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Cambridge Healthtech Institute's Third Annual

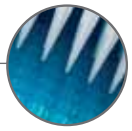
August 22-25, 2011 Marriott Long Wharf, Boston, MA

THE BIOPROCESSING SUMMIT

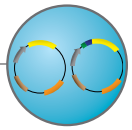
Practical Solutions for Today's Laboratory Challenges

AUGUST 22-23

Optimizing Cell Culture Technology



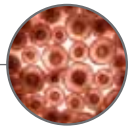
Affinity Protein Purification



Biopreservation

AUGUST 24-25

Optimizing Mammalian Cell Lines



Baculovirus Technology

Scaling Up & Down with Optimized Bioreactors + Disposables

AUGUST 22

Pre-Conference Short Courses

(SC1) Media Optimization to Increase Productivity in Bioreactors

(SC3) Ensuring Operational Excellence in Bioprocessing

AUGUST 23

Dinner Short Course

(SC4) *E.coli* Innovations

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CONFERENCE VENUE AND HOTEL:

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Short Courses*

Pre-Conference Short Courses

Monday, August 22 • 8:30 to 11:30am

SC 1 Media Optimization to Increase Productivity in Bioreactors

To grow mammalian cells, researchers need to provide an optimal *in vitro* environment. The key feature of successful cell growth is the culture medium. 'Achieving Super Soup' requires finesse and know-how in order to combine the right ingredients at the right times under the right conditions to achieve high titers. This workshop will provide a foundation for optimizing cell culture media presented by real-world experts who will also tailor a portion of the course to fit concerns and challenges faced by the workshop participants.

- Feed strategies
- Media formulation
- Oxygen
- Process optimization
- Analytical tools
- Increasing cell densities
- High-throughput protocols

Instructors:

Frederic Girard, Ph.D., Managing Director, Spinnovation Analytical BV

Scott D. Storms, Ph.D., Cell Culture Consulting, LLC

Martin Jordan, Ph.D., Associate Manager, Biotech Process Sciences - Medium Development, Merck Serono

SC 3 Ensuring Operational Excellence in Bioprocessing: PAT, QbD, DoE and Continuous Improvement – An Introductory Overview

Ensuring quality in bioprocesses that comply with regulatory requirements and mitigate risk often results in very high bottom-line costs. Adopting best practices early in the development process and customizing these approaches to operational excellence from other highly competitive industries are currently taking place in biopharmaceutical production. This course will provide both an overview of these approaches and how they work, as well as case studies of how these innovations have been applied in bioprocessing and elsewhere. Appropriate regulatory guidance will also be discussed.

- Quality by Design (QbD)
- Design of Operation (DoE)
- Process Analytical Technology (PAT)
- Continuous Improvement
- Lean Manufacturing
- Six Sigma

Instructors:

Joyce Chiu, M.B.A.,CPIP, Senior Project Manager, Honeywell Safety Products

Susan Dana Jones, Ph.D., Vice President & Senior Consultant, BioProcess Technology Consultants, Inc.

Sheila G. Magil, Ph.D., Senior Consultant, BioProcess Technology Consultants, Inc.

Dinner Short Course

Tuesday, August 23

6:00 to 9:00pm

SC 4 *E.coli* Innovations

Escherichia coli has proven its worth as a protein expression platform. Currently, *E.coli* is not viewed so much as an 'alternative' platform, but as a viable choice for achieving high-level expression of human genes and protein at a reasonable cost. This Dinner Short Course will explore strategies for successful *E.coli* protein expression, including:

- Host cell engineering to improve product quality
- Development of protein expression assays
- Development and optimization of protein purification processes
- Automating high-throughput protein expression and purification
- Scaling up production

Instructors:

Cynthia L. Kinsland, Ph.D., Research Associate, Biotechnology Center, and Head, Protein Production Facility, Cornell University

Francis Rajamohan, Ph.D., Senior Principal Scientist, Molecular and Structural Biology, Pfizer Global Research & Development

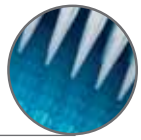
Guido Seidel, Ph.D., Head of Process Development, Deputy Managing Director, Wacker Biotech GmbH

**Separate registration required.*

Cambridge Healthtech Institute's Seventh Annual

Optimizing Cell Culture Technology

Enhancing the Environment for Growing Cells



MONDAY, AUGUST 22

11:30 am Main Conference Registration

OPTIMIZING INSIGHTS TO ENHANCE CELL CULTURE PROCESSES

1:00 pm Chairperson's Opening Remarks

1:10 OPENING KEYNOTE PRESENTATION

High-Throughput Cell Culture Technologies: Challenges and Future Trends

Jianguo Yang, Ph.D., Principal Scientist, Commercial Cell Culture Development, Commercial Process Development, Biologic R&D, Genzyme

Demand for high-throughput (HT) cell culture technologies has increased dramatically in the biopharmaceutical industry because the technologies are of vital importance to cell culture process optimization, media development, and most recently in the Quality by Design (QbD) approaches expected by regulatory agencies. Although HT cell culture technologies have advanced quickly from half-liter to micro-liter scale, there are some major challenges remaining, especially in mammalian cell line and cell culture development, and a true high-throughput cell culture process is yet to come. This presentation will articulate current advances, major challenges and future trends in HT cell culture technologies.

1:45 FEATURED PRESENTATION

Metabolite Profiling of Recombinant Mammalian Cell Lines: Putting the Data to Work

Alan Dickson, Ph.D., Professor, Biotechnology, and Director, Centre of Excellence in Biopharmaceuticals, Faculty of Life Sciences, The University of Manchester

This presentation will focus on metabolite profiling (extra- and intra-cellular) of recombinant mammalian cell lines. In our experience, metabolite profiling is an 'omics approach that offers immediate insights for understanding key processes that determine product yield. I will describe our approach for metabolite harvest and assessment (with a focus on the critical need for generation of physiological concentrations of intracellular metabolites) from cells in suspension culture and illustrate, with case studies, how this approach can lead to enhanced culture performance.

2:15 Approach and Challenges to Developing a Platform Cell Culture Process

Wendy Hsu, Engineer and Group Leader, Early Stage Cell Culture, Genentech, Inc.

Speed to tox and Phase I material production is often key in establishing the competitive advantage for a product. This presentation summarizes Genentech's approach in establishing a platform cell culture process using a new chemically defined media that enables meeting development timelines to tox and PhI material production while establishing basis for late stage development. The presentation highlights challenges to the platform process development from implementation of a new media. The presentation also highlights challenges to the platform process development in accommodating a wide range of culture phenotypes such as high growth and high oxygen uptake rate.

