Seventh Annual PEGS

May 9-13, 2011

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KEYNOTE SPEAKERS

William R. Strohl Ph.D., Vice President, Biologics Research, Biotechnology Center of Excellence, Centocor

Raimund Dutzler Ph.D., Professor, Biochemistry, University of Zurich

Janice Reichert Ph.D., Research Assistant Professor, Tufts Center for the Study of Drug Development, Tufts University School of Medicine

Davinder Gill Ph.D., Vice President and Head, Global Biologics Technologies, Pfizer, Inc.

Allan Bradley Ph.D., FRS, Director Emeritus, Wellcome Trust Sanger Institute

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

Roger A. Sabbadini Ph.D., Founder, Vice President & CSO, Lpath, Inc.; Professor Emeritus, Biology, San Diego State University

Wayne Coco Ph.D., Vice President Global Biologics / Biologics Lead Optimization, Bayer HealthCare AG Global Drug Discovery

Lorenz M. Mayr Ph.D., Executive Director, Unit Head Biology, Protease Platform, Novartis Pharma AG

Douglas Cecchini Ph.D., Director, Technical Development, Biogen Idec, Inc.

DISCOVERY

- Phage & Yeast Display
- Engineering Antibodies
- Antibody Optimization

EXPRESSION

- Difficult to Express Proteins
- Optimizing Protein Expression
- Purifying Antibodies

ANALYTICAL

- Characterization of Biotherapeutics
- Protein Aggregation and Stability
- Immunogenicity

ANTIBODIES

- Antibodies for Cancer Therapy
- Bispecific Antibodies
- Antibody-Drug Conjugates

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EVENT-AT-A-GLANCE

	Sunday 5/8/11 Short Courses		Monday 5/9/11	Tuesday 5/10/11	Wednesday 5/11/11	Thursday 5/12/11	Friday 5/13/11
am	Microfluidics for Antibody Selections & Screening	DISCOVERY	Phage & Yeast Display	Phage & Yeast Display	Engineering Antibodies	Engineering Antibodies	Antibody Optimization
pm	Screening & Selecting Candidate Antibodies	DISCOVERY	Phage & Yeast Display	Phage & Yeast Display	Engineering Antibodies	Antibody Optimization	Antibody Optimization
am	Translational Considerations for Devt of mAbs Focus on Early Disc- Pt. 1	EXPRESSION	Difficult to Express Proteins	Difficult to Express Proteins	Optimizing Protein Expression	Optimizing Protein Expression	Purifying Antibodies
pm	Translational Considerations for Devt of mAbs from Disc to Clinic- Pt. 2	EXPRESSION	Difficult to Express Proteins	Difficult to Express Proteins	Optimizing Protein Expression	Purifying Antibodies	Purifying Antibodies
am		ANALYTICAL	Characterization of Biotherapeutics	Characterization of Biotherapeutics	Protein Aggregation	Protein Aggregation	Immunogenicity
pm	Mass Spec Apps for Drug Discovery & Product Devt	ANALYTICAL	Characterization of Biotherapeutics	Characterization of Biotherapeutics	Protein Aggregation	Immunogenicity	Immunogenicity
am		ANTIBODIES	Antibodies for Cancer Therapy	Antibodies for Cancer Therapy	Bispecific Antibodies	Bispecific Antibodies	Antibody-Drug Conjugates
pm	Phage & Yeast Display Libraries	ANTIBODIES	Antibodies for Cancer Therapy	Antibodies for Cancer Therapy	Bispecific Antibodies	Antibody-Drug Conjugates	Antibody-Drug Conjugates
			Dinner Short Courses	Size Matters in Therapeutic Antibody Design		Changing Guidances and Regulatory Expectations for Biologics Characterization Techniques for Prot Therapeutics: Orthogonal vs Complementary	

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SHORT COURSES*

MORNING

SUNDAY, MAY 8 | 10:00 AM - 1:00 PM

SC1 - MICROFLUIDICS FOR ANTIBODY SELECTIONS AND SCREENING

Integrated Single-Cell Analysis for Antibody Discovery

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

Use of Microfluidics for Ultra High-Throughput Antibody Screening and Selection

David Weitz, Ph.D., Gordon McKay Professor, Applied Physics, Harvard University

Comparing Tools for Antibody Screening

David Weitz, Ph.D., Gordon McKay Professor, Applied Physics, Harvard University

SC2 - TRANSLATIONAL CONSIDERATIONS FOR DEVELOPMENT OF MONOCLONAL ANTIBODIES: FOCUS ON EARLY DISCOVERY *PART 1*

- Considerations for target selection, antibody screening and mAb pre-clinical development
- Antibody affinity and biophysical characterization: Biacore, Kinexa, and FACS
- Pre-clinical Considerations – A science based approach: Design goal, MOA, choice of species, and pre-clinical plans

Mohammad Tabrizi, Ph.D., Sr. Fellow, Head PK/PD, Merck Research Laboratory, MRL-Palo Alto

Cherryl Funelas, Manager, Bioanalytical Development, Takeda San Francisco

Scott Klakamp, Ph.D., Research Fellow, Biophysical Chemistry and Research Informatics, Takeda San Francisco

AFTERNOON

SUNDAY, MAY 8 | 2:00 - 5:00 PM

SC3 - SCREENING & SELECTING CANDIDATE ANTIBODIES

- Strategies for antibody discovery
- Shortening the timeline for identifying ASCs (antibody secreting cells)
- Integrating technology, such as biosensors and microfluidics

David Lowe, Ph.D., Principal Scientist, Display Technology, MedImmune

XiaoDong Yang, M.D., President & CEO, Apexigen, Inc.

Arnout Gerritsen, Ph.D., Director, Assay & Bioanalytical Science, Genmab

SC 4 -TRANSLATIONAL CONSIDERATIONS FOR DEVELOPMENT OF MONOCLONAL ANTIBODIES: FOCUS ON NONCLINICAL DEVELOPMENT TO CLINIC *PART 2*

- Considerations for immunoassay development in support of pharmacokinetic, immunogenicity & biomarker evaluation
- Antibody safety, species selection, introduction to surrogate approaches in development of monoclonal antibodies
- Translation of exposure – Response data from discovery into the clinic in support of FIH dosing

Mohammad Tabrizi, Ph.D., Sr. Fellow, Head PK/PD, Merck Research Laboratory, MRL-Palo Alto

Cherryl Funelas, Manager, Bioanalytical Development, Takeda San Francisco

Scott Klakamp, Ph.D., Research Fellow, Biophysical Chemistry and Research Informatics, Takeda San Francisco

SC5 - BIOLOGICAL MASS SPECTROMETRIC APPLICATIONS FOR DRUG DISCOVERY AND PRODUCT DEVELOPMENT

- Geared for individuals supporting biopharmaceutical drug characterization analyses using mass spectrometry in either discovery or product development
- A novel method for assessing disulfide bond networks will be disussed
- Methods for performing glycosylation analyses, PTM analyses, and stress assessments on drug candidates will be covered

Chair: Jennifer Nemeth, Ph.D., Principal Research Scientist, Biologics Mass Spectrometry & Allied Tech nologies, Centocor R&D, Inc.

Alain Balland, Ph.D., Scientific Director, Analytical & Formulation Sciences, Amgen

Yoshi Hamuro, Ph.D., Director, Analysis, ExSAR

Dariusz Janecki, Ph.D., Research Scientist, Biologics Mass Spec, Centocor R&D, Inc.

Ron Orlando, Ph.D., Professor, Biochemistry and Molecular Biology, Complex Carbohydrate Research Center, University of Georgia

SC6 - PHAGE AND YEAST DISPLAY LIBRARIES AND THEIR SCREENING

- Phage display and construction of phage-displayed peptide, scFv and Fab libraries
- Yeast display and construction of yeast-displayed scFv and Fab libraries
- Selection and screening technologies that are compatible with phage and yeast-display libraries

Jamie K. Scott, M.D., Ph.D., Professor , Canada Research Chair, Molecular Immunity, Molecular Biology & Biochemistry; Faculty of Health Sciences, Simon Fraser University

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

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

DINNER

TUESDAY, MAY 10 | 6:00 – 9:00 PM

SC7 - HOW SIZE MATTERS IN THERAPEUTIC ANTIBODY DESIGN

- Strategies for achieving more powerful and smaller antibody therapeutics
- Designing antibody therapeutics to penetrate tumors and tissue
- Overcoming the challenge of the blood/brain barrier

David Blakey, Ph.D., Chief Scientist, Oncology Discovery, AstraZeneca R&D

K. Dane Wittrup, Ph.D., C.P. Dubbs Professor, Chemical & Biological Engineering, Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

Michael T. Stumpp, Ph.D., CSO, Molecular Partners AG

H. Kaspar Binz, Ph.D., Vice President Technology & Co-Founder, Molecular Partners AG

THURSDAY, MAY 12 | 5:30 – 8:30 PM

SC8 - CHANGING GUIDANCES AND REGULATORY EXPECTATIONS FOR BIOLOGICS

- Update on ICH6 pre-clinical guidance document
- Impact on regulatory changes to design and cost of conducting pre-clinical studies
- Introducing concept of First-in-Human (FIH) trials
- Approaches to optimize initial clinical studies, post TeGenero
- Interactive case study exercises on advancing new biologics into Phase I clinical trials

Joy Cavagnaro, Ph.D., DABT, RAC, President, Access BIO LC

Julia Barrett, M.D,. MPH, Senior Clinical Consultant, Biologics Consulting Group, Inc.

SC9 - CHARACTERIZATION TECHNIQUES FOR PROTEIN THERAPEUTICS – ORTHOGONAL VS. COMPLEMENTARY

- This workshop covers the theory and general application of both traditional and emerging technologies suitable for protein therapeutic characterization, across the applicable size range of 1 nm to 100 um.
- What's the difference between Tm measured by DSC, CD, & DLS? Can DLS be used to confirm SEC results? What's the relevance of protein charge on formulation stability? Can particle counting be achieved in the 100 nm to 1 um size range? What role does protein aggregate "morphology" play?

Kevin Mattison, Ph.D., Principal Scientist, Bioanalytics, Malvern Instruments

Ulf Nobbmann, Ph.D., Senior Applications Specialist, Nanometrics, Malvern Instruments

Jason Sanchez, Ph.D., Product Manager, GPC/SEC Technologies, Malvern Instruments

** Separate Registration Required*

PHAGE AND YEAST DISPLAY OF ANTIBODIES AND PROTEINS

SUNDAY, MAY 8

4:00 - 6:00 pm Main Conference Registration

MONDAY, MAY 9

7:00 am Registration and Morning Coffee

» KEYNOTE SESSION

8:30 Chairperson's Opening Remarks

Lutz Jermutus, Ph.D., Senior Director, Research & Development; Global Head, Technology, MedImmune

8:40 Centocor Antibody Discovery from pIX Phage Display to Cell Line Development

William R. Strohl, Ph.D., Vice President, Biologics Research, Biotechnology Center of Excellence, Centocor

The pathway for antibody discovery at Centocor will be presented, with a focus on the stages that are key components of the development process and technologies that are available. These include a novel pIX human antibody library, and technologies available for optimization, isotype selection, developability, epitope mapping, high content functionality screening, and cell line development.

9:10 Engineering Antibodies for Medical Differentiation

Davinder Gill, Ph.D., Vice President and Head, Global Biologics Technologies, Pfizer, Inc.

The talk will cover key aspects of antibody safety and efficacy as they relate to medical differentiation. This includes new modes of action as well as use of novel modalities. The importance of clear patient benefit in an increasingly crowded biologics area will be discussed.

9:40 Selection of Internalizing Phage Antibodies Using Tumor Cells and Yeast Displayed Tumor Antigens

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

Antibodies that bind cancer cells and are internalized can be used for tumor targeted drug and nucleic acid delivery. We show that such antibodies to specific tumor antigens can be generated by first selecting phage antibody libraries on a tumor cell line expressing the target antigen followed by selection on yeast displaying the same antigen on their surface. Advantages of this approach and specific examples will be covered.

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

11:10 *In vitro* Recombination and HTS Screening Strategies for Potency, Selectivity and Antibody Germlining

Wayne Coco, Ph.D., Vice President Global Biologics / Biologics Lead Optimization, Bayer HealthCare AG Global Drug Discovery

The optimization of antibody leads is important to maximize potency, best exploit animal models, shorten timelines to clinic/market and minimize risk. The choice of diversity to include into *in vitro* recombination libraries will be discussed as will the potential to rapidly and simultaneously affinity mature, alter specificity, germline and sequence optimize.

11:40 Panel Discussion: Trends and Opportunities in Antibody Discovery

Moderator: Lutz Jermutus, Ph.D., Senior Director, Research & Development; Global Head, Technology, MedImmune

- Why would you need more than phage display and hybridomas to create antibody leads?
- Which technologies speed up early antibody CMC?
- How many "good" antibody targets are out there?

How can we drug GPCRs, ion channel and other membrane proteins effectively using monoclonal antibodies?

12:10 pm A Phage Display Approach for Anti-Inflammatory Therapeutic Antibody Discovery

Sponsored by Dyax

Andrew E. Nixon, VP, Lead Discovery & Biochemistry, Dyax

12:40 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:40 Break

LIBRARY DESIGN AND OPTIMIZATION STRATEGIES

2:00 Chairperson's Remarks

Aaron K. Sato, Ph.D., Senior Director, OncoMed Pharmaceuticals, Inc.

2:05 Combining Phage and Ribosome Display for Antibody Optimization

Maria A.T. Groves, Ph.D., Senior Scientist, Lead Generation, MedImmune

The ribosome display technology can be applied to phage display derived antibodies and phage display enriched antibody populations to yield antibodies with high affinity and potency. Here, we will discuss examples where the combination of phage and ribosome display technologies has worked synergistically to produce antibodies with the desired characteristics for therapeutic programs.

2:35 Selection of Artificial Transcription Factors Modulating Breast Cancer Metastasis

Pilar Blancafort, Ph.D., Assistant Professor, Department of Pharmacology, University of North Carolina School of Medicine

This work will describe the isolation of Artificial Transcription Factors (ATFs) made of six finger DNA binding domains linked to transcriptional and epigenetic effector domains. We show that these ATFs activate and/or repress oncogenic and tumor suppressor targets and modulate neoplastic progression in mouse models.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

3:45 Yeast Display: A Versatile Protein Engineering Platform

Cheryl Baird, Ph.D., Senior Research Scientist, Cell Biology & Biochemistry, Pacific Northwest National Laboratory

We routinely use yeast surface display to engineer proteins for biodetection applications. I will present our approach for developing antibodies from immune libraries, as well as recent work engineering novel binding specificities into non-immunoglobulin protein scaffolds.

4:15 Spatially Addressed Antibody Libraries for Rapid and Multiplexed Discovery

Vaughn V. Smider, M.D., Ph.D., Founder, Fabrus LLC; Assistant Professor, Molecular Biology, The Scripps Research Institute

We used synthetic biology and high throughput fermentation and purification to create the first spatially addressed combinatorial protein library. From this library we could identify a range of hits against several targets in multiplexed screening assays. This technology could open up the possibility of cell based functional screens for antibody discovery.

4:45 Problem Solving Breakout Sessions
Concurrent Problem Solving Breakouts are interactive sessions hosted by a moderator to discuss a topic in depth. They are open to all attendees, sponsors, exhibitors, and speakers and provide a forum for discussing key issues and meeting potential partners. *Please pick a topic of your choice and join in.*

5:45 Reception in the Exhibit Hall with Poster Viewing

6:45 End of Day

TUESDAY, MAY 10

8:00 am Morning Coffee

DISPLAYING VIABLE PRODUCTS

8:25 Chairperson's Remarks

8:30 Paired Yeast-Display/Secretory Vectors for Rapid Isolation of Site-Specific Biotinylated Affinity Reagents

Nathalie Scholler, M.D., Ph.D., Assistant Professor, Obstetrics/Gynecology, University of Pennsylvania
We will describe our new platform for high-throughput identification of affinity reagents in two steps. Our platform combines two complementary systems of yeast expression for display and secretion of affinity reagent libraries. Transfers from display to secreted forms that are site-specific biotinylated are easily achieved by gap repair and mating.

9:00 Engineering T cell Receptors by Mammalian Cell Display and Yeast Display

David Kranz, Ph.D., Professor, Biochemistry, University of Illinois, Urbana–Champaign
T cell receptors (TCRs) have potential applications in adoptive T cell therapies and as soluble therapeutics. Despite structural and functional similarities with antibodies, TCRs have proven more difficult to engineer. We have developed strategies to optimize ligand binding properties of TCRs using mutant libraries displayed on mammalian or yeast cells.

9:30 A Filamentous Phage Display System for N-linked Glycoproteins

Matthew P. DeLisa, Ph.D., Associate Professor, Chemical & Biomolecular Engineering, Cornell University
Phage display is one of the most useful methods for isolating interesting mutants from large combinatorial libraries of protein sequences. Our laboratory has recently extended the power of phage display for the production and selective enrichment of phages that display asparagine-linked (N-linked) glycoproteins. The technique has significant potential for studying and engineering any of the steps along the bacterial N-linked protein glycosylation pathway. The nascent field of bacterial glycoengineering now has a new tool for its relatively empty toolbox.

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

10:45 Engineering Protein Posttranslational Modification Enzymes by Phage Display

Jun Yin, Ph.D., Assistant Professor, Chemistry, University of Chicago
We use phage display as a high throughput selection platform to evolve the catalytic activities of Sfp phosphopantetheinyl transferase, biotin ligase and ubiquitin ligase. The engineered posttranslational modification enzymes are equipped with new functions and can be used as tools to study cell biology.

11:15 Cyclotides, a Novel Natural Peptide Scaffold for Drug Discovery

Julio A. Camarero, Ph.D., Associate Professor, Pharmacology and Pharmaceutical Sciences, University of Southern California
Cyclotides are a new emerging family of large plant-derived backbone-cyclized polypeptides (≈28-37 amino acids long) that share a disulfide-stabilized core (3 disulfide bonds) characterized by an unusual knotted. Cyclotides thus appear as promising leads or frameworks for peptide drug design.

