Mass Spectrometry antigen presentation assays, Dendritic cell-T cell assays to measure responses to fully formulated biologics, HLA-peptide Binding Assays, and naïve T cell Proliferation Assays to characterize individual epitopes. I will also discuss how the potential risk of first infusion reactions can be mitigated using whole-blood cytokine release assays.

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

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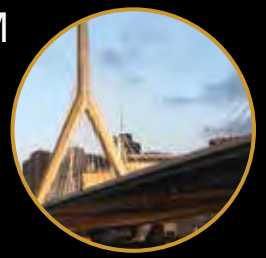


3rd Annual | May 4-5

Immunogenicity Prediction & Mitigation

Understanding and Control from Pioneers in the Field

NEW APPROACHES TO TOLERANCE INDUCTION

4:25 Improving the Efficacy Profile of Biologic Drugs by Addressing Product Immunogenicity with Tolerogenic Nanoparticles

Kei Kishimoto, Ph.D., Chief Scientific Officer, Selecta Biosciences

A case example will be presented with adalimumab in a mouse model of a spontaneous arthritis. Co-administration of the tolerogenic nanoparticles with adalimumab at the beginning of therapy prevent the formation of ADAs, resulting in normalized adalimumab PK and greatly enhanced protection from joint erosion. Other applications will also be discussed.

4:55 Induction of Immunological Tolerance to *E. Coli* Asparaginase by Engineering Erythrocyte Binding

Stephan Kontos, Ph.D., Co-Founder, Director, Research, Anokion SA

We report the application of an antigen-specific immune tolerance technology that harnesses natural immune regulation mechanisms of apoptotic cells to induce tolerance to the *E. coli* chemotherapeutic enzyme L-asparaginase. We demonstrate that engineering an erythrocyte-binding variant of asparaginase (ERY1-ASNase) allows for repeated dosing in mice without the development of anti-asparaginase antibodies, while additionally driving prophylactic immune tolerance that enables non-immunogenic follow-on therapy with wild-type ASNase.

5:25 End of Conference

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

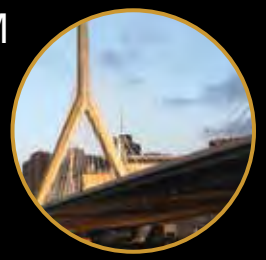
SC11: Overcoming the Challenges of Immunogenicity Assessment

**Separate registration required, please see page 4 for course details.*

8th Annual | May 6-7

Immunogenicity Assessment & Clinical Relevance

Technologies and Strategies for Safe and Efficacious Products in the Clinic



Recommended Pre-Conference Short Course*

SC7: Immunogenicity Risk Assessment and Regulatory Strategies

** Separate registration required, please see page 4 for course details.*

WEDNESDAY, MAY 6

7:00 am Registration and Morning Coffee

MEETING REGULATORY EXPECTATIONS FOR INNOVATORS AND BIOSIMILARS: STRATEGY AND ASSAY METHODOLOGY FOR CHALLENGING PRODUCTS

8:00 Chairperson's Remarks

Boris Gorovits, Ph.D., Director, PDM, Pfizer, Inc.

» 8:10 KEYNOTE PRESENTATION:

Recommendations for the Assessment and Reporting of Clinical Immunogenicity of Therapeutic Proteins and Peptides

Meena Subramanyam, Ph.D., Vice President, Translational Sciences, Biogen Idec, Inc.

To foster a unified approach to assessing and describing immunogenicity, the AAPS Therapeutic Protein Immunogenicity Focus Group convened a team of experts from the industry and regulatory agencies and tasked them with producing a consensus document comprising best practices and recommendations regarding: standardizing terminology; sampling schema for the assessment of ADA in clinical studies; interpretation and presentation of analytical data; and assessment of clinical impact.

8:40 Immunogenicity of Elosulfase Alfa, an Enzyme Replacement Therapy in Patients with Morquio A Syndrome: Results from MOR-004, a Phase 3 Trial

CASE STUDY *Becky Schweighardt, Ph.D., Director, Immunogenicity Assessment, BioMarin Pharmaceutical, Inc.*

Elosulfase alfa is an enzyme replacement therapy (ERT) for the treatment of Morquio A. In a 24-week phase 3 trial, all treated patients developed anti-drug antibodies, and the majority developed neutralizing antibodies (NAb) capable of interfering with cellular receptor binding *in vitro*. Despite the universal development of anti-drug antibodies, elosulfase alfa treatment was both safe and well tolerated and immunogenicity was not associated with lack of treatment effect.

9:10 Case Study on Characterization of Immunogenicity to Multiple Domain Biotherapeutics

UNPUBLISHED DATA *Boris Gorovits, Ph.D., Director, PDM, Pfizer, Inc.*

An evaluation of an ADA response to an MDB based on drug risk factors, drug MOA, patient population and other parameters could facilitate prediction of safety consequences. This presentation will focus on a strategic approach to evaluation of MDB immunogenicity characteristics based on the program development requirements, including non-clinical and clinical translation. Potential issues and concerns will be discussed based on specific case studies.

9:40 Re-Assessment of Immunogenicity Risk Based on Clinical Data: Case Study of a Humanized IgG1 Monoclonal Therapeutic with a Knob-And-Hole Structure

Mauricio Maia, Ph.D., Bioanalytical Sciences, Genentech, Inc.

Initial clinical immunogenicity evaluation plans are often based upon an immunogenicity risk assessment that includes a myriad of molecule and patient factors, but prior to attaining clinical experience. Clinical data can and should modify this assessment. This presentation will describe a case study of a structurally novel biotherapeutic whose risk-based assessment was changed following analysis of clinical immunogenicity data derived from early-stage trials.

10:10 The Challenge of Pre-Existing Antibodies

Steven J. Swanson, Immunology Consultant, Steven J Swanson Consultant

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

NEUTRALIZING ANTIBODY ASSAYS

11:25 Development of Neutralizing Antibody Assays for Antibody Therapeutics with Cell Depletion MOA

Shan Chung, Ph.D., Senior Scientist, Bioanalytical Sciences, Genentech – A Member of the Roche Group

Monoclonal antibodies with mechanisms of action (MOA) involving cell depletion have been used successfully in treatment of a variety of malignant diseases. This presentation will describe development of a neutralizing antibody (NAb) assay for a humanized therapeutic antibody that depletes target tumor cells via effector functions such as antibody-dependent cell-mediated cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC), and antibody-dependent cell-mediated phagocytosis (ADCP). A general guidance on selection of NAb assay format for antibody therapeutics will also be presented.

11:55 Driving Factors for Choice of Immunogenicity/NAb Strategy

UNPUBLISHED DATA *Shalini Gupta, Ph.D., Director, Clinical Immunology, Amgen, Inc.*

Currently a clear strategy for choosing a cell-based or non cell-based assay for the detection of anti-drug neutralizing antibodies is not available. This talk will provide an overview of an AAPS white paper currently being compiled that provides three rationales for selecting the NAb assay format. These include (i) the mechanism of action of the drug; (ii) the risk of NAbs on patient safety and (iii) assay characteristics of the NAb assay. When applied together these 3 aspects can guide the strategy of NAb assay format selection in a consistent manner for the vast majority of biological therapeutics.

12:25 pm ImmunoCAP® ADA Bridging Assay – a Comparison of Different Immunoassay Formats

Sponsored by ThermoFisher SCIENTIFIC

Åsa Marknell DeWitt, Ph.D., Senior Scientist, Diagnostic Partnering, Thermo Fisher Scientific

The ImmunoCAP ADA bridging assay is an anti-drug-antibody assay based on an IVD platform. In this pilot study we have compared technical and inter assay performance of the ImmunoCAP ADA bridging assay with ELISAs to evaluate the robustness of the assays for global transferability. Customized assays are developed for the automated Phadia system, using standardized reagents. The features of the ImmunoCAP solid phase enables further characterization on the same platform, e.g. measurement of specific IgE and specific IgG4.

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

1:55 Session Break

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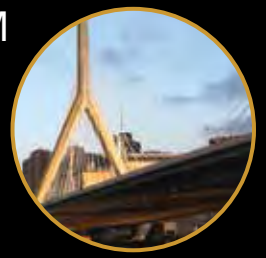
8th Annual | May 6-7

Immunogenicity Assessment & Clinical Relevance

Technologies and Strategies for Safe and Efficacious Products in the Clinic



OVERCOMING TARGET INTERFERENCE

2:10 Chairperson's Remarks
Meena Subramanyam. Ph.D., Vice President, Translational Sciences, Biogen Idec, Inc.

2:15 Case Studies on Troubleshooting Soluble Target Interference in Immunogenicity Assays in the Clinical Space
CASE STUDY *Qiang Qu, Ph.D., Senior Scientist, PDM, Pfizer, Inc.*
Soluble targets that form multimers can result in false positive signals in bridging assays. This presentation will focus on troubleshooting clinical immunogenicity assays with interference from the soluble target multimers found in the circulation of the intended population. Two case studies will be presented with their own distinctive approaches to overcome the target interference, and a general mitigation strategy will be discussed for clinical immunogenicity assay development.

2:45 Strategy for Overcoming Target Interference throughout Development
Olivier Petricoul, Ph.D., Senior Investigator II, DMPK-PK/PD, Novartis Institutes for Biomedical Research
While drug interference is a well-known phenomenon for immunogenicity assays and is routinely characterized and optimized during the development and validation of the assays, interference by the pharmacological target occurs only under particular circumstances and is assessed on a case by case basis. This presentation will review different strategies for overcoming target interference, and case studies will be shown to illustrate how an integrated PK/PD/IG assessment can help to assess the clinical relevance of the immunogenicity assay.

3:15 Meeting or Exceeding Regulatory Expectations for Anti-Drug Antibody Assays
Jim McNally, Ph.D., Senior Principal Scientist, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.
The goal of this talk will be to host an interactive session with the audience to discuss and to share our collective experiences with anti-drug antibody (ADA) assays and to ask the question "Should we meet or exceed expectations?" Are there examples where the pursuit of increased drug tolerance, improved sensitivity and greater characterization of the ADA response results in significant expenditures of time and effort without adding value to the project?

Potential discussion topics:

- Sensitivity of ADA assay vs. biological relevance
- Increased drug tolerance vs. process controls for sample collection
- Clinical impact of pre-existing reactivity

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

4:45 Problem-Solving Breakout Discussions

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

7:00 End of Day

THURSDAY, MAY 7

8:00 am Morning Coffee

IMMUNOGENICITY ASSESSMENT CHALLENGES IN THE CLINIC

8:30 Chairperson's Remarks
Shalini Gupta, Ph.D., Director, Clinical Immunology, Amgen, Inc.

