KEYNOTE SPEAKERS

**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

**Organized by Cambridge Healthtech Institute**

250 First Avenue, Ste 300, Needham MA, 02494
EVENT-AT-A-GLANCE

Sunday 5/8/11 Short Courses

**Monday 5/9/11**

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**Tuesday 5/10/11**

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STAY CONNECTED

Join our group on LinkedIn. Follow us on Twitter @PEGSboston #PEGSboston
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

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

SC4 - TRANSLATIONAL CONSIDERATIONS FOR DEVELOPMENT OF MONOCLONAL ANTIBODIES: FOCUS ON NONCLINICAL DEVELOPMENT TO 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 mass spectrometry in either discovery or product development
• A novel method for assessing disulfide bond networks will be discussed
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, ExSR
Darío Arencibia, 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

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

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

THURSDAY, MAY 12 | 5:30 – 8:30 PM

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

Chair: Jennifer Nemeth, Ph.D., Principal Research Scientist, Biologics Mass Spectrometry & Allied Technologies, Centocor R&D, Inc.
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Ron Orlando, Ph.D., Professor, Biochemistry and Molecular Biology, Complex Carbohydrate Research Center, University of Georgia
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

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* Separate Registration Required
MAY 9-10 | DISCOVERY STREAM

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

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

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.

4:40 Adjourn

For more information, visit pegsummit.com
Cyclotides thus appear as promising leads or frameworks for peptide drug stabilization core (3 disulfide bonds) characterized by an unusual knotted, cyclized polypeptides (≈28-37 amino acids long) that share a disulfide-...
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
Glad 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
Armelle Gaussin, Ph.D., Chief Technology Officer, SELEXIS SA
DNA vectors incorporating versatile epigenetic regulatory elements such as the Selexis Genetic Elements (SGEs) provide a high 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 Hamessing 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
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
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
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, MAY 12

8:00 am Morning Coffee

ENGINEERING FOR SUCCESS FROM THE START

8:30 Chairperson’s Opening Remarks

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 therapeutically 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 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

PEGylated protein. A therapeutic protein was conjugated to linear or two different type of branched PEGs of the same MW. Biophysical, biochemical, and ADMET properties (in rodents and primates) were evaluated for all combinations of the protein-PEG conjugate. Correlation between the biophysical and ADMET 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.

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the essential protein engineering summit | 7
2:40 A Standardized Platform for Antibody Characterization
James R. Carney, Ph.D. Research Biologist, US Army

2:55 Applying Tag-lite® to Therapeutic Antibodies Screening and Characterization: A Review of Recent Findings
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 IL6 receptor pH dependently. This pH dependent binding variant bound to IL6 receptor in plasma but dissociates from IL6 receptor within acidic endosome, which would enable recycling of free antibody to the plasma. This pH dependent binding variant exhibited significantly improved pharmacokinetics and duration of IL6 receptor neutralization compared to Actemra and Actemra variant with increased FcRn binding and affinity maturation to IL6 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 immunoadfinity 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, PEPpePRINT 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. Unrivalled 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

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
difficult to express proteins

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 Computational 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 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
12:25 Sponsored Presentation (Opportunity Available)

12:40 Luncheon Presentation I

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) on Lunch Your Own

1:40 Break

MEMBRANE PROTEINS AND OTHER BEASTS

2:00 Chairperson’s Remarks

2:05 Expression and Purification of Membrane Protein Diacylglycerol Acytransferase

Helping 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 on extracellular fusion proteins.

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

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

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-cellulosic 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, SAC-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.

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
**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. Mayer, Ph.D., Executive Director, Unit Head Biology, Protease Platform, Novartis Pharma AG

Success in drug discovery relies not only on 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 IL23R 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**

**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 upscaling and generation of production cell banks.

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

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’ mAb 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**

**WEDNESDAY, MAY 11**

7:00 am Registration and Morning Coffee

**CHO & MAMMALIAN EXPRESSION SYSTEMS**
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 Microfluidic Analysis for Enhanced Optimization of Recombinant Protein Expression Platforms
Mark Roskey, Ph.D., Senior Vice President, Applied Biology R&D, Caliper Life Sciences
This talk will focus on the use of high throughput microfluidics 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 Pfeffer, 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 valuable 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
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.

