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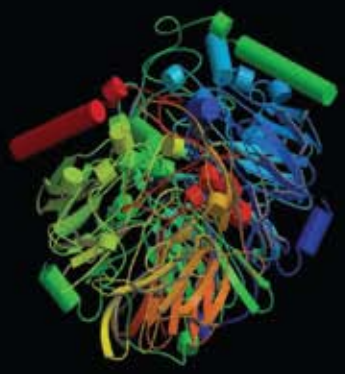

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Sixth Annual PEGS

May 17 -21, 2010

the essential protein engineering summit

KEYNOTE SPEAKERS

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

Yatin Gokarn, Ph.D., Associate Director, Late-stage Pharmaceutical and Process Development, Genentech

Igor A. Kaltashov, Ph.D., Associate Professor, Department of Chemistry, University of Massachusetts, Amherst

David Litzinger, Ph.D., Director, Pharmaceutical Sciences, Amylin Pharmaceuticals, Inc.

James R. Swartz, Ph.D., Department of Bioengineering, Stanford University

Daniela Verthelyi, Ph.D., Chief, Laboratory of Immunology, DTP/ FDA

James A Wells, Ph.D., Department of Pharmaceutical Chemistry, University of California, San Francisco

Herren Wu, Ph.D., Vice President, Antibody Discovery & Protein Engineering, MedImmune

Zhenping Zhu, M.D., Ph.D., Vice President and Global Head, Protein Sciences & Design, Novartis Biologics

DISCOVERY

Phage and Yeast Display
Engineering Antibodies
Antibody Optimization

DEVELOPMENT

Difficult to Express Proteins
Pre-Clinical/Clinical Development
Bispecific Antibodies

FORMULATION

Immunogenicity
Protein Aggregation
Biotherapeutic Targets

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EVENT-AT-A-GLANCE

AM SESSIONS

	Monday 5/17	Tuesday 5/18	Wednesday 5/19	Thursday 5/20	Friday 5/21
DISCOVERY	Phage and Yeast Display	Phage and Yeast Display	Engineering Antibodies	Engineering Antibodies	Antibody Optimization
DEVELOPMENT	Difficult to Express Proteins	Difficult to Express Proteins	Pre-Clinical/Clinical Development	Pre-Clinical/Clinical Development	Bispecific Antibodies
FORMULATION	Immunogenicity	Immunogenicity	Protein Aggregation	Protein Aggregation	Biotherapeutic Targets

PM SESSIONS

	Monday 5/17	Tuesday 5/18	Wednesday 5/19	Thursday 5/20	Friday 5/21
DISCOVERY	Phage and Yeast Display	Phage and Yeast Display	Engineering Antibodies	Antibody Optimization	Antibody Optimization
DEVELOPMENT	Difficult to Express Proteins	Difficult to Express Proteins	Pre-Clinical/Clinical Development	Bispecific Antibodies	Bispecific Antibodies
FORMULATION	Immunogenicity	Immunogenicity	Protein Aggregation	Biotherapeutic Targets	Biotherapeutic Targets

HOTEL & TRAVEL INFORMATION

The Sheraton Boston Hotel

39 Dalton Street
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Discounted Room Rate: $259 s/d
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Please visit our website to make your reservations online or call the hotel directly to reserve your sleeping accommodations. Identify yourself as a Cambridge Healthtech Institute conference attendee to receive the reduced room rate. Reservations made after the cut-off date or after the group room block has been filled (whichever comes first) will be accepted on a space-and-rate-availability basis. Rooms are limited, so please book early.

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PRE-CONFERENCE SHORT COURSES*

SUNDAY, MAY 16

MORNING COURSES 10 AM - 1 PM

(SC1) PHAGE AND YEAST DISPLAY LIBRARIES AND THEIR SCREENING

This workshop is meant to bring the scientist up to speed on the display technologies covered by the main conference. The workshop will provide an overview of:

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

Course Instructors:

Jamie Kathleen Scott, M.D., Ph.D., Professor and Canada Research Chair in Molecular Immunity, Department of Molecular Biology & Biochemistry and Faculty of Health Sciences, Simon Fraser University
Andrew M. Bradbury, M.B., B.S., Ph.D., Staff Scientist, Biosciences, Los Alamos National Laboratory

(SC2) PRECLINICAL SAFETY ASSESSMENT OF BIOLOGICS – UNEXPECTED SAFETY FINDINGS

This short course provides an overview of the most common reasons for encountering unexpected preclinical safety issues during development of monoclonal antibodies in particular. These unexpected issues can arise from:

- Binding to the intended target
- Binding to unanticipated targets
- Anti-drug antibody formation in preclinical species
- Fc- and Fab-mediated interactions

Course Instructors:

Thomas Monticello, DVM, Ph.D., Diplomate ACVP, Executive Director, Toxicology, Amgen
Jeanine Bussiere, Ph.D., DABT, Exec. Dir., Toxicology, Amgen
Nancy Everds, DVM, Diplomate ACVP, Pathology Director, Clinical Pathology, Amgen

(SC3) PROGRAM MANAGEMENT FOR SCIENTISTS

Most scientists train for years in their prospective fields but must learn business management "on-the-fly." This course is designed for scientists who have recently been promoted to program/product manager or are planning ahead.

- Strategic decision making
- Operational planning
- Oversight of resources
- Program management models

Course Instructor:

Patricia Seymour, M.B.A., Senior Consultant, BioProcess Technology Consultants

(SC4) ESSENTIAL CONSIDERATIONS FOR DEVELOPMENT OF ANTIBODY-BASED THERAPEUTICS FROM DISCOVERY TO THE CLINIC

- This introductory course will evaluate critical considerations necessary for effective development of ABTs
- Integration of relevant knowledge with respect to target antigen properties, antibody design criteria such as affinity, isotype selection, pharmacokinetic (PK)-pharmacodynamic (PD) properties, biophysical characterization and antibody cross-reactivity across species from the early stages of antibody development
- Key learnings will include: Considerations for target selection, screening and preclinical development; Affinity and biophysical characterization; Translational Considerations

Course Instructors:

Mohammad Tabrizi, Ph.D., Vice President, Preclinical Development, AnaptysBio, Inc.
Gadi Bornstein, Ph.D., Principal Scientist, AstraZeneca R&D
Scott Klakamp, Ph.D., Research Fellow, Biophysical Chemistry and Bioinformatics, Takeda

AFTERNOON COURSES 2 PM - 5 PM

(SC5) ANTIBODY-DRUG CONJUGATES

- Linker technology and drug characteristics
- Site-specific antibody modifications
- Use of alternative scaffolds for delivery
- Recent clinical proof-of-concept data

Course Instructors:

Pamela A. Trail, Ph.D., Vice President, Oncology, MedImmune, Inc.
Ravi V.J. Chari, Ph.D., Exective Director, Chemistry & Biochemistry, ImmunoGen, Inc. Changshou Gao, Ph.D., Principal Scientist, Antibody Discovery & Protein Engineering, MedImmune
Dario Neri, Ph.D., Professor, Chemistry & Applied Biosciences, Institute of Pharmaceutical Sciences, ETH Zürich
Kirsten Achilles Poon, Senior Toxicology Research Associate, Development Sciences Safety Assessment, Genentech, Inc.

(SC6) ANALYTICAL TOOLS AND METHODS USED IN BIOPHARMACEUTICAL CHARACTERIZATION TO DRIVE THERAPEUTIC DRUG DESIGN 2 PM - 6 PM

- Overview of the common analytical techniques used for performing a structural assessment of biopharmaceuticals, with real-life examples highlighting how they are applied
- Speakers are leaders in structural characterization for biopharmaceutical drug development, and bring a wide breath of experience to the forum
- Discussion will span a range of topics from protein profiling for isoform detection and percent population to peptide mapping for detecting low-level changes to drug product and the identification of post-translational modifications
- Additionally, methods for looking at solvent accessibility and epitope mapping will be presented

Course Instructors:

Jennifer F. Nemeth, Ph.D., Head, Discovery Mass Spectrometry, Centocor R&D, Inc.
Steve Pomerantz, Ph.D., Senior Research Scientist, Centocor R&D, Inc.
Jason C. Rouse, Ph.D., Director, Mass Spectrometry, Analytical Research and Development, Pfizer, Inc.
Sharon Gao, Ph.D., Principle Scientist, Analytical Biochemistry, Biogen Idec
Paul Schnier, Ph.D., Molecular Structure & Design, Amgen, Inc.

(SC7) PHAGE DISPLAY IN VACCINE DEVELOPMENT

- Peptide Mimotopes: Discovery of small peptides that can mimic vaccine antigens
- Vaccine Antigen Epitope Mapping: Use of phage display to discover dominant antigen epitopes
- Phage Based Vaccines: Use of peptides on phage vs. peptides alone for vaccination

Course Instructors:

Aaron K. Sato, Ph.D., Senior Director, OncoMed Pharmaceuticals, Inc.
Danuta Kozbor, Ph.D., Associate Professor of Immunology and Microbiology, Department of Immunology, Roswell Park Cancer Institute
Dimiter S. Dimitrov, Ph.D., Senior Investigator, Protein Interaction Group, National Cancer Institute, NIH
Beka Solomon, Ph.D., Department of Molecular Microbiology & Biotechnology, George S. Wise Faculty of Life Sciences, Tel-Aviv University

(SC8) MEMBRANE PROTEINS - AN IMPORTANT PROTEIN CLASS

- Overview of Membrane Proteins
- Structure & Assembly
- Function & Interactions
- Transporters

Course Instructors:

William A. Cramer, Ph.D., Henry Koffler Professor, Biological Science, Purdue University
Ernst ter Haar, Ph.D., Research Fellow I, Structural Biology, Vertex Pharmaceuticals, Inc.
Robert K. Nakamoto, Ph.D., Professor and Vice Chair, Department of Molecular Physiology & Biological Physics, University of Virginia
Ernst ter Haar, Ph.D., Research Fellow I, Structural Biology, Vertex Pharmaceuticals, Inc.

DINNER SHORT COURSES*

TUESDAY, MAY 18

5:30 PM - 8:30 PM

(SC9) DINNER, PRESENTATIONS AND INTERACTIVE PANEL DISCUSSION - SATISFYING FDA RECOMMENDATIONS IN THE AREA OF PROTEIN AGGREGATE QUANTIFICATION IN PROTEIN THERAPEUTICS

At the close of the day an optional Dinner and Short Course will be hosted at the conference venue. Attendees must register in advance, as seating is limited. This event will feature both presentations and an interactive panel discussion where the audience can bring up specific issues or questions important to their work.

- Overview of immunogenicity studies & conclusions
- FDA recommendations in the area of aggregate quantification
- Common techniques used to characterize protein aggregates & basic principles
- Advantages, disadvantages, and complementarities of each of these techniques

Chair: Kevin Mattison, Ph.D., Senior Bioanalytical Scientist, Product Development, Malvern

Course Instructors:

Thomas M. Laue, Ph.D., Professor, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire
Henryk Mach, Ph.D., Senior Investigator, Bioprocess Analytical and Formulation Sciences, Merck Research Laboratories
Devendra (Davy) S. Kalonia, Ph.D., Professor of Pharmaceutics, University of Connecticut
Mark Pollo, Associate Senior Biophysical Chemist, Bioproduct Research and Development, Eli Lilly

THURSDAY, MAY 20

5:30 PM - 8:30 PM

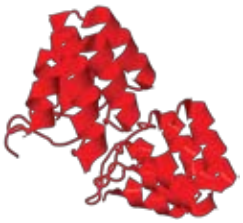
(SC10) AFFINITY TAGS FOR PROTEIN PURIFICATION DINNER, PRESENTATIONS & INTERACTIVE DISCUSSION

- Overview of Affinity Purification
- Types of Affinity Tags
- Comparison of Affinity Tags
- Tag Cleavage/Self-Cleaving Tags
- Alternative Tagging Strategies
- Streamlining Protein Recovery
- Emerging Technologies

Course Instructor:

Alexey Veraksa, Ph.D., Assistant Professor, Biology Department, University of Massachusetts, Boston
William Gillette, Ph.D., Senior Scientitst, Protein Expression Lab, SAIC-NCI Frederick

*Separate Registration Required



Phage and Yeast Display of Antibodies and Proteins

Recommended Short Courses (Details on Page 3)*

SUNDAY, MAY 16

10:00 am – 1:00 pm (SC1) Phage &Yeast Libraries & Screening

2:00 pm – 5:00 pm (SC5) Antibody Drug Conjugates

2:00 pm – 5:00 pm (SC7) Phage Display for Vaccine Dev.

**Separate Registration Required*

MONDAY, MAY 17

7:00 am Registration and Morning Coffee

KEYNOTE PRESENTATIONS

8:30 Chairperson's Opening Remarks

Sachdev Sidhu, Ph.D., Banting & Best Medical Research, University of Toronto

8:40 Phage Display Traps for Protein Conformation and Specific Composition

James A. Wells, Ph.D., Department of Pharmaceutical Chemistry, University of California, San Francisco

Phage display continues to represent one of the most powerful and unbiased selection technologies. One of the key advantages is that one can have complete control of the antigen state and composition without the worry of *in vivo* processing or proteolysis. We'll present two such examples demonstrating the exquisite directed selectivity for a specific enzyme conformation and a peptide composition.

9:10 Research and Development of Next-Generation of Antibody-Based Therapeutics: Challenges and Opportunities

Zhenping Zhu, M.D., Ph.D., Vice President and Global Head, Protein Sciences & Design, Novartis Biologics

Recent clinical success with antibody-based therapeutics has led to an upsurge in the development of these agents. Since 1994 the US FDA has approved 23 therapeutic antibodies. In addition, there are several hundreds of antibodies currently being tested in late-stage, pre-clinical and clinical settings worldwide for a variety of disease indications. This presentation will discuss the current status and future trends, focusing on emerging novel technologies and their impact, in the discovery and development of next generation antibody-based therapeutics.

9:40 Next-Generation Biologics

Herren Wu, Ph.D., Vice President, Antibody Discovery & Protein Engineering, MedImmune

10:10 Grand Opening Coffee Break in Exhibit Hall

11:10 Q&A with Keynote Presenters

Moderator: Lutz Jermutus, Ph.D., Director of Research & Technology, MedImmune

- Will monoclonal antibodies become a commodity for the top ten pharma companies worldwide?
- What will drive differentiation in biologics?
- With greater dependence on publicly funded research for target identification and validation, where will new antibody targets come from?
- What are the advantages for considering next-generation biologics?

> **"PEGS is a great place to hear the latest advances in protein and antibody engineering every year."**
> Principal Scientist, Protein Science, Amgen Inc.

ENHANCING LIBRARY DIVERSITY

11:35 Chairperson's Remarks

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

11:40 Antibody Generation and Engineering Using Adaptor-Directed Phage and Yeast Display of Structure-Based Libraries

Mark Hsieh, Ph.D., Research Fellow, Biologics Research at Merck & Co., Inc.

We will present a novel and integrated platform for antibody generation and engineering using adaptor-directed phage and yeast display of structure-based designer libraries with superior biophysical and biological properties. These antibodies are designed to balance their structural and chemical diversity in capturing the distinct epitopes of different antigens. The adaptor-directed approach is used for functional selection of designed antibody libraries that can be tailored to hit diverse targets or leads. The power of our technology is in generating superior therapeutic antibodies by combining both antibody library design with robust phage and yeast selection systems.

12:10 pm Determination of the True Diversity of a Human Antibody Library and Insights into the Human Antibody Repertoire, Using Next Generation DNA Sequencing

Jaume Pons, Ph.D., Vice President & CSO, Research, Rinat Pfizer

To date, the diversity of large libraries is typically estimated based on the number of colonies obtained after library transformation. This method gives the upper limit of possible diversity of the library, but sequence diversity can be significantly lower. To solve this problem, we have used next-generation DNA sequencing, and adapted bioinformatics methods, to determine the true diversity of antibody libraries. Furthermore, when the libraries are cloned from human donors, deep sequencing also gives information about the human antibody repertoire.

12:40 In Vitro Evolution of Allergy Vaccine Candidates with Reduced IgE-Binding and T-Cell Activation Capacity

Sponsored by attana

Ola Nilsson Ph.D., Department of Medicine Solna, Karolinska Institute

Allergy and asthma to cat (Felis domesticus) affects about 10% of the population in affluent countries. Immediate allergic symptoms are primarily mediated via IgE antibodies binding to B cell epitopes, whereas late phase inflammatory reactions are mediated via activated T cell recognition of allergen-specific T cell epitopes. Allergen-specific immunotherapy relieves symptoms and is the only treatment inducing a long-lasting protection by induction of protective immune responses.

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

MEMBRANE PROTEINS AND CELL-BASED SELECTIONS

2:00 Chairperson's Remarks

Lutz Jermutus, Ph.D., Director of Research - Technology, MedImmune

2:05 Selection and Engineering of Antibodies Targeting Membrane Proteins

Eric V. Shusta, Ph.D., Assistant Professor, Chemical & Biological Engineering, University of Wisconsin, Madison

Membrane proteins are challenging to work with in terms of antibody selection, engineering, and antigen identification as a result of their insolubility in aqueous solutions. We have therefore developed a platform for antibody engineering using cell lysates as antigen sources. Such approaches are compatible with membrane protein targets, subcellular selections, and the rapid assessment of antibody specificity.