8:35 Pre-Existing Antibodies: Are they always Meaningful?
UNPUBLISHED DATA *Lakshmi Amaravadi, Ph.D., Senior Director, Translational Medicine, Biogen Idec, Inc.*
The scientific community and the regulators alike have been performing investigations and evaluations to understand the relevance and potential impact of pre-existing antibodies on safety and efficacy. This presentation will review some of the considerations related to the evaluation of pre-existing antibodies, the experience so far and also present a case study to discuss the implications or lack thereof as it relates to detection of pre-existing antibodies.

9:05 Using Statistical Design of Experiment (DOE) in Assay Development to Reduce Drug Interference in Immunogenicity Assays
Dr Christopher Ehlinger, Senior Associate Scientist, Biologics Clinical Pharmacology
An acid dissociation approach is often used to overcome drug interference in immunogenicity assays for anti-drug antibody (ADA) detection. We utilize a statistical design of experiment (DOE) concept with nonhierarchical 4-Factor Split Plot design to thoroughly evaluate the effects of acid types, acid concentrations, temperature and duration of acidification of acid treatment conditions in the acid dissociation step of immunogenicity assays to improve drug tolerance and more accurately detect ADAs.

9:35 Advances in Improving Drug Tolerance of NAb assays
Christian Vettermann, Ph.D., Scientist, Clinical Immunology, Bioanalytical Sciences/PKDM, Amgen, Inc.
To achieve maximal sensitivity, NAb assays utilize a very low concentration of drug that can be easily neutralized by anti-drug antibodies. Therefore, exogenous drug contained in study samples is one of the most critical interference factors that can preclude NAb detection during the dosing phase. This presentation will focus on current approaches to improve drug tolerance of NAb assays through sample pretreatment and their limitations. The relevance of drug tolerance for the interpretation of study data will be discussed, and a novel strategy for detecting clinically impactful NAbs in the presence of high amounts of drug will be presented.

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

NABS / SAFETY OF IGE ADAS / IMMUNE COMPLEX DISEASE

11:05 Challenges Encountered for Cell-Based Neutralizing Antibodies Assays
Weifeng Xu, Ph.D., Senior Research Investigator, Bioanalytical Sciences, BMS

11:35 Evaluation of Antibodies of IgE Isotype to Omalizumab and their Potential Correlation to Anaphylaxis
CASE STUDY *Sally Fischer, Ph.D., Senior Scientist and Group Leader, Assay Development and Technology, Genentech, Inc.*
To better understand the risk of anaphylaxis in patients with allergic asthma receiving regulatory-approved omalizumab, a recombinant humanized monoclonal antibody, a post-marketing pharmacosurveillance study was initiated in March, 2009. As part of this study, an assay was developed to detect antibody of IgE isotype to omalizumab. This presentation will discuss the challenges and approaches in development of this assay as well as the outcome of this post-marketing commitment.

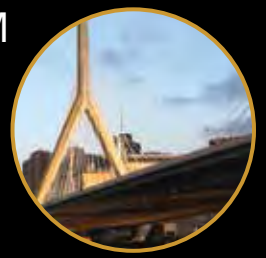
12:05 Cynomolgus Monkey Case Study of Immune Complex Disease
Deborah Finco, Ph.D., Senior Principal Scientist, Drug Safety R&D, Pfizer, Inc.
We developed a method to induce immune complex glomerulopathy (ICG) in non human primaytes (NHPs) using BGG as the immunogen. The goal was to evaluate possible immune related biomarkers to detect early glomerular injury in non-human primates. We investigated: complement receptor 1 levels on erythrocytes; levels of circulating immune complexes complement split products, macrophage chemotactic protein 1, and anti- BGG antibodies. BGG dosing was associated with changes in CR1, CIC, anti-BGG titers and serum complement split products. The utility as biomarkers will be further discussed during the presentation.

12:35 End of Conference

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC11: Overcoming the Challenges of Immunogenicity Assessment
**Separate registration required, please see page 4 for course details.*



Inaugural | May 7-8

Bioassays for Biologics

Techniques and Solutions for Biotherapeutics Development

Recommended Pre-Conference Short Course*

SC11: Overcoming the Challenges of Immunogenicity Assessment

**Separate registration required, please see page 4 for course details.*

Recommended Dinner Short Course*

SC14: Strategic Bioassay Design and Analysis

**Separate registration required, please see page 4 for course details.*

THURSDAY, MAY 7

ASSESSMENT OF MULTI-DOMAIN PROTEINS

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

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

1:50 Assessment of Neutralizing Anti-Drug Antibodies for Multi-Domain Biologics

Boris Gorovits, Ph.D., Director, PDM, Pfizer, Inc.

A growing number of research labs are now working on multi domain biologics (MDB) with a complex and multistep mode of action. As with any biotherapeutic, MDBs present a risk of immune response that could result in various types of clinical sequelae. This presentation will focus on risk-based considerations related to evaluation of neutralizing anti-MDB antibodies, the need and benefits of NAB domain specificity evaluation. Case studies will be presented to support proposed ideas.

2:20 Development and Validation of Novel SPR-Based Assays for Bispecific Molecules

Joerg Moelleken, Ph.D., Senior Scientist, Roche Pharmaceutical Research and Early Development, Large Molecule Research, Roche Innovation Center GmbH

Increasing complexity of novel biotherapeutics like bispecific antibodies or fusion proteins raises new challenges for functional characterization as compared to standard antibodies, since two individual interactions and the inter-dependency of binding events needs to be considered. Novel SPR-based binding assays allow parallel assessment of additional information and therefore can lead to a "total" description of the molecule. These assays be validated and enable fast development.

2:50 Bioassays for Antibody Maytansinoid Conjugates (AMCs) Having Multiple Activities

Gillian Payne, Senior Director, Bioanalytical Science, ImmunoGen, Inc.

All AMCs have potent maytansinoid-directed anti-tumor activity. Some AMCs also have additional antibody-directed anti-tumor activity. A control strategy for such AMCs will be presented.

3:20 iLite Reporter Gene Technology: Assay Sensitivity & Specificity Throughout The Drug Development Life Cycle

Sponsored by EURODIAGNOSTICA BIOMONITOR

Michael G. Tovey, Ph.D, Managing Director, Biomonitor SAS

Innovative, engineered reporter gene cell lines have been developed with a high degree of specificity, and sensitivity for the quantification of the activity of a diverse range of biopharmaceuticals. The same cell line in which drug-induced activity is normalized relative to the expression of an internal standard can be used in drug discovery, for the quantification of drug potency, and for the analysis of functional drug levels and anti-drug neutralizing antibodies in both pre-clinical, and clinical studies and post-market commitments without drug interference or serum matrix effects within 2 to 5 hours. A common normalized assay read-out also allows direct comparisons of the relative activity & immunogenicity of innovator molecules and biosimilars. The iLite technology has been used to develop highly sensitive and specific assays for critical targets including Her2, VEGF2, CD20, FGF21, IL-23, TNFββ and to quantify ADCC activity.

3:50 Refreshment Break

4:20 Problem-Solving Breakout Discussions

5:20 End of Day

5:15 Registration for Dinner Short Courses

FRIDAY, MAY 8

8:00 am Morning Coffee

ASSAY COMPARABILITY CASE STUDIES

8:30 Chairperson's Remarks

Boris Gorovits, Ph.D., Director, PDM, Pfizer, Inc.

8:35 Bridging Discovery to Development, Leveraging Technology for Accelerated Bioassay Development

UNPUBLISHED DATA

Han Li, Ph.D., Senior Research Investigator II, Lead Discovery and Optimization, Bristol Myers Squibb

To support the fast expanding biologics portfolio in BMS, a bioassay core team has been built in the Cellular Resource Group of Lead Discovery and Optimization department for bridging discovery and development. Our core team is to leveraging the discovery assay experiences, cell line development capacity, extensive cell line inventory and state of art technology platforms.

9:05 Application of Cell-Based Assays in Biologics Drug Discovery

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

The use of cell-based assays for primary HTS for identification of therapeutic biologics presents a number of extra challenges, due to sample tolerance and assay sensitivity, and therefore have primarily been used for hit to lead evaluation. We will discuss recent advances in high-throughput sample expression techniques that have opened up new possibilities for cell-based HTS within the biologics industry.

9:35 Improved Consistency and Efficiency by Applying Ready-to-Plate Cells in Immunogenicity Testing

Jenny Hu, MSc, Scientist, Bioanalytical Science, PKDM, Amgen, Inc.

A cell-based bioassay, often used in detecting neutralizing antibodies (NAb) against protein therapeutics, can not only produce inconsistent response due to cell age and culture conditions, but also is labor intensive in maintaining a continuous culture. Here we describe 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.

10:05 Coffee Break

TECHNOLOGIES AND TOOLS FOR BIOANALYTICAL METHOD DEVELOPMENT

10:35 Targeted & Functional Proteomics Approaches for High-Throughput Assays

Manuel Fuentes, Ph.D., Scientist, Medicine, Proteomics Unit, Cancer Research Center, University of Salamanca-CSIC

Targeted proteomics is a powerful approach that enables quantitative analysis of peptides from complex biological samples with high sensitivity and specificity. We report a method for high-throughput, cost-efficient empirical discovery of optimal proteotypic peptides and fragment ions for targeted proteomics applications using *in vitro*-synthesized proteins. We demonstrate that low-abundance targets and empirically derived proteotypic peptides for 98% of the target proteins. We show that targeted proteomic assays developed using our approach facilitate robust *in vivo* quantification of clinically relevant human proteins.

11:05 Acoustic Membrane Micro-Particle: An Emerging Technology in the Ligand Binding Assay Space

CASE STUDY

Shannon D. Chilewski, Research Scientist II, Analytical & Bioanalytical Development, Bristol-Myers Squibb

This presentation will share a case study addressing key points on how we approached the eva

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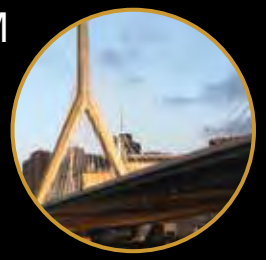

Inaugural | May 7-8

Bioassays for Biologics

Techniques and Solutions for Biotherapeutics Development

the Acoustic Membrane Micro Particle (AMMP) technology. The instrument has an oscillating membrane where an immunocomplex containing the analyte is captured for detection. The membrane is sensitive to mass changes that affect its vibrating frequency in a manner proportional to the analyte's concentration. The main potential advantages over established platforms were sensitivity and throughput. The evaluation focused of 4 main points, which will be reviewed as part of this talk.

11:35 Optimization of a Bioassay for a Multi Component Immunomodulator using Design of Experiment

CASE STUDY

Jasmin Barbara Hebeis, Ph.D., Principal Scientist, CMC Bioassay and Genomics, NDA Analytics

We have developed a potency assay for a multi peptide immunoregulator using an IL-2 ELISpot read-out. This was then optimised using Design of Experiment (DoE). As a result, the assay window and net response were improved considerably, with limited effect on the inter-replicate variability. The method was validated to ICH guidelines and is currently in use for cGMP compliant potency testing for clinical release and stability.

