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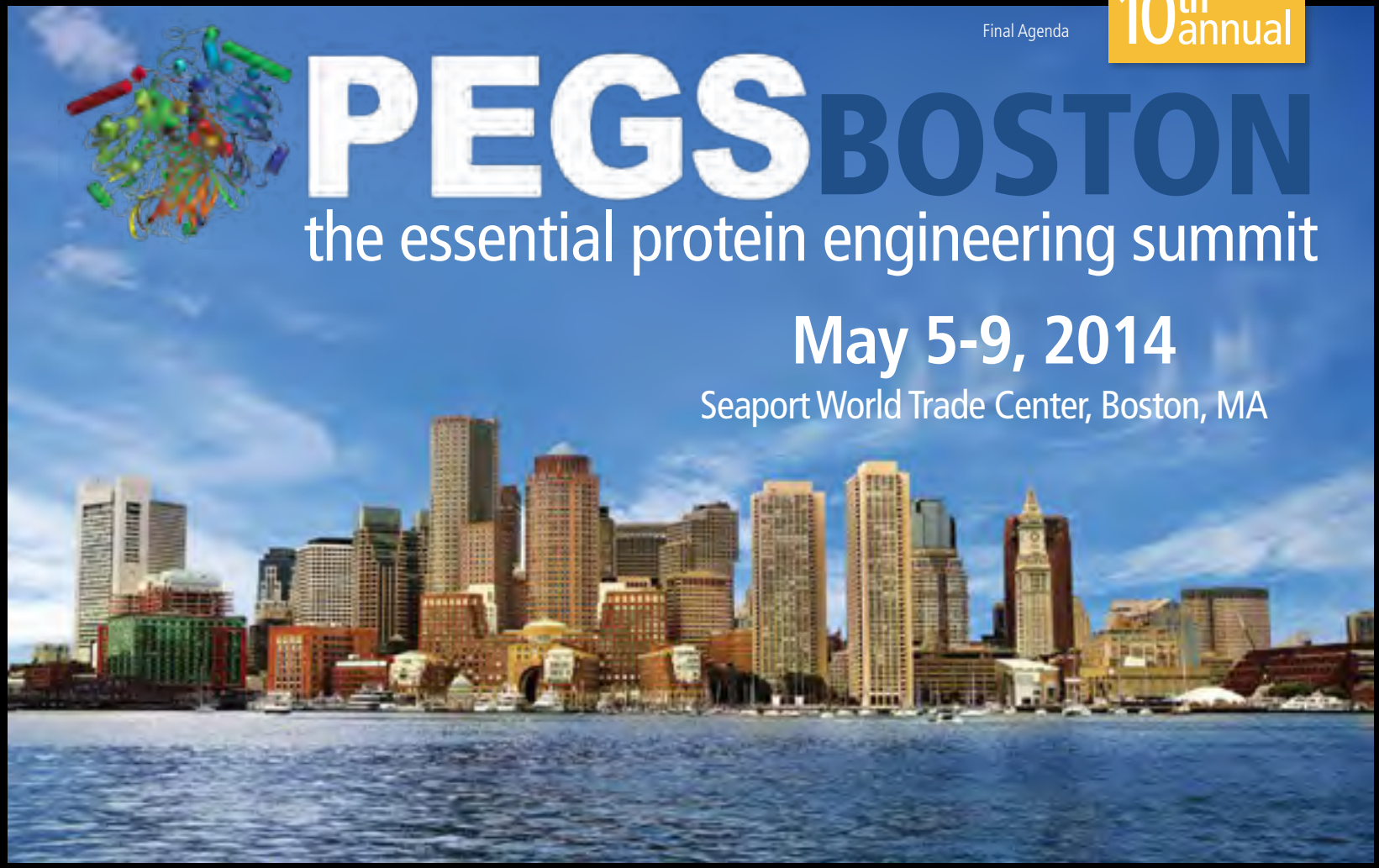

May 5-9, 2014

Seaport World Trade Center, Boston, MA

Plenary Keynote Speakers

Peter CR Emtage, Ph.D.
Vice President, Immune Mediated Therapies, MedImmune

George D. Yancopoulos, M.D., Ph.D.
President, Regeneron Laboratories; CSO, Regeneron Pharmaceuticals, Inc.

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CONFERENCE-AT-A-GLANCE

	CONFERENCE TRACKS: Monday-Tuesday | May 5-6	CONFERENCE TRACKS: Wednesday-Thursday | May 7-8	CONFERENCE TRACKS: Thursday-Friday | May 8-9
ENGINEERING STREAM	Phage and Yeast Display	Engineering Antibodies	Engineering Bispecific Antibodies
ONCOLOGY STREAM	Antibodies for Cancer Therapy	Advancing Bispecific Antibodies	Antibody-Drug Conjugates
THERAPEUTICS STREAM	Biologics for Autoimmune Diseases	Adoptive T Cell Therapy	Peptide Therapeutics
EXPRESSION STREAM	Difficult to Express Proteins	Optimizing Protein Expression	High-Level Expression of Enzymes
ANALYTICAL STREAM	Characterization of Biotherapeutics	Biophysical Analysis of Biotherapeutics	Protein Aggregation and Stability
SAFETY STREAM	PK/PD of Multi-Domain Proteins	Immunogenicity for Regulatory Success	Immunogenicity Prediction and Mitigation
BIOPROCESS STREAM	Scaling Up and Down Strategies	ADC Development & Manufacturing	
	SHORT COURSES*: Sunday, May 4 | 10:00am - 1:00pm	SHORT COURSES*: Sunday, May 4 | 2:00 - 5:00pm	SHORT COURSES*: Tuesday, May 6 | 6:00 - 8:00pm	SHORT COURSES*: Thursday, May 8 | 5:30 - 7:30pm

PLENARY KEYNOTE SPEAKERS

Monday, May 5

Harnessing the Patient's Immune System to Combat Cancer
Peter CR Emtage, Ph.D., Vice President, Immune Mediated Therapies, MedImmune

Building Regeneron's Pipeline: From Trap Technology to the *VelocImmune* Platform to *Veloci-Next*
George D. Yancopoulos, M.D., Ph.D., President, Regeneron Laboratories; CSO, Regeneron Pharmaceuticals, Inc.

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CO-LOCATED EVENT:*

Biologics Formulation & Delivery SUMMIT May 5-7

Advances in molecular biology and biotechnology have allowed for the large-scale production of effective and potent biotherapeutic drugs. Major research issues in protein/peptide delivery include the stabilization of proteins in delivery devices and the design of appropriate target-specific carriers. CHI's Biologics Formulation and Delivery Summit will provide a forum for focused discussions on current challenges and opportunities in delivery of biotherapeutics.

This multi-track summit will discuss various formulation and device-based approaches for designing physiologically relevant, patient friendly, targeted biologics products.

healthtech.com/Biologics-Delivery

*Separate Registration is Required

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HOTEL & TRAVEL INFORMATION

Host Hotel:
Seaport Hotel
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Convention Venue:
Seaport World Trade Center
200 Seaport Boulevard
Boston, MA 02210

Discounted Room Rate: $249 s/d
Discounted Room Rate Cutoff: March 27, 2014

Please call the hotel directly to reserve your sleeping accommodations. You will need to identify yourself as a CHI conference attendee to receive the discounted room rate with the host hotel. Reservations made after the cut-off date or after the group room block has been filled (whichever comes first) will be accepted on a space and rate-availability basis. Rooms are limited, so please book early.

Flight Discounts:

Special discounts have been established with American Airlines for this conference:

- Call American Airlines directly at 1-800-433-1790 and use Conference Code 7654AA
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SHORT COURSES*

SUNDAY, MAY 4 (10:00AM-1:00PM)

SC1: Phage and Yeast Display Libraries

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

James D. Marks, M.D., Ph.D., Professor, Anesthesia & Pharmaceutical Chemistry, UCSF; Chief, Anesthesia and Vice Chairman, Anesthesia & Perioperative Care, San Francisco General Hospital

SC2: Translational Strategies for Development of Monoclonal Antibodies from Discovery to Clinic

Part 1: Focus on Early Discovery

Mohammad Tabrizi, Ph.D., Head, DMPK and Disposition, Merck

Gadi Bornstein, Ph.D., Associate Research Fellow, Centers for Therapeutic Innovation, Pfizer, Inc.

Scott Klakamp, Ph.D., Principal Consultant, SKD Consulting LLC

Randall Brezski, Ph.D., Senior Research Scientist, Biotechnology Center of Excellence, Janssen R&D, Inc.

Isabel Figueroa, Associate Principal Scientist, PK/PD, Merck

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

Vinodh Kurella, Ph.D., Visiting Research Fellow, C3 Bioinformatics, Harvard Medical School

SC4: Novel and Emerging Conjugation Methods for ADCs

Sean Hu, Ph.D., SVP, Biotherapeutics, Dophen Biomed

Ying Sun, Ph.D., Associate Director, Chemistry, Ambrx, Inc.

Florence Lhospice, Director, Pharmaceutical Operations, R&D, Innate Pharma

SC5: Introduction to Adoptive T Cell Therapies

Michelle Krogsgaard, Ph.D., Assistant Professor, NYU Cancer Institute, NYU School of Medicine

Richard Morgan, Ph.D., Vice President, Immunotherapy, Bluebird Bio

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

Michael C. Milone, M.D., Ph.D., Assistant Professor, Pathology and Laboratory Medicine, University of Pennsylvania

SUNDAY, MAY 4 (2:00-5:00PM)

SC6: Translational Strategies for Development of Monoclonal Antibodies from Discovery to Clinic

Part 2: Focus on Nonclinical Development to Clinic

Mohammad Tabrizi, Ph.D., Head, DMPK and Disposition, Merck

Gadi Bornstein, Ph.D., Associate Research Fellow, Centers for Therapeutic Innovation, Pfizer, Inc.

Scott Klakamp, Ph.D., Principal Consultant, SKD Consulting LLC

Randall Brezski, Ph.D., Senior Research Scientist, Biotechnology Center of Excellence, Janssen R&D, Inc.

Isabel Figueroa, Associate Principal Scientist, PK/PD, Merck

SC8: *In silico* Immunogenicity Predictions (Hands-On) Workshop

Vinodh Kurella, Ph.D., Visiting Research Fellow, C3 Bioinformatics, Harvard Medical School

Sinu Paul, Ph.D., Researcher, La Jolla Institute for Allergy & Immunology

SC9: Alternate Display Technologies

John Löfblom, Ph.D., Assistant Professor, Molecular Biotechnology, AlbaNova University Center, Royal Institute of Technology (KTH)

Birgit Dreier, Ph.D., Senior Scientist, Professor Dr. A. Plückthun Laboratory, Biochemistry, University of Zurich

SC10: Measures to Enhance Half-Life and Stability

Javier Chaparro-Riggers, Ph.D., Associate Research Fellow, Protein Engineering, Rinat-Pfizer, Inc.

TUESDAY, MAY 6 (6:00-8:00PM)

SC11: Overcoming the Challenges of Immunogenicity Assessment

Jim McNally, Ph.D., Senior Principal Scientist, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

Shalini Gupta, Ph.D., Director, Clinical Immunology, Amgen, Inc.

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

Stefan Schmidt, Ph.D., Vice President, DSP, Rentschler Biotechnology

Stuart Bussell, Ph.D., Director, Upstream Process Development, Sutro Biopharma

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

SC14: Next-Generation Sequencing in Antibody Discovery for End Users

Tadas Panavas, Ph.D., Principal Scientist, Molecular Protein and Biosciences, Janssen

John Wheeler, Ph.D., Senior Scientist, Biologics Research, Janssen R&D, Pharmaceutical companies of Johnson & Johnson

THURSDAY, MAY 8 (5:30-7:30PM)

SC15: Antibody-Drug Conjugate Therapeutics: Potential and Challenges

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

Robert J. Lutz, Ph.D., Vice President, Translational Research and Development, ImmunoGen, Inc.

SC16: Protein Aggregation: Mechanism, Characterization and Immunogenic Consequences

Elizabeth Topp, Ph.D., Dane O. Kildsig Chair and Head, Industrial and Physical Pharmacy, Purdue University

Daniel Some, Ph.D., Principal Scientist, Wyatt Technology

Michael Marlow, Ph.D., Staff Scientist, Regeneron Pharmaceuticals, Inc.

SC17: Antibody-Based Cancer Immunotherapy

Christian Klein, Ph.D., Head, Oncology Programs; Expert Scientist, Discovery Oncology oDTA, Pharma Research and Early Development (pRED), Roche Glycart AG

Angus M. Sinclair, Ph.D., Scientific Director, Oncology Research, Amgen, Inc.

*Separate Registration is Required

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ENGINEERING STREAM

16th Annual | May 5-6

Phage and Yeast Display of Antibodies and Recombinant Proteins

Tools for Molecular Evolution

Recommended Pre-Conference Short Courses*

Phage and Yeast Display Libraries

Alternate Display Technologies

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

MONDAY, MAY 5

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks

Kristi Sarno, Chair, Greater Boston Chapter, Women in Bio; Director, Business Development, Pfenex, Inc.

8:40 Harnessing the Patient's Immune System to Combat Cancer

Peter CR Emtage, Ph.D., Vice President, Immune Mediated Therapies, MedImmune

With recent FDA approvals, modulation of the immune system is now a clinically validated approach in the treatment of some cancers. At MedImmune, the Oncology Department is developing assets and expertise in Immune Mediated Therapy of Cancer (IMT-C). The challenges from a drug development perspective are multi-fold. The talk will focus on the relevance of preclinical models and translational science to address key issues, including dose selection and rationale combinations.

9:25 Building Regeneron's Pipeline: From Trap Technology to the *VelocImmune* Platform to *VelociNext*

George D. Yancopoulos, M.D., Ph.D., President, Regeneron Laboratories; CSO, Regeneron Pharmaceuticals, Inc.

George D. Yancopoulos, M.D., Ph.D., who is the Founding Scientist, President, Research Laboratories and Chief Scientific Officer of Regeneron Pharmaceuticals, one of the world's top biotechnology companies, will discuss how he and his colleagues exploited a commitment to science and technology to start the company, withstand years of challenges and failures, and emerge with a pipeline of promising technologies and novel/biologics that are beginning to bring hope to countless patients and their families.

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

OPENING SESSION

11:05 Chairperson's Remarks

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

» KEYNOTE PRESENTATION:

11:10 Generating High-Quality Affinity Reagents through Phage Display

Brian K. Kay, Ph.D., Professor and Head, Biological Sciences; LAS Distinguished Professor, University of Illinois, Chicago

Protein scaffolds are an attractive alternative to monoclonal and polyclonal antibodies as a source of high affinity and specific affinity reagents. I describe a method for incorporating mutagenesis into the phage-display pipeline and demonstrating that the resulting affinity reagents can be used for pull-down experiments.

11:40 Next-Generation Sequencing and Ultimate-Generation Peptide Phage Display

Michael Szardenings, Ph.D., Head, Ligand Development Unit, Fraunhofer Institute for Cell Therapy and Immunology; Coordinator JLCI, CNUHH, Hwasun, Korea

An innovative, highly diverse (>109) peptide phage library has been generated with a novel tri-nucleotide synthesis approach, with less than 20 codons per position, perfectly statistically distributed and a peptide diversity outnumbering most libraries. This diversity, in combination with next generation sequencing and novel software for *in silico* allows to determine epitopes after single round panning directly on complete sera from allergy patients or on polyclonal antibodies.

12:10 pm Biological Recognition: Beyond the Antibody

Sponsored by Avacta Life Sciences

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

Antibodies are ubiquitous in life science research; their high affinity and specificity have enabled biological detection in a range of settings, from basic research to clinical diagnostics. Antibodies, however, are not suitable for all applications, and have limitations around targets and applications. Engineered non-antibody protein binders, largely focused on therapeutics, have been developed more recently. Here, I will review existing alternatives to antibodies and present Affimers as next generation reagents for biological recognition.

12:40 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., CSO & Senior Vice President, Research, 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 vaccinia virus. Upon infection of mammalian cells the antibody is not only incorporated into 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.

1:10 Luncheon Presentation II Next-Generation Analysis of Deep Sequencing Data: Bringing Light into the Black Box of Phage Display Experiments

Sponsored by aptaIT

Michael Blank, Ph.D., CSO, AptaIT GmbH

We developed an innovative bioinformatic approach that allows to exploit NGS data with an unprecedented depth to improve the identification of phage display ligands. Besides quality control and optimization of libraries, early identification of rare but high quality ligands otherwise lost in the screening experiment or advanced screening strategies for difficult targets become possible. The wealth of comparative sequence data already obtained from the screening experiment is furthermore useful for subsequent lead optimization.

1:40 Session Break

RATIONAL DESIGN

2:00 Chairperson's Remarks

David C. Lowe, Ph.D., Fellow, R&D, MedImmune, Ltd.

2:05 Enhanced Identification of Antibodies Targeting Specific Structures

Dimiter S. Dimitrov, Ph.D., Senior Investigator, Membrane Structure & Function, National Cancer Institute, NIH

Phage and yeast display methodologies to identify monoclonal antibodies targeting specific parts of a protein molecules will be discussed including sequential and competitive panning and sorting of antibody libraries.

2:35 Designing Antibodies to Bind to Integrin

Ahuva Nissim, Ph.D., Senior Lecturer, Molecular Targeting, Biochemical Pharmacology, William Harvey Research Institute, Queen Mary University of London

To increase the likelihood of developing powerful bio-therapeutics, a structurally-guided scaffold library was engineered based on the NMR structure/function analysis of ligand to tumour cell surface receptor avb6. VH-CDR3 encoding RGD-helix hairpins with helices of differing pitch, length and amino acid composition were built. Lead scFv clones and their corresponding VH-CDR3 derived peptides demonstrated specific inhibition of avb6 mediated activity and selective retention by avb6-expressing, but not avb6-negative, human xenografts.

3:05 Integrating Therapeutic Target Identification with Rapid Yumab Generation

Stefan Duebel, Ph.D., Director, Institute for Biochemistry, Biotechnology & Bioinformatics, Technical University Braunschweig

Using parallel high-throughput generation of Yumabs (human single chain antibodies carrying an Fc part), new systematic screening approaches for the discovery of novel drug targets are now available - offering the additional advantage that the tools used for the discovery are drug lead candidates right away.

3:35 Structure-Based Design of Novel PTM-Specific Antibody Scaffolds

James T. Koerber, Ph.D., Life Science Research Fellow, Pharmaceutical Chemistry, University of California, San Francisco

High-quality monoclonal PTM-specific antibodies have revolutionized our understanding of cell signaling. However, these reagents remain extremely challenging to generate by immunization methods, which are time consuming, expensive, and inefficient. I will discuss a novel method that combines structure-based design with display technologies to enable the rapid, high-throughput generation of renewable, recombinant PTM-specific antibodies.

4:05 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem Solving Breakout Discussions

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

6:45 End of Day

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ENGINEERING STREAM

16th Annual | May 5-6

Phage and Yeast Display of Antibodies and Recombinant Proteins

Tools for Molecular Evolution

TUESDAY, MAY 6

7:45 am Morning Coffee

CELL-BASED DISPLAY TECHNOLOGIES

8:25 Chairperson's Remarks

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

8:30 Ultra-High Affinity Engineered Protein Therapeutics for Treating Metastatic Disease

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

A soluble receptor was used as a therapeutic strategy to inhibit the biological activity of a ligand involved in cancer metastasis. Combinatorial and rational methods were used to engineer variants that bound ligand with affinities in the femtomolar range. The engineered receptors exhibited a remarkable ability to inhibit cancer metastasis in several aggressive tumor models in contrast to the wild-type receptor which was only marginally effective.

9:00 Mammalian Cell Display Allows Co-Selection of Human Antibodies for Functionality and Developability

David King, Ph.D., CSO, AnaptysBio, Inc.

The natural mechanism of antibody maturation, somatic hypermutation (SHM), has been reproduced *in vitro* and coupled with a mammalian cell-based display system to enable antibodies to be generated and directly selected for their functional properties as well as excellent biophysical properties for development. The use of high-throughput sequencing methodologies during this process allows insight into the maturation pathways of antibodies and can be used to rapidly identify optimized antibodies.

9:30 Best Poster Presentations

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

IN VIVO PHENOTYPIC SELECTION

10:40 Chairperson's Remarks

David C. Lowe, Ph.D., Fellow, R&D, MedImmune, Ltd.

10:45 *In vivo* Selection of Antibodies: New Roads Open Up for the Identification of Systemically Accessible Tumor Antigens

Luis Álvarez-Vallina, M.D., Ph.D., Molecular Immunology Unit, Hospital Universitario Puerta de Hierro

One of the most promising strategies for cancer treatment relies on the targeted delivery of antibody-based therapeutics; however, the discovery and validation of novel tumor-associated antigens remains challenging. We have recently developed novel functional approaches to identify antibodies able to deliver a payload to the primary tumor in a xenograft mouse model.

11:15 Phage Display Selection in Stage IV Cancer Patients: Safety of the Procedure, and Tumor-Specificity of Selected Antibodies

Girja Shukla, Ph.D., Associate Professor, Surgery; Member, Vermont Cancer Center, University of Vermont College of Medicine

A phage display selection technique in which a phage-antibody library is infused into cancer patients provides a novel approach for identifying tumor-specific antibodies that recognize both the patient's tumor cells and tumors of other patients. We conclude that these outcomes support the safety and utility of phage-display library panning in human cancer patients for ligand selection and target discovery for cancer treatment and diagnosis.

11:45 Phenotypic Selections Using Tumor and Stromal Cells to Identify Novel Oncology Targets

Louise Slater, Ph.D., Postdoctoral Fellow, Antibody Discovery and Protein Engineering, MedImmune

There is a shortage of validated targets to support therapeutic antibody discovery in different human diseases. While targets do arise from systematic explorations of disease biology, this can be a slow, complicated process. We have developed a phenotypic selection platform for the rapid identification and validation of novel antibody targets on disease-associated cells using phage display. This presentation will introduce phenotypic selections and show data from successful and ongoing projects.

12:15 pm Long-Read, Single-Molecule Sequencing Applications for Protein Engineering

Sponsored by PACIFIC BIOSCIENCES®

Erik Miller, Ph.D., Staff Scientist, Enzymology, Pacific Biosciences

PacBio® SMRT® Sequencing produces unprecedented read lengths and high-accuracy consensus sequencing. These features allow high-throughput sequencing of multi-kilobase constructs with high confidence and low cost, as well as simple identification of coupled mutations separated by thousands of bases in sequence. This talk provides an introduction to PacBio's DNA sequencing technology, an overview of the protein engineering efforts at Pacific Biosciences, and a case study of PacBio sequencing applications in a protein engineering pipeline.

12:45 Lunch on Your Own

1:15-1:45 Ice Cream Break in the Exhibit Hall

DESIGNING ANTIBODIES WITH ROSETTA

2:00 Chairperson's Remarks

Charlie E.M. Strauss, Ph.D., Technical Staff Member & Scientist, Bioscience Division, Los Alamos National Lab

2:05 Computational Prediction and Design of Antibody/Antigen Interactions

Jordan R. Willis, Ph.D., Laboratories of Jens Meiler Ph.D. and James Crowe M.D., Center for Structural Biology and Vaccine Research Center, Vanderbilt University Medical Center

Rosetta design of antibodies that target Influenza, HIV and Rotavirus are an *in silico* solution to enhancing specificity and breadth while providing insight into potential immunogens. Additionally, we use Rosetta for the incorporation of sparse orthogonal experimental data to aid in structure determination of antibody-antigen complexes.

2:35 Applying Rosetta to Antibody Loop Modeling and Docking

Jeffrey Gray, Ph.D., Associate Professor & F. Stuart Hodgson Faculty Scholar, Chemical & Biomolecular Engineering, Johns Hopkins University

The three-dimensional structure of antibodies is key to understanding mechanisms of binding and recognition. I will present latest advances in homology modeling and docking of antibodies, including recent work on the difficult problem of CDR H3 modeling and design applications in thermostability and cross-linking.

3:05 Enhanced Affinity with Improved Stability – The Power of Near-Germline Affinity

Sponsored by AB

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

How many mutations do you need to enhance affinity and how many mutations can your antibody sequence bear without losing stability? AbCheck has developed an extremely powerful tool to completely explore the near to germline sequence space. For up to five mutations from the germline encoded sequence, our libraries encode every possible combination of amino acids in more than 50 randomized positions. The technology delivers significantly improved antibodies and conclusive information about the paratope.

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

Recommended Tuesday Dinner Short Course*

Next-Generation Sequencing in Antibody Discovery for End Users

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

INTRACELLULAR DELIVERY

4:00 Chairperson's Remarks

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

4:15 Selection of Cell Binding and Internalizing Phage Antibodies for Targeted Drug Delivery

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

Antibodies that bind cancer cells and are internalized can be used for tumor targeted drug and nucleic acid delivery. Such antibodies can be selected from phage antibody libraries using the approaches that will be described. An example will also be provided of transitioning a targeted drug delivery vehicle into the clinic.

4:45 Novel Chemical Entities Introduced into Cells via Protein Pump

Bradley L. Pentelute, Ph.D., Assistant Professor, Massachusetts Institute of Technology

I will present a macromolecular delivery platform based on a engineered bacterial transport machine that allows for facile delivery of bioactive peptide variants to the cytosol of cells. We show that the delivered cargo material can disrupt protein-protein interactions in cancer cells and induce apoptosis.

5:15 End of Conference

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15th Annual | May 7-8

Engineering Antibodies

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

Recommended Pre-Conference Short Course*

Measures to Enhance Half-Life and Stability

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

WEDNESDAY, MAY 7

7:00 am Registration and Morning Coffee

SELECTION OF BIOLOGICALLY ACTIVE ANTIBODIES

8:00 Chairperson's Opening Remarks

Gregory P. Adams, Ph.D., Co-Leader, Developmental Therapeutics Program, Fox Chase Cancer Center

» 8:10 KEYNOTE PRESENTATION:
Identifying Functional Antibodies by Direct Expression in Reporter Cells

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

Using "traditional" cell-based screening assays we have generated a number of human antibodies that block cell signaling. We now report a novel system for identifying blocking antibodies by introducing antibody gene populations into ES reporter cells. Exemplified using FGF4 signaling, individual antibody-expressing ES clones exhibiting changes in differentiation outcomes are identified using lineage-specific gene expression allowing isolation of clones that encode and express signal-modifying antibodies.

8:40 Screening Antibody Phage Libraries in Product Format

Partha Chowdhury, Ph.D., Principal Scientist, MedImmune

Despite being a powerful technology for antibody discovery, phage libraries are severely limited because they cannot be directly screened in a relevant product format which is typically IgG. This talk will focus on the development and validation of a new technology that enables batch conversion of scFvs from phage libraries and high throughput screening as IgGs.

9:10 Preclinical Development of T Cell Directed Bispecific DART® Candidates

Ezio Bonvini, M.D., Senior Vice President, Research, MacroGenics, Inc.

Selection of DART clinical candidates proceeds from *in vitro* physicochemical and functional analyses to *in vivo* activity modeling and toxicological assessment. Challenges in this category of products include on-target and off-target effects as well as acute phenomena related to T cell activation and cytokine release. A strategy integrating *in vitro* and *in vivo* studies aimed at defining parameters for clinical translation is discussed.

9:40 The Use of Structure and Rosetta to Design Phage Libraries for Antibody Optimization

Will Somers, Ph.D., Vice President, Global Biotherapeutic Technologies, Pfizer

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

ANTIBODY THERAPEUTICS FOR NEURODEGENERATION

11:10 Pathogenic Protein Targets for Neurodegenerative Disease Immunotherapies

Anne Messer, Ph.D., Professor, Biomedical Sciences, University at Albany; Senior Scientist, Neural Stem Cell Institute

Proteostasis in neurons and other mature cells breaks down as a result of a range of degenerative disease triggers and aging. Engineered antibody fragments are ideal reagents for validating and manipulating target proteins that are known to misfold. This presentation will cover examples of this approach, mainly focused on Huntington's and Parkinson's diseases.

11:40 Passive Immunization of Anti-α-Synuclein Antibodies Attenuate Pathological Synuclein Aggregates and Improve Behavioral Deficits in a Transgenic Mouse Model

Robin Barbour, Head, Antibody Generation, Research, Prothena Biosciences

Over 2 million patients suffer from Parkinson's Disease (PD) in the US/Europe. At this time, there is no proven disease-modifying therapy for PD. PD patients shows abnormal intracellular inclusions called Lewy Bodies, composed of α-synculein, a protein that is also genetically linked to the disease. We will discuss the outcomes of passive anti-α-synuclein immunotherapy studies in a transgenic mouse model of synucleinopathy.

12:10 pm Proprietary and Unique Expression System for Versatile and Ubiquitous Transgene Expression

Sponsored by SELEXIS

Igor Fisch, Ph.D., CEO & Chairman, Selexis SA

Based on proprietary epigenetic regulator elements and leveraging the SURE CHO-M Genome and Transcriptome, Selexis has developed a mammalian expression platform capable of robust transcription and of overcoming complex secretion bottlenecks. This technology has an extensive history of generating high-level, stable expressing cell lines, including cell lines producing difficult-to-express proteins such as Fc:fusions and large multimeric proteins. The extensive characterization of the CHO-M cell line supports comprehensive and effective transfer packages for manufacturing.