2:45 Sponsored Presentation (Opportunity Available)

3:00 Networking Refreshment Break

3:30 POSTER HIGHLIGHT:

Optimization and Modification of Glycosylation Profiles of a Monoclonal Antibody During Mammalian Cell Culture Process Development

Sarath Moses, Ph.D., Senior Scientist, Bioprocess Development, Merck Research Laboratories

4:00 Cost-Efficient and Consistent Single-Batch Manufacturing of Antibody Mixtures

Søren Kofoed Rasmussen, Ph.D., Principal Scientist, Symphogen A/S

Development of combination products consisting for example of two or more antibodies with synergistic properties for treatment of serious human disease is becoming increasingly important. Symphogen has developed a manufacturing platform, Sympress, which allows fast, reproducible and cost-efficient development of antibody mixtures for human therapy of complex diseases like cancer and infections. In 2010, Symphogen started clinical trials with one such product, a combination of two antibodies against the EGFR which has shown clear synergistic properties. The single-batch manufacturing technology comprised in Sympress provides a very attractive solution - with respect to cost, timelines and batch-to-batch consistency - to the CMC challenges linked to development of these types of APIs.

4:30 Breakout Discussions

5:30 Grand Opening Reception with Exhibit & Poster Viewing

7:00 End of Day One

TUESDAY, AUGUST 23

7:30 am Breakfast Presentation (Sponsorship Opportunity Available) **or Morning Coffee**

CULTIVATING CHO CELLS

8:25 Chairperson's Remarks

8:30 Optimizing CHO Cell-Based Bioprocesses

Anthony Rossomando, Ph.D., Senior Director, Biotherapeutics, Alnylam Pharmaceuticals

RNAi technology is being utilized in bioprocessing development to silence genes involved in key cellular pathways that impact biologic protein quality, particularly around decreasing fucosylated glycans to improve antibody-dependent cellular cytotoxicity (ADCC). mRNA levels from genes that affect biotherapeutic

fucosylation and cell viability were significantly reduced (>80%) over a 10-14 day culture period using small interfering RNAs (siRNAs) added directly to CHO cells grown in 3L bioreactors with significant improvements in cell viable density and biologic quality.

9:00 Proteomic Analysis of Recombinant CHO Cells and the Potential for Biomanufacturing Process Improvement

Paula Meleady, Ph.D., Senior Research Scientist and Programme Leader, Proteomics Core Facility, National Institute for Cellular Biotechnology (NICB), Dublin City University

The talk will focus on proteomic approaches we have used to profile poor and good performing recombinant CHO cell lines concentrating on phenotypes related to growth (slow/fast) and productivity (both high/low and sustained productivity). Data will be presented showing outcomes from profiling efforts where phenotypic improvements, using growth as an example, have been achieved following engineering of targets of interest back into recombinant CHO cells.

9:30 CHO Cell Culture Improvements Using a Controlled Nutrient Limiting Feed Strategy

Matthew Gagnon, Scientist, Culture Process Development, BioProcess Research and Development, Pfizer, Inc.

Maintaining an optimal environment is essential to promote a healthy and productive CHO cell culture. A well characterized culture vessel ensures ideal mixing and gas transfer. A balanced initial medium and nutrient addition during culture prevents depletion of necessary metabolites. Finally, preventing the accumulation of certain metabolites inhibitory to both cell growth and productivity is critical. An elegant approach to maintain lactate concentrations at low levels in culture will be described in this talk.

10:00 Sponsored Presentation (Opportunity Available)

10:15 Networking Coffee Break with Exhibit and Poster Viewing

11:00 Site-Specific Antibody Production of Different Antibody Cell Lines

Sinyoung Park, Ph.D., Scientist, Process Development – Upstream, Ambrx, Inc.

Ambrx's proprietary technology enables the production of a site-specific variant of an antibody which is created by incorporation of Ambrx amino acid into the specific location(s) of the molecule. The cell lines containing Ambrx orthogonal t-RNA and tRNA synthetase replace a natural amino acid with an Ambrx unnatural amino acid such as para-acetyl phenylalanine (pAF). The Chinese Hamster Ovary (CHO) cell lines were generated for different types of antibody variants. The cell culture process parameters such as pAF addition time, temperature shift, feed addition, and media selection were examined for different cell lines.

11:30 Fluorinert, An Oxygen Carrier, Improves Cell Culture Performance in Deep Square 96 Well Plates by Facilitating Oxygen Transfer – A Scale-Down Model for Multi-Parallel High Throughput Production Clone Selection

Yung-Shyeng Tsao, Ph.D., Senior Principal Scientist, Cell Culture, Merck

Suspension mammalian cell cultures in 96-well plates often fail to reach high cell density under normal agitation presumably due to limitations in oxygen transfer. Although more vigorous agitation can improve gas transfer in 96-well format, it can also harm mammalian cells. We employed Fluorinert, an artificial blood candidate, to overcome oxygen limitation in 96-well plate and enable a recombinant antibody-producing Chinese Hamster Ovary (CHO) cell line to reach high cell density and antibody titer comparable to that of shake flask culture.

12:00 pm Perfusion of an IgG Producing CHO Cell Line by ATF or by TFF in WAVE Bioreactor

Véronique Chotteau, Ph.D., Animal Cell Technology Group, School of Biotechnology, Division of Bioproduction, KTH - Royal Institute of Technology

Perfusion of an IgG producing CHO cell line was performed in a WAVE Bioreactor™ using either Alternating Tangential Flow or Tangential Flow Filtration. The properties and performances obtained with both filtration systems were compared. Very high cell densities were achieved and could be stably maintained. Then the cell density could be significantly further increased showing the capacity of the system set-up.

12:30 Redefining Cell Line Selection and Process Development using Microbioreactors and Design of Experiments (DoE)

Sponsored by PALL Life Sciences *New Science. New Thinking.*

Tiffany D. Rau, Ph.D., Global Technology & Technical Manager, Pall Corporation

High-throughput bioreactors allow one to efficiently conduct Design of Experiments (DoE) which embodies the principles of Quality by Design. Data will be presented showing the Micro-24 successfully being used in cell line selection and process optimization activities and its scalability to larger bioreactors, demonstrating the advantages of a controlled "high-throughput" bioreactor system that allows rapid, very early stage process development which can contribute to shorter development timelines and lower development costs.