12:05 pm Featured Poster Presentations

Two exceptional posters will be selected by the scientific advisory committee to give brief, 15 minute podium presentations on their work. For more information on presenting a poster, see the registration page.

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

1:05 Refreshment Break

WORKING WITH DIFFERENT ASSAY TYPES

1:35 Chairperson's Remarks

Susan E. Rutberg, Ph.D., Senior Scientist, Analytical Development, Genzyme

1:40 Strategy for the Use of Orthogonal Methods to Characterize New CHO Host Cell Protein Reagents

Carl Co, Ph.D., Scientist, Analytical Development, Biogen Idec

This presentation describes a strategy used to generate new HCP reagents. Multiple orthogonal techniques including 2D-DIGE, 2D Western Blot and sandwich immunoassays are utilized to characterize different antigens and antibodies. Case studies are presented which highlight different challenges in the generation of new HCP reagents.

2:10 A High Performance Non-Radioactive Potency Assay for Measuring Cytotoxicity: A Full Substitute of Chromium-Release Assay Targeting the Regulatory-Compliance Objective

UNPUBLISHED DATA

Alexis Rossignol, Ph.D., R&D Project Manager, Bioassays, Clean Cells

A novel cytotoxicity potency assay will be described, combining all the advantages of the chromium-release assay with a non-radioactive read-out method. Unlike existent non-radioactive assays (LDH release, CD16 engagement, etc.), the new assay specifically measures the lysis of target cells while exhibiting similar performances (sensitivity, accuracy, precision) to the chromium method, revealing great potentialities for standardized ADCC, CDC or apoptosis activity measurement on a fully regulatory-compliant basis.

2:40 Implementation of Statistical Methods during Method Development for a Cell-Based Potency Assay

Susan E. Rutberg, Ph.D., Senior Scientist, Analytical Development, Genzyme

Potency testing for biological therapeutics often relies on a measurement of the relative potency of a test sample compared with a reference standard. A method for accurately comparing the dose response curves that considers parallelism of the data must be selected. The USP guidelines promote following an equivalence testing approach for parallelism testing of bioassay data. A case history demonstrating the adoption of the USP guidelines for the determination of relative potency values will be presented.

3:10 Why Do We Need Dedicated Guidelines to Develop and Validate Relative Potency Assays? Implementation of USP Approach on Binding and Cell-Based Assays

CASE STUDY

Gaël Debauve, Analytical Sciences for Biologicals, Bioassay Development Laboratory, UCB Pharma S.A., Braine-L'Alleud, Belgium

We will review the limitations of classical development/validation approaches (i.e. ICHQ2R1) when applied to relative potency assays and how the USP chapters (1032, 1033 and 1034) were successfully implemented on binding and cell-based assays. Through case studies, we will present how fitting model and equivalence limits were defined and how validation characteristics can support the choice of the assay format.

3:40 Potency Assay Strategies for Accelerated Program Timelines

Zulfia Babadjanova, Associate Principal Scientist, Biologics Analytical Testing, Merck

Potency assays are some of the most technically challenging analytical assays to develop. They often require long lead times and may require specialized reagents or cell lines. However data generated from these assays are critical to understanding a product's stability profile, the impact of manufacturing changes, and for supporting formulation decisions. The challenges of developing high quality potency assays are even more acute when faced with an accelerated program timeline. In this talk, I will discuss potency assay strategies for a biologic on an accelerated timeline.

4:10 End of Conference

Inaugural | May 4-5

Fusion Protein Therapeutics

Engineering Next-Generation Biologics

MONDAY, MAY 4

7:00 am Registration and Morning Coffee

PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks

8:40 Cancer Stem Cells and Mechanisms of Malignant Progression

Robert A. Weinberg, Ph.D., Founding Member, Whitehead Institute for Biomedical Research; Professor, Biology, Massachusetts Institute of Technology

The cell-biological program termed the epithelial-mesenchymal transition (EMT) plays a role in conferring aggressive traits on carcinoma cells. In addition, it generates cancer stem cells (CSCs) that have the ability, following dissemination, to serve as founders of new metastatic colonies. The relationship between these CSCs and the SCs residing in normal tissues, and the participation of the CSCs in metastatic dissemination will be described.

9:25 Building an Antibody Discovery Company in a Crowded Field – the Adimab Story

Tillman Gerngross, Ph.D., CEO, Co-Founder, Adimab

The presentation will cover the evolution of Adimab from its founding in 2007 to becoming one of the few privately held profitable biotech companies in the last decade. Industry trends and specific strategic decisions along the way will be discussed and used to illustrate the importance of integrating finance and scientific information to build successful capital efficient biotech companies.

10:10 Coffee Break

ACHIEVING SUCCESS WITH THERAPEUTIC FUSION PROTEINS

10:45 Chairperson's Remarks

Fredrik Frejd, Ph.D., Chief Scientific Officer, Biotherapy, Affibody AB

10:50 KEYNOTE PRESENTATION:

Engineering Clotting Factor Fc Fusion Proteins for the Treatment of Hemophilia

Jennifer Dumont, Ph.D., Director, Medical Affairs, Biogen Idec, Inc.

Prophylactic clotting factor replacement in patients with hemophilia improves outcomes, but requires frequent injections with conventional therapies. Recombinant fusion of the Fc domain of human IgG1 with clotting factors VIII or IX was performed to extend the half-life of these factors and provide the potential to reduce the frequency of injections needed to control and prevent bleeding in hemophilia A and B patients, respectively. The Fc fusion factors are configured with monomeric factor VIII or IX covalently fused to dimeric Fc. These protein fusion products are now approved for the treatment of hemophilia and the development programs will be discussed.

11:20 FEATURED PRESENTATION:

Therapeutic Fusion Proteins: Current Trends and Challenges

Stefan Schmidt, Ph.D., Vice President, DSP, Rentschler Biotechnology

This talk examines the state-of-the-art in developing fusion proteins for biopharmaceuticals, shedding light on the immense potential inherent in fusion protein design and functionality. First, I will present a comprehensive overview on the current trends, and second, I will address challenges and how to overcome them.

Sponsored by novozymes

11:50 Veltis® Technology: Engineered Albumins for Optimized Serum Half-Life Extension

Karen Bunting, Ph.D., Senior Research Scientist, Molecular Biology and Fermentation, Novozymes Biopharma UK

Short circulatory half-life represents a major obstacle for many protein and peptide-based therapeutic agents, resulting in increased dosing with the consequent risk of side effects and reduced patient compliance. Molecule half-life can be significantly improved by association, conjugation or fusion to albumin, due to both size and recycling via the neonatal Fc receptor (FcRn). We will describe rationally engineered albumins with increased FcRn affinity and their application to improve the pharmacokinetic properties of therapeutic candidates.

Sponsored by BIOSCALE

12:20 pm Luncheon Presentation I to be Announced

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

1:20 Session Break

ENGINEERING ENHANCED PROPERTIES

1:50 Chairperson's Remarks

Mark Distefano, Ph.D., Professor, Chemistry and Medicinal Chemistry, University of Minnesota

1:55 FEATURED PRESENTATION:

PASylation: The Preparation of Fusion Proteins with Extended Plasma Half-Life Based on a Biological Alternative to PEG

Arne Skerra, Ph.D., Professor, Technische Universität Munich; Chief Scientific Officer, XL-protein GmbH

PASylation allows the simple genetic fusion (or chemical coupling) of a therapeutic protein or peptide with a voluminous hydrophilic polypeptide composed of Pro, Ala, and/or Ser to retard kidney filtration. PAS sequences show surprisingly similar biophysical properties to PEG but, in contrast, are biodegradable. PASylation has been successfully applied to antibody fragments, growth hormones, cytokines and other biologics; for example, PAS-leptin fusion proteins show much enhanced satiety effects in mice.

2:25 Re-Engineering Lysosomal Enzyme Therapeutics for the Brain as IgG Fusion Proteins that Penetrate the Blood-Brain Barrier

Ruben Boado, Ph.D., Vice President, R&D, ArmaGen, Inc.

Lysosomal enzymes are large molecule drugs that do not cross the blood-brain barrier (BBB). However, BBB-penetration of enzyme therapeutics is enabled by re-engineering the recombinant enzyme as IgG fusion proteins, wherein the IgG transport domain targets a specific endogenous receptor-mediated transporter within the BBB, such as the human insulin receptor (HIR). The therapeutic domain of the IgG fusion protein exerts the pharmacological effect in the brain once across the BBB.

2:55 Pathogenesis-Mediated Targeted Cytokine Delivery

UNPUBLISHED DATA

Yuti Chernajovsky, Ph.D., FRCP, Emeritus Professor, Molecular Medicine, William Harvey Research Institute, Barts and The London School of Medicine and Dentistry

I will describe how fusion proteins of the latency associated peptide (LAP) from TGFβ with therapeutic cytokines can be used to safely increase the half life of cytokines, confer latency and, using matrix metalloproteinase activity found at sites of disease, specifically release the therapeutic moiety where needed without side effects. A case will be made in favor of the use of latent cytokines as compared to anti-cytokine antibodies due to their novel pharmacodynamic properties.

3:25 Affibody-Based Ligand-Trap that Block IL-17 with Unparalleled *in vivo* Potency and Long Plasma Half-Life

Fredrik Frejd, Ph.D., Chief Scientific Officer, Biotherapy, Affibody AB

Il-17 is a potent inducer of tissue inflammation involved in auto-inflammatory disease. Here we describe the engineering of a ligand trap fusion protein designed to block IL-17 mediated pathology. The ligand trap is based on two small Affibody scaffold domains for IL-17 inhibition, and an albumin binding domain for extended plasma half-life supporting once monthly dosing. The fusion protein has unparalleled potency with complete blocking of the dimeric interleukin.

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

4:35 Problem-Solving Breakout Discussions

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:50 End of Day

CONTINUED

Inaugural | May 4-5

Fusion Protein Therapeutics

Engineering Next-Generation Biologics

TUESDAY, MAY 5

8:00 am Morning Coffee

STRATEGIES FOR ENGINEERING FUSION PROTEIN THERAPEUTICS

8:25 Chairperson's Remarks

Stefan Schmidt, Ph.D., Vice President, DSP, Rentschler Biotechnology

8:30 Enzymatic Assembly of Fusion Proteins

Mark Distefano, Ph.D., Professor, Chemistry and Medicinal Chemistry, University of Minnesota

Fusion proteins prepared by linking domains manifesting different functions have enormous potential for biomedical applications. Chemoenzymatic methods involving the enzymatic incorporation of chemical linkers coupled with bioorthogonal reactions greatly increase the repertoire of possible constructs that can be obtained. This presentation will focus on various protein fusions and assemblies that have been prepared using enzymatic modification with farnesyltransferase and subsequent chemical ligation.