12:40 Luncheon Presentation I: Evaluate Diagnostic Antibody Specificity by Using High Density Protein Microarray Technology

Sponsored by ORIGENE

Donghui Ma, Ph.D., CSO, Immunology, OriGene

Sensitivity and specificity are the two key features for a good diagnostic antibody. High density protein microarray technology is the best technology platform for antibody specificity evaluation. Here we showcase a novel protein microarray technology to evaluate target specificity for a couple of commonly used IHC diagnostic antibodies. Our data suggested that cross-reactivity is one of the reasons to create off-target staining. We will also introduce UltraMAB, the Ultra-specific monoclonal antibodies for anatomic pathology application.

1:10 Luncheon Presentation II
Human Single Domain Antibodies from the Crescendo Mouse

Sponsored by Crescendo Biologics

Joyce Young, Ph.D., Head, Transgenic Platforms, Crescendo Biologics Ltd.

VH single domains are the smallest, most robust antibody fragments with advantages for topical delivery, tissue and tumour penetration, engineering of multivalent products and simple manufacture. The Crescendo Mouse harnesses the benefits of *in vivo* maturation to generate heavy chain antibodies as a source of fully human VH. Data from multiple programmes will be used to illustrate its ability to rapidly generate a high diversity of potent leads with excellent biophysical properties.

1:40 Session Break

HIGH-THROUGHPUT ANTIBODY SELECTION AND ENGINEERING

2:00 Chairperson's Remarks

Partha Chowdhury, Ph.D., Principal Scientist, MedImmune

2:05 High-Throughput Epitope Discovery Using Biosensor Technology

Yasmina Abdiche, Ph.D., Research Fellow, Rinat-Pfizer

We evaluated label-free biosensors that process 96 unique interactions simultaneously and several hundred interactions per experiment. Since cross-blocking of two monoclonal antibodies is necessary but not sufficient for them to bind the same epitope, high-resolution epitope binning assays determined by HT experiments can yield exquisite epitope discrimination. We also demonstrate that an antibody's epitope and functional activity are correlated.

2:35 A High-Throughput Microfluidic Platform for the Discovery of Monoclonal Antibodies

Carl Hansen, Ph.D., Associate Professor, Center for High-Throughput Biology, University of British Columbia, Canada

3:05 A Unified Framework for Computer-Aided Biologics Design

Sponsored by CHEMICAL COMPUTING GROUP

Christopher R. Corbeil, Ph.D., Research Scientist, Chemical Computing Group

Protein engineering plays a pivotal role in modulating the function, activity and physical properties of biologics. Representative strategies employed in protein engineering include rational protein design and directed evolution. In general, disparate work has been done in applying computer-aided biologics design (CABD) to protein engineering for the development of novel biological therapeutics. Here, we establish a unified framework of protein engineering tools and investigate its applicability to modulation of protein properties: affinity and stability.

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

4:20 Droplet Microfluidics to Isolate Antibody-Secreting Cells

John Heyman, Ph.D., Research Associate, School of Engineering and Applied Sciences, Harvard University

Droplet-microfluidics methods are increasingly used for single-cell analysis. Mammalian cells are viable for several hours within 40 pL aqueous drops, which are formed and sorted at rates >500Hz. Cell-secreted molecules remain trapped in the droplets, and in-droplet sandwich-type assays can identify and select cells that secrete desired antibodies. Here we report use of these methods to isolate non-immortalized antibody-secreting cells.

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15th Annual | May 7-8

Engineering Antibodies

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

4:50 New Directions in Discovery of Antibodies from Native Sources Using NGS

Tadas Panavas, Ph.D., Principal Scientist, Molecular Protein and Biosciences, Janssen

With the means of next-generation sequencing combined with selective antigen specific B cell sorting we develop methods to molecularly clone antigen-specific antibodies from native or immunized sources. This technology bypasses the hybridoma fusion step and accelerates the timeline for isolation of mAbs. We compared natural mAbs derived from single B cells with antibodies resulting from artificial pairing of vH and vL from NGS analysis.

5:20 Networking Reception in the Exhibit Hall with Poster Viewing

6:30 End of Day

THURSDAY, MAY 8

7:45 am Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

MODEL-BASED ANTIBODY DEVELOPMENT

8:30 Chairperson's Remarks

Anne Messer, Ph.D., Professor, Biomedical Sciences, University at Albany; Senior Scientist, Neural Stem Cell Institute

8:35 Developing Antibodies against Difficult Targets Using Knowledge-Based Antibody Design

Gregory P. Adams, Ph.D., Co-Leader, Developmental Therapeutics Program, Fox Chase Cancer Center

The most interesting functional targets are often highly conserved between species making them particularly difficult targets for antibody generation. We have overcome prior failures of phage and immunization approaches by employing novel knowledge-based design strategies including homology modeling of the interaction between proteins in order to develop antibodies that specifically engage desired epitopes.

9:05 Analysis of Convergent Antibodies Reveals a Hallmark of Influenza Vaccine Seroconversion

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

In a deep repertoire analysis of antibodies elicited by influenza vaccination of human populations, no completely identical antibodies were seen in any two individuals. Using a "paratope convergence" analysis, highly similar vaccine-specific antibodies appeared in a high proportion of successfully vaccinated individuals, but were absent in those that failed to seroconvert.

9:35 Advancing Experimental and Computational Methods in Next-Generation Sequencing-Based Discovery of Monoclonal Antibodies

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

An outcome of the advancement of the field of systems immunology has been the emergence of next-generation sequencing; specifically its application in large-scale analysis of antibody variable gene repertoires. We have developed experimental and computational methods to help advance NGS of antibody repertoires. I will provide an overview of this research field and it's application towards the discovery and engineering of mAb therapeutics.

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

INTRACELLULAR ANTIBODIES

11:05 Antibody Fragments for Use Inside Cells as Templates for Drug Development

Terence H. Rabbitts, FRS FMedSci, Professor, Molecular Biology, Weatherall Institute of Molecular Medicine, MRC Molecular Hematology Unit, University of Oxford

Cancer cell growth is mediated by intracellular protein complexes that are difficult to disrupt for intervention. We have circumvented these limitations by developing new methods for drug target validation and discovery based on antibody fragments that function as intracellular inhibitors of protein-protein interactions. I will present work targeting mutant RAS in epithelial tumors and LMO2 in T-ALL as goal of employing molecular biology for improved patient treatment.

11:35 Therapeutic Antibodies to Intracellular Targets in Cancer Therapy

David A. Scheinberg, M.D., Ph.D., Chair, Molecular Pharmacology and Chemistry Program, Memorial Sloan-Kettering Cancer Center

ESK1, a human IgG1 mAb, mimics T-cell receptor specificity for a Wilms' tumor protein-derived peptide presented by HLA-A0201 and kills cancer cells via ADCC, suggesting that it could treat a range of cancers while sparing normal tissue. Bispecific formats of ESK are equally effective in mouse models of human cancers. These studies provide POC that TCR mimic mAb constructs can effectively treat cancers while targeting a low-density peptide/HLA epitope.

Sponsored by SCHRÖDINGER. BIOLOGICS

12:05 pm Luncheon Presentation: Improved Antibody Design Using Structure-Based Analysis and Computation

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

In this talk we describe recent successes and advances in predicting the H3 loop of the antibody CDR region, and demonstrate the value of a good structural antibody model for epitope/paratope identification when the model is combined with protein-protein docking. We also discuss how a model for the antibody/antigen complex can be used with *in silico* alanine scanning to identify mutational hot spots.

12:35 End of Conference

Recommended Tuesday Dinner Short Course*

Next-Generation Sequencing in Antibody Discovery for End Users

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

"The meeting was excellent: very well organized, great choice of presenters from academia, government and industry. I have set two collaborative studies during the meeting as a result of the talks and interesting topics."

Principal Investigator, Senior Staff Fellow, Hematology, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration (FDA)

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5th Annual | May 8-9

Engineering Bispecific Antibodies

Harnessing Complexity

THURSDAY, MAY 8

OPENING KEYNOTE SESSION:

1:30 pm Chairperson's Opening Remarks

Robert Mabry, Ph.D., Associate Director, Antibody Discovery and Bispecific Engineering, Adimab LLC

1:40 Bispecific and Bifunctional Antibodies for Modulating Immune Responses in Cancer Therapy

Roland E. Kontermann, Ph.D., Mildred Scheel Professor, Biomedical Engineering, University of Stuttgart

Bispecific and bifunctional antibody fusion proteins allow a targeted delivery and modulation of immunological responses, e.g. by retargeting effector cells of the immune system and activation of immunostimulatory or immunoregulatory signaling pathways. General strategies and new developments in the field will be presented.

2:10 Pathways with FDA: Insight into Regulation, Cocktails vs. Bispecific Antibodies

Kathleen A. Clouse, Ph.D., Director, Monoclonal Antibodies, FDA/CDER/OPS/OBP/DMA

2:40 High-Throughput Bispecifics Generation and Testing

Maria Wendt, Ph.D., Senior Scientific Consultant, Biologics, Genedata

The need for systematic evaluation of large panels of multi-specific antibodies poses new throughput bottlenecks for antibody engineering. Multiple next-generation antibody formats must be tested (e.g. bi- and multi-specifics, KinH, Fab-scFv, IgG-scFv, DVD-Ig, tandem-scFv-Fc), including all parametric variants (e.g. linkers, V-domain order, Fc), which creates huge combinatorial complexity. We present a new technology platform that allows for the systematic design and cloning of large numbers of novel molecules and automates downstream expression, purification, and characterization processes, which substantially increases throughput.

3:10 Refreshment Break in the Exhibit Hall with Poster Viewing

DEVELOPABILITY ASSAYS

3:55 Chairperson's Remarks

Robert Mabry, Ph.D., Associate Director, Antibody Discovery and Bispecific Engineering, Adimab LLC

4:00 Novel Engineering Solutions to the "Common Light Chain Problem" Give Rise to Potent Bispecifics with Favorable Developability Profiles

Robert Mabry, Ph.D., Associate Director, Antibody Discovery and Bispecific Engineering, Adimab LLC

We report here the engineering of multiple VHs that pair with a single light chain against three targets with unrelated epitopes. Bispecific constructs were generated with a common light chain that bind to each target with low picomolar affinities and exhibit favorable biophysical properties similar to benchmarks established by traditional mAbs.

4:30 Engineering Antibody Fc and Fab Regions for Generation of Bispecific and Monovalent Antibodies

Guna Kannan, Ph.D., Principal Scientist and Group Leader, Biologics Optimization, Amgen, Inc.

We have modified the CH3 domain of the Fc region and the light and heavy chain interface of the Fab with targeted mutations in order to generate bispecific antibodies. The engineered bispecific antibodies have desirable *in vivo* and *in vitro* stabilities. The presentation will cover the engineering aspects as well as various strategies used to mitigate the issues encountered during the screening and production stages.

5:00 Close of Day

Recommended Thursday Dinner Short Course*

Antibody-Based Cancer Immunotherapy

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

FRIDAY, MAY 9

7:45 am Continental Breakfast in the Exhibit Hall with Poster Viewing

NOVEL FORMATS

8:30 Chairperson's Remarks

Christian Klein, Ph.D., Head, Oncology Programs; Expert Scientist, Discovery Oncology oDTA, Pharma Research and Early Development (pRED), Roche Glycart AG

8:35 Bispecific DR5-FAP Antibodies: Efficient Tumor-Targeted Induction of Apoptosis for Cancer Therapy

Peter Bruenker, Ph.D., Large Molecule Research, Pharma Research and Early Development (pRED), Roche Glycart AG

We have generated novel bispecific agonistic DR5-FAP antibodies for tumor targeted induction of apoptosis. These tetravalent bispecific molecules specifically induce apoptosis of DR5 positive tumor cells only in the presence of FAP expressed on a second cell line by efficient DR5 cross-linking. *In vivo* studies in mouse xenograft models demonstrated superior efficacy of these bispecific antibodies as compared to the parental agonistic DR5 antibody alone.

9:05 Preclinical Developments with a Fully Human Bispecific Antibody Platform

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

This presentation will describe the generation of a platform technology to generate fully human bispecific antibodies through the combination of Fc modifications that allow selective protein A purification and VelocImmune® derived antibodies that utilize a single defined light chain. Molecular characterization and *in vitro*/*in vivo* data showing the efficacy of this format will be discussed. In addition, preclinical findings with proof-of-principle molecules targeting T cells will be presented.

9:35 DutaMabs: Ultrastable Fully Human Bispecific Antibodies with Two Independent Paratopes in the Fv Region

Kristian Jensen, Ph.D., Vice President, Project Management, R&D, Dutalys GmbH

This presentation will show the fully independent behavior of the two paratopes in DutaMabs, including paratope maturation to low picomolar affinities and describe the most stable antibodies described to date, including lessons learned from engineering the first antibodies with stabilities above boiling point.

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

ENHANCED PROPERTIES

10:45am Chairperson's Remarks

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

10:50 Effective Tumor Killing by Bispecific IgG1-Her2XCD3 Antibodies Generated by Controlled Fab-Arm Exchange

Aran F. Labrijn, Ph.D., Senior Scientist, Antibody Sciences, Genmab BV

This presentation will describe the efficient generation of stable bispecific IgG1 using controlled Fab-arm exchange (DuoBody® platform). We will address the effects of 1) epitope binding, 2) Her2 expression density, and 3) Fc-backbone on T cell mediated tumor killing in a proof-of-concept model using bispecific IgG1-CD3xHER2 antibodies.

11:20 Enhanced Soluble Antigen Clearance by a Chelating Bispecific Antibody

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

Soluble ligands have frequently been targeted by biologics for therapy of cancers and other diseases. Here we present an approach combining potent neutralization and fast clearance by using a bispecific antibody that targets two different epitopes on interleukin-6, inducing formation of large immune complexes that show enhanced binding to FcγRs, are efficiently phagocytosed by macrophages, and are cleared rapidly from circulation.

11:50 Built-In Purification Technologies to Readily Purify Bispecific Heavy Chain Heterodimers

Stanislas Blein, Ph.D., Deputy Director, Antibody Engineering, Biologics Research, Glenmark Pharmaceuticals S.A.

BEAT® antibodies are bispecific heavy chain heterodimers with a built-in purification system that relies on a difference in Protein A affinity between hetero and homodimers. To consistently achieve high levels of purity, we have developed solutions when dealing with bispecific antibodies from the VH3 subclass that would normally interfere. In addition, a second method based on a difference in Protein G affinity was developed to readily purify bispecific heterodimers in two subsequent affinity purification steps. Technology backgrounds and preclinical applications will be presented.

12:20 pm Enjoy Lunch on Your Own

12:50 Session Break

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5th Annual | May 8-9

Engineering Bispecific Antibodies

Harnessing Complexity

INDICATIONS OUTSIDE OF ONCOLOGY

1:35 Chairperson's Remarks

Christian Klein, Ph.D., Head, Oncology Programs; Expert Scientist, Discovery Oncology oDTA, Pharma Research and Early Development (pRED), Roche Glycart AG

1:40 A Bispecific CrossMAb for Ophthalmic Indications

Jörg Thomas Regula, Ph.D., Pharma Research and Early Development (pRED), Large Molecule Research (LMR), Roche Diagnostics GmbH

The CrossMAb technology is an innovative approach to generate a bispecific antibody by IgG domain exchange that retains its IgG-like properties. Applying this technology, a bispecific human IgG1 antibody (CrossMab) depleting two angiogenic factors simultaneously was produced. To accommodate the specific requirements of ophthalmologic indications this CrossMab was adopted by Fc engineering.

2:10 Selection and Formatting of Bispecific Domain Antibodies for Therapeutic Use

Claire Ashman, BSc (Hons), Senior Scientific Investigator, Biopharm Innovation and R&D, GlaxoSmithKline Medicines Research Centre

This talk will provide an update on the preclinical and clinical data of bispecific domain antibody-based drugs that are currently in clinical development. It will cover library design, lead discovery process/engineering and the selection of formats for improved biological, biophysical and pharmacokinetic properties, focussing on the bispecific platforms.

2:40 Generation of an Asymmetric Bispecific IgG Antibody Mimicking the Function of FVIII Cofactor Activity for the Treatment of Hemophilia A

Zenjiro Sampei, Research Scientist, Research Division, Chugai Pharmaceutical Co., Ltd.

An anti-FIXa and FX asymmetric bispecific IgG antibody having the cofactor activity of FVIII was identified. It was optimized multidimensionally to exhibit sufficient FVIII-mimetic activity and enable subcutaneous delivery at long dosing intervals for the treatment of hemophilia A as well as large scale manufacturing of a bispecific IgG antibody. We expect that the clinical candidate ACE910 will provide significant benefits for hemophilia A patients and their families.

3:10 COVA322: A Novel, Bispecific TNF/IL-17A Inhibitor for the Treatment of Inflammatory Diseases Moving towards the Clinic

Dragan Grabulovski, Ph.D., CSO, Covagen AG

Covagen develops bispecific FynomAbs by fusing its fully human Fynomer binding proteins to antibodies. Here we will discuss the results of this process and introduce COVA322, a bispecific TNF/IL-17A inhibitor, which blocks the activity of both cytokines *in vitro* and *in vivo* with picomolar inhibition potencies.

3:40 Structure-Based Design of Novel Bispecifics Platforms

Stephen Demarest, Ph.D., Research Advisor, Lilly Biotechnology Center

The presentation will describe the combination of computational and rational design approaches paired with directed engineering to support the development of novel bispecific antibody platforms with high stability, multiple geometries and multiple valencies. Applications enabled by these Bispecific molecules will be described.

4:10 End of Conference

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4th Annual | May 5-6

Antibodies for Cancer Therapy

Challenging the Current Treatment Paradigm

Recommended Pre-Conference Short Courses*

Translational Strategies for Development of Monoclonal Antibodies from Discovery to Clinic, Part 1: Focus on Early Discovery & Part 2: Focus on Nonclinical Development to Clinic

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

MONDAY, MAY 5

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks

Kristi Sarno, Chair, Greater Boston Chapter, Women in Bio; Director, Business Development, Pfenex, Inc.

8:40 Harnessing the Patient's Immune System to Combat Cancer

Peter CR Emtage, Ph.D., Vice President, Immune Mediated Therapies, MedImmune

With recent FDA approvals, modulation of the immune system is now a clinically validated approach in the treatment of some cancers. At MedImmune, the Oncology Department is developing assets and expertise in Immune Mediated Therapy of Cancer (IMT-C). The challenges from a drug development perspective are multi-fold. The talk will focus on the relevance of preclinical models and translational science to address key issues, including dose selection and rationale combinations.

9:25 Building Regeneron's Pipeline: From Trap Technology to the *VelocImmune* Platform to *VelociNext*

George D. Yancopoulos, M.D., Ph.D., President, Regeneron Laboratories; CSO, Regeneron Pharmaceuticals, Inc.

George D. Yancopoulos, M.D., Ph.D., who is the Founding Scientist, President, Research Laboratories and Chief Scientific Officer of Regeneron Pharmaceuticals, one of the world's top biotechnology companies, will discuss how he and his colleagues exploited a commitment to science and technology to start the company, withstand years of challenges and failures, and emerge with a pipeline of promising technologies and novel/biologics that are beginning to bring hope to countless patients and their families.

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

TRENDS IN IMMUNOTHERAPY

11:05 Chairperson's Remarks

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

11:10 Glass Half-Empty or Half-Full? Potential Mechanisms of Non-Response to Immunomodulatory Antibodies

Robert H. Pierce, M.D., CMO, OncoSec Medical, Inc.

11:40 Mechanisms by Which Tumor Antigen-Specific Antibodies Enhance and Skew Tumor Antigen-Specific Cellular Immune Responses

Neil Gildener-Leapman, M.D., Instructor, Otolaryngology, University of Pittsburgh Medical Center

This talk will describe the ability of tumor antigen targeted mAb to enhance cellular immunity, to skew the T lymphocyte response in the tumor microenvironment, with implications for novel combination therapeutic strategies.

12:10 pm Selected Poster Presentation: Chemically Programmed Bispecific Antibodies in DART Format

Even Walseng, Ph.D., Senior Research Associate, Cancer Biology, The Scripps Research Institute

12:25 Selected Poster Presentation: Annotation of the Heavy Chain Immunoglobulin Gene Locus in Cynomolgus Monkeys by High-Throughput Antibody Repertoire Sequencing

Ina Hellmann, Ph.D., Department of Biosystems Science and Engineering, ETH Zürich

12:40 Enjoy Lunch on Your Own

1:40 Session Break

2:00 Chairperson's Remarks

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

2:05 Antibodies as Mediators of Anti-Tumor Immunity

Robert A. Anders, M.D., Ph.D., Associate Professor, Pathology, Johns Hopkins School of Medicine

We have developed a functional proteomics approach to identify antibody targets of the immune response. Using immunized sera from patients responding to immunotherapy, we have identified a panel of antigenic and tolerating proteins and have studied their role in preclinical models. These data and their clinical and diagnostic implications will be discussed.

» 2:35 KEYNOTE PRESENTATION:

Recent Advances in Cancer Immunotherapy

Michael B. Atkins, M.D., Deputy Director, Georgetown-Lombardi Comprehensive Cancer Center; Professor, Oncology and Medicine, Georgetown University Medical Center

This talk will cover the immune checkpoints CTLA-4 and PD-1. Antibodies targeting these molecules, used alone or in combinations, can restore anti-tumor immunity and produce rapid and sustained tumor responses in patients with a variety of advanced malignancies leading to broad-based clinical development efforts.

3:05 PD-1 Immunotherapy

Gordon Freeman, Ph.D., Associate Professor, Medicine, Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School

3:35 Novel MHC Class I Antibody Fusions for Cancer Treatment

Hendrik Knoetgen, Ph.D., Head, LMR Penzberg & pRED, Roche Diagnostics GmbH

Here we describe a novel recombinant format of viral peptide-MHC class I IgG fusion proteins. Our results show for the first time that recombinant pMHC class I full length antibody fusions successfully recruit pre-existing virus specific CD8+ T cells from human PBMCs and effectively trigger eradication of the targeted tumor cells.

4:05 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem Solving Breakout Discussions

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

6:45 End of Day

TUESDAY, MAY 6

7:45 am Morning Coffee

CANCER INITIATING CELLS, NOVEL TARGETS AND SIGNALING

8:25 Chairperson's Remarks

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

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ONCOLOGY STREAM

4th Annual | May 5-6

Antibodies for Cancer Therapy

Challenging the Current Treatment Paradigm

8:30 Therapeutic Antibodies Targeting Glypican-3 in Liver Cancer

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

Heparan sulfate proteoglycans (HSPGs) are important modulators of cell signaling during development and disease. We have generated antibodies specific for oncofetal antigen glypican-3. The antibodies inhibit liver cancer cell proliferation and xenograft tumor growth in mice via inactivating 'YAP signaling' and other signaling pathways. HSPGs may be a novel class of potential targets for antibody-based cancer therapy.

9:00 Evaluation of T Cell Agonists for Cancer Immunotherapy

Jeong Kim, Scientist, Cancer Immunology, Genentech, Inc

Productive immune responses to tumors are hypothesized to require T cell costimulation. OX40 is a costimulatory molecule that is expressed on activated effector T and Treg cells. Agonistic antibodies targeting OX40 are predicted to counteract the immunosuppressive tumor microenvironments and promote T cell dependent anti-tumor immunity via two distinct mechanisms, activation and expansion of antigen experienced T cells and inhibition of T cell suppression.

9:30 Therapeutic Targeting of Signaling Pathways Critical for Cancer Stem Cells

Timothy Hoey, Ph.D., Senior Vice President, Cancer Biology, OncoMed Pharmaceuticals, Inc.

Cancer stem cells (CSCs) mediate tumor progression, metastasis, and drug resistance. We have developed new biologics that antagonize key CSC signaling pathways including Notch, Wnt and RSPO-LGR. Currently, we have five therapeutics advancing in clinical testing, as well as others in preclinical development. These agents inhibit tumor growth through multiple mechanisms including mediating a reduction of CSC frequency.

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

10:45 BNC101: A Highly Selective, Humanized Antibody Targeting LGR5 on Cancer Stem Cells

Christopher L. Reyes, Ph.D., Vice President, Research & Development Biologics, Bionomics, Inc.

Using our validated CSC Rx Discovery platform, we have developed multiple novel therapeutic monoclonal antibodies that target key cancer stem cell receptors overexpressed in solid cancers. We will review BNC101, and how in preclinical studies it blocks the growth of cancer stem cells derived from primary patient tumors both *in vitro* and *in vivo*.

11:15 Tumor Antigen-Specific Antibody-Based Immunotherapy of Malignant Disease, Cancer Initiating Cells and Disease Recurrence

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

Following a description of the characteristics of cancer initiating cells (CICs) and the markers used for their identification in various types of cancer, we will provide evidence to suggest that disease recurrence is caused by the lack of eradication of CICs by the TA-specific mAb-based immunotherapy. In addition, we will describe potential strategies to overcome this resistance.

11:45 Using Peptide Conjugation to Create Brain-Penetrant mAbs for Targeting Metastatic Brain Tumors

Jean Lachowicz, Ph.D., CSO, R&D, Angiochem

While targeted therapy with mAbs has dramatically increased survival rates in patients with extracranial tumors, metastatic tumors in the brain remain untreated due to inability of mAbs to cross the blood-brain barrier. We have engineered peptides (Angiopeps) which utilize receptor-mediated transcytosis to enter the brain and achieve therapeutic brain concentrations. Angiopep-mAb conjugates have been shown to be brain-penetrant.

12:15 pm Luncheon Presentation I: A Look Inside Genentech's Protein Sciences Organization

Sponsored by Genentech, A Member of the Roche Group

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

12:45 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:15-1:45 Ice Cream Break in the Exhibit Hall

2:00 Panel Discussion: Industry-Academic Collaboration

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

Panelists: Stuart A. Aaronson, M.D., Aron Professor and Founding Chair, Emeritus, Oncological Sciences, Icahn School of Medicine at Mount Sinai

Michelle F. Browner, Ph.D., Platform Innovation & Partnership Management, Johnson & Johnson Innovation Center

Christine A. Jost, Ph.D., Associate Director, Technology Ventures Office, Beth Israel Deaconess Medical Center

3:05 Targeting of Solid Tumors with Bi-Specifics and Bi-Specific ADC's – Achieving Novel Biologies and Drug-Like Properties

Sponsored by zymeworks

David Poon, Ph.D., Director, External R&D and Alliances, Zymeworks Inc.

A robust, developable and manufacturable bi-specific platform will be discussed as the foundation to engineer novel anti-solid tumor antibodies. Unlike combination therapies, these bi-specifics demonstrate enhanced tumor decoration, tumor diffusion and retention, internalization, and effector functions. Supported with *in vivo* efficacy studies, a number of bi-specifics and bi-specific ADC modalities will be discussed.

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

IMPACT OF TECHNOLOGY ON CLINICAL EFFICACY

4:15 Discovery and Development of GAZYVA (obinutuzumab, GA101): A Glycoengineered Type II CD20 Antibody for the Therapy of Chronic Lympocytic Leukemia

Christian Klein, Ph.D., Head, Oncology Programs; Expert Scientist, Discovery Oncology oDTA, Pharma Research and Early Development (pRED), Roche Glycart AG

We have found that GAZYVA is the only glycoengineered Type II CD20 antibody in clinical trials. Its preclinical properties as they relate to clinic and clinical data from the CLL11 trial will be reviewed.

4:45 Trastuzumab Induces Phosphorylation of EGFR Family Receptors to Mediate CSK-Homologous Kinase-Coupled Growth Inhibitory Pathway

Wen Jin Wu, M.D., Ph.D., Senior Investigator, Monoclonal Antibodies, Office of Biotechnology Products, Office of Pharmaceutical Science, Center for Drug Evaluation and Research, FDA

We have found that overexpression of CHK not only mimics trastuzumab treatment to mediate ErbB2 phosphorylation and more, but also enhances both trastuzumab-induced ErbB2 phosphorylation and degradation. Moreover, CHK overexpression combined with trastuzumab exerts an additive effect on cell growth inhibition. Our data demonstrates that CHK is a downstream effector of ErbB2 mediating trastuzumab-induced growth inhibition.

5:15 End of Conference

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2nd Annual | May 7-8

Advancing Bispecific Antibodies to the Clinic for Oncology

Recommended Tuesday Dinner Short Course*

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

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

WEDNESDAY, MAY 7

7:00 am Registration and Morning Coffee

BISPECIFIC ANTIBODIES, COMBINATIONS AND MIXTURES

8:00 Chairperson's Opening Remarks
Rakesh Dixit, Ph.D., DABT, Vice President, R&D, MedImmune (AstraZeneca Biologics)

» 8:10 KEYNOTE PRESENTATION:

Smart Strategies for Developing Bispecifics, Combinations and Mixture of Antibodies
Rakesh Dixit, Ph.D., DABT, Vice President, R&D, MedImmune (AstraZeneca Biologics)
This talk will cover an overview of bispecifics biologics, combinations and mixtures. It will also review technological advances in developing bispecific biologics and will discuss what distinguishes mixtures from combinations. CMC and regulatory considerations as well as strategies to develop bispecifics vs. combinations or mixtures will be shared.

9:10 Dual Variable Domain – Ig (DVD – Ig™) Platform: Some Opportunities and Challenges for Developing the Next Generation of Cancer Therapies
Tariq Ghayur, Ph.D., Senior Principal Scientist & Research Fellow, AbbVie Bioresearch Center

9:40 An Efficient Route to Generate Bispecific Antibodies with Natural Architecture from Distinct Half-Antibodies
Christoph Spiess, Ph.D., Scientist, Antibody Engineering and Structural Biology, Genentech, Inc.
The presentation will cover a technology to use the knobs-into-holes technology to generate bispecific antibodies with non-common light chains. Individual half-antibodies are purified, combined and finally the bispecific antibody purified. The versatility and robustness of the approach will be demonstrated by a broad set of bispecific antibodies.