3D CELL CULTURE

1:55 Chairperson's Remarks

2:00 High-Throughput 3D and Micropatterned Cell Culture

Shuichi Takayama, Ph.D., Professor, Biomedical Engineering, Macromolecular Science and Engineering, College of Engineering, University of Michigan

Our laboratory specializes in developing microfluidic tools to control cellular microenvironments. Microfluidic approaches to cell culture, however, are typically cumbersome and challenging to perform in high-throughput formats using conventional liquid handling tools. In this presentation, I will describe recent high throughput cell culture technology developed in our laboratory that incorporates microfluidic concepts but without use of microchannels and in formats compatible with standard 96, 384, and 1536 well technologies. One technology is a 384-well format hanging drop cell culture plate that makes spheroid formation, culture, and subsequent drug testing on the obtained 3D cellular constructs as straightforward as conventional 2D cultures. We show that drugs with different modes of action produce distinct responses in the physiological 3D cell spheroids compared to conventional 2D cell monolayers. Specifically, the anti-cancer drug 5-fluorouracil (5-FU) has higher anti-proliferative effects on 2D cultures whereas the hypoxia activated drug commonly referred to as tirapazamine (TPZ) are more effective against 3D cultures. I will also describe the use of aqueous two phase system to perform micropatterned gene expression or knockdown, and to micropattern embryonic stem cell niches to modulate their differentiation towards neuronal cells.

2:30 Cells in Gels in Paper: High-Throughput Platform for Investigation of Cell Function in 3D Tissues

Ratmir Derda, Ph.D., Assistant Professor, Department of Chemistry, University of Alberta

In vitro 3D culture is an important model for tissues ***in vivo***. Cells in different locations of 3D tissues are physiologically different, because they are exposed to different concentrations of oxygen, nutrients, and signaling molecules. The majority of cell-based assays based on 3D cultures, however, can only detect the average behavior of cells in 3D construct. Isolation of cells from specific regions of 3D cultures is possible, but relies on low-throughput techniques such as tissue sectioning. We developed a simple method for generation and analysis of complex 3D tissue structures. Spotting of cells suspended in extracellular matrix (ECM) gel onto the ordinary filter paper creates 200 micron-thick slabs of ECM gel containing cells. Stacking the sheets assembles 3D multilayer constructs. Peeling apart the sheets of paper "sections" the cultures into 200-micron-thick cell-containing slabs. The number of cells plated initially in each layer determines the spatial distribution of cells in the stacked 3D cultures. Multilayer culture, thus, generate 3D tumor models with well-defined gradients of oxygen and nutrients. This capability made it possible to examine the 3D migration/invasion of cells and their susceptibility to therapeutic agents.

3:00 Three-Dimensional Cell Culturing Through Magnetic Levitation

Thomas C. Killian, Ph.D., Professor, Physics and Astronomy, Rice University

3D cell culturing through magnetic levitation, developed at Rice University and the University of Texas MD Anderson Cancer Center and marketed by Nano3D Biosciences (n3D) [www.n3dbio.com], is a new paradigm in cell culturing that provides the advantages of 3D cell culturing in a much simpler platform that can easily be incorporated into existing protocols and diagnostics. It is based on magnetization of cells using magnetic-nanoparticles and levitation of the cells in spatially varying magnetic fields. I will describe the general technique and results with a variety of cell lines and primary cells, with an emphasis on primary human lung cells cultured as monoculture and co-culture at the air-media interface, kidney cells used in a wound healing test for toxicology studies, and controlled manipulation and shaping of human gliobalstoma and normal human astrocytes co-culture for invasion assays.

3:30 Networking Refreshment Break with Exhibit and Poster Viewing

4:15 INTERACTIVE PANEL: How will Mammalian Cell Culture be Further Innovated?

As mammalian cell culture moves forward meeting increased demands for ever higher titer, how will the task of culturing cells be innovated? What are the emerging technologies and approaches that will bring cell culture to new heights?

Please join this interactive panel discussion as cell culture experts share their insights on how cell culture will be innovated to provide adequate capacity for the biologics industry.

Moderator: Tiffany D. Rau, Ph.D., Global Technology & Technical Manager, Pall Corporation

Panelists:

Paula Meleady, Ph.D., Senior Research Scientist and Programme Leader, Proteomics Core Facility, National Institute for Cellular Biotechnology (NICB), Dublin City University

Yung-Shyeng Tsao, Ph.D., Senior Principal Scientist, Cell Culture, Merck

James C. Warren, Ph.D., Principal Development Engineer, Vaccine Manufacturing Sciences and Commercialization, Merck & Co., Inc.

Jianguo Yang, Ph.D., Principal Scientist, Commercial Cell Culture Development, Commercial Process Development, Biologic R&D, Genzyme

5:15 End of Conference

6:00 – 9:00 pm SC 4 - Dinner Short Course: *E.coli* Innovations (Separate registration required; see page 3 for details.)

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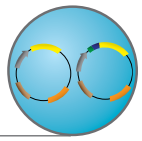
Cambridge Healthtech Institute's Third Annual

Affinity Protein Purification

Improving Speed, Quality and Cost



MONDAY, AUGUST 22

11:30 am Main Conference Registration

AFFINITY TAGS

1:00 pm Chairperson's Opening Remarks

1:10 FEATURED PRESENTATION
Affinity Tags, Their Uses and Removal

Paul Ramage, Ph.D., CPC, Protease Platform, Senior Research Investigator, Novartis Pharma AG

Affinity tags are widely used in protein science. Some are used to boost expression (both soluble and insoluble), some to increase solubility and many to specifically capture target proteins, especially when poorly expressed. In my talk I shall describe the tagging strategies we use for isolating recombinant proteases and related proteins, as well as the advantages and disadvantages of using such strategies.

1:45 Self-Cleaving Affinity Tags: A New Platform for Biologics Manufacturing?

David Wood, Ph.D., Associate Professor, Chemical & Biomolecular Engineering, Ohio State University

The development of self-cleaving affinity tag technology has the potential to provide a new platform for biologics manufacturing, and several systems have been developed. The use of these technologies, however, will require an understanding of their impact on widely accepted downstream processes, as well as new validation methods for safe adoption and regulatory approval. This talk will examine these issues, with an emphasis on the specific opportunities for self-cleaving tags, as well as the remaining barriers to their application. This examination will include examples of how existing canonical processes might be impacted by the adoption of self-cleaving tag methods.