9:00 Development of Affibody® C5 Inhibitors for Versatile and Efficient Therapeutic Targeting of the Terminal Complement Pathway

Patrik Strömberg, Ph.D., Project Leader, R&D; Principal Scientist, Nonclinical Safety and Pharmacology, Swedish Orphan Biovitrum AB (SOBI)

We are developing protein therapeutics against complement component C5, utilizing the innovative Affibody scaffold for protein targeting. During lead generation and optimization, large efforts were made to optimize PK/PD properties, i.e., maximizing the plasma persistence of this small protein while maintaining inhibitory potency. In particular, pioneering studies with a novel albumin binding domain (ABD) technology were performed that ultimately generated the first clinical candidate from this program.

9:30 Functional Assay Strategies for Bispecific Antibodies and Fusion Proteins

UNPUBLISHED DATA *Jörg Moelleken, Ph.D., Senior Scientist, Roche Pharmaceutical Research and Early Development, Large Molecule Research, Roche Innovation Center Penzberg*

The increasing complexity of novel biotherapeutics comprising of bispecific antibodies and fusion proteins raise new challenges for functional characterization as compared to standard antibodies. Besides varying binding sides, additional biologically relevant aspects like bi-specificity must be addressed now. This presentation shows points to consider relevant from lead identification until lead characterization.

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

TRAIL (TUMOR NECROSIS FACTOR-RELATED APOPTOSIS-INDUCING LIGAND) FUSION PROTEINS

10:50 Development of TRAIL-Based Bifunctional Proteins Platform for Targeted Anticancer Therapy

Jerzy Pieczykolan, Ph.D., Head, Research and Principal Investigator, Adamed Group

11:20 Hexavalent Agonists Targeting Receptors of the Tumor Necrosis Factor Superfamily

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

Apogenix has engineered TRAIL mimetics with three Apo2L/TRAIL protomer subsequences genetically fused into one polypeptide chain. This trivalent single-chain TRAIL-receptor-binding domain (scTRAIL-RBD) was fused to a mutated Fc-part of human IgG1 to create a hexavalent scTRAIL-RBD dimer (scTRAIL-RBD-Fc). The underlying engineering concept was successfully transferred to CD40-ligand (CD154), resulting in a hexavalent CD40-agonist (scCD40L-RBD-Fc) suitable for clinical development. We will present our results on both agonists and discuss their impact on the design of novel TNFR super-family targeting biologics.

11:50 Cancer Therapy with TR3, a Genetically Stabilized TRAIL-Based Drug Platform with Increased Activity, Stability, and Targeting Capabilities

Dirk Spitzer, Ph.D., Instructor in Surgery, Washington University School of Medicine

Soluble TRAIL has a tremendous potential as a cancer drug but cannot form bioactive trimers when produced from monomeric cDNAs in mammalian cells. We solved these limitations by designing a head-to-tail fusion protein, resulting in the constitutive TRAIL trimer TR3. This new drug platform is extremely versatile, since it is generically extensible in modular fashion, while the domain stoichiometry is strictly controlled. Here, we will emphasize the latest optimization strategies performed on our MUC16-targeted cancer drug Meso-TR3.

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

ANTIBODY FUSIONS

2:00 Chairperson's Remarks

Dirk Spitzer, Ph.D., Instructor in Surgery, Washington University School of Medicine

2:05 Potential Role of LEC/Antibody Fusion Protein in the Immunotherapy of Cancer

Alan L. Epstein, M.D., Ph.D., Professor, Pathology, University of Southern California Keck School of Medicine

A novel fusion protein consisting of the human chemokine LEC and a human antibody that targets degenerative regions of tumors has been found to be an effective reagent for the immunotherapy of cancer. Used with inhibitors of tumor-induced immunosuppression, experimental tumors show dramatic regression after IV treatment. Due to its broad applicability and unique mechanism of action, this reagent has high potential in enhancing current immunotherapy approaches and vaccine technology.

2:35 Antibody-IFN Fusion – A Combination of ADC and Targeted Immunotherapy

Sanjay D. Khare, Ph.D., President and CEO, ImmunGene, Inc.

ImmunGene's proprietary technology empowers antibodies by genetically engineering them with the tumor cell-killing cytokines, thereby combining the exquisite specificity of antibodies with the potent cytotoxic effects of cytokines. Antibody-cytokine fusion proteins are designed to be inactive systemically (against healthy cells) at the therapeutic doses, but stable in the bloodstream while efficiently targeting and killing cancer cells. This approach spares non-targeted (healthy) cells and thus reduces many of the known toxic effects of systemically administered cytokines while greatly enhancing the anti-tumor activity of antibodies.

3:05 Sponsored Presentation *(Opportunity Available)*

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

CONQUERING DISEASE

4:25 Cancer Stem Cell Therapeutics

Agamemnon A. Epenetos, Ph.D., Chairman, Trojan Technologies, Ltd.

It is likely that cancer stem cells, (CSCs) may be a key reason for the failure of current therapies. The NOTCH pathway is an important pathway in cancer stem cells. We have generated a hybrid protein (TR4) which translocates into the nucleus, suppresses NOTCH and eliminates human tumor growth; along with microparticles (MPs) derived from mesenchymal cells loaded with microRNAS. These MPs can fuse with tumors and affect tumor growth.

4:55 Discovery and Development of Novel Ig-GAIM Fusion NPT088 for Alzheimer's Disease

CASE STUDY *Richard A. Fisher, Ph.D., Chief Scientific Officer, NeuroPhage Pharmaceuticals*

NPT088 is an Ig fusion displaying two copies of the General Amyloid Interaction Motif (GAIM) that targets misfolded protein assemblies. GAIM activities include potent (nM) binding to multiple types of amyloid fibrils, inhibition of misfolded protein assembly, cytoprotection from oligomer mediated toxicity, and disruption of amyloid structure. NPT088 has been tested in transgenic disease models, and after systemic administration NPT088 mediates reduction of pathology and improvements in behavior and cognition.

5:25 End of Conference

CONTINUED

Inaugural | May 4-5

Fusion Protein Therapeutics

Engineering Next-Generation Biologics

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC12: Production Challenges for Complex Biologics: ADCs, Bispecific & Fusion Proteins

**Separate registration required, please see page 4 for course details.*

5th Annual | May 6-7

Engineering ADCs

Pushing the Envelope in ADC Design with Novel Payloads, Linkers and Conjugation Chemistries

Recommended Pre-Conference Short Course*

SC12: Production Challenges for Complex Biologics - ADCs, Bispecifics & Fusion Proteins

**Separate registration required, please see page 4 for course details.*

WEDNESDAY, MAY 6

7:00 am Registration and Morning Coffee

NOVEL PAYLOADS & LINKERS

8:00 Chairperson's Remarks

Peter Park, Ph.D., Vice President, Biology, Mersana Therapeutics

» 8:10 KEYNOTE PRESENTATION:

Lessons from Kadcyla™: The Future of ADCs in Oncology and Beyond

Fred Jacobson, Ph.D., Staff Scientist, Kadcyla™ Technical Development Leader, Protein Analytical Chemistry, Genentech, Inc.

8:40 Fleximer Next-Generation ADCs: Creating ADCs for Low Expression Targets and Improving Therapeutic Index

Natalya Bodyak, Ph.D., Senior Director, Biology, Mersana Therapeutics

Mersana has developed novel, next-generation antibody-drug conjugation platforms which enable the creation of highly differentiated ADCs for a variety of solid tumor targets and that overcome many of the limitations of existing ADC approaches. The development and application of Mersana's Fleximer-based Dolaflexin ADC platform will be described, and its potential to address low-expression antigens and potentially improve clinical outcomes for a variety of cancer patients will be highlighted.

9:10 Drug and Cytokines: Synergistic Payloads for Monoclonal Antibodies

Dario Neri, Ph.D., Professor, Department of Chemistry and Applied Biosciences, Swiss Federal institute of Technology (ETH Zurich)

This presentation will illustrate preclinical and clinical experience, gained in collaboration with Philogen, related to the development of human antibodies which target components of the pathological extracellular matrix and which can be "armed" with cytotoxic drugs and/or with cytokines. A comparative analysis will be presented.

9:40 Cancer Stem Cell Targeting with Antibody-Drug Conjugate Payloads and Linker Technologies

UNPUBLISHED DATA

Sourav Sinha, Ph.D., CEO, Oncolinx

A challenge with current antibody-drug conjugates (ADCs) is to improve patient outcomes by circumventing drug resistance, disease recurrence, and cancer stem cells. We explore a novel cytotoxic payload, Azonafides, that can be integrated into ADC platforms. This cytotoxin is more stable in circulation, has unique mechanisms of action, and is derived from natural products. Azonafides create an exciting clinical opportunity to improve the therapeutic window, efficacy, and safety of ADCs.

10:10 Homogeneous ADCs Bearing Two Different Payloads Show Strong Synergistic Killing Effect *in vivo*

Sean Hu, Ph.D., Senior Vice President, Biotherapeutics Discovery, Dophen Biomed

Two different toxins were conjugated site-specifically to the endogenous glutamine residues of one mAb molecule by engineered transglutaminase in a single step reaction at >95% yield. Such a homogeneous hybrid (ADC) displays strong synergy in tumor cell killing in both *in vitro* cell based assays and xenograft mice in comparison to ADCs with each toxin individually.

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

11:25 A pH-Tunable Linker: The Next Generation of Versatile Linkers for ADC

UNPUBLISHED DATA

Cindy Jan Choy, Ph.D., Postdoctoral Researcher, Chemistry, Washington State University

We have discovered a novel pH-sensitive chemical linker scaffold that can be tuned to release molecules at various pH values. The tunability of a pH-triggered phosphoramidate linker is advantageous for intracellular drug release because it allows the tailoring of the drug release profile to meet specific application needs; an attribute that is absent in current linker technologies. In addition, the pH-triggered phosphoramidate linker does not require intracellular enzymatic action to initiate drug release from the ADC.

11:55 Enabling Splicing Inhibitors as ADC Payloads

Edmund Graziani, Ph.D., Head, Bioconjugation Chemistry and Natural Products Discovery, Pfizer, Inc.

Antibody-drug conjugates (ADC's) for the treatment of refractory malignancies is an area of intense focus across the pharma industry and to date more than 30 ADC's are in clinical trials. A majority of these utilize microtubule inhibitors (MTI's) such as Auristatin or Maytansine as the payload. Discovery of novel payload class to further advance this field would undoubtedly enhance the utility of the antibody-drug conjugate based anticancer drugs. This talk will focus on the discovery and enablement of a novel class of spliceostatin-based splicing inhibitors as ADC payloads.

12:25 pm Sortase-Mediated Generation of Site-Specifically Conjugated Next-Generation ADCs for Treatment of Cancer

Sponsored by NBE therapeutics

Ulf Grawunder, Ph.D., CEO, NBE-Therapeutics Ltd.

