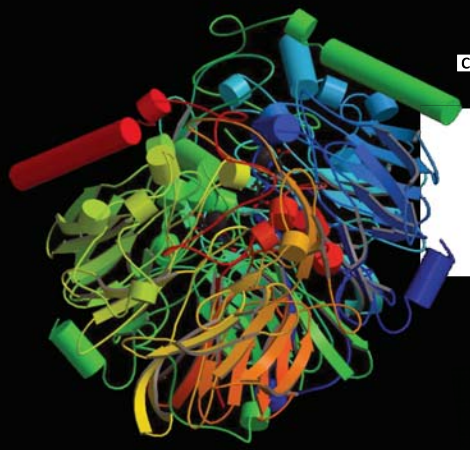
Register Early and SAVE!



Cambridge Healthtech Institute's

PEGS Europe

Protein Engineering Summit

6-8 October 2009
Exhibition Grounds
Hannover | Germany

Held in Conjunction with:

BIO TECHNICA
Hannover, 6–8 October 2009

Europe's No.1 Event in Biotechnology and Life Sciences

6-7 October

Third Annual
Improving Protein Expression through Innovation

Inaugural
Phage Display of Therapeutic Antibodies

7-8 October

Inaugural
Next Generation Technologies for Protein Science

Third Annual
Antibodies from Bench to Bedside

Keynote Speakers

Trevor Wilkinson, Ph.D., Head, Protein Sciences, MedImmune Ltd

Joerg Standfuss, Ph.D., Senior Post-Doctoral Researcher, MRC-Laboratory of Molecular Biology

Andreas Plückthun, Ph.D., Professor of Biochemistry, University of Zürich

Debbie Law, Ph.D., Chief Scientific Officer, Ablynx nv

Georg Feger, Ph.D., Site Manager, Geneva Research Center, Vice President, Research Head of NBE Technologies, Merck Serono S.A.

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

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Sponsoring Society: ProteinSociety.org

Cambridge Healthtech Institute
250 First Avenue, Suite 300 • Needham, Massachusetts 02494
Telephone: 781-972-5400 Toll-free in the U.S. 888-999-6288 • Fax: 781-972-5425

PEGSummitEUROPE.com

SUMMIT-AT-A-GLANCE

MONDAY, 5 OCTOBER		
16:00-18:30	Conference Registration	
18:30	BIOTECHNICA Opening and EUROPEAN BIOTECHNICA AWARD Ceremony plus Reception	
TUESDAY, 6 OCTOBER		
08:30-19:00	Conference Registration	
09:00-18:00	Exhibit Viewing	
09:00-12:30	**Track 1: Improving Protein Expression through Innovation**	**Track 2: Phage Display of Therapeutic Antibodies**
12:30-13:45	Lunch for Purchase in the Exhibit Hall and Exhibit Viewing	
14:00-17:30	**Track 1: Improving Protein Expression through Innovation**	**Track 2: Phage Display of Therapeutic Antibodies**
17:45-19:00	Interactive Breakout Discussion Groups	
19:00-21:00	CHI Reception	
WEDNESDAY, 7 OCTOBER		
09:00-12:30	**Track 1: Improving Protein Expression through Innovation**	**Track 2: Phage Display of Therapeutic Antibodies**
12:30-13:45	Lunch for Purchase in Exhibit Hall and Exhibit Viewing	
13:00-17:30	Conference Registration	
14:00-17:30	**Track 3: Next Generation Technologies for Protein Science**	**Track 4: Antibodies from Bench to Bedside**
18:30	BIOTECHNICA Night: Beer Hall, full dinner reception, a traditional German band	
THURSDAY, 8 OCTOBER		
09:00-12:30	**Track 3: Next Generation Technologies for Protein Science**	**Track 4: Antibodies from Bench to Bedside**
12:30-13:45	Lunch for Purchase in Exhibit Hall and Exhibit Viewing	
14:00-17:30	**Track 3: Next Generation Technologies for Protein Science**	**Track 4: Antibodies from Bench to Bedside**
17:30	Conference Adjourns	

Hotel Information

Conference Venue: Hanover Exhibition Grounds
Deutsche Messe | Messegelände
30521 Hannover | GERMANY

Host Hotel:
Please visit the conference website for the most up to date information regarding hotel accommodations.
PEGSummitEurope.com

Online: PEGSummitEurope.com
Email: reg@healthtech.com
Fax: 781-972-5425

Exhibit & Sponsorship Opportunities

Whether you are ready to present an exciting new technology, preparing for a new product launch, or need feedback on a specific idea, PEGS Europe offers the perfect platform for you to present to a high-level, targeted audience.

The Biotechnica exhibit hall will host 13,000 attendees over the course of the event. Co-location with Biotechnica will allow you to exhibit as part of the larger event and reach your target audience in the PEGS Europe session rooms, with an expected attendance of 400 PEGS delegates.

Exhibit in the PEGS Pavilion in the Biotechnica hall, and you will be located in the central location for all PEGS delegates. Traffic-building programs will be in place to ensure delegates visit this pavilion.

Sponsors will get the opportunity to participate in three networking events offered to you free-of-charge by Biotechnica & CHI:

- Monday evening - pre-conference keynote presentation & reception
- Tuesday evening - an exclusive dinner reception for PEGS attendees
- Wednesday evening - a second social hosted by Biotechnica in the Bavarian Beer hall, complete with dinner and a traditional German band

These receptions are an excellent opportunity to network with your target audience. Attendance is included in selected sponsorship packages.

SPONSORSHIP OPPORTUNITIES:

Podium Presentations
A 15 or 30 minute podium presentation as part of the main conference.
(May also include a table-top in the foyer during the exclusive PEGS Tuesday evening dinner reception.)

Coffee Breaks (exclusive per break)
Coffee breaks will be held in close proximity of the conference sessions. Table-top will be available for sponsoring company to display corporate product literature

Session Chair (exclusive per break)
An executive from your company will chair a session (a group of talks) on the main conference program. Includes a brief introduction to the entire session and the individual speakers

Exhibitor Information
Exhibitors at PEGS Europe will enjoy facilitated networking opportunities with more than 400 high-level decision-makers. Speak face-to-face with prospective clients and showcase your latest product, service or solution.

Marketing support from CHI and Biotechnica will include

- combined brochure mailings of 260,000
- email campaigns of 1 million impressions

For more information on sponsorship and exhibit opportunities, please contact Carol Dinerstein; 781-972-5471 or dinerstein@healthtech.com

About Cambridge Healthtech Institute (CHI)

Founded in 1992, Cambridge Healthtech Institute (www.chicorporate.com) is the industry leader offering the preeminent source of information to leading researchers and business experts from top pharmaceutical, biotech, and academic organizations. Delivering an assortment of resources such as events, reports, publications and eNewsletters, CHI's portfolio of products include Cambridge Healthtech Institute Events, Pharmaceutical Strategy Series, Barnett International, Insight Pharma Reports, Marketing Services, and Cambridge Healthtech Media Group.

About BIOTECHNICA

Geared to "Turning ideas into value" BIOTECHNICA 2009 invites you to Europe's leading gathering for biotechnology and life sciences, staged annually in Hannover, Germany. For three days the exhibition halls, the conference rooms and the Partnering meeting boxes will be alive with exhibitors and visiting professionals from all over the world, together with investors and distinguished speakers from business, science and politics - all here to discuss the latest products, innovations, research findings and market opportunities. Maximize your sales prospects. From research and product development, equipment, process technology and services to production and marketing: the exhibition section of BIOTECHNICA charts the biotech industry's value-adding chain from start to finish. Alongside the big industry players and SMEs, which have their own stands at the show, young and emerging biotech firms and scientific establishments are given ideal opportunities to showcase their work at the many group display stands representing national and international BioClusters and industry associations. Reduce time and cost by making BIOTECHNICA the event of your choice in 2009. You can close deals, find business or research partners, discuss politics and forms of financing with experts and meet old and new friends - all this under one roof in just three days! All details at www.biotechnica.de

COSMIX Cosmix is a development stage biotechnology company that is using proprietary technologies to develop a range of biotherapeutic agents as well as highly specific binding peptides for use in the diagnostic, imaging and biopurifications industries. The Company uses innovative mRNA Display Technology to generate highly selective affinity ligands as reagents for its partners in the life science industry. Its bioprocessing products enable an improved efficiency of current bioprocessing procedures. In addition, the Company is developing novel biotherapeutics that offer the ability to be more cost effective, safer and less toxic. Cosmix intends to utilize its proprietary approaches to build its own proprietary drug pipeline. Cosmix, Cosmix Verwaltungs GmbH, is comprised of two subsidiaries Cosmix Molecular Biologicals GmbH in Braunschweig, Germany, focused on products and services for the life science industry, and Cosmix Therapeutics LLC in the US, focused on the development of D-peptides as therapeutics.