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

11:10 Multispecific T Cell Products for Cancer Immunotherapy
Nabil M. Ahmed, M.D., MPH, Assistant Professor, Pediatrics Center for Cell and Gene Therapy, Baylor College of Medicine
Targeted T cells are emerging as effective non-toxic therapies for cancer. Multiple elements, however, contribute to the overall pathogenesis of cancer through both distinct and redundant mechanisms. Hence, targeting multiple cancer-specific markers simultaneously could result in better therapeutic efficacy by offsetting antigen escape tumor cell variants and by providing a holistic approach by simultaneously targeting elements of the tumor microenvironment.

11:40 Challenges and Opportunities in Developing Highly Effective Antibody Mixtures
Mikkel Wandahl Pedersen, Ph.D., Director, Cancer Biology, Symphogen A/S
Antibody mixtures are emerging as a promising alternative to monoclonal and bi-specific antibodies. This talk will address some of the opportunities and challenges associated with development of highly effective antibodies mixtures.

12:10 pm Enjoy Lunch on Your Own

1:40 Session Break

CHECKPOINT REGULATION:
Multi-Specifics and Their Potential Use as Immune Checkpoint Regulators

2:00 Chairperson's Remarks
David M. Hilbert, Ph.D., CSO & Head, R&D, Zyngenia, Inc.

» 2:05 KEYNOTE PRESENTATION:

Engineering Antibodies for Cancer Immunotherapy
Louis M. Weiner, M.D., Director, Lombardi Comprehensive Cancer Center, Georgetown University Medical Center
Contemporary antibody engineering has long focused on improving cancer therapy through the manipulation of protein structures. This remains important, but it is more important than ever to consider tumor targets, immune targets and how tumors adapt to immune attack or signaling perturbation initiated by antibody therapy. These issues will be discussed with a particular emphasis on targeting the EGF receptor network in human cancer.

2:35 Bispecific Antibody Targeting CD47 Aiming at Increasing Phagocytosis of Cancer Cells
Nicolas Fischer, Ph.D., Head, Research, NovImmune SA
CD47 is a ubiquitously expressed transmembrane receptor with multiple functions in cell-to-cell communication. Its interaction with SIRPα expressed in macrophages and DCs inhibits their phagocytic function. Overexpression of CD47 in cancer cells is often observed and it is believed to help cancer cells escape immune surveillance. We have generated bispecific antibodies (BsAbs) that preferentially neutralize CD47-SIRPα interaction on cancer cells.

3:05 Development and Manufacturing of a Common Light Chain Bispecific Antibody: MCLA-128 as a Case Study
Lex Bakker, Ph.D., Chief Development Officer, Merus
MCLA-128 is an ADCC-enhanced human common light chain bispecific IgG1 antibody targeting HER2 and HER3. MCLA-128 demonstrates potent inhibition of HER2:HER3 heterodimer signaling and robust anti-tumor activity in a trastuzumab-resistant xenograft model. It is produced in CHO cells using low fucose expression technology and Merus' proprietary CH3 engineering to force bispecific IgG heterodimerization. A robust purification process was developed resulting in ultra pure MCLA-128 at high process yields. MCLA-128 is currently undergoing cGMP manufacturing to allow clinical evaluation in a planned first in human phase I study.

3:20 Sponsored Presentation *(Opportunity Available)*

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

4:20 Problem Solving Breakout Discussions

5:20 Networking Reception in the Exhibit Hall with Poster Viewing

6:30 End of Day

THURSDAY, MAY 8

7:45 am Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

BIODISTRIBUTION

8:30 Chairperson's Remarks
Stanley R. Frankel, M.D., Executive Director, Medical Sciences, Amgen Rockville, Inc.

8:35 A Critical Evaluation of Disease-Homing Properties of Bifunctional Antibody Products
Dario Neri, Ph.D., Institute of Pharmaceutical Sciences, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology Zurich

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Advancing Bispecific Antibodies to the Clinic for Oncology

My laboratory has worked for the last 18 years in the field of armed antibody therapeutics, in collaboration with Philogen. In this lecture, I will present biodistribution results in animal models of disease and imaging results in patients, outlining their relevance for therapeutic application.

9:05 PET Imaging in Antibody Development: Immuno-PET

Guus van Dongen, Ph.D., Professor, Radiology and Nuclear Medicine, Preclinical Imaging, VU University Medical Center Amsterdam

In this presentation the potential and QA/QC aspects of PET imaging with radiolabeled monoclonal antibodies during preclinical and clinical antibody development will be described and illustrated. Related to this, the European Infrastructure for Translational Medicine (EATRIS) will be introduced, which supports pharma and biotech companies in their translational drug development programs.

CLINICAL PROGRESS

9:30 Chairperson's Remarks

Stanley R. Frankel, M.D., Executive Director, Medical Sciences, Amgen Rockville, Inc.

» 9:35 KEYNOTE PRESENTATION:

Engineering Antibodies with Potent and Broad Inhibitory Activity against HIV

David D. Ho, M.D., Scientific Director & CEO, Aaron Diamond AIDS Research Center; Irene Diamond Professor, The Rockefeller University

Dr. Ho's group has been engineering antibodies that could be used to block HIV transmission. Specifically, his team has constructed over 100 antibody molecules, most of which are bispecific with one arm directed to one of the viral receptors and one arm directed to an element on the viral envelope glycoprotein. Extremely potent antibodies have been identified and characterized as candidates for clinical development for the purpose of HIV prevention.

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

11:05 Bispecific T cell Engagers (BiTEs®): Progress in Clinical Development

Stanley R. Frankel, M.D., Executive Director, Medical Sciences, Amgen Rockville, Inc.

11:35 Multispecific Antibody Molecules for Treatment of Cancer

Alexey Lugovskoy, Ph.D., Vice President, Therapeutics, Merrimack Pharmaceuticals

Multispecific antibodies have a strong potential to overcome tumor resistance to targeted therapies and chemotherapies, and they have proven difficult to develop due to both suboptimal design and poor pharmaceutical properties. Network Biology approach overcomes these complexities and accelerates the discovery of active and manufacturable therapeutic molecules. This approach will be illustrated by the case studies of multispecific antibodies for the treatment of cancer developed at Merrimack Pharmaceuticals.

12:05 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

12:35 End of Conference

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4th Annual | May 8-9

Antibody-Drug Conjugates

Novel Payloads, Linkers & Conjugation, Target Expression & Internalization

Recommended Pre-Conference Short Course*

Novel and Emerging Conjugation Methods for ADCs

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

THURSDAY, MAY 8

CLINICAL UPDATES

1:30 pm Chairperson's Opening Remarks
Pamela A. Trail, Ph.D., Vice President, Oncology, Regeneron Pharmaceuticals

1:40 Examination of ADC Safety: Dose-Limiting Toxicities with ADCs: A Clinical Update
Flavia Brunstein, M.D., Ph.D., Safety Science Leader, Early Development, Genentech
The concept of an ADC is to improve the "therapeutic window" of cancer chemotherapy. This presentation will examine the therapeutic windows for representative ADCs in clinical development. A discussion of efficacy and toxic liabilities of specific ADCs will provide such a vision as we peer into the therapeutic window of such agents.

2:10 Clinical Development of ADCs at Seattle Genetics
Nancy Whiting, Pharm.D., Senior Medical Director, Seattle Genetics
In addition to a broad clinical development program with Seattle Genetics' approved ADC ADCETRIS (brentuximab vedotin), the company has multiple other ADC programs in its pipeline. This talk will highlight novel targets and ADCs in development with a focus on recent clinical data.

2:40 Site Specific ADC Generation Using SMARTag™ Technology
Sponsored by Catalent
David Rabuka, Ph.D., CSO, Redwood Bioscience
Dr. David Rabuka from Redwood Bioscience will present a protein engineering platform, SMARTag™ Technology, that enables precise, programmable, site- specific chemical protein modification. Redwood Bioscience generates ADCs with enhanced efficacy, safety, stability by utilizing this proprietary aldehyde-tagging technology and novel linker chemistries. The presentation will highlight data demonstrating SMARTag™ ADC efficacy and safety in preclinical tumor models and PK studies.

3:10 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 4:00 Phase I Experience with SAR566658: An Anti-CA6-SPDB-DM4 ADC
Anne Bousseau, Head, Early Development Projects Oncology, Sanofi-Aventis
SAR566658 is the third ADC progressed to the clinic by Sanofi. CA6 is a MUC-1 glycotope specifically expressed on certain cancers. This talk will highlight the first results of the Phase I trial, as well as the lessons learned accumulated from the 3 projects that will help designing the next molecules.

4:30 *In vitro-in vivo* Molecular Integrity of Antibody-Drug Conjugates: Applying Learning to Clinical Measurements for ADCs
Dan Rock, Ph.D., Scientific Director, Pharmacokinetics and Drug Metabolism, Amgen, Inc.
Antibody-drug conjugates (ADC) represent the fusion of a small and large molecule wherein the efficacy and tolerability of ADC molecules are governed by molecular integrity and targeted delivery of the cytotoxic small molecule. Factors affecting the ADC stability are reviewed and the subsequent impact on ADC disposition is considered in the context of clinical monitoring.

5:00 Close of Day

Recommended Thursday Dinner Short Course*

Antibody-Drug Conjugate Therapeutics: Potential and Challenges

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

FRIDAY, MAY 9

7:45 am Continental Breakfast in the Exhibit Hall with Poster Viewing

THE IMPORTANCE OF TARGET EXPRESSION & INTERNALIZATION IN MAKING A GOOD ADC

8:30 Chairperson's Remarks
Adeela Kamal, Ph.D., Associate Director, Oncology Research, MedImmune

8:35 Strategies for Efficient ADC Target Discovery and Lead Selection
Adeela Kamal, Ph.D., Associate Director, Oncology Research, MedImmune
Lessons learned from target identification and validation will be discussed as well as the importance of target expression and internalization and approaches to select a lead ADC - a case study.

9:05 Translational Modeling and *in vivo* Imaging in the Design and Development of Antibody-Drug Conjugates
Shu-Wen Teng, Scientist, Millennium Pharmaceuticals, The Takeda Oncology Company
Successful ADC development requires both consideration of patient characteristics (such as antigen expression and tumor vascularity), and ADC optimization (including antibody binding affinity and payload potency). To gain insights into the effect of these design choices, we constructed a mechanistic mathematical model of ADC efficacy, which integrates experimental findings from *in vivo* imaging, *in vitro* viability, and xenograft activity studies.

9:35 Imaging: Value-Added in Preclinical and Clinical ADC Development
Neil Bander, M.D., Professor, Weill Cornell Medical College
Imaging yields unique information by providing a functional and quantitative view of antibody targeting and uptake into tumor both in the preclinical setting as well as clinical trials. It provides a valuable assessment of target quality in an *in vivo* context and a patient's potential to benefit. It can make the difference between ADC product success and failure.

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

10:50 A Novel Approach to ADCs for Targets with Low Expression
Timothy B. Lowinger, Ph.D., CSO, Mersana Therapeutics, Inc.
The application of Fleximer® to antibody-drug conjugate (ADC) design can provide numerous advantages, including significantly higher capacity for drug payload; utilization of alternative payloads not suitable for direct conjugation; and improvement of physicochemical properties. In particular, benefits of the Fleximer approach for ADCs directed at low expression targets will be presented.

11:20 PANEL DISCUSSION: Target Expression
Moderator: Pamela A. Trail, Ph.D., Vice President, Oncology, Regeneron Pharmaceuticals
Panelists: Peter U. Park, Ph.D., Vice President, Biology, Mersana Therapeutics
Nancy Whiting, Pharm.D., Senior Medical Director, Seattle Genetics
Dan Rock, Ph.D., Scientific Director, Pharmacokinetics and Drug Metabolism, Amgen, Inc.
Neil Bander, M.D., Professor, Weill Cornell Medical College

- What are the characteristics of a good ADC target?
- Is there a minimal level of target expression required for ADC or does this vary for different drug payloads/linkers/targets?
- Tumor vs. normal: what is an acceptable difference in expression?
- How do you gauge what is acceptable efficacy for ADC against a particular target?
- What types of models are most informative?
- What are the target tissues that are most concerned for ADC? Based on previous clinical data?
- What can we learn by employing imaging technologies (pre-clinically and in Phase 1 trials)?

NOVEL PAYLOADS AND LINKERS

11:50 Developing Novel Linker-Drugs for Use in ADCs
Thomas Pillow, Ph.D., Scientist, Discovery Chemistry, Genentech
Combining the specificity of a monoclonal antibody with the cell killing ability of a cytotoxic agent is an outstanding method for treating cancer. Assembling the correct combination of these three components is key to this strategy: antibody, linker, and cytotoxic drug. This presentation briefly reviews some of the successful applications of this technology and discusses the future directions of linkers and cytotoxic drugs.

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4th Annual | May 8-9

Antibody-Drug Conjugates

Novel Payloads, Linkers & Conjugation, Target Expression & Internalization

Sponsored by NBE therapeutics

12:20 pm Luncheon Presentation: Development of Homogenous "Next-Generation" Antibody Drug Conjugates by Enzymatic Conjugation

Ulf Grawunder, Ph.D., CEO, NBE-Therapeutics Ltd.

Recently approved antibody drug conjugates (ADCs) have shown to be highly potent anti-tumor drugs, exceeding the efficacy of conventional antibodies therapies. All current ADCs in clinical use are generated by chemical conjugation of drugs to antibodies leading to heterogeneous ADCs. Here, we present a novel enzymatic conjugation platform that allows generation of homogenous ADCs with defined drug-to-antibody ratios, and by which the drug conjugation site can precisely be controlled.

12:50 Session Break

1:35 Chairperson's Remarks

Peter Kiener, Ph.D., CSO, Ambrx, Inc.

1:40 Development of IMGN289, a Novel EGFR-Targeting Antibody-Maytansinoid Conjugate

Yulius Setiady, Ph.D., Principal Scientist, Discovery Research, ImmunoGen, Inc.

EGFR is a validated target for cancer therapy. To address limitations of current EGFR therapies, we have developed IMGN289, an ADC which combines a novel anti-EGFR antibody and the cytotoxic payload, DM1. IMGN289 is active against EGFR-overexpressing tumor regardless of their dependency on the EGFR pathway.

2:10 Enabling Conjugations of Problematic ADC Payloads

Russell Dushin, Ph.D., Associate Research Fellow, Worldwide Medicinal Chemistry, Pfizer, Inc.

The physicochemical characteristics of small molecules considered as payloads for conjugation to antibodies can have a profound effect upon the success of their conjugation. This presentation highlights some of the challenges we've faced in conjugating problematic payloads and the steps we've taken to overcome these challenges by altering the composition of the linker and through exploration of alternative modes of conjugation.

2:40 Development of SYD985 – A Second Generation Duocarmycin Anti-HER2 ADC with Superior Therapeutic Window

Marco Timmers, Ph.D., CSO, New Molecular Entities, Synthon Biopharmaceuticals

This presentation highlights Synthon's second generation Linker-Drug technology and its complementarity with novel proprietary duocarmycin payloads, yielding highly stable and potent ADCs. Emphasis is given to SYD985, a second-generation duocarmycin anti-HER2 ADC. Improved CMC characteristics, efficacy in patient-derived xenografts and lack of toxicity in cynomolgus monkeys resulted in a superior therapeutic window compared to Roche's Kadcyla (T-DM1).

3:10 A Universal Chemically Driven Approach for the Synthesis of Homogeneous ADCs

David Jackson, Ph.D., Principle Scientist, ADC Discovery, Igenica, Inc.

Igenica has invented novel site-specific linkers to enable the synthesis of homogeneous ADCs. The linkers are compatible with a variety of different ADC payloads and can be applied directly to any antibody without prior modification. Analytical data, functional activity, and efficacy of these ADCs in two different tumor models will be presented.

NOVEL CONJUGATION METHODS

3:30 Location Matters: Site of Conjugation Modulates Stability and Pharmacokinetics of Antibody-Drug Conjugates

Jaume Pons, Ph.D., Senior Vice President, CTO, Pfizer, Inc. Biotech Unit R&D Group; CSO, Rinat

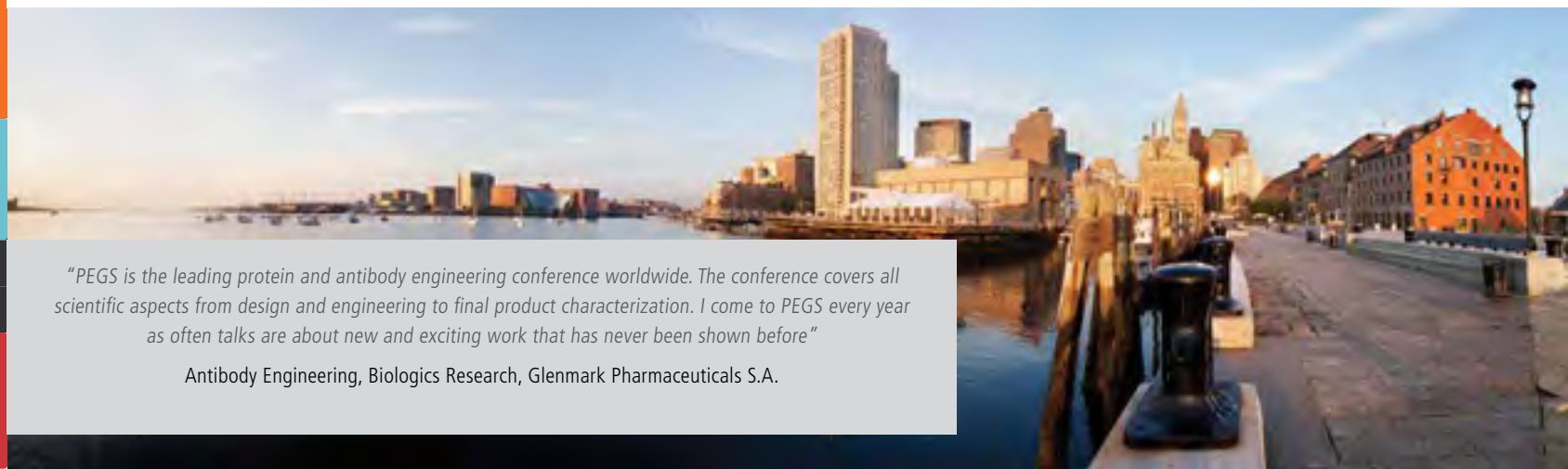
To understand the role of the conjugation site, we developed an enzymatic method for site-specific antibody-drug conjugation using microbial transglutaminase. We show that the conjugation site has significant impact on ADC stability and pharmacokinetics in a species dependent manner. With this method, it is possible to produce homogeneous ADCs and tune their properties to maximize the therapeutic window.

3:50 Producing Homogeneous ADCs with Combination Warheads

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

Cell-free protein synthesis methods have been developed for production of homogeneous therapeutic proteins, including ADCs. Many variants can be expressed in hours and rapidly assessed for function. The power and utility of the platform to design and manufacture single species antigen-targeted combination warheads as well as the stability and pharmacokinetics of these homogeneous ADCs will be described.

4:10 End of Conference



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Inaugural | May 5-6

Biologics for Autoimmune Diseases

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

Recommended Pre-Conference Short Course*

Strategy for Entering the Biosimilars Market

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

MONDAY, MAY 5

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks
Kristi Sarno, Chair, Greater Boston Chapter, Women in Bio; Director, Business Development, Pfenex, Inc.

8:40 Harnessing the Patient's Immune System to Combat Cancer
Peter CR Emtage, Ph.D., Vice President, Immune Mediated Therapies, MedImmune

With recent FDA approvals, modulation of the immune system is now a clinically validated approach in the treatment of some cancers. At MedImmune, the Oncology Department is developing assets and expertise in Immune Mediated Therapy of Cancer (IMT-C). The challenges from a drug development perspective are multi-fold. The talk will focus on the relevance of preclinical models and translational science to address key issues, including dose selection and rationale combinations.

9:25 Building Regeneron's Pipeline: From Trap Technology to the *VelocImmune* Platform to *VelociNext*
George D. Yancopoulos, M.D., Ph.D., President, Regeneron Laboratories; CSO, Regeneron Pharmaceuticals, Inc.

George D. Yancopoulos, M.D., Ph.D., who is the Founding Scientist, President, Research Laboratories and Chief Scientific Officer of Regeneron Pharmaceuticals, one of the world's top biotechnology companies, will discuss how he and his colleagues exploited a commitment to science and technology to start the company, withstand years of challenges and failures, and emerge with a pipeline of promising technologies and novel/biologics that are beginning to bring hope to countless patients and their families.

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

11:05 Chairperson's Remarks
Ronald Herbst, Ph.D., Senior Director, Autoimmune Diseases, MedImmune

» 11:10 KEYNOTE PRESENTATION:

Biologics for Systemic Lupus Erythematosus
William Stohl, M.D., Ph.D., Professor, Medicine, Rheumatology, Keck School of Medicine, University of Southern California

With FDA approval of a biologic therapeutic for SLE, optimism abounds for approval of additional agents. Candidates include: biologics to effect B cell depletion/inactivation or generation of regulatory B cells; biologics to effect T cell tolerance, blockade of T cell activation/differentiation, or altered T cell trafficking; and biologics targeting individual cytokines. As understanding of SLE pathogenesis continues to expand, additional therapeutic targets will be identified.

CLINICAL AND PRECLINICAL UPDATES OF BIOLOGIC THERAPIES FOR AUTOIMMUNE DISEASES

12:10 pm Embracing Complexity: Understanding IVIg to Rationally Engineer Novel Therapeutics
Tony Manning, Ph.D., Vice President, Research, Momenta Pharmaceuticals

12:40 Luncheon Presentation I *(Sponsorship Opportunity Available)*

1:10 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:40 Session Break

2:00 Chairperson's Remarks
Lawren Wu, Ph.D., Senior Scientist, Immunology, Genentech, Inc.

2:05 NI-0101, a Noncompetitive Inhibitor Targeting TLR4 with the Potential to Become the First Personalized Treatment in Rheumatoid Arthritis (RA)
Marie Kosco-Vilbois Ph.D., Chief Scientific Officer, NovImmune SA, Switzerland

As diverse TLR4 activators are upregulated in many diseases, NI-0101, currently in Phase I, blocks TLR4 in a ligand-independent manner. Synovial fluids from RA patients contain various TLR4 ligands and induce cytokines from patients' blood- and tissue-derived cells, with the levels correlating to NI-0101's blocking potential. These results indicate that NI-0101 is a promising strategy for the treatment of RA with levels of TLR4 ligands circulating in patients used as biomarkers to distinguish responders to anti-TLR4 therapy.

2:35 Clinical Update of MEDI 551 (Anti-CD19 Antibody) for Autoimmune Disease
Ronald Herbst, Ph.D., Senior Director, Autoimmune Diseases, MedImmune

Human cluster of differentiation (CD) antigen 19 is a B cell-specific surface antigen and an attractive target for B cell depletion. MEDI-551 is an affinity-optimized and afucosylated CD19 mAb with enhanced antibody-dependent cellular cytotoxicity (ADCC). MEDI-551 is currently in several phase 1/2 clinical studies, including B cell malignancies, systemic sclerosis (SSc) and relapsing remitting multiple sclerosis (RRMS).

3:05 Cytokine Modulation by Protein Therapeutics in Anterior and Posterior Ocular Disorders
Christian Dombrowski Ph.D., Senior Scientist, Eleven Biotherapeutics, Inc.

Cytokines, chemokines, and growth factors mediate anterior and posterior eye diseases. A novel soluble receptor inhibitor of IL -17A and IL -17A with potential for treating uveitis and AMD was engineered, along with an IL -6 inhibitor with potential for treating diabetic macular edema. Our lead product, EBI-005 was designed and engineered for the topical treatment of dry eye disease and has evidence of biological activity in a clinical study.

3:35 IL-1a/b DVD-Ig™: From Design to Clinic for Autoimmune Indications
Tariq Ghayur, Ph.D., Senior Research Fellow, AbbVie

4:05 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem Solving Breakout Discussions

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

6:45 End of Day

TUESDAY, MAY 6

7:45 am Morning Coffee

BISPECIFIC ANTIBODIES FOR AUTOIMMUNE DISEASES

8:25 Chairperson's Remarks
Tariq Ghayur, Ph.D., Senior Research Fellow, AbbVie

8:30 Development of a Human IgG4 Bispecific Antibody for Dual Targeting of IL -4 and IL -13 Cytokines
Lawren Wu, Ph.D., Senior Scientist, Immunology, Genentech, Inc.

Interleukins IL -4 and IL -13 have been implicated in the pathogenesis of asthma and allergy. We have extended a previously developed bispecific antibody technology to develop a human IgG4 bispecific antibody targeting both IL -4 and IL -13. Our work broadens the range of therapeutic bispecific antibody platforms to include both human IgG1 and IgG4 isotypes, resulting in the generation of an anti-IL -4/IL -13 bispecific suitable for clinical studies.

9:00 Proof-of-Concept Studies of B-Lymphocyte Targeted Bispecific DART® Molecules for Autoimmune Disorders
Syd Johnson, Ph.D., Vice President, Antibody Engineering, MacroGenics, Inc.

To address limitations of existing B cell targeted therapies, we have developed MGD010, a bispecific Dual-Affinity ReTargeting (DART) molecule that coligates the inhibitory FcγRIIb (CD32B) receptor and the BCR component, CD79B, to inhibit B cell activation and dampen autoimmunity. Preclinical studies have demonstrated the ability of CD32BxCD79B DARTs to preferentially inhibit activated B cells through activation of the CD32B pathway.

9:30 XmAb5871: An FcgRIIb-Enhanced Anti-CD19 Antibody for Nondepleting B Cell Inhibition
John Desjarlais, Ph.D., Vice President, Research, Xencor

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

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Inaugural | May 5-6

Biologics for Autoimmune Diseases

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

EMERGING BIOLOGIC FORMATS

10:45 mRNA-Engineered Mesenchymal Stem Cells as Targeted Drug Factories

Oren Levy, Ph.D., Instructor in Medicine, Harvard Medical School

MSCs are promising candidates for cell-based therapy to treat inflammatory diseases and are compelling to consider as vehicles for delivery of biological agents. We harnessed mRNA transfection to rapidly target systemically administered MSCs to inflamed sites to which they delivered an immunosuppressive cytokine, significantly reducing local inflammation. This platform may be used for cell-based targeted delivery of therapeutics to disease sites.

11:15 AVX-470, An Oral Anti-TNF Antibody for Inflammatory Bowel Disease

Barbara S. Fox, Ph.D., CEO, Avaxia Biologics, Inc.

Avaxia is developing gut-targeted antibody therapeutics – antibodies designed to be taken orally and to act locally in the GI tract. AVX-470 is Avaxia's lead product, an orally-delivered polyclonal anti-TNF antibody in clinical development for inflammatory bowel disease.

11:45 SOBI002, a Small Affibody-ABD Fusion Protein Targeting Complement Factor C5 as a Next-Generation Biologic for Autoimmune Disease

Patrik Strömberg, Ph.D., Principal Scientist, Drug Design and Development, Swedish Orphan Biovitrum (Sobi), Sweden

SOBI002 is composed of a C5 targeting Affibody molecule fused to an albumin binding domain. *In vivo*, this molecule displays long terminal half-life, high subcutaneous bioavailability and durable pharmacodynamic effects. No dose-limiting toxicity of SOBI002 was observed in repeat dose studies in monkey and rat. Based on these results, a study to evaluate safety, tolerability, PK and PD of SOBI002 in man is warranted.

12:15 pm Luncheon Presentation I *(Sponsorship Opportunity Available)*

12:45 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:15-1:45 Ice Cream Break in the Exhibit Hall

IMMUNE MODULATION AND TOLERANCE INDUCTION STRATEGIES

2:00 Chairperson's Remarks

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

2:05 Strategies Underlying Tolerance Induction with Antibodies as Combination Therapy

Herman Waldman, Ph.D., Emeritus Professor of Pathology, Therapeutic Immunology Group, Sir William Dunn School of Pathology, University of Oxford, United Kingdom

Current immunosuppression is often long-term and it penalizes the whole immune system, as well as inflicting many unwanted side effects. If we could harness some of the key mechanisms of tolerance that the body uses, then we might be able to minimize the duration and quantity of drugs given. The talk will summarize approaches to using short-term exposure to anti-lymphocyte antibodies to achieve this end.

2:35 Inducing Antigenic-Specific B Cell Tolerance using Antigenic Liposomes Displaying CD22 Ligands

Matthew Macauley, Ph.D., Researcher, Paulson Laboratory, Chemical Physiology, The Scripps Research Institute

New strategies are needed for antigen-specific suppression of undesired antibody responses. Liposomes displaying both antigen and glycan ligands of the inhibitory B cell co-receptor CD22, induce a tolerogenic program that selectively causes apoptosis in B cells. Since inhibitory antibodies to FVIII are problematic for hemophilia A patients, we used this approach to induce tolerance to FVIII in a hemophilia mouse model, allowing for effective administration of FVIII to prevent bleeding.

3:05 HL161, a Novel Anti-FcRn Antibody as a New Therapeutic Option for Autoimmune Diseases

Sponsored by HANALL BIOPHARMA

Seung Kook Park, Ph.D., MBA, CEO, Vice President, HanAll BioPharma Co.,Ltd.