Antibody drug conjugates (ADCs) have recently been proven to be highly potent anti-tumor drugs, typically exceeding the efficacy of conventional monoclonal antibodies (mAbs). ADCs are currently produced by chemical conjugation of the small-molecule toxin to the mAb through lysine or cysteine side chains, leading to heterogeneous mixtures that present challenges with respect to analytical characterization and manufacturing. Furthermore, the individual components of these mixtures behave differentlywith respect to their pharmacokinetic, efficacy, and safety profiles. As a consequence, there is great interest in the further development of drug conjugation technologies, with a particular focus on site-specific payload conjugation. Here, we present an enzymatic conjugation platform called SMACTM (sortase-mediated antibody conjugation) technology that allows for efficient generation of homogenous ADCs with pre-defined drug-to-antibody ratios. Data will be presented demonstrating that SMACTM technology is capable of producing homogeneous ADCs with high potencies for tumor killing *in vitro* and *in vivo*.

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

1:55 Session Break

SITE-SPECIFIC CONJUGATION TECHNOLOGIES

2:10 Chairperson's Remarks

David Rabuka, Global Head, R&D, Chemical Biology, Catalent Pharma Solutions

2:15 New Site-Specific, Traceless Antibody Conjugation Methodology

UNPUBLISHED DATA

Gonçalo Bernardes, Ph.D., Group Leader, Royal Society University Research Fellow, Department of Chemistry, University of Cambridge

Our work explores the interplay between effector molecules, targeting ligands and site-specific protein conjugation chemistry to create safer, more selective and efficient cancer therapeutics. This lecture will cover recent examples of emerging areas in our group in (i) site-specific modification of antibodies via Aza-Michael addition at chemically installed dehydroalanine residues – a new traceless drug-release strategy at slightly acidic pH and (ii) use of carbon monoxide (CO) as an immunomodulator signalling molecule for applications in cancer therapeutics.

2:45 Engineering Site-Specific ADCs

Pam Thompson, Ph.D., Scientist I, Antibody Discovery and Protein Engineering, MedImmune

Antibody-Drug Conjugates (ADCs) are commonly produced by conjugating cytotoxic drugs to antibodies through lysine side chains or native cysteine thiols, which yield heterogeneous conjugates with complex biophysical properties. To limit these liabilities, we have designed, characterized, and validated antibody variants which allow precise control of the site of conjugation. The strategies presented herein for engineering site-specific ADCs allow for controlled drug loads, optimal serum stability, and potentially decreased off-target toxicity.

CONTINUED

5th Annual | May 6-7

Engineering ADCs

Pushing the Envelope in ADC Design with Novel Payloads, Linkers and Conjugation Chemistries

3:15 Sponsored Presentation *(Opportunity Available)*

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

4:45 Site Specific ADC Generation Using SMARTag™ Technology

David Rabuka, Global Head, R&D, Chemical Biology, Catalent Pharma Solutions

- Enabling precise, and programmable, site-specific chemical protein modification
- The development of novel conjugation chemistry resulting in ADCs with enhanced stability
- Linker chemistry that optimises the potency of the cytotoxic payload

5:15 Site-Specific Conjugation by BTG Improves the Therapeutic Index of ADC *In Vivo*

Delphine Bregeon, Ph.D., Scientist, Innate Pharma

We describe the *in vitro* and *in vivo* characterization of four novel ADCs that are based on the anti-CD30 antibody cAC10, which has the same polypeptide backbone as ADCETRIS®, and compare the results with the latter. Bacterial transglutaminase (BTG) was exploited to site-specifically conjugate derivatives of monomethyl auristatin E (all comprising a cleavable linker) to the glutamines at position 295 and 297 of cAC10, thereby yielding homogeneous ADCs with a DAR of 4. The results suggest that homogenous BTG ADCs display improved pharmacokinetics and better therapeutic indexes compared to chemically modified ADCs with variable DARs.

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

7:00 End of Day

THURSDAY, MAY 7

8:00 am Morning Coffee

ENGINEERING ADCs FOR IMPROVED PROPERTIES

8:30 Chairperson's Remarks

Andreas Pahl, Ph.D., CSO, Heidelberg Pharma

8:35 Engineering of Amanitin-Based ADCs to Improve the Therapeutic Index

Andreas Pahl, Ph.D., CSO, Heidelberg Pharma

Payloads of today's ADCs are exclusively based on compounds acting on microtubules or DNA suffering from various limitations. New generations of payloads enter the field including Heidelberg Pharma's amanitin, a highly effective inhibitor of the eukaryotic RNA Polymerase II. Due to its unique mode of action and its hydrophilicity this toxin differs from well-known payloads. We will present new developments on engineering amanitin-based ADCs to improve the tolerability thereby improving the therapeutic index.

9:05 An EGFR Targeting Antibody-Drug Conjugate Engineered for Increased Tumor Specificity

UNPUBLISHED DATA *Christopher Thanos, Ph.D., Director, New Molecular Entities, New Molecular Entities, Halozyme Therapeutics*

Cancers with KRAS/BRAF mutations and EGFR+ genotypes are resistant to EGFR targeting agents and are a significant unmet medical need. We hypothesized that an anti-EGFR ADC could be active against these tumors. In an effort to eliminate the known dermal toxicity associated with anti-EGFR therapy, we engineered an EGFR targeting mAb with significant binding to EGFR+ tumors and attenuated binding to human skin in murine xenografts. The corresponding ADC demonstrated significant activity against multiple KRAS/BRAF mutated tumors *in vivo*, suggesting a possible new approach for treatment over a broad range of tumor types.

NEW FORMATS & DESIGNS - NEXT GEN ADCs, ALTERNATIVE AND NON ANTIBODY PROTEIN CONJUGATES

9:35 Meditopes: Development of Noncovalent Peptide-Fab Interaction to Rapidly and Specifically Add Functionality to mAbs

Krzysztof Bzymek, Ph.D., Staff Scientist, Drug Discovery and Structural Biology, Core Department of Molecular Medicine, Beckman Research Institute of City of Hope

mAbs require chemical conjugation and/or extensive re-engineering to deliver toxins, imaging agents and other functionalities to diseased tissues. Herein, we present the discovery of a novel cyclic peptide (aka a meditope) that binds to the cavity of cetuximab Fab. While this binding site is unique to cetuximab, it can be grafted on to mAbs. Studies will be presented highlighting the rapid and efficient functionalization of mAbs.

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

11:05 Peptide-ADCs Cross the Blood-Brain Barrier and Extend Survival in Mice with Intracranial HER2-Positive Tumors

Jean Lachowicz, Ph.D., CSO, R&D, Angiochem

ADC therapy for metastatic brain tumors requires that the mAb crosses the blood-brain barrier. We have successfully engineered peptides (Angiopeps) which utilize Receptor-mediated transcytosis to enter brain. A three-way conjugation between Angiopep, cytotoxic and mAb results in a targeted cytotoxic that can reach tumors in the brain. Survival studies in mice with brain-implanted tumor cells were conducted to select the optimal peptide/linker/payload combination, which resulted in significant improvement in survival.

11:35 OptiLinked Antibody Fragments for ADCs

Ioanna Stamati, Ph.D., Team Leader, Bioconjugation, Antikor Biophama Ltd.

Fragment based ADCs offer the prospect of a wider therapeutic window due to a controllable PK profile and better tumour penetration. Using OptiLinked anti-HER2 scFvs high DAR (≈12) ADCs were synthesised using various payloads. These retained solubility and exhibited limited/no aggregation even at high DAR. This is further demonstrated by the *in vivo* PK profile of the ADCs which is similar or slower to that of the free antibody.

Sponsored by AMUNIX

12:05 pm Tumor-Targeted Drug Delivery via XTEN, a Protein-Polymer with Precisely Controlled Chemical Composition

Volker Schellenberger, Ph.D., President and CEO, R&D and Strategy, Amunix, Inc.

Amunix developed a hydrophilic protein-polymer (XTEN™) that can be used for half-life extension and drug delivery. XTEN is stable in circulation but rapidly degraded upon internalization. XTEN facilitates the orthogonal conjugation of multiple toxins and targeting moieties with precisely controlled stoichiometry. The hydrophilic nature of XTEN allows high drug loads and reduces toxicity resulting from non-specific internalization. XTEN-drugs can linked to many tumor-specific ligands such as peptides, scaffolds, and antibody fragments and full antibodies.

12:35 End of Conference

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC13: Physicochemical and Biophysical Characterization of Antibody-Drug Conjugates

**Separate registration required, please see page 4 for course details.*

5th Annual | May 7-8

ADCs: Preclinical and Clinical Updates

Leveraging Lessons Learned in Preclinical and Early Clinical to Strategize for the Future

THURSDAY, MAY 7

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

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

» 1:50 KEYNOTE PRESENTATION:

ADCs: Building on the Past, Delivering on the Present and Optimizing for the Future
Clay B. Siegall, Ph.D., President, CEO and Chairman of the Board, Seattle Genetics, Inc.
Antibody-drug conjugates represent an increasingly important therapeutic approach for the treatment of cancer, with two ADCs currently approved by the FDA and dozens of other programs progressing through clinical trials and preclinical development. This presentation will highlight ADCETRIS® (brentuximab vedotin) and other ADCs in development. In addition, advances in ADC technology will be discussed.

TRANSLATIONAL CONSIDERATIONS

2:20 Optimizing ADC-Based Therapies in Cancer
Robert Lutz, Ph.D., Vice President, Translational Research and Development, ImmunoGen, Inc.
Our growing clinical experience with antibody-maytansinoid conjugates is leading to an enhanced understanding regarding critical attributes for their success. This presentation will highlight a recent clinical/translational R&D effort leading to a change in the treatment paradigm of an ADC.

2:50 Antibody-Drug Conjugates: Translational Considerations
CASE STUDY *Isabel Figueroa, Ph.D., Principal Scientist, DMPK and Disposition, Biologics Discovery Operations, MRL Biologics*
Antibody-Drug Conjugates (ADCs) are increasingly employed as novel targeted therapies. ADCs combine the exquisite selectivity of targeted antibodies and high potency of small molecule drugs with the aim in achieving the desired therapeutic objectives. Successful strategies for the development of the lead ADC candidates will require comparative investigations and integration of knowledge with respect to target- and modality-related considerations across species. Here, we have attempted to address some of the key translational considerations critical for early development of ADCs in an integrated fashion.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Refreshment Break

4:20 Problem-Solving Breakout Discussions

5:20 End of Day

5:15 Registration for Dinner Short Course(s)*

Recommended Dinner Short Course(s)*

SC13: Physicochemical and Biophysical Characterization of Antibody-Drug Conjugates
**Separate registration required, please see page 4 for course details.*

FRIDAY, MAY 8

8:00 am Morning Coffee

TRANSITIONING TO THE CLINIC

8:30 Chairperson's Remarks
Alan Rigby, Ph.D., Vice President, Antibody-Drug Conjugate Biology, Eli Lilly and Company

8:35 Preclinical Development of IGN786: A Homogeneous Antibody-Drug Conjugate Directed Against C16orf54 for the Treatment of Hematological Malignancies
Jason Damiano, Ph.D., Director, Discovery Research, Igenica Biotherapeutics
Using Igenica's proprietary proteomics-based target discovery technology, C16orf54 was identified as a novel cell-surface antibody target. C16orf54 is overexpressed with high prevalence in primary CLL and AML tumor specimens and has restricted expression in normal tissues. Using Igenica's proprietary SNAP technology, a homogeneous ADC directed against C16orf54 was developed. The IGN786 clinical candidate is highly efficacious in C16orf54-expressing xenograft models.