Media Partners:

Cambridge Healthtech Institute's Third Annual

Improving Protein Expression through Innovation

6-7 October 2009

MONDAY, 5 OCTOBER

16:00-18:30 **Conference Registration**

18:30 **BIOTECHNICA Opening and EUROPEAN BIOTECHNICA AWARD Ceremony plus Reception**

TUESDAY, 6 OCTOBER

08:30-19:00 **Conference Registration**

OPENING KEYNOTE SESSION

09:00-09:05 **Chairperson's Remarks**

09:05-09:35 **Protein Tools for Antibody Discovery: Taming Complex and Difficult Proteins**

Trevor Wilkinson, Ph.D., Head, Protein Sciences, MedImmune Ltd

The expression and purification of target proteins to support the development of therapeutic antibodies remains a significant challenge. An additional challenge is the requirement to support diverse activities (e.g. biochemical screening, phage and ribosome display) and to produce species variants of the human target proteins to facilitate pharmacology and toxicology studies. To support these activities we have developed a number of platforms to allow expression and purification of challenging proteins. In this presentation I will outline the capabilities developed at MedImmune and provide some case study examples of protein expression and purification.

09:35-10:05 **Thermostable Mutants for the Crystallographic Study of GPCR Activation**

Joerg Standfuss, Ph.D., Senior Post-Doctoral Researcher, MRC-Laboratory of Molecular Biology

G protein-coupled receptors (GPCRs) allow the transmission of chemical signals across the cellular membrane. GPCRs are encoded by ~800 human genes and include ~30% of all known drug targets. Due to their low stability and low natural abundance structural investigations of GPCRs have long been limited to wild-type rhodopsin. To lift this limitation we use wave bag bioreactors for large-scale production of mutant receptors in insect and mammalian cells. Alanine scanning and structural design yielded thermostable mutants that enabled us to crystallize active and inactive receptor conformations and to solve the first structure of a recombinantly produced GPCR.

PROGRESS IN PROTEIN EXPRESSION

10:05-10:35 **Cell-Free Expression of Membrane Proteins**

Frank Bernhard, Ph.D., Lab Leader, Institute of Biophysical Chemistry, Goethe University-Frankfurt

Cell-free expression eliminates most central problems associated with the conventional cellular production of membrane proteins and it allows completely new expression approaches by the direct synthesis of membrane proteins into defined artificial environments like detergent micelles or liposomes. We demonstrate the cell-free production of diverse groups of membrane proteins involved in transport, efflux, signaling, metabolism or biosynthesis in mg amounts by automated throughput optimization strategies. The quality of selected membrane proteins including eukaryotic solute carriers, G-protein coupled receptors and transporters has been evaluated by a number of complementary techniques. Pharmaceutically important targets such as G-protein coupled receptors or Alzheimer's disease related proteins can be produced in high quality in less than 24 hours and we present new strategies for their specific labeling and their functional as well as structural evaluation in particular by NMR spectroscopy.

10:35-11:00 **Coffee Break** *Sponsored by* sloning BioTechnology

11:00-11:30 **Secreted Expression of Self-Assembling Proteins in *Pichia pastoris***

Catarina Ferreira da Silva, M.Sc., Bioprocess Engineering, Wageningen University and Research Centre

Custom-made self-assembling proteins, resembling proteins like collagen or silk, may have a broader medical and pharmaceutical application if they could be produced in an animal-free way. The optimization of *Pichia pastoris* as a host organism for the production of these proteins will provide a new system for the synthesis of innovative protein materials with well-defined conformations and properties.

11:30-12:00 **Lemo21(DE3): A Generic *E. coli*-based Protein Overexpression Platform Guaranteeing Maximum Yields**

Jan-Willem de Gier, Ph.D., Associate Professor, Department of Biochemistry & Biophysics, Stockholm University/Xbrane Bioscience AB

A simple generic method for optimizing protein overexpression in *Escherichia coli* is still lacking. Therefore, we have engineered the Lemo21(DE3) strain. Lemo21(DE3) is tunable for protein overexpression and conveniently allows optimizing overexpression of any given soluble and membrane protein by using only a single strain rather than a multitude of different strains.

12:00-12:15 **Comparative Study on Autologous Expression Improvement in Human Cells by Gene Optimization: Results and Applications** GENEART THE GENE OF YOUR CHOICE

Hans Buegl, Ph.D., Head, Marketing and Sales, GENEART AG

We report the largest gene expression study on synthetic optimized genes in mammalian cells to date. Fifty human genes from the NCBI Entrez database representing different protein classes such as protein kinases, cytokines, membrane proteins and transcription factors, were optimized for increased mRNA half-life and protein expression in human cells. Expressed protein levels in HEK 293T cells were quantified and compared. The results clearly indicate a significant improvement of expression yield with optimized constructs compared to respective wildtype versions. Therefore, gene synthesis is not only a versatile manner to obtain individualized genes but also allows for autologous expression increase in most cases.

12:15-12:30 **Sponsored Presentation** *(Opportunity Available)*

12:30-13:45 **Lunch for purchase in the Exhibit Hall and Exhibit Viewing**

PROTEIN EXPRESSION FOR CMC AND CHALLENGING PROTEINS

14:00-14:05 **Chairperson's Remarks**

Trevor Wilkinson, Ph.D., Head, Protein Sciences, MedImmune Ltd

14:05-14:35 **EnBase: Novel High Cell Density Culture-Based Screening Platform for Recombinant Protein Production and Bioprocess Development**

Peter Neubauer, Ph.D., Professor, Department of Bioprocess Technology, Institute of Biotechnology, Technische Universität Berlin

EnBase is a unique microbial cultivation platform for high cell density growth in micro-well plate and shake flask formats. It is based on the principle of the glucose-limited fed-batch technology but applies an enzyme controlled internal delivery system for the controlled supply of glucose which allows easy scaling to any cultivation volume, including microwell cultures. Here we demonstrate that EnBase works well for the production of a large number of recombinant proteins in various shake flask and micro-well plate formats. Interestingly, aside from 10-20x higher cell densities compared to shaken cultures, and an equal growth in parallel cultures, in a number of examples the amount of the soluble active form of the target product was significantly increased per cell unit. Scalability of the Enbase technology has been shown in 100 liter cultivations.

14:35-15:05 **Helmholtz Protein Sample Production Facility for Large Scale Production of Protein Samples for Structural Analysis**

Joop van den Heuvel, Ph.D., Group Leader, Structural Biology - Protein Sample Production Facility, Helmholtz Centre for Infection Research

The Helmholtz PSPF is a unique infrastructure for the production of pure proteins in adequate amounts for biochemical and 3-dimensional structural studies by X-ray crystallography and NMR spectroscopy. The PSPF is a German-wide open access support facility for structural biologists and will participate in the European infrastructure initiative INSTRUCT (EU Frameworkprogram 7). A broad package of advanced techniques are now available that allow protein expression in a range of cultivation systems.