2:35 Selection of Single-Domain Antibodies Targeting Brain Vasculature and Their Optimization for Imaging and Therapeutic Applications

Danica Stanimirovic, M.D., Ph.D., Director, Neurobiology, National Research Council, Canada

One of the principal hurdles for translation of both emerging therapeutics and molecular imaging agents for CNS diseases is their delivery across the blood brain barrier. This talk will provide two examples of the selection of single domain antibodies targeting brain vessels using protocols of subtractive panning of phage display libraries against cells or generation of immune libraries against selected brain vascular target(s) and their optimization for applications in brain imaging and therapy.

3:05 Refreshment Break, Poster and Exhibit Viewing

3:45 Harnessing Somatic Hypermutation for Antibody Discovery and Optimization

David King, Ph.D., Vice President, Research, Anaptys Bio

The natural process for antibody generation in man encompasses gene recombination and affinity maturation through AID-induced somatic hypermutation (SHM). AID-induced SHM has been recreated *in vitro* using a novel mammalian cell display system. This allows SHM to be carried out in controlled conditions with either single antibody heavy and light pairs, resulting in affinity maturation of a specific antibody, or with libraries of antibody genes allowing novel antibody specificities to be discovered and optimized.

4:15 Dissecting and Engineering High-Affinity Antibody-Antigen Interactions: Application to Viral Epitopes

Jonathan R. Lai, Ph.D., Assistant Professor, Department of Biochemistry, Albert Einstein College of Medicine

Detailed analysis of factors governing high-affinity antibody-antigen interactions is crucial to understanding how natural antibodies evolve, and provides information for designing and selecting functional antibody libraries *de novo*. We used phage-based technologies to understand the molecular basis of a high-affinity HIV-1 antibody, and are developing strategies for identification of new neutralizing viral antibodies from *de novo* designed repertoires. This work will provide novel reagents for studying viral membrane fusion and explore new avenues for therapeutic or diagnostic applications.

4:45 Problem Solving Break-Out Sessions

Table 1: Antibody-Drug Conjugates

Moderator: Pamela A. Trail, Ph.D., Vice President, Oncology, MedImmune, Inc.

Table 2: Comparing Phage and Yeast Display Libraries

Moderator: Mark Hsieh, Ph.D., Research Fellow, Biologics Research at Merck & Co., Inc.

Table 3: Selection and Engineering of Antibodies Targeting Membrane Proteins

Moderator: Eric V. Shusta, Ph.D., Assoc. Professor, Chemical & Biological Engineering, Univ. of Wisconsin, Madison

- Display platform choice and how it relates to cellular preparations used: whole cells, fractionated cells, detergent-solubilized cells
- Selections/Engineering against known vs. unknown membrane targets
- Identification of unknown membrane antigens targeted by selected antibodies
- Designer antibody selections for cell-specific targeting (e.g. subtractive methods) and function (e.g. endocytosis)

Table 4: Strategies for Building Novel Scaffold Libraries

Moderator: Balaji Rao, Ph.D., Assistant Prof., Chemical Engineering, North Carolina State

- Choosing a scaffold
- What areas on the scaffold does one mutagenize?
- Constructing a library using a screening platform (yeast display, phage display etc.)
- Assessing the quality of the library generated

Table 5: Use of Next Gen Sequencing Platform to Bypass Primary Screening

Moderator: Nicolas Fischer, Ph.D., Head of Protein Engineering, NovImmune SA

- Next generation sequencing platforms and their suitability for different library formats
- Use of NSG at different steps of display technology
- Bypassing primary screening or complementing it?
- Implications for better library design

5:45 Networking Cocktail Reception in the Exhibit Hall

TUESDAY, MAY 18

8:00 am Registration and Morning Coffee

ALTERNATIVE SCAFFOLDS AND DISPLAY SYSTEMS

8:25 Chairperson's Opening Remarks

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

8:30 *de novo* Selection of High Affinity Antibodies from Synthetic Antibody Libraries Displayed on Phage as pIX-Fusion Proteins

John Wheeler, Ph.D., Senior Research Scientist, Biologics Research, Centocor

We report here the first combinatorial synthetic Fab libraries displayed on pIX, constructed on twelve scaffolds representing frequently used genes in human antibodies. After selection on a diverse panel of proteins, numerous specific, nanomolar-affinity Fabs were isolated. Applying an integrated affinity maturation process, selected antibodies yielded low picomolar affinities.

9:00 Next-Generation Sequencing Technologies Applied to Antibody Display: By-Passing Primary Screening

Nicolas Fischer, Ph.D., Head of Protein Engineering, NovImmune SA

In recent years novel technologies have allowed unprecedented DNA sequencing capacity that has revolutionized whole genome sequencing. We have applied the Illumina sequencing platform to different steps of phage display selection of antibody fragments. We used a specially designed scFv library in order to follow the evolution of virtually all antibody sequences during the selection process. This approach also allows for the direct identification of potential hits without upfront activity screening.

9:30 Engineered Bispecific Proteins that Target Multiple Tumor Vasculature Receptors

Jennifer Cochran, Ph.D., Assistant Professor, Bioengineering, Stanford Medical Center

There is significant crosstalk between the cell signaling pathways of receptors expressed on the tumor vasculature; therefore, bispecific agents that target multiple receptors offer promise for improved inhibition of tumor angiogenesis and metastasis. We used a natural growth factor ligand as a scaffold to engineer bispecific proteins that bind to both VEGFR and alphavbeta3 integrin with low nanomolar affinities. These engineered proteins strongly inhibit ligand-mediated receptor phosphorylation and cell proliferation compared with protein variants that bind only one receptor, and are currently being evaluated in murine tumor models.

10:00 Coffee Break, Poster and Exhibit Viewing

10:45 A "Super-Library" of Alternate Scaffolds for Engineering Molecular Recognition

Balaji Rao, Ph.D., Assistant Professor, Chemical Engineering, North Carolina State University

A "super-library" of alternate scaffolds for engineering molecular recognition. We have created a "super-library" of alternate scaffold proteins where multiple different topologies have been randomized. Here we present our results comparing this super-library with a single-scaffold library having much higher sequence diversity. A comparison of yeast surface display and mRNA display methods for library screening, in the context of this problem, is also presented.

11:15 Phage-Encoded Bicyclic Peptides

Christian Heinis, Ph.D., Professor, Laboratory of Therapeutic Peptides and Proteins, Ecole Polytechnique Fédéral de Lausanne (EPFL)

With Sir Greg Winter, I had developed at the Laboratory of Molecular Biology (LMB) in Cambridge, UK, combinatorial libraries of phage-encoded bicyclic peptides by chemically cyclizing linear peptides on phage. From these libraries, we were able to isolate peptide macrocycle structures with high affinity and specificity for disease related serine proteases.

11:45 Generation of Nanobodies® with fM Affinities: Exploration of Different Methods for Affinity Maturation

Joost Kolkman, Ph.D., Associate Director, Discovery, Ablynx

Nanobodies® are therapeutic proteins based on the smallest functional domain of heavy chain antibodies, which occur naturally in camels and llamas. To further expand our capabilities for generating Nanobodies® with desired characteristics we have been developing innovative display methods using Pichia pastoris. This presentation will focus on the versatility of Pichia surface display and we will discuss the advantages in comparison with other display technologies.

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

ENGINEERING ANTIBODY STABILITY AND DEVELOPABILITY

2:00 Chairperson's Remarks

David Lowe, Ph.D., Head, Display Technology, RI & A, MedImmune, Inc.

2:05 Thermodynamic and Information-Based Design of IgG-Like Bispecific Antibodies

Stephen J. Demarest, Ph.D., Senior Scientist, Protein Chemistry, Biogen IDEC, Inc.

We use thermal unfolding experiments to define stability constraints within antibody and scFv molecules. We have devised sequence-based methodologies to generate highly stable antibody domains for the construction of robust IgG-like bispecific antibodies. Some successful protein engineering applications will be described.

2:35 Aggregation-Resistant Human Antibody Domains through Directed Evolution

Daniel Christ, Ph.D., Senior Lecturer, Garvan Institute of Medical Research and Senior Lecturer (conj.), Faculty of Medicine, The University of New South Wales

Human antibody variable domains tend to aggregate in isolation. In addition, the aggregation-propensities of larger antibody therapeutics are often influenced by their variable domains. We have recently demonstrated that human variable domains can be engineered to resist aggregation. The engineered domains withstand challenging conditions, such as high temperature and acidic pH. Progress on the development of repertoires of such domains will be discussed. Aggregation-resistant single domains are a promising class of antibody fragments and provide robust building blocks for the generation of larger antibody therapeutics.

3:05 Antibody Selection from Immunoglobulin Gene Libraries Expressed in Mammalian Cells

Sponsored by VACCINEX

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

Utilizing a vaccinia virus based library technology we have developed an antibody discovery technology that enables efficient selection of full length IgG antibodies from highly diverse immunoglobulin gene libraries expressed in mammalian cells. This technology can be used either for de novo antibody selection or for the robust conversion of a non-human antibody into a panel of fully human antibodies with similar or even improved affinity and functional activity. This technology has a number of advantages, including a built in selection for full length IgG antibodies that are efficiently expressed in mammalian cells.

3:35 Refreshment Break, Poster and Exhibit Viewing

4:15 Designing Quality in Antibodies: In silico Aggregation Screening and Protein Engineering methodologies to Improve Developability and Safety Profiles.

Jesús Zurdo, Ph.D., Head, Advanced Protein Technologies, Lonza Biologics plc

Protein aggregation and low stability imposes severe restraints in the development of biopharmaceuticals, potentially increasing the risks of undesired immune responses in patients. Predictive algorithms can be used during lead selection to screen out polypeptides with aggregation / stability issues early on in the development process. Such methodologies have also been successfully applied to re-designing therapeutic antibodies with improved stability properties.

4:45 Human Antibody Discovery and Optimization in Yeast

Michael J. Feldhaus, Ph.D., Senior Director, Antibody Engineering, Adimab, Inc.

We have developed an integrated platform for the discovery and optimization of human IgGs in yeast. Unprecedented speed from antigen to panels of human IgG protein is attained. Selection of binders within the IgG format results in desirable bioprocess phenotypes for the selected antibodies.

5:15 End of Conference

Difficult to Express Proteins

Exploring New Paradigms in Expression Science

MONDAY, MAY 17

7:00 am Registration and Morning Coffee

IMPROVING PERFORMANCE FROM THE GROUND UP

8:30 Chairperson's Opening Remarks

Norman Garceau, Ph.D., Chief Scientific Officer, Blue Sky Biotech, Inc.

8:40 KEYNOTE PRESENTATION

Breaking the Cell Wall Barrier for Difficult-to-Produce Natural and Supernatural Products

James R. Swartz, Ph.D., Bioengineering, Stanford University

9:10 Screening Approaches to Solving Expression and Solubility Problems Using Novel Tagging and Detection System

Geoffrey Waldo, Ph.D., Team Leader, Biosciences, Los Alamos National Laboratories

We use a 15 amino acid tag, 'FPmicroTag', from a novel fluorescent protein to screen for soluble, stable protein complexes, find compact soluble protein domains and well-behaved multidomain proteins in living cells and in the test tube. The fluorescent detection system is stable and even 9 M urea does not perturb fusion protein behavior. We apply this to protein trafficking, protein interaction detection, high-throughput measurement of soluble protein in living cells, and engineering proteins for stability and solubility.

9:40 Applications and Expansions of Expression Modules That Tag Mammalian Membrane Proteins

Li Lin, Ph.D., Cardiovascular Sciences, National Institute on Aging, NIH

The recombinant expression of mammalian membrane proteins has been a major stumbling block in efforts to dissect their biological functions and determine their structures. It is also often difficult to generate effective antibodies to membrane proteins. To overcome these difficulties, we have designed, and generated, a set of expression modules that facilitate subcloning, expression, and detection of mammalian membrane proteins. The applications of these modules are further expanded to study the configuration of membrane proteins on cell surface, and to study signal transduction.

10:10 Grand Opening Coffee Break in Exhibit Hall

11:10 Evaluating Host Cell Differences for Difficult to Generate Proteins

Jennitte Stevens, Ph.D., Senior Scientist, Protein Science, Amgen

11:40 Meeting the Gene Expression Challenges Posed by Heterologous Polyketide Biosynthesis

Blaine A. Pfeifer, Assistant Professor, Chem. & Biological Eng., Tufts University

The last 15 years have seen a steady increase in efforts to heterologously produce polyketides through engineering-friendly organisms like *Escherichia coli*. However, many polyketide synthases are large proteins (>300 kDa) with unique structural and higher order assembly characteristics. In addition, the pathways needed for successful heterologous reconstitution may require up to 20 coordinately expressed genes before full biosynthesis would be expected. These challenges remain key technical hurdles to realizing the full potential of heterologously produced polyketide natural products, and this presentation will specifically address routes our group has taken to meet these challenges.

12:10 pm Dual Purpose Aminoacyl-tRNA Synthetases

A. James Link, Ph.D., Professor, Chemical Engineering & Molecular Biology, Princeton University

Much effort in the last decade has been placed on the engineering of aminoacyl-tRNA synthetases (aaRS) for the incorporation of unnatural amino acids into recombinant proteins. In this talk we describe strains of *E. coli* that harbor a single genomic copy of an engineered methionyl-tRNA synthetase (MetRS). The MetRS can ligate either the unnatural amino acid, azidonorleucine, or its natural substrate, methionine to methionyl-tRNA. Thus, these strains can be considered "dual purpose" organisms, the genetic code of which changes as a function of environment. The use of these strains for protein production and several other studies will be discussed.

12:40 Presentation

Sponsored by novozymes Rethink Tomorrow

Chris Finnis, Ph.D., Manager, Molecular Biology, Novozymes Inc

12:55 Luncheon Presentation I

Sponsored by Thermo SCIENTIFIC

Human *In Vitro* Translation Systems for Rapid, High Fidelity Protein Production

Brian Webb, Ph.D., Platform Manager, Proteomics R&D, Thermo Fisher Scientific

Current in vitro expression systems suffer from low yields or inaccurate post-translational modifications. E.coli- and wheat germ-based in vitro systems cannot glycosylate proteins and protocols involving rabbit reticulocyte lysates in combination with canine microsomal membranes produce low amounts of protein and are inefficient at glycosylation. We report here the development of novel in vitro systems derived from human cell lines that yield biologically active glycoproteins with up to 15-fold more protein than rabbit reticulocyte lysates

EXPRESSING PROTEINS FOR STRUCTURE

2:00 Chairperson's Remarks

Philip Laible, Ph.D., Argonne National Laboratory

2:05 Assessment of the Importance of Sample Purity on Membrane-Protein Crystallization in Different Systems

Philip Laible, Ph.D., Argonne National Laboratory

Practical guidelines are needed to increase the efficiency of membrane protein crystallization. The difficulty in purifying active membrane protein samples and the high costs associated with producing such samples require extremely pragmatic approaches. We have investigated the effects of commonly encountered impurities on various membrane protein crystallization regimes, and we report that the lipidic-cubic-phase based crystallization methodology is more robust than crystallization in detergent environments in its ability to tolerate contaminations in the forms of protein, lipid, or other general membrane components.

2:35 Expression, Refolding and Purification of a Human IL-17A Variant for Structural Studies

Bingyuan Wu, Ph.D., Research Scientist, Molecular and Protein Biosciences, Centocor, Inc.

In this study, the expression of a human IL-17A variant in *E. coli* was optimized. The protein was isolated as inclusion bodies and refolded in a buffer containing arginine, glycerol and a redox coupling agent. The refolded rhIL-17A variant was subsequently purified using a combination of cation-exchange, reversed phase and fluoroapatite chromatography. The purified product was active, homogeneous and crystallizable. This presentation describes an example of expression and purification method development to overcome the challenges of a difficult protein.

3:05 Refreshment Break, Poster and Exhibit Viewing

GLYCOSYLATION

3:45 A Robust, Automated, High-Throughput Quantitative HPLC-Based Platform for Glycan Analysis with Computer-Assisted Data Interpretation

Pauline Rudd, B.Sc., LRIC, MA (OXON), Ph.D., NIBRT Professor , Glycobiology, University College Dublin, Medical Sciences, NIBRT

Features include (i) sample immobilization (96-well plates), glycan release, and fluorescent labeling; (ii) quantitative HPLC analysis, including monosaccharide sequence and linkage information for charged and neutral glycans; (iii) automatic structural assignment from HPLC profiles via web-based software that accesses our experimental database (GlycoBase) and (iv) software (autoGU) that progressively analyzes data from exoglycosidase digestions giving a refined list of final structures (v) detection at <0.5% of total glycan pool (vi) sialic acid speciation (vi) compatible with MS and CE technologies.

4:15 Engineering N-Glycosylation in the Baculovirus Expression System

Christoph Geisel, Department of Molecular Biology, University of Wyoming

Insect cell hosts used in the baculovirus expression system typically produce glycoproteins with truncated N-glycans, whereas glycoproteins from mammalian cells bear extended N-glycans. This difference is caused by the presence of a deleterious processing enzyme as well as a lack of glycosyltransferases in insect cells relative to mammalian cells. We have engineered insect cells to express glycosyltransferases, thus allowing the production of mammalian-like N-glycans. Recently, we identified genes encoding processing enzymes in commonly used cells lines, which allows us to further improve their glycosylation potential.