11:45 The RaPID Display of Non-Standard Peptides

Hiroaki Suga, Ph.D., Professor, Bioorganic Chemistry Lab, Graduate School of Science, The University of Tokyo
Genetic code reprogramming enables us to ribosomally express cyclic peptides containing non-standard residues such as N-methyl amino acids. The integration of this method with a *in vitro* display system, referred to as RaPID (Random Peptide Integrated Discovery) display, provides a new means of the discovery of non-standard peptides against a wide variety of therapeutic targets.

12:15 pm Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:15 Break

APPLYING HT SEQUENCING TO ANALYSIS OF SELECTION EXPERIMENTS

2:00 Chairperson's Remarks

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

2:05 Next-Generation Sequencing: Applications and Pitfalls

Chris Detter, Ph.D., Group Leader, Genome Science, Bioscience Division, Los Alamos National Laboratory
For close to 20 years, we were used to a wonderfully accurate and stable sequence product. Today, that has all changed. Recent technological advances have dramatically changed how we use genome sequencing to answer important scientific questions in health, environment and security. The Next Generation Sequencing era we find ourselves in has released what seems to be an endless spectrum of potential. Opportunities and caveats will be explored.

2:35 Technology Development for Immune Sequencing

Francois Vigneault, Ph.D., Post-Doctoral Ragon Institute Fellow/Church Laboratory, Harvard Medical School, Wyss Institute
We are developing enabling technologies to leverage the information registered in the human immune repertoire. Recent advance in next-generation sequencing have allowed us to survey the immune response in time across a few individuals following flu vaccination. We are also conducting small cohort immune sequencing analysis of Rheumatoid arthritis and HIV elite controllers patients. Finally, we are also working on the next set of technologies to enable this field of research further.

3:05 Sponsored Presentations *(Opportunities Available)*

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

4:15 Deep Sequencing of Captured CDRH3 Repertoires for Accelerated Antibody Discovery

Nicolas Fischer, Ph.D., Head, Research Department, NovImmune SA
Using a natural or synthetic CDR3 capture approach, multiple scFv libraries were generated. Deep sequencing of the initial diversity and after each selection round provided insights into sequence evolution against different targets. The resulting extensive sequence information and clone enrichment profiles allow for library quality assessment and by-passing primary screening thus accelerating antibody discovery.

4:45 "Third Wave" Antibody Discovery by V Gene Repertoire Mining in Animals and Humans

George Georgiou, Ph.D., Cockrell Endowed Chair Professor, Chemical & Biomedical Engineering and Molecular Genetics & Microbiology, University of Texas, Austin
We have developed a technology for the discovery of antibodies by mining the repertoire in relevant B subpopulations in animals and in patients. Comparisons of the V gene repertoires in different settings and the implications for Ab discovery will be discussed.

5:15 End of Conference

ENGINEERING ANTIBODIES

WEDNESDAY, MAY 11

7:00 am Registration and Morning Coffee

ANTIBODY DISCOVERY STRATEGIES AND TOOLS

8:30 Chairperson's Opening Remarks

8:40 Multidimensional Glycan Arrays for Selection and Characterization of Carbohydrate-Binding Antibodies

Jeffrey C. Gildersleeve, Ph.D., Chemical Biology Laboratory, Center for Cancer Research, National Cancer Institute-Frederick

Carbohydrate-binding antibodies are used extensively for basic research and have clinical applications as therapeutic agents and diagnostics. We have developed a carbohydrate microarray or "glycan array" containing hundreds of carbohydrate antigens immobilized on a glass microscope slide. To enhance diversity, the array contains variations in both carbohydrate structure and presentation. The array provides a high-throughput tool for evaluating antibody-antigen interactions.

9:10 Elicitation of Structure-Specific Antibodies by Epitope Scaffolds: Application to HIV-1 Vaccine Design

Gilad Ofek, Ph.D., Senior Scientist, Vaccine Research Center, National Institute of Allergy and Infectious Diseases, National Institutes of Health

A key challenge for vaccine design has been the elicitation of antibodies against epitopes that are immunorecessive, cryptic, or transient in their native context. We employ computational techniques to transplant a vulnerable neutralizing HIV-1 determinant into acceptor protein scaffolds - epitope scaffolds - and demonstrate that epitope scaffolds readily elicit antibodies that recognize the pre-determined shape of the epitope. Epitope scaffolds thus provide a means for eliciting structure-specific antibodies against HIV-1 and against other pathogens for which vaccines are sought.

9:40 Tools for the Evaluation of Disulfide-Mediated Heterogeneity Characteristic to IgG2 Monoclonal Antibodies

Nathan A. Lacher, Ph.D., Analytical R&D, Pfizer BioTherapeutics R&D

The development of analytical methodologies to study disulfide-mediated isoforms that are present in IgG2 antibodies as a result of differences in the disulfide connectivity within the hinge region will be reviewed. The application of these tools for comparability, bioprocess development, and *in vivo* assessment will also be discussed.

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

11:10 Exploiting Potent Chromatin Remodelling Elements to Rapidly Identify Relevant Monoclonal Antibody Variants in Stable CHO Cell Lines

Sponsored by SELEXIS

Armelle Gaussin, Ph.D., Chief Technology Officer, SELEXIS SA

DNA vectors incorporating versatile epigenetic regulatory elements such as the Selexis Genetic Elements (SGEs)providehigh transcription rates and prevent transgene silencing, yielding cell clones with increased and stable expression. Thus, combined with optimized gene transfer methods, these vectors can be used to generate high-producer stable cell lines in short time frames and with little screening efforts. This unique feature opens up the possibility of relying on a single stable expression system throughout the drug development process, allowing the identification of relevant monoclonal antibody variants and high expressing clones at the same time. This novel set up allows considerable time and labour saving by screening top lead candidates in a production ready platform.

11:40 Harnessing the Human Immune Response to Fight Infectious Disease

Roger Beerli, Ph.D., Head, Human mAb Discovery, Intercell AG

Sophisticated *in vivo* processes that shape the immune repertoire afford endogenous human antibodies with high affinity, minimal immunogenicity and minimal off-target reactivity. Natural human mAbs are therefore an attractive alternative to antibodies developed by other means. We isolate human mAbs directly from the B lymphocytes of naturally exposed or immunized human subjects using a proprietary platform technology involving mammalian cell display. Here, the mammalian cell display platform will be discussed and several pre-clinically validated natural human mAbs against infectious disease targets will be described.

12:10 pm De-risking Strategies of Therapeutic Antibodies

Sponsored by Lonza

Philippe Stas, MBA, Head Applied Protein Services, Lonza

In order to reduce the high attrition rate of therapeutic antibodies in clinical development, rational design strategies will be presented, including avoidance of immunogenicity and the optimization of aggregate propensity and other drug characteristics.

12:40 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:10 Break

GETTING IT DONE

1:30 Chairperson's Remarks

1:35 A Novel Integrated Data Management Platform for Biologics R&D

Christoph Freiberg, Ph.D., Senior Scientist, Head of Biologics Data Platform Project, Biologics Research, Bayer HealthCare Pharmaceuticals, Wuppertal/Germa

We have implemented an enterprise-level software solution together with our partner Genedata to comprehensively support biologics R&D activities. We show how we have integrated all steps from HT biologics screening to cell line development into one workflow.

2:05 Design, Production and Efficacy of Antibody-Peptide Fusions for Oral Treatment of Neonatal *Cryptosporidium spp*. Infection

Michael Imboden, Ph.D., Director, Research and Development, ioGenetics LLC

Effective drugs are needed to treat *Cryptosporidium parvum* and *C. hominis* infections in livestock and humans. Specific targeting of the parasite *in vivo* is achieved through genetically engineered fusions comprising monoclonal antibodies linked to innate immunity peptides toxic to the parasite while well-tolerated by the mammalian host. Efficacy of oral treatment against neonatal cryptosporidiosis in mice is presented.

2:35 In-silico Protein Engineering: Computational Methods used in the Design and Study of Macromolecular Systems

Sponsored by accelrys®

Francisco Hernandez-Guzman, Product Manager, Life Sciences, Accelrys

As new biologics based therapies or diagnostics continue to gain interest, there is an increased need for computational tools that can assist researchers characterize, model and predict the behavior of their molecules. So, whether you're interested in generating a structure in absentia of experimentally determined structures, or are looking to understand protein stability and the effect of site-directed mutagenesis, or you want to study molecular motion as a function of time, or are looking to accelerate your development and reduce the experimental burden, modern computational algorithms can be used effectively to make rational decisions for the design of novel biological based molecules. In this presentation, we will present a

short overview of some of these computational methods commonly used in the study of biologics.

2:50 Novel Biosensor Technologies and Analysis Approaches Mimicking Natural Environments

Sponsored by attana

Ian A. Nicholls, Linnaeus University, Sweden

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

3:50 Problem Solving Breakout Sessions

Concurrent Problem Solving Breakouts are interactive sessions hosted by a moderator to discuss a topic in depth. They are open to all attendees, sponsors, exhibitors, and speakers and provide a forum for discussing key issues and meeting potential partners. *Please pick a topic of your choice and join in.*

4:50 Reception in the Exhibit Hall with Poster Viewing

6:00 End of Day

THURSDAY, MAY12

8:00 am Morning Coffee

ENGINEERING FOR SUCCESS FROM THE START

8:30 Chairperson's Opening Remarks

8:35 OptCDR: A Computational Framework for the Design of Complementarity Determining Regions for Targeted Epitope Binding

Robert Pantazes, Chemical Engineering Department, The Pennsylvania State University

Here we present our Optimal Complementarity Determining Regions (OptCDR) method for designing antibody CDRs that bind any specified antigen. The method can be used to design either nanobodies (heavy chains by themselves) or scFvs (heavy and light chains). Several thera-peutically relevant systems are used to demonstrate the efficacy of the method.

9:05 Llama Derived Single Domain Antibodies for Ricin Detection

Ellen R. Goldman, Ph.D., Research Scientist, Center for Bio/Molecular Science and Engineering, Naval Research Laboratory

We selected high affinity, highly specific single domain antibodies (sdAb) towards ricin from an immune library. These sdAb bind four distinct epitopes on ricin; many have sub nM affinities and are able to refold and bind antigen after heat denaturation. The best sdAb pair provided ricin detection to at least 0.1 ng/ml and excellent discrimination *versus* non-toxic RCA 120.

9:35 Selecting and Characterizing Llama Single Domain Antibodies Against High Consequence Pathogens and Toxins with a View to Ruggedizing Immunoassays

Andrew Hayhurst, Ph.D., Associate Scientist, Virology and Immunology, Texas Biomedical Research Institute

Unlike conventional IgG and recombinant derivatives, single domain antibodies (sdAb) are unique in being able to refold after denaturation. Therefore, sdAb appear to be ideal ligands for developing rugged antigen capture assays for stockpiling, resource poor and cold-chain free environments. We have generated and characterized sdAb specific for Filoviruses and the seven botulinum neurotoxin serotypes using semi-synthetic and immune approaches.

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

11:05 Polyreactivity Increases the Apparent Affinity of Anti-HIV Antibodies by Heteroligation

Hugo Mouquet, Ph.D., Postdoctoral Associate, Molecular Immunology - Nussenzweig Laboratory, The Rockefeller University

Although cross-reactivity to self-antigens or polyreactivity is strongly selected against during B-cell development, it is a common serologic feature of certain infections in humans, including HIV, Epstein-Barr virus and hepatitis C virus. Seventy-five percent of the 134 monoclonal anti-HIV-gp140 antibodies cloned from six patients with high titres of neutralizing antibodies are polyreactive. Despite the low affinity of the polyreactive combining site, heteroligation demonstrably increases the apparent affinity of polyreactive antibodies to HIV.

11:35 Screening and Characterization of Fully Human Antibodies from Velocimmune® Mice using Real-Time Label-Free Interaction Analysis

Matthew C. Blome, Ph.D., Scientist, Therapeutic Proteins,

Regeneron Pharmaceuticals, Inc.During antibody development, generation of high quality binding interaction data is essential for identifying antibodies with potential therapeutic use. However, many challenges can occur throughout the screening and characterization phase of development. Such challenges include the analyses of target antigen proteins with a propensity for nonspecific binding and the analyses of large numbers of unpurified antibody supernatant samples. This presentation will discuss how different label-free interaction analysis platforms are used to overcome these various challenges and how they can facilitate the identification and characterization of potential therapeutic antibodies.

12:05 pm End of Conference

MAY 12-13 | DISCOVERY STREAM
ANTIBODY OPTIMIZATION

THURSDAY, MAY 12

12:00 pm Registration

EARLY PLANNING FOR LATER SUCCESS

1:30 Chairperson's Opening Remarks

1:40 Correlating Biophysical and ADME Properties of a Protein Conjugated to Linear or Branched PEG

Yulia Vugmeyster, Principal Research Scientist, Pharmacokinetics, Dynamcs, and Metabolism, Pfizer

Modulation of pharmacokinetics (PK) profiles of therapeutic proteins by conjugation of polyethylene glycol (PEG) is widely used in the biopharmaceutical industry. We studied the effects that PEG structure and the conformation of the resulting conjugates have on the PK profile of a PEGylated protein. A therapeutic protein was conjugated to linear or two different type of branched PEGs of the same MW. Biophysical, biochemical, and ADME properties (in rodents and primates) were evaluated for all combinations of the protein-PEG conjugate. Correlation between the biopshysical and ADME profiles and species differences are discussed.

2:10 A Germline Knowledge-Based Computational Approach for Determining Antibody Complementarity Determining Regions

Shanrong Zhao, Ph.D., Researcher, In Silico Informatics, Centocor Discovery Research

Determination of complementarity determining regions (CDRs) in an antibody is essential for antibody engineering and optimization. Based upon the mapping between a mature antibody and its corresponding germline gene segments, a computational algorithm was developed for automatic determination of CDRs. The algorithm has been proven to be very fast, robust, and has been recently extended into *in silico* antibody engineering.

2:40 A Standardized Platform for Antibody Characterization

Sponsored by BIO-RAD

James P. Carney, Ph.D. Research Biologist, US Army

2:55 Applying Tag-lite® to Therapeutic Antibodies Screening and Characterization: A Review of Recent Findings

Sponsored by cisbio

Stéphane Martinez, Tag-lite® Product Manager, Cisbio Bioassays

GPCRs and other cell surface receptors such as RTKs are privileged targets in small molecule and biotherapeutic screening. The optimization of Tag-lite® technology platform, a combination of HTRF® and self-labeling technologies for the study of cell surface biomolecule interactions, has recently boosted the way a large number of assay configurations could be set up for investigating receptor biology and pharmacology under multiple angles. This presentation will detail a number of cases studies for antibody screening and characterization, assessed through ligand binding assays, and receptor function.

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

4:00 Problem Solving Breakout Sessions

Concurrent Problem Solving Breakouts are interactive sessions hosted by a moderator to discuss a topic in depth. They are open to all attendees, sponsors, exhibitors, and speakers and provide a forum for discussing key issues and meeting potential partners. *Please pick a topic of your choice and join in.*

5:00 Close of Day

FRIDAY, MAY 13

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

LOOKING TO THE FUTURE

8:30 Chairperson's Opening Remarks

8:35 DARPins: Therapeutic Proteins Beyond Antibodies

H. Kaspar Binz, Ph.D., Vice President, Technology & Co-Founder, Research & Development, Molecular Partners

The DARPins platform allows generation of novel therapeutic candidates beyond what is possible with antibodies or antibody fragments. Affinity, specificity, PK and payloads can be engineered at will to create drugs that comply with very ambitious target product profiles. This process will be highlighted and illustrated with different examples. In addition, the latest clinical data on MP0112, a VEGF-antagonistic DARPin with best-in-class drug potential for the treatment of ocular neovascularization diseases will be presented.

9:05 Antibody Recycling by Engineered pH-Dependent Antigen Binding Improves the Duration of Antigen Neutralization

Tomoyuki Igawa, Researcher, Genome Antibody Research Product Department, Chugai Pharmaceutical Co., Ltd.

Anti-IL6 receptor antibody, Actemra, was engineered to bind to IL-6 receptor pH dependently. This pH dependent binding variant bound to IL-6 receptor in plasma but dissociates from Il-6 receptor within acidic endosome, which would enable recyling of free antibody to the plasma. This pH dependent binding variant exhibited significantly improved pharmacokinetics and duration of IL-6 receptor neutralization compared to Actemra and Actemra variant with increased FcRn binding and affinity maturation to IL-6 receptor. pH dependent binding technology enabled generation of second generation Actemra, and can also be applied to other antibodies targeting various antigens to generate long-acting antibodies.

9:35 Biointeraction Analysis by High-Performance Affinity Chromatography: Kinetic Studies of Immobilized Antibodies

David S. Hage, Professor, Chemistry Department, University of Nebraska

A system based on high-performance affinity chromatography was developed for characterizing the binding, elution and regeneration kinetics of immobilized antibodies. This information was provided by using a combination of the frontal analysis, split-peak analysis and peak decay analysis methods and was tested using immunoaffinity supports that contained monoclonal antibodies for 2,4-dichlorophenoxyacetic acid (2,4-D) and related compounds.

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

THE MANY FACETS OF OPTIMIZATION

11:05 Comprehensive Epitope Mapping with Amino Acid Resolution

Volker Stadler, Ph.D., CEO, Management Board, PEPperPRINT GmbH

Based on a new platform technology, we are able to provide custom peptide microarrays in a uniquely fast and cost effective manner. These microarrays are used for the comprehensive characterization of mono- and polyclonal antibody responses with amino acid resolution. Unrivaled spot densities with more than 1,000 peptides per square centimeter considerably reduce the sample consumption to finally elucidate antibody responses on the molecular level.

11:35 SnugDock: Paratope Structural Optimization During Antibody-Antigen Docking Compensates for Errors in Antibody Homology Models

Aroop Sircar, Ph.D., Post Doc. Computational Scientist-Antibody Design, Protein Engineering & Antibody Technologies (P.E.A.T.), EMD Serono Research Institute, Inc.