15:05-15:35 **Sponsored Presentation** *(Opportunity Available)*

15:35-16:00 **Refreshment Break**

Online: PEGSummitEurope.com

Email: reg@healthtech.com

Fax: 781-972-5425

16:00-16:30 Preparation of Stable Isotope-Labeled Cannabinoid Receptor CB2 for NMR Structural Studies

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

The peripheral cannabinoid receptor, CB2, a heptahelical G protein-coupled membrane receptor, has become one of the most sought after pharmaceutical targets. Structural studies on CB2 by NMR spectroscopy and other biophysical techniques will contribute greatly into the development of novel specific ligands targeting this receptor. In order to study CB2 at functional conditions, reconstitution of the purified receptor into liposomes is required. The ability of CB2-proteoliposomes to activate G-proteins in response to agonist binding was studied as a function of lipid composition and detergent concentration. The fermentation protocol was adapted to expression in minimal media supplemented with stable isotope-labeled tryptophan, and yielded 2 mg of 15N-tryptophan-labeled CB2 from 1L of culture. An efficient incorporation of the isotope was confirmed by mass spectrometry. We further adapted fermentation procedures for uniform labeling of CB2 with 13C and 15N that produced over 3 mg/L of labeled material. Functionally active 15N/13C labeled CB2 was reconstituted into liposomes, and is being currently analyzed by solid state NMR.

16:30-17:00 Library-Based Construct Screening for Difficult-to-Express Proteins: Influenza Polymerase as a Case Study

Darren Hart, Ph.D., Team Leader, High-Throughput Protein Technologies, European Molecular Biology Laboratory

The ESPRIT construct screening technology has been developed at EMBL to identify soluble constructs of "difficult-to-express" protein targets that resist the classical approach of bioinformatics and PCR cloning. In each experiment, 30,000 individual constructs are assayed in parallel for yield and solubility using a highly automated colony array format. Results will be presented on the influenza polymerase that has, prior to this study, proved intractable due to the absence of homologues required for multiple sequence alignments. Previously unsuspected domains were expressed and characterized structurally by X-ray crystallography and NMR, providing insights into the mechanisms of virus replication.

17:00-17:30 Poster Spotlight Presentations

17:30-17:45 Move to Breakout Discussion Groups

17:45-19:00 Interactive Breakout Discussion Groups

Mammalian Expression Systems: Options for Producing Difficult-to-Express Proteins

Moderator: Trevor Wilkinson, Ph.D., Head, Protein Sciences, MedImmune Ltd

- Mammalian expression systems - current options
- Optimising protein expression - current best practice and options
- Solutions to low expression of target proteins

GPCRS: Overcoming Cell Free Expression Challenges

Moderator: Frank Bernhard, Ph.D., Lab Leader, Institute of Biophysical Chemistry, Goethe University Frankfurt

Expression of GPCRs has traditionally been difficult, no matter the host chosen. Expression in cell-free systems can also be difficult. This roundtable will discuss:

- Specific problems in expression of GPCRs
- Challenges and benefits of cell free systems
- Shifting the bottleneck in GPCR production from high level
- Synthesis to appropriate quality control
- Quality improvement of cell-free produced GPCRs

Production of Complex Biopharmaceuticals with Moss Bioreactors

Moderator: Eva L. Decker, Ph.D., Researcher, Plant Biotechnology, Faculty of Biology, Freiburg University

The production of proteins in moss bioreactors offers new and interesting solutions to protein expression challenges.

- Characteristics of moss expression
- Deciding which proteins work best in mosses
- Solving expression problems with mosses

Saving Time and Costs for Antibody Expression in Mammalian Cells

Moderator: Gerald Casperson, Ph.D., BioTherapeutics Center of Emphasis, Pfizer Discovery Research

Discussion will include:

- Expression challenges in mammalian cells
- Time-saving strategies
- Cost-saving strategies
- Big pharma perspective on savings plans

E. coli Expression Systems: Making the Right Choices to Enhance Expression

Moderator: Ian Hodgson, Ph.D., Head, Molecular Biology, Research and Development, Avecia Biologics

As the workhorse host for protein expression, *E. coli* has been used both at the bench level and at the industrial level. However, there are still many choices to be made during the process to enhance the eventual outcomes. We will discuss:

- Evaluating and choosing the correct expression route
- Shortening process development time
- Increasing yields

19:00-21:00 CHI Reception *(Sponsorship Opportunity Available)*

21:00 Close of Day

WEDNESDAY, 7 OCTOBER

TAKING IT TO THE NEXT LEVEL

09:00-09:05 Chairperson's Remarks

09:05-09:35 Thermostabilisation Allows Purified GPCRs to be Used for Drug Discovery

Markus Koglin, Ph.D., Head, Structural Sciences Group, Heptares Therapeutics Limited

09:35-10:05 Production of Complex Biopharmaceuticals with Moss Bioreactors

Eva L. Decker, Ph.D., Researcher, Plant Biotechnology, Faculty of Biology, Freiburg University

The moss *Physcomitrella patens* is emerging as a highly beneficial alternative expression system for the production of complex recombinant pharmaceuticals (e.g. glycoproteins) for which tissue culture-based production in photobioreactors has been established. In contrast to microorganisms plants perform protein modifications strongly resembling those of human cells. However, certain plant-specific protein-linked sugar residues were shown to be immunogenic, a fact that restricts the use of plants in biopharmaceutical production. The availability of the moss genome sequence facilitated the identification of genomic loci for enzymes involved in plant-specific modifications. Using targeted gene replacements, moss strains were created with non-immunogenic humanised glycan patterns.

10:05-10:35 Sponsored Presentation *(Opportunity Available)*

10:35-11:00 Coffee Break

11:00-11:30 Therapeutic Antibody Production in Mammalian Cells at Lab Scale: Comparison, Adaptation and Implementation of Strategies for Time and Cost Savings

Gerald Casperson, Ph.D., BioTherapeutics Center of Emphasis, Pfizer Discovery Research

We have explored a variety of options for laboratory-scale (up to several grams) production of biotherapeutic antibodies from mammalian cells, including large scale transient transfection with PEI and other lipids, baculovirus transduction and production from stably-transfected pools of cells. We have also evaluated process improvements such as fed-batch strategies to increase productivity. We will discuss implementation and impact of improvements that allow rapid production of gram quantities of antibody therapeutics suitable for evaluation in animal models.

11:30-12:00 Achieving Exceptional Yields in CHO and PER.6® Cell Lines Enables Full Pre-Clinical Evaluation of Candidates without the Need for CMO Scale Up

Bram Bout, Ph.D., Chief Executive Officer, Board of Directors, Bioceros BV

New High Expression Level Cell Lines in combination with innovative disposable culturing systems allow for sufficient volumes of test material to be produced at a laboratory scale (20 liter) to enable a complete pre-clinical characterisation and safety evaluation. This, without the need of a costly and time consuming scale up to a GMP CMO facility, as was classically the case. Furthermore, these novel production methods allow the use of serum free culture media, making a seamless transition to GMP CMO possible, further negating the classical adaptation necessity and allowing for a swift commencement of Phase 1 clinical testing.

12:00-12:30 *E. coli* Expression Systems: New Tools for Improved Process Development of Biopharmaceuticals

Ian Hodgson, Ph.D., Head, Molecular Biology, Research and Development, Avecia Biologics

We have developed expression systems which have been specifically designed to enable rapid evaluation of the optimal expression route in *E. coli* (Intracellular, Soluble/Insoluble, or Periplasmic secretion), whilst enabling high overall yields, with minimal process development time. We will describe the design of the system, and demonstrate their use in a number of real case studies. In addition we will describe some recent enhancements to the system utilising novel components.

12:30-13:45 Lunch for Purchase in the Exhibit Hall and Exhibit Viewing

13:45 Close of Improving Protein Expression through Innovation conference

Cambridge Healthtech Institute's Inaugural

Phage Display of Therapeutic Antibodies

6-7 October 2009

Letter from the Scientific Advisory Board

"Building on the success of the annual PEGS Summit in Boston, we are happy to support Cambridge Healthtech Institute in organizing the Inaugural Phage Display of Therapeutic Antibodies event in Europe. This meeting promises to be a fantastic way to hear the latest protein engineering science, network with scientists that are at the forefront of research, and discover solutions to the challenges facing the field. We hope you join us and learn how to leverage display methodologies for new protein therapeutic entities."