As we develop new technologies for protein purification, we sometimes overlook old methods that can be greatly improved. We have modified these columns.

In the past decade, continuous chromatography has evolved and can now be used in the production of chemical APIs for two decades, i.e. the so-called SMB-process. Continuous chromatography has been successfully applied in the large-scale production of chemical APIs for two decades, i.e. the so-called SMB-process. 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.

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.
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-Papastolis, 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 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 Naive 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 naive 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., Executive 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
Characterization of the products of these pathways. This presentation will focus especially on oxidative and photolytic chemical degradation are known such as hydrolytic, oxidative and photolytic degradation of proteins, all of which may contribute to immunogenicity. Several pathways of chemical degradation present an important problem for the design of stable formulations of therapeutic proteins. Chemical degradation may require 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 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.

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 biological attributes, and minimize potential chemical liabilities, such as post-translational modification (PTM). We have developed an MS-based system coupled with both-end quantitation and identification software for the rapid analysis of defined PTMs to enable narrowing 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 Przybylinski, 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 affinity-bound 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 lectin-carbohydrate 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 Malty, 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 Scanning Calorimetry (DSC) profile of abatacept shows two major transitions with melting temperatures of 58°C and 83°C. 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
Yqing 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 carbohydrate 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.
CHARACTERIZATION OF PROTEIN AGGREGATION

2:00 Chairperson’s Remarks
Satish Malviya, Ph.D., Senior Research Investigator, Biologics Process and Product Development, Bristol-Myers Squibb

2:05 Huge Aggregates: Removing the Cloak of Invisibility
Donna Luis, 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 potential 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
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 scat tering. 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**

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**THURSDAY, MAY 12**

**8:00 am Morning Coffee**

**CONTROLLING AND OVERCOMING AGGREGATION AND PARTICULATE FORMATION**

**8:30 Chairperson’s Remarks**

Devendra (Davy) S. Kelonia, 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**

Vinay 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)**

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?

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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
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
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

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.

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 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. Meso Scale Discovery 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 coated plates. Streptavidin Gold meets the most rigorous demands of the community.

12:15 Luncheon Presentation II (Sponsorship Opportunity Available) or Lunch on Your Own

1:05 Break

1:15 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

Cristina 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

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MAY 9-10 | ANTIBODIES STREAM

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 major 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 anti-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

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

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, Paris 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
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.

4:15 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.

4:45 Problem Solving Breakout Sessions
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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 ‘Tbody’ 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. Nastr, Ph.D., Head, Antibody Technologies, EMD Serono Research Center, Inc.

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

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
CONSTRUCTING BISPECIFICS WITH IMPROVED PROPERTIES

8:20 Chairperson’s Opening Remarks and Overview of Bispecific Antibodies
Patrick Baueraue, 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

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

9:40 Heavy-Light Chain Fab Crossover: A Generic Approach for the Production of Bispecific IgG Antibodies
Christian Klein, Ph.D., Discovery Oncology cDTA, Pharma Research and Early Development (pRED), Roche Glycyst AG

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

11:40 Pan-Specific Antibodies Targeting Redundant Signaling Pathways in Autoimmunity
Marie Kosco-Vilbois, Ph.D., CSO, Novimmune SA, Geneva

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

2:05 TRIBILITY™: Building Trispecificity by Fab-scFv Fusions
Nico Mertens, Ph.D., MBA, Director, Antibody Engineering, Biotecnol SA

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

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 TCell ReceptorLike 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

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

**BISPECIALS 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 bispes 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 End of Conference
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 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

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.
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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 Spectrometric 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

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• Antibody Optimization
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