2:15 The three A's of Biologicals are Activity, Activity, Activity: Case Study of Guiding Process Development Towards Biological Specific Activity though Bioactivity and *in Vitro* Kinetic Assays

Sponsored by fortéBIO

Oren Beske, Ph.D., Vice President, in Vitro Services, Aragen Biosciences

Monitoring quality and activity of a biological are essential during manufacturing development. This study describes significant bioactivity loss after adoption to an industrial CHO platform. Using the ForteBio Octet, an in vitro binding assay was rapidly developed, revealing a faster dissociation constant for the inactive form. Alternative clones and upstream processes were developed to increase specific activity. Both the bioactivity assay and the ForteBio kinetic assay were used to track product quality during process development.

2:45 Sponsored Presentation
(Opportunity Available)

3:00 Networking Refreshment Break

3:30 Visible Heme Tags for Protein Affinity Purification and Quantification

Kara L. Bren, Ph.D., Professor, Chemistry, University of Rochester

A heme tag imparts intense color to a target protein for visual tracking during expression in *E. coli* and purification. Heme tags also can be utilized in affinity purification and protein quantification. Developments in heme tags will be discussed including achievement of tagging in the *E. coli* cytoplasm as well as periplasm.

4:00 High-Recovery Tandem Affinity Purification Tags

Yifeng Li, Ph.D., Technical Director, Protein Production Core Facility, Department of Biochemistry, The University of Texas Health Science Center

TAP coupled with mass spectrometry constitutes a powerful tool for the characterization of protein complex associated with a given target protein. This talk reviews several alternative TAP tags with improved efficiency and/or flexibility. In particular, a newly developed SBP-His tandem tag will be discussed in more detail.

4:30 Breakout Discussions

5:30 Grand Opening Reception with Exhibit and Poster Viewing

7:00 End of Day One

TUESDAY, AUGUST 23

7:30 am Breakfast Presentation (Sponsorship Opportunity Available) **or Morning Coffee**

OPTIMIZING PURIFICATION

8:25 Chairperson's Remarks

8:30 Protein Production in *S. cerevisiae* for Systems Biology Studies

Naglis Malys, Experimental Officer, Faculty of Life Sciences, University of Manchester

Proteins, collectively with metabolites, nucleic acids, lipids and other intracellular molecules, form biological systems that involve networks of functional and physical interactions. To understand these interactions and the many other characteristics of proteins in the context of biochemical networks and systems biology, research aimed at studying medium and large sets of proteins is required. This either involves an investigation focused on individual protein activities in the mixture (e.g. cell extracts) or a protein characterisation in the isolated form. Here I provide an overview on the currently available resources and strategies for isolation of proteins from Saccharomyces cerevisie. The use of standardised gene expression systems is discussed and protein production protocols applied to the data generation pipeline for systems biology are described in detail.

9:00 Engineering Proteases with Switchable Activity

Philip N. Bryan, Ph.D., Professor, Department of Bioengineering, University of Maryland; Owner, Potomac Affinity Proteins, LLC

We will describe the engineering of highly-specific proteases which are tightly regulated by small molecules. The ability to control protease specificity and activity creates a vast potential for building enzyme-based nanodevices. The substrate protein contains the cognate sequence of the protease. The trigger

of the protease is a specific small molecule. In this scheme the protease occupies a role analogous to a transistor in an electronic circuit and is able to mediate such functions as detection, purification, activation, or inactivation (destruction) of other proteins. The substrate protein and the triggering molecule will vary from application to application. For example, we have developed a protein purification system (the Profinity eXact Purification System, Bio-Rad). This method uses a simple protease machine for protein purification and provides the conceptual foundation for other devices based on triggered proteases.

9:30 Identification of an FHL1 Protein Complex Containing ACTN1, ACTN4, and PDLIM1 Using Affinity Purifications and Mass Spectrometry Based Protein–Protein Interaction Analysis

Anthony Gramolini, Ph.D., Professor, Department of Physiology, University of Toronto

Affinity tagged constructs of cardiac and skeletal muscle-relevant proteins were expressed, and metal affinity chromatography was used to purify the protein together with interacting proteins. When analyzed by gel-free liquid chromatography mass spectrometry (LC-MS) we identified putative interacting complexes. Follow-up biochemical and imaging experiments were used to validate and extend these findings.

10:00 Sponsored Presentation (Opportunity Available)

10:15 Networking Coffee Break with Exhibit and Poster Viewing

11:00 Substrate Selectivity and Kinetics for Fe(II)-Dependent gamma-Hydroxybutyrate Dehydrogenase from Ralstonia Eutropha

Stanley M. Parsons, Ph.D., Professor, Department of Chemistry and Biochemistry, Neuroscience Research Institute, University of California, Santa Barbara

The gene for iron(II)-dependent gamma-hydroxybutyrate dehydrogenase (GHB-DH; EC 1.1.1.61) from the bacterium Ralstonia eutropha was fused to the gene for glutathione S -transferase in an expression vector, and 161 ± 32 mg of fusion protein was isolated from 1 L of induced *E. coli*. The purified fusion protein was used to test 42 natural and synthetic compounds structurally related to the human drug of abuse GHB for substrate activity. When testing otherwise normal human urine or blood using a prescribed protocol, GHB-DH will detect only ingested GHB.

11:30 Application of Thermal Shift Assay in the Stability Optimization of Aurora B Kinase Domain

Payal Sheth, Ph.D., Investigator, Protein Science Department, Merck Research Laboratory

AFFINITY CHROMATOGRAPHY

12:00 pm Classical and Affinity Chromatography Employed in Obtaining BACE and JAK Proteins

Thomas L. Emmons, Ph.D., Senior Scientist, Pfizer, Inc.

The catalytic domains of tagged aspartyl protease BACE-1 and BACE-2 and tyrosine kinases JAK-2/-3 and TYK-2 have been purified to homogeneity by using a combination of classical and tag affinity chromatography, as well as (in the instance of BACE-1 and BACE-2) a ligand specific affinity chromatography. Tag removal by BACE-1 and BACE-2 autocleavage or by JAK-2/-3 and TYK-2 cleavage with specific proteases was performed as needed. High quality enzymes were obtained for kinetic and inhibition studies and to obtain crystals that yielded high resolution 3D structures for inhibitor optimization. The purification of a double tagged full length kinase will be discussed as well. Finally, yields, optimization, throughput, reproducibility and scalability of the purification processes will be presented along with in depth characterizations of the purified product to establish its authenticity and activity.