H. Kaspar Binz, Ph.D., Vice President, Technology & Co-Founder, Molecular Partners AG
Lutz Jermutus, Ph.D., Senior Director, Technology, MedImmune Ltd.
Sachdev Sidhu, Ph.D., Associate Professor, Banting & Best Department for Medical Research and Department of Molecular Genetics, University of Toronto
Richard W. Wagner, Ph.D., President and Chief Executive Officer, SRU Biosystems, Inc.
Gregory A. Weiss, Ph.D., Associate Professor, Department of Chemistry, Molecular Biology & Biochemistry, University of California, Irvine
K. Dane Wittrup, Ph.D., J.R. Mares Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

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PHAGE DISPLAY OF THERAPEUTIC ANTIBODIES

OPENING KEYNOTE SESSION

09:00-09:05 **Chairperson's Remarks**

09:05-09:35 **Combinatorial and Evolutionary Protein Engineering**

Andreas Plückthun, Ph.D., Professor of Biochemistry, University of Zürich

Display, selection and iterative evolution has been used in three sce narios. First, to generate binding proteins for therapy, using Designed Ankyrin Repeat Proteins (DARPins). Second, to build a modular system to detect and discriminate linear protein sequences in a sequence-specific manner, using Armadillo Repeat Proteins. Third, to stabilize targets such as GPCRs by directed evolution such that they can be stabilized for structural studies.

09:35-10:05 **Bringing Nanobodies to the Clinic**

Debbie Law, Ph.D., Chief Scientific Officer, Ablynx nv

Nanobodies® are therapeutic proteins based on the smallest functional fragments of heavy chain antibodies, which occur naturally in the Camelidae family, including camels and llamas. Due to their inherent biophysical properties, Nanobodies can combine the advantages of both small molecule and traditional monoclonal antibody therapeutics. This presentation will focus on these next-generation biologics and provide examples of how Nanobodies can be formatted to generate clinical candidates with the desired biological activities including selectivity, high potency, and appropriate half-life.

OPENING KEYNOTE SESSION

10:05-10:35 **Strategies for a Competitive Biologics Portfolio**

Georg Feger, Ph.D., Site Manager, Geneva Research Center, Vice President, Research Head of NBE Technologies, Merck Serono S.A.

Biotherapeutics based on cytokines, growth factors, receptorbodies and monoclonal antibodies are an essential part of today's medical treatment. The desire for more efficacious treatment with fewer side effects is driving a new innovation cycle that promises to extend the addressable target space, to deliver new binding scaffolds, to increase potency and manufacturability. A balanced portfolio approach to generate a sustainable and competitive biologics portfolio will be discussed.

10:35-11:00 **Coffee Break** *Sponsored by* sloning BioTechnology

INCREASING EFFICIENCY OF LIBRARIES AND SELECTION

11:00-11:30 **Yeast Surface Display**

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

We have developed an integrated platform for the discovery and optimization of human IgGs in the baker's yeast *Saccharomyces cerevisiae*. A novel form of synthetic library has been designed and constructed that reproduces key features of the preimmune human VHCDR3 repertoire. The abundance of nanomolar-affinity lead antibodies in this repertoire expressed in yeast is 100-fold greater than that from published data for premier phage antibody libraries. Unprecedented speed from antigen to panels of human IgG protein is attained. Optimization of affinity and expression are robust and rapid within the platform.

11:30-12:00 **Microdroplets for Directed Evolution**

Florian Hollfelder, Ph.D., Department of Biochemistry, University of Cambridge

The potential of water-in-oil microdroplets, generated in microfluidic devices, for future applications in protein engineering is discussed. Catalytic single-cell assays, protein expression from single cells, and cell-free protein expression can be quantitatively monitored. Thermal and isothermal PCR reactions from single DNA molecules bring about 'monoclonal' droplets with multiple gene copies. The droplet compartment can also be used to create a covalent genotype-phenotype linkage in 'SNAP-tag display'. This display system can be engineered to provide a multivalent display systems to take advantage of avidity effects for selections from naive libraries.

12:00-12:30 **Combining Chemical Protein Synthesis and mRNA Display in a Mirror Image Approach to Generate D-Peptides as a New Generation of Drugs** COSMIX

Peter Wagner, Ph.D., Chief Executive Officer, COSMIX molecular biologicals GmbH

Cosmix combined its powerful, proprietary technologies, mRNA display and chemical protein synthesis, to generate D-peptides as next generations of drugs. Mirror images of validated targets are chemically synthesized, applied to mRNA display selections and corresponding, identified binding L-peptides are turned into D-peptides to recognize corresponding natural targets in a highly, stereoselective manner of high affinity. Here we demonstrate the Proof of Concept and show the advances to develop a VEGF-binding D-peptide suitable for a wide range of indications.

12:30-13:45 **Lunch for Purchase in the Exhibit Hall and Exhibit Viewing**

ANTIBODY FRAGMENTS AND SCAFFOLDS BY PHAGE DISPLAY

14:00-14:05 **Chairperson's Remarks**

14:05-14:35 **Synthetic PDZ Domains for Functional Genomics**

Sachdev Sidhu, Ph.D., Banting & Best Department for Medical Research and Department of Molecular Genetics, University of Toronto

PDZ domains are peptide-recognition modules that recognize C-terminal sequence to assemble signaling complexes. We have significantly expanded the PDZ family specificity range by engineering synthetic domains that target novel C-terminal sequences. Synthetic PDZ domains represent a new class of affinity reagents that can be tailored for the recognition of peptide motifs in natural proteins to enable numerous functional genomics applications.

Online: PEGSummitEurope.com

Email: reg@healthtech.com

Fax: 781-972-5425

14:35-15:05 Engineered Cystine Knot Miniproteins for Diagnostics and Therapy

Harald Kolmar, Ph.D., Department of Biochemistry, Technical University of Darmstadt

Due to their outstanding inherent stability, as well as their small size of only around 30 amino acid residues, cystine knot miniproteins (knottins) are an attractive class of agents for the development of peptide-based pharmaceuticals. Potent and selective knottins with predefined binding characteristics were obtained by rational protein design as well as by combinatorial library screening using phage and bacterial display strategies.

15:05-15:35 Sponsored Presentation *(Opportunity Available)*

15:35-16:00 Refreshment Break

IMMUNOCONJUGATES FOR CANCER THERAPY: FROM DISCOVERY TO CLINIC

FEATURED PRESENTATION

16:00-16:30 Development of an EphA2 Antibody Drug Conjugate for the Treatment of Cancer

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

The use of monoclonal antibodies (MAbs) to selectively deliver highly po tent cytotoxic drugs to tumors can both improve efficacy and reduce sys temic toxicity. It is important to consider each of the components, the MAb and its target antigen, the linker, and the cytotoxic drug, during the design of an antibody drug conjugate (ADC). In particular, the choice of an appropriate target antigen is critical to the efficacy and safety of the ADC. The antigen should be expressed in high density on malignant cells, have limited normal tissue expression, and be internalized following ADC binding. This presentation will focus on the design and development of ADCs consisting of human antibodies against EphA2, a tyrosine kinase receptor that is over-expressed on a variety of malignant tumors.

16:30-17:00 Combining Radioimmunotherapy and Antivascular Agents: Using Human *Ex Vivo* Phage Display Selection to Derive Clinically Relevant Targeting Moieties

Tim Meyer, M.D., Ph.D., Senior Lecturer in Medical Oncology, UCL Cancer Institute, University College London

The results of a recently completed Phase 1 trial combining the CEA targeting antibody 131I-A5B7 with combretastatin A4 Phosphate will be presented. In addition, a novel strategy for deriving clinically relevant scFvs using *ex vivo* human organ perfusion will be presented.