4:45 Problem Solving Break-Out Sessions

Enhancing Cytoplasmic Expression in Mammalian Cells

Host: Dominic Esposito, Ph.D. (Contractor), Principal Scientist, Group Leader, Clone Optimization Group, Protein Expression Laboratory, Advanced Technology Program, SAIC-Frederick, Inc.

- Effects of promoters, enhancer, and other elements on transient protein production
- Transient transfection vs lentiviral transduction
- Ways to monitor protein expression and solubility using fusion tags
- High-throughput mammalian protein expression techniques

Getting a Handle on Proteins Using the Right Tag

Host: Geoffrey Waldo, Ph.D., Team Leader, Biosciences, Los Alamos National Laboratories

- Tagging objectives: Purification or detection or both.
- Library screening requirements (host, protein, library size, property to be screened for).
- Survey of some protein tagging systems (pros and cons, specificity, size, expense, readout format).
- Examples of tagging and library screening

Mammalian membrane proteins: how to break the bottleneck

Host: Li Lin, Ph.D., NIH/NIA/IRP

- Choice of expression hosts
- Ways to monitor/detect membrane protein in cells and tissues (epitope tagging and generating effective antibodies)
- Proteomics studies of membrane protein complexes
- Structure-function study of membrane proteins

- Membrane protein and signal transduction

Novel Analytical Techniques/Tools for the Characterization of Biopharmaceuticals

Host: Jennifer F. Nemeth, Ph.D., Principal Research Scientist and Head, Discovery Mass Spectrometry, Centocor Research and Development

- New and improved technologies
- Novel methods
- Software characterization programs
- Bioinformatics options for biopharmaceutical characterization

5:45 Networking Cocktail Reception in the Exhibit Hall

TUESDAY, MAY 18

EXPRESSING "FINICKY PROTEINS:" CASE STUDIES IN SUCCESS

8:25 Chairperson's Opening Remarks

Jean-Luc Lenormand, Ph.D., HumProTher Laboratory, Université Joseph Fourier

8:30 HaloTag® Based Purification of Functional Proteins from Mammalian Cells *Sponsored by* Promega

Rachel Friedman Ohana Ph.D., Senior Research Scientist, Research and Development: Cellular Proteomics, Promega Corporation

Obtaining high yields of functional mammalian proteins containing relevant post-translational modifications remains a critical challenge; we addressed this with a new method for purification of intracellular mammalian proteins from their native location. This approach is based on a protein fusion tag, HaloTag, which provides efficient protein purification through covalent immobilization coupled with proteolytic tag removal. We have used this method to purify intracellular proteins including 5 kinases from different kinase families and obtained milligram levels of pure proteins from 1 L cultures. All proteins were tested for activity and shown to be functional.

9:00 Employing Rhodobacter sphaeroides to Functionally Express and Purify Human G Protein-Coupled Receptors

Ankita Roy, Ph.D., NIEHS, NIH

Functional production of most recombinant GPCRs is one of the main bottlenecks to obtaining structural information. We used a novel bacterial expression system based on the photosynthetic bacterium *Rhodobacter sphaeroides* for this purpose. The advantage of employing *R. sphaeroides* as a host lies in the fact that it provides much more membrane surface per cell compared to other typical expression hosts. We tested this system for the expression of some class A GPCRs. The system can be extended for other "difficult to express and crystallize" membrane proteins in general.

9:30 Comparison of High-Throughput Techniques for the Expression of Protein Complexes

Gyorgy Babnigg, Ph.D., Scientist, Biological Sciences, Argonne National Laboratory

While Structural Genomics pipelines have extensive experience with the expression of single proteins in high-throughput fashion, the generation of protein complexes is labor intensive using current techniques. Most of the existing techniques are not compatible with HTP operations or are not economical at that scale. We developed recently a technique compatible with high-throughput operation for the expression of protein complexes and the results of this comparative study are presented.

10:00 Coffee Break, Poster and Exhibit Viewing

10:45 Production of Recombinant Proteoliposomes for Therapeutic Uses

Jean-Luc Lenormand, Ph.D., HumProTher Laboratory, Université Joseph Fourier

The use of recombinant proteoliposomes containing therapeutic membrane proteins is a recently developed technology that allows biologically active proteins to penetrate across the plasma membrane of eukaryotic cells. One of the bottlenecks in this powerful delivery system lies in the production of functional therapeutic membrane proteins, mainly due to their biophysical characteristics. This presentation describes the methodology for the production of bioactive proteoliposomes containing therapeutic, proapoptotic membrane proteins synthesized with an optimized cell-free expression system. This system can be easily adapted for producing "difficult to express proteins."

11:15 Co-Expression of AMPK Subunits in Insect Cells Yields a Stable Heterotrimer

Lata Ramanathan, Ph.D., Senior Scientist, Protein Sciences, Schering-Plough Research Institute

11:45 Elimination of Bacterial Toxicity of the Gene Encoding the Tfg1 Subunit of *S. cerevisiae* TFIIF

Alfred S. Ponticelli, Ph.D., Associate Professor, Biochemistry, School of Medicine and Biomedical Sciences, State University of New York, Buffalo

Biochemical studies of the yeast *S. cerevisiae* RNA polymerase II basal transcription machinery have been hampered by difficulties in the production of recombinant transcription factor IIF (TFIIF), specifically due to the extreme toxicity of the gene encoding the Tfg1 subunit in *E. coli*. I will report on the elimination of TFG1-associated toxicity in *E. coli* through the identification and mutational inactivation of both a functional *E. coli* promoter and an internal translation initiation site within the N-terminal coding region.

12:15 pm Expression of a Vaccine Antigen Candidate Protein in the *Pseudomonas Fluorescens*-Based Pfenex Expression Technology

Bruce Carpick, Ph.D., Principal Scientist, Biochemistry Research, Sanofi Pasteur

Expression of soluble and active protein is critical to the success of any protein based vaccine or therapeutic product development program. This is quite challenging given the complexity of the proteins being expressed in recombinant systems today. This case study will describe the expression of a particularly challenging antigen using Pfenex Expression Technology. The presentation will cover the small scale parallel screening of hundreds of unique expression strains and subsequent in vitro a nd in vivo pre-clinical testing of the antigen produced.

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

UNIQUE HOSTS AND TOOLS

2:00 Chairperson's Remarks

Dominic Esposito, Ph.D., SAIC Frederick, Inc.

2:05 Expression Plasmids and Production of EGFP in Stably Transfected *Acanthamoeba*

Erik A. Bateman, Ph.D., Research Associate Professor, Microbiology & Molecular Genetics, University of Vermont

Stable transfection of *Acanthamoeba castellanii* for promoter analysis and protein expression has been characterized. Expression plasmids containing the TBP, TPBF or GAPDH gene promoters from Acanthamoeba were constructed. The promoters for *Acanthamoeba* TPBF and GAPDH genes were used to drive expression of enhanced green fluorescent protein (EGFP) in stably transfected Acanthamoeba. Purification from lysates of 22-ml cultures yielded approximately 1.1 milligrams of EGFP, a value that extrapolates to 50 milligrams per liter of cell culture. Results suggest that *Acanthamoeba* is a useful system for production of recombinant proteins.

2:35 The Science of Solubility: Structure/Function Studies of Chimeric NusA Fusion Tags Provides Insight into Protein Solubility Enhancement

Dominic Esposito, Ph.D., Group Leader, Clone Optimization Group, Protein Expression Laboratory, Advanced Technology Program, SAIC-Frederick, Inc.

Enhancement of solubility of heterologous proteins in E. coli is often necessary if these proteins are to be produced at significant levels. We investigated the ability of homologs of the *E. coli* NusA protein to act as solubility enhancers, and in the process have discovered that very subtle differences in NusA protein sequence can have remarkable effects on the ability to solublize partner proteins. These results help to better understand the characteristics of the NusA protein which lead to its function as a solubility tag, and may lead to the production of more efficient solubility tags.

3:05 Functional Assembly of Membrane-Associated Protein Complexes on a Derivatized Lipid Template for HTS – a SmartScreen™ Technology Review *Sponsored by* BlueSky Biotech

Scott Gridley, Ph.D., Head of Product Development, Blue Sky Biotech

3:20 Advancing Synthetic Gene Design *Sponsored by* DNA 2.0

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

Gene synthesis offers immense flexibility in the tailoring of genes for practical uses. Capturing the value of this flexibility, however, is greatly limited by lack of understanding of the interactions between gene sequence features and host expression systems. DNA2.0 has developed a novel approach to interrogate the gene design preferences of expression hosts to maximize production from synthetic genes. Applications of this approach for a number of target proteins in several different host organisms will be discussed.

3:35 Refreshment Break, Poster and Exhibit Viewing

4:15 A Versatile Viral System for Expression and Depletion of Proteins in Mammalian Cells

Eric Campeau, Ph.D., Program in Gene Function and Expression, University of Massachusetts Medical School

The ability to express or deplete proteins in living cells using viral vectors has become essential to the study of biological processes. We recently published a collection of 59 vectors that comprise an integrated system for constitutive or inducible expression of cDNAs, shRNAs or miRNAs, and use a wide variety of drug selection markers. This system can be easily expanded to accommodate new designs and technologies to rapidly screen expression conditions or protein levels that would ensure maximal expression and biological activity.

4:45 Development of Algal Chloroplasts as a Novel Bioreactor for the Production of Pharmaceutical Proteins

Shengwu Ma, Ph.D., Plantigen Inc.; University of Western Ontario

Eukaryotic microalgae have recently received significant attention as a promising alternative to plant, bacteria or mammalian cell bioreactors for the production of recombinant pharmaceutical proteins, because of their simple growth requirements, ease of manipulation and high growth rate. The unicellular green alga Chlamydomonas reinhardtii is particularly attractive as a bioreactor since high levels of foreign protein accumulation have been achieved in its chloroplast. Apart from being easily transformed with foreign DNA, stable transgenic strains and high production volumes in full containment can be obtained with C. reinhardtii within a relatively short time. Furthermore, C. reinhardtii is a green alga which is generally recognized as safe (GRAS) for use as a food ingredient and therefore has the potential as a carrier for direct oral delivery of therapeutic proteins. In this presentation, I will review the progress made in the use of C. reinhardtii chloroplasts for the production of high-value therapeutic proteins, with particular reference to the expression of diabetes-associated autoantigen human glutamic acid decarboxylase (hGAD65) using the algal chloroplast organelle.

5:15 End of Conference

Immunogenicity of Therapeutic Biologics

Recommended Short Courses (Details on Page 3)*

SUNDAY , MAY 16

10:00am-1:00pm (SC2) Preclinical Safety Assessment of Biologics – Unexpected Safety Findings

2:00 pm – 5:00 pm (SC5) Antibody Drug Conjugates

Nancy Everds, DVM, Diplomate ACVP, Pathology Director, Clinical Pathology, Amgen

**Separate Registration Required*

MONDAY, MAY 17

7:00 am Registration and Morning Coffee

HOW DO YOU BEGIN?

8:30 Chairperson's Opening Remarks

8:40 KEYNOTE PRESENTATION

Thinking about Product Immunogenicity: From Tolls to Packaging

Daniela Verthelyi, Ph.D., Chief, Laboratory of Immunology, DTP/FDA

9:10 Immunogenicity Issues with Biosimilars: The Need for Comparability Assessment

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

Assessment of unwanted immunogenicity is important for ensuring the safety of biotherapeutics including biosimilar products. A comparative evaluation of relative immunogenicity of the biosimilar and the innovator product using an appropriate testing strategy and methods for antibody detection is a requirement for approval of a biosimilar product. Some examples of the immunogenicity issues with biosimilars and the current guidance available will be presented.

9:40 Importance of T cells to Antibody Response

Sara J. Brett, Ph.D., Department of Immunology, GlaxoSmithKline

This presentation will give an overview about the role of CD4+ T cells in regulation B cell and antibody responses. It will focus on the cellular and molecular interactions required to induce an antibody response to foreign antigens. The mechanisms of regulation of the antibody response to self antigens will be summarised and the potential mechanisms which result in breaking of self tolerance and the generation of auto-antibody responses will be discussed. The relevance of basic immunology of T cell regulation to the generation of an antibody response will be discussed in the context of clinical anti-drug antibody responses observed during therapy with protein agents such as monoclonal antibodies with examples from some case studies.

10:10 Grand Opening Coffee Break, Poster and Exhibit Viewing

11:10 Development of Point-of-Care Assay for Detection of Anti-Drug Antibodies

Tatiana Plavina, Ph.D., Scientist, Clinical Science & Technology, Biogen Idec

Given the speed and growing flexibility required to support drug development and increasing emphasis on individualized medicine, deployment to the point of patient care of a rapid and simple-to-perform test detecting the presence of anti-drug antibodies (ADA) may be desirable both in the clinical development and commercial settings. The feasibility of developing point-of-care ADA assay using a lateral flow platform was established. Materials and custom reagents were evaluated against desired specifications for ADA detection, and key areas requiring optimization were defined and will be discussed.

11:40 Protein Structures Responsible for Immunogenicity of Biologics

Barend Bouma, Ph.D., COO & Head, R&D, Crossbeta Biosciences

This presentation will report on the immune response and breaking of tolerance against interferon-alpha with conformational changes, accompanied by adoption of amyloid-like crossbeta structure and misfolding. For several biologics the level of crossbeta structure increases upon prescribed storage, and results indicate that misfolding of therapeutic proteins is a risk factor for immunogenicity. Methods for detecting potentially harmful misfolded protein entities with crossbeta structures will be described together with affinity matrices under development to remove harmful entities with crossbeta structures from biopharmaceutical preparations.

12:10 pm Potential Clinical Adverse Consequences Related to the Immunogenicity of Therapeutic Biologics

Jacques Descotes, M.D., Pharm.D., Ph.D., Fellow ATS, Professor and Head, Poison Center and Pharmacovigilance Department, Lyon University Hospitals

This presentation will report on the potential adverse consequences related to the immunogenicity of therapeutic biologics in treated patients. These include alterations in biopharmacokinetics or declining efficacy due to the development of neutralizing anti-drug antibodies as well as acute or delayed immune-mediated hypersensitivity reactions. Examples of therapeutic biologics for which a sufficient amount of nonclinical, clinical and post-marketing data is available will be used to illustrate the incidence, clinical outcome, pathogenesis and management of these adverse events.

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

CASE STUDIES: DEALING WITH IMMUNOGENICITY

2:30 Chairperson's Remarks

Sara J. Brett, Ph.D., Department of Immunology, GlaxoSmithKline

2:35 Selected Poster Presentations

3:05 Networking Refreshment Break, Poster and Exhibit Viewing

3:45 Non-Clinical Case Studies of the Interplay of Pharmacokinetics, Pharmacodynamics and Immunogenicity

Holly W. Smith, Ph.D., Senior Research Scientist, Investigative Toxicology, Eli Lilly and Company

Demonstrating adequate exposure to active drug in the presence of anti-drug antibodies is a complex formula of evaluating the format of the PK assay, the quantitative nature of the PD marker, and/or the interpretation of the immune-relatedness of the adverse event. We present examples of "complicated" immunogenicity assessments.

4:15 Review of the Immunogenicity of Therapeutic Insulins

S.Edwin Fineberg, M.D., Professor Emeritus Indiana University, School of Medicine and Clinical Professor of Medicine, UAB (Birmingham) School of Medicine

The factors affecting insulin antibody formation will be discussed including molecular structure, site of delivery and characteristics of recipients will be reviewed. Clinical trial data regarding insulin analogs and native insulins will be presented with special attention to data from inhaled insulin trials. Lastly, data will be presented regarding impact of insulin antibodies on clinical efficacy, insulin resistance and hypoglycemia.

4:45 Break-Out Sessions

ASK THE EXPERTS

Table 10: Current Practices in Clinical Immunogenicity Assessment

Catherine Wang, Ph.D., Manager, Clinical Immunology, Biopharmaceutical R&D, GlaxoSmithKline

Table 11: What is the Best Way to Manage the Clinical Program When Significant Immunogenicity/Immunotoxicity is Observed in Preclinical Studies

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

Table 12: Preclinical Screening for Immunogenicity Using in Silico, in Vitro and in Vivo Techniques; What's the Buzz

Anne S. De Groot, M.D., CEO & CSO, EpiVax, Inc.; Professor and Director, Institute for Immunology and Informatics, University of Rhode Island

Table 13: Role of Product Impurities and Innate Immunity in Product Immunogenicity

Daniela Verthelyi, Ph.D., Acting Chief, Laboratory of Immunology, DTP/FDA

5:45 Networking Cocktail Reception in the Exhibit Hall

6:45 End of Day

TUESDAY, MAY 18

8:00 am Registration and Morning Coffee

FACTORS DRIVING IMMUNOGENICITY: THE SCIENCE

8:25 Chairpersons' Opening Remarks

Laurent Audoly, Ph.D., Senior Director, Biologics Research, Merck Research Labs and Anne S. De Groot, M.D., CEO & CSO, EpiVax, Inc.; Professor & Director, Institute for Immunology and Informatics, University of Rhode Island

8:30 How Cells Resist Human Treg Suppression: A Role in Autoimmunity?