9:05 Advances in ADC Development at Pfizer Oncology
Puja Sapra, Ph.D., Senior Director, Oncology Research Unit, Pfizer, Inc.
This presentation will highlight the innovations made in Pfizer in terms of development of novel linker-payloads, conjugation chemistries and target identification for ADC development. Case studies will be used to elaborate on the multifaceted optimization required to yield a viable clinical candidate. Highlights from late stage preclinical and clinical ADCs will be discussed including candidates targeting tumor-initiating cells and Notch pathway. Finally, translational biology and combination strategies to enable clinical development of ADCs will be discussed.

9:35 Molecular Integrity of Antibody-Drug Conjugates: Applying Preclinical Learnings to the Clinic
Brooke Rock, Ph.D., Senior Scientist, Pharmacokinetics and Drug Metabolism, Amgen, Inc.
Characterizing the mechanisms of ADC instability and release of free cytotoxin are germane in the design of ADCs. Understanding the mechanism behind release of the cytotoxin is important in both the efficacy of the ADC as well as toxicity profile. Factors affecting the ADC stability will be reviewed and the subsequent impact on ADC disposition will be considered in the context of clinical monitoring.

10:05 Coffee Break

10:35 mAbXcite: A Novel Immunotherapy Platform that Initiates a Robust Anti-Cancer Immune Response by Recruiting and Activating Neutrophils
UNPUBLISHED DATA *Ifat Rubin-Bejerano, Ph.D., Co-Founder and CSO, ImmuneXcite, Inc.*
mAbXcite is a platform that exhibits a lasting immune response that is initiated by neutrophils. mAbXcite constructs of two validated antibodies, trastuzumab and cetuximab, as well as a syngeneic antibody demonstrate significantly greater efficacy in resistant tumor models. Mice that show complete regression or stasis do not grow tumors upon rechallenge, suggesting a memory response that is initiated by neutrophils.

11:05 Engineering and Clinical Development of Antibody-Targeted Nanotherapeutics
Daryl C. Drummond, Ph.D., Vice President, Discovery, Merrimack Pharmaceuticals
The use of nanotherapeutics provides a novel and highly effective platform for developing next generation antibody-drug conjugates. These novel immunotargeted nanotherapeutics are engineered with the antibody indirectly conjugated through the lipidic carrier, and with a wide range of possible payloads. An ErbB2-targeted pegylated liposomal doxorubicin is currently showing promising preclinical and early clinical activity, and is currently being evaluated in a Phase II trial in metastatic breast cancer.

CONTINUED

5th Annual | May 7-8

ADCs: Preclinical and Clinical Updates

Leveraging Lessons Learned in Preclinical and Early Clinical to Strategize for the Future

11:35 Toward Clinical Development of the Novel HER2-Targeting Antibody-Drug Conjugate SYD985

UNPUBLISHED DATA

Patrick Groothuis, Ph.D., Principal Scientist, Preclinical Pharmacology, Synthon Biopharmaceuticals B.V.

SYD985 is a novel anti-HER2 antibody-drug conjugate (ADC) based on the monoclonal antibody trastuzumab, a cathepsin B-sensitive dipeptide linker (valine-citrulline (vc) motif) and a unique prodrug seco-duocarmycin-hydroxybenzamide-azaindole. *In vitro* and *in vivo* studies exemplify that SYD985 is a promising therapeutic modality for cancer patients with moderate or even low HER2 levels in tumors.

12:05 Anti-Tumor Activity of the Antibody-Drug Conjugate (ADC), BT-062, Against CD138-Positive Solid Tumors

Kurt Schönfeld, Ph.D., Manager, Research Immunology, Global Research, Biotest AG

BT-062 is an ADC comprising a chimeric anti-CD138 antibody conjugated to the maytansinoid DM4. CD138 has long been recognized as being highly expressed on multiple myeloma (MM), and findings previously reported include BT-062's highly selective cytotoxic activity against CD138-positive MM cells. Here, we show the potential of BT-062 as a treatment for CD138-positive solid tumors.

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

1:05 Refreshment Break

CLINICAL UPDATES ON ADCs

1:35 Chairperson's Remarks

Alan Rigby, Ph.D., Vice President, Antibody-Drug Conjugate Biology, Eli Lilly and Company

1:40 pm Clinical Results with SN-38-Conjugated Antibody-Drug Conjugates in Patients with Metastatic Solid Cancers

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

2:10 Clinical Perspective of ADC Development

Michael K. Bauer, Ph.D., Senior Vice President, Clinical Development, Genmab

- Mechanism of action of HuMax-Tissue Factor-ADC
- Translation of preclinical research into the clinic
- Striking the right balance between patient safety and charting unknown clinical territory
- Beyond dose-escalation
- Patient selection - why, when and how

2:40 Clinical Development of Auristatin-Based ADCs at Seattle Genetics

Nancy Whiting, Pharm.D., BCOP, Executive Director & Head, Medical Affairs, Seattle Genetics

In addition to a broad clinical development program with Seattle Genetics' approved ADC ADCETRIS® (brentuximab vedotin), the company has multiple other auristatin-based ADC programs as well as novel pyrolobenzodiazepine dimer-based ADCs in its pipeline. This talk will highlight novel auristatin-based ADCs in development with a focus on recent clinical data.

3:10 Tumor Selective Anti-EGFR Antibody-Drug Conjugates for Multiple Indications

Ed Reilly, Ph.D., Senior Research Fellow, Project Director, Oncology Discovery, Abbvie

Most approved EGFR antibodies are unsuitable for use as antibody-drug conjugates (ADCs) because of on target toxicities. We have developed EGFR-directed ADCs that bind to a tumor selective epitope thereby limiting the effects of the toxin on normal cells while maintaining a high degree of activity on EGFR-overexpressing tumor cells. Early promising clinical data, including durable objective responses, in subjects with EGFR-positive tumors will be presented.

3:40 AGS67E, An Anti-CD37 Monomethyl Auristatin E (MMAE) Antibody-Drug Conjugate for NHL, CLL & AML

Leonard M. Reyno, M.D., Senior Vice President and Chief Medical Officer, Agensys, Inc.

Our growing clinical experience with antibody-maytansinoid conjugates is leading to an enhanced understanding regarding critical attributes for their success. This presentation will highlight some recent efforts to incorporate this translational knowledge into the future development of these compounds.

4:10 End of Conference

Inaugural | May 4-5

Fusion Protein Therapeutics

Engineering Next-Generation Biologics

MONDAY, MAY 4

7:00 am Registration and Morning Coffee

PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks

8:40 Cancer Stem Cells and Mechanisms of Malignant Progression

Robert A. Weinberg, Ph.D., Founding Member, Whitehead Institute for Biomedical Research; Professor, Biology, Massachusetts Institute of Technology

The cell-biological program termed the epithelial-mesenchymal transition (EMT) plays a role in conferring aggressive traits on carcinoma cells. In addition, it generates cancer stem cells (CSCs) that have the ability, following dissemination, to serve as founders of new metastatic colonies. The relationship between these CSCs and the SCs residing in normal tissues, and the participation of the CSCs in metastatic dissemination will be described.

9:25 Building an Antibody Discovery Company in a Crowded Field – the Adimab Story

Tillman Gerngross, Ph.D., CEO, Co-Founder, Adimab

The presentation will cover the evolution of Adimab from its founding in 2007 to becoming one of the few privately held profitable biotech companies in the last decade. Industry trends and specific strategic decisions along the way will be discussed and used to illustrate the importance of integrating finance and scientific information to build successful capital efficient biotech companies.

10:10 Coffee Break

ACHIEVING SUCCESS WITH THERAPEUTIC FUSION PROTEINS

10:45 Chairperson's Remarks

Fredrik Frejd, Ph.D., Chief Scientific Officer, Biotherapy, Affibody AB

10:50 KEYNOTE PRESENTATION:

Engineering Clotting Factor Fc Fusion Proteins for the Treatment of Hemophilia

Jennifer Dumont, Ph.D., Director, Medical Affairs, Biogen Idec, Inc.

Prophylactic clotting factor replacement in patients with hemophilia improves outcomes, but requires frequent injections with conventional therapies. Recombinant fusion of the Fc domain of human IgG1 with clotting factors VIII or IX was performed to extend the half-life of these factors and provide the potential to reduce the frequency of injections needed to control and prevent bleeding in hemophilia A and B patients, respectively. The Fc fusion factors are configured with monomeric factor VIII or IX covalently fused to dimeric Fc. These protein fusion products are now approved for the treatment of hemophilia and the development programs will be discussed.

11:20 FEATURED PRESENTATION:

Therapeutic Fusion Proteins: Current Trends and Challenges

Stefan Schmidt, Ph.D., Vice President, DSP, Rentschler Biotechnology

This talk examines the state-of-the-art in developing fusion proteins for biopharmaceuticals, shedding light on the immense potential inherent in fusion protein design and functionality. First, I will present a comprehensive overview on the current trends, and second, I will address challenges and how to overcome them.

Sponsored by novozymes

11:50 Veltis® Technology: Engineered Albumins for Optimized Serum Half-Life Extension

Karen Bunting, Ph.D., Senior Research Scientist, Molecular Biology and Fermentation, Novozymes Biopharma UK

Short circulatory half-life represents a major obstacle for many protein and peptide-based therapeutic agents, resulting in increased dosing with the consequent risk of side effects and reduced patient compliance. Molecule half-life can be significantly improved by association, conjugation or fusion to albumin, due to both size and recycling via the neonatal Fc receptor (FcRn). We will describe rationally engineered albumins with increased FcRn affinity and their application to improve the pharmacokinetic properties of therapeutic candidates.

Sponsored by BIOSCALE

12:20 pm Luncheon Presentation I: Development of a Generic Anti-PEG Antibody Assay Using BioScale's Acoustic Membrane MicroParticle Technology

Shannon D. Chilewski, MSc, Research Scientist II, Analytical and Bioanalytical Development, Bristol-Myers Squibb

In cases where established technologies cannot deliver on the assay sensitivity requirements set by a specific drug development program, alternative platforms may need to be evaluated. This presentation will share a case study on the application of the Acoustic Membrane Micro Particle (AMMP) technology for PK determination of a domain antibody and cover results on accuracy and precision and selectivity assessments. The second case study will cover the development of an immunogenicity assay on the AMMP where none of the established platforms were able to achieve adequate sensitivity.