17:00-17:30 Vascular Tumor Targeting: From the Bench to the Clinic

Dario Neri, Ph.D., Professor, Chemistry & Applied Biosciences, Institute of Pharmaceutical Sciences, ETH Zürich

The recent identification of good-quality markers of angiogenesis opens new avenues for the antibody-based selective delivery of therapeutic agents to primary tumors and metastatic sites.

17:30-17:45 Move to Breakout Discussion Groups

17:45-19:00 Interactive Breakout Discussion Groups

Antibody Fragments and Scaffolds

Moderator: Sachdev Sidhu, Ph.D., Associate Professor, Banting & Best Department for Medical Research and Department of Molecular Genetics, University of Toronto

- Limitations of conventional igg antibodies in terms of production, delivery and efficacy
- Features and caveats to be considered in the design and application of igg alternatives
- Advantages and disadvantages of antibody fragments relative to iggs
- Advances in alternative scaffolds beyond the immunoglobulin fold
- Key application niches for antibody fragments and alternative scaffolds

Delivery into Tumors

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

- Targeted nanoparticles
- Immunotoxins & antibody-drug conjugates
- Vascular targeting
- Micropharmacokinetics

Immunoconjugates for Cancer Therapy

Moderator: Dario Neri, Ph.D., Professor, Chemistry & Applied Biosciences, Institute of Pharmaceutical Sciences, ETH Zürich

- Action at the tumor cell (e.G., Internalizing antibodies) vs. Effector functions with cross-fire effect (e.G., Adept, radionuclides)
- Antibodies against cell membrane antigens vs. other possible targets (e.G., Ecm components)
- Effector functions: radionuclide vs. cytokine vs. drug vs. other toxic moieties
- Integration of imaging and therapy

Increasing Efficiency of Libraries and Selection

Moderator: Andreas Plückthun, Ph.D., Professor of Biochemistry, University of Zürich

Engineering Approaches to Minimize Aggregation and/or Immunogenicity

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

- Selections for solubility
- Selections for thermostability
- Designing libraries for solubilization
- Screens for thermostability and solubility

19:00-21:00 CHI Reception *(Opportunity Available)*

WEDNESDAY, 7 OCTOBER

09:00-18:00 Exhibit Viewing

ENGINEERING IMPROVEMENTS IN PROPERTIES

09:00-09:05 Chairperson's Remarks

09:05-09:35 Engineering of Therapeutic Antibodies for Optimal Affinity and Biophysical Properties

Christilyn Graff, Ph.D., Senior Scientist, Protein Engineering, Biogen Idec

Selection of a therapeutic antibody hinges on both affinity for the target and appropriate biophysical properties, including propensity to aggregate, solubility, and stability. This presentation will cover the many approaches that one can take using phage display to improve antibodies with known good affinity for the target, but sub-optimum biophysical properties. Approaches presented include engineering the variable and constant domains of the antibody, as well as using families of antibodies to guide design of improved mutants. As different approaches can yield a range of results, it is advantageous to explore multiple routes to a solution.

09:35-10:05 Thermostability Engineering of a Soluble T-Cell Receptor Using Phage Display

Geir Åge Løset, Ph.D., Post-doctoral Fellow, Molecular Biosciences, University of Oslo

We have used phage display to engineer a soluble T-cell receptor to increased solubility and decreased susceptibility to aggregation. Random mutations were introduced in the V regions and mutants resistant to thermal denaturation were selected. Co-expression of the chaperone FkpA was critical for success – a finding of strong general interest for all combinatorial selection regimes. This is the first example to date of thermostability engineering of a soluble T-cell receptor by phage display.

10:05-10:35 Sponsored Presentation *(Opportunity Available)*

10:35-11:00 Coffee Break

TARGETING TRANSMEMBRANE PROTEINS

11:00-11:30 Phage Display and Engineering of Membrane Proteins

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

Representing about a third of the human proteome, membrane proteins contribute key roles in molecular sensing, signaling, and transportation. Roughly half of all pharmaceuticals target membrane proteins. Despite their importance, membrane proteins have remained off-limits to phage display. Using a new type of helper phage, the Weiss Laboratory has reported display and engineering of membrane proteins.

11:30-12:00 Comprehensive Identification of Tumor-Associated Antigens via Isolation of Human Monoclonal Antibodies that May be Therapeutic

Yoshikazu Kurosawa, Ph.D., Director, Professor, Institute for Comprehensive Medical Science, Fujita Health University

We succeeded in identification of 28 tumor-associated antigens (TAAs) that were preferentially and abundantly expressed on the surface of malignant cells and in isolation of 435 human monoclonal antibodies (mAbs) that specifically bound to one of the 28 TAAs. I am going to present the strategy and the data showing how we can select proper targets for therapeutic Abs from among the TAAs and what characters are required for mAbs to be therapeutic reagents against solid cancers.

12:00-12:30 Apoptosis-Inducing ICAM-1 Antibody has Broad and Potent Anti-Myeloma Activity *in Vivo*

Björn Frendéus, Ph.D., BioInvent International AB

We previously developed combined target and drug discovery methodology enabling isolation of tumor cell apoptosis-inducing antibodies from the *in vitro* CDR shuffled human antibody library n-CoDeR®. Among several antibodies targeting different tumor cell associated receptors with documented apoptosis-inducing properties, antibodies specific for intercellular adhesion molecule-1 (ICAM-1) - a receptor not previously associated with tumor cell apoptosis – were obtained. We here characterize the ICAM-1 specific antibody BI-505 with respect to *in vivo* anti-tumor activity in different well-established myeloma disease models and explore mechanisms underlying its anti-tumor activity. Preliminary data indicate that the BI-505 epitope is frequently and highly expressed on plasma cells from multiple myeloma patients.

12:30-13:45 Lunch for Purchase in the Exhibit Hall and Exhibit Viewing

13:45 Close of Phage Display of Therapeutic Antibodies conference

Cambridge Healthtech Institute's Inaugural

Next Generation Technologies for Protein Expression

7-8 October 2009

WEDNESDAY, 7 OCTOBER

13:00 **Conference Registration**

ENGINEERING A BETTER EXPRESSION PROCESS

14:00-14:05 **Chairperson's Remarks**

14:05-14:35 **Development of a Novel Gateway-based Vector System for Efficient, Multiparallel Protein Expression in *Escherichia coli*, Insect and Mammalian Cells.**

Felix Freuler, M.S., Scientific Technical Leader I, Center for Proteomic Chemistry, Novartis Institutes for BioMedical Research (NIBR)

We have generated a series of Gateway vectors which were improved with some new features: Kanamycin resistance for protein expression in *E. coli*, HRV 3C protease cleavage sites, novel solubilization tags and last but not least the capability to combine diverse N- and C-terminal extensions. This set of customized Gateway vectors proved to be highly useful for overexpression of a broad range of proteins in various hosts.

14:35-15:05 **New Ways of Establishing Production Cell Lines for Structural Biology**

Konrad Büssow, Ph.D., Project Group Leader, Structural Biology, Helmholtz Centre for Infection Research

Site directed, recombinase mediated cassette exchange (RMCE) has the potential of establishing stable mammalian producer cell lines fast and with reproducible expression strength and stability. We have established CHO master cell lines for RMCE for structural biology using a GFP vector and FACS sorting of high producer cells. A CHO Lec cell line was used, that is glycosylation deficient and produces glycoproteins that can be deglycosylated and crystallized efficiently. Establishing CHO production cell lines for target proteins by RMCE was fast (less than one month), reproducible and yielded cell lines that compare favorably to traditional production cell lines. Protein was produced by fermentation and crystals were obtained of deglycosylated, purified proteins.

15:05-15:35 **Protein Science Technologies in Industrial Process Development**

Philine Dobberthien, Process Science / Downstream Development, Boehringer Ingelheim Pharma GmbH & Co KG

This presentation will introduce novel technologies developed in the downstream development unit to accelerate process development and to enhance the knowledge and understanding of the behaviour of biomolecules we are handling. Downstream processes at Boehringer Ingelheim are designed to minimize the time to tox and time to clinical material, while maintaining a focus on the development of a customized process for each individual product. With the complexity of biological compounds and the increasing regulatory requirements, it is critical to have flexibility in the development process in order to insure the highest product quality and safety standards. Novel technologies based on biochemical and physical characterization, the implementation of automation and high-throughput techniques allow us to individually streamline process development timelines while increasing the amount of data used to make critical process decisions leading to rationally designed processes. This presentation will also describe how our novel technologies have impact on later stages of development and scale-up leading to integrated processes.