Clare Baecher-Allan, Ph.D., Assistant Professor of Neurology, Center for Neurologic Diseases, Brigham and Women's Hospital, Harvard Medical School

Decreased regulatory T cell suppression has been associated with a number of human autoimmune diseases. We have found that specific sub-populations of human Tregs isolated from patients with MS exhibit kinetically distinct deficiencies suggestive of different modes of regulation. Non-regulatory CD4 T cells produce factors that can inhibit the activity of human Tregs. Modulating the production or activity of such resistance factors could be therapeutically advantageous for the treatment of autoimmunity.

9:00 The Potential for Clinical Tolerance: New Targets for Co-stimulatory Molecule Blockade

John Iacomini, Ph.D., Associate Professor of Medicine, Assistant Director, Scientific Affairs, Transplantation Research Center, Brigham and Women's Hospital and Children's Hospital Boston, Harvard Medical School

In this presentation I will focus on the use of co-stimulatory molecule blockade strategies in transplantation. I will also focus on targeting co-inhibitory pathways and their potential for transplantation. Lastly, I will highlight recent work from our laboratory suggesting a role for Th17 cells in transplant rejection and novel co-stimulatory molecule blockade strategies that could be used to target these cells.

9:30 Relevance of Glycosylation to Recombinant Therapeutic Proteins and Monoclonal Antibodies

Jeremy P. Kunkel, Ph.D., Research Scientist, Centre for Biologics Research, Biologics and Genetic Therapies Directorate, Health Products and Food Branch, Health Canada

10:00 Coffee Break, Poster and Exhibit Viewing

10:45 A Novel Homogeneous Biotin-Digoxigenin Based Assay for the Detection of Human Anti-Therapeutic Antibodies in Autoimmune Serum

Julia Qiu, Ph.D., Scientist, Bioanalytical Research & Development, Genentech, Inc.

Homogeneous Biotin-Digoxigenin based bridging assay format was selected as an immunogenicity screening platform to replace the existing BioVeris ECL ATA assays at Genentech based on our evaluation of several available technologies. The presentation will cover the development, challenge, and qualification of a clinical Biotin-DIG ATA assay in RA matrix, as well as the investigational result of other potential interferences on the Biotin-DIG platform. The comparison of the assay performance between the homogeneous Biotin-DIG assay and the previous BioVeris ECLA will also be presented.

11:15 Molecular Determinants of T Cell Epitope Recognition in Timothy Grass Allergy

Alessandro D. Sette, Ph.D., Principal Investigator, Vaccine Discovery, La Jolla Institute for Allergy & Immunology

We have performed an in depth characterization of the epitope recognized in timothy grass, their lymphokine profile, their allergen of origin, HLA binding restriction and other immunological parameters. The results illustrate the mechanisms by which particular epitopes are recognized in the context of T cell responses directed against timothy grass allergens.

11:45 Immunization to Ameliorate Atherosclerotic Cardiovascular Diseases

Mark Carvlin, Ph.D., COO, CardioVax

Atherosclerosis involves the formation of inflammatory arterial lesions and is one of the most common causes of death globally. Recently, it has become apparent that the immune system may confer athero-protecting effects which blunt athero-promoting effects. We have shown that immunization with a formulation that selectively activates the athero-protective pathway can reduce atherosclerosis by up to 70%. In this presentation I will describe the translational work we are performing to advance CVX-210-H from the laboratory into clinical practice.

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

INNOVATIVE APPROACHES FOR PREDICTION

2:00 Chairperson's Remarks

2:05 Computational Simulations of the Immune System: Applications for Vaccine Development

Vladimir Brusic, Ph.D., Director, Bioinformatics, Cancer Vaccine Center, Dana-Farber Cancer Institute

Bioinformatic applications in vaccinology focus on the analysis of pathogen diversity, profiling of human immune system, management of immunological data, and mathematical modeling of the immune system. Predictive models development requires several cycles of experimental validation and refinement. We will present examples of recent developments in computational vaccinology and discuss how these tools are combined in an integrative large-scale system, including our experience with the Human ImmunoGrid project.

2:35 A Human Lymphoid Organ Model (HuALN) for Predictive Testing of Immunogenicity, Immunotoxicity and Immune Functions *in vitro*

Christoph Giese, Ph.D., Director, Cell and Tissue Services, ProBiogen

Biopharmaceutical drugs such as antibodies or cytokines may bear the risk of unexpected immunogenicity in the patient. Human tissue based models which emulate immune organ function are conceived to bridge the gap between early lead optimization and the pre-clinical development stage in immunotoxicity and predictive immunogenicity. The model of the Human Artificial Lymph Node (HuALN) is designed to investigate induced immune responses *in vitro*. The 3D organoid model can be used for long-term culture and repeated dosing. Cytokine release, antibody secretion, cellular functionality and tissue formation are monitored.

3:05 Nanoliter Scaled Immunoassay Performed on a Compact Disc: Maximizing Effectiveness in Pre-Clinical Biotherapeutic Development *Sponsored by*

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

Preclinical and clinical development of biotherapeutic agents is often challenged by data quality, slow turnaround time and delays due to slow assay development. Nano-liter scaled immunoassays on the Gyrolab™ workstation utilize innovative microfluidics on a compact disc that automates the assay workflow for reduced matrix interference and results in an hour. The system allows for up to 4 log dynamic range to minimize the need to dilute samples and repeat analyses. This talk will focus on case studies highlighting the use of the Gyrolab in therapeutic protein development and immunogenicity of biotherapeutics from early discovery to clinical trials.

3:20 Sponsored Presentation II *Sponsored by*

Handling Allergenicity Risks in Clinical Development of Biologicals

Jörgen Dahlström, Ph.D., Senior Scientific Manager, Phadia

3:35 Networking Refreshment Break, Poster and Exhibit Viewing

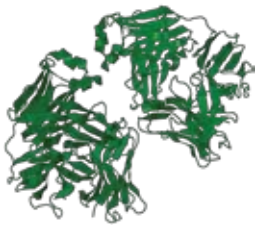
4:15 Vaccine Development in Enhanced Hu-NSG Chimeric Mice

Robert T. Woodland, Ph.D., Department of Molecular Genetics and Microbiology, University of Massachusetts Medical School

Humanized mice present a potentially unique opportunity to model the human immune response *in vivo*. We show these mice when appropriately supplemented with critical human cytokines will produce de novo immune responses to challenge with both T cell dependent and T cell independent antigens. The use of these mice as a platform for vaccine development will be discussed.

4:45 End of Conference

> "The new landscape of drug discovery is highlighted by open innovation- PEGS is the ideal forum for sharing our collective ideas for increasing R&D productivity."
>
> Chief Executive Officer, Blue Sky Biotech



Engineering Antibodies

Creating Solutions for Antibody Discovery and Development

WEDNESDAY, MAY 19

7:00 am Registration and Morning Coffee

DISCOVERY

8:30 Chairperson's Opening Remarks
George Georgiou, Ph.D., Professor, Chemical Engineering, University of Texas, Austin

8:40 Unique Combination of Computational Modeling, Antibody Engineering and Cell Biology
Birgit Schoeberl, Ph.D., Vice President, Discovery, Merrimack Pharmaceuticals

We will discuss the importance of disease context with respect to the design of monoclonal or bispecific antibodies. In addition, we will address the importance of growth factor receptor signaling crosstalk and how these insights drive the antibody design and engineering.

9:10 Importance of Early and Complete Characterization of Antibodies in the Lead Selection Process
Shrikant Deshpande, Ph.D., Senior Director, Protein Chemistry, Medarex, a wholly owned subsidiary of Bristol-Myers Squibb Co.

Selection of a lead candidate from a pool of antibodies is a critical step in product development. A wrong lead selected will result in major development issues. Understanding the biophysical and analytical characteristics of a pool of antibodies using a variety of tests will not only help select ideal leads, but also reduce or eliminate development issues.

9:40 Case Study: Engineered Human Antibody CH2 Constant Domains (Nanoantibodies) as Novel Candidate Therapeutics
Rui Gong, Ph.D., Postdoctoral Visiting Fellow, Protein Interaction Group, CCRNP, CCR, NCI-Frederick

Isolated immunoglobulin constant CH2 domains (nanoantibodies) are promising as scaffolds for selection of binders with potential effector functions. The binders against HIV-1 were selected and identified from several large libraries based on CH2 scaffold. However, CH2 domain is relatively unstable to thermally induced unfolding, which limits the use of CH2 as scaffold. A stabilized CH2 mutant (m01) with an additional disulfide bond was engineered and characterized, which can be used for the development of candidate therapeutic antibodies with increased stability.

10:10 Coffee Break, Poster and Exhibit Viewing

11:10 A Computational-Experimental Strategy for the Isolation of Antigen-Specific Antibodies from Immunized Animals
George Georgiou, Ph.D., Professor, Chemical Engineering, University of Texas, Austin

We have developed a computational-experimental strategy for the isolation of antigen-specific antibodies from immunized animals. This methodology is simple, fast and requires neither cloning nor screening. In addition, and to complement Ab isolation from immunized animals we have developed an improved bacterial display system for affinity maturation, for Fc engineering and *de novo* antibody discovery.

11:40 Analytical Methods to Characterize and Evaluate the Mode of Action of Antibody Drug Conjugates
Vangipuram Rangan, Ph.D., Director, Protein Chemistry, Medarex, a wholly owned subsidiary of Bristol-Myers Squibb Co.

Antibody drug conjugates (ADC) are emerging platform technology where antibodies are used as targeting agents to deliver payloads to the tumor site. In order to characterize ADCs as well as to understand their mechanism of action, one has to develop various analytical methods and assays that are unique to ADCs. This presentation describes several analytical methods that are employed to characterize ADCs being developed at Medarex, a wholly owned subsidiary of BMS.

12:10 pm Luncheon Presentation I: Slonomics® - An Innovative Toolbox for the Precise Engineering of Immunoglobulin Repertoires
Sponsored by sloning BioTechnology
Thomas Waldmann, Ph.D., Dir., Sci. & Technology Support, Sloning BioTechnology GmbH

Slonomics®, a proprietary genetic engineering platform, uses standardized DNA triplets as building blocks. It allows for introducing multiple codons in parallel at any desired sequence position. The ability to precisely control the individual frequency of up to 20 specific codons per position results in genetically diverse libraries with unique molecular profiles. The technology easily allows for combining complex positional mutation strategies with diversifying the length of randomized regions. Therefore, synthetic antibody libraries of highest quality can be created that mimic the design of naturally occurring immunoglobulin repertoires.

12:40 Luncheon Presentation II: Best Practices in the Design of Antibody Models Using In-Silico Methods
Sponsored by accelrys®
Francisco G. Hernandez-Guzman, Ph.D., Accelrys, Inc.

As the pharmaceutical, biotech and academic labs continue their research in antibodies as alternative therapeutic agents to classical small molecule therapy, more and more scientists are looking for structural information to help their understanding of antibody-antigen interactions, as well as various other biophysical properties. By leveraging the high homology within the antibody family, one can successfully build reliable models with a high degree of molecular detail. In this presentation, we will explore the process of building a homology for an Fab domain. We will highlight a process that has shown to give high quality models and we will discuss some of the challenges that one has to watch for during the model building process. We will also emphasize methodologies used to refine the Complimentary Determining Regions (CDRs) of the antibody, and in particularly explore some approaches that can be used to increase the reliability of modeling the challenging H3 loop.

EPITOPES, MAPPING AND ANALYSIS

1:30 Chairperson's Remarks

1:35 Application of H/D-Exchange for Epitope Screening to Assist with Candidate mAb Selection
Jennifer Nemeth, Ph.D., Principal Research Scientist, Biologics Research, Centocor Research and Development

Hydrogen/deuterium-exchange (H/D-Ex) coupled with mass spectrometry is having an impact in the biopharmaceutical arena in the area of epitope mapping and lead selection. As the use of the technology is still quite novel for biopharmaceutical applications, this talk is timely and relevant in this era of intelligent drug design. An example of the utility of this technology is highlighted during lead selection in a monoclonal antibody (mAb) drug program. As the timelines and sample amounts were limited, hydrogen/deuterium-exchange (H/D-Ex) was chosen for mapping out the epitopes on the target antigen, as opposed to more traditional techniques. Based on the results, lead and back-up mAbs were selected that had desirable epitopes for further product development.

2:05 A Multi-Fc-Species System for Recombinant Antibody Production
Stefan Dübel, Ph.D., Professor, Technical Institute of Braunsweig

2:35 Use of Disposable Label-Free Real-Time Biosensors in Epitope Binning Monoclonal Antibodies
Sponsored by fortéBIO
Yasmina Noubia Abdiche, Ph.D., Senior Principal Scientist, Rinat Laboratories-Pfizer Inc.

This talk introduces a novel 384-well platform based on bio-layer interferometry (BLI) detection equipped with disposable fiber-optic tips that can be used for characterizing antibody interactions. Rerackable banks of 16 biosensors move to samples without any microfluidics, which opens up the possibility of immobilizing and regenerating batches of ligands on- or off-line to expedite screening. We compare data generated using BLI with those obtained by SPR to highlight the advantages of using this label-free real-time biosensor platform in the context of epitope binning monoclonal antibodies.

2:50 Deriving and Epitope Mapping Antibodies Targeting Membrane Proteins
Sponsored by integral
Benjamin Doranz, Ph.D., President and CSO, Integral Molecular

Integral Molecular's Lipoparticle technology provides an innovative solution for presenting structurally intact membrane protein antigens, including GPCRs and ion channels, at concentrations 10-100x higher (50-200pmol/mg) than in cells or membrane preparations. This enabled us to derive high titer serum responses (>1:500) against membrane proteins of interest and to characterize resulting antibodies using techniques such as biosensor analysis. Once MAbs are isolated, our Shotgun Mutagenesis Mapping technology enabled us to rapidly identify both linear and conformationally complex epitopes that distinguish MAb binding sites.

3:15 Networking Refreshment Break, Poster and Exhibit Viewing

3:50 Problem Solving Break-Out Sessions

***In vitro* Screening or Immunization? Isolating Biologically Active Antibodies**
Host: George Georgiou, Ph.D., Professor, Department of Biomedical Engineering, University of Texas at Austin

CMC issues with ADCs
Host: Vangipuram S. Rangan, Ph.D., Director, Protein Chemistry, Medarax Inc. a subsidiary of Bristol-Myers Squibb

- Importance of identification of site of conjugation in current ADC platforms
- Random conjugation versus site-specific conjugation
- Importance of analytical methods

Engineered Antibody Domains
Host: Rui Gong, Ph.D., Postdoctoral Visiting Fellow, Protein Interaction Group, CCRNP, CCR, NCI-Frederick

Increasing Efficiency of Phage Display Libraries and Selection
Host: Prof. Dr. Stefan Dübel, Technische Universität Braunschweig, Institute of Biochemistry and Biotechnology

- Pitfalls in library making
- Controlling display valency
- QC of libraries
- Tuning of panning conditions to get what you want

Stability Prediction Parameters: How Well They Perform in the Real World?
Host: Shrikant Deshpande, Ph.D., Medarex Inc, a subsidiary of Bristol-Myers Squibb

- How can we predict the stability of the antibodies in the real world based on early screening techniques such as DSC, aggregation propensity
- Acclerated deamidation studies: How well they correlate with the in vivo situation?"

4:50 Networking Cocktail Reception in the Exhibit Hall

6:00 End of Day

THURSDAY, MAY 20

8:00 am Registration and Morning Coffee

EPITOPES, MAPPING AND ANALYSIS, CONT.

8:30 Chairperson's Opening Remarks
Stefan Dübel, Ph.D., Professor, Technical Institute of Braunsweig

8:35 Structure-Based Prediction of Antibody Epitopes
Julia Ponomarenko, Ph.D., Senior Scientist, Computational Biology, Skaggs School of Pharmacy & Pharmaceutical Science, San Diego Supercomputer Center, University of California, San Diego

Prediction of antibody epitopes, or antibody binding patches on the surface of protein antigens, remains challenging yet highly desirable for the design of vaccines and immunodiagnostics. In this work, we ask whether a comprehensive analysis of sequence and structural properties of three-dimensional structures of antibody-protein complexes enables reliable prediction of epitopes, or this task is still infeasible, given our current knowledge of protein antigenicity and antibody repertoire.

ANTIBODIES AS PAYLOAD SPECIALISTS

9:05 A Novel Approach to Antibody Drug Conjugates
James Prudent, Ph.D., CEO, Research & Development, Centrose LLC

Despite the potential of the antibody drug conjugate concept, a key complication in the development of effective ADCs exists: drug-antibody cell internalization followed by active drug separation. In order to circumvent this, we envisioned that a new class of ADCs where internalization and antibody-drug separation would not be required could be developed. Data will be presented that shows this concept is valid and may be broadly applicable.

EXPRESSION, CHARACTERIZATION AND PURIFICATION

9:35 A Paradigm Shift in Protein Expression Enabling Lead Selection Concomitant with Isolation of the Production Cell Line
Sponsored by SELEXIS
Andrew Sandford, Selexis S.A.