Local docking using SnugDock with the lowest-energy Rosetta Antibody homology model produced more accurate predictions than standard rigid-body docking. SnugDock can be combined with ensemble docking to mimic conformer selection and induced fit resulting in increased sampling of diverse antibody conformations. The combined algorithm produced four medium (Critical Assessment of rediction of Interactions-CAPRI rating) and seven acceptable lowest-interface-energy predictions in a test set of fifteen complexes. Structural analysis shows that diverse paratope conformations are sampled, but docked paratope backbones are not necessarily closer to the crystal structure conformations than the starting homology models. The accuracy of SnugDock predictions suggests a new genre of general docking algorithms with flexible binding interfaces targeted towards making homology models useful for further high-resolution predictions.

12:05 Exploiting Nanobody® Advantages to Target Challenging Proteins: from Discovery to in vivo Proof-of-Concept for an anti-CXCR4 Nanobody

Hilde Revets, Senior Research Fellow, Ablynx

Nanobodies are therapeutic proteins based on the smallest functional fragments of heavy-chain only antibodies. These stable, naturally evolved single-domain binding structures can target less accessible epitopes and can be formatted into highly potent drug candidates for challenging targets including GPCRs and ion channels. Here we describe the isolation of two highly selective monovalent Nanobodies, 238D2 and 238D4, against the chemokine receptor CXCR4 by using whole cell immunization, phage display, and counter selection method including the use of lipoparticles (Integral Molecular). Epitope mapping using the Shotgun Mutagenesis technology platform from Integral Molecular showed that the Nanobodies bind to distinct but partially overlapping sites in the extracellular loops. Short peptide linkage of the Nanobodies resulted in significantly increased potency and affinity and this biparatopic Nanobody effectively induced the mobilization of CD34+ stem cells in cynomolgus monkey.

12:35 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:05 Break

CUTTING EDGE CASE STUDIES

1:25 Chairperson's Remarks

1:30 Fc Optimization – A Pre-Clinical and Clinical Update

Greg A. Lazar, Ph.D., Associate Director, Protein Engineering, Xencor, Inc.
Fc engineering has moved from theoretical promise to therapeutic reality. We have advanced a pipeline of optimized antibodies and Fc fusions tuned for improved pharmacologic properties. *In vitro,* pre-clinical, and clinical data support the developability, safety, and activity of these next generation biologics.

2:00 SComputational Design of Proteins Targeting the Conserved Stem region of Influenza Hemagglutinin

Timothy Whitehead, Ph.D., Senior Fellow, Department of Biochemistry, University of Washington

Computational methods were used to design two proteins that bind a neutralizing epitope of the influenza hemagglutinin (HA) from the 1918 H1N1 pandemic virus. After affinity maturation, two of the designed proteins bind H1 and H5 HAs with low-nanomolar affinity. The crystal structure of one design in complex with 1918/H1 HA revealed that the actual binding interface is nearly identical to that in the computational design model. Such designed proteins may be useful for both diagnostics and therapeutics.**2:30 Refreshment Break**

3:00 Engineering Host Cell Lines to Reduce Terminal Sialylation of Secreted Antibodies

Michael F. Naso, Ph.D., Biologics Research, Centocor Research and Development, Inc.

3:30 Site-Directed Mutagenesis for Improving Biophysical Properties of VH Domains

Jamshid Tanha, Ph.D., Institute for Biological Sciences, National Research Council of Canada
The variable domains of camelid heavy chain antibodies (VHHs) provide an attractive therapeutic option due to their high stability in the gastrointestinal tract environment. I will present the isolation and characterization of toxin-specific VHHs as well as their mutant versions with improved gastrointestinal tract stability. With favorable characteristics such as high production yield, potent toxin neutralization and intrinsic stability, the aforementioned VHHs are attractive systemic therapeutics.

4:00 End of Conference

MAY 9-10 | EXPRESSION STREAM

DIFFICULT TO EXPRESS PROTEINS

SUNDAY, MAY 8

4:00 - 6:00 pm Main Conference Registration

MONDAY, MAY 9

7:00 am Registration and Morning Coffee

HITTING THE GROUND RUNNING

8:30 Chairperson's Opening Remarks

» **OPENING KEYNOTE PRESENTAION**
8:40 Novel Tools for the Overexpression of Transport Proteins

Raimund Dutzler, Ph.D., Professor, Biochemistry, University of Zurich
The recent success in the structure determination of membrane proteins is tied to the possibility to characterize large numbers of homologues of a particular protein family in different expression systems to identify candidates with superior biochemical properties. I will discuss a novel tool that allows the rapid generation of expression constructs for all common pro- and eukaryotic expression systems and discuss its application to different ion transport families.

9:10 The Importance of Characterization in Successful Protein Production

Jeff Culp, Ph.D., Associate Research Fellow, Primary Pharmacology Group, Pfizer Research and Development
It is much easier to express a protein than it is to produce a fully functional protein for use in Drug Discovery. Specific examples will be described of the importance of proper protein charaterization to eliminate potential mistakes. Guidlines will be suggested to aid the protein production specialist. Examples will include proteins intended for use in target screens, NMR, protein crystallization and biophysical characterization.

9:40 Refolding, Purification, and Characterization of the Ectodomain Complex of the CGRP Receptor

Norzehan Abdul-Menan, Ph.D., Senior Staff Investigator, Structural Biology, Vertex Pharmaceuticals, Inc.
The calcitonin gene-related peptide receptor is a heterodimer of two membrane proteins: calcitonin receptor-like receptor (CLR) and receptor activity-modifying protein 1 (RAMP1). CLR is a class B G-protein-coupled receptor, possessing a large N-terminal extracellular domain (ECD) for ligand recognition and binding. Heterodimerization of CLR with RAMP1 provides specificity for CGRP peptide. The expression, purification, and refolding of the heterodimer of the ectodomain from inclusion bodies will be presented. The refolded complex forms a stable, monodisperse complex and is competent to bind ligands.

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

11:10 Integrated Upstream and Downstream Optimization as the Key for the Development of Complex Biologics

Michaela Wendeler, Ph.D., Scientist I, Biopharmaceutical Development, MedImmune
For complex biotherapeutics with extensive posttranslational modifications, changes in upstream process conditions can significantly impact product quality and alter requirements for downstream processing. This case study illustrates the challenges of understanding and controlling the impact of process conditions on protein attributes and demonstrates the course of integrated upstream and downstream development that led to the successful implementation of a robust manufacturing process.

11:40 Poster Spotlight Presentation

Sponsored by DNA 2.0

12:10 pm Advancing Synthetic Gene Design for Optimal Protein Expression

Mark Welch, Ph.D., Director, Gene Design, DNA2.0, Inc.
Advances in gene design and synthesis have enabled greater insight into the workings of the genetic code. This includes how changes in gene sequences can impact the expression of encoded proteins through mechanisms including codon bias, mRNA stability, and translation initiation. Natural gene sequences have been shaped in response to many different evolutionary pressures, but are rarely optimal for "biotechnological fitness". Here we present how gene design variables such as codon choice and mRNA structure predictably affect the yield of heterologous protein expression, often by up to orders of magnitude increase in expression levels. Host systems validated include mammalian cell lines (CHO/HEK293), yeast (S.cerevisiae/P.pastoris/K.lactis),E.coli and more.

12:25 Sponsored Presentation (Opportunity Available)

12:40 Luncheon Presentation I

Sponsored by Thermo SCIENTIFIC

High-Yield *in vitro* Protein Expression System for Functional Protein Synthesis using Immortalized Human Cell Lines

Penny Jensen, Ph.D., Research Scientist, Proteomics Research and Development, Thermo Fisher Scientific

Culturing of mammalian cells for the purpose of protein expression is a time consuming and expensive process. An effective alternative is cell-free expression (i.e., *in vitro* translation) using extracts prepared from mammalian cells. Several immortalized human cell lines, including HeLa, HuH7, and HEK293 have been used to prepare translationally competent extracts. These results along with information regarding our optimized *in vitro* expression system based on HeLa extracts for producing several hundred micrograms of recombinant protein per ml of reaction, expression of multiple proteins in a single reaction, and high-throughput compatibility of our system will be discussed.

1:10 Luncheon Presentation II (Sponsorship Opportunity Available) or Lunch on Your Own

1:40 Break

MEMBRANE PROTEINS AND OTHER BEASTS

2:00 Chairperson's Remarks

2:05 Expression and Purification of Membrane Protein Diacylglycerol Acyltransferase

Heping Cao, Ph.D., Principal Research Scientist, Southern Regional Research Center, US Department of Agriculture

DGAT knockout mice are resistant to diet-induced obesity and lack milk secretion. DGAT genes have been isolated from many organisms, but progress in characterization of the enzymes has been slow because DGATs are membrane-associated and difficult to express and purify. We developed a procedure for full-length DGAT expression in *E. coli* and yeast. This study represents the first description of a procedure for producing full-length recombinant DGAT protein from any species using an *E. coli* expression system.

2:35 Recent Progress in Production of Human Membrane Protein Targets and Use in Drug Discovery

Niek Dekker, Ph.D., Principal Scientist, Discovery Enabling Capabilities & Sciences, AstraZeneca R&D Molndal

Results will be presented on the expression of human ion channels in various eukaryotic expression systems. Total protein expression levels have been analyzed using Western blotting and radio-ligand binding. Target localization has been analyzed using confocal microscopy, and functional properties have been studied using electrophysiology. The combined approaches provided good insight in quality of produced targets in the various expression systems. The successful mg-scale production of a human ligand-gated ion channel will be presented including biophysical verification of ligand-binding properties using circular dichroism and isothermal titration calorimetry. Progress on crystallization of this target and ongoing engineering efforts will be presented. In addition, examples of production of other membrane proteins including GPCRs will be discussed.

3:05 Refreshment Break in Exhibit Hall with Poster Viewing

3:45 A Sensitive Fluorescent Method for Rapidly Identifying and Characterizing Lead Membrane Protein Constructs

Christopher Koth, Ph.D., Scientist, Structural Biology, Genentech, Inc.

A number of features of membrane proteins render them challenging targets for the structural biologist, among which the most important is the difficulty in obtaining sufficient quantities of properly folded and homogeneous protein. To address this, we have developed a simple, high-throughput procedure to rapidly characterize and optimize membrane protein solubility, homogeneity and aggregation state in various buffers/detergents. This method has aided in the purification of several membrane protein targets including GPCRs and ion channels.

4:15 From Clones to Crystals on a Shoestring Budget

Jian Payandeh, Ph.D., Pharmacology, University of Washington

The success of a membrane protein structural biology project may warrant a "try everything" approach, but this is seldom feasible. I will describe practical aspects to achieving high-level expression and sample homogeneity in a standard laboratory setting. Key considerations in devising a streamlined and cost-effective screen will be highlighted, and examples from our current structural biology efforts will be detailed.

4:45 Problem Solving Breakout Sessions

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5:45 - 6:45 Reception in the Exhibit Hall with Poster Viewing

TUESDAY, MAY 10

8:00 am Morning Coffee

THE TOOLS FOR SUCCESS

8:25 Chairperson's Remarks

Geoffrey S. Waldo, Ph.D., Bioscience Division, Los Alamos National Laboratory

8:30 The Use of the Improved *E. coli* Cell-Free Protein Synthesis for Structural Biology

Takanori Kigawa, Ph.D., Team Leader, Protein Preparation Team, RIKEN Systems and Structural Biology Center

We have been developing and using *E. coli* cell extract-based cell-free system. Our developments improved the efficiency, productivity, and throughput of our system, enabling us to use the system as one of the standard expression methods. We have determined more than 200 X-ray structures and 1,300 NMR structures of proteins/protein domains using our system as the protein production method.

9:00 Optimization of *in vitro* High-Throughput Chemical Lysis of *Escherichia coli*

Geoffrey S. Waldo, Ph.D., Bioscience Division, Los Alamos National Laboratory

9:30 Production of Multifunctional Chimaeric Enzymes in Plants: A Promising Approach for Degrading Plant Cell Wall from Within

Ling Yuan, Ph.D., Associate Professor, Plant & Soil Sciences, Univ. of Kentucky

Biological processing of biomass requires a large number of ligno-cellulolytic enzymes that are expensive to produce at industrial scales. We address this hindrance by creating multidomain, multifunctional single enzymes and producing these novel proteins in plants. The advantages of this approach include cost reduction in enzyme production, ease in vector construction and plant transformation, and improved biomass feedstock digestibility.

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

10:45 Fine Tuning HIV-1 Envelope Glycoprotein Expression for Pre-Clinical Immunogen Testing

George Sellhorn, Ph.D., Staff Scientist, Viral Vaccines, Seattle Biomedical Research Institute

The HIV-1 Envelope (Env) glycoprotein is a heavily glycosylated trimer of two non-covalently associated heterodimeric subunits and is the sole target on anti-HIV-1 for neutralizing antibodies. High-throughput production of soluble, recombinant versions of Env for pre-clinical comparative evaluation faces several challenges including: inherently low expression levels, heterogeneity in glycosylation, weak inter-subunit association and aggregation. Here we discuss recent improvements in Env production and purification.

11:15 Galectin-1 as a Fusion Partner for the Production of Soluble and Folded Human Beta-1,4-glycosyltransferase-T7 in *E. coli*

Pradman K. Qasba, Ph.D., Chief, Structural Glycobiology Section, SAIC-Frederick, Inc., Ctr for Cancer Research Nanobiology Program, NCI-Frederick

Galectin-1 as a fusion partner for the production of soluble and folded glycosyltransferases in *E. coli*. The expression of recombinant glycosyltransferases in *E. coli* often produces aggregated proteins known as

inclusion bodies. We show that Galectin-1, which binds a beta-galactoside or a hydrophobic protein sequence, can be used as a fusion partner to produce several recombinant glycosyltransferases as soluble folded fusion proteins in *E. coli.*

11:45 Co-Expression of Proteins in Bacteria: Application to the Production of Soluble Core Histone Protein Complexes and Beyond

Robert N. Dutnall, Ph.D., Assistant Professor, Chemistry & Biochemistry, Sect. of Molecular Biology, Div of Biological Sciences, University of San Diego
Co-expression is a viable strategy for producing multiprotein complexes for biochemical and biophysical studies that has several advantages over expressing components individually. We have used co-expression to produce soluble core histone complexes in bacteria that can be purified by simple chromatographic techniques, facilitating studies of chromatin structure and transcription regulatory proteins. We describe strategies to create expression plasmids to produce two or more proteins in various combinations for optimal complex production, solubility or activity.

12:15 pm Expression of an Antibody Fragment Utilizing the Pfenex Expression Technology Platform

Georg Klima, Ph.D., Head Process Science Microbial, Boehringer Ingelheim Biopharmaceuticals
This case study will describe how the Pfenex Expression Technology™ platform was applied to rapidly screen and identify an optimal production strain and fermentation process for a proprietary antibody fragment (Fab). Data comparing expression results between Pfenex Expression Technology and other hosts will be presented.

12:45 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

CREATIVE PROBLEM-SOLVING

2:00 Chairperson's Remarks

2:05 Production of Novel Proteins Therapeutics for Cancer Treatment

Sayed Goda, Ph.D., Director, Research and Training, Shafallah Medical Genetics Center
This work shows for the first time the production of an enzyme is commonly used for cancer treatment that is much more efficient than the wild type one. The work also includes the isolation and molecular characterization of a natural new form of the enzyme. The two forms of the enzyme would solve many of the problems facing ADEPT techniques for cancer treatment.

2:35 Incorporation of Unnatural Amino Acids into Viral Proteins

Sabrina Lusvarghi, Ph.D., Researcher, HIV Drug Resistance Program, National Cancer Institute, NCI-Frederick
Incorporation of unnatural amino acids with unique biophysical properties into proteins has emerged as an important tool in chemical biology. In particular, our group has used different strategies for the insertion of a variety of unnatural amino acids into viral proteins. Methods of incorporation, as well as application of different non-natural analogs, will be described in this presentation.

Sponsored by
integral

3:05 Production and Epitope Mapping of Antibodies Targeting Membrane Proteins

Benjamin Doranz, Ph.D., President and CSO, Integral Molecular, Inc.
Lipoparticles containing high concentrations of structurally-intact GPCRs, ion channels, transporters, and oligomeric proteins have been used to generate high titer serum responses (>1:1000) against these conformationally complex proteins. Upon mAb isolation, Shotgun Mutagenesis Epitope Mapping has been used to identify conformational epitopes on structurally diverse proteins, including GPCRs and viral Envelope proteins, by mapping their interactions with mAbs directly within cells in the proteins' native structures.

3:35 Refreshment Break in Exhibit Hall with Poster Viewing

4:15 Poster Spotlight Presentation

4:45 Co-Expression of Ferrochelatase Allows for Complete Heme Incorporation into Recombinant Proteins Produced in *E. coli*

Brian R. Crane, Ph.D., Assistant Professor, Chemistry and Chemical Biology, Cornell University
We have determined that recombinant proteins expressed in *E. coli* often contain less than a full complement of heme because they rather are partially incorporated with free-baseporphyrin. Porphyrin-incorporated proteins have similar spectral characteristics as the desired heme-loaded targets, and thus are difficult to detect, even in purified samples. We present a straightforward and inexpensive solution to this problem that involves the co-expression of native ferrochelatase with the protein of interest. The method is shown to be effective for proteins that contain either Cys- or His-ligated hemes.

5:15 End of Conference

OPTIMIZING PROTEIN EXPRESSION

WEDNESDAY, MAY 11

7:00 am Registration and Morning Coffee

CHO & MAMMALIAN EXPRESSION SYSTEMS

8:30 Chairperson's Opening Remarks

» 8:40 OPENING KEYNOTE PRESENTATION:

Protein Expression in Drug Discovery – New Challenges, New Solutions

Lorenz M. Mayr, Ph.D., Executive Director, Unit Head Biology, Protease Platform, Novartis Pharma AG

Success in drug discovery relies not only the appropriate selection of molecular targets, but also on the availability of high-quality recombinant protein and cell lines in sufficient amounts and on short time. Whereas protein expression has long been viewed as a mature science with no need for further improvement, current trends in drug discovery show an increased demand for fast & efficient production systems for recombinant proteins and protein complexes to cope with the demands for protein in sufficient amounts needed for modern hit discovery (HTS, FBS, structure) and lead optimization in discovery research.