15:35-16:00 **Refreshment Break**

16:00-16:30 **Sponsored Presentation** *(Opportunity Available)*

16:30-17:00 **Affinity Partitioning of Proteins Tagged with Choline-Binding Modules in Aqueous Two-Phase Systems**

Isabel Velasco, Ph.D., Assistant Researcher, Research and Development, Biomedal

We present a novel procedure for affinity partitioning of recombinant proteins fused to a choline-binding module (C-LytA or LYTAG) in an aqueous two-phase system (ATPS) containing poly(ethylene glycol) (PEG). Proteins tagged with the C-LytA module have affinity to the PEG-rich phase, whereas subsequent addition of the natural ligand choline specifically shifts their localization to the PEG-poor phase by displacement of the polymer from the binding sites. These systems show interesting advantages both for laboratory and industry as they are cost-effective, easy to scale up and suitable for continuous operation. Many variables can be manipulated to improve the partition, and compatibility with detergents allows the purification of membrane proteins. We have successfully purified diverse recombinant proteins with the choline binding polypeptide tag by affinity partitioning in ATPS. This process avoids some disadvantages of the solid affinity supports such us resin cost, preparation and recycling, column fouling or changes in the stability of the adsorbed proteins. The high purity degree from crude extracts in few simple steps (>98%), its cost-effectiveness and the easy scalability of the process make the affinity partitioning of proteins tagged with choline binding protein (LYTAG) a promising system for either basic research and industrial biotechnology.

17:00-17:30 **Poster Spotlight Presentations**

18:30 **BIOTECHNICA Night: Beer Hall, full dinner reception, a traditional German band**

THURSDAY, 8 OCTOBER

UTILIZING NEXT GENERATION METHODS AND TECHNOLOGIES

09:00-09:05 **Chairperson's Remarks**

09:05-09:35 **Influencing Transgene Expression via Modifications of the Coding Sequence**

Asli Bauer, Ph.D., Senior Scientist, Molecular Microbiology and Gene Therapy, University of Regensburg

The efficacy of transgene expression is significantly enhanced by RNA and codon optimization. A decrease of CpG content in the ORF, applied to circumvent epigenetic mechanisms of gene silencing, results in extremely low expression yields. Multi parameter RNA- and codon optimization results in enhanced de novo-synthesis of gfp and epo RNA in the nucleus and in the cytoplasm. Furthermore, RNA- and codon optimization lead to a dramatically prolonged gene expression in vivo.

09:35-10:05 **Interfering Peptides Targeting Extended Protein Interaction Surfaces**

Katja Arndt, Ph.D., Principle Investigator, Freiburg Institute for Advanced Studies, School of Life Sciences, University of Freiburg

Protein-protein interactions play important roles in numerous diseases, yet, targeting extended protein interaction surfaces still remains a huge challenge for today's antibody and protein engineering. We use semi-rational design in combination with selection systems to generate peptides interfering with transcription factor-mediated gene expression. Phage display selection was compared to *in vivo* selection based on protein-fragment complementation assay, and both methods succeeded in selecting specific peptide inhibitors with high stability. Implementing competitive and negative design aspects resulted in major energetic differences between desired and non-desired states, thereby allowing simultaneous selection for affinity and specificity. Different strategies will be discussed for targeting the oncoproteins Myc, Jun and Fos using tailored D- and L-peptides.

10:05-10:35 **Sponsored Presentation** *(Opportunity Available)*

10:35-11:00 **Coffee Break**

11:00-11:30 **Creating New Enzymes: High-Throughput Protein Expression Optimization of Monomeric TIM Libraries using EnBase™ Technology**

Mari Ylianttila, Ph.D., Post Doctoral Fellow, Department of Process and Environmental Engineering, University of Oulu

Our aim is to build a platform of TIM variants (Kealases) with a widened substrate range based on monomeric Triosephosphate Isomerase. In order to screen for active enzymes with novel reactions and to optimize the process for recombinant protein production we utilize the EnBase™ technology to set up a high-throughput for process optimization and for high-throughput crystallization of the mutants. EnBase™ enables a fed-batch like cultivation in small scale, from 120 µl up to 1 L. The method is based on the enzymatic release of substrate from a gel at the bottom of the growth vessel (e.g. microtiter plate). Due to the controllable growth rate in the EnBase™ system the cultivation mimics a large fed-batch process. High cell densities ensure high protein yields; slow growth rates ensure high amounts of soluble protein per cell.

11:30-12:00 **Biosynthesis of Folded Cyclotides inside Living Bacterial Cells: A Convenient Route for Generation of Genetically-Encoded Cyclotide-Based Libraries**

Julio Camarero, Ph.D., Associate Professor, Pharmaceutical Sciences and Toxicology, School of Pharmacy, University of Southern California

The cyclotide MCoTI-II is a powerful trypsin inhibitor recently isolated from the seeds of *Momordica cochinchinensis*, a plant member of cucurbitaceae family. We report for the first time the *in vivo* biosynthesis of natively-folded MCoTI-II inside live *E. coli* cells. Our biomimetic approach involves the intracellular backbone cyclization of a linear cylotide-intein fusion precursor mediated by a modified protein splicing domain. The cyclized peptide

time the *in vivo* biosynthesis of natively-folded MCoTI-II inside live *E. coli* cells. Our biomimetic approach involves the intracellular backbone cyclization of a linear cylotide-intein fusion precursor mediated by a modified protein splicing domain. The cyclized peptide then spontaneously folds into its native conformation. The use of genetically engineered *E. coli* cells containing mutations in the glutathione and thioredoxin reductase genes considerably improves the production of folded MCoTI-II *in vivo*. Biochemical and structural characterization of the recombinant MCoTI-II confirmed its identity. Biosynthetic access to correctly-folded cyclotides allows the possibility of generating cell-based combinatorial libraries that can be screened inside living cells for their ability to modulate or inhibit cellular processes.

12:00-12:30 Protein Folding on an Industrial Scale
Ole Fuetterer, Ph.D., Scil Proteins GmbH

12:30-13:45 Lunch for Purchase in the Exhibit Hall and Exhibit Viewing

APPLICATIONS

14:00-14:05 Chairperson's Remarks

14:05-14:35 Engineering Enzymes for Prodrug Activation Therapy
Kristian Müller, Junior Professor, Department of Biology, University of Freiburg
Tailored enzymes for tumor targeting facilitating prodrug activation therapies will enable the combination of the best properties of biologics and small molecules in highly effective approaches. We optimized key properties of the enzyme TEM beta-lactamase. Using a perturbation-compensation approach in combination with directed evolution based on NExT DNA shuffling, we raised the half-life time in a protease assay 13-fold, the kcat in a heat stress test at 60°C from zero to over 1000/s and the melting temperature over 28°C while maintaining the catalytic substrate spectrum and activity at low temperatures. We generated fusions with scFv antibody fragments and receptor ligands, addressed the problem of immunogenicity, and also optimized the split enzyme.

14:35-15:05 cGMP Production of Therapeutic Antibody-Cytokine Fusion Proteins
Leonardo Giovannini, Ph.D., Head, Protein Production, PHILOGEN S.p.A.
The complete cGMP production flow of an antibody-cytokine fusion protein for clinical use will be discussed with specific focus on clone selection, master and working cell bank preparation, fermentation, protein purification and final filling.