From discovery to manufacturing, approach es to protein expression vary widely depending on the type of protein being expressed, application of use, amount required, project timeline and the preferences of the scientist conducting the research. This variability often necessitates expression system reformatting which can extend timelines, impact protein quality and compromise fundamental preclinical decision. Selexis SA has developed an uncomplicated and efficient approach allowing for the expression an identification of lead molecules while isolating the Production Cell Line.

10:05 Coffee Break, Poster and Exhibit Viewing

11:05 DARPins as Alternative to Antibodies
Michael T. Stumpp, Ph.D., CSO and Co-Founder, Molecular Partners AG

DARPins are a novel class of high-affinity, low-immunogenicity protein drugs that combine the advantages of antibodies and small molecule drugs. The favorable properties of DARPins enable the fast generation and production of a variety of drug candidates for different indications. Examples of how to generate DARPins and select therapeutic drug candidates with superior characteristics will be discussed. A best-in-class therapeutic program, called MP0112, the lead DARPin to treat ocular neovascularization diseases, will be presented.

11:35 Fc N-linked Oligosaccharides and their Effect on Recombinant IgG1 Monoclonal Antibody Binding to Protein-A and Protein-G
Georgeen Gaza-Bulseco, M.S., Senior Research Scientist, Abbott Bioresearch Center

Effects of N-linked oligosaccharides in the Fc region of a recombinant IgG1 on the binding to Protein-A and Protein-G were investigated. Deglycosylated antibodies eluted later from Protein-A but earlier from Protein-G resins than glycosylated antibodies when a decreasing pH gradient was used. In addition, presence of different types of oligosaccharides affected elution of the antibodies. Antibody glycosylation status had no effect on antigen binding suggesting that differences in elution profiles were due to structural changes in the CH2-CH3 domain interface under low pH conditions.

12:05 pm End of Conference

THIRD ANNUAL MAY 19 - 20, 2010

Pre-Clinical/Clinical Development of Therapeutic Antibodies

Recommended Short Courses (Details on Page 3)*

SUNDAY, MAY 16

2:00 – 5:00 pm (SC8) Membrane Proteins - An Important Protein Class

THURSDAY, MAY 20

5:30 – 8:30 pm (SC 10) Affinity Tags for Protein Purification - Dinner Presentations & Discussions

**Separate Registration Required*

WEDNESDAY, MAY 19

7:00 am Registration and Morning Coffee

TOXICOLOGY

8:30 Chairperson's Opening Remarks

Jeffrey A. Engelhardt, D.V.M., Ph.D., DACVP, President and Pathologist, Engelhardt Consulting, Inc., and SNBL USA, Ltd.

8:40 OPENING KEYNOTE PRESENTATION

Revealing the "Magic" of Monoclonal Antibodies
Joy Cavagnaro, Ph.D., President, Access BIO

Monoclonal antibodies have been used as experimental therapy and as essential research tools since the beginning of the 1980s. Initially considered as the ultimate realization of Paul Ehrlich's concept of a "magic bullet," monoclonal antibodies have evolved over the past three decades. This presentation will reveal the "tricks of the trade" that have enabled the successful development and approval of monoclonal antibodies for diagnosis and treatment and include a brief glimpse into the future.

9:10 Recommendations for Nonclinical PK Comparability Study Designs for Monoclonal Antibodies
Wendy Putnam, Ph.D., Scientist, Pharmacokinetics and Pharmacodynamics, Genentech, Inc.

Nonclinical pharmacokinetic studies may be required to demonstrate comparability of therapeutic antibodies following manufacturing changes during clinical development and post-approval. This presentation will discuss when and how to conduct nonclinical PK comparability studies. Factors to consider in designing comparability studies will be discussed, including selection of study species, dose/regimen, PK endpoint, acceptance criteria, and sample size. Case studies of the use of nonclinical PK comparability studies in the development of therapeutic monoclonal antibodies will be reviewed, together with lessons learned.

9:40 The Role of Pharmacokinetics in the Design, Conduct and Interpretation of Toxicology Studies with Antibody-Based Biotherapeutics
Stanley A. Roberts, Ph.D., D.A.B.T., Principal, SAR Safety Assessment LLC

Understanding the disposition of antibody-based therapeutics is critical for selecting the best new drug candidates. Principles and strategies will be reviewed that detail the studies necessary for assuring that compounds with the appropriate efficacy and safety attributes are selected for development. Specific case histories will be discussed that provide examples of how the pharmacokinetic characteristics are determined and their impact on toxicology studies. The potential impact on the development program, including human studies, will also be discussed.

10:10 Coffee Break, Poster and Exhibit Viewing

TOX - SAFETY

11:10 Nonclinical Reproductive and Developmental Toxicity Testing Strategies with Antibody Therapeutics

William J. Breslin, Ph.D., Senior Research Advisor, NSD Safety Assessment, Eli Lilly and Company

Because antibodies (Ab) therapeutics are highly target and species specific, they may not demonstrate active pharmacology in standard rat, mouse or rabbit models. As a result, nonhuman primate, homologous molecule, or transgenic models may be required for the evaluation of nonclinical reproductive and developmental toxicity. The application of these nontraditional strategies for reproductive and developmental toxicity using Ab therapeutics will be addressed using examples from previous and ongoing drug development programs.

11:40 Translational Safety for Therapeutic Antibodies: Protecting Subjects and Enabling Risk:Benefit Decisions During Early Clinical Development

Andrew Erdman, M.D., Global Safety Medical Director, Amgen

The transition from preclinical to clinical development is a critical milestone in drug development, with safety as the critical concern. This talk will discuss tactics, strategies and resources designed to ensure the safety of subjects in early clinical trials, identify and manage any risks to subjects and the development program as a whole, and provide the necessary safety information to enable early risk:benefit development decisions.

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

TOX - TESTING MODELS

1:30 Chairperson's Remarks

Stanley A. Roberts, Ph.D., D.A.B.T., Principal, SAR Safety Assessment LLC

1:35 Species Selection: The Foundation of the Nonclinical Toxicology Program

Marque Todd, Ph.D., Regulatory Strategy Lead, Drug Safety Research & Development, Pfizer, Inc.

Selection of relevant species for the nonclinical development of biotherapeutics is foundational for the entire development program. Several aspects need to be addressed before the most relevant species can be selected and compared with the similar human data: target sequence homology, target distribution, target binding and affinity and biological activity. Assessment of potential immunogenicity may also be important. Several different techniques exist that can aid the nonclinical scientist in collecting and assessing data for species selection. These various aspects of species selection will be addressed in the presentation.

2:05 Surrogates: Their Use, Qualification and Challenges

Janet Clarke, Ph.D., D.A.B.T., Senior Director, Pharmacotoxicology, Biogen Idec

Surrogates can serve a useful role in providing safety data when use of the clinical candidate is limited by lack of activity in animal models. Circumstances to consider when to use or not use a surrogate antibody, and how to "qualify" a surrogate for use to represent a safety assessment of the clinical candidate will be discussed with reference to specific examples. Finally, scientific, financial and regulatory challenges will be outlined.

2:35 Real Time Cell Surface Interaction Analysis: A Focus on Lectin-Cell Glycan Interactions

Sponsored by attana

Staffan Grenklo, Ph.D, Cell Biologist, Attana AB

In today's quest for new therapeutic drugs, it is increasingly important to obtain early and informative data on potential agents in order to save time and costs. Combining biosensor technologies contributing to detailed information on molecular interactions with an experimental approach, as close as possible to the natural environment of action, increases the chances of selecting the optimal candidate already in the pre-clinical phase.

2:50 Biomolecule Production Using PEI-Mediated Transient Transfection

Sponsored by Polyplus transfection

Alain Cuzange, Ph.D., Polyplus-Transfection

Transient gene expression in mammalian cells is an attractive alternative for recombinant protein & antibody production. Chemically-defined media supporting the growth of non-adherent cells are commonly used. The use of the cationic polymer, polyethylenimine (PEI), a well-known synthetic delivery reagent, for transfection is covered by a patent from which Polyplus-transfection™ is the worldwide exclusive licensee. Our latest generation of linear PEI is more efficient than the previous branched polymers for transfection into mammalian cells. An overview of the properties and different qualities of PEIs used in bioproduction will be presented.

3:05 Networking Refreshment Break, Poster and Exhibit Viewing

3:50 Problem Solving Break-Out Sessions

We present these one-hour moderated discussion groups to allow researchers the opportunity to network and exchange information with colleagues from around the world in a small-group setting. Each table will address a scientific topic that is related to the meeting to enhance in-depth discussion and interactive problem solving with the potential for establishing collaborations. You will select a topic group, sit down at the selected table, and join the discussion.

Table 1. Toxicologists & Clinicians – We're Talking, But Are We Communicating?

Moderator: Meredith Rocca, Ph.D., D.A.B.T., Director, Nonclinical Safety Evaluation, Elan Pharmaceuticals

- Detailed toxicology summaries are included in the IB, but are they giving clinicians the information they need? A non-adverse finding in a rat may be unacceptable in a clinical study
- Changes in clinical chemistry over baseline may concern toxicologists, but not clinicians if they are within the normal range

Table 2. Cross Species Specificity – The Challenge Faced When Characterizing Targets

Moderator: Shane Olwill, Ph.D., Director, Research & Development, Fusion Antibodies Ltd.

- How do you develop an antibody with cross species efficacy?
- Designing antigens to conserved epitopes
- Where do you go if your target is not conserved in small animal models?
- Murine surrogates and benchmarking results

Table 3: Data Integration – Do You Need to Work Across Silos?

Moderator: Jeffrey A. Engelhardt, DVM, Ph.D., DACVP, President and Pathologist, Engelhardt Consulting, Inc., and SNBL USA, Ltd.

This discussion will address various ways to work across discipline "silos" to achieve an accurate gap analysis for the available study data. There are many reasons for the formation of the silos with an equal or greater number of ways to tunnel under or break through them. Without a quality gap analysis, the dossier is liable to have unintended holes that will raise questions during the validation and ev aluation process by a regulatory agency.

A quality nonclinical assessment requires input from pharmacology, PKDM, toxicology, manufacturing, and clinical.

- How do you address different levels of understanding of drug development?
- How do you address team leaders that need to be "in charge?"
- How do you know what data to ask for?
- What are the drivers for the silos in your organization?
- What are some tactics to overcome these drivers?
- Do you have any trump cards that you can play?
- How much lead time do you have to prepare the documents?

Table 4: The ICH S6 Addendum – How Will It Change Your Nonclinical Safety Evaluation Strategy?

Moderator: Marque Todd, MS, DVM, DABT, Regulatory Strategy Lead, Drug Safety R&D, Pfizer, Inc.

- The ICH S6 Addendum covers 5 key topics: species selection, study design, immunogenicity, reproductive and developmental toxicity and assessment of carcinogenic potential – do you understand the impact of the potential changes to your nonclinical development strategy?
- Changes in the addendum can impact both early and late-stage nonclinical strategies
- Changes can streamline your development plan and save resources and time

Table 5: What is Biologically Relevant?

Moderator: Staffan Grenklo, Ph.D., Cell Biologist & International Account Manager-Attana AB

- Is measuring on pure samples good enough?
- How to measure binding to complex structures?
- How to bridge the gap between in vitro assays and bio assays?

Table 6: Toxicologists & Clinicians – We're Talking, But Are We Communicating?

Moderator: Meredith Rocca, Ph.D., D.A.B.T., Director, Nonclinical Safety Evaluation, Elan Pharmaceuticals

- Detailed toxicology summaries are included in the IB, but are they giving clinicians the information they need? A non-adverse finding in a rat may be unacceptable in a clinical study
- Changes in clinical chemistry over baseline may concern toxicologists, but not clinicians if they are within the normal range

Table 7: Cross Species Specificity – The Challenge Faced When Characterizing Targets

Moderator: Shane Olwill, Ph.D., Director, Research & Development, Fusion Antibodies Ltd.

Table 8: Data Integration – Do You Need to Work Across Silos?

Moderator: Jeffrey A. Engelhardt, DVM, Ph.D., DACVP, President and Pathologist, Engelhardt Consulting, Inc., and SNBL USA, Ltd.

- How do you address different levels of understanding of drug development?
- How do you address team leaders that need to be "in charge?"
- How do you know what data to ask for?
- What are the drivers for the silos in your organization?
- What are some tactics to overcome these drivers?
- Do you have any trump cards that you can play?
- How much lead time do you have to prepare the documents?

Table 9: The ICH S6 Addendum - How Will It Change Your Nonclinical Safety Evaluation Strategy?

Moderator: Marque Todd, MS, DVM, DABT, Regulatory Strategy Lead, Drug Safety R&D, Pfizer, Inc.

- The ICH S6 Addendum covers 5 key topics: species selection, study design, immunogenicity, reproductive and developmental toxicity and assessment of carcinogenic potential – do you understand the impact of the potential changes to your nonclinical development strategy?
- Changes in the addendum can impact both early and late-stage nonclinical strategies
- Changes can streamline your development plan and save resources and time

Table 10: What is Biologically Relevant?

Moderator: Staffan Grenklo, Ph.D., Cell Biologist & International Account Manager-Attana AB

- Is measuring on pure samples good enough?
- How to measure binding to complex structures?
- How to bridge the gap between in vitro assays and bio assays?

Table 11: What Types of Non-Clinical Studies are Required for an IND?

Moderator: Stanley Roberts, Ph.D., D.A.B.T., Principal, SAR Safety Assessment, LLC

- What are the non-clinical strategies for filing an IND as applied to a variety of biotherapeutic classes?
- What types of non-clinical studies (i.e., efficacy, PK/disposition and toxicology) are needed?
- Other issues to discuss include: the timing of studies, how to problem-solve scientific challenges and how to select/manage collaborations with partners (e.g., universities and CRO'S)

4:50 Networking Cocktail Reception in the Exhibit Hall

6:00 End of Day

THURSDAY, MAY 20

8:00 am Registration and Morning Coffee

NOVEL THERAPIES IN DEVELOPMENT

8:30 Chairperson's Opening Remarks

Janet Clarke, Ph.D., D.A.B.T., Senior Director, Pharmacotoxicology, Biogen Idec

8:35 Targeting GPCRs with Therapeutic Antibodies

Hai Yan, Ph.D., Scientific Director, Protein Science, Amgen, Inc.

GPCRs have traditionally been considered intractable targets for antibody development. However, significant developments has been made recently to develop therapeutic antibodies that target GPCRs. This talk will address novel approaches and how they compare with traditional antibodies generated against soluble proteins. Through innovation, these new approaches have opened the potential to target one of the most important cell surface targets for large molecule therapy.

9:05 Fsn0503: A Novel Cathepsin S Specific Antibody that Blocks Angiogenesis and Tumor Invasion

Shane Olwill, Ph.D., Director, Research & Development, Fusion Antibodies Ltd.

Fsn0503, a novel monoclonal antibody that targets and inhibits Cathepsin S activity, attenuates invasion of a range of tumour cell lines. It significantly reduces in vitro microtubule formation by HUVEC cells and vessel outgrowth in the ex vivo rat aortic ring model. Fsn0503 also impairs tumor growth and neovascularisation in the HCT116 xenograft model by reducing the surface area of large vessels. Our data indicates that Fsn0503 is an experimental therapeutic which may have significant clinical utility.

9:35 Development of Antibody Drug Conjugates: An Emerging New Class of Drugs

Carmel Lynch, Ph.D., Senior Director, Nonclinical Science & Clinical Pharmacology, Seattle Genetics

Antibody-drug conjugates (ADCs) are an emerging class of drugs for the treatment of cancer. The goal is to enhance delivery of a cytotoxic agent to tumor cells via targeting of an antigen on the surface of the tumor and to spare normal cells that do not express the antigen, thereby reducing toxicity. The ADC, brentuximab vedotin (SGN-35), delivers the antitubulin agent monomethyl auristatin E (MMAE) to CD30-positive malignant cells by binding specifically to CD30 on the cell surface and releasing MMAE inside the cell via lysosomal degradation. Subsequent binding of MMAE to tubulin disrupts the microtubule network, leading to cell cycle arrest and apoptosis. The nonclinical studies conducted to support development of brentuximab vedotin will be presented, in particular the toxicity studies that enabled an IND and Phase 1 clinical trials in humans. The preliminary safety and antitumor activity of brentuximab vedotin in patients with relapsed or refractory CD30 positive hematologic malignancies such as Hodgkin Lymphoma will also be discussed.

10:05 Coffee Break, Poster and Exhibit Viewing

PRE-CLINICAL STRATEGIES

11:05 Nonclinical Regulatory Strategy and Interacting with Regulators

Jeffrey A. Engelhardt, D.V.M., Ph.D., DACVP, President and Pathologist, Engelhardt Consulting, Inc., and SNBL USA, Ltd.

Presenting nonclinical drug safety data and interacting with health authorities around the globe can create a challenge for the toxicologist. Each regulatory agency has its own personality and protocol relative to how sponsor-requested meetings are conducted and how briefing documents are viewed. This talk will look at various strategies for the development of summary documents and how they can facilitate the scientific discussions and insights on some of the complexities for a scientist working in the international regulatory arena.