» 9:25 FEATURED PRESENTATION:

High-Level Recombinant Protein Production in CHO Cells Using Lentiviral Vectors and the Cumate Gene-Switch

Bernard Massie, Ph.D., Director, Bioprocess Center, Institute of Research and Biotechnology, Research Council of Canada; President, l'Association de Thérapie Génique du Québec (ATGQ)

Fast and efficient production of recombinant proteins for structural and functional studies is a crucial issue for research and for industry. To this end, we have developed an efficient system to generate, in less than 6 weeks, pools of CHO cells stably expressing high-level of recombinant proteins (>100 mg/L). This system takes advantage of the efficient gene delivery of lentiviral vectors (LVs) in highly active transcription sites, coupled with the powerful cumate-regulated promoter that, not only allow for inducible gene expression, but is also 8-fold stronger in CHO cells than the optimized CMV5 promoter.

9:55 Transient Expression of an IL-23R Extracellular Domain Fc Fusion Protein in CHO vs. HEK Cells Results in Improved Plasma Exposure

John Trauger, Ph.D., Group Leader, Genomics Institute of the Novartis Research Foundation

We found that the plasma exposure in mice of an IL-23R extracellular domain Fc fusion protein (IL23R-Fc) was improved about 30-fold when the protein was prepared by transient transfection of CHO vs. HEK cells. Characterization of the CHO- and HEK-expressed IL23R-Fc proteins indicated that the difference in their *in vivo* plasma exposure is due to differential glycosylation.

10:25 Coffee Break in the Exhibit Hall with Poster Viewing

USING microRNAs TO ENHANCE PROTEIN EXPRESSION IN CHO

11:10 microRNAs: New Tools to Manipulate Protein Expression in CHO Cells

Niall Barron, Ph.D., Program Leader, Mammalian Cell Engineering, National Institute for Cellular Biotechnology, Dublin City University

The ability of miRNAs to influence protein expression is now recognized as a fundamental layer of regulation within the cell. We will provide a brief overview of their biogenesis, genomic organization and mode of action, and then go on to describe some of the approaches we have taken to examine their potential application in the bioprocessing area, with particular emphasis on CHO cell engineering.

11:40 mRNA Stability and Antibody Production in CHO Cells: Improvement through Gene Optimization

Shuangping Shi, Ph.D., Associate Principal Scientist, Bioprocess Development, Merck Research Lab, Merck & Co.

Gene optimization substantially enhances antibody production in Chinese hamster ovary (CHO) cells. When gene optimization was applied to the heavy and light chain genes of a therapeutic antibody, we observed increased antibody production in transient transfection as well as in stable clones. It is also demonstrated that elevated heavy chain mRNA level was associated with the increase of antibody production. Further analysis suggests that the increased antibody expression is attributable to enhanced mRNA stability resulting from gene optimization.

12:10 pm Luncheon Presentation I

Sponsored by ICOSAGEN CELL FACTORY

Fast, Simple and Efficient Method for Production of Biologics using Stable Extrachromosomal Expression System

Mart Ustav, Ph.D., Founder and CEO, Icosagen Cell Factory Ltd

Icosagen Cell Factory has developed efficient technological platform (QMCF Technology) for production of various recombinant proteins, antibodies and VLPs in mammalian (CHO or 293) cell system. Main goal of QMCF technology is stable maintenance and replication of appropriate expression plasmid, fast and feasible upscale and generation of production cell banks.

12:40 pm Key Aspects of Managing Early Phase Development Programs for Long Term Success

Sponsored by FUJIFILM Diosynth

George Koch, CSO, Fujifilm Diosynth Biotechnologies

Highlight several CMC best practices for preclinical activities. From selection of a cell line to release of the first clinical batch, product and process developers make decisions that have timeline, financial, and regulatory consequences.

1:10 Break

ESCHERICHIA COLI & CLONAL CELL PRODUCTION

1:30 Chairperson's Remarks

1:35 Production of Antibody Mixtures and Bispecifics from Single Clonal Cells

John de Kruif, Ph.D., CSO, Merus Biopharmaceuticals BV

Pre-clinical and clinical studies demonstrate that mixtures of antibodies (mAbs) and bispecific mAbs represent next-generation biopharmaceuticals with improved specificity and efficacy. We have approached the manufacturing complexity of producing and developing these formats by using human mAbs that share the same identical germline-encoded light chain ('single VL'). Transfection of cells with genetic constructs encoding 2 or 3 different 'single VL' mAbs results in the production of bispecific antibodies or mixtures of antibodies by clonal cells. Clonal cell lines show stable expression and high production levels for all mAb specificities even after > 60 passage doublings and show growth characteristics consistent with conventional mAb production cell lines. We show that native mass spectrometry-based analytical methods allow quantitative measurement of all antibody species in a complex mixture and that cation exchange chromatography can be used to efficiently separate bispecifics from the parental mAbs. This technology facilitates the pharmaceutical production of next generation therapeutic antibodies based on intact IgG molecules.

2:05 Optimization of Protein Expression in *E. coli:* Best Practices and Unusual Tricks for the Production of Protein

Suitable for Structural Studies

Rebecca Page, Ph.D., Assistant Professor, Biology and Principal Investigator, Molecular Biology & Cell Biology & Biochemistry, Brown University
I will be presenting both best practices and unusual ('last ditch') methods that are used to successfully express both prokaryotic and eukaryotic proteins in *E. coli*. Topics to be covered include: solubility tags, purification tags, chaperones and *in vivo* refolding, soluble expression through protein co-expression, and toxins and eukaryotic kinases.

2:35 Automated Microfludic Analysis for Enhanced Optimization of Recombinant Protein Expression Platforms

Sponsored by Caliper LifeSciences

Mark Roskey, Ph.D., Senior Vice President, Applied Biology R&D, Caliper Life Sciences
This talk will focus on the use of high throughput microfludics based electrophoretic analysis for cell culture optimization and clone selection. Applications discussed will include construct selection, factorial experiment design, analysis of antibody yield and purity, and glycan analysis.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

3:50 Strategies for the Use of *E.coli* as an Expression Host for Challenging Proteins

Bingyuan Wu, Ph.D., Research Scientist, Molecular & Protein Biosciences, Centocor R&D, Inc.
Escherichia coli has been a workhorse for recombinant protein expression due to its well-studied biology, fast growth, and high expression level. However, the expression of mammalian proteins in *E. coli* often turns out to be challenging. Here a few case studies will be presented on obtaining those difficult proteins using *E. coli* as an expression host.

4:20 The Challenges and Opportunities for Heterologous Reconstitution of Polyketide and Isoprenoid Natural Product Pathways through *E.coli*

Blaine Pfeifer, Ph.D., Assistant Professor, Chemical and Biological Engineering, Tufts University
Polyketide and isoprenoid natural products display an impressive therapeutic range that has provided a strong motivation for new technologies to better access this medicinal potential. Equally motivating are the technical challenges associated with production processes reliant on the native host systems responsible for most polyketide and isoprenoid compounds. As a result, heterologous biosynthesis has gained noticeable traction over the last 15 years as a viable route to clinically-relevant natural products. This talk will feature recent successful examples of polyketide and isoprenoid natural products produced heterologously through *E. coli*. Emphasis will be placed on the technical challenges and strategies associated with functional gene transfer and expression within this alternative host.

4:50 Reception in the Exhibit Hall with Poster Viewing

6:00 End of Day

THURSDAY, MAY 12

8:00 am Morning Coffee

YEAST

8:30 Chairperson's Remarks

8:35 The Power of Yeast for Protein Expression

Christine Lang, Ph.D., Professor, Institute for Microbiology and Genetics, Institute of Biotechnology, Technical University of Berlin
Both yeasts *Saccharomyces cerevisiae* and *Pichia pastoris* are widely recognized and used as robust hosts for recombinant protein expression. These systems are well suited for parallel cloning and expression, and we have used yeast in a comparative expression study of mammalian cDNAs in structural genomics projects. Both yeasts proved to be reliable hosts giving overall expression success rates of 50 – 60% of cDNAs tested. Using different host systems in parallel and varying affinity tags for isolation, bottlenecks in the expression and production of sufficient amounts of soluble proteins can be overcome.

9:05 Yeast-Based Antibody Discovery Platform Enables the Selection of High Expressing Monoclonal Antibodies

Piotr Bobrowicz, Ph.D., Associate Director, Technology & Platform Development, Adimab, Inc.
Adimab has developed a yeast-based antibody discovery platform. The technology inherently isolates antibodies that express well because antibody expression in eukaryotic organism is part of the selection process. Identification of high expressing IgGs at a very early stage ultimately reduces the time and cost to develop antibody therapeutics.

9:35 Production of Recombinant Proteins in the Methylotrophic Yeast *Pichia pastoris*

James M. Cregg, Ph.D., Research Professor, Keck Graduate Institute of Applied Life Science
As systems for the production of recombinant proteins, yeasts combine the growth and genetic manipulation advantages of bacteria with the ability to perform important post-translational modifications such as proper folding, proteolytic processing, disulfide bridge formation and glycosylation. *Pichia pastoris* expression strains are easy to scale up from shake-flask cultures to large-volume fermenter cultures growing at cell densities of greater than 100 grams/liter, dry cell weight. The *P. pastoris* system is particularly valued for its ability to secrete recombinant proteins. Since the organism secretes only low levels of native proteins, the recombinant protein is often the major protein species in the medium.

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

BACULOVIRUS & INSECT CELLS

11:05 The Baculovirus-Insect Cell Expression System: An Overview and Update

Donald L. Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming
The baculovirus-insect cell system is now well established as a tool for recombinant protein production. This presentation will include a description of this system and its relative strengths and weaknesses. In addition, it will include a discussion of recent developments facilitating the isolation of recombinant baculovirus expression vectors and efforts to humanize protein glycosylation pathways in the lepidopteran insect cell lines that serve as hosts for these vectors.

11:35 Insect Cells for Cytokine Production and Stem Cell Mediated Gene Therapy Applications

Satya Prakash, Ph.D., Professor, Biomedical Engineering, McGill University
Recombinant proteins produced in insect cell systems are useful in molecular biology research and in production of specialized proteins and other applications. Insect cells have been used to produce recombinant protein productions using the BEVS (baculovirus expression vector system) and other systems. Recently we have shown their prospects in excellent expression of therapeutic proteins. Here we discuss the application of this system in producing human interleukin-7, a cytokine protein that may become a valuable supplementary agent for immunotherapeutic treatments in patients with HIV infection, immunodeficiency and other diseases. In addition, we will introduce a new concept of using insect cells in stem cell-mediated gene therapy applications using polymeric membrane microcapsules.

12:05 pm End of Conference

PURIFYING ANTIBODIES

THURSDAY, MAY 12

12:00 pm Registration

PURIFICATION STRATEGIES

1:30 Chairperson's Opening Remarks

» 1:40 OPENING KEYNOTE PRESENTATION:

Can the Antibody Purification Platform be Improved?

Douglas Cecchini, Ph.D., Director, Technical Development, Biogen Idec, Inc.
In recent years, technological development for the purification of monoclonal antibodies and Fc fusion proteins has, to some extent, reached a plateau. However, new challenges posed by highly productive cell culture processes, the increasing demands on multi-product manufacturing facilities, and the Quality by Design initiative would benefit from further improvements to purification technologies. A number of innovative approaches that address these challenges will be presented.

» 2:10 FEATURED PRESENTATION:

Purification of Antibody Fragments and Alternative Protein Scaffolds using the Strep-Tag, the His-Tag and Other Affinity Tags

Arne Skerra, Ph.D., Professor, Biological Chemistry, Technical University of Munich
The quick purification of recombinant proteins under standardized conditions is crucial for their functional optimization, in particular during biological drug discovery and development. While many affinity tags have been proposed over the years, only few offer the beneficial features of high purification efficiency, re-use of the affinity matrix, native elution and minimal interference with protein structure and function. A survey of established affinity tags and some case studies of Fab fragments, Anticalins and PASylated biologicals will be presented.

Sponsored by Semba Biosciences

2:40 Continuous mAb Purification using Simulated Moving Bed: Taking the Chromatography Platform to the Next Level

Alla Zilberman, Ph.D., Director, Applications, Semba Biosciences, Inc.
Chromatography as a bioprocessing platform has not kept pace with the demand for higher flexibility, higher productivity and lower costs in the purification of protein A based pharmaceuticals. Continuous multicolumn protein separations through simulated moving bed chromatography elevate the chromatographic platform by conversion of the conventional batch process to a continuous process. Several purification methods including the "industry-standard" Protein A and size exclusion chromatography can be performed continuously on an automated bench top Octave™ Chromatography System. The results demonstrate more efficient use of chromatography media, reduced resin and buffer consumption, and higher throughput, making continuous chromatography an improved alternative to single column methods.

2:55 Sponsored Presentation (Opportunity Available)

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

4:00 Options for the Production and Purification of Fab Antibody Fragments

Gavin Wild, Ph.D., Senior Scientist, Antibody Biology, UCB New Medicines
Antibody fragments such as Fab offer a structurally simply and physically robust format for therapeutic candidates. The purification and subsequent conjugation of antibody fragments at scale bring several challenges which must be overcome. A number of options for robust, efficient, and scalable processes have been developed by exploitation of the target molecule properties, combined with a range of chromatography matrices. Downstream purification case studies covering the harvest/extraction, primary capture and subsequent polishing steps for Fab expressed in both mammalian and E.coli systems will be presented.

4:30 mAb Downstream Filtration Development: A Platform Approach for Variable Feed Streams

Bruno Marques, Ph.D., Investigator, Biopharmaceutical Development, GlaxoSmithKline
In order to de-bottleneck high-producing monoclonal antibody (MAb) processes at the commercial scale, highly efficient, cost-effective, and predictable platform downstream unit operations are required. This paper presents the development of robust downstream filtration steps – employing depth, nano-, ultra-, and membrane filter technology – capable of scaling up to 20,000 L bioreactors with MAb titers of 3 g/L and above. By utilizing a statistical approach to experimental design, various filter fouling models, as well as high-throughput systems to alter buffer conditions, we were able to identify a combination of operating parameters and raw materials capable of processing MAbs with different biophysical properties, impurity profiles, and formulation requirements.

5:00 Close of Day

FRIDAY, MAY 13

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

INNOVATING ANTIBODY PURIFICATION

8:30 Chairperson's Remarks

8:35 Innovation in Antibody Purification: Are Old Ways Better than New?

William W. Ward, Ph.D., Associate Professor, Biochemistry & Microbiology; Director, CREBB, School of Environmental and Biological Sciences, Rutgers University
As we develop new technologies for protein purification, we sometimes overlook old methods that can be greatly improved. We have modified one of the earliest methods for purifying antibodies, ammonium sulfate precipitation, improving this method to the extent that it now out-performs affinity chromatography on Protein-A. Used to purify therapeutic monoclonal antibodies, our substitute method eliminates the need to validate total removal of Protein-A, a potentially harmful ligand that always leaches from these columns.

9:05 Purifying Antibodies from Complex Biological Milieu with Nanoparticles: Exquisite Specificity, Maximum Yield

David O'Connell, Ph.D., Senior Scientist, School of Medicine, University College Dublin
We have engineered a set of nanoparticles with well-defined biological characteristics to specifically extract immunoglobulins from complex milieu including bacterial, fungal and cell line expression systems. The retrieval process can even be applied to human serum and represents an enabling approach for bench scientists and companies alike. This cutting-edge development can easily be scaled up to industrial scale. Specific examples from each system will be shown.

9:35 Continuous Chromatography (MCSGP) for the Purification of Conventional mAbs and Next-Generation Therapeutics

Massimo Morbidelli, Ph.D., Professor, Institute of Chemical and Bioengineering, Department of Chemistry and Applied Biosciences, ETH Zurich
Continuous chromatography has been successfully applied in the large-scale production of chemical APIs for two decades, i.e. the so-called SMB-process. In the past decade, continuous chromatography has evolved and can now be

used for biomolecules purifications with the MCSGP-process. In the case studies presented here, the application and process development for a mixed-mode, a CIEX, an HIC, and an SEC step run in continuous chromatography mode is shown for mAb capture and polish applications (e.g. aggregate removal). In addition, the unique ability of the MCSGP process to purify in preparative scale mAb charge variants is shown with experimental data from Avastin, Herceptin and other conventional mAbs. The benefit of continuous MCSGP chromatography versus batch chromatography in terms of purity, yield, throughput and buffer consumption is demonstrated and the application to other next-generation therapeutics is discussed.

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

OPTIMIZING PURIFICATION PROCESSES

11:05 Development of Downstream Bioprocesses with PAT Approaches and/or QbD Concepts

Judy Chou, Ph.D., Vice President, R&D, Tanvex Biologics, Inc.

11:35 Progress in Downstream Processing of Monoclonal Antibodies: Past, Present and Future

Greg Zarbis-Papastoitsis, Ph.D., Senior Director, Protein Production & Analytical Development, Eleven Biotherapeutics

The presentation will touch on the evolution of downstream processing through the last 30 years of antibody production, starting with the low titer cell culture and traditional downstream processes, to the current intensified fermentation processes and the evolution of single use technologies. The talk will cover topics such as choice of purification technologies as well as its effects on manufacturing facilities and cost of goods.

12:05pm Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:05 Break

SCREENING INNOVATIONS TO ENHANCE ANTIBODY PURIFICATION

1:25 Chairperson's Remarks

Daniel ForcinitiDaniel Forciniti, Ph.D., Professor, Chemical and Biological Engineering Department, Missouri University of Science and Technology

1:30 Using Robotics and High Throughput Screening to Develop Early Stage Purification Processes

Paul McDonald, Associate Scientist, Early Stage Purification, Genentech, Inc.