15:05-15:35 Sponsored Presentation *(Opportunity Available)*

15:35-16:00 Refreshment Break

16:00-16:30 Going Double-Digit with *Pichia*: High-Level Expression of Human Serum Albumin and Transferrin as Well as Fusion Proteins Driven by AOX1 Promoter Library
Roland Weis, Head, Research & Development, Biotechnology, VTU Technology
Although *Pichia pastoris* nowadays is a state-of-the-art host for recombinant expression with extraordinary capabilities for the secretion of heterologous proteins, only few examples of expression titers as high as >5g/L are reported. We report recombinant protein yields exceeding 10 g/L employing our proprietary AOX1-promoter library for expression of human serum albumin, human serum transferring(s) as well as fusion proteins thereof. Different cloning and expression strategies were assessed to improve expression titers, and parameter scouting in 1L bioreactors resulted in an optimized fermentation protocol, executed in 5L fermentations. As a result of downstreaming approaches, high purity and quality of the described proteins was achieved. Relying on the AOX1-promoter library, several other (human) recombinant proteins were expressed to titers between 2 and 7 g/L.

16:30-17:00 "Proteome Scale" *in vitro* Antibody Selections: Lessons from Pilot Projects and Use of the Antibody Genes for Functional Genomics
Stefan Dübel, Ph.D., Director, Biotechnology, Technische Universität Braunschweig
Started by work within the NGFN SMP Antibody Factory, a highly integrated and MTP-based pipeline for the generation of antibodies to any antigen was established and validated by making binders to individual SH2 domains within a Pilot Project of the Structural Genomics Consortium (SGC). We have further used various scFv genes for the functional analysis of the target gene. After subcloning into a mammalian expression vector, the scFv genes induced a functional knock down of the target antigen.

17:00-17:30 Automated Parallel Protein Chromatography in a 96-Array Format
Juergen Friedle, Ph.D., Senior Vice President, Marketing, Atoll GmbH
This presentation will discuss innovative technology for parallel chromatography used in resin and method screening, process analytics and depletion of abundant components. This method utilized 8 independent columns operating simultaneously, compression packed with any available resin. It is suited to process a large number of samples and fully automated. Results are available in days instead of months.

17:30 Close of Next Generation Technologies for Protein Expression conference

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Cambridge Healthtech Institute's Third Annual

Antibodies from Bench to Bedside:
Engineering the Next Generation of Antibodies

7-8 October 2009

WEDNESDAY, 7 OCTOBER

13:00 **Conference Registration**

14:00-14:05 **Chairperson's Remarks**

OVERCOMING BOTTLENECKS

14:05-14:35 **Production of Recombinant Antibody Fragments in Cold Adapted Bacteria: An Alternative to Conventional Microbial Systems**

Maria Giuliani, Organic Chemistry and Biochemistry, University of Naples "Federico II"

Inclusion body formation is a major limiting factor for recombinant antibody fragment production in conventional prokaryotic expression systems. The solubility of recombinant proteins can be successfully improved by reducing the temperature of the production process. We developed a novel expression system for recombinant antibody fragment production at low temperatures based on the use of a psychrophilic bacterium as the recombinant expression host. The new cold expression system has been tested for recombinant production of several antibody formats (Fab, scFv, Vhh) and all of them were recovered in soluble form correctly secreted in the bacterial periplasm.

14:35-15:05 **An XBP-1 Dependent Bottle-Neck in Production of IgG Subtype Antibodies in Chemically Defined Serum-Free Chinese Hamster Ovary (CHO) Fed-Batch Processes**

Hitto Kaufmann, Ph.D., Boehringer Ingelheim Pharma GmbH & Co. KG, BP Process Science

15:05-15:35 ***In Vitro* Affinity Maturation of Cardiac Diagnostic Antibodies for Improved Diagnostic Assay Sensitivity**

Susan Brophy, Ph.D., Lab Manager, Antibody Research, Abbott Laboratories

For many years, cardiac biomarkers have been used to diagnose and monitor heart conditions and help determine the appropriate medical treatment. Two cardiac biomarkers, B-type natriuretic peptide (BNP) and troponin I (TnI), are prominently employed for heart failure and heart attacks, respectively. In order to further improve the sensitivity of Abbott's cardiac diagnostic immunoassays, antibody engineering using yeast surface display was employed on both a mouse anti-human BNP antibody and a mouse anti-human TnI antibody. Affinity matured antibodies (AM) were identified with a 2-10 fold improvement in affinity predominately evident in the off-rate. In addition, chimeric antibodies with a human IgG1 scaffold were expressed to minimize heterophilic interference and reduce the amount of expensive heterophilic blocking reagents used in sandwich immunoassays. Currently, the BNP AM1 Ab and the TnI AM1 Ab are being evaluated for utility in prototype immunoassays with the anticipation that improved assay sensitivity will allow for earlier detection of heart injury.

15:35-16:00 **Refreshment Break** *Sponsored by* sloning BioTechnology

16:00-16:15 **"ADLib®" An Innovative Solution in Antibody Technology** *Sponsored by* CHIOME

Hidetaka Seo, Ph.D., Senior Director, Research & Development, Chiome Bioscience Inc.

ADLib® (Autonomously Diversifying Library) System could be a platform technology to identify monoclonal antibodies quickly and efficiently *in vitro* against multiple targets, even tough antigens, which couldn't be obtained by the conventional methods.

16:15-16:30 **Sponsored Presentation** *(Opportunity Available)*

16:30-17:00 **ImmunoRNase Fusion Proteins Targeting Lymphomas**

Thomas Schirrmann, Ph.D., Department of Biotechnology, Technische Universität Braunschweig

"ImmunoRNases" represent a class of immunoenzymes that employ ribonucleases (RNases) as cytotoxic effector component. They do not show appreciable immunogenicity or non-specific toxicity, and are expected to not cause severe adverse effects known from many classical immunotoxins and their plant or bacterial toxin domains. Recently, we developed a novel immunoRNase design by fusing a CD30 specific single chain Fv (scFv) fragment to the IgG1 Fc moiety and the pancreatic RNase. This immunoRNase construct was very efficiently produced in mammalian cells as homodimeric protein that specifically bound to CD30+ lymphoma cells and inhibited tumor growth at low nanomolar concentrations.

17:00-17:30 **Spotlight Poster Presentations**

18:30 **BIOTECHNICA Night: Beer Hall, full dinner reception, a traditional German band**

THURSDAY, 8 OCTOBER

NEW STRATEGIES FOR EXISTING TECHNOLOGIES

09:00-09:05 **Chairperson's Remarks**

09:05-09:35 **Alternative Strategies to Generate Humanized Antibodies Against Pathogenic Antigens**

Andreas W. Stuke, Ph.D., Principal Investigator, Infection Biology, German Primate Centre (DPZ)

Naive full-length human monoclonal antibodies (mabs) are becoming an important tool to combat infectious human diseases. Mabs are usually generated by protein immunization of laboratory animals and subsequent hybridoma cell production. We isolated anti-prion protein (PrP) IgG-class mabs by nucleic acid mediated immunization of PrP-knock-out mice. Humanization of mabs was done by cloning of the heavy and light chains into a new eukaryotic expression vector bearing human constant regions. However, in the future mab generation will become possible by direct immunization of human peripheral blood mononuclear cells (PBMCs) to induce mab secreting plasma cells. Thus, immunization of animals and laborious humanization by genetic engineering will become redundant.

09:35-10:05 **Affinity-Optimized™ Antibodies with Improved Biodistribution Properties**

Ilia Tikhomirov, M.Sc., Manager, Strategic Research, Translational Research, YM BioSciences, Inc.

Traditionally, antibody development has focused on highest affinity candidates. However, this approach results in the antibodies targeting all tissues expressing the antigen, which causes side-effects and makes such antibodies poor candidates for conjugation to toxins. In some clinical situations, such as in many types of malignancies, antigens are frequently over-expressed at disease site compared to normal tissues. This presents an opportunity to develop antibodies that rely on avidity for stable attachment to cellular surface. Such antibodies will be better tolerated and represent ideal candidates for targeting toxins to the disease sites.