11:35 Nonclinical Dosing Strategies to Support First-in-Human (FIH) Clinical Studies

Meredith Rocca, Ph.D., DABT, Director, Nonclinical Safety Evaluation, elan Pharmaceuticals

Therapeutic antibodies pose unique challenges when designing FIH clinical studies and the nonclinical studies to support them. Although the general principles of nonclinical toxicity testing are the same for therapeutic antibodies and small molecule drugs, a case-by-case approach to therapeutic antibody study design is often required due to factors such as long half-life, the potential for immunogenicity, and the possibility of performing the FIH study in a patient population. Factors to consider and successful nonclinical dosing strategies will be presented.

12:05 pm End of Conference

Protein Aggregation in Biopharmaceutical Products

Mechanistic, Analytical Formulation and Process Development Challenges

Recommended Short Courses (Details on Page 3)*

SUNDAY, MAY 16

10:00 am – 1:00 pm (SC 4) Essential Considerations for Development of Antibody-Based Therapeutics from Discovery to the Clinic

2:00 pm – 6:00 pm (SC 6)Analytical Tools and Methods Used in Biopharmaceutical Characterization to Drive Therapeutic Drug Design

TUESDAY, MAY 18

5:30 pm – 8:30 pm (SC 9) Dinner, Presentations and Interactive Panel Discussion - Satisfying FDA Recommendations in the Area of Protein Aggregate Quantification in Protein Therapeutics

**Separate Registration Required*

WEDNESDAY, MAY 19

7:00 am Registration and Morning Coffee

MECHANISTIC PERSPECTIVES ON AGGREGATION

8:30 Chairperson's Opening Remarks

David Litzinger, Ph.D., Director, Pharmaceutical Sciences, Amylin Pharmaceuticals, Inc.

8:40 KEYNOTE PRESENTATION

Good Proteins, Bad Environment: The Role of Ions in Governing Stability, Solubility, and Viscosity of Proteins

Yatin Gokarn, Ph.D., Associate Director, Late-stage Pharmaceutical and Process Development, Genentech

9:10 The Role of Physical Stress on Aggregate Formation during Processing and Storage of Biotherapeutic Proteins

Mark Pollo, Associate Senior Biophysical Chemist, Bioproduct Research and Development, Eli Lilly & Co.

A major challenge for production and delivery of proteins is to preserve the physical and chemical stability after exposure to varying processing and storage conditions. We have performed studies utilizing biophysical methods to monitor changes in higher-order structures and formation of non-native species for an antibody exposed to physical stresses, including agitation and freeze-thaw. The formation of different aggregate types resulting from different physical stresses and outline rational, evidenced based controls for minimizing protein perturbation.

9:40 Proximity Energies and Protein Aggregation

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

The weak, short-range electrostatic and electrodynamic forces between molecules dominate solution behavior, including solubility. These forces become significant at high concentrations. The potential energies that result in these forces are called proximity energies. Thinking about high concentration solutions using a framework of proximity energies clarifies a number of solution phenomena, and can lead to formulation changes that will optimize solubility. Proximity energies will be described, along with solvent and solute properties that influence them.

10:10 Coffee Break, Poster and Exhibit Viewing

11:10 Solution Factors Affecting Aggregation in a High Concentration Antibody Solution

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

This talk will focus on the importance of solution properties of a monoclonal antibody at high concentrations. The ionic strength affect can both reduce or enhance aggregation depending on the protein-protein interactions in solution. The solution storage modulus or elastic behavior correlates with the extent of aggregation at various pH conditions.

11:40 A Case Study of Process Stress Induced Aggregation

Carl "Charlie" Hitscherich Jr., Ph.D., Associate Director, Protein Pharmaceutical Development, Biogen Idec

When optimizing processing conditions for unit operations downstream the traditional purification unit operations one must closely monitor the impact that processing conditions can have on aggregation. This talk will provide several bench scale and manufacturing scale examples of where process stress leads to increased aggregate levels in the final drug product. The talk will also discuss the approach that Biogen Idec takes to minimize increases in aggregation levels during scale up and processing

12:40 Luncheon Presentation II: Rapid Assessment of Aggregation in Protein-Based Pharmaceuticals *Sponsored by* Enzo Life Sciences

Wayne F. Patton, Ph.D., Chief Scientific Officer, Enzo Life Sciences

A homogenous fluorescence-based assay is described for investigating the impact of adverse conditions that a protein product might be exposed to during manufacture, storage, shipping, freeze/thaw cycles, oxygen exposure, light, and physical stress. The assay facilitates assessment of the impact that these conditions might have on drug safety and quality and can be performed using a simple fluorimeter, microplate reader or RT-PCR instrument. Sub-visible particles are detectable without a requirement for sample separation, solvent exchange or dilution. The assay has been benchmarked using a wide range of practical applications.

TOOLS AND METHODS FOR ANALYSIS

1:30 Chairperson's Remarks

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

1:35 Biophysical Techniques to Explore Protein Aggregation or Aggregation Propensity

Min Huang, Ph.D., Principal Scientist, Pharmaceutical Research and Development, Global Biologics, Pfizer, Inc.

Protein aggregation poses a considerable challenge in the manufacturing and delivery of biopharmaceuticals. This talk will present some case studies employing some new biophysical analytical techniques to characterize protein aggregation as well as their aggregation propensities. These techniques could potentially be useful orthogonal tools to understand and characterize protein aggregation.

2:05 Analysis of Subvisible Particles in Protein Therapeutics: Methods and Applications

Shawn Cao, Ph.D., Principal Scientist, Process and Product Development, Amgen, Inc.

The subvisible particles that might be present in protein therapeutics have been identified by the regulatory agencies as a potential safety issue. Analytical methods are needed for the monitoring and control of these subvisible particles, and to study the mechanism of particle formation. The methods available to subvisible particle analysis, their strengths and weaknesses, and some case studies showing how these techniques can be applied to address particle characterization during the product lifecycle will be discussed in this presentation.

2:35 DLS Characterization of High Concentration Protein Formulations in Shelf Life Studies *Sponsored by* Malvern

Kevin Mattison, Ph.D., Senior Bioanalytical Scientist, Research & Development, Malvern Instruments Ltd.

Dynamic light scattering (DLS) is a common technique for detecting protein aggregation. While historically delegated to dilute solutions, technological advances have moved DLS instrumentation into the realm of high concentration measurements. The ability to measure at high concentration however, does not negate the possibility of physical effects such as multiple scattering, restricted diffusion, and particle interactions, all of which can lead to erroneous interpretation of DLS results. This presentation highlights approaches to addressing high concentration effects.

3:05 Networking Refreshment Break, Poster and Exhibit Viewing

3:50 Problem Solving Break-Out Sessions

Interactive break-out discussion groups are interactive, guided discussions hosted by a facilitator or set of co-facilitators to discuss some of the more poignant questions facing the industry. Delegates will join a table of interest to them and become an active part of the discussion at hand. It is an informal yet informative format that allows attendees to learn from each other and make some new contacts. To get the most out of this interactive session and format please come prepared to: share examples from your work, vet some ideas with your peers, be a part of group interrogation and problem solving, and, most importantly, participate in active idea sharing.

4:50 Networking Cocktail Reception in the Exhibit Hall

6:00 End of Day

THURSDAY, MAY 20

8:00 am Registration and Morning Coffee

APPROACHES FOR MANAGING OR PREVENTING AGGREGATION ISSUES

8:30 Chairperson's Opening Remarks

Greg Walsh, Senior Scientist, Technology Development, Genzyme

8:35 KEYNOTE PRESENTATION

Improving Physicochemical Properties of Biopharmaceutical Drug Candidates

David Litzinger, Ph.D., Director, Pharmaceutical Sciences, Amylin Pharmaceuticals, Inc.

Often drug candidates in discovery and development have undesirable chemical and physical instability. This presentation will focus on options for modifying the drug molecules to improve their physicochemical properties such as chemical stability, solubility, and to lessen their potential for aggregation. Changes that will be discussed include creating analogs, chemical conjugation, and other modifications.

9:05 Protein Structure Alteration and Aggregation in Liquid Formulations: What Impact on the Drug Product Features and How to Monitor These Issues?

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

State-of-the-art development for therapeutic proteins is presently focusing on liquid formulations, requiring high concentration formulations(> 100 mg/mL). It needs properly assessing and carefully monitoring the compatibility of the protein with the container and the stabilizing excipients, as well as the stability of the protein in the formulation over time. Structure alteration and aggregation are among the most striking issues, the latter triggering immunogenic reactions upon repeated subcutaneous administration. This talk will focus on case studies using the appropriate combination of biophysical methods (fluorescence, thermal analysis, circular dichroism, dynamic light scattering, analytical ultracentrifugation, etc.) to show structural modifications of the protein in the formulations and study the effect of excipients on these modifications. Clinical impact will also be discussed.

9:35 Case Studies of Monoclonal Antibody Aggregation: Lessons Learned from Apparently Stable Molecules

Tia Estey, Ph.D., Scientist II, Protein Pharmaceutical, Development, Biogen-Idec

The presentation will highlight a number of case studies in which unexpected aggregation behavior was observed during the development of monoclonal antibody formulations. Examples of processing and long-term stability challenges will be presented. For each of the case studies, the origins of physical instability as well as formulation and development mitigation strategies will be discussed. The audience will gain a better understanding of some of the drivers behind the aggregation of monoclonal antibodies, how process stresses can contribute to aggregation, how to characterize aggregation in order to get at the root cause, and potential solutions to this problem.

10:05 Coffee Break, Poster and Exhibit Viewing

11:05 Monoclonal Antibody Aggregation Intermediates Visualized by Atomic Force Microscopy

Henryk Mach, Ph.D., Senior Investigator, Bioprocess Analytical and Formulation Sciences, Merck Research Laboratories

In this work we present the use of an atomic force microscopy to examine morphology of monoclonal antibody aggregates. Despite varying in primary structure, most antibodies studied exhibited aggregation intermediates consisting of several monomers. The manner of subsequent condensation of these oligomers appeared to differ between the antibodies.

11:35 Structure-Based Engineering of a Monoclonal Antibody for Improved Solubility

Sam Wu, Ph.D., Senior Research Scientist, Biologics Research, Centocor R&D, Inc.

Three structure-based engineering approaches were employed in antibody solubility: 1) modifying the isoelectric point, 2) decreasing the overall surface hydrophobicity, and 3) re-introduce an N-linked carbohydrate moiety within a complementarity-determining region (CDR) sequence. We have demonstrated that all three approaches led to improved solublility and that adding an N-linked carbohydrate to the CDR was the most effective route for enhancing the solubility of this antibody, in which an aggregation "hot spot" overlapped with residues in contact with the target antigen.

12:05 pm End of Conference

SEVENTH ANNUAL

MAY 20 - 21, 2010

Antibody Optimization

Fine-Tuning Affinity, Specificity, and Efficacy

THURSDAY, MAY 20

12:00 pm Registration

TARGETING, SPECIFICITY AND AFFINITY

1:30 Chairperson's Opening Remarks

1:40 Conferring Meaningful Anti-Tumor Activity to Monoclonal Antibodies by Linking Cell Killing Agents

Ravi V. Chari, Ph.D., Executive Director, Chemistry & Biochemistry, ImmunoGen, Inc.

A majority of antibodies developed against cancer targets display only modest cell killing activity to be therapeutically useful. Linking highly cytotoxic cell killing agents to antibodies to provide Antibody-Drug Conjugates (ADCs) offers a means to enhance the anti-tumor activity of antibodies. Multiple ADCs that utilize ImmunoGen's maytansinoid cell killing agents are currently undergoing clinical evaluation and promising results are emerging. This talk will review ImmunoGen's approaches to design each ADC to achieve the best performance for the specific cancer target.

2:10 Recombinant Human Multi-Domain Fusion Proteins

Stefan Barth, Ph.D., Department of Pharmaceutical Product Development, Fraunhofer IM

Under pathological conditions, activated and dysregulated macrophages play a decisive role in the development of numerous inflammatory processes including progression of cancer. The high affinity receptor for IgG (CD64) is highly expressed on monocytes and macrophages is a prime target for therapeutic intervention. We have generated novel recombinant multi-domain immunotherapeutics by fusing different cytotoxic enzymes to a single chain fragment derived from the CD64-specific human antibody H22. Final aim is the application of tailor-made immunofusions not only considering the targeting moiety, but also the appropriate cytotoxic agent to specifically destroy diseased cells.

2:40 Design and Produce Better Antibodies with Antigen Profiler *Sponsored by* Thermo SCIENTIFIC

Matt Baker, Proteomics Business Development Director, Thermo Fisher Scientific

Antibodies play a key role in many research and preclinal projects and can be a serious limiting factor in the progression of the project when existing commercial antibodies do not perform as needed or no commercial antibodies are available. Thermo Scientific has combined years of experience in antibody development along with advanced antigen design algorithms and targeted antigen display to overcome many the challenges of generating robust antibodies. See how antibodies can be designed and optimized to perform in specific applications through better technology.

3:10 Networking Refreshment Break, Poster and Exhibit Viewing

4:00 Optimizing Antibody Homogeneity and Development: Lessons Learned from Structural and Functional Studies

Alain Beck, Ph.D., Head of Department, Physico-Chemistry, Institut de Recherche Pierre Fabre

High-resolution Mass Spectrometry methods in combination with ultra-performance separation techniques are now routinely used at all stages of antibody discovery and development to assess their structure. As a consequence, these new analytical tools result also in the identification of minor components like charge variants, glycoforms, disulfide bridge isoforms and other low level molecular species. Lessons learned from the impact of these micro-variants on the stability and the PK/PD will be discussed and illustrated by the design of the next generation of optimized antibody-leads with higher homogeneity, stability and potency.

4:30 Antibody-Drug Conjugates to Improve Therapeutic Index

Wei Liao, Ph.D., Senior Research Scientist, Project Team Leader, BioTherapeutic Center of Emphasis, Pfizer, Inc.

Antibody-drug conjugates (ADC) are an effective way to reduce toxicity and to enable site-specific drug delivery. In this presentation, we will discuss the strategies used to meet the challenges to generate the conjugates, and to develop analytical methods, including functional bioassays.

5:00 End of Day

FRIDAY, MAY 21

7:45 am Continental Breakfast in the Exhibit Hall

HALF-LIFE, SENSITIVITY AND EFFICACY

8:30 Chairperson's Opening Remarks

Gerald Casperson, Ph.D., Associate Research Fellow, Biotherapeutics, Pfizer Global Research & Development

8:35 Trastuzumab Conjugate for the Treatment of Trastuzumab-Resistant Human Breast Cancer: Increasing Magnitude and Duration of Response

Wen Jin Wu, Ph.D., Principal Investigator, Division of Monoclonal Antibodies, OBP/OPS/CDER, Food and Drug Administration

Our laboratory in the Division of Monoclonal Antibodies at FDA has investigated the mechanisms underlying trastuzumab-resistance and is pursuing new ways to increase the magnitude and duration of the response to the trastuzumab treatment. Using a Rac1 specific inhibitor, NSC23766, to treat trastuzumab-resistant cells, we found that trastuzumab-resistant cells became sensitive to the trastuzumab treatment. We plan to develop a new molecular entity (NME), whereby trastuzumab will be covalently conjugated with NSC23766.

9:05 Fc-Optimized Monoclonal Antibody for HER2- Expressing Tumors

Jeffrey L. Nordstrom, Ph.D., Director, Product Development Research, MacroGenics, Inc.

We have developed an anti-HER2 mAb with an Fc engineered for increased binding to both alleles of the CD16A activating Fc receptor and decreased binding to the inhibitory receptor, CD32B. The optimized Fc enhances ADCC activity against low-expressing HER2+ tumor lines and enhanced antitumor activity against HER2+ xenografts in mice transgenic for the low-binding allele of human CD16A. Breast cancer patients carrying the low-binding allele have reduced clinical responses to trastuzumab; the Fc-optimized anti-HER2 mAb could potentially benefit these patients.

9:35 Optimization of a Monoclonal Antibody for Improved Anti-Tumor Efficacy

Gerald Casperson, Ph.D., Associate Research Fellow, Biotherapeutics, Pfizer Global Research & Development

We will describe the optimization of an antibody which has recently entered the clinic for Oncology indications. We engineered this antibody to greatly enhance its efficacy and to minimize the likelihood of immunogenicity. We plan to disclose the target and will describe the process and technology used for optimization including data from both *in vitro* and *in vivo* pharmacology.

10:05 Coffee Break, Poster and Exhibit Viewing

WHEN LESS IS MORE: ANTIBODY FRAGMENTS

11:05 Recombinant Immunotoxins for the Treatment of Hematologic Malignancies

Robert J. Kreitman, Ph.D., Principal Investigator, Laboratory of Molecular Biology, National Cancer Institute, National Institutes of Health

Recombinant immunotoxins, containing a fragment of a monoclonal antibody (Mab) genetically fused to a protein toxin, kill cells by binding to the cell, internalizing, and transporting a toxin fragment to the cytoplasm where it catalytically inhibits protein synthesis, stimulating apoptosis. Unlike naked MAbs, they do not require ADCC or CDC, and unlike radioimmunotherapy, they do cause bystander damage to normal marrow cells. Recombinant immunotoxins with clinical activity, particularly in hairy cell leukemia, include LMB-2, targeting CD25, and BL22 and its improved version HA22 (CAT-8015), targeting CD22.