12:30 Luncheon Presentation (Sponsorship Opportunity Available) **or Lunch on Your Own**

ANTIBODY AFFINITY PURIFICATION

1:55 Chairperson's Remarks

2:00 A Recovery Platform for the Initial Purification of His-Tagged Proteins Derived from *E. coli* Inclusion Bodies

Liliana T. Yee, Research Associate, Purification Development, Genentech/Roche

During recombinant protein production in *E. coli*, the target protein may be associated with the insoluble phase following cell lysis and centrifugation. Protein purification from the insoluble phase can be challenging due to the presence of: aggregated species, misfolded proteins, and/or inclusion bodies (due to high levels of expression, cell induction, and/or growth conditions), as well as cell debris and DNA released in the cell lysis step. In this presentation, we will describe our recovery platform for the initial extraction and chromatography for his-tagged proteins that are expressed as inclusion bodies in *E. coli*. This procedure allows for the initial isolation of this class of proteins independent of expression levels, allowing us the flexibility to scale this laboratory process to support a wide range of production needs.

2:30 Affinity Purification of a New Marker for Kidney Failure from Multiple Biological Sources

Kevin Rupprecht, Ph.D., Principal Research Scientist, Abbott Diagnostics Analytical Chemistry R&D, Abbott Laboratories

This talk will detail our use of a monoclonal antibody affinity column to purify NGAL (Neutrophil Gelatinase-Associated Lipocalin) from a variety of sources. We have isolated NGAL from neutrophils, lymphocytes, a leukocyte lysate, neutrophil granules and urine. This protein naturally binds iron siderophores. The siderophore co-purifies with the NGAL indicating the purified material is in a native conformation. The material isolated is very pure (>99%) and we have thoroughly characterized it. We present data comparing and contrasting the material from the various sources including carbohydrate content, siderophore content and dimer content.

3:00 From Quantitative Protein Complex Analysis to Disease Mechanism

Karsten Boldt, Ph.D., Professor, Medical Proteome Center, Centre for Ophthalmology, University of Tuebingen

Using an affinity-based quantitative proteomic approach, we show that the Leber's Congenital Amaurosis (LCA) associated protein lebercilin specifically interacts with intraflagellar transport (IFT) complex A and complex B members. By quantitative complex comparison we demonstrate that LCA-associated nonsense mutations specifically disrupt the interaction with the IFT proteins. This implicates a disruption of IFT dependent protein transport in photoreceptors as the cause for LCA which was confirmed by inactivation of lebercilin in mice.

3:30 Networking Refreshment Break with Exhibit and Poster Viewing

4:15 Antibody Affinity Purification Using Nickel Particles

Zhiyu Li, Ph.D., Assistant Professor, Pharmaceutical Sciences, Philadelphia College of Pharmacy, University of the Sciences

Magnetic separation using functionalized magnetic adsorbent particles are emerging as reliable and convenient techniques in biomacromolecules

(proteins and DNAs) purification and cells isolation. In this study, a novel method using Protein A -coated nickel ferromagnetic particles for affinity purification of antibody has been proposed and confirmed. Protein netting/ caging method has been utilized to stabilize Protein A on nickel particle surface and limit protein leaching during affinity purification. IgG in mouse serum can be quickly isolated for as short as 5 minutes. In addition, the separation procedure is gentle, scalable, efficient and economical. Protein coated and netted nickel particles will not only be utilized in affinity purification but can also be further modified through functional groups of amino acids for other chromatographic applications.

4:45 Expanding the Repertoire of Split Proteins as Versatile Tools for Ttagging, Detection, and Purification

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

GFP, RFP and 'SNAP' are a convenient genetically encoded tags for labeling proteins, but are bulky and can perturb protein behavior or cause misfolding and aggregation. In 2005 we published a split GFP that has become widely used in protein production, cell-based assays, and library screening campaigns. We now report a new split fluorescent protein that is orthogonal to the original GFP. We describe its characterization and validation in protein applications. This unusually stable protein remains fluorescent in 7 M GndHCl when reconstituted from its two fragments. We also describe new color variants of our original split GFP. We describe the new applications that are possible using these orthogonal tags, including multiplex tagging, enhanced FRET experiments without causing protein misfolding, host-pathogen interactions, and tracking protein complex formation in living cells. These tools should also enable new TAP MS applications and library screens for proteins with improved solubility and stability. Mix and match tools for improving protein crystallization are another area hinted at.

5:15 End of Conference

Cambridge Healthtech Institute's Inaugural

Biopreservation

Assuring Purity, Viability, and Productivity of Cell Lines

MONDAY, AUGUST 22

11:30 - 1:00pm Conference Registration

1:00 Chairperson's Opening Remarks

CELL BANKING: DIVERSITY BRINGS SOLUTIONS

FEATURED PRESENTATION

1:10 Cryopreservation: The Quest for Best Practices

John G. Baust, Ph.D., UNESCO Chair & Professor; Director, Institute of Biomedical Technology, Binghamton University; Editor-in-Chief, Biopreservation & Biobanking

Typical "best practice guidelines" originating from various biobanks and biobanking consortia do not contain guidance related to preservation practices that would result in standardized outcomes. That is: few offer quantitative direction on the matter of the development of state-of-the-art cryopreservation protocols compatible with sample recovery from one or more biobanks that would yield equivalent specimen quality. With cryopreservation methodologies slowly emerging from the "structural" to a "molecular" perspective in which strategies are employed to mitigate disruptive, damaging and lethal aspects of oxidative stressors, we are now have knowledge of the cell-based factors that limit biobank standardization. This presentation will review novel approaches to improved cell preservation methodologies designed to enable biobanks to adopt standardized, outcome-driven, preservation protocols.

2:15 Biopreservation Methods for Cell Therapy Products

Kelvin G.M. Brockbank, Ph.D., President and CSO, Cell & Tissue Systems, Inc.

Biopreservation for regenerative medicine products containing living cells will be discussed drawing primarily upon experience with cardiovascular and orthopedic cell and tissue models. There are two major approaches to cell and tissue biopreservation in use: either traditional freezing methods or ice-free vitrification. Both approaches have pros and cons, and which should be employed depends upon the cell/tissue type and the final product design. Some future cell therapy products may also be freeze dried for ambient room temperature storage.