10:05-10:35 **Sponsored Presentation** *(Opportunity Available)*

10:35-11:00 **Refreshment Break**

11:00-11:30 **Antibody Optimisation: Insights from Affinity and Specificity Maturation Studies**

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

Antibody characteristics such as affinity and specificity can be readily and rapidly engineered *in vitro* using phage and ribosome display technologies. Here we present case studies from a number of therapeutic antibody programs, where affinity for the human antigen and/or cross-reactivity with an animal homologue of the target antigen has been greatly increased. Insights from solved antibody / antigen co-crystals are also considered.

11:30-12:00 **Albumin Binding Technology Transforms HER2-imaging Molecules to Therapeutic Candidates**

Fredrik Frejd, Ph.D., Project Manager, Biotherapeutics, Affibody AB

Affibody molecules are 7 kDa scaffold affinity proteins with very rapid *in vivo* kinetics, and a HER2-binding. Affibody molecules have proven to be highly suitable for tumor imaging in patients. Fast blood clearance is, however, not always optimal for therapeutic applications. Therefore, an improved femtomolar affinity albumin binding protein (ABD) was fused to the tumor targeting molecule to allow for extended circulation half life. Higher dose to the tumor, longer residence time in blood and drastically decreased dose to the kidneys are some of the new properties of the Affibody molecule when fused to ABD, allowing for complete eradication of xenografts in a murine model.

12:00-12:30 A Therapeutic Antibody with Ability to Inhibit Cancer Cells and Tumor-Associated Counterparts and Enhance Antitumor Immunity

Yan Wu, M.D., Group Leader, Antibody Technology, ImClone Systems

To date, the most difficult challenge to cancer intervention is to control metastasis that accounts for most death of patients with cancer and to enhance antitumor immunity that is seriously weakened in cancer patients. Antibody-directed therapeutics have been primarily based on targeting a specific receptor or molecule that is either expressed or/and functional in cancer cells or tumor-associated cells. Antibody combination and bispecific antibodies targeting cancer cells and other factors have been demonstrated to be effective in tumor treatment compared to single antibody based monotherapy. We will present an approach to achieving greater antitumor efficacy by using an antibody targeting one growth receptor exerting multi-functions in cancer cells and tumor-associated counterparts to inhibit tumor growth, metastasis, angiogenesis, stroma and immunosuppression as well as enhance antitumor immunity.

12:30-13:45 Lunch for Purchase in the Exhibit Hall and Exhibit Viewing

PROGRESS WITH ANTIBODY AND ANTIBODY-LIKE THERAPEUTICS

14:00-14:05 Chairperson's Remarks

14:05-14:35 Development of a Humanised Antibody for the Treatment of Venezuelan Equine Encephalitis Virus

Stuart Perkins, Ph.D., Team Leader, Biomedical Sciences, Defense Science and Technology Laboratory (DSTL)

Venezuelan Equine Encephalitis (VEE) virus causes epidemics and endemics in North and South America and is a potential bio-warfare agent, to which there are no available medical countermeasures. We have humanised a murine-derived antibody and assessed the biological activity of this molecule *in vitro*. We have also demonstrated that this antibody is able to provide protection in a small animal model of aerosol infection.

14:35-15:05 Probodies: Engineering Systemic Specificity into Antibody Therapeutics

James West, Ph.D., Director, Research, CytomX Therapeutics, LLC

In this presentation we show how our proprietary bacterial display technologies, eCPX and CliPS, were used to discover unique masking-peptides that block antibody combining regions, and to discover and optimize peptide-substrates specific for proteases overexpressed in tumors. We also show how the masking-peptides and protease substrates are combined, and tethered to antibody variable domains to generate Probodies specific for validated tumor targets. *In vitro* results, including direct binding and inhibition of biological activity, show that Probodies are strongly inhibited by a tethered masking-peptide, efficiently activated by specific protease activity, and when activated are equally potent as the unmodified antibody. Furthermore, we present *in vivo* biodistribution data demonstrating that anti-VEGF Probodies distribute to, and are specifically activated in human tumor xenografts, while remaining inactive in normal tissues.

15:05-15:35 Sponsored Presentation *(Opportunity Available)*

15:35-16:00 Refreshment Break

16:00-16:30 Translational Research in the Development of Novel Nanobody®-Based Therapies: From Bench to Bedside

Josi Holz, M.D., Chief Medical Officer, Ablynx na

The talk will illustrate the utilities of the Nanobody® platform to rapidly generate clinical drug candidates. Translational research from discovery to drug development and the use of biomarkers will be discussed in 2 case studies of Ablynx's clinical candidates targeting platelet aggregation and bone resorption.

16:30-17:00 Single Domain Antibodies from Llamas and Sharks as Novel Therapeutic Tools in Immunity and Infection

Friedrich Koch-Nolte, Ph.D., Deputy Director, Institute of Immunology, University Medical Center Hamburg-Eppendorf

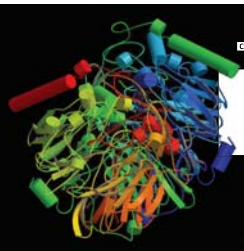
Most antibodies are composed of two heavy and two light chains. Both chains contribute to the antigen binding site, which usually is flat or concave. In addition to these conventional antibodies, camelids and sharks produce antibodies composed only of heavy chains. The antigen binding site of these unusual antibodies (designated VHH and VNAR, respectively) is formed only by a single chain. The CDR3 region of these single domain antibodies (sdAbs, also known as nanobodies) possesses the extraordinary capacity to form long fingerlike extensions that can extend into cavities on antigens, e.g. the active site crevice of enzymes. Other advantageous features of nanobodies include their small size, high solubility, thermal stability, refolding capacity, and good tissue penetration *in vivo*.

17:00-17:30 Powerful and Fast: DARPin Therapeutics

H. Kaspar Binz, Ph.D., Vice President, Technology, 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. We have validated several DARPin drug candidates in a variety of disease models. DARPins can be tailored to the format of choice allowing the generation of ideal drugs. A best-in-class therapeutic program illustrating the potency of the DARPin therapeutic platform will be presented.

17:30 Close of Antibodies from Bench to Bedside conference



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6-7 October (choose one) and 7-8 October (choose one)

❒ **Track 1:** Improving Protein Expression
❒ **Track 2:** Phage Display
❒ **Track 3:** Next Generation Technologies for Protein Science
❒ **Track 4:** Antibodies from Bench to Bedside

INDIVIDUAL CONFERENCE PRICING

Early Registration Deadline until 26 June	❒ €935	❒ €470	
Advance Registration Deadline until 4 September	❒ €1045	❒ €525	❒ €150
Registrations after 4 September and on-site	❒ €1195	❒ €595	

Please select the SINGLE conference you will be attending:

❒ **Track 1:** Improving Protein Expression
❒ **Track 2:** Phage Display
❒ **Track 3:** Next Generation Technologies for Protein Science
❒ **Track 4:** Antibodies from Bench to Bedside

DISCOUNTS*

❒ Poster Discount	❒ €35 Off	❒ €35 Off

COMPLIMENTARY BIOTECHNICA EVENTS

I plan to attend:

❒ Monday, 5 October - BIOTECHNICA Opening and EUROPEAN BIOTECHNICA AWARD Ceremony plus Reception
❒ Wednesday, 7 October - BIOTECHNICA Night – Original Bavarian Beer Hall, full dinner reception, and band.

❒ I cannot attend but would like to purchase PEGS Europe CD for €600 (plus shipping). Massachusetts delivery will include 6.25% sales tax.
❒ Please send information on exhibiting and opportunities to present workshops
❒ Please send information on BIOTECHNICA's Partnering, an online networking tool

3. PAYMENT INFORMATION

❒ 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: ❒ 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 Keycode below:

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Present a Poster and Save €35!

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 **3pm EST** on **11 September, 2009**. 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 Europe**

Title

CHI Insight Pharma Reports
A series of reports that evaluate the salient trends in pharmaceutical technology, business, and 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.

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Additional Registration Details
Each registration includes all conference sessions, posters and exhibits, food functions, and access to 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 €75 processing fee per conference.
- Request a refund minus the cost (€600) 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.