11:35 Engineered Avibodies Optimized for Clinical Diagnosis and Therapy

Peter Hudson, Ph.D., CSO, Avipep Laboratories, Avipep Pty, Ltd.

Avibodies are scFvs that self-associate into multivalent dimers or trimers and provide unique and superior properties to enhance therapeutic payloads (radionuclides, toxins, drugs etc). We have evaluated several oncology applications and have optimized tumor-to-blood ratios for imaging and therapy whilst reducing undesired renal accumulation. Increasing the apparent molecular weight by PEG derivatization plus radio-labeling provides high xenograft tumor uptake (over 50% ID/gm) and with a biodistribution profile optimal for therapy or *in vivo* imaging.

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

1:05 Break

STABILITY, GLYCOSYLATION, IMMUNOGENICITY AND HUMANIZATION

1:25 Chairperson's Remarks

Ira Pastan, Ph.D., Head, Molecular Biology Section, NCI, NIH

1:30 Antibody Therapeutics: Isotype and Glycoform Selection

Roy Jefferis, Ph.D., Professor of Molecular Immunology University of Birmingham, Division of Immunity & Infection

Antibody therapeutics may be developed to achieve one, or more, of several outcomes: i) killing of cells or organisms, e.g. cancer cells, bacteria; ii) neutralization of soluble molecules, e.g. cytokines, toxins; iii) acting as agonists or antagonists of cellular receptors. Consequently the choice of antibody isotype is a critical decision; however, functional activity is also dependent on the IgG-Fc glycoform. Glycosylation and protein engineering may be employed to generate antibody formats and homogeneous IgG glycoforms considered optimal for given clinical indications.

2:00 Early Stage Engineering to Improve Pharmaceutical Properties of Antibodies

Alexey Lugovskoy, Ph.D., Head of Molecular Modeling and NMR, Drug Discovery, Biogen IDEC, Inc.

Unfavorable pharmaceutical properties of antibodies can limit their potential as drugs. To mitigate this risk we apply structure-guided engineering approaches in early antibody discovery programs. We will present examples where stability and solubility of antibodies were improved and discuss the incorporation of these technologies in cycle one design.

2:30 Networking Refreshment Break

3:00 Deimmunizing Non-Human Proteins

Ira Pastan, Ph.D., Head, Molecular Biology Section, NCI, NIH

Many non-human proteins have useful therapeutic properties, but their use is limited because of their immunogenicity. We have shown immunotoxins which contain portions of Pseudomonas exotoxin A have therapeutic benefit in leukemias where the immune system is suppressed. To make immunotoxins useful in patients with normal immune systems, we have mapped and removed by mutation all 7 major B cell epitopes. The new immunotoxin (HA22-LR-8X) has full cytotoxic activity and anti-tumor activity yet has very low immunogenicity in mice. Our approach should be useful to deimmunize other foreign proteins.

3:30 Antibody Optimization from Pharmacokinetic-Pharmacodynamic Perspectives

Liang Zhao, Ph.D., Clinical Pharmacology Reviewer, FDA/CDER/OTS/OCP

PK-PD provides critical quantitative measures for antibody drug candidates, not only at the discovery stage, but also at late phases of development cycle. It integrates any knowledge available of drugs in the same category, dosing needs for therapeutic effect, mechanism of action, disease progression, shared characteristics of antibody drugs, and clinical outcomes. Overview from all these perspectives will greatly benefit new antibody drug design from scratch

4:00 Probodies: Site-Directed Antibodies to Improve Therapeutic Indices

Nancy Stagliano, Ph.D., CEO, CytomX Therapeutics, LLC

Although antibodies are highly specific for their target, the target itself is often not confined to diseased tissues. Mechanism-based activities of antibodies cause side effects, the need for dose delay and reduction and potentially reduced therapeutic benefit. In addition, their high potency allows for fewer targets that can be safely and effectively drugged. Protease-activated antibodies, Probodies, are a new, discovery-stage therapeutic with the potential for dramatically improved therapeutic indices. In the circulation, Probodies exist in a masked or inactive state. In contrast, endogenous proteases within diseased tissues activate Probodies locally and produce the desired therapeutic effect. Using our proprietary approach to engineering therapeutic antibodies, we will describe our early stage oncology programs including Probodies to EGFR and a cancer stem cell target, including preclinical *in vivo* data.

4:30 End of Conference

Revival of Bispecific Antibodies: The Way Forward?

THURSDAY, MAY 20

12:00 pm Registration

SELECTION CRITERIA FOR BISPECIFIC ANTIBODIES: HOW DO YOU DECIDE WHEN TO USE THEM AND WHICH IS A BETTER CHOICE?

1:30 Chairperson's Opening Remarks

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

1:40 FEATURED PRESENTATION

Bispecific Antibodies: Developments and Current Perspectives

Roland Kontermann, Ph.D., Professor, Biomedical Engineering, Institute of Cell Biology & Immunology, University of Stuttgart

The concept of using bispecific antibodies for tumor therapy was developed more then 20 years ago. Initial clinical trials have failed because of low efficacy, severe side effects and immunogenicity of the hybridoma-derived bispecific antibodies. New developments in the field of antibody engineering have led to second-generation bispecific antibodies and a revival of these molecules for tumor therapy.

2:10 Single Chain Immunoglobulins – A New Way to Generate Bispecific Antibodies

Thomas Schirrmann, Ph.D., Senior Scientist, Institute of Biochemistry and Biotechnology, Technische Universität Braunschweig

Single chain immunoglobulins (scIgGs) only require the assembly of two identical polypeptide chains thus promising to facilitate heterologous production, surface display, among others, and opening new ways for the improved generation of bispecific antibodies. The production in mammalian cells resulted in a majority of homodimeric scIgG molecules with high apparent affinity to their antigen. Based on the scIgG and scFv-Fc format we further demonstrate the generation of tetravalent bispecific antibodies which are still being encoded by a single gene.

2:40 Sponsored Presentations *(Opportunities Available)*

3:10 Networking Refreshment Break, Poster and Exhibit Viewing

4:00 Efficient Chemical Approaches to Bispecific Antibodies and Antibodies of High Valency

Carlos F. Barbas III, Ph.D., Kellogg Professor, The Skaggs Institute for Chemical Biology, Department of Chemistry, The Scripps Research Institute

Efficient chemical programming approaches have been developed that provide for versatile and economically viable routes to bispecific antibodies and high-valency therapeutic antibodies. These approaches are further augmented with our development of a new tyrosine ligation reaction for bioconjugation. These approaches are applicable to chemically programmed antibodies, vaccines, and the modification of virtually any therapeutic antibody.

4:30 Chimeric Antigen Receptors Arm T-Cells to Fight Cancer

Hinrich J. Abken, M.D., Professor, Internal Medicine I, University of Cologne

Research into redirecting the cellular immune response against cancer resulted in the development of chimeric antigen receptors which consist of a single-chain antibody fragment, specific to a tumour-associated antigen, fused to a component of the T-cell receptor complex. Upon antigen binding on tumor cells, chimeric antigen receptor primes the engrafted T-cell for anti-tumour activity. Mouse tumor models indicate remarkable efficacy and clinical trials have been initiated.

5:00 Problem-Solving Break-Out Sessions

Table 1: Targeting Stem Cells with Bispecific Antibodies

Moderator: Lawrence G. Lum, M.D., D.Sc., Professor Medicine, Professor of Immunology and Microbiology, Scientific Director of Immunotherapy and BMT, Barbara Ann Karmanos Cancer Institute

- What types of cells can induce regeneration of myocardium?
- How do we get the cells to the site and remain at the site?
- What types of functions related to stem cells or other cells can be induced for tissue repair?
- How can we assess whether infusions of the cells actually repaired cardiac tissue?

Table 2: Bispecific Antibodies for Tumor Therapy

Moderator: Roland Kontermann, Ph.D., Professor, Biomedical Engineering, Institute of Cell Biology & Immunology, University of Stuttgart

Table 3: Challenges in Developing Bispecific Antibodies

Moderator: To be Announced

6:00 End of Day

FRIDAY, MAY 21

7:45 am Continental Breakfast in the Exhibit Hall

CREATING A BISPECIFIC – A VARIETY OF APPROACHES

8:30 Chairperson's Opening Remarks

Michael J. Feldhaus, Ph.D., Senior Director, Antibody Engineering, Adimab, Inc.

8:35 Strand Exchange Engineered Domain (SEED), a Protein Engineering Strategy Designed to Create a Heterodimer Protein Scaffold

Marco Muda, Ph.D., Binders & Protein Engineering, EMD Serono Research Institute, Inc.

Engineered antibody and antibody-like proteins are the emerging "State of the Art" for development of the Next Generation Biologics. We will present the development of a heterodimer protein scaffold with critical antibody properties and with the added potential of efficiently generating multifunctional therapeutics. This heterodimeric protein platform has potential to open new opportunities through new mechanism of action, increased specificity and delivering combination therapy in one molecule.

9:05 Engineering Antibodies to Concurrently Target Multiple Disease Mediators

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

The characterization of oligospecific antibodies designed to concurrently target multiple disease mediators is presented. These oligospecific antibodies were generated by genetically linking single-chain Fv fragments to the N-termini of antibody heavy and light chains, and to the C-terminus of the antibody CH3 domain. A multidisciplinary approach combining biochemical, biophysical, *ex vivo*, and *in vivo* methods was employed to fully characterize these oligospecific antibodies. The broad applicability of these engineered oligospecific antibodies and their potential use as the next generation of biological drugs to treat complex diseases is discussed.

9:35 bis-Fabs: A New Platform for Bispecific Molecules

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

A new approach using controlled chemistry to produce bispecific antibodies will be described. The technology has uncovered unexpected insights into antibody structure and function relationships. The application of these molecules to drug discovery and basic research will be described.

10:05 Coffee Break, Poster and Exhibit Viewing

11:05 Trifunctional Antibodies: What's so Different?

Horst Lindhofer, Ph.D., Founder & CEO, Trion Pharma GmbH

The trifunctional antibody catumaxomab consisting of two independent antigen binding sites for EpCAM and CD3 as well as the Fc region enables the formation of tri-cell complexes with tumor cells, T cells and accessory cells (e.g. monocytes, macrophages, natural killers or dendritic cells). Catumaxomab showed strong anti-tumor efficacy and a clinically significant prolongation of puncture-free survival in a pivotal phase II/III trial with patients suffering from malignant ascites, an advanced disease manifestation of e.g. ovarian, breast or gastric cancer.

11:35 Combining mABs and dABs: Generation of Dual-Targeting Antibodies and Their Preclinical Development

Paul Hamblin, Ph.D., Manager, Discovery Biopharm, GlaxoSmithKline

Domain Antibodies (dAbs) are the smallest functional binding fragments of human antibodies. By combining different dAbs, or through fusion of dAbs and mAbs, we are creating a suite of novel bispecific agents that offer enhanced efficacy in a range of indications. We will show that these molecules will provide differentiated, developable biopharmaceuticals, and by virtue of their modular nature offer up a pipeline of further such molecules in the future.

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

BISPECIFICS IN CANCER THERAPY

1:25 Chairperson's Remarks

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

1:30 Bispecific Antibodies for Effective Engagement of T Cells in Cancer Therapy

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

By transiently connecting T and cancer cells with bispecific BiTE antibodies, T cells are activated and potently kill attached cancer cells. Examples for the clinical activity of two different BiTE antibodies in lymphoma, leukemia and solid tumor patients will be given.

2:00 Catumaxomab (Removab): The First Approved Bispecific, Trifunctional Antibody

Diane Seimetz, Ph.D., CSO, Executive Vice President, Drug Development, Fresenius Biotech

Catumaxomab is worldwide the first approved bispecific, trifunctional antibody. The presentation will cover the major steps taken in the drug development and approval process. Considerations for life cycle management will be given.

2:30 Networking Refreshment Break

3:00 CVX-241 - A Bispecific Covx-Body Targeting Angiogenesis

Gary Woodnutt, Ph.D., Vice President, Biology, CovX Pharmaceuticals, Inc., Pfizer

The utility of molecules that interact with two (or more) targets or that can interact in two places on the same target is generating much interest. The CovX technology enables rapid discovery and evaluation of bispecific molecules that can be used in many therapeutic settings. I will discuss the development of one such CovX body (CVX-241) which is currently in clinical development.

3:30 mAb2: Novel Bispecific Antibodies that are Minimally Changed from IgG

Kevin FitzGerald, Ph.D., MBA, CEO, f-star GmbH

We have developed two novel antibody formats: Fcab, in which antigen-binding sites are introduced into a human Fc fragment and mAb2, in which additional binding sites are engineered into the Fc of an intact antibody. Fcabs allow therapeutic candidates to be isolated that, despite being one third the size of IgG, retain all normal antibody functionalities (antigen binding, effector functions and long half life) while mAb2 provides the opportunity to add additional functionality, specificity, selectivity or potency to existing antibodies.

4:00 Targeting T Cells to Tumors and Stem Cells for Myocardial Repair with Bispecific Antibodies

Lawrence G. Lum, M.D., DSc, Professor Medicine, Professor of Immunology and Microbiology, Scientific Director of Immunotherapy and BMT, Barbara Ann Karmanos Cancer Institute

Platform technology was developed using chemically heteroconjugation of commercially available monoclonal antibodies to target T cells for cancer therapy and to target stem cells to repair myocardial injury. Evidence for inducing an endogenous immune response to metastatic breast cancer in a phase I clinical trial done with anti-CD3 x anti-Her2/neu bispecific antibody armed activated T cells will be presented. Evidence for targeting stem cells to myocardial infarcts will be presented.

4:30 End of Conference

INAUGURAL MAY 20 - 21, 2010

Biotherapeutic Targets

The Bioanalytical Challenges of Optimizing Next-Generation Protein Therapeutics

Recommended Short Course (Details on Page 3)*

THURSDAY, MAY 20

5:30 pm – 8:30 pm (SC 10) Affinity Tags for Protein Purification - Dinner Presentations & Interactive Discussions

**Separate Registration Required*

THURSDAY, MAY 20

12:00 pm Registration

EMERGING TOOLS & TECHNOLOGIES

1:30 Chairperson's Opening Remarks

Mitchell Ho, Ph.D., Head, Antibody Therapy Unit, Laboratory of Molecular Biology, National Cancer Institute, National Institutes of Health (NIH)

1:40 OPENING KEYNOTE PRESENTATION

Emerging Mass Spectrometry-Based Tools to Characterize Higher Order Structure and Dynamics of Biopharmaceuticals

Igor A. Kaltashov, Ph.D., Associate Professor, Department of Chemistry, University of Massachusetts, Amherst

Among several MS-based techniques, targeting protein higher order structure and dynamics, hydrogen/deuterium exchange (HDX) has demonstrated the greatest promise vis-à-vis conformational analysis of biopharmaceutical products. Several examples of biopharmaceutical products (interferon beta 1a, velaglucerase, etc.) will be used to illustrate the utility of HDX MS and related techniques as a means of characterizing protein drugs in terms of their conformational integrity, stability and functional competence with high predictive value.

2:10 Quantitative Method for Measurement of Antibody Internalization using Fluorescent Imaging

Inna Vainshtein, Ph.D., Scientist II, Global PK-PD & Bioanalysis, MedImmune

Quantitative assessment of internalization is important in development of antibody therapeutics. Despite a number of publications describing antibody-mediated receptor internalization, quantitative assessment of this process has not been extensively presented. Target-mediated internalization may increase antibody clearance and result in non-linear pharmacokinetic (PK) profiles. For immunotoxins, internalization could effect efficiency of toxin delivery into the target cells. We have developed a quantitative image-based method for measurement of antibody internalization. Examples will be presented to demonstrate the application of this methodology to development of therapeutic antibodies.

2:40 Antibody Screening using Multiplexed SPR *Sponsored by* BIO-RAD

John Corbin, Ph.D., Sr. Scientist, XOMA US LLC

Understanding how an antibody exerts a therapeutic effect in vivo often depends on knowing the mechanism by which the antibody impacts the targeted signaling pathways at a molecular level. This is especially relevant for XOMA 052, an anti-IL-1 antibody that regulates the activity of the cytokine by a novel mechanism of differentially modulating the kinetic parameters of IL-1 binding to its cognate receptors. Biophysical studies using techniques such as surface plasmon resonance (SPR) are a powerful approach for characterizing therapeutic antibody mechanism of action as well as a facile technique for mechanistic screening of antibodies. Analysis of multiple molecular interactions in parallel using multiplexed SPR offers several advantages over conventional SPR including increasing throughput and the ability to conduct side-by-side comparisons of binding kinetics under different conditions. This presentation will highlight the use of surface plasmon resonance to elucidate antibody mechanism of action

2:55 Antibody Screening Using Multiplexed SPR *Sponsored by* PhyNexus

Lee Hoang, Ph.D., Manager, Research & Development, PhyNexus Inc.