Various autoimmune diseases are characterized by the involvement of pathogenic autoantibodies in pathogenesis. HL161, a novel anti-FcRn antibody, suppresses autoimmunity against autoantigen through dual modes of action: increasing catabolism of pathogenic autoantibodies and decreasing antigen presentation with MHC class I and II by blocking FcRn, thereby exerting a therapeutic effect on various autoimmune diseases. The clinical candidate will be finally selected through the monkey PK/PD study in 3Q, 2014.

3:20 Sponsored Presentation *(Opportunity Available)*

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

4:15 Antigen-Specific Immunotherapy for Autoimmune Diseases

David Wraith, Ph.D., Professor of Experimental Pathology, School of Cellular and Molecular Medicine, University of Bristol, United Kingdom

Antigen-specific immunotherapy is disease modifying and efficacious. The use of whole antigens for SIT is, however, associated with unacceptable side effects. Apitopes are T cell epitopes designed to modulate immune response to self-antigens or allergens while minimizing the side effects of SIT. This lecture reviews the design and MOA of tolerogenic epitopes and will discuss results of recent clinical trials in allergic and autoimmune diseases.

4:45 The MCAM/Laminin 411 Interaction Provides a TH17 Specific Mechanism for T Cell Entry into the CNS

Ken Flanagan, Ph.D., Senior Scientist, Cell Biology, Prothena Biosciences

Expression of MCAM/CD146 is enriched on TH17 cells. The ligand for MCAM is laminin 411, a molecule critical in T cell infiltration into tissues. Anti-MCAM antibodies inhibit the interaction with laminin 411. The specificity of MCAM expression on TH17 cells combined with the binding of MCAM exclusively to laminin 411 defines a targetable TH17/vascular interaction, to specifically inhibit a particularly pathogenic immune cell population.

5:15 End of Conference

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Inaugural | May 7-8

Adoptive T Cell Therapy

New Targets and Strategies for Immune-Driven Diseases

Recommended Pre-Conference Short Course*

Introduction to Adoptive T Cell Therapies

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

WEDNESDAY, MAY 7

7:00 am Registration and Morning Coffee

STRATEGIES FOR TARGET DISCOVERY, SELECTION & VALIDATION

8:00 Chairperson's Opening Remarks

Nancy L. Parenteau, Ph.D., Co-Founder, President & CSO, Ingenium BioTherapy Corporation

» 8:10 OPENING KEYNOTE PRESENTATION:

Engineered T Cell Therapies for Cancer

Marcela V. Maus, M.D., Ph.D., Director, Translational Medicine and Early Clinical Development, Translational Research Program, Abramson Cancer Center, University of Pennsylvania

This presentation will provide background on T cell biology and costimulation as well as the synthetic biology of chimeric antigen receptors and how they were developed. Preclinical data and clinical data in leukemia and preclinical and early-phase translation of engineered T cells in several cancers will also be presented.

8:40 Innovative Approaches to Effective T cell Transfer Therapy of Cancer

Daniel J. Powell, Jr., M.D., Assistant Professor, Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania

The adoptive transfer of tumor-reactive T cells has emerged as a "game changer" in the effective treatment of melanoma and leukemias, but challenges exist to its widespread application in other malignancies. This presentation focuses on improved methodologies and approaches that allow for isolation of rare tumor-reactive TILs from non-melanoma cancers, and the development of systems that better enable gene-engineered T cells to persist after infusion, that focus their cytolytic activity on cancers cells, not normal organ tissues, and that permit versatility in antigen targeting to broaden patient access to this promising new immunotherapeutic approach. These next generation strategies will be discussed and stand to improve the efficacy, safety and access to CAR T cell therapy for cancer.

9:10 A Pipeline for Generating Affinity-Enhanced TCRs for Adoptive T Cell Therapy

Ellen Border, D.Phil., Senior Scientist, Protein Engineering, Adaptimmune Ltd.

This presentation outlines the processes comprising Adaptimmune's TCR pipeline, beginning with target antigen selection and validation. TCRs directed towards these antigens are isolated and characterized, using a range of assays, and a subset is selected for affinity optimization. Panels of affinity enhanced mutants are then tested for efficacy and specificity in cells to identify lead candidates for full preclinical assessment, and progression to clinical trials.

9:40 Predictive Biomarkers in Adoptive T Cell Therapy Using Tumor-Infiltrating Lymphocytes

Laszlo Radvanyi, Ph.D., Professor, Melanoma Medical Oncology, University of Texas , MD Anderson Cancer Center

This talk will present work on a comprehensive project identifying predictive biomarkers in TIL-treated patients both on the infused T cells, as well as biomarkers in tumor microenvironment of tumors from TIL treated patients. We have identified a number of candidate biomarkers that can be validated in further trials and also shed light on the mechanism of action of TIL and how tumor microenvironment factors regulate T-cell infiltration and TIL response.

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

STRATEGIES FOR T CELL ENGINEERING

11:10 Engineering Genetic Resistance to HIV in T Cells

Matthew Porteus, M.D., Ph.D., Associate Professor, Pediatrics (Cancer Biology), Stanford School of Medicine

We have used the tools of genome editing to demonstrate the feasibility and power of genetically "stacking" multiple anti-HIV genes in creating cells that are resistant to both CCR5-tropic and CXCR4-tropic HIV. This presentation will discuss that work and the future directions we are exploring to translate the concept into therapy for patients with HIV.

11:40 Enhancing the IQ of CAR T Cells

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

Targeted eradication of cancer by adoptive transfer of antigen specific T cells is the subject of intensive clinical exploration. While many of the key conceptual and technical barriers that have previously limited translation to human clinical trials have been overcome, as reflected by the growing number of FDA IND-supported studies in progress, significant refinement is needed to evolve this therapeutic modality for reproducibly effective and safe applications in the oncology clinic. This talk will focus on technologies in development that utilize principles of synthetic biology and bioengineering to equip CAR T cells with regulated functional outputs.

12:10 pm Sponsored Presentation *(Opportunity Available)*

12:40 Luncheon Presentation I *(Sponsorship Opportunity Available)*

1:10 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:40 Session Break

CHIMERIC ANTIGEN RECEPTOR DESIGN

2:00 Chairperson's Remarks

2:05 The Principles of Chimeric Antigen Receptor Design

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

A multitude of CARs have been reported over the past decade, targeting an array of cell surface tumor antigens. Their biologic functions have dramatically changed following the introduction of tripartite receptors comprising a costimulatory domain, termed second-generation CARs. These have recently shown clinical benefit in patients treated with CD19-targeted autologous T cells and represent a new class of drugs with exciting potential for cancer immunotherapy.

2:35 ErbB-Targeted CAR T Cell Immunotherapy of Cancer: A Strategy to Maximize the Window of Therapeutic Opportunity

John Maher, Consultant and Senior Lecturer in Immunology, Department of Research Oncology, King's College London

We have developed a CAR named T1E28z that targets the extended ErbB network. Engineered T cells are expanded and enriched using a co-expressed IL-4-responsive chimeric cytokine receptor. Efficacy of the resultant "T4 immunotherapy" has been demonstrated in several tumor models *in vivo*, without significant accompanying toxicity. To de-risk this approach in man, phase 1 testing will be performed in patients with head & neck cancer.

NEW TECHNIQUES IN T CELL THERAPY

3:05 Dynamic Intravital Tracking of Immune Cell Migration and Interaction with Single Cell Resolution

Alex Y. Huang, M.D., Ph.D., Associate Professor, Pediatrics, Pathology & Biomedical Engineering; Director, Pediatric Hematology-Oncology Fellowship Program, Rainbow Babies & Children's Hospital, Case Western Reserve University School of Medicine

To improve efficacy and to understand the biology of how adoptive T cell therapy works *in vivo*, attention must be paid to how immune cells behave and interact within host tissue and tumor microenvironment. The application of intravital two-photon microscopy in preclinical animal models allows the visualization and tracking of these intricate mutli-cellular processes in 3-dimensions over time. In turn, these observations yield new insights into cellular biology that were previously under-appreciated using traditional experimental tools. These novel insights promise to provide new scientific rationale in designing next generation adoptive T cell therapy.

3:20 Sponsored Presentation *(Opportunity Available)*

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

4:20 Problem Solving Breakout Discussions

5:20 Networking Reception in the Exhibit Hall with Poster Viewing

6:30 End of Day

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Inaugural | May 7-8

Adoptive T Cell Therapy

New Targets and Strategies for Immune Driven Diseases

THURSDAY, MAY 8

7:45 am Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

INCREASING SPECIFICITY AND PREVENTING TOXICITY

8:30 Chairperson's Remarks

8:35 Influence of T Cell Receptor Affinity on Efficacy and Specificity of T Cells

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

We have examined the impact of the affinity of the alpha-beta TCR for the pepMHC cancer antigens on both efficacy and specificity. There are advantages and disadvantages of using higher affinity TCRs in adoptive T cell therapies. TCR affinity and target selection will both influence potential efficacy and safety issues, and these are addressed using several mouse and human systems.

9:05 Harnessing the Power of Costimulatory Molecules to Genetically Improve Adoptive T Cell Immunotherapy

Cyrille Cohen, Ph.D., Senior Lecturer, Laboratory of Tumor Immunology, Bar-Ilan University Visiting Scientist, Surgery Branch, NCI, NIH

In this presentation, we will share our recent results dealing with the manipulation of the 4-1BB and PD1 pathways using chimeric molecules to enhance anti-tumor activity of genetically-engineered T cells both *in vitro* and *in vivo*. We will also present a novel tumor-targeting approach using a class of chimeric receptors specific for a broad spectrum of malignancies.

9:35 Safely and Effectively Combining TCR and CAR T Cell Therapies for Cancer

Malcolm Brenner, M.D., Ph.D., Professor, Departments of Pediatrics and Medicine; Stem Cells and Regenerative Medicine (STaR) Center; Program in Translational Biology & Molecular Medicine; Director, Center for Cell and Gene Therapy, Baylor College of Medicine

As we learn how to make effector T cells more active against cancer cells, the dangers of off-target or off-organ toxicity and of life-threateningly explosive immune responses have become more evident. By making use of a combination of native and chimeric receptors on the same cell and by incorporating cellular rheostats we hope to increase the accuracy of T cell targeting of tumors and regulate the speed with which they became activated, thereby increasing the value of this approach.

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

FUTURE PERSPECTIVES: FROM OFF-THE-SHELF THERAPIES TO NK CELLS

11:05 NK Cells, Their Receptors and Cancer and Transplantation

Jeffrey S. Miller, M.D., Deputy Director, Masonic Cancer Center; Deputy Director, Clinical and Translational Sciences Institute; Director, Cancer Experimental Therapeutics Initiative, University of Minnesota

We have performed a number of clinical trials using autologous and allogeneic NK cells which will be reviewed. IL-15, a natural cytokine that is critical for NK cell development and homeostasis will be discussed. I will discuss NK cell receptor immunogentics and their importance in predicting transplantation outcomes. Lastly, I will review how NK cells can be targeted to tumors by bispecific killer engagers (BiKEs) and discuss the future of NK cell therapeutics.

» 11:35 CLOSING KEYNOTE PRESENTATION:

Democratizing Gene Therapy – Off-the-Shelf T Cells Can be Engineered from One for Many

Laurence J.N. Cooper, M.D., Ph.D., Grant Taylor, W.W. Sutow and Margaret Sullivan Distinguished Professor in Pediatrics; MDACC Section Chief, Cell Therapy, Children's Cancer Hospital, Division of Pediatrics (Unit 907); Associate Director, CCIR; Director, Immunology Laboratory of Physician Scientists, Department of Immunology, MD Anderson Cancer Center

The infusion of T cells genetically modified to express a CD19-specific chimeric antigen receptor (CAR) has resulted in dramatic anti-tumor effects. However, this approach to immunotherapy relies on real-time generation of CAR+ T cells that are manufactured for a given recipient. We have developed an alternative approach whereby T cells can be pre-prepared from a healthy donor and infused into multiple recipients when the patient needs them, rather than when the biologic product is available.

12:05 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

12:35 End of Conference

Recommended Thursday Dinner Short Course*

Antibody-Based Cancer Immunotherapy

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

"I have really enjoyed attending PEGS. I was very impressed with the quality of the science and interactions at this event. I attended the "Immunogenicity for Regulatory Success" meeting and find myself still reviewing the slides that were presented on those topics. Thanks for making those available. I believe that the panel members, as experts in the field, were able to provide a higher level view covering the discovery, generation and clinical/therapeutic potential of non-conventional antibody formats. This was especially useful for those attendees who are either still new in the field or who only are involved with one facet of the drug discovery process."

Senior Director Biologics Generation, AbbVie Bioresearch Center

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Inaugural | May 8-9

Peptide Therapeutics

Conquering Disease

THURSDAY, MAY 8

THE PROMISE OF PEPTIDES

1:30 pm Chairperson's Opening Remarks

Irwin Chaiken Ph.D., Professor, Biochemistry and Molecular Biology Drexel University College of Medicine

» 1:40 OPENING KEYNOTE PRESENTATION:

Pharmaceutical Protein & Peptide Engineering: From Once Daily to Once Weekly GLP-1 Dosing

Jesper Lau, Ph.D., Vice President, Diabetes Protein & Peptide Chemistry, Novo Nordisk A/S

Proteins and peptides play unique roles in human physiology and are thus excellent templates for drug discovery. However, endogenously secreted proteins/peptides have many limitations when translated directly into pharmaceuticals. Poor half-life, bioavailability, pharmaco-dynamics, chemical and biophysical stability typically need to be significantly improved in order to transform a protein/peptide into a convenient drug. Tailored engineering of GLP-1 will be discussed based on Novo Nordisk case stories.

2:10 FEATURED PRESENTATION:
Highly Constrained Bicyclic Peptides (Bicycles): A Novel Class of Therapeutics

Christophe Bonny, Ph.D., CSO, Bicycle Therapeutics, Ltd.

The Bicycle technology is based on repertoires of peptides displayed on the surface of bacteriophages which can be modified with organochemical scaffolds to create a diverse array of constrained peptides. These repertoires have been extensively used for iterative selections to identify high affinity binding peptides for a wide array of targets, including receptors, interleukins and proteases. The bicycle peptides show antibody-like properties such as low to sub-nanomolar affinities and exquisite selectivity, but in a 100-fold, chemically synthesized format. Due to their small size, these small entities extravasate and penetrate tumours much more efficiently than antibodies. Results will be presented that exemplify the potential of the technology and its application to deliver cytotoxic payloads to tumour cells.

2:40 Veltis® – An Innovative Platform Technology for the Half-Life Extension of Biotherapeutics

Sponsored by novozymes

Darrell Sleep, Ph.D., Director, Biopharma R&D, Novozymes Biopharma

Veltis® from Novozymes Biopharma is an innovative albumin based half-life extension technology that offers improvements In therapeutic window by allowing greater control over dose frequency, dose quantity and drug tolerability. In this presentation I will describe the science behind the engineering of the albumin molecules, that powers the Veltis platform and exemplify the technology with some case study examples.

3:10 Refreshment Break in the Exhibit Hall with Poster Viewing

RESISTING PROTEASE ACTIVITY & STAPLED PEPTIDES

4:00 Stapled Peptide Drugs: Nature's α–Helix to Breakthrough Medicines

Tomi Sawyer, Ph.D., Adjunct Professor, University of Massachusetts, University of Massachusetts Medical School, and Northeastern University Center for Drug Discovery

4:30 A General Method for Making Peptide Therapeutics Resistant to Serine Protease Degradation; Application to Dipeptidyl Peptidase IV Substrates

William Bachovchin, Ph.D., Professor, Developmental, Molecular & Chemical Biology, Sackler School of Graduate and Biomedical Sciences, Tufts University

Incorporating a tertiary substituted beta carbon into the P1' position directly C-terminal to a serine proteases cleavage site renders peptides highly resistant to cleavage by serine proteases without significantly affecting biological activity. Thus far the method has been show to invariably work for six substrates of DPP4 including GLP-1 as well as for substates of DPP8, FAP?, alpha-lytic protease, trypsin, and chymotrypsin.

5:00 Close of Day

Recommended Tuesday Dinner Short Course*

Overcoming the Challenges of Immunogenicity Assessment

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

FRIDAY, MAY 9

7:45 am Continental Breakfast in the Exhibit Hall with Poster Viewing

IMPROVING QUALITIES

8:30 Chairperson's Remarks

Hong Moulton, Ph.D., Associate Professor, Senior Researcher, Biomedical Sciences, Oregon State University

8:35 PK Modulation of Haptenylated Peptides via Non-Covalent Antibody Complexation

Ulrich Brinkmann, Ph.D., Scientific Director, Pharma Research and Early Development, Roche

We applied noncovalent complexes of digoxigenin (Dig) binding antibodies with digoxigeninylated peptide derivatives to modulate their pharmacokinetic properties. We observed more prolonged weight reduction in a murine diet-induced obesity (DIO) model with antibody-complexed peptides compared to unmodified peptides. We conclude that antibody-hapten complexation can be applied to modulate the PK of haptenylated peptides and in consequence improve the therapeutic efficacy of therapeutic peptides.

9:05 AlbudAb: A Versatile Serum Half-Life Extension Platform for Peptides

Oliver Schon, Ph.D., Manager, Biopharm Innovation, GlaxoSmithKline

This talk will provide an update on the preclinical and clinical data of therapeutic drugs that include the AlbudAbTM half-life extension technology. It will cover lead discovery process/engineering and the selection of formats for improved biological, biophysical and pharmacokinetic properties, focussing on key *in vivo* and clinical data.

9:35 Novel ApoA-I Mimetic Peptides for the Treatment of Cardiovascular Disease

Alan T. Remaley, M.D., Ph.D., Section Chief, Lipoprotein Metabolism Laboratory, National Institutes of Health (NIH)

ApoA-I is the major protein component of High Density Lipoproteins and mediates the efflux of excess cellular cholesterol by the ABCA1 transporter. We have synthesized apoA-I mimetic peptides that are as effective as full-length protein in mediating cholesterol by the ABCA1 transporter. ApoA-I mimetic peptides show great promise in the replacement of the full-length protein for the acute treatment of patients with acute coronary syndrome.

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

INNOVATING PEPTIDE THERAPEUTICS

10:50 SELECTED POSTER PRESENTATION
#303 VDAC1-Based Peptides as Potential Therapeutics for Cancer: Proof of Concept in Chronic Lymphocytic Leukemia and Glioblastoma

Varda Shoshan-Barmatz, Ph.D., Director & Investigator, Life Sciences, Ben Gurion University

11:20 Apolipoprotein E Derived Peptides with Anti-Atherosclerosis and Insulin Sensitizing Effects

Jan Johansson, Ph.D., CEO and President, Artery Therapeutics, Inc.

Artery Therapeutics, Inc. has developed ABCA1 ligand peptides derived from the C-terminal of apoE with anti-atherosclerosis and anti-diabetic actions confirmed in cell and animal models. The lead peptide candidate drug holds great promise for the treatment of macro-vascular complications in diabetes as myocardial infarct and stroke.

11:50 Peptides with a Defined Structure: Half-Life Extended Affibody Molecules with High Potency and Stability Allowing for Alternative Delivery Routes

Fredrik Frejd, Ph.D., CSO, Vice President R&D, Biopharma, Affibody AB

Affibody molecules are 58 aa peptides with a defined helical structure allowing generation of high affinity, high specificity binders for a broad range of targets. The half-life of Affibody molecules and other therapeutic peptides can be extended up to several weeks by applying Affibody's Albumod technology based on an albumin binding peptide domain. Results from oral administration of a half-life extended peptide for treatment of metabolic disease will be shown.

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Inaugural | May 8-9

Peptide Therapeutics

Conquering Disease

12:20 pm Luncheon Presentation
Improving Drug Properties by Glycosylating Peptides via Chemical Synthesis

Sponsored by GlyTech, Inc.

Michael F. Haller, Ph.D., Business Development, GlyTech, Inc.

Peptides are often developed via chemical synthesis, and are devoid of glycans. Glycans are naturally-occurring sugars that can dramatically affect drug properties, such as binding, efficacy, and pharmacokinetics. Creating glycosylated peptides via a chemically synthetic route can capture the benefits of glycosylation without the need to resort to mammalian-based cell culture. This presentation will illustrate chemical synthesis methodologies for these molecules.

12:50 Session Break

CLICK CHEMISTRY, CONJUGATION & PENETRATION

1:35 Chairperson's Remarks

Joyce A. Schroeder, Ph.D., Professor, Molecular and Cellular Biology, Program in Cancer Biology, BIO 5 Institute, Arizona Cancer Center, University of Arizona

1:40 Inactivating HIV-1 Using Peptide Triazoles and Their Nanoparticle Conjugates

Irwin Chaiken Ph.D., Professor, Biochemistry and Molecular Biology Drexel University College of Medicine

Blocking initial entry of HIV-1 into host cells remains a compelling yet elusive means to prevent infection and virus spread. Recent progress will be presented showing how peptide triazole inhibitors of HIV-1 Env gp120 can block cell receptor interactions and inactivate the virus surface protein before cell encounter, providing a platform to develop peptidomimetic and nanoparticle-conjugated derivatives to prevent AIDS transmission and treat already-infected individuals.

2:10 Using Engineered Peptides to Deliver Peptide/Protein Therapeutics into Cells

Jean-Philippe Pellois, Ph.D., Associate Professor, Biochemistry and Biophysics, Texas A&M University

Proteins do not penetrate cells and this reduces their use as therapeutic tools. To solve this problem, we have developed several agents that deliver proteins into cells by promoting endocytosis and by escaping very efficiently from endosomes. Remarkably, this approach does not lead to deleterious effects on cell physiology. The relevance of these findings for the design of future drug delivery agents will be discussed.

2:40 Intracellular Peptide-Based Breast Cancer Therapeutics

Joyce A. Schroeder, Ph.D., Professor, Molecular and Cellular Biology, Program in Cancer Biology, BIO 5 Institute, Arizona Cancer Center, University of Arizona

The Epidermal Growth Factor Receptor (EGFR) is highly expressed in basal breast cancer and represents an important clinical target. MUC1 is a regulator of EGFR, and we have developed a MUC1-based peptide therapeutic that causes tumor-specific loss of EGFR. This peptide, PMIP, inhibits tumor growth and invasion in mouse models of breast cancer. IND-enabling studies are underway to move PMIP towards clinical trials.

3:10 Peptide Delivery of a Therapeutic Nucleic Acid Analog

Hong Moulton, Ph.D., Associate Professor, Senior Researcher, Biomedical Sciences, Oregon State University

Morpholino oligos bind complementary RNA to block translation, modify splicing, or inhibit ncRNA activity. They can bind pathogen RNA or modify genetic disease. Unmodified Morpholinos do not readily cross the plasma membrane. Cell-penetrating peptides conjugated to Morpholinos allow systemic administration of antisense in animals. Preclinical studies for Duchenne muscular dystrophy illustrate the promise and barriers for application of CPP-Morpholino conjugates for treatment of human disease.

3:40 Characterization of a New Brain-Penetrant Angiopep2-Neurotensin Derivative (ANG2002) with Antinociceptive Properties

Philippe Sarret, Ph.D., Professor, Physiology and Biophysics, University of Sherbrooke

The tridecapeptide neurotensin (NT) plays an important role in many neurological processes including physiology of pain. However, the peptide does not cross the blood-brain barrier. A brain-penetrant NT derivative, ANG2002, has been created by conjugating NT to Angiopep2, a 19 AA peptide designed to cross the blood-brain barrier by receptor-mediated transcytosis. ANG2002 is an effective analgesic when dosed systemically to rodents, including in models of neuropathic and cancer pain.

4:10 End of Conference

"I found the meeting to be very interesting as you have the complete story of protein therapeutics; from biochemistry to chemical engineering. I came away with a number of new ideas, and many more new contacts."

Professor, Chemistry, Clemson University

"The small group discussion attracted more interest and participation than I expected. After a few minutes everyone seemed to open up and we had quite a good give and take session. I enjoyed participating and thought the entire conference was comprehensive and stimulating."

Senior Scientific Manager, Genentech

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9th Annual | May 5-6

Difficult to Express Proteins

Harnessing Innovation to Improve Expression and Function

Recommended Pre-Conference Short Courses*

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

***In silico* Immunogenicity Predictions (Hands-On) Workshop**

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

MONDAY, MAY 5

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks
Kristi Sarno, Chair, Greater Boston Chapter, Women in Bio; Director, Business Development, Pfenex, Inc.

8:40 Harnessing the Patient's Immune System to Combat Cancer
Peter CR Emtage, Ph.D., Vice President, Immune Mediated Therapies, MedImmune
With recent FDA approvals, modulation of the immune system is now a clinically validated approach in the treatment of some cancers. At MedImmune, the Oncology Department is developing assets and expertise in Immune Mediated Therapy of Cancer (IMT-C). The challenges from a drug development perspective are multi-fold. The talk will focus on the relevance of preclinical models and translational science to address key issues, including dose selection and rationale combinations.

9:25 Building Regeneron's Pipeline: From Trap Technology to the *VelocImmune* Platform to *Veloci-Next*
George D. Yancopoulos, M.D., Ph.D., President, Regeneron Laboratories; CSO, Regeneron Pharmaceuticals, Inc.
George D. Yancopoulos, M.D., Ph.D., who is the Founding Scientist, President, Research Laboratories and Chief Scientific Officer of Regeneron Pharmaceuticals, one of the world's top biotechnology companies, will discuss how he and his colleagues exploited a commitment to science and technology to start the company, withstand years of challenges and failures, and emerge with a pipeline of promising technologies and novel/biologics that are beginning to bring hope to countless patients and their families.

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

USING THE SCIENCE TO YOUR ADVANTAGE

11:05 Chairperson's Remarks
Benjamin Doranz, Ph.D., President & CSO, Integral Molecular Inc.

» KEYNOTE PRESENTATION:

11:10 Construct and Expression Optimization of the G Protein-Coupled Neurotensin Receptor for Structure Determination
Reinhard Grisshammer, Ph.D., Biotechnology Core Laboratory, National Institute of Diabetes and Digestive and Kidney Diseases
In the past few years, we started to see an explosion in the field of GPCR structure determination with structures of more than 20 unique receptors now deposited in the Protein Data Bank. This exciting progress required a tremendous amount of methods development contributed by many laboratories. I will discuss our approaches that led to successful overproduction, crystallization and structure determination of the neurotensin receptor NTS1 bound to its peptide agonist.

11:40 Artificial Environments and Quality Modulation of Cell-Free Expressed GPCRs: Case Studies of the Human Endothelin and Gonadotropin Releasing Hormone Receptors
Erika Orbán, Ph.D., Postdoctoral Fellow, Institute of Biophysical Chemistry, Goethe University
Protocol development and defining the optimal biosynthetic environment for functionally folded and stable membrane protein samples is a complex issue and requires systematic evaluation of numerous additives. We present case studies for the optimization of cell-free expression protocols of the human Endothelin and Gonadotropin Releasing Hormone receptors. The co- and post-translational solubilization of the synthesized GPCRs in several hydrophobic environments including nanodiscs, amphipols and surfactants was analyzed.

12:10 pm Discovery of MAbs Against Difficult GPCRs, Ion Channels, and Transporters
Sponsored by integral
Benjamin Doranz, Ph.D., CSO, Integral Molecular, Inc.
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.

12:40 Luncheon Presentations *(Sponsorship Opportunities Available)*

1:40 Session Break

NOVEL TECHNOLOGIES TO "GET IT DONE"

2:00 Chairperson's Remarks

2:05 TAPBOOST Technology: Novel Technology to Enhance the Production of Hard-to-Produce Therapeutic Recombinant Proteins
Akinori Hishiya, Ph.D., Director, Biology, Boston Strategics Corporation
A proprietary protein (TAPBOOSTER) is expressed together with the therapeutic protein. The TAPBOOSTER protein binds to targeted proteins and enhances its production specifically. TAPBOOSTER has successfully enhanced the production of many therapeutic recombinant proteins including monoclonal antibodies and Fc fusion proteins. The technology is particularly effective in enhancing the production of proteins where incorrect folding may result.

2:35 Rapid Screening of Membrane Protein Expression in Transiently Transfected Insect Cells
Hao Chen, Ph.D., Sr. Scientist, Protein Technologies, Amgen, Inc.
Membrane proteins play critical roles in many biological processes and constitute the majority of all drug targets. However, producing correctly folded and stable membrane proteins is often difficult and requires intensive protein engineering and optimization. Here, we present a rapid method for screening membrane protein expression in insect cells.

3:05 Cell-Free Systems: Functional Modules for Synthetic and Chemical Biology
Marlitt Stech, MSc, Cell-Free Protein Synthesis, Fraunhofer IBMT-Potsdam
Here we present recent advances for the synthesis of glycoproteins, proteins containing disulfide bridges, membrane proteins, and fluorescently labeled proteins. The basis for the expression of these difficult-to-express target proteins is a translationally active cell extract which can be prepared from eukaryotic cell lines such as *Spodoptera frugiperda* 21 (Sf21) and Chinese hamster ovary (CHO) cells.

3:35 High-Yield Membrane Protein Expression from *E. coli* Using an Engineered Outer Membrane Protein F Fusion
Bryan Berger, Ph.D., Head, Berger Lab; Assistant Professor, Chemical Engineering, Lehigh University
An *Escherichia coli*-based membrane protein overexpression system utilizing an engineered bacterial outer membrane protein F (pOmpF) fusion has been developed. Full-length human receptor activity-modifying protein 1 (RAMP1) was expressed using pOmpF, solubilized in FC15 and purified to homogeneity. Our approach provides a useful, complementary approach to achieve high-yield, full-length membrane protein overexpression for biophysical studies.