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

1:20 Session Break

ENGINEERING ENHANCED PROPERTIES

1:50 Chairperson's Remarks

Mark Distefano, Ph.D., Professor, Chemistry and Medicinal Chemistry, University of Minnesota

1:55 FEATURED PRESENTATION:

PASylation: The Preparation of Fusion Proteins with Extended Plasma Half-Life Based on a Biological Alternative to PEG

Arne Skerra, Ph.D., Professor, Technische Universität Munich; Chief Scientific Officer, XL-protein GmbH

PASylation allows the simple genetic fusion (or chemical coupling) of a therapeutic protein or peptide with a voluminous hydrophilic polypeptide composed of Pro, Ala, and/or Ser to retard kidney filtration. PAS sequences show surprisingly similar biophysical properties to PEG but, in contrast, are biodegradable. PASylation has been successfully applied to antibody fragments, growth hormones, cytokines and other biologics; for example, PAS-leptin fusion proteins show much enhanced satiety effects in mice.

2:25 Re-Engineering Lysosomal Enzyme Therapeutics for the Brain as IgG Fusion Proteins that Penetrate the Blood-Brain Barrier

Ruben Boado, Ph.D., Vice President, R&D, ArmaGen, Inc.

Lysosomal enzymes are large molecule drugs that do not cross the blood-brain barrier (BBB). However, BBB-penetration of enzyme therapeutics is enabled by re-engineering the recombinant enzyme as IgG fusion proteins, wherein the IgG transport domain targets a specific endogenous receptor-mediated transporter within the BBB, such as the human insulin receptor (HIR). The therapeutic domain of the IgG fusion protein exerts the pharmacological effect in the brain once across the BBB.

2:55 Pathogenesis-Mediated Targeted Cytokine Delivery

UNPUBLISHED DATA

Yuti Chernajovsky, Ph.D., FRCP, Emeritus Professor, Molecular Medicine, William Harvey Research Institute, Barts and The London School of Medicine and Dentistry

I will describe how fusion proteins of the latency associated peptide (LAP) from TGFβ with therapeutic cytokines can be used to safely increase the half life of cytokines, confer latency and, using matrix metalloproteinase activity found at sites of disease, specifically release the therapeutic moiety where needed without side effects. A case will be made in favor of the use of latent cytokines as compared to anti-cytokine antibodies due to their novel pharmacodynamic properties.

3:25 Affibody-Based Ligand-Trap that Block IL-17 with Unparalleled *in vivo* Potency and Long Plasma Half-Life

Fredrik Frejd, Ph.D., Chief Scientific Officer, Biotherapy, Affibody AB

Il-17 is a potent inducer of tissue inflammation involved in auto-inflammatory disease. Here we describe the engineering of a ligand trap fusion protein designed to block IL-17 mediated pathology. The ligand trap is based on two small Affibody scaffold domains for IL-17 inhibition, and an albumin binding domain for extended

CONTINUED

Inaugural | May 4-5

Fusion Protein Therapeutics

Engineering Next-Generation Biologics

plasma half-life supporting once monthly dosing. The fusion protein has unparalleled potency with complete blocking of the dimeric interleukin.

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

4:35 Problem-Solving Breakout Discussions

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:50 End of Day

TUESDAY, MAY 5

8:00 am Morning Coffee

STRATEGIES FOR ENGINEERING FUSION PROTEIN THERAPEUTICS

8:25 Chairperson's Remarks
Stefan Schmidt, Ph.D., Vice President, DSP, Rentschler Biotechnology

8:30 Enzymatic Assembly of Fusion Proteins
Mark Distefano, Ph.D., Professor, Chemistry and Medicinal Chemistry, University of Minnesota
Fusion proteins prepared by linking domains manifesting different functions have enormous potential for biomedical applications. Chemoenzymatic methods involving the enzymatic incorporation of chemical linkers coupled with bioorthogonal reactions greatly increase the repertoire of possible constructs that can be obtained. This presentation will focus on various protein fusions and assemblies that have been prepared using enzymatic modification with farnesyltransferase and subsequent chemical ligation.

9:00 Development of Affibody® C5 Inhibitors for Versatile and Efficient Therapeutic Targeting of the Terminal Complement Pathway
Patrik Strömberg, Ph.D., Project Leader, R&D; Principal Scientist, Nonclinical Safety and Pharmacology, Swedish Orphan Biovitrum AB (SOBI)
We are developing protein therapeutics against complement component C5, utilizing the innovative Affibody scaffold for protein targeting. During lead generation and optimization, large efforts were made to optimize PK/PD properties, i.e., maximizing the plasma persistence of this small protein while maintaining inhibitory potency. In particular, pioneering studies with a novel albumin binding domain (ABD) technology were performed that ultimately generated the first clinical candidate from this program.

9:30 Functional Assay Strategies for Bispecific Antibodies and Fusion Proteins
UNPUBLISHED DATA *Jörg Moelleken, Ph.D., Senior Scientist, Roche Pharmaceutical Research and Early Development, Large Molecule Research, Roche Innovation Center Penzberg*
The increasing complexity of novel biotherapeutics comprising of bispecific antibodies and fusion proteins raise new challenges for functional characterization as compared to standard antibodies. Besides varying binding sides, additional biologically relevant aspects like bi-specificity must be addressed now. This presentation shows points to consider relevant from lead identification until lead characterization.

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

TRAIL (TUMOR NECROSIS FACTOR-RELATED APOPTOSIS-INDUCING LIGAND) FUSION PROTEINS

10:50 Leading TRAIL to the Clinic: Improving Pharmacokinetics, Identifying Sensitizers and Selecting Cancer Types
Xiangwei Wu, Ph.D., Associate Professor, Clinical Cancer Prevention, MD Anderson Cancer Center
Interest in TRAIL has increased following the observation that TRAIL can selectively kill a wide variety of human cancer cells without harm normal cells. However, results from clinical trials of TRAIL-based therapy are disappointing. We will describe our approaches in improving TRAIL's performance by generating Fc fusion TRAIL, identifying best drugs to work with TRAIL, and selecting subpopulation of patients who may benefit from TRAIL-based therapy.

11:20 Hexavalent Agonists Targeting Receptors of the Tumor Necrosis Factor Superfamily
Oliver Hill, Ph.D., Vice President, Molecular Biology, APOGENIX GmbH
Apogenix has engineered TRAIL mimetics with three Apo2L/TRAIL protomer subsequences genetically fused into one polypeptide chain. This trivalent single-chain TRAIL-receptor-binding domain (scTRAIL-RBD) was fused to a mutated Fc-part of human IgG1 to create a hexavalent scTRAIL-RBD dimer (scTRAIL-RBD-Fc). The underlying engineering concept was successfully transferred to CD40-ligand (CD154), resulting in a hexavalent CD40-agonist (scCD40L-RBD-Fc) suitable for clinical development. We will present our results on both agonists and discuss their impact on the design of novel TNFR super-family targeting biologics.

11:50 Cancer Therapy with TR3, a Genetically Stabilized TRAIL-Based Drug Platform with Increased Activity, Stability, and Targeting Capabilities
Dirk Spitzer, Ph.D., Instructor in Surgery, Washington University School of Medicine
Soluble TRAIL has a tremendous potential as a cancer drug but cannot form bioactive trimers when produced from monomeric cDNAs in mammalian cells. We solved these limitations by designing a head-to-tail fusion protein, resulting in the constitutive TRAIL trimer TR3. This new drug platform is extremely versatile, since it is generically extensible in modular fashion, while the domain stoichiometry is strictly controlled. Here, we will emphasize the latest optimization strategies performed on our MUC16-targeted cancer drug Meso-TR3.

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

ANTIBODY FUSIONS

2:00 Chairperson's Remarks
Dirk Spitzer, Ph.D., Instructor in Surgery, Washington University School of Medicine

2:05 Potential Role of LEC/Antibody Fusion Protein in the Immunotherapy of Cancer
Alan L. Epstein, M.D., Ph.D., Professor, Pathology, University of Southern California Keck School of Medicine
A novel fusion protein consisting of the human chemokine LEC and a human antibody that targets degenerative regions of tumors has been found to be an effective reagent for the immunotherapy of cancer. Used with inhibitors of tumor-induced immunosuppression, experimental tumors show dramatic regression after IV treatment. Due to its broad applicability and unique mechanism of action, this reagent has high potential in enhancing current immunotherapy approaches and vaccine technology.

2:35 Antibody-IFN Fusion – A Combination of ADC and Targeted Immunotherapy
Sanjay D. Khare, Ph.D., President and CEO, ImmunGene, Inc.
ImmunGene's proprietary technology empowers antibodies by genetically engineering them with the tumor cell-killing cytokines, thereby combining the exquisite specificity of antibodies with the potent cytotoxic effects of cytokines. Antibody-cytokine fusion proteins are designed to be inactive systemically (against healthy cells) at the therapeutic doses, but stable in the bloodstream while efficiently targeting and killing cancer cells. This approach spares non-targeted (healthy) cells and thus reduces many of the known toxic effects of systemically administered cytokines while greatly enhancing the anti-tumor activity of antibodies.

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Inaugural | May 4-5

Fusion Protein Therapeutics

Engineering Next-Generation Biologics

3:05 Extended Q&A

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

CONQUERING DISEASE

4:25 Cancer Stem Cell Therapeutics

Agamemnon A. Epenetos, Ph.D., Chairman, Trojan Technologies, Ltd.

It is likely that cancer stem cells, (CSCs) may be a key reason for the failure of current therapies. The NOTCH pathway is an important pathway in cancer stem cells. We have generated a hybrid protein (TR4) which translocates into the nucleus, suppresses NOTCH and eliminates human tumor growth; along with microparticles (MPs) derived from mesenchymal cells loaded with microRNAS. These MPs can fuse with tumors and affect tumor growth.

4:55 Discovery and Development of Novel Ig-GAIM Fusion NPT088 for Alzheimer's Disease

CASE STUDY

Richard A. Fisher, Ph.D., Chief Scientific Officer, NeuroPhage Pharmaceuticals

NPT088 is an Ig fusion displaying two copies of the General Amyloid Interaction Motif (GAIM) that targets misfolded protein assemblies. GAIM activities include potent (nM) binding to multiple types of amyloid fibrils, inhibition of misfolded protein assembly, cytoprotection from oligomer mediated toxicity, and disruption of amyloid structure. NPT088 has been tested in transgenic disease models, and after systemic administration NPT088 mediates reduction of pathology and improvements in behavior and cognition.