2:45 Networking Refreshment Break

3:15 Automated Cryobank of Microorganisms: Unique Possibilities for Long-Term Authorized Depositing of Commercial Microbial Strains

Speaker to be Announced

Liconic Instruments automated –80°C Tube Store becomes an extremely useful, simple and intuitive system for a long-term storage of microorganisms at optimum conditions without the loss of their valuable properties. Unique "real time" online database of microorganisms can be organized on basis of sample management software of the STC Tube Store. This database will enable depositors to monitor their samples and climatic conditions in the repository during storage. Such kind of store provides an authorized access to the deposited commercial strains of microorganisms and gives possibilities to intensify the search of new microbial cultures, keeping in mind the huge soil microbe's biodiversity and a necessity to mobilize genetic resources of microorganisms for an agricultural production

3:45 High-Throughput Preparation of Biomaterials in a CLIA Lab

Lynn Bry, M.D., Ph.D., Director, Partners Biorepository for Medical Discovery Associate Medical Director, BWH Clinical Laboratories Associate Director, Partners Center for Personalized Genomic Medicine

This talk will discuss methods used to prepare blood products, including cellular preparations for transfusion into recipient patients, and other methods for collecting and processing materials from clinical laboratories for research use.

4:15 Moderated Small-Group Breakout Discussions

5:30 Grand Opening Reception with Exhibit and Poster Viewing

7:00 End of Day One

TUESDAY, AUGUST 23

7:30am Breakfast Presentation (Sponsorship Opportunity Available) **or Morning Coffee**

STEM CELLS: BIOPRESERVATION FOR THERAPY

8:25 Chairperson's Remarks

8:30 Bioprocessing and Cell Storage Methods for Human Progenitor and Stem Cells

Mary Pat Moyer, Ph.D., CEO and Chief Science Officer, INCELL Corporation LLC

Integrated strategies, combined with new reagents and other tools for GMP bioprocessing and storage of cells derived from various tissues, are important to bringing new cell and immunotherapy products to clinical applications. Stored cells from living and cadaveric donor tissues (e.g., adipose, bone marrow, blood, skin), either alone or in combination with other products, have unique needs and similar requirements. These will be reviewed with regard to time and temperature of storage and in the context of their therapeutic, diagnostic or research applications.

9:00 Serum Free Cryopreservation of Adult Stem Cells

Ram Devireddy, Ph.D., Associate Professor, Mechanical Engineering, Louisiana State University

Developing effective techniques for the cryopreservation of human adipose derived adult stem cells could increase the usefulness of these cells in tissue engineering and regenerative medicine. Unfortunately, the use of serum and a commonly used cryoprotectant chemical dimethyl sulfoxide (DMSO) during cryopreservation storage restricts the direct translation of adult stem cells to in vivo applications. Our results suggest that post-thaw cell viability, adipogenic and osteogenic differentiability can be maintained even when they are frozen in the absence of serum and DMSO.

9:30 Hematopoietic Stem Cell Growth and Cryopreservation: Removing Animal Proteins from the Culture and Optimizing the Freeze Curve for Long Term Storage

Linda L. Kelley, Ph.D., Director, Connell O'Reilly Cell Manipulation Core Facility Dana Farber Cancer Institute

The talk will focus on the use of human platelet lysate (PL) as growth media to replace fetal bovine serum (FBS) for growth of bone marrow-derived mesenchymal stem cells (MSC). Data demonstrate that MSC grown in PL have a shorter doubling time, remain phenotypically characteristic of MSC and maintain

multilineage differentiation capability. Secondly, the talk will emphasize the importance of controlled-rate freezing and optimized freezing conditions for long-term storage and maximal recovery of hematopoietic stem cells.

10:00 Networking Coffee Break with Exhibit and Poster Viewing

CHO CELLS: BIOPRESERVATION FOR PRODUCTION

10:45 Genotoxic Assessment on CHO-Cells of Three Cryoprotectants Commonly Used for Human Oocyte Vitrification

Blandine Courbière, M.D., Ph.D., Medical Faculty, Laboratory of Environmental Mutagenesis and Biogenotoxicology, Université de la Méditerranée Aix-Marseille II

The aim of our work was to evaluate the possible genotoxic activity of three cryoprotectants extensively used in vitrification techniques: dimethyl sulfoxide, ethylene glycol, and propylene glycol. For this purpose, a Chinese Hamster Ovary cell line, commonly used in genetic toxicology, was used to assess i) the induction of DNA primary lesions by the comet assay and ii) the persistence of chromosomal damages (micronuclei) by the micronucleus assay.

11:15 Cryopreservation of High Density Recombinant CHO Cell Banks

James Moldenhauer, M.S., Senior Scientist, Manufacturing Science & Technology, Eli Lilly and Company

Seed train expansion of recombinant CHO cells from a Working Cell Bank (WCB) cryovial for eventual inoculation into a bioreactor remains a manually-intrusive process that is time consuming and labor intensive, often requiring several sub-cultivations in shake flasks of increasing volumes. The frequent handling of cell cultures is a potential source of contamination at each expansion step, as well as a possible cause of variability in the final cell inoculum used for bioreactor seeding. By increasing the viable cell density of the WCB, one could reduce or eliminate the need for shake flask expansion steps prior to inoculation of a bioreactor. Along with minimizing aseptic open culture manipulations, reduction or elimination of cell expansion steps could increase scheduling flexibility for pilot plants and/or commercial production facilities. We have demonstrated the feasibility of a novel method for cryopreservation of GS-CHO cells as a "pelletized cell bank" used as a high density cell inoculum for direct seeding of bioreactors.

11:45 Cryopreservation to Maintain Continuity of the CHO Cell Line

Yvonne A. Reid, Ph.D., Manager, Scientist, Cell Biology Program, American Type Culture Collection

Chinese hamster ovary (CHO) cell line was derived from the ovary of the Chinese hamster in the 1960s. Since then it has become one of the most commonly used cell line for biological, medical and commercial applications including the production of therapeutic proteins. For these very important activities, cryopreservation of CHO cells ensures reproducibility and continuity of the cell line.

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

CRYOPRESERVATION: MEETING THE DEMANDS OF SCALE-UP AND PRODUCTION

1:55 Chairperson's Remarks

2:00 Cryopreservation and Long-Term Storage of Mammalian Cell Lines in 50 - 100 mL Cryobags

Rüdiger Heidemann, Ph.D., Group Leader, Cell Culture Development, Bayer HealthCare LLC

This presentation will discuss the cryopreservation of a recombinant mammalian cell line in cryobags suitable for GMP-type cell banks. It will highlight the challenges and differences compare to conventional banking procedures using cryo vials. In addition recovery data for the long-term storage in liquid nitrogen of these cryobags are presented.