4:05 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem Solving Breakout Discussions

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

6:45 End of Day

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EXPRESSION STREAM

9th Annual | May 5-6

Difficult to Express Proteins

Harnessing Innovation to Improve Expression and Function

TUESDAY, MAY 6

7:45 am Morning Coffee

EXPRESSION FOR STRUCTURE, DRUG DISCOVERY AND OPTIMIZATION

8:25 Chairperson's Remarks

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

8:30 Nanolipoprotein Particles (NLPs) for Supporting Solubilization and Characterization of Membrane Proteins

Matthew A. Coleman, Ph.D., Adjunct Professor, Radiation Oncology, University of California, Davis School of Medicine

We have developed new ways to tune and produce apolipoprotein nanoparticles for use in membrane protein production. The method has been used for drug screening, functional analysis of SNPs. Novel data will be presented for the production and characterization of full length membrane bound proteins that have been difficult to obtain let alone characterize (ERBB2, EGFR and GPCRS).

9:00 Recovering Costly Labeled GPCRs from Dilute Solutions

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

NMR studies of G protein-coupled receptors require milligram quantities of stable isotope-labeled receptors, either reconstituted in lipid bilayers or stabilized in detergent micelles. We report optimized preparation of functional, labeled cannabinoid receptor expressed by fermentation in minimal media of a defined composition, & high yield recovery from dilute extracts by TA chromatography on His-Tag/ Rho-Tag and His-tag/ Flag-tag resins.

9:30 Expressing Challenging Targets for Drug Discovery

Rick Davies, Ph.D., Reagents and Assay Development, AstraZeneca, Inc.

Targets for drug discovery projects are becoming more diverse and challenging. They are chosen based on evidence linking them to human disease and not on the challenges, which need to be overcome to express these proteins in suitable quantity and quality to support small molecule drug discovery projects. A number of examples of recent AZ projects will be presented, in which difficult expression/ purification challenges have been overcome.

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

BREAKING BARRIERS TO EXPRESSION

10:45 Cell Biological Underpinnings Behind Difficult-to-Express Human IgGs

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

11:15 Strategy to Address the Issues of IgG4 Fab-Arm-Exchanges and the Protein Tools Prepared for *in vitro* and *in vivo* Studies of the Exchanges

Jacques Dumas, Ph.D., Head, Protein Production, Vitry Biologics SCP, Vitry Research Center, Sanofi

11:45 Adenosine Receptor Expression: Yeast as an Engineered Host

Anne Skaja Robinson, Ph.D., Catherine and Henry Boh Professor, Engineering; Chair, Chemical and Biomolecular Engineering, Neuroscience Program Faculty Member; Professor and Chair, Chemical and Biomolecular Engineering, Tulane University

G-protein coupled receptors (GPCRs) are a diverse class of therapeutically important proteins and are implicated in nearly every aspect of our physiology. We have generated various yeast strains that express the human adenosine receptors, including A2aR, hA2bR and several chimeras, and will describe here the transcriptional and post-transcriptional regulation of protein expression and trafficking to the plasma membrane.

12:15 pm Luncheon Presentation I
A Holistic Approach for Manufacturing Difficult-to-Express Proteins

Sponsored by WACKER

Andreas Anton, Ph.D., Director, Contract Development, Scil Proteins Production

Biopharmaceuticals are attractive therapeutic alternatives to classical small molecules due to their high target specificity and hence reduced side effects. However, the production of therapeutic proteins is much more challenging, and it is commonly said that the product is actually the process. Here we will present an integral approach to improve the manufacturing efficiency for difficult-to-express proteins in order to reduce cost of goods. Selected case studies will be shown for productivity and process efficiency improvement using a unique *E. coli* secretory system and a matrix-based screening technology for refolding of insoluble proteins

12:45 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:15-1:45 Ice Cream Break in the Exhibit Hall

ENHANCING THE PROCESS

2:00 Chairperson's Remarks

David O'Connell, Ph.D., Director, Masters Programs in Biotechnology, School of Biomolecular & Biomedical Research, University College Dublin; Conway Institute of Biomolecular & Biomedical Research, UCD Belfield

2:05 Insights into How to Design Assays and Correctly Plan for Candidate Profiling in the Most Cost-Effective, Rapid and Dynamic Way

David O'Connell, Ph.D., Director, Masters Programs in Biotechnology, School of Biomolecular & Biomedical Research, University College Dublin; Conway Institute of Biomolecular & Biomedical Research, UCD Belfield

We have optimized the approach for very sensitive determination of the specificity and promiscuity of many important classes of proteins in the biotherapeutic pipeline. This presentation highlights solutions to key concerns for the industry in developing attritional strategies for candidate protein molecules through optimized assay protocols on new generation proteome chips.

2:35 Expression of Mammalian Glycoproteins and Other Difficult to Express Proteins with the Vankyrin-Enhanced Baculovirus Expression System

Kendra Steele, Ph.D., Research Scientist, ParaTechs Corp.

The vankyrins are genes derived from polydnaviruses that significantly delay death and lysis of baculovirus-infected cells while enhancing recombinant protein production. ParaTechs' vankyrin-enhanced technology markedly improves the baculovirus expression system by overcoming one of its main limitations. The vankyrin technology is also evaluated with cells developed for mammalian glycoprotein expression.

3:05 New Tools for Difficult Expression Problems: New Solubility Partners and Endotoxin Free DNA and Protein

Sponsored by Lucigen Simplifying Genomics

David Mead, CEO, Lucigen Corp.

Lucigen will present a suite of new solubility fusion partners within a robust enzyme-free cloning platform, including a novel fluorescent protein that provides an instant visual report of the amount of soluble, active protein. In addition, attendees will learn about novel competent *E. coli* cells lacking lipopolysaccharide (LPS) for endotoxin-free protein and DNA production.

3:20 Non-Viral Adeno Associated Virus-Based Platform for Stable Expression of Antibody Combination Therapeutics

Sponsored by excelimmune

Elizabeth Reczek, Ph.D., President & CSO, Excelimmune, Inc

Antibody Combination Therapeutics (ACTs) are a novel class of polyvalent biopharmaceuticals, uniquely suited for the treatment of complex diseases. Excelimmune has developed an AAV-based, virus-free recombinant protein expression platform capable of rapid and consistent production of complex antibody mixtures in a single batch format.

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

4:15 Expression and Purification of Soluble Porcine CTLA-4 in Yeast *Pichia pastoris*

Zhirui Wang, DVM, Ph.D., Assistant Professor, Harvard Medical School; Technical Director, MGH-DF/HCC Recombinant Protein Expression and Purification Core, Transplantation Biology Research Center, Massachusetts General Hospital

Glycosylation analysis using PNGase F demonstrated the N-linked glycosylation on *Pichia pastoris* expressed soluble porcine CTLA-4. To improve the expression level and facilitate the downstream purification we mutated the two potential N-linked glycosylation sites with non-polarized alanines by site-directed mutagenesis. Removal of the two N-glycosylation sites significantly improved the soluble porcine CTLA-4 expression and purification using yeast *Pichia pastoris* system.

4:45 Primary Structure Inspections to Improve Initial Expressions

Brian Chiswell, Ph.D., Owner and Founder, Dimensions BioSciences

The objective of the preliminary inspection is to determine the constrained residues within or near a domain to increase the stability and solubility of a construct while maintaining its native activity. Potential binding sites, domain boundaries, areas of disorder & areas of flexibility should be considered before subcloning. Optimization of a construct should also be done information becomes available.

5:15 End of Conference

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4th Annual | May 7-8

Optimizing Protein Expression

Enhancing Expression Systems

WEDNESDAY, MAY 7

7:00 am Registration and Morning Coffee

PROTEIN EXPRESSION IN CHO CELLS

8:00 Chairperson's Opening Remarks

Alexei Yeliseev, Ph.D., Staff Scientist and Head, Protein Expression Group, LMBB, NIH

8:10 Engineering Recombinant Proteins for Improved Manufacturability in CHO Cells

Sujeewa D Wijesuriya, Ph.D., Senior Scientist, XOMA (US) LLC

Case studies will be presented that identify manufacturability issues with two recombinant proteins. First, we greatly improved expression of CAB-2, a hybrid recombinant protein, by eliminating unproductive mRNA coding sequences. Second, we established that light chain was responsible for poor expression and high aggregate levels in a recombinant antibody. Light chain shuffling yielded an antibody with high binding affinity, and improved expression and product quality.

8:40 Development and Optimization of a Suspension CHO-EBNA Transient Gene Expression System

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

Recent advances in mammalian expression hosts for protein expression have led to their increased utilization in efforts to meet the challenge of generating large amounts of functional proteins for drug discovery research. We present the engineering of a suspension CHO-EBGS cell line and subsequent optimization of polyethyleneimine-mediated transient gene expression using a factorial experimental design approach. Data from a case study will be presented highlighting why this high-yielding, high-throughput CHO-EBGS expression system has become an integral expression tool within the Reagents and Assay Development (RAD) department at AstraZeneca.

9:10 Aeration Strategies and the Control of Interfacial Stress in Mammalian Cell (CHO) Culture

Daniel G. Bracewell, Ph.D., Reader, Biochemical Engineering, University College London

Understanding gas transfer is critical to the design and scale-up of bioreactor conditions with landmark events being the use of stirred tank reactors for penicillin in 1944 and discovery of surfactants for mammalian cell culture in 1968. The advent of biosimilars and the commodification of antibodies challenges the depth of our understanding. We present our recent results on the subject in this context.

9:40 Estimation of Metabolic Rewiring in CHO Cell Culture Using Combined ^{13}C-Metabolic Flux Analysis

Woo Suk Ahn, Ph.D., Research Associate, Bioinformatics and Metabolic Engineering, Massachusetts Institute of Technology (MIT)

^{13}C-Metabolic flux analysis (^{13}C-MFA) is a powerful methodology to quantify intracellular metabolism using stable isotopic tracers. We introduced multiple tracers in parallel to quantify CHO central metabolism. Here, we revealed metabolic rewiring from growth to non-growth phase. In addition, by design of multiple isotopic tracers, we achieved high accuracy and resolution of flux values. This technology enables us to identify and optimize CHO cellular metabolism.

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

EXPRESSION STRATEGIES

» 11:10 KEYNOTE PRESENTATION:
The Production of Complex Proteins in Drug Discovery: Challenges & Solutions

René Assenberg, Ph.D., Research Investigator, Novartis Pharma AG

Recently there's been a trend towards greater complexity of proteins targeted for drug discovery. The production challenges of such proteins require a range of different tools, including different expression systems, novel protein engineering and analytical approaches. This talk will outline some of the challenges our group faces in this area, with emphasis on glycoproteins and protein complexes, as well as the solutions we deploy.

11:40 FEATURED PRESENTATION:
Protein Expression Technologies - Evolution or Revolution?

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

I will give an overview of protein expression at AstraZeneca Pharmaceuticals, including: An overview of established protein expression technologies; Novel trends and demands for proteins in hit discovery and lead optimization; Novel technologies and trends for protein expression in drug discovery research; Case studies for difficult-to-express proteins and protein complexes; Finding the balance between in-house efforts and outsourcing, and summary and outlook.

12:10 pm From Strep-Tag® to Super-StrepTactin®

Sponsored by iba Solutions For Life Sciences

Thomas Schmidt, Ph.D., COO, IBA GmbH

The widely used Strep-tag®/Strep-Tactin® purification system provides highly pure and functional proteins from crude lysates of any host after one chromatographical step only. We have now developed a new Strep-Tactin®, called Super-StrepTactin®. Super-StrepTactin® has been designed for the very stable binding of Twin-Strep-tag fusion proteins (T1/2=13h) with the provision that binding can still be reversed under physiological conditions. This opens new application fields for Strep-tag users beyond purification, particularly new assay capabilities in drug discovery processes.

12:25 Superior Protein Yields in CHO and HEK-293 Cells Using a Novel Highly Efficient Reagent for Transient Transfection

Sponsored by Polyplus transfection THE DELIVERY EXPERTS

Géraldine Guérin-Peyrou, Bioproduction Product Specialist, Polyplus-transfection

Low transfection efficiency of CHO cells is a major bottleneck hampering protein production in Transient Gene Expression (TGE). Polyplus-transfection, with its 10+ year expertise in transfection, will present superior results obtained in CHO and HEK-293 cells with its novel, technically advanced reagent.

12:40 Luncheon Presentation I: Engineering of Genes, Proteins and Pathways for Systematic Optimization of Therapeutic Protein Production

Sponsored by DNA 2.0

Mark Welch, Ph.D., Director, Gene Design, DNA2.0 Inc.

1:10 Luncheon Presentation II Lessons from DNA Viruses: Customized and Flexible Protein Production in CHO Cells

Sponsored by ICOSAGEN CELL FACTORY

Meelis Kadaja, Ph.D., CSO, Icosagen Cell Factory

By combining favorable features of DNA viruses, Icosagen has developed technology for fast and efficient production of recombinant proteins in CHO cells. Our QMCF Technology is flexible and can be tailored for the optimal expression of each protein. It is also suitable for cell bank generation and long-term protein production.

1:40 Session Break

BACULOVIRUS / INSECT CELLS

2:00 Chairperson's Remarks

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

2:05 A Novel Baculovirus Vector for Production of Non-Fucosylated Recombinant Glycoproteins

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

The inability to provide human-type protein glycosylation patterns has precluded the use of baculovirus-insect cell systems for therapeutic glycoprotein production. Recent glycoengineering efforts have advanced the platform through the creation of improved systems that can produce recombinant glycoproteins with human-type, complex, terminally sialylated N-glycans. We produced the first baculovirus-insect cell systems capable of producing non-fucosylated recombinant glycoproteins, including antibodies, and characterized their capabilities.

2:35 Insect Cell Culture for Rapid GMP Manufacturing of Seasonal and Pandemic Influenza Vaccines

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

We developed a universal process for the generation of recombinant baculovirus banks for seasonal and pandemic influenza antigens, as well as for the expression and purification of these antigens at large scale. Less than 30 days is required for the introduction of new antigens to GMP manufacturing. Influenza seasonal vaccine Flublok, containing three different hemagglutinin antigens, can be manufactured during two months.

3:05 The Impact of Scalable Transfection: Maximizing CHO Antibody Production Using Flow Electroporation to Accelerate Development Timelines

Sponsored by MaxCyte

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

CHO transient gene expression (TGE) greatly accelerates antibody development by eliminating the need to change cell backgrounds during scale up to biomanufacturing. Flow electroporation enables scalable transient transfection of a variety of CHO cell lines producing sufficient quantities of antibodies for early and mid-stage antibody development. The production of antibody titers >1g/L yielding multiple grams of antibody from a single transfection, as well as the rapid generation of stable CHO cell lines will be discussed.

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

4:20 Problem Solving Breakout Discussions

5:20 Networking Reception in the Exhibit Hall with Poster Viewing

6:30 End of Day

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4th Annual | May 7-8

Optimizing Protein Expression

Enhancing Expression Systems

THURSDAY, MAY 8

7:45 am Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

YEAST, ALGAE & EUKARYOTIC CELLS

8:30 Chairperson's Remarks

Peter B. Heifetz, Ph.D., President and CTO, OrPro Therapeutics, Inc.

8:35 Examples of Successful Application of Yeast Expression System for Therapeutic Protein Discovery, Optimization and Production

Piotr Bobrowicz, Ph.D., Director, Open Innovation, Adimab, LLC

Yeast cells offer an effective and highly adaptable system for the production of proteins. The development of cells with modifications in the secretory pathway in combination with expression vector optimization overcame several of the past limitations. This talk will provide an overview of the recent improvements with examples of how a yeast expression system can be successfully applied to therapeutic protein discovery, optimization and production.

9:05 Specialized Expression – Lessons Learned from Photosynthetic Platforms

Peter B. Heifetz, Ph.D., President and CTO, OrPro Therapeutics, Inc.

A key goal of utilizing specialized expression systems for recombinant proteins is to enable superior products by leveraging unique platform characteristics. The chloroplast organelles of microalgae combine prokaryotic gene expression with a folding milieu that facilitates assembly of complex, eukaryotic proteins. The promises and pitfalls of such a strategy will be discussed in light of lessons learned at Rincon Pharmaceuticals.

9:35 Cell-Free Protein Expression Based on Extracts from Eukaryotic Cells

Stefan Kubick, Ph.D., Group Manager, Fraunhofer Institute for Biomedical Engineering IBMT

We developed a production procedure of translationally active lysates from cultured eukaryotic cells. The integrity of subcellular ER-derived components was demonstrated in these lysates by showing signal peptide cleavage as well as glycosylation of cell-free expressed proteins. Moreover, we expanded our cell-free protein expression system by the insertion of an orthogonal tRNA/synthetase pair to facilitate the cotranslational and site directed incorporation of non-canonical building blocks.

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

ESCHERICHIA COLI

11:05 Large-Scale Expression of a Functional GPCR in *E. coli*: Optimizing Expression Tags and Fermentation Conditions

Alexei Yeliseev, Ph.D., Staff Scientist and Head, Protein Expression Group, LMBB, NIH

We optimized production of human cannabinoid receptor CB2, a G protein-coupled receptor, involved in regulation of immune response, in *E. coli* by testing several expression vectors, expression hosts, and different combinations of expression and affinity tags. We further optimized fermentation conditions by developing a defined medium, temperature, aeration and mode of induction to maximize the yield of a stable isotope-labeled receptor suitable for NMR studies.

11:35 Optimizing Protein Expression with the Three Ss of Cell Free Protein Synthesis – Simplicity, Speed, and Scalability

Stuart Bussell, Ph.D., Senior Director, Fermentation/Upstream Development, Sutro Biopharma

Cell free protein synthesis (CFPS) facilitates protein expression optimization with its simplicity, speed, and scalability. Once extracts are produced industrially, protein expression is reduced to standard DNA production processes and rapid CFPS. CFPS is complete in 8-10 hours, scales smoothly from the microliter to the 100 liter (and presumably larger) scale, and produces as much as 1 g/L of complex biologics in fully active form.

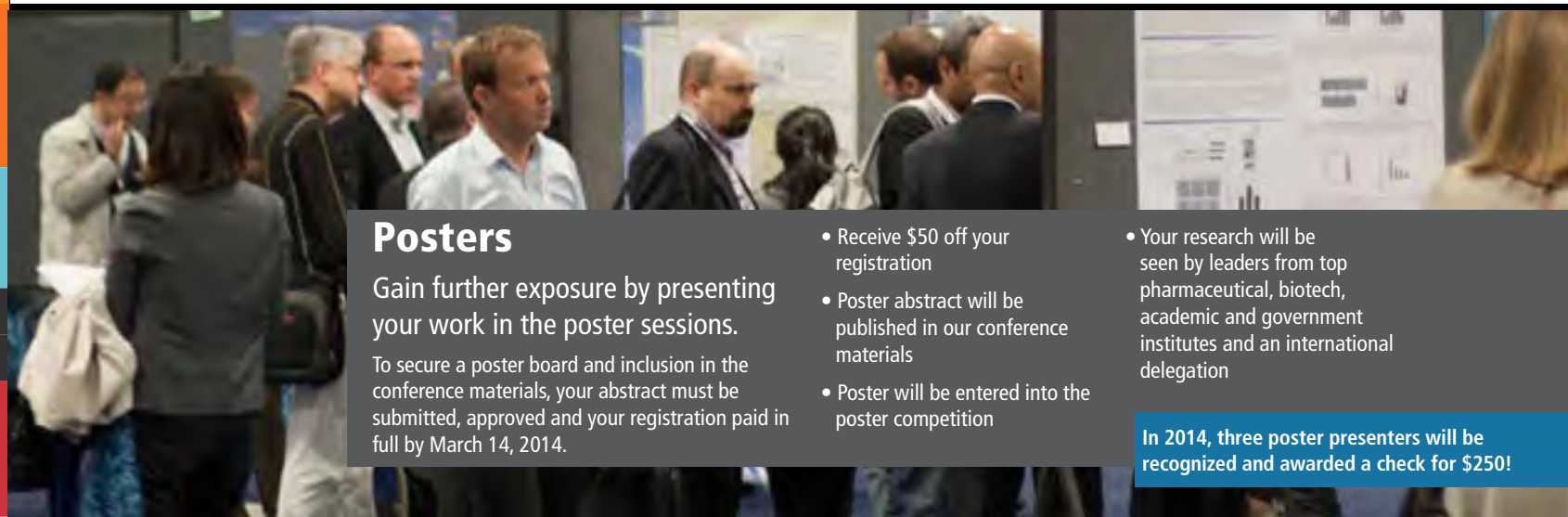
12:05 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

12:35 End of Conference

Recommended Thursday Dinner Short Course*

Protein Aggregation: Mechanism, Characterization and Immunogenic Consequences

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



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Inaugural | May 8-9

High-Level Expression of Enzymes

From Biotherapeutics to Food Science and Bioenergy

Recommended Pre-Conference Short Courses*

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

***In silico* Immunogenicity Predictions (Hands-On) Workshop**

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

Recommended Thursday Dinner Short Course*

Protein Aggregation: Mechanism, Characterization and Immunogenic Consequences

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

THURSDAY, MAY 8

THE SCIENCE FOR SUCCESS

1:30 pm Chairperson's Opening Remarks
Markku Saloheimo, Ph.D., VTT Technical Research Centre of Finland

1:40 Class A β-Lactamases as Versatile Scaffolds to Create Hybrid Enzymes: Applications from Basic Research to Medicine
Marylene Vandevenne, Ph.D., Laboratory of Enzymology and Protein Folding, Centre for Protein Engineering, Institute of Chemistry, University of Liege
Designing hybrid proteins is a major aspect of protein engineering and covers a very wide range of applications from basic research to medical applications. This review focuses on the use of class A β-lactamases as versatile scaffolds to design hybrid enzymes (referred to as β-lactamase hybrid proteins, BHPs) in which an exogenous peptide, protein or fragment thereof is inserted at various permissive positions. We discuss how BHPs can be specifically designed to create bifunctional proteins, to produce and to characterize proteins that are otherwise difficult to express, to determine the epitope of specific antibodies, to generate antibodies against nonimmunogenic epitopes, and to better understand the structure/function relationship of proteins.

2:10 The Cargo and the Transport System: Secreted Proteins and Protein Secretion in *Trichoderma reesei (Hypocrea jecorina)*
Markku Saloheimo, Ph.D., VTT Technical Research Centre of Finland
We discuss T. reesei secreted enzymes and proteins that have been studied, such as proteases, laccase, tyrosinase and hydrophobins. Investigation of the *T. reesei* secretion pathway has included molecular characterization of the pathway components functioning at different stages of the secretion process as well as analysis of the stress responses caused by impaired folding or trafficking in the pathway or by expression of heterologous proteins.

2:40 Sponsored Presentation *(Opportunity Available)*

2:55 Sponsored Presentation *(Opportunity Available)*

3:10 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Problem Solving Breakout Discussions

5:00 Close of Day

FRIDAY, MAY 9

7:45 am Continental Breakfast in the Exhibit Hall with Poster Viewing

ENGINEERING FOR BETTER SOLUBILITY & PURIFICATION

8:30 Chairperson's Remarks

8:35 Bacterial Expression Strategies for Several *Sus scrofa* Diacylglycerol Kinase Alpha Constructs: Solubility Challenges
Becky Tu-Sekine, Ph.D., Research Associate, Biological Chemistry, Johns Hopkins University School of Medicine
We pursued several strategies for expressing either full-length *Sus scrofa* diacylglycerol kinase (DGK) alpha or the catalytic domain (alphacat) in *Escherichia coli*. Alphacat could be extracted, refolded, and purified from inclusion bodies, but when subjected to analytical gel filtration chromatography, it elutes in the void volume, in what we conclude are microscopic aggregates unsuitable for X-ray crystallography.

9:05 Engineering *Escherichia coli* for Soluble Expression and Single Step Purification of Active Human Lysozyme
Karl E. Griswold, Ph.D., Thayer School of Engineering; Molecular and Cellular Biology Program, Dartmouth University
In the ongoing battle against drug-resistant bacterial pathogens, there is growing interest in lytic cell wall hydrolases as prospective therapeutic agents. Facile and scalable production of such bactericidal enzymes can, however, bottle-neck both early stage discovery & downstream development of promising therapeutic candidates. We describe the creation of efficient microbial production systems through biomolecular and strain engineering.

9:35 High Level Expression using the Drosophila S2 Expression System
Wian De Jongh, Ph.D., CSO, ExpreS2ion Biotechnologies
The Drosophila S2 system is particularly well suited to the expression of secreted complex proteins. ExpreS2ion has developed methods to speed-up screening of protein variants in small scale, as well as to significantly increase expression of individual variants. Examples of expressed antigens and enzymes will be discussed, as well as examples of process development leading to significantly increased expression.

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

ALTERNATE HOSTS AND STRATEGIES

10:50 Evaluation of Butyrate-Induced Production of a Mannose-6-phosphorylated Therapeutic Enzyme Using Parallel Bioreactors
Chikkathur N. Madhavarao, Ph.D., Senior Staff Fellow,Therapeutic Proteins, OBP, OPS, CDER, FDA (Invited)
We have evaluated the effect of adding butyrate to bioreactor production cultures of human recombinant β-glucuronidase produced from CHO-K1 cells, with an emphasis on CQAs. Using this approach we found that butyrate treatment increased β-glucuronidase production up to ~3-fold without significantly affecting the catalytic properties of the enzyme. However, M6P content in β-glucuronidase was inversely correlated with the increased enzyme production.

11:20 High-Throughput Construct Screening and Rational Strategies for Structural Platform Establishment: Case Studies of Difficult Kinases
Jacques Dumas, Ph.D., Head, Protein Production, Vitry Biologics SCP, Vitry Research Center, Sanofi
We present case studies for which we spent variable time to find the right construct. For the last cases we started a collaboration with EMBL Grenoble which established a platform called ESPRIT (Expression of Soluble Proteins by Random Incremental Truncation) allowing the selection of
tracks of soluble constructs in *E. coli*. We further pursue our efforts in expression and purification optimizations. Structures were solved at 2.0Å.

11:50 The Production and Characterization of a New Active Lipase from *Acremonium alcalophilum* using a Plant Bioreactor
Rima Menassa, Ph.D., Southern Crop Protection and Food Research Centre, Agriculture and Agri-Food Canada

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

12:50 Session Break

OVERCOMING PROBLEMS & CHALLENGES

1:35 Chairperson's Remarks
Matthew H. Coleman, Ph.D., Senior Biomedical Staff Scientist, Lawrence Livermore National Laboratory

1:40 Genome-Encoded *Bacillus cereus* E33L AmpD Displays Lytic Properties against *Bacillus anthracis*: Identifying and Characterizing Novel Antimicrobial
Matthew H. Coleman, Ph.D., Senior Biomedical Staff Scientist, Lawrence Livermore National Laboratory
We have identified a genome-encoded, non-prophage gene AmpD, from B. cereus E33L with lytic capabilities against B. anthracis. Normal approaches using *E. coli* faiiled to produce the protein due to cellular toxicity. We were able to produce this protein at levels greater than 1 mg/mL when we applied cell free exprity. We were able to produce this protein at levels greater than 1 mg/mL when we applied cell free expression technologies.

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Inaugural | May 8-9

High-Level Expression of Enzymes

From Biotherapeutics to Food Science and Bioenergy

2:10 Expression, Characterization, Crystallographic and Inhibition Studies of DXR from Human Pathogens

Yongcheng Song, Ph.D., Assistant Professor, Pharmacology, Baylor College of Medicine

1-Deoxy-D-xylulose-5-phosphate reductoisomerase (DXR) in the non-mevalonate isoprene biosynthesis pathway is essential for most pathogenic bacteria and apicomplexan parasites. We present expression and purification of DXR proteins from *E. coli*, *P. falciparum* and T. gondii as well as the biochemical, biophysical (including X-ray crystallography) and inhibition studies of these enzymes.

2:40 Engineering of Human L-Asparaginase: Amino-Terminal Exposure of the Catalytically Critical Threonine Residue in the Bacterially Produced Enzyme

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

Asparaginases hydrolyze L-asparagine in the blood, thus depriving leukemic cells from the external source of this natural amino acid. To replace therapeutically used bacterial enzymes, we pursue the design of human asparaginases. We developed a co-expression system to expose the catalytically critical threonine residue at the N-terminus of the β-subunit.

3:10 Aggresomes: A Putative New Type of Self-Assembling, Immobilized Biocatalyst

Jose-Luis Corchero, Ph.D., Senior Scientist, Nanobiotechnology Group, Univ Autonoma de Barcelona; Bioengineering, Biomaterials and Nanomedicine, Centro de Investigación Biomédica en Red (CIBER-BBN)

To study and characterize aggresomes properties (architecture, enzymatic activity, composition, stability and reusability), a purification protocol for such structures has been established, taking into consideration GLA optimal pH to preserve its enzymatic activity. Taking all the results together, we propose aggresomes as a novel type of carrier-free, self-assembled immobilized biocatalyst, with intriguing putative applications in both biotechnological and biomedical fields.

3:40 Closing Remarks

4:00 End of Conference

Student Fellowship

Present Your Poster to 1,600+ Protein Engineering Researchers

Student Fellowship Award Winners will attend the 10th 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 14, 2014.