High-throughput screening can be used to accelerate the development of purification processes for therapeutic antibodies. We have developed screens using batch binding on 96-well filter plates to evaluate the fit of antibodies to our chromatography processes. The simultaneous screening of a large number of conditions allows us to identify operating conditions for antibodies with a variety of characteristics. The screens are applied during an initial molecule assessment and during the development of off-platform antibodies. In addition, they can be applied to the development of platforms for new classes of antibodies. Case studies will be presented where high-throughput screening has accelerated the development of antibodies that represent both a good and poor fit in the purification platform.

2:00 Production and Purification of Soluble VH Domains Derived from a Naïve Human VH Library

Csaba Pazmany, Senior Scientist, Head, Throughput Production and Purification, X-Body BioSciences

We have established a robust high-throughput *E. coli* expression platform to produce soluble VH domains identified from a naïve human VH library for binding and affinity screening. A single-step purification process yields highly pure, monomeric and stable proteins for rapid lead characterization and selection. Extrinsic and intrinsic factors that may contribute to the solubility of these VH antibody fragments will be discussed.

2:30 Refreshment Break

PURIFYING ANTIBODIES FROM TRANSGENIC SOURCES

3:00 Purification of Human Antibodies Expressed in Plants using Liquid/Liquid Extraction

Daniel Forciniti, Ph.D., Professor, Chemical and Biological Engineering Department, Missouri University of Science and Technology

The use of liquid/liquid extraction for the purification of transgenic human antibodies will be discussed. The method will be illustrated by the purification of a de-glycosylated antibody expressed in corn. The effects of glycosylation on the purification strategy will also be discussed.

3:30 GMP-Compliant Production of a Full-Sized mAb in Tobacco Plants

Stephan Hellwig, Ph.D., Head, Manufacturing, Integrated Production Platforms, Fraunhofer IME

A process was developed for the production of an HIV-binding humanized full-sized monoclonal antibody in greenhouse-grown tobacco plants. The process was scaled up to 200 kg leaf biomass and clinical-grade API for topical administration. IME was one of the first players when using plants as an expression system for biopharmaceuticals was in its infancy, and one of the first to produce an API under GMP. IME holds a manufacturing license for antibodies produced in plants. The talk will highlight the special features of downstream processing from this unusual source and quality control of the purified bulk.

4:00 Strategies for Purification of Human Polyclonal Antibodies from Transgenic Bovine Plasma

Jin-an Jiao, Ph.D., Execitove Vice President, Product Development and Manufacturing, Hematech, Inc.

Hematech is developing a novel technology platform to produce human polyclonal antibodies in transgenic cattle for a wide variety of therapeutic applications, including immune deficiency, infectious diseases, cancers, and biodefense. Due to the complicated nature of the feedstock material (transgenic bovine plasma) and the product (human polyclonal antibodies), specific purification methods are required to achieve high yields and purity of polyclonal human antibodies with minimal levels of bovine impurities. We have developed unique purification methods using caprylic acid fractionation and llama VHH ligand as affinity ligands.

4:30 End of Conference

BIOPHYSICAL & BIOCHEMICAL CHARACTERIZATION OF BIOTHERAPEUTICS

SUNDAY, MAY 8

4:00 - 6:00 pm Main Conference Registration

MONDAY, MAY 9

7:00 am Registration and Morning Coffee

LATEST TOOLS FOR BIOPHARMACEUTICAL CHARACTERIZATION

8:30 Organizer's and Chairperson's Opening Remarks

Micah Lieberman, Executive Director, Conferences, Cambridge Healthtech

» 8:40 OPENING KEYNOTE PRESENTATION:

Introductory Presentation: Overview of Current Analytical Technologies in the Biopharmaceutical Characterization Field, and Where Changes are Required to Address Unmet Needs

Jennifer Nemeth, Ph.D., Principal Research Scientist, Biologics Mass Spectrometry & Allied Technologies, Centocor R&D, Inc.

There are a wide range of analytical tools for the assessment and characterization of biopharmaceuticals. Generally, a set of tools and processes are established, and the path to making changes down the line can be difficult, even in a discovery environment. Obstacles to change are not necessarily related to SOPS and regulations, but to lack of development time and hesitancy to "do something different." Here, an examination of advances in standard technologies, or a new look at little-used ones, will be provided, and proposals on how these technologies might enhance the biopharmaceutical discovery/development process will be presented.

9:10 Characterization of Heterogeneous Proteins by Ion/Ion Chemistry Coupled with Ion Mobility Mass Spectrometry

Paul Schnier, Ph.D., Principal Scientist, Molecular Structure, Amgen, Inc.

Electrospray ionization mass spectrometric (ESI-MS) analysis of heterogeneous proteins often results in complex, unresolved spectra. Here we demonstrate how ion-ion chemistry can be used to enable the analysis of heterogeneous proteins by mass spectrometry. We demonstrate how anions generated with a home built glow discharge source can be used to manipulate the charge states of ESI generated ions, greatly reducing the spectral congestion typically observed for polydisperse molecules. Additionally, we demonstrate how ion-ion chemistry can be used to selectively charge strip protonated protein ions to simplify ESI mass spectra of proteins which form extensive non-specific metal adducts.

9:40 Novel Chemical Pathways of Protein Degradation: Characterization of Products and Immunogenicity

Christian Schöneich, Ph.D., Professor, Chair, Pharmaceutical Chemistry, University of Kansas

Chemical degradation presents an important problem for the design of stable formulations of therapeutic proteins. Chemical degradation may trigger aggregation and/or fragmentation, and lead to novel epitopes on proteins, all of which may contribute to immunogenicity. Several pathways of chemical degradation are known such as hydrolytic, oxidative and photolytic pathways. This presentation will focus especially on oxidative and photolytic pathways with focus on novel reactions of peptide and protein cysteine, cystine, and methionine in both solution and the solid state, and on the characterization of the products of these pathways.

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

11:10 Relative Sensitivity of Common Biophysical Methods and Conventional Chromatographic and Functional Assays to Changes in Protein Higher Order Structure

Andrew Kosky, Ph.D., Senior Group Leader, Early Stage Pharmaceutical Development, Genentech

We have compared commonly used biophysical methods (e.g. circular dichroism and Fourier-transform infrared spectroscopy) and conventional chromatographic and functional assays to determine which types of methods are most sensitive to higher order structural changes in proteins. Our results demonstrate that commonly used biophysical techniques are often less sensitive than conventional purity and potency assays to the types of structural changes that impact protein function *(in vitro)* and overall therapeutic protein product quality.

11:40 A Platform Independent Analysis System for the Characterization of Chemical Liability in Biotherapeutics

Steven Pomerantz, Ph.D., Senior Research Scientist, Centocor R&D, Inc.

After winnowing the biochemical diversity through various characterizations and assays, a biotherapeutic development program may still be faced with several candidate molecules with equivalent affinity or bioactivity. One criterion for the selection of a lead candidate molecule is its developability, a suite of requirements to maximize the desirable chemical and biophysical attributes, and minimize potential chemical liabilities, such as post-translational modification (PTM). We have developed an MS-based system coupled with back-end quantitation and identification software for the rapid analysis of defined PTMs to enable screening of larger panels of candidate molecules to ensure maximum information availability for selection of the therapeutic lead.

12:10 pm On-line SAW-Bioaffinity-Mass Spectrometry: New Bioanalytical Application in Detection, Structure Determination and Quantification of Biomolecular Protein-Ligand Interactions from Biological Material

Michael Przybylski, Ph.D.,Professor, Chair, Laboratory of Analytical Chemistry and Biopolymer Structure Analysis, University of Konstanz, Germany

In recent years, bioaffinity analysis using biosensors such as surface plasmon resonance has become an established technique for the detection and quantification of biomolecular interactions; however, a severe limitation of biosensors is their lack of providing structure information of affinity-bound biopolymer ligands. Bioaffinity- mass spectrometry is a new, combined analytical approach for the detection, quantification, and structure determination of affinity-bound ligands. We have developed an online combination of a surface acoustic wave (SAW) biosensor with electrospray ionization mass spectrometry (SAW-ESI-MS) that enables the direct structure determination and quantification of affinitybound ligands dissociated from a protein-ligand complex on a gold chip. An interface for the coupling of SAW-biosensor chip and ESI-MS provides a sample concentration and in-situ desalting step for the MS analysis of the ligand eluate solution. First applications of the online SAW-MS combination with chip- immobilized antibody and polypeptide ligands show broad bioanalytical application to the simultaneous, label-free structure determination and quantification of biopolymer- ligand interactions, as diverse as antigen-antibody and lectincarbohydrate complexes. Dissociation constants (KD) are determined in the milli- to nanomolar range directly from biological material, such as cell lysate and brain homogenate.

12:40 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:40 Break

BIOPHYSICAL CHARACTERIZATION OF THERAPEUTIC PROTEINS

2:00 Chairperson's Remarks

Andrew Kosky, Ph.D., Senior Group Leader, Early Stage Pharmaceutical Development, Genentech

2:05 Interpretation and Misinterpretation of Biophysical Analysis in Characterization, Formulation and Process Development of Protein Therapeutics, and its Application in High Throughput Formulation Screening

Haripada Maity, Ph.D., Principal Scientist, Formulation Development, ImClone Systems, a wholly owned subsidiary of Eli Lilly & Co.

Protein structure is stabilized enthalpically and enthalpy-entropy compensation makes protein marginally stable. Biophysical analysis plays a unique role in characterizing higher-order structure and evaluating the stability of complex protein molecules. This presentation will discuss a variety of case studies that involve (i) prediction of optimized formulation based on structure and conformational stability and caveats in the use of accelerated stability data in formulation selection, (ii) cautionary notes for the analysis of accelerated stability samples, (iii) understanding different thermal and thermodynamic stability parameters, (iv) steady-state and kinetic analysis in the optimization of protein stability in low pH for process development, (v) sensitive biophysical methods for comparability assessment, and (vi) challenges in the use of biophysical techniques in high throughput formulation screening.

2:35 Challenges in Testing and Characterization of Bionanotherapeutics

Nanda Subbarao, Ph.D., Senior Consultant, Analytical CMC, Biologics Consulting Group

The physiological action of Bionanotherapeutics depends strongly on the size and morphology of the nanoparticles; therefore, their testing and characterization must include methods which address these parameters. Characteristics of the nanoparticle matrix and its interaction with the drug has to be studied, in addition to analytical methods commonly required for all biotherapeutics. Methods useful for characterization, lot release and stability studies on bionanotherapeutics and common ways in which nanoparticles interfere with these assays will be presented.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

3:45 Composition-Dependent Properties of Monoclonal Antibody Formulations

Jonas Fast, Ph.D., Formulation Scientist, Pharmaceutical and Analytical R&D Biologics, F. Hoffmann-La Roche

During development of a monoclonal antibody formulation, significant composition-dependent physical bulk properties and chemical degradations were observed. The driving forces of these observations were investigated in several systems.

4:15 Correlation between the Differential Scanning Profile, Binding Activity and Bioactivity of Abatacept

Satish Mallya, Ph.D., Senior Research Investigator, Biologics Process and Product Development, Bristol-Myers Squibb

Abatacept (CTLA4Ig) is a fusion protein that has been approved for the treatment of rheumatoid arthritis. The Differential Scaning Calorimetry (DSC) profile of abatacept shows two major transitions with melting temperatures of 58C and 83C. This presentation will discuss the correlation between the transitions, ligand binding activity and bioactivity of abatacept.

4:45 Problem Solving Breakout Sessions

Concurrent Problem Solving Breakouts are interactive sessions hosted by a moderator to discuss a topic in depth. They are open to all attendees, sponsors, exhibitors, and speakers and provide a forum for discussing key issues and meeting potential partners. *Please pick a topic of your choice and join in.*

5:45 - 6:45 Reception in the Exhibit Hall with Poster Viewing

TUESDAY, MAY 10

8:00 am Morning Coffee

ASSAY DEVELOPMENT

8:25 Chairperson's Remarks

Arvind Srivastava, Ph.D., Director, Formulation Development, ImClone Systems, a wholly owned subsidiary of Eli Lilly & Co.

8:30 Assessing Manufacturability, Expression and Formulation in Discovery

Yiqing Feng, Ph.D., Associate Director, Biologics Research, Biotechnology Center of Excellence, Centocor R&D, Inc.

It takes a long time for biotech drugs in Discovery Research to reach the market, and developing these drugs is a big investment. Well-behaving molecules can be developed relatively fast, while others cost a significant amount more time and resources. A process to assess the molecular properties suitable for development in discovery will be presented.

9:00 Strategies of Product Quality Profiling for Process Characterization

Christine Chan, Ph.D., Senior Manager, Bioanalytics & Formulation, Genzyme

This presentation will discuss the application of complementary analytical tools for monitoring protein product heterogeneity including variations in subunit dissociation, fragment size, covalent modifications, aggregation and particle size distribution. The techniques include HPLC, capillary electrophoresis and mass spectrometry, as well as biophysical methodologies. Examples on characterization of different proteins through the manufacturing process are reviewed.

9:30 Strategies on Development and Optimization of Cell Assays for Potency Measurement

Inder Patel, Ph.D., Manager, Bioanalytical Services, ImClone Systems, a wholly owned subsidiary of Eli Lilly & Co.

Monoclonal antibodies represent a rapidly growing class of biologics developed for a number of unmet medical needs. Bioassays play a key role for measuring the potency during drug development process including product release, stability testing, in-process sample testing, and comparability studies. The presentation will focus on key issues impacting bioassays such as cell line, ligand, and other factors causing variability in the assay and attempts to control this variability to generate accurate, reliable and robust assay.

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

PRODUCT CHARACTERIZATION AND COMPARABILITY

10:45 Characterizing a Protein Gel

Osi Esue, Ph.D., Senior Engineer, Pharmaceutical Development, Genentech

Although extensively studied, the mechanism of protein-protein interactions remains highly elusive and is of increasing interest in drug development. We show the assembly of a monoclonal antibody, using multivalent carboxylate ions, into highly-ordered structures. While the presence and function of similar structure *in vivo* is not known, this may present a possible unexplored scope of structure-function relationship of antibodies. Using a variety of analytical tools, we characterize the physical and biochemical properties of these structures.

11:15 Product Characterization Methods and Acceptance Criteria in Comparability Studies

Brent Kendrick, Ph.D., Scientific Director, Process Development and Analytical Sciences, Amgen

Product comparability studies are designed to evaluate the potential impact of manufacturing process changes on quality, safety and efficacy of the drug product (per ICH Q5E). The scope and depth of the study will vary by product, by nature of the process change, and by the clinical / commercial development stage. This presentation will cover approaches for selection of characterization methods and acceptance criteria to supplement lot release tests used in comparability studies.

11:45 Biocomparability and Biosimilarity: Current Strategies and Guidances

Shefali Kakar, Ph.D., Senior Fellow, Clinical Pharmacology, Oncology Business Unit, Novartis

Biological comparability can be assessed by examining the physiochemical, pre-clinical and clinical characteristics of the molecule. The presentation will primarily focus on: a. Current guidances from EMEA and FDA for biocomparability and the current strategies for the extent of physiochemical, pre-clinical and clinical characterization based on the stage of development; b. Emerging guidances on biosimilarity and their implications on the pre-clinical and clinical development program for biosimilars; and c. Use of Biomarkers in the biocomparability exercise: Are we there yet?

12:15 pm Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:15 Break

CHARACTERIZATION OF PROTEIN AGGREGATION

2:00 Chairperson's Remarks

Satish Mallya, Ph.D., Senior Research Investigator, Biologics Process and Product Development, Bristol-Myers Squibb

2:05 Huge Aggregates: Removing the Cloak of Invisibility

Donna Luisi, Ph.D., Senior Principal Scientist, Pharmaceutical Research & Development, Pfizer

Development of therapeutic antibodies has become an important component of drug therapy over the past 20 years. The large size and complex structure of antibodies presents a unique challenge to develop a stable liquid formulation. Understanding the potentially complex protein-protein interactions under the conditions our drug encounters is critical in understanding its overall behavior. These interactions can lead to denaturation, aggregation, and precipitation, all of which can cause a change in visual appearance. One major issue of antibody visual appearance is opalescence.

2:35 Quantification of Posttranslational Modifications in Recombinant Protein Using Stable Isotope Labeled Internal Standard (SILIS) and Mass Spectrometry. Principles, Applications and Performances

Xinzhao Grace Jiang, Ph.D., Senior Scientist, Process and Product Development, Amgen

With the increased attention to Quality by Design for biopharmaceutical products, there is a demand for an accurate quantification method to monitor Critical Quality Attributes during the product lifecycle. To address this need we have developed a method to quantify the posttranslational modifications (PTM) in recombinant proteins using Stable Isotope Labeled Internal Standards (SILIS). With the application of SILIS, the level of PTMs can be accurately and precisely determined based on the measured MS signal intensity ratio, e.g; 15N labeled versus the non-labeled enzymatic peptide. Several examples using microbial and mammalian expressed recombinant proteins will be shown to demonstrate the advantages of this method, which include superior accuracy and precision. Additionally, the SILIS method demonstrated extended linear dynamic range expressed in accurate quantification up to at least 4 orders of magnitude concentration ranges. This performance is maintained on three different types of mass spectrometers. Furthermore, we demonstrate that lengthy chromatographic separations may not be required to obtain quality results, offering an opportunity to significantly shorten the method run time. The results using SILIS indicate the potential of this methodology in rapid assessment of multiple PTMs in a single analysis.

3:05 Sponsored Presentations (Opportunities Available)

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

4:15 Tools, Tools, Tools and Even More Tools! How to Predict Immunogenicity in Silico, in Vitro and in Vivo – an Overview

Melody Sauerborn, Ph.D., Utrecht Institute for Pharmaceutical Sciences, Department of Pharmaceutics, Utrecht University

With about 200 new products in the pipeline, recombinant human (rh) therapeutics are becoming the most dominant class of drugs. One of the reasons rh therapeutics were created was to avoid recognition by the immune system due to foreign origin. Nevertheless, rh therapeutics induced formation of anti-drug antibodies. Aggregation of the therapeutic protein became a major concern and due to the improvement in bioanalytical techniques, detection of aggregates and other protein-structure related issues are increasingly being addressed and dealt with. In the process of rh drug development, protein aggregation can hardly be avoided, thus there is a need to predict the immunogenic potential of rh therapeutics in context of the immune system. Today, three methods are available to predict immunogenicity: in silico, in vitro and in vivo. This presentation will give an overview of these current tools and discuss their pro and cons.