5:25 End of Conference

5:30 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC12: Production Challenges for Complex Biologics: ADCs, Bispecific & Fusion Proteins

**Separate registration required, please see page 4 for course details.*

Inaugural | May 6-7

Peptide Therapeutics

Conquering Disease

Recommended Pre-Conference Short Course*

SC12: Production Challenges for Complex Biologics: ADCs, Bispecific & Fusion Proteins

**Separate registration required, please see page 4 for course details.*

WEDNESDAY, MAY 6

7:00 am Registration and Morning Coffee

BICYCLICS AND CHARACTERIZING PEPTIDES

8:00 Chairperson's Remarks

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

» 8:10 KEYNOTE PRESENTATION:

Development of Bicyclic Peptides for Therapeutic Application

UNPUBLISHED DATA *Christian Heinis, Ph.D., Professor, Therapeutic Peptides and Proteins, École Polytechnique Fédéral de Lausanne (EPFL)*

Bicyclic peptides have two macrocyclic rings that can bind to protein targets much like antibodies interact through CDRs, but they have around a 100-fold smaller mass. The small size allows chemical synthesis and brings advantages in therapeutic applications as, for example, good tissue penetration. We have recently developed new bicyclic peptide formats that will be presented.

8:40 FEATURED PRESENTATION:

High Affinity Bicyclic Peptides: Application to Payloads in Oncology

Christophe Bonny, Ph.D., Chief Scientific Officer, Bicycle Therapeutics Limited

The Bicycle technology is based on repertoires of peptides that can be modified with organochemical scaffolds to create a diverse array of constrained peptides. The bicycle peptides show antibody-like properties such as low to sub-nanomolar affinities and exquisite selectivity, but in a 100-fold smaller, chemically synthesized format. Bicycle Therapeutics will present *in vivo* POC data from its preclinical programs demonstrating the power of its technology to deliver cytotoxic payloads to tumor cells.

CHARACTERIZING PEPTIDES FOR GREATER FINESSE

9:10 Peptide Therapeutics and the Quest for Differentiated Medicines

Maria Ufret, Ph.D., Scientist, Chemistry, Ipsen Bioscience, Inc.

Peptides possess a unique potential to function as receptor agonists, targeting agents or bifunctional molecules, yet peptides remain an underrepresented modality in pharmaceutical development pipelines. Strategies that synergize both biological screening tools along with chemical approaches to deliver peptide therapeutic leads against targets not readily addressed by small molecules or antibodies will be presented.

9:40 Understanding the Mechanism of Physical Instability of Peptide Pharmaceuticals

UNPUBLISHED DATA *Karolina Zapadka, Ph.D. Candidate, Formulation Group, MedImmune, LLC*

Aggregation and amyloid fibril formation of peptides and proteins is a widespread and intensively studied problem. Hence, the ability to understand the formation and proliferation of aggregates under specific conditions is of critical importance along with developing ways to control the process. This study has worked towards a better understanding of the mechanism of the aggregation and amyloid fibrillation of human GLP-1 as a model peptide.

10:10 Identifying Novel Drug Leads: Proteome-Wide Screening of Peptide Motifs that Inhibit Protein-Protein Interactions

UNPUBLISHED DATA *Philip M. Kim, Ph.D., Associate Professor, The Donnelly Centre for Cellular and Biomolecular Research, Banting and Best Department of Medical Research, Molecular Genetics and Computer Science, University of Toronto*

I will present our novel technology platform that allows us to screen all peptide motifs in the human proteome as inhibitors of protein-protein interactions. Briefly, we have devised a strategy that expresses each peptide motif intracellularly and can monitor the phenotype it causes. We do so using a pooled strategy, and screen about 500,000 peptide motifs. We thereby identify many novel target interactions whose inhibition shows very strong and specific phenotypes in cell lines.

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

PEPTIDE ADVANCES

11:25 Use of Cell Penetrating Peptides to Mute Physiologically Deleterious Signal Cascades

Jamie L. Wilson, Ph.D., Research Associate, Boston University School of Medicine

We are controlling signal transductions initiated by G-protein coupled and tyrosine kinase receptors by targeting receptor motifs which link to specific signal cascades with cell penetrating peptides (CPP). Similarly we are also controlling downstream signal point. We have used the hypoxic rat model of Pulmonary Hypertension *in vivo* and human pulmonary artery smooth muscle cell migration in culture as physiologic targets to demonstrate the potential of control through the CPP.

11:55 Ligand-Independent Inhibitory Peptides (SCHOOL Peptides) in Medicine: Recent Advances and Future Perspectives

CASE STUDY *Alexander B. Sigalov, Ph.D., President and Founder, SignaBlok, Inc.*

New model of cell signaling, the Signaling Chain HOmoOLigomerization (SCHOOL) model, and peptides that employ novel, ligand-independent mechanisms of receptor inhibition (SCHOOL peptides) will be briefly reviewed. As an exemplary use case, preclinical studies of the SCHOOL peptide inhibitor of TREM-1 receptor in free and nanoparticle-bound forms in cells and animal models of cancer and sepsis will be presented.

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

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

1:55 Session Break

GASTROINTESTINAL DISEASE

2:10 Chairperson's Remarks

Jeffrey Wang, Ph.D., Associate Professor, Pharmaceutical Sciences, Western University of Health Sciences

2:15 Role of Guanylate Cyclase Agonists in the Regulation of Gastrointestinal Function and Treatment of Gastrointestinal Diseases

Mark Currie, Ph.D., Senior Vice President, Chief Scientific Officer & President, R&D, Ironwood Pharmaceuticals, Inc.

In the current talk, we will focus on the actions of linaclotide, a synthetic 14-amino acid peptide GCC agonist, on animal models of abdominal pain and intestinal transit and the relationship of these actions for the treatment of intestinal dysfunction in irritable bowel sydrome with constipation (IBS-C) and chronic constipation (CC) patients by examining the effect of linaclotide treatment on the abdominal symptoms associated with IBS-C, including abdominal pain.

2:45 Orally Stable Peptides for Gastrointestinal Diseases

UNPUBLISHED DATA *Dinesh V. Patel, Ph.D., President & CEO, Protagonist Therapeutics*

Targeted therapy in the field of GI diseases is currently dominated by injectable antibodies. Protagonist is pursuing the discovery and development of orally stable peptides based NCEs as a safer and superior choice for targeted treatment of inflammatory bowel diseases (IBD, Crohn's and Ulcerative Colitis). R&D progress towards orally stable antagonists of alfa4beta7 integrin, a clinically validated IBD specific target, will be highlighted.

3:15 Sponsored Presentation *(Opportunity Available)*

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

4:45 Problem-Solving Breakout Discussions

CONTINUED

Inaugural | May 6-7

Peptide Therapeutics

Conquering Disease

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

7:00 End of Day

THURSDAY, MAY 7

8:00 am Morning Coffee

IMPROVING PROPERTIES

8:30 Chairperson's Remarks

Jamie L. Wilson, Ph.D., Research Associate, Boston University School of Medicine

8:35 Cysteine Perfluoroarylation and Ultra Rapid Peptide Synthesis

Bradley L. Pentelute, Ph.D., Pfizer-Laubach Career Development Assistant Professor, Chemistry, Massachusetts Institute of Technology (MIT)

Here we report a novel and robust method for macrocyclization of unprotected peptides using cysteine arylation. This chemistry allowed for peptide modifications that imparted favorable cell penetration and proteolytic stability. In addition, we describe a rapid flow solid phase peptide synthesis methodology that enables incorporation of an amino acid residue in 1.5 minutes. To demonstrate the broad applicability of this method, it was employed to synthesize hundreds of peptides and proteins.

9:05 XTEN – A Biodegradable and Monodisperse PEG Alternative for Monthly Dosing of Peptides

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

Amunix has developed XTEN, a protein-based polymer that mimics the biophysical properties of PEG. XTEN is monodisperse, extremely hydrophilic, and it contains conjugation sites in precisely controlled locations. XTEN is stable in circulation but readily degraded upon internalization which eliminates the risk of long-term polymer accumulation associated with PEG. XTEN offers class-leading monthly dosing.

9:35 Targeted Peptide-Directed Ablation of Adipose Stromal Cells Suppresses Obesity and Cancer Progression in Animal Models

Mikhail Kolonin, Ph.D., Associate Professor and Director, Center For Metabolic and Degenerative Diseases, University of Texas Health Science Center

As shown by our studies, adipose stromal cells (ASC), not only serve as adipocyte progenitors, but also promote cancer through supporting vasculature. We recently characterized a peptide that specifically targets ASC (Daquinag et al. Cell Stem Cell 2011) and used it to design a targeted pro-apoptotic peptide ablating ASC *in vivo* (Daquinag et al., in press). We show that in mice this compound suppresses overgrowth of white fat tissue and inhibits tumor growth.

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

DELIVERY

11:05 Patient-Focused Peptide Delivery

CASE STUDY *Leila Hassani-Beniddir, PharmD & Ph.D., Scientist-Novel Drug delivery Technologies, Peptides Development-CMC, Ipsen*

The high potency and specificity of peptides have made them attractive drug candidates with several blockbuster molecules. Recent advances in peptide delivery technologies are opening up the possibility of developing oral, nasal, buccal, transdermal and inhaled routes for a wider range of peptides, with many in late stage development and close to market. Recent developments in novel peptide delivery technologies will be reviewed with an emphasis on key factors that might determine their success.

11:35 Lipid Conjugates for Peptide Drug Delivery

CASE STUDY *Jeffrey Wang, Ph.D., Associate Professor, Pharmaceutical Sciences, Western University of Health Sciences*

The use of peptides as therapeutic drugs offers many advantages. However, the delivery of peptides often faces challenges due to their inherently unfavorable pharmacokinetic properties. Lipid conjugation is one of the practical approaches to improve these properties and two lipid-peptide conjugates (recombinant insulin detemir and liraglutide) are approved for clinical use. This presentation will include a discussion of the rationale for lipid conjugation, along with several case studies.

12:05 pm Sponsored Presentation *(Opportunity Available)*

12:35 End of Conference

5:15 Registration for Dinner Short Courses

Recommended Dinner Short Course*

SC14: Strategic Bioassay Design and Analysis

Separate registration required, please see page 4 for course details.

HOTEL & TRAVEL INFORMATION

Host Hotel:
Seaport Hotel
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Convention Venue:
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Reservations: Go to PEGSummit.com

Discounted Room Rate: $259 s/d
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We understand that you have many choices when making your travel arrangements. Please understand that reserving your room in the CHI room block at the conference hotel allows you to take full advantage of the conference sessions, events and networking opportunities, and ensures that our staff will be available to help should you have any issues with your accommodations.

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For sponsorship and exhibit information, please contact:

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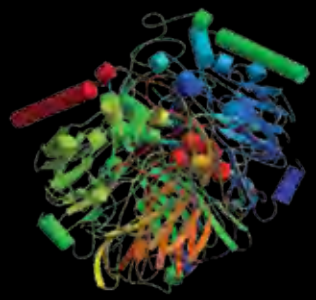

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