STUDENT FELLOWSHIP DETAILS:

- Full-time graduate students and Ph.D. candidates are encouraged to apply for the PEGS the essential protein engineering summit Student Fellowship. Applications are due by February 14.
- Interested students must complete the 2014 Student Fellowship Application and are required to present a scientific poster (title and abstract are due at the time of the application).
- All applications will be reviewed by the scientific review committee and accepted students will be notified no later than February 21 if they have been accepted for the 2014 Student Fellowship.
- ADDED BONUS! Poster competition features cash prize winners.
- Accepted 2014 Student Fellows will receive a discounted conference registration rate of $295*, which must be paid by March 14.
- This fellowship is limited to 20 students and is for the Premium Conference Package Only. Excludes Short Courses.
- All accepted 2014 Student Fellows will be asked to help promote the conference at their college and throughout their social media networks.
- Students not accepted for the 2014 Student Fellowship can still register at a discounted rate of $595*, and will not be required to present a poster.

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4th Annual | May 5-6

Characterization of Biotherapeutics

The Changing Analytical Function in an Era of New Product Formats

Recommended Pre-Conference Short Courses*

Translational Strategies for Development of Monoclonal Antibodies from Discovery to Clinic, Part 1: Focus on Early Discovery & Part 2: Focus on Nonclinical Development to Clinic

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

MONDAY, MAY 5

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks

Kristi Sarno, Chair, Greater Boston Chapter, Women in Bio; Director, Business Development, Pfenex, Inc.

8:40 Harnessing the Patient's Immune System to Combat Cancer

Peter CR Emtage, Ph.D., Vice President, Immune Mediated Therapies, MedImmune

With recent FDA approvals, modulation of the immune system is now a clinically validated approach in the treatment of some cancers. At MedImmune, the Oncology Department is developing assets and expertise in Immune Mediated Therapy of Cancer (IMT-C). The challenges from a drug development perspective are multi-fold. The talk will focus on the relevance of preclinical models and translational science to address key issues, including dose selection and rationale combinations.

9:25 Building Regeneron's Pipeline: From Trap Technology to the *VelocImmune* Platform to *Veloci-Next*

George D. Yancopoulos, M.D., Ph.D., President, Regeneron Laboratories; CSO, Regeneron Pharmaceuticals, Inc.

George D. Yancopoulos, M.D., Ph.D., who is the Founding Scientist, President, Research Laboratories and Chief Scientific Officer of Regeneron Pharmaceuticals, one of the world's top biotechnology companies, will discuss how he and his colleagues exploited a commitment to science and technology to start the company, withstand years of challenges and failures, and emerge with a pipeline of promising technologies and novel/biologics that are beginning to bring hope to countless patients and their families.

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

11:05 Chairperson's Remarks

Hubert Kettenberger, Ph.D., Principal Scientist, Large Molecule Research, Roche Diagnostics GmbH, Germany

» 11:10 KEYNOTE PRESENTATION:
Regulatory Challenges for Protein Therapeutics

John Alvino, Senior Manager, Global Regulatory CMC, MedImmune

Common regulatory challenges exist among protein therapeutics but there are unique concerns for novel molecules. This talk will present specific and general concerns for innovative non-mAb therapeutics which are becoming increasingly more important and are now in preclinical pipelines. Finally, the presentation will conclude with a case study highlighting a fusion protein which utilizes a nonstandard manufacturing process, illustrating the challenges with determining specifications, comparability and process validation for a novel molecule.

CHARACTERIZATION OF ANTIBODY-DRUG CONJUGATES

11:40 Novel ADC Chemistry for Improved Stability and Pharmacokinetics

Robert Lyon, Ph.D., Associate Director, Protein Chemistry, Seattle Genetics

Drug-linker stability is a key attribute of an ADC. We have developed a new conjugation chemistry that allows for the generation of stable ADCs using native IgG1 antibodies. ADCs prepared with this method exhibit increased ADC exposure resulting in potent activity coupled with diminished toxicity.

12:10 pm Advances in Antibody Characterization and Collaborative Workflows

Sponsored by accelrys®

Ken Butenhof, Ph. D., Senior Application Field Scientist, Accelrys, Inc.

Antibody discovery is driven by complex time consuming experimental processes involving numerous teams. Evolving technologies enable researchers to make more informed decisions early in the process. Here we suggest collaborative and comprehensive capabilities in antibody characterization and development: capabilities to analyze, annotate, predict 3-dimensional structures, mutation energies for stability and binding affinity, electrostatics properties, aggregation propensity, developability and more. Collaborative environments for registration, workflow and sharing will be discussed.

12:40 Luncheon Presentation I: Deconvoluting Receptors Targeted by Antibodies and Protein Ligands Using the Retrogenix Cell Micorarray Platform

Sponsored by RETROGENIX® SPOTTING YOUR TARGET

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

Selecting antibodies by phenotype, rather than against a pre-determined target, leads to novel, disease-relevant antibody targets. Retrogenix's Cell Microarray technology overcomes the target deconvolution hurdle, with high success rates. The technology also provides a powerful approach to identify potential off-target activities to guide lead selection, and to identify previously unknown receptors of protein ligands.

1:10 Luncheon Presentation II: High Throughput Analysis and Characterization Methods for Improved Process Development Workflows

Sponsored by PerkinElmer® For the Better

Alissa Thompson, NA Biotherapeutics Product Specialist, PerkinElmer

The development of Biotherapeutics is a complex and lengthy process and there is a need for techniques which can increase profitability, productivity and improve the speed of development. Process development can involve multiple complex steps and PerkinElmer offers solutions to simplify and improve the workflow. The LabChip® GXII microfluidic technology enables the rapid analysis.

1:40 Session Break

2:00 Chairperson's Remarks

2:05 Making and Characterizing Antibody-Maytansinoid Conjugates for Preclinical Research and Development

Nicholas Yoder, Ph.D., Scientist, Biochemistry, ImmunoGen, Inc.

Antibody-maytansinoid conjugates (AMCs) show promise for the treatment of many cancer indications, as exemplified by the FDA approval of Kadcyla for Her2-positive breast cancer. Robust protein chemistry is required to provide material for early stage AMC research and lead selection. Sophisticated analytical techniques are employed to understand crucial molecular and biological properties of AMCs. Both these topics will be discussed in the context of candidate therapeutic development.

2:35 Role of Analytics in the Development of Antibody-Drug Conjugates

Samadhi Vitharana, Ph.D., Senior Scientist, Core Sciences & Technologies, Takeda California

Monoclonal antibodies linked to cytotoxic payloads known as antibody-drug conjugates represent an emerging technology in clinical oncology. ADCs utilize the specificity of a mAb to deliver a cytotoxic drug to targeted tumor cells. Chemistry of the linker, cytotoxic drug and sites of attachment often result in complex and heterogeneous drug product preparations. Analytics to evaluate different architectures of ADCs will be discussed.

3:05 Analytical Characterization of Fleximer-Based ADC

Alex Yurkovetskiy, Ph.D., Senior Director, Chemistry, Mersana Therapeutics

ADC design utilizing biodegradable polymer scaffolds for drug payload immobilization provides remarkable flexibility in the selection of targeting ligand format, active agent type/density and bioconjugation strategy. This ADC subclass requires development of new approaches to characterize ADC composition, stability, and pharmacokinetics. The analytical methods developed for characterization of polyacetal-based ADCs is presented.

3:35 Investigation into Temperature-Induced Aggregation of an Antibody-Drug Conjugate

Heather Flores, Scientist, Late Stage Pharmaceutical Development, Genentech, Inc.

We explored the effect of thermal stress on the physical stability of an ADC and the effects of conjugation on the ADC secondary and tertiary structures. Analysis showed that for species with high drug loading, conjugation does not measurably alter the secondary structure, but it does render the CH2 domain less stable to thermal stress. The variable domain of the antibody may also contribute to the extent of aggregation.

4:05 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem Solving Breakout Discussions

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

6:45 End of Day

TUESDAY, MAY 6

7:45 am Morning Coffee

CHARACTERIZATION OF BISPECIFIC ANTIBODIES

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ANALYTICAL STREAM

4th Annual | May 5-6

Characterization of Biotherapeutics

The Changing Analytical Function in an Era of New Product Formats

8:25 Chairperson's Remarks

Josh Pearson, Ph.D., Senior Scientist, Biochemistry & Biophysics Group, Pharmacokinetics & Drug Metabolism, Amgen, Inc.

8:30 Mammalian Co-Culture for Single-Reactor Bispecific Production

Whitney Shatz, Senior Research Associate, Genentech

The past few years have seen significant developments in the field of bispecific antibody production and characterization. Most of these technologies involve producing each half separately, and relying on an *in vitro* heterodimerization step for bispecific assembly. Using mammalian co-culture, we have devised a production method involving a single reactor to efficiently produce native architecture IgG bispecifics with 2 distinct light chains.

9:00 Assay Selection for Studying Impurities in Bispecific Antibodies

Hubert Kettenberger, Ph.D., Principal Scientist, Large Molecule Research, Roche Diagnostics GmbH, Germany

9:30 The Platform Analytical Strategy for Characterization of Kλ-body® Bispecific Products

Sylvain Raimondi, Ph.D., Head, Analytical Unit, Novimmune

The κλ-body is a bispecific antibody format having a molecular structure identical to that of a fully human monoclonal antibody (i.e., an absence of linkers, mutations or protein purification tags). The talk explores the development of analytical tools to be used with this format. These are used to assess product quality and stability for both in-process and release samples and will highlight novel chromatographic and impurity detection methods.

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

COMPARABILITY AND BIOSIMILARITY

10:45 Analytical Characterization Strategies for Biosimilar Development

Otmar Hainzl, Ph.D., Lab Head, Biophysical Characterization, Sandoz Biopharmaceuticals, Germany

Thorough characterization of a biosimilar candidate in comparison with the reference product at all stages of technical development is the basis for demonstration of similarity and a targeted clinical development program. This presentation will give an overview on characterization strategies for biosimilar development, with case studies on product variant characterization and the impact on structure/function.

11:15 Clinical Pharmacology of Biosimilars: Assessing Similarity in PK, PD and Immunogenicity

Shefali Kakar, Ph.D., Director, Oncology Clinical Pharmacology, Novartis

11:45 Considerations in the Development of Formulations for Biosimilars

Kelly Neelon, Ph.D., Associate Director, Drug Product Formulation and Development, Momenta Pharmaceuticals

With the development of biosimilar products companies face challenges that are different than those faced during novel product development. One of these challenges is to develop a formulation in which the drug product has comparable attributes to the branded product. This talk will discuss considerations for developing alternative formulations for biosimilars with the goal of achieving comparable product quality attributes and stability profiles.

12:15 pm Advances and Challenges in the Analytical Characterization of Biosimilar Products

Sponsored by Pfenex Inc.

Jeff Allen, Ph.D., Director, Analytical Biochemistry & Protein Purification, Pfenex Inc.

At the core of every biopharmaceutical development program is the challenge to successfully produce active and high quality protein, however for biosimilars additional challenges arise in demonstrating the comprehensive analytical comparability to the reference product. Utilizing our technology, Pfenex has rapidly accelerated the development of a biosimilar candidate, demonstrated analytical biosimilarity and progressed the product into clinical trials.

12:45 Luncheon Presentation Automated Chemical Denaturation as a Tool to Evaluate Protein Stability and Optimize the Formulation of Biologics

Sponsored by AVIA BIOSYSTEMS

Ernesto Freire, Ph.D., Professor, Biology and Biophysics, Johns Hopkins University

Automated chemical denaturation provides an accurate way of measuring protein stability under many different solvent or formulation conditions, yielding reliable thermodynamic stability parameters. Contrary to temperature denaturation, chemical denaturation is reversible under a majority of conditions, especially for monoclonal antibodies, fusion proteins and other proteins of therapeutic interest. The dynamic range of the technique permits stability measurements over protein concentrations spanning five orders of magnitude, allowing measurements in the important 100mg/mL concentration range. In addition, chemical denaturation experiments performed in the presence of ligands provide enough information to determine binding affinities from chemical denaturation shifts. In this presentation, the fundamentals of automated chemical denaturation and its application to the evaluation of protein stability and optimization of formulation conditions will be discussed.

1:15-1:45 Ice Cream Break in the Exhibit Hall

CHARACTERIZATION CHALLENGES FOR EMERGING BIOLOGICS

2:00 Chairperson's Remarks

Kelly Neelon, Ph.D., Associate Director, Drug Product Formulation, Drug Product Development, Momenta Pharmaceuticals

2:05 Biophysical Characterization Combined with Proteolytic Assays for Assessing Stability of Therapeutic Proteins *in vitro*

Josh Pearson, Ph.D., Senior Scientist, Biochemistry & Biophysics Group, Department of Pharmacokinetics & Drug Metabolism, Amgen, Inc.

Biophysical techniques and quantitative protease assays may be used for early assessment of the stability of therapeutic proteins *in vitro*. Sequence dependent proteolytic liabilities and the intrinsic instability of a protein can limit its functional half-life and pharmacological activity *in vivo*. *In vitro* assays will be presented for defining the achievable pharmacokinetic profile of a therapeutic protein and the potential engineering options.

2:35 Factors Affecting Ocular Pharmacokinetics of Protein Therapeutics

Leslie Dickmann, Ph.D., Scientist, Preclinical and Translational Pharmacokinetics, Genentech

The molecule characteristics governing clearance and biodistribution of protein therapeutics after intravitreal injection are poorly understood. This presentation will highlight recent investigations into the effect of molecular weight, charge, and binding to FcRn on ocular pharmacokinetics. Results from these studies will allow for development of ocular protein therapeutics with optimized pharmacokinetics.

3:05 Biopharmacetical Characterization According to ICH Q6B Harmonized Guidelines

Sponsored by SGS

Kenneth H. Warrington, Jr., Ph.D., Biopharmaceutical Specialist, SGS Life Science Services

SGS Life Sciences' range of services dedicated to biopharmaceutical characterization focus on the most recent technical and regulatory advances. A biologic characterization strategy designed to confirm structural and physicochemical properties will be presented in accordance with a uniform set of internationally accepted principals for characterization of new and biosimilar biopharmaceutical products (ICH Q6B).

3:20 Sponsored Presentation *(Opportunity Available)*

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

4:15 Comparability Characterization of Protein Vaccine Antigens

Marina Kirkitadze, Ph.D., Deputy Director, Analytical Research & Development, Sanofi Pasteur, Canada

Advances in analytical tools now permit extensive characterization packages for purified recombinant proteins, a significant progression from the traditional characterization by manufacturing processes. Regulatory drivers and analytical approaches used to examine product comparability are discussed and two case studies are described in detail to demonstrate the comparability of pre- and post-change product at different stages of development.

4:45 Challenges and Strategic Approaches for Characterization of Host Cell Proteins in Biopharmaceuticals

Monika Meier, Ph.D., Postdoctoral Researcher, Development Analytics, Roche Diagnostics GmbH, Germany

Host cell proteins (HCPs) are process-related impurities and a potential critical quality attribute in the development of protein-based pharmaceuticals. Here, the characterization of rare reagents for CHO-HCP quantification and the application of an alternative high-throughput method for HCP quantification are discussed. Additionally, advanced orthogonal approaches for characterization of HCPs in general and API associated HCPs in particular for conventional and new product formats are described.

5:15 End of Conference

Recommended Tuesday Dinner Short Course*

Overcoming the Challenges of Immunogenicity Assessment

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

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2nd Annual | May 7-8

Biophysical Analysis of Biotherapeutics

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

Recommended Tuesday Dinner Short Course*

Overcoming the Challenges of Immunogenicity Assessment

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

WEDNESDAY, MAY 7

7:00 am Registration and Morning Coffee

8:00 Chairperson's Opening Remarks
Jennifer Nemeth, Ph.D., Program Leader, Biologics Research, Janssen R&D

8:10 FEATURED PRESENTATION: Subvisible Particulate Matter in Therapeutic Protein Injections: USP<787> and Extended Characterization Using Orthogonal Methods
Satish Singh, Ph.D., Research Fellow and Group Leader, Pfizer; Member, 787 Expert Panel, U.S. Pharmacopeial Convention (USP)

USP<787> is a new chapter that addresses the limitations of USP<788> for therapeutic proteins. This talk will cover the key aspects of USP<787> and discuss the orthogonal methods for characterization of these proteinaceous aggregates in the context of risk assessments during product development.

HIGH-THROUGHPUT AND HIGH RESOLUTION ANALYSIS

8:40 Automation, Acceleration and Enhancement of Analytical Assays for Biotherapeutics
Markus Haindl, Ph.D., Group Leader, Research & Development, Roche Diagnostics GmbH, Germany

Conventional methods for characterization of therapeutic proteins show limitations with respect to speed and compatibility with the growing demand for high-throughput formats. We developed improved and rapid analytical assays for bioprocess development and characterization of biotherapeutics. In combination with an enhancement of assay automation we are able to significantly accelerate process development and PC/PV studies.

9:10 Utility of Hydrogen/Deuterium Exchange Mass Spectrometry for Probing Higher Order Structure of Biotherapeutics
Guodong Chen, Ph.D., Principal Scientist, Bioanalytical and Discovery Analytical Sciences, Bristol-Myers Squibb

One of the key challenges in biotherapeutics characterization is how to define the higher order structures that often dictate their biochemical functions. Classical biophysical methods do not provide detailed conformational information. HDX-MS has emerged as a powerful technology for probing higher order structure of biotherapeutics. This presentation highlights recent developments and applications of HDX-MS in higher order structure analysis.

9:40 High-Throughput Solution-Based Measurement of Antibody-Antigen Affinity and Epitope Binning
Yingda Xu, Ph.D., Group Leader, Protein Analytics, Adimab

Advances in antibody discovery have allowed for the selection of hundreds of high affinity antibodies against many therapeutically relevant targets. This has necessitated the development of reproducible, HT analytical techniques to characterize the output from these selections. Here we report the use of FortéBio for rapid kinetic profile screening and epitope binning, while using MSD for fast and accurate solution phase based KD measurement.

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

11:10 Application of Ultrahigh-Resolution Mass Spectrometry to the Characterization of Antibody Biotherapeutics
Heather DeGruttola, Scientist, Mass Spectrometry and Biophysical Characterization, Pfizer

The presentation will discuss the application of an LC/MS characterization method for mAbs that demonstrates rapid, definitive detection of modifications at the subunit/domain level, including deamidation and oxidation. In addition, rapid confirmation of the amino acid sequence and the detection of potential sequence variants at the subunit/domain level during early stages of process development will be addressed.

11:40 Developing Automated Ribosome Display Selections and Various High-Throughput Screenings
Jonas Schaefer, Ph.D., Head, High-Throughput Laboratory, Biochemistry, University of Zurich, Switzerland

Reliable methods for the selection and screening of affinity reagents in parallel are key to cover today's demand of specific binders. Our laboratory has developed a semi-automated high-throughput pipeline, aiming at an improved robustness of the overall process, while decreasing its time and cost requirements. This approach has generated binders that specifically recognize different, non-overlapping epitopes at their targets with high affinities.

12:10 pm Molar Mass, Size, Conjugation and Interactions: Light Scattering Tools for Biophysical Characterization
Sponsored by WYATT TECHNOLOGY
Dan Some, Ph.D., Principal Scientist, Wyatt Technology Corporation

Biophysical techniques based on static and dynamic light scattering address many of the key analytical challenges in biotherapeutic R&D, from early candidate selection through scale-up, formulation, characterization and comparability studies. This seminar will review light scattering technology and instrumentation, then present select examples illustrating how Wyatt's light scattering solutions facilitate rapid and effective development of biologics including mAbs, ADCs, PEGylated and other proteins.

12:40 Luncheon Presentation I Biomolecular Binding Kinetics Assays Using Different Label-Free Platforms: Discriminating Sense From Non-Sense
Sponsored by PALL Life Sciences and fortéBIO A Division of Pall Life Sciences
Vishal Kamat, Ph.D., Scientist, Biomolecular HTS Center, Therapeutic Proteins, Regeneron Pharmaceuticals

The study of protein-protein interaction has always been in the forefront of drug discovery. Different real-time label-free biosensors are currently available to study various aspects of protein binding. Kinetics profile of monoclonal antibodies binding to their target is one of the key factors that guide the selection of lead therapeutic antibodies. So, accurate measurement of antibody binding kinetics is important. Various factors that could influence binding kinetics measurements and optimization of these parameters for accurate kinetics and affinity characterization of monoclonal antibodies will be presented. Comparison of binding kinetics profile for monoclonal antibodies against multiple targets measured using Surface Plasmon Resonance (SPR) and Biolayer Interferometry (BLI) will be also be presented.

1:10 Luncheon Presentation II Surface Plasmon Resonance (SPR) & Differential Scanning Calorimetry (DSC) for Analysis of Critical Quality Attributes
Sponsored by GE Healthcare
Paul E. Belcher, Ph.D., Development Leader, GE Healthcare, Life Sciences

A range of analytical techniques are used to characterize and monitor CQAs in various stages of drug development and in comparability studies. Through case studies attendees will gain understanding of how SPR (Biacore™) and DSC (MicroCal™) can be used for analysis of binding activity and higher order structure. Case studies include characterization of IgG/Fc receptor interactions, active concentration measurements, and the use of specific epitope characterizing reagents for detection of changes in antibody higher order structure.

1:40 Session Break

MOLECULAR ASSESSMENT

2:00 Chairperson's Remarks
Jonas Schaefer, Ph.D., Head, High-Throughput Laboratory, Biochemistry, University of Zurich, Switzerland

2:05 "Hammerhug" Selection Strategy Incorporating Thermal Challenge, Functional and Biophysical Screening
William"Jonny" Finlay, Ph.D., Director, Pfizer, Ireland

We generated a tetravalent bispecific molecule targeting two inflammatory mediators for synergistic immune modulation. Phage-displayed 3B4 CDR-mutant libraries were used in an aggressive "hammer-hug" selection strategy that incorporated thermal challenge, functional, and biophysical screening. This approach identified leads with improved stability and > 18-fold, and 4,100-fold higher affinity for both human and cynomolgus CXCL13, respectively.

2:35 Developability Assessment through Molecular Modeling and Small-Scale High-Throughput Experiments
Naresh Chennamsetty, Ph.D., Research Investigator, Bristol-Myers Squibb

Early assessment of developability is beneficial in selecting an optimal protein candidate in discovery and in guiding formulation approaches. We discuss modeling and high throughput experimental tools to address the developability issues of aggregation and oxidation. Aggregation is assessed using Spatial-Aggregation-Propensity (SAP) model along with kosmotrope-based solubility assay. The oxidation of methionine residues is assessed using molecular simulation models based on solvent assessable area and 2-shell water coordination number.

3:05 Applications of Surface Plasmon Resonance for Studying Amyloidogenic Peptides/Proteins
Sponsored by BIO-RAD
Marco Gobbi, Head, Laboratory Pharmacodynamics & Pharmacokinetics, IRCCS, "Mario Negri" Institute for Pharmacological Research

A growing number of important human diseases are associated with the aggregation of amyloidogenic peptide/proteins. Surface Plasmon Resonance allows to obtain information hardly accessible with other approaches, regarding the binding events underlying assemblies growth, the recognition and

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Biophysical Analysis of Biotherapeutics

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

characterization of the toxic aggregates, and the screening and identification of potential inhibitors.

3:20 Sponsored Presentation *(Opportunity Available)*

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

4:20 Use of Developability Data to Help Drive Lead Selection of a Bispecific Therapeutic

Jennifer Nemeth, Ph.D., Program Leader, Biologics Research, Janssen R&D

Two lead bispecific antibodies were recently assessed using developability assays for differentiation and lead selection. Assays included analytical structural assessments, amino acid risk assessments, molecule interaction and concentratability assessments, and large-scale expression in proposed manufacturing cell lines. The resultant data package allowed for a clear decision on candidate selection and proposed back-up molecules. A lead was recommended for advancement into product development and is currently under review by the therapeutic area for declaration as a New Molecular Entity.

4:40 High-Throughput Heterogeneity Analysis of Antibodies and Antibody-Like Molecules

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

Multispecific antibodies and antibody-like molecules broaden the therapeutic application of IgGs, but they can be challenging to engineer and manufacture. To address this we first use a network biology approach to identify key design parameters followed by iterative rational engineering, rapid design cycles and high-throughput screening assays to reduce heterogeneity. Our approach selects for potential therapeutic candidates with robust pharmaceutical properties.

5:20 Networking Reception in the Exhibit Hall with Poster Viewing

6:30 End of Day

THURSDAY, MAY 8

7:45 am Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

CHALLENGES IN BIOPHYSICAL ANALYSIS

8:30 Chairperson's Remarks

Scott Klakamp, Ph.D., Principal Consultant, Biophysical Chemistry, SKD Consulting LLC

8:35 New Characterization and Computational Methods for Understanding Protein Aggregation

Ewa Marszal, Ph.D., Chemist, Hematology, Office of Blood Research and Review, Center for Biologics Evaluation and Research, FDA

This presentation will cover recent advancements in our understanding of the role of aggregation-prone regions in folding, structure stability, and protein function. Also, new methods for aggregates quantitation, characterization, and result-visualization tools will be discussed.

9:05 The Use of Mass Spectrometry to Probe the Domain Stability of IgG and DVD-Ig Biotherapeutics

Chris Chumsae, Senior Scientist, Protein Analytics, AbbVie Bioresearch Center

A technique has been developed which can measure the domain level stability of an IgG. Domain stability probing (DSP) exploits the sensitivity and selectivity of LC/MS peptide mapping. The technique uses partial denaturation and differential alkylation to monitor the inherent stability of individual domains. DSP is a powerful technique that can help evaluate the drug-like properties of recombinant monoclonal antibodies and DVD-Ig therapeutics.

9:35 Measuring Free Thiols of Bispecific Monoclonal Antibodies

Steven Orcutt, Research Scientist, Janssen

Confirmation of native structural integrity for therapeutic immunoglobulins can be achieved through accurate determination of unpaired cysteine residues. As several bispecific antibody platforms utilize hinge reduction and subsequent oxidation for heavy chain exchange, verification of disulfide pairing and measuring free thiols after re-oxidation is critical. Novel methods to characterize product candidates early in development are described.

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

11:05 Biacore Surface Matrix Effects on the Binding Kinetics and Affinity of an Antigen/Antibody Complex

Scott Klakamp, Ph.D., Principal Consultant, Biophysical Chemistry, SKD Consulting LLC

Unexpectedly, in the characterization of an antigen/mAb complex, the observed binding kinetics depended upon the sensor chip used, suggesting negatively charged carboxyl groups were adversely impacting the Biacore kinetic results. The results revealed that as the negative-charge on the biosensor surface decreased, the binding kinetics and KD approached more closely the binding parameters measured in solution.

11:35 Integrating Structural Bioinformatics and Protein Analysis to Identify and Characterize Novel Pathways in Cell Death and Viral Immunity

Frederic Pio, Ph.D., Associate Professor, Molecular Biology & Biochemistry, Simon Fraser University, Canada

A protein superfamily highly represented in the cell death machinery is called death domain. Structural bioinformatics, biochemical and reverse genetics can be integrated to identify and characterize new candidate proteins. The findings presented include discovery of the death domain subfamily Pyrin/DAPIN/PAAD and the biophysical and functional characterization of members of the HIN200 family that are novel components of viral innate immunity.

12:05 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

12:35 End of Conference

Recommended Thursday Dinner Short Courses*

Antibody-Drug Conjugate Therapeutics: Potential and Challenges

Protein Aggregation: Mechanism, Characterization and Immunogenic Consequences

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

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7th Annual | May 8-9

ANALYTICAL STREAM

Protein Aggregation and Stability in Biopharmaceuticals

Analytic, Formulation, Manufacturing and Regulatory Challenges

Recommended Pre-Conference Short Courses*

Translational Strategies for Development of Monoclonal Antibodies from Discovery to Clinic, Part 1: Focus on Early Discovery & Part 2: Focus on Nonclinical Development to Clinic

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

THURSDAY, MAY 8

AGGREGATION AND INTEGRATED DEVELOPABILITY ASSESSMENT

1:30 pm Chairperson's Opening Remarks

Elizabeth Topp, Ph.D., Dane O. Kildsig Chair and Head, Industrial and Physical Pharmacy, Purdue University

» 1:40 KEYNOTE PRESENTATION:
Protein Aggregation: Characterization to Support Clinical Development

Jamie Moore, Ph.D., Senior Scientist & Director, Early Stage Pharma Development, Genentech, Inc.

Aggregation of protein therapeutics can be defined as self-associating monomeric subunits. In order to understand the impact of aggregates on safety, efficacy and immunogenicity, the aggregates need to be characterized with regard to size, reversibility, conformation, covalent modifications and morphology. This presentation will review case studies evaluating aggregates and their potential impact on clinical development.

2:10 Strategy for Integrated Developability Assessment to Select Candidates for Clinical Development

Hubert Kettenberger, Ph.D., Principal Scientist, Roche Diagnostics GmbH

At the time of selection of a lead molecule (e.g. mAbs, bispecific mAbs, fusion proteins) from a series of lead candidates, it is desirable to assess their stability and physico-chemical properties in order to avoid liabilities during further development. A "developability assessment" results in a prediction of the anticipated development effort for a new lead molecule, using in-silico and small-scale in-vitro methods under short timelines.