2:30 Optimizing Mammalian Cell-Line Cryopreservation and Revival through Effective Detection and Depletion of Non-Viable Cells

Christopher Gregory, Ph.D., Professor, MRC Centre for Inflammation Research, University of Edinburgh; CSO, ImmunoSolv Ltd.

An often forgotten consequence of cryopreservation is the pro-apoptotic stress response caused by storage at low temperature. Thus, viability assessments of cells immediately following revival are often erroneous because they fail to take account of the rapid cell death responses (sometimes referred to as "delayed onset" cell death responses) that subsequently occur when the cells are cultured at physiological temperatures. In this presentation, the effective measurement of cell viability – including assessment of the commitment of apparently viable cells to apoptosis post-revival – will be considered. Furthermore, the beneficial effects of dead-cell removal on culture re-establishment, illustrated with antibody-producing cell lines and human embryonic stem cells, will be demonstrated.

3:00 Disposable Technology in Cell Banking and Expansion to Meet Demanding Process Timelines

Eric Becker, Ph.D., Associate Director, Mammalian Cell Culture Process, Boehringer Ingelheim Pharma GmbH & Co. KG

This presentation will provide an overview over current cell banking activities and topics such as long term storage and new strategies in cell expansion.

3:30 Networking Refreshment Break With Exhibit and Poster Viewing

4:15 INTERACTIVE PANEL: How will Mammalian Cell Culture be Further Innovated?

As mammalian cell culture moves forward meeting increased demands for ever higher titer, how will the task of culturing cells be innovated? What are the emerging technologies and approaches that will bring cell culture to new heights?

Please join this interactive panel discussion as cell culture experts share their insights on how cell culture will be innovated to provide adequate capacity for the biologics industry.

Moderator: Tiffany D. Rau, Ph.D., Global Technology & Technical Manager, Pall Corporation

Panelists:

Paula Meleady, Ph.D., Senior Research Scientist and Programme Leader, Proteomics Core Facility, National Institute for Cellular Biotechnology (NICB), Dublin City University

Yung-Shyeng Tsao, Ph.D., Senior Principal Scientist, Cell Culture, Merck

James C. Warren, Ph.D., Principal Development Engineer, Vaccine Manufacturing Sciences and Commercialization, Merck & Co., Inc.

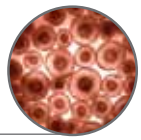
Jianguo Yang, Ph.D., Principal Scientist, Commercial Cell Culture Development, Commercial Process Development, Biologic R&D, Genzyme

5:15 End of Conference

Cambridge Healthtech Institute's Third Annual

Optimizing Mammalian Cell Lines

Enhancing Expression



WEDNESDAY, AUGUST 24

7:30 am Registration & Morning Coffee

CELL LINE DEVELOPMENT

8:25 Chairperson's Remarks

8:30 OPENING KEYNOTE PRESENTATION

Cell Engineering in a Genomics Era

Michael Betenbaugh, Ph.D., Professor, Chemical & Biomolecular Engineering, Whiting School of Engineering, Johns Hopkins University

The advent of the Chinese Hamster Genome will transform the ways in which cell and metabolic engineering occur in the coming decades. We will now have access to much greater amounts of genomic, proteomic, metabolomics, and glycomics data. How this information is used to alter cell behavior by genetic manipulation or environmental changes will shape mammalian biotechnology in the coming decades. In this presentation, we will outline several ways in which we are utilizing genomic data to alter mammalian cell performance. In one case study, we are evaluating the role of microRNAs in the activation of the apoptosis cascade. Chinese hamster ovary (CHO) cells were induced to undergo apoptosis by exposing the cells to nutrient-depleted media. A microarray comparison of known microRNA's in CHO cells exposed to fresh or depleted media revealed up-regulation of the mouse miR-297-669 cluster in CHO cells, including the specific microRNA Mmu-miR-466h. We further hypothesized that up-regulated mmu-miR-466h inhibits anti-apoptotic genes and induces apoptosis and a combination of bioinformatics and experimental tools predicted 38 anti-apoptotic targets. Several genes were selected from this anti-apoptotic subset based on nucleotide pairing complimentarity. The inhibition of the mmu-miR-466h lowered the expression levels of these genes, increased cell viability, and decreased apoptosis activity. In separate studies, we are applying proteomic tools to CHO cells and evaluating what proteins may be critical to optimizing bioprocessing.

9:00 FEATURED PRESENTATION

Novel Vector Technologies for Enhanced CHO Cell Line Development

Thomas Jostock, Ph.D., Technology Network Leader, Integrated Biologics Profiling, Novartis Pharma AG

The current Novartis CHO platform allows generation of high yielding production cell lines with short cycle times. Our strategy for further optimising speed and yield of the platform combines internal efforts with systematical screening and evaluation of external know-how. By integrating internal and external technologies, we are aiming for further reducing cycle times and screening efforts of cell line development. Some novel vector technologies that we have evaluated to improve our platform towards high yielding fast processes, including a new selection marker and a targeted integration technology, will be presented.

9:30 Early Markers of Production Instability of Recombinant Chinese Hamster Ovary Cell Lines

Ulrich Göpfert, Ph.D., Senior Research Scientist, Pharma Research and Early Development (pRED), Biologics Research, Roche Diagnostics GmbH

Production instability of manufacturing cell lines can be associated with methylation and silencing of the heterologous promoter. We have established methylation-specific real-time qPCR for the rapid and sensitive measurement of hCMV-MIE methylation in multiple cell lines and provide evidence that hCMV-MIE methylation and transgene copy numbers can be used as early markers to predict production instability of recombinant CHO cell lines. These markers should provide the opportunity to enrich stable producers early in cell line development and allow developers to put more emphasis on other criteria, such as product quality and bioprocess robustness.

10:00 Networking Coffee Break with Exhibit and Poster Viewing

10:45 Development of a High Yielding, Scalable CHO Transient Expression System

Gary Pettman, Team Leader, Early Expression and Supply, MedImmune

A rapid and productive expression strategy is required to meet the increasing requirements for research grade material during early drug development. The development, optimisation and implementation of a scalable, high yielding proprietary CHO transient expression system will be presented. The system has been successfully scaled up to 250L and is capable of expressing several hundred mg/L of recombinant protein and is used routinely to provide multi-gramme quantities of pre-clinical grade material for Biopharmaceutical development.