4:45 Shedding Light on Protein Aggregates: Fluorescent Dyes

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

Noncovalent, extrinsic fluorescent dyes are applied in various fields of protein analysis, including aggregate characterization. I will discuss the use of such dyes, including strengths and weaknesses, present an online dye fluorescence detection method for size exclusion chromatography and asymmetrical flow field-flow fractionation to characterize thermally induced aggregates of monoclonal antibodies, and present applications of dyes for polysorbate-containing protein formulations.

5:15 End of Conference

PEGS SUNDAY AFTERNOON WORKSHOP

(please see page 3)

SUNDAY, MAY 8 | 2:00 - 5:00 pm

[SC5] Biological Mass Spectrometric Applications for Drug Discovery and Product Development

Chair: Jennifer Nemeth, Ph.D., Principal Research Scientist, Biologics Mass Spectrometry & Allied Technologies, Centocor R&D, Inc.

Alain Balland, Ph.D., Scientific Director, Analytical & Formulation Sciences, Amgen

Yoshi Hamuro, Ph.D., Director, Analysis, ExSAR

Dariusz Janecki, Ph.D., Research Scientist, Biologics Mass Spectrometry, Centocor R&D, Inc.

Ron Orlando, Ph.D., Professor, Biochemistry and Molecular Biology, Complex Carbohydrate Research Center, University of Georgia

This workshop is geared to those individuals supporting biopharmaceutical drug characterization analyses using mass spectrometry in either discovery or product development.

Aspects that will be covered in the workshop include:

- A novel method for assessing disulfide bond networks
- Methods for performing glycosylation analyses
- Methods for conducting PTM analyses
- Methods for performing stress assessments on drug candidates

PROTEIN AGGREGATION AND STABILITY IN BIOPHARMACEUTICAL PRODUCTS

WEDNESDAY, MAY 11

7:00 am Registration and Morning Coffee

UNDERSTANDING THE MECHANICS OF AGGREGATION

8:30 Chairperson's Opening Remarks

Thomas Laue, Ph.D., Professor, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire

8:40 Addressing Particulate and Aggregation Issues of Therapeutic Protein Products

Li Shi, Ph.D., Senior Director, Senior Director, BioAnalytics and Formulation, CPD, Genzyme

Biological product quality control is a critical effort in ensuring the success of the manufacturing, final product safety and efficacy, and process consistency. In addition to process control, formulation design and formulation/fill/finish process development are also responsible for the final product's critical quality attributes. One of the common challenges of protein biopharmaceutical quality evaluation is the aggregation during process, handling, and under the situation of process deviation. In addition, the presence of foreign particles in parenteral protein products is often a manufacturing process and product release challenge. This presentation will review related expectation and elaborate general strategies and scientific approaches used in addressing those protein aggregation and particulate issues.

9:10 Mechanistic Understanding of Reversible Self Association in Therapeutic Monoclonal Antibodies

Sathish Hasige, Ph.D., Senior Scientist, Formulation Sciences, MedImmune

Successful development of a therapeutic protein requires complete characterization of aggregates and related complexes. Unlike irreversible aggregation, reversible self-association (RSA) typically arises from relatively weak non-covalent protein interactions. Both the potential for increased viscosity and higher size can result in manufacturability issues. Also RSA of therapeutic proteins can have a potential impact on immunogenicity and potency. This talk will provide a mechanistic understanding of reversible self association and process control strategy to mitigate and prevent RSA in mAb's.

9:40 The Importance of Protein Surface Charge on Biological Activity, Inherent Structural Stability, and Formulation Shelf Life

Kevin Mattison, Ph.D., Principal Scientist, Bioanalytics, Malvern Instruments

Sponsored by

Malvern

There is a growing interest in the measurement of protein charge, as a means of predicting formulation characteristics. A common technique for measuring protein charge is electrophoretic light scattering (ELS). Historically, the low scattering of proteins have made ELS measurements somewhat challenging. Recent advances in ELS technology however, have led to significant reductions in both the minimum sample volume and the experimental limitations under which protein samples can be measured. This paper highlights these improvements using a series of antibody formulations.

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

11:10 Amyloidogenic Regions and Interaction Surfaces Overlap in Globular Aggregating Proteins

Salvador Ventura, Ph.D., Group Leader, Institut de Biotecnologia i Biomedicina, Universitat Autonoma de Barcelona

Protein aggregation underlies a wide range of human disorders. The polypeptides involved in these pathologies might be intrinsically unstructured or display a defined 3D-structure. Little is known about how globular proteins aggregate into toxic assemblies under physiological conditions, where they display an initially folded conformation. Protein aggregation is, however, always initiated by the establishment of anomalous protein-protein interactions. Therefore, in the present work, we have explored the extent to which protein interaction surfaces and aggregation-prone regions overlap in globular proteins associated with conformational diseases.

ORTHOGONAL CHARACTERIZATION TOOLS AND PHYSIOLOGICAL EFFECTS

11:40 Aggregates, Particulates: Why is there a Need for Orthogonal Characterization Tools and What are the Adverse Physiological Effects

Joel Richard, Ph.D., Senior Director, Head, Vice President, Drug Product Development, Pharmaceutical Development, Ipsen

A major critical quality attribute for liquid formulations of biologics is the level of aggregates and particulates. Their key features (size, morphology, reversibility) have to be characterized, in order to anticipate potential related safety issues. For this purpose, orthogonal characterization methods have to be implemented so as to get a comprehensive mapping of the characteristics of aggregates and particulates. Practical approaches based on appropriate combination of analytical tools for the in-depth characterization of aggregates and particulates will be highlighted. The adverse physiological effects related to their presence in the formulations, e.g. induction of immune response, will also be discussed.

12:10 pm Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:10 Break

DETECTING AND PREDICTING AGGREGATION

1:30 Chairperson's Remarks

Robert Forbes, Ph.D., Professor of Biophysical Pharmaceutics, School of Pharmacy, University of Bradford

1:35 Novel Approaches to Predicting Aggregation Rates

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

This presentation will focus on new approaches to rapidly and quantitatively estimating real-time aggregation rates based on accelerated data and/or biophysical properties. Comparison with conventional methods for different proteins as a function of pH and excipient concentrations shows predictability across a range of systems, with reduced time and material consumption. The methods also provide useful data for mechanistic modeling of aggregation pathways.

2:05 Fast Assessment and Prediction of Protein Aggregation Trends

Andreas Bommarius, Ph.D., Professor, Chemical & Biomolecular Engineering and Chemistry & Biochemistry, Georgia Institute of Technology

In the present work, diffusion and aggregation kinetics of the globular

model proteins lysozyme and BSA were studied in sodium-salt solutions of different composition and ionic strength using dynamic light scattering. We find a strong correlation between the concentration dependent protein diffusivity in stable solutions and the kinetics of protein aggregation in unstable solutions of similar composition but higher salt content. Our findings suggest a fast and convenient new way to assess a protein's specific tendency to aggregate in different types of electrolytes and buffer solutions.

2:35 Sponsored Presentations *(Opportunities Available)*

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

3:50 Problem Solving Breakout Sessions

Concurrent Problem Solving Breakouts are interactive sessions hosted by a moderator to discuss a topic in depth. They are open to all attendees, sponsors, exhibitors, and speakers and provide a forum for discussing key issues and meeting potential partners. *Please pick a topic of your choice and join in.*

4:50 Reception in the Exhibit Hall with Poster Viewing

6:00 End of Day

THURSDAY, MAY 12

8:00 am Morning Coffee

CONTROLLING AND OVERCOMING AGGREGATION AND PARTICULATE FORMATION

8:30 Chairperson's Remarks

Devendra (Davy) S. Kalonia, Ph.D., Professor of Pharmaceutics, Department of Pharmaceutical Sciences, University of Connecticut

8:35 Strategy to Control Protein Aggregation and Particulate Formation in an Antibody Drug Product

Arvind Srivastava, Ph.D., Director, Formulation Development, ImClone Systems, a wholly owned subsidiary of Eli Lilly & Co.

Protein aggregates and particulates are a major issue in biological therapeutic development because of their potential to cause undesirable immunogenic reactions and other safety concerns. It is possible to influence the rate of aggregate and particulate formation during product storage and handling by carefully selecting formulation components. The formulation strategy to control aggregate and particulate formation in various stress conditions will be discussed in the presentation. The effect of formulation component quality on product stability will also be discussed.

9:05 Hydrophobic Interactions: A Key Player in Aggregation of Antibodies at High Concentrations

Vineet Kumar, Ph.D., Senior Research Scientist, Global Formulation Sciences, Parenterals, Abbott

The importance of hydrophobic interactions in governing protein aggregation especially at high concentrations is underestimated especially because of the overestimation of the charge-charge long-range interactions. Examples wherein hydrophobic interactions play the major part will be discussed. Attendees will learn: (1) What are the major forces that govern aggregation at high concentrations, (2) How to overcome aggregation issues by formulation approaches, and (3) Analytical techniques to make use of during such investigations.

9:35 Analysis of Protein Aggregation by Size Exclusion Chromatography in Combination with Ultra Performance Liquid Chromatography (UPLC)

Sponsored by Waters

Paula Hong, Ph.D., Senior Applications Chemist, Chemistry Operations, Waters Corporation

Size-exclusion chromatography (SEC) is often used to measure protein aggregates and other size variants in biopharmaceuticals. Current silica-based HPLC SEC methods are time-consuming and unreliable due to variability in protein recovery, retention time, peak shape, and resolution, as well as irreproducibility between columns. In this presentation, we will demonstrate how UPLC technology dramatically improves productivity and bioseparation quality for SEC.

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

11:05 Design of Antibodies Fragments with Drug Like Properties

Leonardo Borras, Ph.D., Head, Protein Engineering, Research & Development, ESBATech (Alcon)

Using binding free energy prediction and antibody homology models we have achieved reducing aggregation in antibodies by modulating the VL-VH domain interaction. This presentation will discuss in detail our method for reducing aggregation in antibody fragments and provide several results validating this computational protein design approach.

11:35 Revolutionary Approach to Building Nano-Scale Capability to Size Biopharmaceuticals and their Aggregation Potential

Robert Forbes, Ph.D., Professor of Biophysical Pharmaceutics, School of Pharmacy, University of Bradford

The talk will present results from a novel technology developed over two years from a consortium team approach (including end-users, innovator and academia) addressing the need to size biopharmaceuticals and their aggregates at high-concentrations, using nL sample sizes concentrations and without sample dilution.

12:05 pm End of Conference

PEGS DINNER WORKSHOP *(please see page 3)*

THURSDAY, MAY 12 | 5:30 - 8:30 pm

[SC9] Characterization Techniques for Protein Therapeutics – Orthogonal vs. Complementary

This workshop covers the theory and general application of both traditional and emerging technologies suitable for protein therapeutic characterization, across the applicable size range of 1 nm to 100 um. Historically, quantification of protein aggregates in pharmaceutical formulations had been assessed almost exclusively using size exclusion chromatography (SEC) in the nm size range and light obscuration in the micron size range. Given recent concerns regarding the potential of undesirable immune responses to protein aggregates, the FDA is recommending 1) the use of orthogonal techniques to support SEC results, and 2) an expansion of the technology portfolio to include those suitable for particle sizes beyond the upper limits of SEC. This workshop covers the range of technologies suitable for satisfying these FDA recommendations, with a focus on orthogonality vs complementarity, using real world examples.

What's the difference between Tm measured by DSC, CD, & DLS?

- Can DLS be used to confirm SEC results?
- What's the relevance of protein charge on formulation stability?
- Can particle counting be achieved in the 100 nm to 1 um size range?
- What role does protein aggregate "morphology" play?

UNDERSTANDING AND OVERCOMING IMMUNOGENICITY OF PROTEIN THERAPEUTICS

THURSDAY, MAY 12

12:00 pm Registration

PROTEIN AGGREGATION AND IMMUNOGENICITY

1:30 Chairperson's Opening Remarks

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

» OPENING KEYNOTE PRESENTATIONS

1:40 Understanding the Impact of Aggregates on Immunogenicity

Jack Ragheb, Ph.D., Senior Regulatory Research Officer and Principal Investigator, Division of Therapeutic Proteins, FDA

Large protein aggregates are known to be produced during the pharmaceutical manufacturing of therapeutic protein products. However, our understanding of how protein aggregate attributes such as size contribute to this immunogenicity is very limited. This talk will focus on subvisible protein aggregates, how they may interact with the immune system, and the potential impact these particles could have on a product's safety and efficacy profile.

2:10 Protein Aggregation and Immunogenicity: The Formulation Matters

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

In this talk I will present product-related risk factors for protein immunogenicity, with a focus on aggregation. Clinical case studies illustrating the importance of the formulation in relation to protein immunogenicity will be presented. Moreover, theoretical considerations and pre-clinical studies pointing to which types of aggregates (including subvisible particles) may serve as a risk factor will be discussed.

2:40 Immunogenicity Assay Formats: Pros and Cons

Sponsored by GYROS

Robert A. Durham, Ph.D., Manager, Field Applications Scientist, Gyros US, Inc.

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

4:00 Problem Solving Breakout Sessions

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5:00 Close of Day

FRIDAY, MAY 13

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

REGULATORY CONSIDERATIONS AND GUIDANCE

8:30 Chairperson's Remarks

Narendra Chirmule, Ph.D., Executive Director, Clinical Immunology, Amgen

8:35 Key Considerations when Thinking about Product Immunogenicity

Daniela Verthelyi, Ph.D., Chief, Laboratory of Immunology, Therapeutic Proteins, FDA

Protein immunogenicity plays a key role in the safety and efficacy of therapeutic proteins. This talk will review critical product attributes that impact on immunogenicity, present a few case studies and briefly describe recent studies on the role of innate immune response modulating impurities in protein immunogenicity.

9:05 Practical Implementation of Immunogenicity Testing: "Rightsourcing" Strategies for Small and Large Companies

Joy Cavagnaro, Ph.D., DABT, RAC, President, Access BIO

This presentation will discuss the alignment of regulatory expectations with the practical implications of implementing immunogenicity testing during early stages of clinical development. As with other areas of biopharmaceutical development, resource optimization and risk mitigation strategies differ between virtual (very small), small and large companies. For example considering how and when to use qualified vs. validated assays to achieve the goal of risk minimization for the patient, molecule and company? Scenarios will be developed highlighting timing and resource implications for developing appropriate immunogenicity testing strategies.

NON-CLINICAL AND CLINICAL ASSESSMENT OF IMMUNOGENICITY

9:35 Case Study: Translation from Pre-Clinical Testing to Clinical Implementation

Jaya Goyal, Ph.D., Principal Investigator, Clinical Science and Technology, Biogen IDEC

The traditional ELISA assays, used routinely for immunogenicity evaluations, provides adequate sensitivity but interference from the circulating drug somewhat restricts the use of ELISA to support long term and frequent dosing with high levels of drug. Numerous analytical methods have been utilized industry wide that provides further improvements in terms of sensitivity, specificity and drug tolerance. This case study highlights that for immunogenicity evaluation during the course of pre-clinical and clinical development of macromolecules, careful consideration of study species/population, dose levels and anticipated levels of circulating drug is required prior to the selection of assay configuration.

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

11:05 Case Study: Pre-Existing Antibodies in Humans: Prevalence, Complexity and Potential Impact on Immunogenicity Risk

Li Xue, Ph.D., Senior Research Scientist II, Immunogenicity Sciences, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

Pre-existing antibodies have been observed for many protein biotherapeutics and complicate the evaluation of true immunogenicity responses post treatment. This talk will present a few case studies

investigating the source of pre-existing antibodies in humans. The potential impact on immunogenicity risk will be discussed based upon historical clinical immunogenicity data analysis.

11:35 Risk-Based Immunogenicity Assessment of a Novel One-Armed Antibody

Alyssa Morimoto, Ph.D., Scientist, Bioanalytical Research & Development, Genentech

MetMAb is a novel, monovalent antibody that acts as an antagonist against the receptor tyrosine kinase Met. Binding of MetMAb to Met blocks ligand binding and prevents HGF dependent Met activation and cell proliferation. MetMab is currently in development for the treatment of patients with solid tumors. The risk-based strategy being utilized to assess the non-clinical and clinical immunogenicity of MetMAb will be discussed.

12:05 pm A Streptavidin Coated Plate for Long-Term Clinical Studies

Sponsored by MSD Meso Scale Discovery

Robert Umek, Ph.D., Director of External Scientific Affairs, Meso Scale Discovery

There is increasing demand for a streptavidin coated plate that satisfies the demands of long-term clinical trials, especially for immunogenicity studies. The nature of immunogenicity assays requires that performance be of exceptional uniformity across plates, within and between plate lots. In addition, practitioners seek to minimize the validation required for each new incoming lot of plates. MSD® has made substantial investments in optimizing the production and characterization of reagents and manufacturing processes associated with the production of Streptavidin coated plates. Streptavidin Gold meets the most rigorous demands of the community. The plates are subject to seven independent measurements of plate uniformity in a well-defined QC process. Streptavidin Gold is also characterized by a guaranteed binding capacity. Furthermore, the plates maintain performance through a shelf life of 30 months, reducing the frequency of new lot validations for end users. Data supporting the exceptional performance of Streptavidin Gold has been collected from over 4000 plates comprising 200 production lots over a two year period.