Characterization of therapeutic candidates requires that proteins are well purified post expression. We have developed a platform that completely automates purification, enrichment and desalting of functional proteins eliminating bottlenecks associated with traditional protein purification techniques and expediting multiple stages of the discovery process. Examples of how the platform is utilized in biomarker analysis, process and assay development, and immunogenicity will be presented. Protein separations in small-scale extraction columns with optimized conditions enabling functional and analytical tests will be discussed as well.

3:10 Refreshment Break, Poster and Exhibit Viewing

4:00 Combining Label Free Assay Platforms to Support Therapeutic Antibody Development from Identification of Candidate Antibodies through Pre-Clinical Development

Robin Barbour, Director, Antibody Technology, Elan Pharmaceuticals

Label free technologies can impact antibody development from the earliest phase through entry into the clinic and beyond. In this presentation, we compare and contrast three optically-based label free technologies, the Biacore T100, the Forte-Bio Octet, and SRU bind in their ability to screen antibodies from tissue culture supernatants and then to characterize the resultant positives for affinity, kinetics, epitope binding and domain binding. During the presentation, the advantages and disadvantages of each technology will be highlighted.

4:30 Proteomic Profiling of Novel Protein Targets by Selective Epitope Inhibition and SILAC/MS Analysis

Christian Freund, Ph.D., Principal Investigator/Group leader, Structural Biology, FMP/Free University of Berlin

We have a developed a rapid and robust method for addressing specificity of protein-protein interactions by a combined inhibitor/SILAC/MS approach. As exemplified by intracellular adaptor domains involved in disease processes, we show that deconvolution of epitopes is possible. This allows one to define the contribution of individual interaction sites for the assembly of molecular machines (e.g., the spliceosome) or signaling pathways.

5:00 End of Day

FRIDAY, MAY 21

7:45 am Continental Breakfast in the Exhibit Hall

LIGAND BINDING ASSAYS

8:30 Chairperson's Opening Remarks

Igor A. Kaltashov, Ph.D., Associate Professor, Department of Chemistry, University of Massachusetts, Amherst

8:35 Affinity, Avidity, and Assay Limits – What is My Assay Measuring?

Eric Day, M.B.A., Scientist II, Biogen Idec. Inc.

Affinity is a measure of the binding strength between ligand and receptor. It has a precise mathematical definition and with the appropriate tools can be measured directly or indirectly. As such, affinity provides a rigorous parameter to monitor the development of protein therapeutic candidates, for example in antibody humanization. Avidity arises when measuring multivalent or multicomponent binding events. It is not, however, precisely mathematically defined. It is a parameter that depends not only on the intrinsic affinity of the interaction of interest but also on the system in which the interaction is measured. In complex systems, the avidity and affinity components of the observed binding cannot be separated. The limits of an assay are quickly reached in highly avid systems, such that the measurement no longer reflects the strength of an interaction but becomes a simple titration of the number of binding sites available. Examples of monovalent, multivalent and multicomponent receptor-ligand binding systems will be used to demonstrate the information that can and cannot be obtained from a particular assay design. Common techniques such as SPR (Biacore), FACS and ELISA will be discussed.

9:05 Design of Experiments: Case Studies from a Bioanalytical Lab

Franklin Spriggs, Ph.D., Scientist, PDM, Pfizer Global R&D Groton Labs

This presentation and discussion will provide a general introduction to DOE, briefly examine the different kinds of designs available, and finally review a few cases demonstrating the utility and limitations of DOE in a bioanalytical method development.

9:35 Affinity, Avidity, and Assay Limits – What is My Assay Measuring?

Eric Day, M.B.A., Scientist II, Biogen Idec, Inc.

10:05 Coffee Break, Poster and Exhibit Viewing

FREE VS. TOTAL

11:05 Free vs. Total Ligand Binding Assays: Points to Consider in Drug Development

Jihong Yang, Ph.D., Scientist, Bioanalytical Research & Development, Genentech, Inc.

Pharmacokinetic (PK) assays have long been used as an indispensible method to quantify recombinant biotherapeutic IgG exposure *in vivo*. Need for a "Free" or "Total" PK assay depends on many factors. This talk will give case studies on both "free" and "total" PK assays and the impact on the PK analysis.

11:35 Free and Total Immunoassays for Monoclonal Antibodies to Soluble Targets and Target as Biomarker

Lindsay King, Ph.D., Senior Principal Scientist, PDM Regulated Biotherapeutics, Pfizer, Inc.

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

OPTIMIZING FOR ONCOLOGY

1:25 Chairperson's Remarks

Robin Barbour, Director, Antibody Technology, Elan Pharmaceuticals

1:30 The Mesothelin-CA125/MUC16 Interaction

Mitchell Ho, Ph.D., Head, Antibody Therapy Unit, Laboratory of Molecular Biology, National Cancer Institute, National Institutes of Health (NIH)

Ovarian cancer and malignant mesothelioma frequently express both mesothelin and CA125 (also known as MUC16) at high levels on the cell surface. The interaction between mesothelin and CA125 may facilitate the implantation and peritoneal spread of tumors by cell adhesion, whereas the detailed nature of this interaction is still unknown. We identified a region at the N-terminal of cell surface mesothelin required and sufficient for its binding to CA125. The identified CA125-binding domain significantly inhibits cancer cell adhesion and merits evaluation as a new therapeutic agent for preventing or treating peritoneal malignant tumors.

2:00 Hyaluronan: The Glue that Holds a Tumor Together

Curtis Thompson, Ph.D., Director, Pharmacology, Halozyme Therapeutics

Halozyme Therapeutics is developing a novel enzyme therapeutic (PEGPH20) in Phase I clinical trials. The enzyme degrades hyaluronan, the principal ligand for CD44, a tumor stem cell marker. By disrupting the tumor matrix, PEGPH20 depletes both matrix and growth factor support of progressing malignancies.

2:30 Networking Refreshment Break

OPTIMIZING PROPERTIES

3:00 Immunogenicity: Regulatory and Technical Overview with Case Studies of Assay Challenges

Eric Wakshull, Ph.D., Senior Scientist & Group Leader, Bioanalytical Research & Development Department, Genentech, Inc.

The assessment of anti-protein therapeutic immunogenic responses is an essential component of drug safety evaluation during both the preclinical and clinical development phases. This presentation will briefly describe the regulatory landscape regarding immunogenicity assessment, touching briefly on the various white papers and regulatory guidances now available. An introduction to the methodological approaches commonly used to measure anti-protein therapeutic antibodies will be provided and some cases studies on the most common assay interference issues and their possible solutions will also be discussed.

3:30 Determination of the Mechanism of Action of an Antibody using Orthogonal Approaches

Victor H. Obungu, Ph.D., Senior Research Scientist, Biotechnology Discovery Research, Eli Lilly and Company

A neutralizing anti FasL antibody for potential therapeutic applications was generated. In order to determine its mechanism of action, several complimentary approaches were used to determine its epitope. These studies revealed the epitope and gave an understanding of the mechanism of neutralizing activity for this antibody.

4:00 The Impact of Shed Target Antigen on the Quantitation of Therapeutic mAb and its Pharmacokinetics Implication

Bing Kuang, Ph.D., Principal Scientist, Pharmacokinetics, Pharmacodynamics, and Metabolism, Pfizer, Inc.

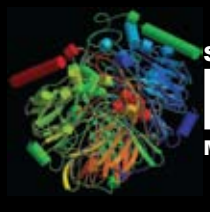
Many therapeutic monoclonal antibodies are designed to target membrane-bound cell surface targets. The membrane-bound proteins, however, may shed their extracellular domain through limited proteolysis. The shed or circulating target antigen in serum would compete with binding of the therapeutic mAb and affect its pharmacokinetic evaluation. Quantifying and distinguish the levels of free and bound form of mAb is therefore important to the characterization of the pharmacokinetics and pharmacodynamics of therapeutic antibody.

4:30 End of Conference

SPONSORSHIP

"It was a great opportunity to see what's new both in the speaker sessions and the vendor show. I was also able to get significant networking accomplished. It was quite useful on all counts."

President and Chief Scientific Officer, Takeda Pharmaceuticals, San Francisco



Sixth Annual
PEGS
May 17 - 21, 2010

PEGS – the essential protein engineering summit is coming off a record setting 2009. This year's event will prove to be even better. PEGS will assemble international innovation leaders who are striving to learn the newest approaches and technologies in the field of life science that will enable the next generation of biologics. Become a sponsor and exhibitor and get the opportunity to network, influence, and interact with over 1,000 of the world's leading protein engineering scientists and executives.

SPONSORSHIP INFORMATION

CHI offers comprehensive sponsorship packages which include presentation opportunities, exhibit space, branding, as well as the use of the pre- and post-show delegate list.

Sponsorships allow you to achieve your objectives before, during and long after the event. Any sponsorship can be customized to meet your company's needs and budget.

OPPORTUNITIES INCLUDE:

Agenda Presentations

Speak to a captive audience about your latest product or service. This sponsorship includes a 15-minute or 30-minute podium presentation within the scientific agenda. You can also choose a luncheon presentation. This opportunity includes a 30-minute podium presentation to delegates in the session room. Both of these packages include exhibit space, branding and use of the delegate mailing lists.

Invitation-Only VIP Dinner/Hospitality Suite

Sponsor will select its top prospects from the pre-registration list for a night of networking at a local venue. To insure optimum face-to-face networking, CHI will work closely with sponsor to develop an invitation format and guest list.

Your company can also host a hospitality suite at the host hotel to accommodate a larger group of delegates. CHI can customize any dinner or reception to meet your needs and budget.

Focus Groups

CHI will gladly provide you the opportunity to host a focus group on-site at the PEGS Summit. This exclusive gathering can be useful to conduct market research, gather feedback on a new product idea and gather marketing intelligence from industry experts on a specific topic.

Other Promotional Opportunities

- Literature Chair Drop in the session room
- Exhibit Hall Reception
- Hotel Room Drop
- Badge Lanyards (SOLD)
- Conference Tote Bags
- Conference Padfolio or Notebook
- Tote Bag Insert
- Program & Exhibit Guide Sponsor

Exhibit Hall

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

Submit a Scientific Poster

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

To customize your sponsorship or exhibit package, contact:
Carol Dinerstein
Director, Exhibit & Sponsorship Sales
Cambridge Healthtech Institute
Phone: 781-972-5471; Fax: 781-972-5470
dinerstein@healthtech.com

2010 SPONSORS & EXHIBITORS AS OF 1/8/2010:

- Aragen Bioscience
- Attana
- BAC B.V. The Affinity Experts
- Bio Rad Labs
- Blue Sky Biotech
- Blue Stream Laboratories
- Caliper Life Sciences
- Crown Bioscience
- DNA 2.0
- Eden Biodesign
- ForteBio
- GENEART Inc.
- GENEWIZ
- GenScript
- GYROS
- Integral Molecular
- Lonza
- Lyophilization Services of New England, Inc.
- Malvern Instruments
- New England Biolabs
- Novozymes
- Paragon Bioservices
- Pfenex, Inc.
- Polyplus-transfection
- Precision Antibody
- Promega
- Proteos, Inc.
- QIAGEN
- Sapidyne Instruments
- Selexis
- Sloning Biothechnology
- STEMCELL Technologies Inc.
- TGA Sciences
- TTP Labtech
- Vaccinex

Sixth Annual

PEGS

May 17 - 21, 2010

Fax or mail registration to: Cambridge Healthtech Institute
250 First Avenue, Suite 300,Needham, Massachusetts 02494
T: 781-972-5400 or toll-free in the U.S. 888-999-6288 • F: 781-972-5425 • www.healthtech.com

1. Registration Information:

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❒ Mr. ❒ Ms. ❒ Mrs. ❒ Dr. ❒ Prof.

Name

Job Title Div./Dept.

Company

Address

City/State/Postal Code

Country

Telephone Fax

Email*

*Email is not a mandatory field. However, by excluding your email you will not receive notification about online access to pre-conference presenter materials, conference updates and networking opportunities. Delivery Preferences: How would you prefer to receive notices from CHI: EMAIL: ❒ Yes ❒ No FAX: ❒ Yes ❒ No

2. Pricing Information:

Short Course Pricing

	Commercial Rate	Academic, Gov't, Hospital Affiliated
1 Short Course	❒ $595	❒ $295
2 Short Courses	❒ $895	❒ $495
3 Short Courses	❒ $1195	❒ $695

Sunday, May 16

Morning Courses 9am - 12pm

❒ SC1 Phage and Yeast Display Libraries and Their Screening
❒ SC2 Safety of Biologics - Dealing with Unexpected Toxicity with Recombinant Proteins
❒ SC3 Program Management for Scientists
❒ SC4 Development of Antibody-Based Therapeutics from Discovery to the Clinic

Afternoon Courses 2pm - 5pm

❒ SC5 Antibody-Drug Conjugates
❒ SC6 Analytical Tools and Methods Used in Biopharmaceutical Characterization (2pm - 6pm)
❒ SC7 Phage Display in Vaccine Development
❒ SC8 Membrane Proteins

Dinner Short Courses

Tuesday, May 18

❒ SC9 Dinner, Presentations and Interactive Panel Discussion - Satisfying FDA Recommendations in the Area of Protein Aggregate Quantification

Thursday, May 20

❒ SC10 Dinner, Presentations - Affinity Tags for Protein Purification

Please select the package below based on the options you will most likely attend.

		ADVANCE RATE until March 26, 2010	REGULAR RATE after March 26, 2010
❒ **PREMIUM:** (Includes access to conference options I, II, III)	Best Value	❒ $2,650	❒ $2,795
		❒ $1,345	❒ $1,495
❒ **STANDARD:** (Includes access to either conference options I & II, OR II & III)		❒ $2,245	❒ $2,445
		❒ $1,125	❒ $1,225
❒ **BASIC:** (Includes access to either conference options I, II, OR III)		❒ $1,445	❒ $1,595
		❒ $725	❒ $795

3. Program Selections:

Based on your pricing package, please select the programs you will most likely attend. NOTE: Choose one program per option.

CONFERENCE OPTIONS

I. (May 17-18)	**II.** (May 19-20)	**III.** (May 20-21)
❒ **Phage Display**	❒ **Engineering Antibodies**	❒ **Antibody Optimization**
❒ **Difficult to Express Proteins**	❒ **Pre-Clinical/Clinical Development**	❒ **Bispecific Antibodies**
❒ **Immunogenicity**	❒ **Protein Aggregation**	❒ **Biotherapeutic Targets**

Poster Discount ❒ **$50 off**

Hotel Discount ❒ **$150 off - see web site for details. Hotel Conf. #:**_____

REGISTER 3 — 4th IS FREE

Individuals must register for the same conference or conference combination an submit completed registration forms together for discount to apply. Please reproduce this registration form as needed

❒ I cannot attend but would like to purchase the PEGS event CD for $750 (plus shipping). Massachusetts deliveries will include 6.25% sales tax.

❒ Please send information on exhibiting and sponsorship opportunities.

4. Payment Information

❒ Enclosed is a check or money order payable to Cambridge Healthtech Institute, drawn on a U.S. bank, in U.S. currency.

❒ Invoice me, but reserve my space with credit card information listed below.

Invoices unpaid two weeks prior to conference will be billed to credit card at full registration rate. Invoices must be paid in full and checks received by the deadline date to retain registration discount. If you plan to register on site, please check with CHI beforehand for space availability.

❒ Please charge: ❒ AMEX (15 digits) ❒ Visa (13-16 digits) ❒ MasterCard (16 digits)

Card # Exp. Date

Cardholder

Signature

Cardholder's Address (if different from above)

City/State/Postal Code

Country

Please refer to the Registration Code below:

Commercial Rate	Academic, Gov't, Hospital Affiliated

PRESENT A POSTER AND SAVE $50

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

To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by **April 7, 2010.** Register online, or by phone, fax or mail. Indicate that you would like to present a poster and you will receive abstract submission instructions via email.
I am interested in presenting a poster at

❒ **PEGS**

Title _____

CHI INSIGHT PHARMA REPORTS

A series of reports that evaluate the salient trends in pharmaceutical technology, business, and therapy markets. Keep abreast of the latest advances in pharmaceutical R&D, their potential applications and business impacts, and their current and future position in the marketplace. For a list of reports, visit InsightPharmaReports.com, or contact Rose LaRaia, rlaraia@healthtech.com, 781-972-5444

ADDITIONAL REGISTRATION DETAILS

Each registration includes all conference sessions, posters and exhibits, food functions, and a copy of the conference proceedings link.

GROUP DISCOUNTS

Special rates are available for multiple attendees from the same organization. Contact David Cunningham at 781-972-5472 to discuss your options and take advantage of the savings.

HANDICAPPED EQUAL ACCESS

In accordance with the ADA, Cambridge Healthtech Institute is pleased to arrange special accommodations for attendees with special needs. All requests for such assistance must be submitted in writing to CHI at least 30 days prior to the start of the meeting.

Substitution/Cancellation Policy

In the event that you need to cancel a registration, you may:

- Transfer your registration to a colleague within your organization
- Credit your registration to another Cambridge Healthtech Institute program
- Request a refund minus a $100 processing fee per conference
- Request a refund minus the cost ($750) of ordering a copy of the CD.

NOTE: Cancellations will only be accepted up to two weeks prior to the conference.

Program and speakers are subject to change.

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

PEGSummit.com