2:40 Importance of Orthogonal Methods in the Analysis of Protein Aggregation: Case Studies

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

3:10 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Problem Solving Breakout Discussions

5:00 Close of Day

Recommended Tuesday Dinner Short Course*

Overcoming the Challenges of Immunogenicity Assessment

Recommended Thursday Dinner Short Course*

Protein Aggregation: Mechanism, Characterization and Immunogenic Consequences

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

FRIDAY, MAY 9

7:45 am Continental Breakfast in the Exhibit Hall with Poster Viewing

APPROACHES TO STABILITY PREDICTION: METHODS AND MECHANISMS

8:25 Chairperson's Remarks

Jamie Moore, Ph.D., Senior Scientist & Director, Early Stage Pharma Development, Genentech, Inc.

8:30 Methodologies to Assess Aggregation Propensities and Stability of Proteins in Biopharmaceutical Development

Malgorzata Tracka, MS, Scientist II, Formulation Sciences, MedImmune

Inapt biophysical features of macromolecules have potential to adversely impact drug product quality, activity, immunogenicity, and manufacturability. Emerging technologies that provide information about biophysical properties are in demand to guide drug development process. Here we will present case studies utilising various Light Scattering (LS) and fluorescence methodologies which have provided important data directing formulation development.

8:50 Mapping Aggregation Hotspots in mAbs with H/D Exchange Mass Spectrometry

David Weis, Ph.D., Assistant Professor, Chemistry, University of Kansas

Development of stable protein formulations remains challenging because of a lack of mechanistic understanding of excipients-protein interactions. We have used amide H/D exchange and mass spectrometry to identify excipient-induced changes in backbone flexibility in an IgG1 mAb. We found that an increase in flexibility in a short, hydrophobic segment of the C_H2 domain correlates with accelerated aggregation and loss of thermal stability.

9:15 An Accurate Analysis for the Determination of the Extent and Mechanism of Aggregation and the Stability of Proteins

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

We have developed a molecular biophysical approach using 2D IR correlation spectroscopy to determine the sequential order of events of the aggregation process during thermal perturbation. This method also allows for the determination of the relative stability of the protein and the extent of aggregation. Two case studies will be presented: The first involves IgG2a and the second are related calcium binding proteins.

9:40 Utilizing Biophysical Tools to Understand Protein Solution Behavior

Donna Luisi, Ph.D., Senior Principal Scientist, Biopharmaceutical R&D, Pfizer

There are many challenges faced in the development of a therapeutic protein. Development of high protein concentration formulations is one such challenge. High protein concentration can lead to a number of complications; one outcome of a high protein formulation can be viscosity behavior. This talk will focus on utilizing biophysical tools to predict and improve viscosity behavior for the proteins of interest.

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

MINIMIZING AGGREGATION: ENGINEERING STRATEGIES AND NOVEL FORMULATION METHODS

10:50 Improving Aggregation Resistance of Single-Domain Antibodies by Increasing Their Net Negative Charge

Kendrick Turner, Ph.D., Postdoctoral Fellow, Center for Bio/Molecular Science and Engineering, U.S. Naval Research Laboratory

Single-domain antibodies are highly soluble, however some possess isoelectric points near neutral pH, which limits their solubility in physiological buffers. We found that by introducing negatively charged amino acids on surface-exposed residues improved both resistance to aggregation as well as enhanced stability. In addition to aggregation resistance, antibodies were able to maintain their binding activity after heating.

11:20 Engineering Antibodies to Mitigate Aggregation/Self-Association

Chris Lloyd, Ph.D., Scientist, Antibody Discovery & Protein Engineering, MedImmune Ltd.

Undesirable physicochemical properties hinder development of therapeutic antibodies, due to issues during manufacturing, storage and *in vivo* administration. This talk highlights a an antibody displaying such characteristics and details how these problems were overcome using *in silico* structural modelling and antibody engineering, leading to an antibody that exhibited both the original functional attributes and improved biophysical properties.

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Protein Aggregation and Stability in Biopharmaceuticals

Analytic, Formulation, Manufacturing and Regulatory Challenges

11:50 Ultra-High Concentration Antibody Nanoparticle Dispersions are Reversible, Retain Bioactivity and Are Not More Immunogenic

Jennifer Maynard, Ph.D., Assistant Professor, Chemical Engineering, University of Texas, Austin

We have created nanometer-sized antibody clusters, in which proteins are "self-crowded" to favor the compact folded state. As shown with experiment and theory, the size of these equilibrium nanoclusters may be tuned reversibly by varying multiscale colloidal interactions with an extrinsic crowding agent and pH. Upon dilution, protein molecules released from the clusters are stable, as shown both *in vitro* and *in vivo* in mice.

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

12:50 Session Break

AGGREGATION OF BIOPHARMACEUTICALS *IN VIVO*: A NEW RESEARCH AND DEVELOPMENT FIELD

1:35 Chairperson's Remarks

Maria Barbosa, Ph.D., CA Consultants; former Senior Principal Scientist, Bioanalytical Sciences, Bristol-Myers Squibb

1:40 FEATURED PRESENTATION: Screening Methods to Study Aggregation of New Monoclonal Antibody Candidates in Human Plasma and Human Serum

Chakravarthy Narasimhan, Ph.D., Senior Principal Scientist, Bioprocess Development, Merck & Co.

Analytical methods based on light microscopy, 90° light-scattering and SPR allowed the characterization of aggregation that occur when antibodies are mixed with plasma and serum. The binding of sera components to new and marketed mAbs was measured and correlated with known serum binding properties of the antibodies. The analytical techniques used proved to be valuable as a screening tool to study the intrinsic and buffer-dependent aggregation.

2:10 FEATURED PRESENTATION: Studies of the Aggregates Formed when Therapeutic Protein Solutions are Mixed with Human Plasma and Whole Blood: A New Research and Development Field

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

After injection of a clear protein solution, aggregation can form at the injection site in tissue or in the blood stream. The talk will present new data on the characterisation of the aggregates formed *in vitro* when different formulations of therapeutic proteins are mixed with human plasma and blood. A model for the aggregation will be presented and some clinical implications of the aggregation induced by biopharmaceuticals will be discussed.

PHYSIOLOGICAL EFFECTS OF PROTEIN AGGREGATION:

Special Shared Session with *Immunogenicity Prediction and Mitigation*

2:40 Are Aggregates Really Immunogenic? Relevance of Current *in vitro* and *in vivo* Test Systems in Understanding Physiological Immune Response to Aggregated Particles

Narendra Chirmule, Ph.D., Executive Director, Clinical Immunology, Amgen, Inc.

Protein aggregates resulting from self association may potentially activate the early phase of the immune system. This talk evaluates the threshold of immune response to the number and size of particles and the relevance of the readout in such assays to the performance of a real time formulation. The impact of immune modulation due to diseased state and concomitant medications on the *in vitro* assay readout is also evaluated.

3:10 Aggregation of Human Recombinant Monoclonal Antibodies Enhances Their Presentation by Dendritic Cells *in vitro*

Andrea Kiessling, Ph.D., Head, Biologics Immunosafety, Pre-Clinical Safety (PCS), NIBR Novartis Pharma AG

Subvisibleproteinaceous particles are present in all therapeutic protein formulations and their impact on immunogenicity is the focus of intense discussions. In order to interrogate the early dendritic cell-driven events that initiate CD4 T cell dependent humoral adaptive immune responses, aggregated monoclonal antibodies were tested in dendritic cell cultures. In this talk I will elute on the specific changes we observed in peptide presentation.

3:40 Biological Impact of Aggregates: Immunogenicity, Biodistribution, *in vivo* Response

Vasco Filipe, Ph.D., Research Scientist, ADOCIA

The correlation between aggregates and immunogenicity has been known for several decades, but the most immunogenic type of aggregates and mechanisms behind aggregate-related immunogenicity are not yet known. Two different studies will be presented: (i) the biodistribution of IgG1 monomers vs aggregates upon subcutaneous (SC) and intravenous (IV) administration in mice was monitored and their propensity to stimulate an early immune response was measured; (ii) the immunogenicity of different type of IgG1 aggregates was tested in immune tolerant transgenic mice.

4:10 End of Conference

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2nd Annual | May 5-6

PK/PD of Multi-Domain Proteins

Bench to Bedside Translation of Bispecifics, ADCs, and Antibody Fragments

Recommended Pre-Conference Short Courses*

Translational Strategies for Development of Monoclonal Antibodies from Discovery to Clinic, Part 1: Focus on Early Discovery & Part 2: Focus on Nonclinical Development to Clinic

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

MONDAY, MAY 5

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks
Kristi Sarno, Chair, Greater Boston Chapter, Women in Bio; Director, Business Development, Pfenex, Inc.

8:40 Harnessing the Patient's Immune System to Combat Cancer
Peter CR Emtage, Ph.D., Vice President, Immune Mediated Therapies, MedImmune

With recent FDA approvals, modulation of the immune system is now a clinically validated approach in the treatment of some cancers. At MedImmune, the Oncology Department is developing assets and expertise in Immune Mediated Therapy of Cancer (IMT-C). The challenges from a drug development perspective are multi-fold. The talk will focus on the relevance of preclinical models and translational science to address key issues, including dose selection and rationale combinations.

9:25 Building Regeneron's Pipeline: From Trap Technology to the *VelocImmune* Platform to *Veloci-Next*
George D. Yancopoulos, M.D., Ph.D., President, Regeneron Laboratories; CSO, Regeneron Pharmaceuticals, Inc.

George D. Yancopoulos, M.D., Ph.D., who is the Founding Scientist, President, Research Laboratories and Chief Scientific Officer of Regeneron Pharmaceuticals, one of

the world's top biotechnology companies, will discuss how he and his colleagues exploited a commitment to science and technology to start the company, withstand years of challenges and failures, and emerge with a pipeline of promising technologies and novel/biologics that are beginning to bring hope to countless patients and their families.

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

PK/PD, ADME AND MOLECULAR CONSTRUCT DESIGN

11:05 Chairperson's Remarks

» 11:10 OPENING KEYNOTE PRESENTATION: Application of PK/PD in Modality Design
Mohammad Tabrizi, Ph.D., Head & Senior Fellow, PK/PD, Merck

With scientific advances, it is now possible to rapidly and effectively generate highly tailored and specific antibody-based therapeutics that interact with a diverse array of soluble or cell-associated target antigens. Additionally, engineering advances have made it possible to generate modalities that bind two or more unique targets within a single molecular entity or deliver potent payloads to specific targets. In this presentation, application of PK/PD for the design of novel and specific modalities will be discussed.

11:40 Which Parameters Do I Need to Optimize for Design of a Successful Antibody-Drug Conjugate: A Modeling and Simulation Approach to Understand PK and PD Drivers of ADC Disposition and Response
Alison Betts, Modeling and Simulation Leader, Associate Research Fellow, Translational Research Group, Pharmacokinetics, Dynamics & Metabolism, Pfizer Global R&D

This presentation will include a review of the processes involved in cellular and whole body disposition of ADCs, along with novel experimental approaches to measure these processes. It will also show a proposed mechanistic model for predicting tumor payload concentrations of ADCs, and linkage to tumor regression data using a pharmacodynamic model of tumor growth and cell kill.

12:10 pm Sponsored Presentation
Speaker to be Announced

Sponsored by GYROS

12:40 Luncheon Presentation I *(Sponsorship Opportunity Available)*

1:10 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:40 Session Break

NEW STRATEGIES FOR BISPECIFICS AND ADCs

2:00 Chairperson's Remarks

2:05 Limits of Tumor Targeting in Immunotherapy: Theory & Experiment
K. Dane Wittrup, Ph.D., J.R. Mares Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

Targeted agents such as immunocytokines are often developed with the intention of achieving improved therapeutic index via a compartment-specific targeting moiety. Simple PK/PD theoretical analyses of intravenously administered agents suggests that strong limits exist for this approach, and we have experimentally validated key predictions of this analysis.

2:35 Considerations for Design of Bispecific Modalities
Isabel Figueroa, Associate Principal Scientist, PK/PD, Merck

Bi-specific antibodies (BsAb) are based on the concept that the blockage or neutralization of two targets will result on superior drug performance when compared to monoclonal antibody therapy. However, their observed therapeutic effect will depend on the kind and extent of pharmacological interaction between the neutralization or binding of both targets. In this talk, we discuss how the BsAb properties theoretically impact their expected therapeutic performance.

3:05 PK Optimization and Preclinical PK of Novel Bispecific Antibody against FIXa and X for the Treatment of Hemophilia A
Kenta Haraya, Researcher, Chugai Pharmaceutical Co., Ltd.

A novel bispecific antibody against FIXa and X was generated for the treatment of hemophilia A. Clinical candidate, ACE910, was generated by improving the pharmacokinetics through minimizing non-specific binding and reducing isoelectric point. Preclinical study of ACE910 demonstrated long half-life and high subcutaneous bioavailability in cynomolgus monkey. Details of the preclinical pharmacokinetic analysis of this bispecific antibody will be discussed.

3:35 Applying PK/PD Principles to Optimize Development of Antibody Maytansinoid Conjugates
Joe Ponte, Ph.D., Senior Scientist, Immunogen, Inc.

This talk will address current challenges in optimizing and developing ADCs and the role PK/PD can play in addressing some of the concerns.

4:05 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem Solving Breakout Discussions

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

6:45 End of Day

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2nd Annual | May 5-6

PK/PD of Multi-Domain Proteins

Bench to Bedside Translation of Bispecifics, ADCs, and Antibody Fragments

TUESDAY, MAY 6

7:45 am Morning Coffee

PK/PD CONSIDERATIONS FOR ADCs

8:25 Chairperson's Remarks

8:30 Understanding the Insights into the ADME of Antibody-Drug Conjugate (ADC) Impacts ADC Development

Ben-Quan Shen, M.D., Senior Scientist, PKPD, Genentech, Inc.

Understanding the ADME of ADC plays an important role in ADC development, given the complexity of ADC molecules. In this talk, a variety of bioanalytical approaches, incorporating strategies for large molecules and small molecules, will be discussed. In addition, case studies on the ADME of a few leading ADCs and their impacts will be presented.

9:00 Utilizing PK/PD Modeling and Simulation to Guide the Discovery and Development of ADCs

Dhaval K. Shah, Ph.D., Assistant Professor, Pharmaceutical Sciences, School of Pharmacy and Pharmaceutical Sciences, University at Buffalo

The talk will introduce a diverse set of mathematical PK/PD/TD models available to support ADC programs at different drug development stages. It will also demonstrate the use of mathematical models to understand ADC disposition, to guide the discovery of ADCs, and to aid a precision medicine approach.

9:30 Presentation to be Announced

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

NOVEL MODELING TECHNIQUES FOR *IN VIVO* PK

10:45 Predicting the Distribution of Biologics Across Multiple Length Scales – From Subcellular to Whole Body PK

Greg Thurber, Ph.D., Assistant Professor, Chemical Engineering & Biomedical Engineering, University of Michigan

Biologics form complex interactions throughout multiple tissues in the body that must be understood to more efficiently develop these agents. The impact of these interactions can affect the cellular, tissue, and organ distribution. By incorporating these molecular events with multiscale mechanistic models and iteratively carrying out computer simulations alongside *in vivo* experiments, we will be able to efficiently design agents and actively scale them to the clinic.

11:15 Integration of QSPR and Mechanistic PD Models to Predict *in vivo* PK/PD Profiles of Chemically Related Compounds

Donald E. Mager, Ph.D., Associate Professor, Pharmaceutical Sciences, University at Buffalo

11:45 Mechanism-Based PK/PD Modeling of Antibody-Drug Conjugate Disposition and Action

Siddharth Sukumaran, Ph.D., Associate Scientist, Pharmacokinetics and Pharmacodynamics, Genentech, Inc.

ADCs are often produced and administered as a heterogeneous mixture of antibodies with different drug to antibody ratio (DAR). In addition to affecting drug efficacy and toxicity, DAR impacts drug deconjugation and proteolytic clearance of antibody. Integrated PK/PD models were developed by incorporating known mechanisms of ADC and TDC disposition and action to describe and predict complex PK and efficacy profiles. These models can be used to guide further optimization and development.

12:15 pm Luncheon Presentation I *(Sponsorship Opportunity Available)*

12:45 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:15-1:45 Ice Cream Break in the Exhibit Hall

PK/PD AND COMBINATION THERAPIES

2:00 Chairperson's Remarks

2:05 PK/PD Considerations for Design of Combination Therapies

Ayse Meric Ovacik, Senior Scientist, Biologics DMPK & Disposition, Merck

PK/PD considerations for designs of combination therapies include adequate drug-drug interaction evaluation. It is particularly important to assess outcome of combination therapy in terms of synergy and/or additivity and to inform combination therapy design with quantitative approaches. In this talk, we will summarize critical considerations of a combination therapy design with a PK/PD aspect.

2:35 Bispecific Antibodies: Key Mechanistic PK/KD Considerations Using Case Study Examples

Pratap Singh, Ph.D., Senior Principal Scientist, Pfizer, Inc.

Bispecific antibodies offer a promising approach to hit two targets simultaneously using a single biological entity but several challenges exist towards their successful development. In this presentation, few case study examples will be provided to illustrate utility of mechanistic modeling in guiding affinity optimization, PK/PD/Tox study design and human dose projections of bispecific antibodies.

3:05 Sponsored Presentation *(Opportunity Available)*

3:20 Sponsored Presentation *(Opportunity Available)*

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

LINKING PK/PD AND IMMUNOGENICITY

4:15 An Integrated Analytical Strategy for Biologics

Peter Lloyd, Head, PK/PD, Biologics, Novartis

PK, PD and potential immunogenicity (IG) of therapeutic proteins cannot be investigated in isolation. An integrated approach is needed which takes into account the interdependency of PK/PD/IG assays. This presentation will focus on the use of an integrated bioanalytical strategy to effectively interpret the behaviour of protein therapeutics.

» 4:45 CLOSING KEYNOTE PRESENTATION:
Impact of Immunogenicity on PK Profiles of Novel Large Molecule Constructs

Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen

An assessment of immunogenicity in single dose and multiple dose studies on clearance of novel drug constructs will be discussed and compared to fully human monoclonal antibodies.

5:15 End of Conference

Recommended Tuesday Dinner Short Course*

Overcoming the Challenges of Immunogenicity Assessment

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

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SAFETY STREAM

6th Annual | May 7-8

Immunogenicity for Regulatory Success

Non-Clinical, Preclinical and Clinical Strategies for Risk Assessment and Smooth Interaction with the Regulatory Authorities

Recommended Pre-Conference Short Course*

Overcoming the Challenges of Immunogenicity Assessment

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

WEDNESDAY, MAY 7

7:00 am Registration and Morning Coffee

ASSAYS, INTERPRETATION AND STANDARDS

8:00 Chairperson's Opening Remarks

Meena Subramanyam, Ph.D., Vice President, Translational Medicine, Biogen Idec, Inc.

8:10 Latest Trends in Neutralizing Antibody Detection and the Clinical Relevance of Immunogenicity Assessment

Shalini Gupta, Ph.D., Director, Clinical Immunology, Amgen, Inc.

This talk will provide a summary of an AAPS white paper currently being compiled that focuses on NAb assay strategy selection for biologicals with varied mechanisms of action. In addition, the clinical relevance of immunogenicity assessment will be presented via case studies.

8:40 International Bioassay Standardization for the Quantification of Neutralizing Antibodies

Michael G. Tovey, Ph.D., INSERM Director, Research, Laboratory of Biotechnology and Applied Pharmacology, ENS-Cachan

Validated standardized assays are key to obtaining reliable data and regulatory approval, in particular for cell-based assays recommend by regulatory authorities for the detection of neutralizing anti-drug antibodies. The EMA initiative to establish a common assay and the E.U. initiative ABIRISK to develop common validated cell-based assays for the quantification of immunogenicity will be presented.

9:10 Fc Fc Interactions in Bridging Immunogenicity Assays for IgG4 Monoclonal Antibody Therapeutics

Michael Partridge, Ph.D., Staff Scientist, Bioanalytical Sciences, Regeneron Pharmaceuticals, Inc.

Human IgG4 antibodies are known to interact with other IgG4s via their Fc. In bridging immunogenicity assays, IgG4 Fc-Fc contacts generate increasing signal over time for the negative control, reducing assay sensitivity and complicating confirmation cut point determination. Increasing background signal over time is especially problematic for automated analysis, as reagents are prepared in advance and used over several hours during a run. This presentation will discuss these interactions and the impact they have on immunogenicity assays for IgG4 drugs.

9:40 Evaluation of Immunogenicity for Enzyme Replacement Biotherapeutics

Yongchang Qiu, Ph.D., Group Director and Head, Bioanalytical and Biomarker Development, Shire, Inc.

Replacement enzymes are a special class of protein therapeutics that often need to be taken up by the target cells for efficacy. In addition, they have endogenous counterparts and are highly glycosylated. Several marketed enzyme replacement therapies serve as treatment for critically ill patients, many of whom are children. This talk will outline the unique challenges in the assessment of immunogenicity of replacement enzymes including cross-reactive immunologic materials (CRIM) testing.

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

IMMUNE COMPLEXES AND HYPERSENSITIVITY

11:10 Case Study on Identification and Potential Impact of Immune Complexes

Binodh Desilva, Ph.D., Executive Director, Bioanalytical Sciences & Biologics, Bristol-Myers Squibb

This presentation will describe immune complexes that have been observed regarding their frequency and where they form, and attempt to provide an explanation for their occurrence. It will discuss methodologies for identifying and characterizing them, their relationship with tox results and their long term impact with complement deposition in the issues.

11:40 Assessment of Biotherapeutic Drug Allergenicity

Robert G. Hamilton, Ph.D., D.ABMLI, F.AAAAI, Professor of Medicine and Pathology, Johns Hopkins University School of Medicine

This lecture will overview the basic pathophysiology at the basis of the immediate type hypersensitivity response and methods for assessing the presence and relative level of drug specific IgE antibody. Recent consensus guidelines will be overviewed that suggest an approach for validation of the IgE antibody assay in the absence of a positive drug-specific human IgE antibody serum.

12:10 pm 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 and difficult issues to address in drug design and development. I will provide an overview of the best tools for immunogenicity risk management, 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.

12:40 Luncheon Presentation I *(Sponsorship Opportunity Available)*

1:10 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:40 Session Break

INTERESTING CASE STUDIES

2:00 Chairperson's Remarks

2:05 The Evaluation of Immunogenicity in Remsima Clinical Studies: From Development to Global Regulatory Approval

Alex Kudrin, M.D., MBA, MRCP, MFPM, Vice President & Head,Global Development, Celltrion, Inc.

The presentation will cover the data generated to support recent EU approval of the biosimilar infliximab and challenges that needed to be addressed throughout the development of the product. In addition, some switch-related immunogenicity and safety data will be presented.

2:35 Pre-Existing Antibodies

Mary Birchler, Investigator, Clinical Immunology, GlaxoSmithKline, Inc.

Pre-existing antibodies in treatment-naïve subjects have been often detected during clinical ADA assessments. However, limited information on prevalence, physiological effect, and impact on post treatment ADA induction is available. This talk will address pre-existing antibody characterization and implications for immunogenicity management and strategies during clinical studies.

3:05 Case Study on Pre-Existing Reactivity and Risk Mitigation

Jim McNally, Ph.D., Senior Principal Scientist, Biotherapeutics research, Pfizer, Inc.

Pre-existing reactivity to biotherapeutics can result in extensive bioanalytical investigations and delays for clinical sample testing. An increase in the frequency of observations of pre-existing reactivity led us to implement a plan to identify this reactivity as early as possible in the drug development process. Our goal is tomitigate risk indrug candidate selection and to inform the development of clinical bioanalytical assays for a proactive testing strategy.

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

4:20 Problem Solving Breakout Discussions

5:20 Networking Reception in the Exhibit Hall with Poster Viewing

6:30 End of Day

THURSDAY, MAY 8

7:45 am Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

IMMUNOGENICITY RISK ASSESSMENT

8:30 Chairperson's Remarks

Binodh Desilva, Ph.D., Executive Director, Bioanalytical Sciences & Biologics, Bristol Myers Squibb

8:35 Strategy for Immunogenicity Risk Assessment

Meena Subramanyam, Ph.D., Vice President, Translational Medicine, Biogen Idec, Inc.

The risk of clinical consequences of immunogenicity can be effectively mitigated with a comprehensive evaluation of therapeutic-specific and patient-population specific risk factors. This talk will focus on investigating the potential risk factors, characterizing their effects on immunogenicity in non-clinical and clinical studies, understanding the nature of concerns and potential data requirements, and development of a risk management plan.

9:05 Case Study on Re-Assessment of Immunogenicity Risk Based on Clinical Data

Eric Wakshull, Ph.D., Senior Scientist and Group Leader, Bioanalytical Sciences, Genentech, Inc.

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6th Annual | May 7-8

Immunogenicity for Regulatory Success

Non-Clinical, Preclinical and Clinical Strategies for Risk Assessment and Smooth Interaction with the Regulatory Authorities

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 any clinical experience. Clinical data can and should modify this assessment. This talk will present a case study of a structurally novel biotherapeutic whose risk-based assessment was changed following analysis of immunogenicity data derived from early clinical trials.

9:35 Impact of Immunogenicity on Clinical Endpoints

Kyra J. Cowan, Ph.D., Scientist, BioAnalytical Sciences, Genentech, Inc.

The value of immunogenicity data lies in the integration of that data with safety, pharmacokinetics, and efficacy endpoints. A clinical trial was designed and executed to evaluate the safety and efficacy of different dose levels and dosing regimens of a biotherapeutic for age-related macular degeneration. This talk will describe the approaches taken for the analysis of anti-therapeutic antibodies (ATAs) in patient sera for this study, and how the results informed the interpretation of ATA impact on clinical endpoints.

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

COMBINATION THERAPY AND COMPLEX MIXTURES OF DRUGS

11:05 Combination Biologic Therapy Development: Impact on Immunogenicity Evaluation

Lakshmi Amaravadi, Ph.D., Senior Director, Translational Medicine, Biogen Idec, Inc.

Assessment of potential interferences of one biologic on the other need to be evaluated in the analytical assays to ensure appropriate interpretation of the data and outcomes in preclinical and clinical studies. In this presentation, one such example of a combination biologic evaluation in a preclinical setting with assay evaluations and impact on immunogenicity as a monotherapy vs. combination therapy will be discussed.

11:35 Non-Biologic Complex Drugs and Immunogenicity: Copaxone and Regulatory Considerations for Complex Drugs

J. Michael Nicholas, Ph.D., Vice President, Specialty Life Cycle Initiatives, Teva Pharmaceuticals

Nonbiologic Complex Drugs (NBCD) comprise a complex heterogenous mixture of closely related, macromolecular components that cannot be isolated, quantified, and/or fully characterized. COPAXONE®, a NBCD, is a highly complex heterogeneous mixture of synthetic proteins /polypeptides with immunomodulatory activity. This case study will examine immunogenicity profiles of NBCDs and implications for the regulatory science of complex drugs.

12:05 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

12:35 End of Conference

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6th Annual | May 8-9

SAFETY STREAM

Immunogenicity Prediction and Mitigation

Risk Factors, Predictive Tools and Immune Tolerance Approaches

THURSDAY, MAY 8

» KEYNOTE SESSION: IMMUNOGENICITY REDUCTION AND CONTROL

1:30 pm Chairperson's Opening Remarks

Bonnie Rup, Ph.D., Research Fellow, Immunogenicity Sciences Lead, Pfizer, Inc.

1:40 Measures to Control Immunogenicity to Interferon Beta

Florian Deisenhammer, Ph.D., Clinical Department of Neurology, Innsbruck Medical University

We have learned a few lessons as to which factors contribute to immunogenicity of different recombinant preparations of Interferon beta (IFNb), such as route and frequency of administration, drug formulation including pegylation, aggregation, affinity of antibody binding and binding site. Also, patients' characteristics influence immunogenicity outcomes. How these factors contribute to controlling immunogenicity will be discussed.

2:10 New Approach to B and T Epitope Removal from Immunotoxins with Retention of High Cytotoxic Activity

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

Recombinant Immunotoxins are hybrid proteins that kill cancer cells. RITs have produced complete remissions in over 50% of patients with drug resistant Hairy Cell Leukemia with impaired immune systems, but are less active in patients with normal immunity. I will describe new highly active immunotoxins predicted to have low immunogenicity in humans as a result of experimental approaches for the identification and removal of B and T cell epitopes.

2:40 Immunogenicity Risk Assessment Using Human *in silico* and *in vitro* Tools

Sponsored by Lonza

Noel Smith, Ph.D., Senior Group Leader, Lonza Biologics

Incorporating immunogenicity 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 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.

3:10 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Problem Solving Breakout Discussions

5:00 Close of Day

Recommended Thursday Dinner Short Course*

Protein Aggregation: Mechanism, Characterization and Immunogenic Consequences

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

FRIDAY, MAY 9

7:45 am Continental Breakfast in the Exhibit Hall with Poster Viewing

PREDICTION OF IMMUNOGENICITY

8:30 Chairperson's Remarks

Steven J. Swanson, Ph.D., Executive Director, Medical Sciences (Clinical Immunology), Amgen, Inc.

8:35 Mathematical Modeling of Immunogenicity for Candidate Selection and Prediction of Effect on Clinical Efficacy

Tim Hickling, Ph.D., Associate Research Fellow, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

Early prediction of the incidence of ADAs to therapeutic proteins will facilitate candidate selection and clinical trial design. This model integrates key parameters for such predictions: ADA incidence and magnitude, and the impact of ADAs on PKPD. Initial attempts at model validation with clinical data will be described as well as application of this approach to selecting clinical drug candidates and predicting immunogenicity.