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

1:05 Break

IMMUNOGENICITY OF ANTIBODIES USED FOR CANCER THERAPY

1:25 Chairperson's Remarks

Maria Barbosa, Ph.D., Senior Principal Scientist, Bioanalytical Sciences, Bristol-Myers Squibb

1:30 An FDA Perspective on the Immunogenicity of Monoclonal Antibody Products

Laurie Graham, Ph.D., Biologist, Division of Monoclonal Antibodies, FDA

2:00 Case Study: Immune Modulation and Immunogenicity of Ipilimumab, a Fully Human Anti-CTLA-4 Monoclonal Antibody, in Patients with Advanced Pre-Treated Melanoma

Eric Masson, Pharm.D., Group Director, Clinical Pharmacology, Oncology-Immunology, Bristol-Myers Squibb

Ipilimumab is a fully human monoclonal antibody against CTLA-4, a negative regulator of T-cell activation. Ipilimumab is a T-cell potentiator that specifically blocks the inhibitory signal of CTLA 4, resulting in T cell activation, proliferation, tumor lymphocyte infiltration leading to tumor cell death. Ipilimumab therapy demonstrated in a randomized clinical trial to improve overall survival of patients with advanced melanoma. The pharmacodynamics of ipilimumab on immune cells, the assessment of immunogenicity, and their impact on pharmacokinetics, efficacy and safety will be discussed.

2:30 Refreshment Break

DEVELOPMENT AND QUALIFICATION OF CELL-BASED ASSAYS

3:00 Sponsored Presentation *(Opportunities Available)*

3:30 Using Various Platforms and Design of Experiments in Development and Qualification of Cell-Based Assays to Detect Neutralizing Antibodies

Corinna Krinos-Fiorotti, Ph.D., Senior Research Scientist II, Pharmacokinetics, Dynamics and Metabolism, Pfizer

This case study-based presentation will describe development and qualification of cell-based assays to detect neutralizing antibodies against three therapeutics. It will highlight critical parameters to consider when transferring a cell-based assay to an external laboratory. During assay development, DoE was used to assess optimal assay conditions. Qualification data were obtained using positive control polyclonal antibodies against each drug. The cell-based assays were shown to reproducibly detect neutralizing antibodies to each drug in human serum.

4:00 Impact of Immunogenicity on PKPD

Narendra Chirmule, Ph.D., Executive Director, Clinical Immunology, Amgen

Several intrinsic and extrinsic factors contribute to the challenges in ability to measure the drug in a precise and accurate manner. In addition, induction of an immune response to therapeutic proteins results in additional complexities in analysis of the pharmacokinetic profile, toxicity, safety, and efficacy of this class of molecules. The goal of this presentation is to provide an overview of impact of immunogenicity on PKPD of therapeutic proteins, using examples of molecules in development.

4:30 End of Conference

MEDIA PARTNERS

ANTIBODIES FOR CANCER THERAPY: Exploiting Successful Strategies

SUNDAY, MAY 8

4:00 - 6:00 pm Main Conference Registration

MONDAY, MAY 9

7:00 am Registration and Morning Coffee

» KEYNOTE PRESENTATIONS

8:30 Chairperson's Opening Remarks

Yan Chen, Ph.D., Vice President, Antibody Engineering, X-Body, Inc.

8:40 Antibodies for Cancer: Past, Present and Future

Janice Reichert, Ph.D., Research Assistant Professor, Tufts Center for the Study of Drug Development, Tufts University School of Medicine

The majority of development programs for monoclonal antibodies have focused on cancer, resulting in nearly a dozen marketed products and a variety of novel antibody modalities in clinical study. An overview of development and approval trends for novel anti-cancer mAbs, including bispecific antibodies and antibody-drug conjugates, will be discussed.

9:10 Kymouse Platform to Generate Highly Selective, Potent and Well-Tolerated Human Antibody-Based Biopharmaceuticals

Allan Bradley, Ph.D., FRS, Director Emeritus, Wellcome Trust Sanger Institute

9:40 Sphingosine-1-Phosphate Antibodies as Potential Agents in the Treatment of Cancer and Age-Related Macular Degeneration

Roger A. Sabbadini, Ph.D., Founder, Vice President & CSO, Lpath, Inc.; Professor Emeritus, Biology, San Diego State University

Bioactive lipids are novel targets for antibody therapeutic drug discovery. The bioactive lipid, Sphingosine-1-Phosphate (S1P), is a pleiotropic extracellular signaling molecule thought to be dysregulated in a variety of disease conditions, including cancer. In this presentation, Dr. Sabbadini will discuss the tumorigenic and angiogenic roles of S1P and the use of the ant-S1P antibody, sonepcizumab, to neutralize dysregulated S1P in cancer patients. S1P as a potential tumor biomarker is also discussed.

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

DIRECT KILLING OF CANCER CELLS

11:10 Overview of the Role of FC-Gamma Receptors and the Roles in Antibody Efficacy

Raphael Clynes, M.D., Ph.D., Associate Professor, Pulmonary & Allergy & Critical Care, Columbia University

Antitumor antibodies establish the paradigm that engineered therapeutic antibodies should engage activatory over inhibitory Fc receptors. I will discuss my research on the immunoregulation of dendritic cells in immunity and inflammation demonstrating that antitumor antibodies drive T cell responses that are relevant to efficacy.

11:40 Antibody scFv-Based Chimeric Immune Receptors for Optimized Adoptive T Cell Therapy of Cancer

Daniel J. Powell Jr., Ph.D., Research Assistant Professor, Pathology & Lab Medicine; Deputy Director, Cell & Vaccine Production Facility, University of Pennsylvania

Chimeric immune receptors (CIRs) couple the high affinity binding of antibody scFv with the intracellular signaling domains of the T cell receptor and costimulatory molecules for the specific retargeting of T lymphocytes to tumor antigens. Accordingly, CIR expressing T cells mediate the specific killing of cancers cells *in vitro,* and deliver potent antitumor activity *in vivo.*

12:10 pm Sponsored Presentations

(Opportunities Available)

12:40 Luncheon Presentation

Sponsored by attana

Kinetics on Cells-Bridging the Gap Between Traditional Biosensor and Cell Based Assay

Teodor Aastrup, Ph.D., CEO, Attana AB

Two typical examples where the Attana Cell 200 proved to be beneficial as the first biosensor in the world that measures molecular interactions label free directly on cell surfaces will be presented.

1:10 pm Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:40 Break

NEW APPROACHES TO IMMUNOTHERAPY

2:00 Chairperson's Remarks

Horacio G. Nastri, Ph.D., Head, Antibody Technologies, EMD Serono Research Center, Inc.

2:05 The Promise and Challenge of Therapeutic Antibodies in Oncology: A Regulatory Perspective

Wendy Weinberg, Ph.D., Senior Investigator and Chief, Molecular Oncology, Monoclonal Antibodies, Office of Biotechnology Products, CDER/FDA

Technical advances and increased understanding of molecular targets have made antibody therapeutics among the fastest growing sector of drug development. New strategies in protein design, expression systems, and manufacturing provide unique regulatory challenges to ensure the safety and consistency of these complex products.

2:35 Discovery and Characterization of hMAB Targeting an RTK Implicated in Metastasis by Live Cell Screening and Interrogation of Fully Human Libraries with Deep Sequencing

Yan Chen, Ph.D., Vice President, Antibody Research, X Body Biosciences, Inc.

We describe a novel platform for rapid generation of hMABs that employs interrogation of fully human libraries by deep sequencing. This human library captures the full naïve antibody repertoire and can be screened for binding to targets on living cells. Sequencing of thousands of hits provide an early read on the function, affinity and specificity of lead candidates. Label-free metastasis assays and 384 well affinity determinations in complex fluids are deployed in the screening process.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

3:45 Next-Generation Therapeutic Proteins for the Treatment of Solid Tumors: Pre-Clinical and Interim Phase I Results

Laurent Audoly, Ph.D., CSO, Pieris AG

Anticalins have been characterized in multiple pre-clinical disease models to demonstrate their potency, efficacy, and unique differentiating features. The presentation will provide an update on PRS050 (VEGFA) currently being dosed in an open Phase I clinical trial, as well as pre-clinical *in vivo* proof-of-concept for PRS110 (cMet). Characteristics of drug-like properties and manufacturability line of sight will be emphasized, and bispecific anticalins

(Duocalins) will be reviewed.

4:15 Induction of HER-2/Neu-Specific Immunity During Combination Trastuzumab and Chemotherapy

Keith Knutson, Ph.D., Associate Professor, Immunology, College of Medicine, Mayo Clinic

The immunologic efficacy of monoclonal antibody therapy is thought to be passive. Recent translational studies however show that combination chemotherapy and trastuzumab induces HER-2/neu-specific immunity. Importantly, these immune responses are linked to clinical outcomes. The findings suggest that, under the appropriate conditions, monoclonal antibody therapy may act as a vaccine ensuring protection from disease recurrence.

4:45 Problem Solving Breakout Sessions

Concurrent Problem Solving Breakouts are interactive sessions hosted by a moderator to discuss a topic in depth. They are open to all attendees, sponsors, exhibitors, and speakers and provide a forum for discussing key issues and meeting potential partners. *Please pick a topic of your choice and join in.*

5:45- 6:45 Reception in the Exhibit Hall with Poster Viewing

TUESDAY, MAY 10

8:00 am Morning Coffee

IMPROVING THERAPEUTIC EFFICACY

8:25 Chairperson's Remarks

Soldano Ferrone, M.D., Ph.D., Professor, Department of Immunology, University of Pittsburgh Cancer Institute

8:30 Development of First-In-Class Antibodies Targeting iNKT Cells for Treatment of Inflammatory Diseases and Cancer

Alem Truneh, Ph.D., Co-founder & CSO, NKT Therapeutics, Inc

9:00 Redirecting Effector T cell with Antibody Specificity Using Cancer-Specific Chimeric Receptors

Zelig Eshhar, Ph.D., Professor, Immunology, The Weizmann Institute of Science

Redirection of effector T cells with antibody type specificity using chimeric receptor (the 'T-body' approach) is an attractive approach for adoptive therapy of cancer. It combines together the specificity of antitumor antibodies with the potent effector function of T cells.

9:30 Monoclonal Antibody-Based Immunotherapy of Malignant Diseases

Soldano Ferrone, M.D., Ph.D., Professor, Department of Immunology, University of Pittsburgh Cancer Institute

Convincing evidence indicate that tumor antigen (TA)-specific monoclonal antibodies (mAb) are effective in the treatment of several malignant diseases, including non-Hodgkin lymphoma, breast carcinoma and colon carcinoma. The mechanisms underlying the therapeutic efficacy of TA-specific mAb will be reviewed. In addition the potential mechanisms underlying the therapeutic efficacy of TA-specific mAb in only a percentage of patients will be discussed.

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

10:45 Targeting Glypican-3 and Mesothelin for Liver Cancer Therapy

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

We study the role of Glypican-3 in cancer with a focus on its potential as a therapeutic target for hepatocellular carcinoma and develop novel human monoclonal antibodies. We also study mesothelin as a novel therapeutic target for cholangiocarcinoma.

11:15 Panel Discussion: Overcoming Challenges of Bringing New Technologies to Market

Moderator: Horacio G. Nastri, Ph.D., Head, Antibody Technologies, EMD Serono Research Center, Inc.

Panelists:

Daniel J. Powell Jr., Ph.D., Research Assistant Professor, Pathology & Lab Medicine; Deputy Director, Cell & Vaccine Production Facility, University of Pennsylvania

Keith Knutson, Ph.D., Associate Professor, Immunology, College of Medicine, Mayo Clinic

Xiaodong Yang, M.D., President & CEO, Apexigen, Inc.

Peter J. Hudson, FTSE, Ph.D., Director, Victorian Cancer Biologics and CSO, Avipep Pty Ltd.

- Optimization approaches
- Reducing Immunogenicity
- Extending half-life
- Humanization alternatives
- Tailoring effector function

12:15 pm Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:15 Break

EMERGING COMPANIES AND TRENDS IN ONCOLOGY

2:00 Chairperson's Remarks

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

2:05 Humanized Antibody Approach for Developing Best-In-Class Antibody Therapeutics for Cancer Treatment

Xiaodong Yang, M.D., President & CEO, Apexigen, Inc.

Monoclonal antibodies derived from rabbits have large diversity, high affinity and recognize unique epitopes and antigen homologues of different species such as mouse and human. Unique aspects of the rabbit immune system and Apexigen's humanized rabbit antibody technologies offer the possibility that humanized antibodies may become best-in-class therapeutics for cancer.

2:35 Development of Anti-hVEGFR-2(KDR) Neutralizing Fully Human Antibody for Cancer Treatment

Jin-San Yoo, Ph.D., President & CEO, PharmAbcine, Inc.

I will talk about the pre-clinical data of our novel anti-KDR neutralizing fully human antibody, Tanibirumab, which has unique cross-species cross reactivity. I will also introduce our novel platform for dual targeting multi functional next generation antibody therapeutics blocking VEGF-KDR and Angiopoietin-Tie2 pathways, DIG-KT, one of our DIG-body scaffold.

3:05 Sponsored Presentation

To Be Announced

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

4:15 Therapeutic Antibodies Targeting Key Pathways of Solid Tumor Cancer Stem Cells

John Lewicki, Ph.D., Executive Vice President, Research & Development, OncoMed Pharmaceuticals

Cancer Stem Cells (CSCs) are a subpopulation of cells that drive the progression of solid tumors. We have generated antibodies targeting the key pathways that regulate CSCs. The presentation will describe novel antibodies that inhibit the Notch or Wnt pathways and impede tumor progression by selectively eliminating CSCs.

4:45 Engineered Diabodies for Diagnosis and Therapy of Prostate and Ovarian Cancer

Peter J. Hudson, FTSE, Ph.D., Director, Victorian Cancer Biologics and CSO, Avipep Pty Ltd.

Diabodies are stable, single-chain antibody fragments that can achieve spectacular tumor load (over 70% ID/gm) with fast blood clearance. Avipep has designed the diabody surface to accept exactly four payload molecules which have included half-life extenders, radioisotopes and/or cytotoxic drugs. Diabodies have been tuned to maximize tumor load and minimize off-site toxicity, including avoiding kidney uptake. An optimized ADC (drug loaded) format has demonstrated efficient inhibition of human xenograft tumor growth in mice.

5:15 End of Conference

RESURGENCE OF BISPECIFIC ANTIBODIES: The Future of Antibody Development

WEDNESDAY, MAY 11

7:00 am Registration and Morning Coffee

CONSTRUCTING BISPECIFICS WITH IMPROVED PROPERTIES

8:20 Chairperson's Opening Remarks and Overview of Bispecific Antibodies

Patrick Baeuerle, Ph.D., CSO & Senior Vice President, R&D, Micromet

8:40 The Impact of Fab-Arm Exchange on the Development of Antibody Therapeutics

Janine Schuurman, Ph.D., Associate Director, Strategic Research, Genmab BV
IgG4s are dynamic molecules that undergo Fab arm exchange by swapping an IgG4 heavy chain and attached light chain for a heavy-light chain pair from another IgG4 molecule. Thereby IgG4 antibodies acquire bispecific binding properties. The relevance of Fab arm exchange for immunotherapy is demonstrated and discussed.

9:10 COMBODY: One-Domain Antibody Multimer with Improved Avidity

Bin Gao, Ph.D., Professor and Director, The Centre for Molecular Immunology, Institute of Microbiology, CAS
The smallest possible antigen binding domain has been built into a multimer molecule, dubbed as Combody, by fusing to a coiled-coil structure derived from cartilage oligomeric matrix protein. Combody has high avidity to its antigen and can be multiple specific and possibly, has improved pharmacokinetics.

9:40 Heavy-Light Chain Fab Crossover: A Generic Approach for the Production of Bispecific IgG Antibodies

Christian Klein, Ph.D., Discovery Oncology oDTA, Pharma Research and Early Development (pRED), Roche Glycart AG
We describe a generic method for the production of bivalent bispecific IgG1 antibodies based on the crossover of domains within the Fab region of one half of a bispecific antibody combined with the knobs-into-holes technology. Based on this approach, we describe a bispecific CrossMab targeting VEGF-A and Angiopoietin-2 with potent anti-tumoral and anti-angiogenic efficacy.

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

11:10 Bispecific/Multispecific SCORPION Scaffold for Autoimmune Diseases and Oncology

Phillip Tan, Ph.D., Associate Director, Research, Emergent Biosolutions
Using our SCORPION scaffold, we have generated bispecific and multispecific molecules to target multiple soluble ligands and multiple receptors on various cell types. These novel molecules often show potent and unique properties compared to single agents alone. Different case studies will be presented.

11:40 Pan-Specific Antibodies Targeting Redundant Signaling Pathways in Autoimmunity

Marie Kosco-Vilbois, Ph.D., CSO, NovImmune SA, Geneva
In certain diseases, targeting a single protein might not be sufficient to achieve efficacy and this has prompted the development of innovative formats that allow for multiple targeting. We describe the isolation and engineering of antibodies that are selectively cross-reactive and neutralize more than one target thus leading to improved neutralization of redundant signaling pathways.

12:10 pm Luncheon Presentations (Sponsorship Opportunity Available) or Lunch on Your Own

1:10 Break

1:30 Chairperson's Remarks

Nazzareno Dimasi, Ph.D., Senior Scientist, Antibody Discovery & Protein Engineering, MedImmune

1:35 Efficient Cell-Mediated Cytotoxicity Using Bispecific Domain Antibodies for Cancer Therapy

Patrick Chames, Ph.D., Principal investigator, Antibody Therapeutics and Immunotargeting (ATI), INSERM, France
We are developing new bispecific antibodies, easy to produce and capable of circumventing most of the limitations faced by today's therapeutic antibodies, including Fc receptor polymorphism, glycosylation issues, competition with endogenous IgG and binding to inhibitory receptors. The latest results obtained with these bispecific fragments will be discussed.

2:05 TRIBODY™ : Building Trispecificity by Fab-scFv Fusions

Nico Mertens, Ph.D., MBA, Director, Antibody Engineering, Biotecnol SA
Tribodies are antibody fragment manifolds based on fusion to Fab-chains. The molecular structure allows easy engineering of bispecific, bivalent bispecific, trispecific or multivalent reagents. Tribodies behave superior as compared to scFv-scFv constructs. This is probably due to better PK properties of these intermediate sized molecules, and to the multivalent targeting. Tribodies hold much potential to be developed as a new generation of biopharmaceuticals, as they can target multiple antigens with a single molecule.