9:05 Immunogenicity Prediction Studies with a Recently Terminated Factor VII Analogue Project

Kasper Lamberth, Ph.D., Head, Immunogenicity Prediction & Tolerance, Novo Nordisk A/S

The development of an rFVIIa analogue (Vatreptacog alfa) was recently discontinued due to the development of ADAs in a phase 3 trial. This analogue has three mutations compared to endogenous rFVIIa. We applied different immunogenicity prediction tools, *in silico* algorithms and different formats of *ex vivo* T cell assays to identify an immunogenicity prediction platform capable of distinguishing between the analogue and the endogenous molecule.

9:35 Integrated Application of a Risk Assessment Toolkit for Investigation of an Immunogenic Monoclonal Antibody Therapeutic

Bonnie Rup, Ph.D., Research Fellow, Immunogenicity Sciences Lead, Pfizer, Inc.

This presentation reviews nonclinical and clinical findings, addresses assessment of potential underlying causes; application of ADA characterization; *in silico*, and *in vitro* dendritic and T cell cellular assays; and how the observations fit in with potential increased immunogenicity risk associated with some biotherapeutic targets. This study demonstrates growing benefits to developing a predictive and investigative tool kit.

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

IMMUNOGENICITY REDUCTION AND TOLERANCE INDUCTION

10:50 Recent Advances with Immune Tolerance Induction for Enzyme Replacement Therapy

Sue Richards, Ph.D., Global Deputy and Head, Clinical Laboratory Sciences, DSAR, SANOFI/Genzyme

As we gain more experience, the effect of antibodies becomes more evident. With inborn errors of metabolism, patients receiving replacement therapy can be at higher risk for developing antibodies, some associated with clinical consequences. Strategies have been investigated to mitigate unwanted immune responses to provide improved therapeutic benefit. Recent advances and case studies using immune tolerance induction for ERT will be discussed.

11:20 Immune Tolerance Induction in Hemophilia A Mice Treated with Factor VIII Fc Fusion Protein

Sriram Krishnamoorthy, Ph.D., Scientist, Preclinical and Clinical Development (Hemophilia), Biogen Idec, Inc.

Many hemophilia A patients treated with therapeutic factor VIII (FVIII) produce Nabs to the product, thus rendering this therapy ineffective. Methods to identify immunodominant epitopes in FVIII and the generation of T cell clones against FVIII have helped modulate this undesirable response. Novel approaches to induce tolerance using IgG fusion proteins and specific T regulatory cells will be discussed.

11:50 Reverse Vaccination via S.C. Route to Mitigate Immunogenicity

Sathy Balu-Iyer, Ph.D., Associate Professor, Pharmaceutical Sciences, SUNY-University at Buffalo

This presentation will explain the principle of reverse vaccination via the sc route to mitigate immunogenicity of therapeutic proteins. It will outline the primate studies and the disease models investigated and describe the types of aggregate identified, providing evidence for small aggregates acting as adjuvants.

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

12:50 Session Break

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6th Annual | May 8-9

SAFETY STREAM

Immunogenicity Prediction and Mitigation

Risk Factors, Predictive Tools and Immune Tolerance Approaches

RISK FACTORS FOR IMMUNOGENICITY

1:35 Chairperson's Remarks

Sue Richards, Ph.D., Global Deputy and Head, Clinical Laboratory Sciences, DSAR, SANOFI/Genzyme

1:40 Understanding the Immune Response against Erythropoiesis Stimulating Agents that Can Lead to Pure Red Cell Aplasia

Steven J. Swanson, Ph.D., Executive Director, Medical Sciences (Clinical Immunology), Amgen, Inc.

Anti-erythropoietin antibodies associated with cases of antibody-mediated PRCA have different characteristics than those observed in subjects that do not have PRCA. PRCA-associated antibodies tend to be of the IgG4 subclasss, have a higher circulating level, bind to the protein region of erythropoietin, and are more likely to have neutralizing capability. This underscores the value of developing and validating clinically relevant assays.

2:10 Designing and Engineering a Protein Therapeutic for Topical Treatment of Ocular Surface Inflammatory Disorders to Have Low Immunogenic Potential

Joseph Kovalchin, Ph.D., Associate Director, Pharmacology, Eleven Biotherapeutics, Inc.

A novel protein therapeutic was designed and engineered for topical treatment of ocular surface inflammatory disorders, with low immunogenic potential. This entailed computer algorithms to suggest amino acid sequences with low HLA binding potential. These were correct as shown by *in vitro* T cell assays. Animal studies suggested that topical administration results in lower immune response to the drug, probably due to low systemic exposure.

PHYSIOLOGICAL EFFECTS OF PROTEIN AGGREGATION:

Special Shared Session with *Protein Aggregation and Stability*

2:40 Are Aggregates Really Immunogenic? Relevance of Current *in vitro* and *in vivo* Test Systems in Understanding Physiological Immune Response to Aggregated Particles

Narendra Chirmule, Ph.D., Executive Director, Clinical Immunology, Amgen, Inc.

Protein aggregates resulting from self association may potentially activate the early phase of the immune system. This talk evaluates the threshold of immune response to the number and size of particles and the relevance of the readout in such assays to the performance of a real time formulation. The impact of immune modulation due to diseased state and concomitant medications on the *in vitro* assay readout is also evaluated.

3:10 Aggregation of Human Recombinant Monoclonal Antibodies Enhances Their Presentation by Dendritic Cells *in vivo*

Andrea Kiessling, Ph.D., Head, Biologics Immunosafety, Pre-Clinical Safety (PCS), NIBR Novartis Pharma AG

Subvisibleproteinaceous particles are present in all therapeutic protein formulations and their impact on immunogenicity is the focus of intense discussions. In order to interrogate the early dendritic cell-driven events that initiate CD4 T cell dependent humoral adaptive immune responses, aggregated monoclonal antibodies were tested in dendritic cell cultures. In this talk I will elute on the specific changes we observed in peptide presentation.

3:40 Biological Impact of Aggregates: Immunogenicity, Biodistribution, *in vivo* Response

Vasco Filipe, Ph.D., Research Scientist, ADOCIA

The correlation between aggregates and immunogenicity has been known for several decades, but the most immunogenic type of aggregates and mechanisms behind aggregate-related immunogenicity are not yet known. Two different studies will be presented: (i) the biodistribution of IgG1 monomers vs aggregates upon subcutaneous (SC) and intravenous (IV) administration in mice was monitored and their propensity to stimulate an early immune response was measured; (ii) the immunogenicity of different type of IgG1 aggregates was tested in immune tolerant transgenic mice.

4:10 End of Conference

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BIOPROCESS STREAM

Scaling Up & Down Strategies for Protein Production

Ensuring Efficiency & Quality

MONDAY, MAY 5

7:00 am Registration and Morning Coffee

» PLENARY KEYNOTE SESSION

8:30 Chairperson's Opening Plenary Remarks
Kristi Sarno, Chair, Greater Boston Chapter, Women in Bio; Director, Business Development, Pfenex, Inc.

8:40 Harnessing the Patient's Immune System to Combat Cancer
Peter CR Emtage, Ph.D., Vice President, Immune Mediated Therapies, MedImmune

With recent FDA approvals, modulation of the immune system is now a clinically validated approach in the treatment of some cancers. At MedImmune, the Oncology Department is developing assets and expertise in Immune Mediated Therapy of Cancer (IMT-C). The challenges from a drug development perspective are multi-fold. The talk will focus on the relevance of preclinical models and translational science to address key issues, including dose selection and rationale combinations.

9:25 Building Regeneron's Pipeline: From Trap Technology to the *VelocImmune* Platform to *Veloci-Next*
George D. Yancopoulos, M.D., Ph.D., President, Regeneron Laboratories; CSO, Regeneron Pharmaceuticals, Inc.

George D. Yancopoulos, M.D., Ph.D., who is the Founding Scientist, President, Research Laboratories and Chief Scientific Officer of Regeneron Pharmaceuticals, one of the world's top biotechnology companies, will discuss how he and his colleagues exploited a commitment to science and technology to start the company, withstand years of challenges and failures, and emerge with a pipeline of promising technologies and novel/biologics that are beginning to bring hope to countless patients and their families.

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

PROCESS DEVELOPMENT

11:05 Chairperson's Remarks
Stefan Schmidt, Ph.D., Vice President, DSP, Rentschler Biotechnology

» 11:10 OPENING KEYNOTE PRESENTATION:

Bioprocess Scale-Up Strategies for Rapid Process Development – A QbD Perspective
Kumar Dhanasekharan, Ph.D., Director, Process Development, Cook Pharmica LLC

The talk will discuss the different scale-up approaches for both upstream and downstream development such as high-throughput approaches, platform based methods and traditional approaches to optimize a particular output or set of outputs, such as productivity/yield while maintaining product quality. Scale-dependent and scale-independent parameter considerations and selection will also be discussed. Case study examples will be used to illustrate key points.

11:40 CHO Small-Scale Model Development and Scale-Up Strategies for Glycoprotein Production
Siguang Sui, Ph.D., Development Scientist I, Upstream Development, Alexion Pharmaceuticals, Inc.

When a cell culture process was scaled from 2L to a 200L bioreactor, significantly lower productivity was observed at the larger scale. With CFD modeling, engineering approaches were implemented to develop and characterize the small-scale model to meet the requirement for both productivity and product quality attributes including purity, sialylation, and glycosylation. Strategies for scaling-up this process at 10,000L scale are proposed.

12:10 pm Sponsored Presentation *(Opportunity Available)*

12:25 Protein Aggregate and Contaminant Removal by Mixed Mode Chromatography

Sponsored by PALL Life Sciences / forteBIO A Division of Pall Life Sciences

Yamuna Dasarathy, Ph.D., Director, Marketing, Pall Life Sciences

Aggregation has been found to be a cause of immunogenicity and it reduces productivity of a process by impacting purity, recovery and yield. Additionally, host cell proteins that are inherent to all production processes can reduce efficacy. Some biopharmaceuticals show a penchant for aggregating in solution and once formed they must be removed during process development resulting in maximum degree of purity. Mixed mode chromatography can be used to remove aggregates and other trace contaminants including host cell proteins and we will present a case study to elucidate how mixed mode chromatography can be used in high throughput process development mode in designing a robust purification process.

12:40 Luncheon Presentation I *(Sponsorship Opportunity Available)*

1:10 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:40 Session Break

SCALING UP & DOWN STRATEGIES

2:00 Chairperson's Remarks

2:05 Case Studies for Utilization of Conventional and CFD Approaches for Successful Scale-Up and Scale-Down of Bioreactor Processes for Monoclonal Antibodies
Michelle LaFond, Director, Bioreactor Scale-Up and Development, Regeneron Pharmaceuticals

More recently, use of both conventional and computational fluid dynamic approaches to develop scale-down, pilot-scale models of production bioreactors have resulted in improved process understanding and more successful transfer for late stage processes. The new scale-down models are more predictive of manufacturing and are used to map out impact of scale-up parameters to process performance. Case studies of both approaches will be discussed.

2:35 A Universal Manufacturing Platform for Vaccine and Protein Therapeutic Production
Elena Feshchenko, Ph.D., Associate Director, GeneXpress, Protein Sciences Corporation

Protein Sciences' proprietary baculovirus expression technology (BEVS) is used to produce high quality recombinant proteins quickly, reliably and at a low cost. The key advantage of this recombinant protein manufacturing platform is that a universal "plug and play" process is used for producing a broad range of protein based therapeutic vaccines for both human and veterinary use.

3:05 Strategies and Considerations for Scaling a CHO Fed-Batch Process
Yun Jiang, Ph.D., Senior Scientist Project Team Leader Upstream, Drug Design & Development, Swedish Orphan Biovitrum AB

From process development to commercial manufacturing, scale-up and scale-down are critical to developing a robust process and maintaining product quality. Here we share our experience with a CHO fed-batch process. The process has been scaled up to 3000L at two CMOs for production of clinical materials. The process has also been characterized with a 2L scale-down model and is now successfully validated for commercial production.

3:35 Scale-Up and Scale-Down Strategies for CHO Cell Clarification and Monoclonal Antibody Purification
Rachel Behan Wollacott, Ph.D, R&D Scientist II, MassBiologics

With the universal adoption of "platform" technologies in the biopharmaceutical industry, it is important to have scale-down process models to quickly demonstrate that a new molecule will fit the platform process. We will present our work concerning small-scale cell clarification with microfiltration. We will also present our strategies for high-throughput purification development and discuss scalability of MAb purification conditions from 96-well plates to chromatography columns.

4:05 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem Solving Breakout Discussions

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

6:45 End of Day

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Inaugural | May 5-6

BIOPROCESS STREAM

Scaling Up & Down Strategies for Protein Production

Ensuring Efficiency & Quality

TUESDAY, MAY 6

7:45 am Morning Coffee

BIOREACTOR PROCESSING & OPTIMIZATION

8:25 Chairperson's Remarks
Hao Chen, Ph.D., Principal Scientist, Merck

8:30 Case Study: Improving the Comparability and Predictability of a Scale-Down Model for Monoclonal Antibody Production Processes
Scott Camberg, MS, Principal Scientist, Process Development, Amgen

9:00 Using Models to Address Scale-Related Challenges in Industrial Fermentation Technology
Krist Gernaey, Ph.D., Professor, Center for Process Engineering and Technology (PROCESS), Chemical and Biochemical Engineering, Technical University of Denmark
This lecture will focus on scaling problems, and on the tools – experimental methods and modeling tools – available to support scale-up. Reaction kinetics can be assumed constant across scales, and process development is based on exploiting knowledge on reaction kinetics obtained at small scale to predict performance at production scale. Mathematical models, validated with sufficient experimental data, can be a great help in this exercise.

9:30 A Comparative Study Between Bench-Top Single Use Bioreactor Vessels and Their Counterpart Reusable Glass Vessels
Kamal Rashid, Ph.D., Director, Biomanufacturing Education and Training Center, Worcester Polytechnic Institute
Large scale single-use stirred-tank bioreactor systems have been on the market for a number of years now, but until recently single-use bench-scale stirred-tank bioreactors have not been commercially available. With the development of the New Brunswick CelliGen® BLU pitched-blade bioreactor in 2009 and other brands, single-use bench-top stirred-tank bioreactors have become a reality. At present, few research based publications are available on the utility of these bioreactors for bench-scale production of recombinant products. The objective of this study was to perform multiple comparisons with these single use bioreactors and the traditional glass vessel counterparts.

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

DISPOSABLES

10:45 Downstream Processing: Disposable Options in Processing of Complicated Feed Streams within Bioprocessing Operations
Michael Jarpe, Ph.D., Vice President, Biologics Development, Allergan
The process development, scale-up and manufacture of vaccine candidates as well as the characterization and IND filing of vaccine or therapeutic products are currently the bottlenecks in bioprocesses. In this presentation, we will explore the different upstream and downstream options for the process development and manufacturing of products focusing on cost-effective disposable and flexible options for facility integration.

11:15 Benefits of Disposables in Non-Platform Manufacturing of Fusion Protein
Stefan Schmidt, Ph.D., Vice President, DSP, Rentschler Biotechnology
In selected case studies, we demonstrate how to overcome the typical difficulties of processing fusion proteins such as low titer, lack of an affinity matrix, tendency to aggregate etc. Strategies in the context of fusion proteins are summarized, highlighting approaches such as utilization of disposable equipment or DoE to accelerate their process development and scale up for clinical applications.

11:45 Evaluation of Single-Use Bioreactors for Perfusion Processes
Richard Pearce, Commercial and Operations Director, Merck BioDevelopment
The aim of our study was to combine standard single use bioreactors with different perfusion technologies and to compare productivity and molecule quality. Without any modification of the Single Use Bioreactor, we were able to demonstrate the compatibility with a mAb perfusion process with a significant increase in productivity. This study demonstrates the flexibility of existing disposable bioreactors to new bioprocessing technologies.

12:15 pm Luncheon Presentation I
Automation of Small Scale Purification Enables Accelerated Process Development
Sponsored by PerkinElmer For the Better
Andrew Barry, MS, Director, Applications & Biology R&D, PerkinElmer
Small scale protein purification presents opportunities for accelerated process development of biotherapeutic molecules. The PerkinElmer Janus BioTx Pro and Pro-Plus Workstations were developed as intuitive, flexible, automated devices capable of performing parallel small-scale analytical protein purification. In order to understand the capabilities of a robotic platform to miniaturize chromatographic purification of proteins that is predictive of higher scale purification platforms while offering advantages in speed and number of samples processed, a series of experiments were performed comparing the Janus BioTx Pro Plus system with GE AKTA Express chromatography.

12:45 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:15-1:45 Ice Cream Break in the Exhibit Hall

SCALING UP

2:00 Chairperson's Remarks
Yamuna Dasarathy, Ph.D., Director, Marketing, Pall Life Sciences

2:05 Case Studies on Scaling Up a Monoclonal Antibody Purification Process for Clinical Manufacturing at a CMO – The Good, Bad and Ugly
Yun Bai, Ph.D., Associate Director, Process Development, Ambrx, Inc.
Despite the fact that monoclonal antibody products have been around for a long time and a significant amount of effort has been made in developing platform processes for mAb production, each mAb product is unique and constantly challenges the platform process. An appropriate and effective PD strategy is, therefore, necessary to leverage the platform knowledge to the distinctiveness of the individual mAb molecule in order to minimize PD time and risk while maintaining process efficiency and robustness. This presentation will focus on several case studies from a mAb project which is currently in the clinical manufacturing stage. Detailed process development and scale-up data will be presented and discussed to demonstrate the challenges often encountered in mAb PD and manufacturing. 2:35 Large-Scale Automation of Plasmid DNA Purifications for Transient Mammalian Protein Expression
Mark R. Nagel, Senior Research Associate, GE Service Manager, Protein Chemistry, Genentech, Inc.
Advancing research projects require increased amounts of proteins and plasmid DNA. Here we describe the development of a preparative three series large-scale automated (LSA) plasmid DNA purification process utilizing the GE Akta Xpress. This new process includes physical modifications of the Xpress flow paths, incorporates unique Unicorn programs that isolate a single flow path for each of the serial purifications and has specialized cleaning programs.

3:05 Identification and Risk Mitigation of a Critical Process Parameter during Antibody Process Scale-Up
Susan Dana Jones, Ph.D., Vice President and Senior Consultant, BioProcess Technology Consultants, Inc.
Jonathan Mitschelen, Ph.D., Vice President, Upstream Process Development, Cytovance Biologics
Rapid process development of a therapeutic monoclonal antibody was performed to enable production of Phase 1 clinical material at the 100 – 200 L scale. Working against a tight timeline, process parameters were not rigorously defined during process development or Phase 1 production. When the process was scaled to 1,000 L for Phase 2 production, cell growth was slower and productivity was much lower than anticipated. A detailed review and risk assessment of available development and manufacturing data was performed and depletion of a single nutrient was identified as the most likely cause. This talk will present the risk assessment and the successful outcome of an increased process control strategy on the performance of the scaled up process.

3:20 Sponsored Presentation *(Opportunity Available)*

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

SCALING DOWN

4:15 Scaling Down with High Cell Densities: Evaluating the TAP AMBR250 Microbioreactor for High-Throughput Fermentation Process Development
Bob Kuczenski, Ph.D., Engineer II, Genentech
The majority of *E. coli* fermentation process development at Genentech is performed at the 10 L pilot scale, which while costly, scales well to production scale. We will present our evaluation of the TAP AMBR250 bioreactor and discuss how this automated platform could increase throughput and reduce cost in fermentation process development.

4:45 Mammalian Cell Culture Process Scale-Down Model Development in Single-Use Bioreactors
Hao Chen, Ph.D., Principal Scientist, Merck
Despite the convenience of set-up and improved automation, Single-Use Bioreactors have unique challenges as scale-down models for mammalian cell culture. Here, we explored using Single-Use Bioreactors as scale-down models at four different scales (15 mL - 200 L). Multivariate Data Analysis (MVDA) tools are applied to establish effective models for fed-batch process up to 12,000 L scale.

5:15 End of Conference

Recommended Tuesday Dinner Short Course*

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

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

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Inaugural | May 7-8

ADC Development and Manufacturing

Overcoming ADC Production Challenges from Early Development to Commercial

Recommended Pre-Conference Short Course*

Novel and Emerging Conjugation Methods for ADCs

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

WEDNESDAY, MAY 7

7:00 am Registration and Morning Coffee

8:00 Chairperson's Opening Remarks
Peter U. Park, Ph.D., Vice President, Biology, Mersana Therapeutics, Inc.

PROCESS DEVELOPMENT AND CMC CHALLENGES

8:10 FEATURED PRESENTATION:
ADC Process Development and Scale-Up Strategy from Early Phase Development to Commercial
Nitya G. Ray, Ph.D., Senior Vice President, Manufacturing, Process Sciences/ Manufacturing, Progenics Pharmaceuticals, Inc.
ADCs require innovative approaches to manufacturing process development and scale-up. This presentation will address process development and manufacturing strategies for ADCs from early phase clinical development to commercial. Critical considerations for process development with emphasis on systems approach, control of conjugated species and scale-up will be presented. Finally, Progenics' ADC therapeutic program, currently in phase 2 clinical development to treat prostate cancer, will be discussed.

8:40 FEATURED PRESENTATION:
Development and Manufacture of ADCs – The Seattle Genetics Perspective
Nathan C. Ihle, Ph.D., Executive Director, CMC Strategy & Management, Seattle Genetics, Inc.
Due to the hybrid nature of ADCs, their production is more complex than for typical biological products. CMC strategies for developing manufacturing processes and product quality characterization will be discussed. Key factors in Seattle Genetics' selection of manufacturers for clinical and commercial production of ADCs, as well as future trends for ADC manufacturing will also be presented.

9:10 Antibody-Drug Conjugates: Challenges and Critical Considerations for Developing Early-Phase Clinical Manufacturing Processes
Marie M. Zhu, Ph.D., Director, Process Sciences, Technical Operations, Agensys Inc., an affiliate of Astellas, Inc.
Developing a scalable and robust process that generates ADC products with desired drug-to-antibody ratio and consistent product quality attributes is important for clinical manufacturing. We will share the challenges experienced during developing ADC processes. Further, through case studies, we will discuss critical aspects in ADC process development and will elucidate development strategies that resulted in successful process scale-up and tech transfer for ADC production.

9:40 Effective Manufacturing of Antibody Drug Conjugates
Aad van de Leur, MSc, COO, Biopharmaceutical Development, Synthon Biopharmaceuticals B.V.
Synthon recently finished the construction and qualification of a new ADC GMP manufacturing plant. The implications on facility design to handle larger batch sizes to meet biopharmaceutical industry standards for safe, effective and reliable manufacturing will be discussed. The challenges and different approaches to develop a robust conjugation process as well as results of this conjugation process including preclinical data will be presented.

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

DEVELOPABILITY OF ADC – OVERCOMING HETEROGENEITY AND TUMOR RESISTANCE

11:10 Next-Generation Antibody-Drug Conjugates Designed with Fleximer™ Platforms Enable High Drug-Loading (DAR >15) of Payloads with Excellent Biochemical Properties and Pharmacokinetics and Potent Anti-Tumor Activity
Peter U. Park, Ph.D., Vice President, Biology, Mersana Therapeutics, Inc.
The application of biodegradable, polyacetal polymer Fleximer™ to ADC design can provide numerous advantages, including significantly higher capacity for drug payload, the improvement of physicochemical properties for ADC, especially with highly hydrophobic payloads and the use of protein recognition scaffolds beyond the commonly used IgGs. Examples of these benefits achieved using Mersana's polyacetal-based conjugation system to create and characterize next-generation ADCs will be presented.

11:40 Addressing Tumor Heterogeneity and Resistance: Production of Homogeneous Multispecific ADCs with Combination Warheads
Trevor Hallam, Ph.D., CSO, Sutro BiopharmaSpeaker
Cell–free protein synthesis methods have been developed for production of homogeneous therapeutic proteins, including ADCs. Many variants can be expressed in hours and within days, production of chosen variants can be scaled to generate clinical materials. The power and utility of the platform to design and manufacture single species bispecific and multispecific antigen-targeted antibodies with conjugated combination warheads will be described.

Sponsored by CONCORTIS

12:10 pm ADC-2x, the Development of Multifunctional ADCs
David Miao, CTO, Concortis Biosystems, The ADC company of Sorrento Therapeutics, Inc.
Conventional ADCs, targeting one type of cancer antigen and bearing one class of payload, promise to vastly improve cancer treatment. Nevertheless there is an urgent need to further increase the therapeutic window of ADCs by discriminating the tumor cells from normal tissues and preventing the development of multiple drug resistance. To maximize the potentials of ADC therapeutics, we have developed a new category of multifunctional ADCs, i.g., ADC-1.2, ADC-2.1 and ADC-2.2. Designs, technologies and data of enhanced potencies will be presented.

12:40 Luncheon Presentation I *(Sponsorship Opportunity Available)*

1:10 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:40 Session Break

FORMULATION AND STABILITY OF ADC

2:00 Chairperson's Remarks
Peter U. Park, Ph.D., Vice President, Biology, Mersana Therapeutics, Inc.

2:05 Pfizer Case Study of ADC Formulation and Process Optimization
Shannon MacMilian, MSc, Principal Scientist, Biotherapeutic Pharmaceutical Sciences R&D, Pfizer, Inc.

2:35 Optimizing ADC Development Using PK/PD Modeling and Simulation
Dhaval K. Shah, Ph.D., Assistant Professor, Department of Pharmaceutical Sciences, School of Pharmacy and Pharmaceutical Sciences, SUNY Buffalo
The talk will introduce different PK/PD/TD models employed for ADC development, and will demonstrate: (1) how to employ the models to gain insight into ADC disposition, and (2) how to use M&S to aid clinical development and discovery of ADCs.

3:05 Oral Poster Presentation
New Site-Specific Conjugation Based on Bacterial Transglutaminase
Delphine Bregeon, Ph.D., R&D Scientist, Innate Pharma
Here, the work relates to ADCs synthesis through BTG approach based on site-specific modification of mAbs with single point mutations. Stability, pharmacokinetics, as well as *in vitro* and *in vivo* efficacy of resulting BTG-ADCs were investigated. ADCETRIS®, brentuximab vedotin, has been used as comparator, hence for consistency BTG-ADCs have been conjugated with the different linkage strategies (one-step and two-step) containing the same protease sensitive moiety as ADCETRIS®, i.e. valine-citrulline-PAB-MMAE. BTG two-step process leads to ADCs with DAR of exactly 2.0 or 4.0 for antibodies with N297S or N297Q single point mutation respectively.

3:20 Sponsored Presentation *(Opportunity Available)*

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

4:20 Problem Solving Breakout Discussions

5:20 Networking Reception in the Exhibit Hall with Poster Viewing

6:30 End of Day

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Inaugural | May 7-8

ADC Development and Manufacturing

Overcoming ADC Production Challenges from Early Development to Commercial

THURSDAY, MAY 8

7:45 am Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

ANALYTICAL CHARACTERIZATION

8:30 Chairperson's Remarks

Alex Lazar, Ph.D., Head, Analytical and Pharmaceutical Sciences, Immunogen, Inc.

8:35 Analytical Challenges in Characterization of Heterogeneities of Antibody-Drug Conjugates: A Case Study

April Xu, Ph.D., Senior Principal Scientist, BioBtx-ARD, Pfizer

It is important to characterize the heterogeneity of an ADC to understand both process consistency and product stability. In this presentation, a case study will be presented on how heterogeneity in an ADC is characterized. In particular, the application of improved analytical techniques using capillary electrophoresis and protein mass spectroscopy are applied to characterized the heterogeneities due to drug load distribution.

9:05 Considerations about Analytical Methods Used for the Measurement of the Level of Unconjugated Antibody (UmAb) Present in Maytansinoid ADCs

Alex Lazar, Ph.D., Head, Analytical and Pharmaceutical Sciences, Immunogen, Inc.

Maytansinoid ADCs are biotherapeutic agents for the treatment of cancer. They are manufactured by chemically attaching a cytotoxic agent to a targeting antibody. A specific attribute of ADC drug product is unconjugated antibody content. The presentation will describe several analytical methods based on different separation principles that have been considered for the measurement of the levels of unconjugated antibody in ADC drug product.

9:35 Strategies and Challenges in Bioassay Development for ADCs

Debra M. Meyer, BSc, Senior Principal Scientist, Analytical R&D, Biotherapeutics Pharmaceutical Sciences, Pfizer, Inc.

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

OUTSOURCING AND SUPPLY CHAIN CHALLENGES

11:05 Challenges of Outsourcing ADCs - Perspectives from the Client

Deborah Meshulam, Director, Contract Manufacturing, ImmunoGen, Inc.

ImmunoGen develops ADCs consisting of its proprietary maytansine derivatives attached to tumor-targeting antibodies. The conjugation process is complex and involves development and transfer for both small and large molecules. Some of the manufacturing challenges will be discussed from a client's perspective involving efficient sourcing for different components of ADC materials, selecting the right CMOs, and ensuring CMOs have the capacity and capability to manufacture ADCs.

11:35 Establishing a Fully Outsourced Supply Chain for an ADC

Jesper Valbjørn, Vice President, CMC Operations, Genmab A/S

The talk will cover the challenges of establishing an ADC supply chain in a fully outsourced model from a small biotech perspective. The process of establishing the supply chain for an ADC increase significantly in complexity compared to the supply chain for a monoclonal antibody. Implications of internal and external processes for an ADC CMC development program will be discussed.

12:05 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

12:35 End of Conference

Recommended Tuesday Dinner Short Course*

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

Recommended Thursday Dinner Short Course*

Antibody-Drug Conjugate Therapeutics: Potential and Challenges

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

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