2:35 Dual Variable Domain (DVD)–Ig™ Platform: Understanding the Biology of DVD–Ig™ Format to Build Therapeutic Dual-Specific Biologics

Tariq Ghayur, Ph.D., Senior Research Fellow, Abbott Bioresearch Center
The DVD-Ig™ technology enables us to attach the target binding domain of one mAb on to an existing mAb via flexible linkers. We have now converted the construction, expression, purification and functional/physicochemical characterization of these molecules into a high throughput platform. Lessons learned from these studies will be discussed.

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

3:50 Sponsored Presentations (Opportunities Available)

4:20 Problem Solving Breakout Sessions
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5:15 Reception in the Exhibit Hall with Poster Viewing

6:00 End of Day

THURSDAY, MAY 12

8:00 am Morning Coffee

IMMUNE CELL ENGAGEMENT

8:30 Chairperson's Remarks

Michael J. Feldhaus, Ph.D., VIce President, Antibody Discovery, Adimab, LLC.

8:35 Engineering Immune Effector Molecules for Cancer Immunotherapy

Yoram Reiter, Ph.D., Professor, Molecular Immunology & Biology, Technion-Israel Institute of Technology; Founder, Applied Immune Technologies (AIT), Ltd.
Two approaches for cancer immunotherapy will be presented that take advantage of the immune system key effector molecules: antibodies and TCR. In one approach, viral-specific potent CTLs are recruited to kill tumor cells. In the second, the specificity of TCRs are mimicked by high affinity unique antibodies,termed T-Cell Receptor-Like Antibodies (TCRLs). Examples and applications of these new approaches to cancer immunotherapy will be presented.

9:05 Tetravalent Bispecific TandAbs for Recruiting NK and T Cells

Melvyn Little, Ph.D., CSO, Vorstand, Affimed Therapeutics
Tetravalent bispecific TandAbs comprised only of antibody variable domains have been created for the highly effective recruitment and activation of either NK cells or T cells to kill tumor cells. TandAbs are quite stable with a molecular weight of 105-110 kDa. Two binding sites for each target provide high avidity. Affimed´s lead product, a TandAb targeting Hodgkin's Lymphoma cells, recently entered clinical trials (October, 2010). This presentation will provide an overview of the TandAb technology and pre-clinical/clinical development.

9:35 Dual-Targeting Triplebodies for a Highly Specific Elimination of Cancer Cells

Georg H. Fey, Ph.D., Professor, Genetics, Biology Department, Friedrich-Alexander University Erlangen-Nuremberg
Single chain triplebodies (sctbs) carry 3 scFv antigen binding sites, two for surface antigens on a cancer cell, the third recruits an effector cell for redirected lysis. When binding 2 different antigens on the same cancer cell, these agents can achieve preferential lysis of double-positive cancer cells over single-positive normal cells through "dual targeting".

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

BISPECIFICS REACHING THE CLINIC

11:00 Chairperson's Remarks

Michael J. Feldhaus, Ph.D., VIce President, Antibody Discovery, Adimab, LLC.

11:05 Systems Design of Bispecific Antibodies

Ulrik Nielsen, Ph.D., Senior Vice President & CSO, Merrimack Pharmaceuticals
We have built a pipeline of novel experimental therapies. Using a systems approach – a combination of experimental and computational biology – we have designed a series of bispecific antibodies which each address a specific cancer biology. We will
discuss our experience with bispecifics from discovery through currently ongoing Phase 1/2 clinical trials.

11:35 Recruiting T Cells for Cancer Therapy by BiTE Antibodies in Clinical Trials

Tobias Raum, Senior Director, Lead Discovery, Human Antibody Technologies, Micromet
BiTE antibodies are single-chain bispecific antibodies directing cytotoxic T cells to target-expressing cancer cells, leading to highly efficient lysis of target cells. CD19-specific Blinatumomab has shown very high response rates in NHL and ALL patients in phase 1 and 2 clinical trials. Clinical data and recent developments will be presented.

12:05 pm End of Conference

MAY 12-13 | ANTIBODIES STREAM

ANTIBODY–DRUG CONJUGATES

THURSDAY, MAY 12

12:00 pm Registration

COUPLING STRATEGIES: LINKING DRUG TO ANTIBODY

1:30 Chairperson's Opening Remarks

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

1:40 Understanding the Influence of Conjugation Site on the Stability and Biological Activity of Antibody-Drug Conjugates

Keyang Xu, Ph.D., Scientist, BioAnalytical Sciences, Genentech, Inc.
Site-specific conjugation generates homogeneous ADCs. Drug deconjugation of the ADC is studied both *in vitro* and *in vivo* using novel analytical approaches to evaluate the impact of conjugation site on the ADC's stability and biological activity.

2:10 Strategies to Control Stoichiometry and Site of Cysteine-Directed Antibody Drug Conjugation

Nazzareno Dimasi, Ph.D., Senior Scientist, Antibody Discovery & Protein Engineering, MedImmune
Classical ADC platforms often rely on the random modification of sulfhydryl, amine, or carboxyl groups and thus have unpredictable stability, solubility, and product quality. Here we discuss our effort to engineer cysteine into antibody Fc-region to address the challenges pertaining to classical ADCs and provide the data of our engineered antibodies with predefined sites and stoichiometries to improve conjugation efficiency and product homogeneity.

2:40 Sponsored Presentations (Opportunities Available)

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

4:00 Problem Solving Breakout Sessions
Concurrent Problem Solving Breakouts are interactive sessions hosted by a moderator to discuss a topic in depth. They are open to all attendees, sponsors, exhibitors, and speakers and provide a forum for discussing key issues and meeting potential partners. *Please pick a topic of your choice and join in.*

5:00 Close of Day

FRIDAY, MAY 13

7:45 am Continental Breakfast with Exhibit & Poster Viewing

DELIVERING DRUG PAYLOADS

8:30 Chairperson's Remarks

Robert Hollingsworth, Ph.D., Director, Cancer Biology, MedImmune, Inc.

8:35 Antibody-Drug Conjugates: Targeted Drug Delivery for Cancer

Django Sussman, Ph.D., Principal Scientist, Experimental Therapeutics, Seattle Genetics, Inc.
The use of monoclonal antibodies for the delivery of anticancer drugs to tumor cells has been the subject of a great deal of investigation. There are several aspects of antibody-drug conjugate (ADC) design that influence activity, safety, and specificity. This talk will present recent advances in ADC development relative to the antigen target, the drug/linker combination, and the mode and multiplicity of drug/linker attachment to the antibody delivery vehicle.

9:05 Antibody-Conjugated Nanoparticles for Targeted Drug Delivery

Dafne Mueller, Ph.D., Group Leader, Institute of Cell Biology & Immunology, University of Stuttgart
Nanoparticles such as liposomes and polymers are versatile carrier systems for delivery of therapeutic molecules, e.g. chemotherapeutic drugs, siRNA and proteins. Conjugation of antibodies, antibody fragments or antibody-mimetic scaffolds to the particle surface allow for active delivery to target cells, e.g. for tumor therapy. Binding to target cells has been shown to promote intracellular uptake and can improve selectivity and therapeutic efficacy. Examples for the generation and application of various targeted nanoparticulate drug carriers will be presented.

9:35 *In vivo* Chemistry for Pretargeted Radioimmunoimaging and Radioimmunotherapy of Cancer

Marc S. Robillard, Ph.D., Senior Scientist, Bio-Molecular Engineering, Philips Research
The inverse-electron-demand Diels-Alder reaction was used for non-invasive pretargeted tumor imaging in mice. An antibody conjugate with trans-cyclooctene was administered to tumor-bearing mice and the resulting chemically-tagged tumors were subsequently reacted with an 111In-labeled tetrazine probe in a remarkable 52-57 % chemical yield *in vivo*, clearly visualized by SPECT/CT imaging. To extend this proof of principle to effective radioimmunotherapy (RIT) our work next centered on increasing the tumor/non-tumor ratio by optimizing the CC49-TCO modification grade and blood clearance, and improving probe dosing. This contribution will address these studies and other system and protocol improvements towards pre-targeted RIT in LS174T-tumored mice.

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

ANTIBODY TARGETS

11:00 Chairperson's Remarks

Peter Park, Ph.D., Senior Director, Discovery Research, ImmunoGen, Inc.

11:05 Unnatural Amino Acids for Site Specific Immunotoxin and Multivalent Antibody Platforms

Vaughn V. Smider, M.D., Ph.D., Founder, Fabrus LLC; Assistant Professor, Molecular Biology, The Scripps Research Institute
Genetically encoded unnatural amino acids provide a means to produce well characterized antibody conjugates. Additionally, singly labeled antibody fragments can be used with orthogonal chemistries or nucleic acids to produce novel hetero- or homo- multimers that cannot be made using genetic fusion techniques.

11:35 Target Selection for Antibody-Drug Conjugates

Véronique Blanc, Ph.D., Head, Cancer Biology, Biologics Discovery, Sanofi-Aventis
Lessons learned from the clinic will be reviewed, along with understanding the impact of target selection on ADCs. Pre-clinical evaluation of ADCs will be discussed.

12:05 pm Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:05 Break

CLINICAL RESULTS

1:25 Chairperson's Remarks

Peter Park, Ph.D., Senior Director, Discovery Research, ImmunoGen, Inc.

1:30 Discovering and Designing Immunotoxins for the Treatment of Solid Cancers

Glen MacDonald, Ph.D., CSO and Vice President, Operations, Viventia Biotechnologies, Inc.
Conventional antibody-based biologics have resulted in modest clinical benefit for solid cancers. We have engineered antibody-toxin fusion proteins to create a pipeline of highly potent anti-cancer agents designed for use against solid cancers. Our unique discovery approach, molecular design rationale, biological characterization and clinical experience with these molecules are presented.

2:00 Directing and Enhancing Therapeutic Antibodies by Light

Colin Self, B.Sc., M.B., B.Chir., Ph.D., D.Sc., FRCPath, FRSC, CEO, BioTransformations Ltd. and The Medical School, Newcastle upon Tyne
Anti-T-cell antibodies are extremely potent with great potential in cancer therapy. This potency needs careful control and direction to tumor sites. We achieve this by rendering the antibodies light-dependant, thus controlling where they are active within the body. Local tumor illumination provides systemic effects, significantly affecting both primary and secondary-metastatic cancers.

2:30 Networking Refreshment Break

3:00 IMGN529: A Novel Antibody-Maytansinoid Conjugate for Hematological Malignancies

Peter Park, Ph.D., Senior Director, Discovery Research, ImmunoGen, Inc.
IMGN529 is an antibody-maytansinoid conjugate for the treatment of certain hematological tumors. It uses the Targeted Antibody Payload (TAP) technology employed by trastuzumab-DM1 and other clinical-stage antibody-maytansinoid conjugates. A TAP compound is composed of a tumor-targeting monoclonal antibody with a derivative of the potent anti-mitotic microtubule agent, maytansine, attached covalently using an engineered linker. This presentation will discuss the pre-clinical evaluation of IMGN529.

3:30 Phase II Data of the Anti-CD22 Antibody-Calicheamicin Conjugates and Next Generation ADCs

Hans-Peter Gerber, Ph.D., Senior Director, Bioconjugate Group, Center for Integrative Biology and Biotherapeutics (CIBB), Pfizer Biotherapeutics
CMC-544 (inotuzumab ozogamicin), an anti-CD22 immuno-conjugate of calicheamicin, is currently being evaluated in B-cell non-Hodgkin's lymphoma (B-NHL) patients. I will describe the mechanism of action and the pharmacology of calicheamicin conjugates and provide an overview of clinical trials. The pre-clinical ADC pipeline at CIBB and novel ADC targets will be discussed.

4:00 SGN-35: Proof-of-Principle for Antibody-Drug Conjugates

Andres Forero, M.D., Professor, Medicine, Hematology & Clinical Oncology; Director, Clinical Protocols and Data Management Shared Facility, Comprehensive Cancer Center, University of Alabama, Birmingham
This presentation will cover the complete development of SGN35 from pre-clinical evaluation to FDA approval.

4:30 End of Conference

SPONSORSHIP & EXHIBIT INFORMATION

PEGS – the essential protein engineering summit, is coming off a very successful 2010 event. This year's summit will prove to be even better. PEGS will assemble international innovation leaders who are striving to learn the newest approaches and technologies in the field of life science that will enable the next generation of biologics.

Become a sponsor and exhibitor and get the opportunity to network, influence, and interact with over 1,000 of the world's leading protein engineering scientists and executives.

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These presentations include a 30 minute podium presentation in the session room to all delegates. Invite session attendees to enjoy lunch on your company's behalf while you give your talk.

INVITATION-ONLY VIP DINNER/HOSPITALITY SUITE

Sponsor will select invitees from the conference pre-registration list for an evening of networking at the hotel or a top local venue. CHI will extend invitations, conduct follow-up and monitor responses. Reminder cards will be placed in the badges of those delegates who will be attending.

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- Literature Distribution
- Badge Lanyards (SOLD)
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- And more…

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EXHIBIT HALL

Exhibitors will enjoy face-to-face networking with qualified end users. PEGS is the perfect place to launch a new product to your target audience, the PEGS delegates. Showcase your latest technologies or solutions and walk away with new business leads.

SUBMIT A SCIENTIFIC POSTER

Savvy exhibitors promote their expertise in the exhibit hall and display their scientific poster for all to view. Poster presenters and the poster titles will be posted on the website.

To customize your sponsorship or exhibit package, contact:

Carol Dinerstein, Director, Business Development, Cambridge Healthtech Institute
Phone: 781-972-5471| Fax: 781-972-5470 | Email: dinerstein@healthtech.com

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The Sheraton Boston Hotel

39 Dalton Street
Boston, MA 02199
Phone: 617-236-2000 | Fax: 617-236-1702

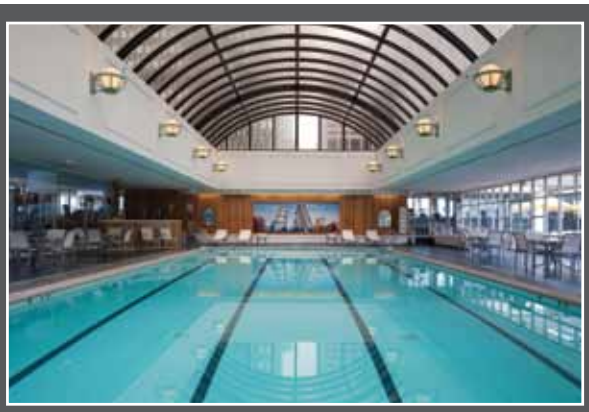
Discounted Room Rate: $239 s/d

Discounted Room Rate Cut-off Date:
April 8, 2011

Please book your reservation online or call the hotel directly, to make your room reservation. Please identify yourself as a Cambridge Healthtech Institute conference attendee to receive the reduced room rate. **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.**

Travel Information

For additional travel information please visit www.PEGSummit.com



Reserve your hotel room and save $150 off your conference registration.*

*You must book your reservation under the PEGS room block for a minimum of four nights at the Sheraton Boston Hotel.

Pricing and Registration Information

PRE-CONFERENCE SHORT COURSES

SUNDAY, MAY 8

Morning Courses 10:00 am-1:00 pm

- **SC1** Microfluidics for Antibody Selection and Screening
- **SC2** Translational Considerations for Development of Monoclonal Antibodies: Focus on Early Discovery (Pt. 1)

Afternoon Courses 2:00 -5:00 pm

- **SC3** Screening and Selecting Candidate Antibodies
- **SC4** Translational Considerations for Development of Monoclonal Antibodies: Focus on Nonclinical Development to Clinic (Pt. 2)
- **SC5** Biological Mass Spectolmetric Applications for Drug Discovery and Product Development
- **SC6** Phage and Yeast Display Libraries and their Screening

Dinner Short Courses

TUESDAY, MAY 10 | 6:00 - 9:00 PM

- **SC7** How Size Matters in Therapeutic Antibody Design

THURSDAY, MAY 12 | 5:30 - 8:30 pm

- **SC8** Changing Guidances & Regulatory Expectations for Biologics
- **SC9** Characterization Techniques for Protein Therapeutics: Orthogonal vs Complementary

SHORT COURSE PRICING

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		Commercial Rate	Academic, Gov't, Hospital Affiliated
		REGULAR RATE after April 8, 2011	
PREMIUM: (Includes access to conference options I, II, III)	Best Value	$2,825	$1,505
STANDARD: (Includes access to either conference options I & II, OR II & III)		$2,475	$1,235
BASIC: (Includes access to either conference options I, II, OR III)		$1,625	$805

CONFERENCE OPTIONS

I. May 9 - 10	II. May 11 -12	III. May 12 -13
• Phage & Yeast Display	• Engineering Antibodies	• Antibody Optimization
• Difficult to Express Proteins	• Optimizing Protein Expression	• Purifying Antibodies
• Characterization of Biotherapeutics	• Protein Aggregation and Stability	• Immunogenicity
• Antibodies for Cancer Therapy	• Bispecific Antibodies	• Antibody-Drug Conjugates

How to Register: PEGSummit.com

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Please use keycode PEG F when registering

CONFERENCE DISCOUNTS

- Poster Discount ($50 Off)
- Hotel Discount ($150 Off) *See page 27*

For Poster Information, visit PEGSummit.com website. Deadline to submit is April 1.

Register 3 - 4th Is FREE: Individuals must register for the same conference or conference combination and submit completed registration form together for discount to apply. Please reproduce this registration form as needed.

Group Discounts Available! Special rates are available for multiple attendees from the same organization. For more information on group discounts contact David Cunningham at +1-781-972-5472

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Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link.

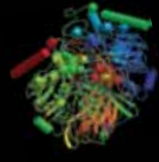
To view our handicap information and our substitutions/cancellations policy, go to http://www.healthtech.com/regdetails

Video and/or audio recording of any kind is prohibited onsite at all CHI events.

To purchase conference proceedings visit PEGSummit.com

PRESENT A POSTER AND SAVE $50

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by **April 1, 2011**. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact **jring@healthtech.com**



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