11:15 Development of Predictive Methods for Cell Line Selection and Process Development

Arnaud Perilleux, Scientist, Upstream Processing, Biotech Process Sciences, Merck Serono SA

This study focuses on the development of a robust fed-batch platform process in a 96-deep well plate system for cell line screening and process development. The system is aimed at screening hundreds of cell lines in suspension with a feeding system and a run duration which are in line with the platform bioreactor process used at Merck Serono. The cell line screening system demonstrated cell line specific culture performances which are in good agreement with those of cultures carried out at larger scales (spin tubes and lab-scale bioreactor cultures) and are predictive in terms of final titer. Challenges such as scale alignment, robustness of the 96-deep well plate system, integration of robotic liquid handling systems and high throughput analytics will be discussed. Additionally, the 96-deep well plate cultivation system can be efficiently used to complement existing development tools with increased throughput and enhanced potential for Design of Experiment (DoE) approaches. This new method was implemented to develop media and feeds for next generation upstream platform processes.

11:45 Micro-24 Microbioreactor: "High-throughput" bioreactors redefining cell line optimization and process development…Today

Tiffany D. Rau, Ph.D., Global Technology & Technical Manager, Pall Corporation

New tools and methods are available to screen and develop processes under controlled conditions earlier than ever before to allow ones organization to deliver a robust cell line and process earlier and also generate data for Quality by Design (QbD) initiatives. One tool that compliments QbD and delivering a robust platform for manufacturing is the Micro-24 Microbioreactor which is a 24 well reactor system where pH, dissolved oxygen and temperature are monitored and controlled.

12:00 pm Sponsored Presentation (Opportunity Available)

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

CELL LINE SELECTION

1:55 Chairperson's Remarks

2:00 Optimal Selection of Cell Lines Producing Biopharmaceutical Human IgGs

Jolanda Gerritsen, Ph.D., Technology Expert, Cell Line Development, Genmab B.V.

Timelines and productivity are of the utmost importance in generating monoclonal antibody producing CHO cell lines. Therefore, we first implemented high-throughput automated picking of high producing clones both after transfection and sub-cloning using ClonePixFL (Genetix). Secondly, we employed miniaturized cell culture using sensor dish reader and µ-24 reactor systems (Applikon). These modifications reduced timelines as they require less expansion work due to their smaller scale. Furthermore, it considerably increased throughput in terms of the number of cell lines that can be screened, which as an additional advantage, can be grown under controlled fed-batch conditions, closely mimicking those in a bioreactor. As a result, the most optimal production cell lines for large-scale manufacturing are selected with faster timelines. This presentation highlights our novel high throughput and miniaturized cell line development process and provides insight into these specific improvements regarding time lines and product yield.

2:30 Applying Quality by Design Principles to Candidate Selection and Cell Line Development

Susan Dana Jones, Ph.D., Vice President and Senior Consultant, BioProcess Technology Consultants

Interweaving production cell line development with final candidate selection in an application of QbD is a further approach to reducing overall development timelines and insuring product quality. Such early product assessments demand earlier development of robust and reliable analytical methods to insure proper and timely results that can inform the decision making needed to select the lead candidate product from among the many that are under consideration and then to identify the cell line that produces the highest quality product. This talk will show how the integration of candidate selection, early analytical development, and cell line development can lead to more effective products that can be produced at lower cost.

3:00 Utilization of Non-AUG Initiation Codons in a Flow Cytometry-Based Method for Efficient Selection of Recombinant Cell Lines

Christine DeMaria, Ph.D., Senior Scientist, Therapeutic Protein Expression, Genzyme Corp.

This high-throughput clone selection method utilizes a cell surface reporter to predict the expression level of any recombinant therapeutic protein. The reporter, which lacks a native translation initiation codon, is placed in the 5' UTR of the therapeutic so that both open reading frames are translated from the same mRNA. Flow cytometry sorting of uncloned pools is used to isolate high producing cell lines based on reporter expression. Subsequent flow cytometry screening during clone expansion enables resources to be focused solely on clones with both high and stable therapeutic expression.

3:30 Networking Refreshment Break with Exhibit and Poster Viewing

TRANSFECTION / ELECTROPORATION

4:15 Flow-Through Electroporation Based on Constant Voltage for Large-Volume and Enhanced Cell Transfection

Chang Lu, Ph.D., Associate Professor, Chemical Engineering, Virginia Tech

Here we present a novel flow-through electroporation method for delivery of DNA into cells with a processing rate up to ~20 ml/min based on disposable microfluidic chips, a syringe pump, and a low-cost direct current (DC) power supply that provides a constant voltage. Our technique eliminates the use of a pulse generator and the associated cost. More importantly, we show that by harnessing hydrodynamic effects of the flow, our technique enables the entire membrane surface to become uniformly permeabilized and this leads to greatly improved delivery and transfection. Our technique provides a drastically simple and effective approach to electroporation-based cell transfection.

4:45 Nanochannel Electroporation–Giving Cells a Shot

L. James Lee, Ph.D., Helen C. Kurtz Professor, Chemical and Biomolecular Engineering; Director, NSF Nanoscale Science and Engineering Center for Affordable Nanoengineering of Polymer Biomedical Devices (CANPBD), The Ohio State University

We describe a new technology, nanochannel electroporation (NEP) allowing transfection of many small sized and delicate cells with precise control over dose and timing. Cell mortality from NEP is virtually zero. We show dose control effects on a variety of transfection agents such as oligonucleic acids, molecular beacon, quantum dots and efficient delivery of large plasmid DNA. Dosage controlled delivery to multiple cells is not achievable with any existing techniques.

5:15 Networking Reception, Last Chance for Poster and Exhibit Viewing

6:45 End of Day

THURSDAY, AUGUST 25

7:30 am Breakfast Presentation (Sponsorship Opportunity Available) **or Morning Coffee**

OPTIMIZING PROPERTIES

8:25 Chairperson's Remarks

8:30 Analysis of the RNAi Pathway for Improved siRNA Design

S. Patrick Walton, Ph.D., Associate Professor, Chemical Engineering & Materials Science, Michigan State University

RNA interference (RNAi) provides a powerful means for down regulating the expression of a specific gene in mammalian cells. However, selection of the most active short, interfering RNA (siRNA) against a target is generally accomplished by guided trial-and-error.

We will discuss our results on the interactions of siRNAs with other molecular components of the RNAi pathway and how these interactions inform siRNA design and selection.

9:00 Monitor and Control of Glycosylation in Mammalian Cell Bioprocesses

Michael Butler, Ph.D., Distinguished Professor, Animal Cell Technology, Microbiology, University of Manitoba

Critical culture parameters control the glycosylation profile of proteins secreted from mammalian cells in culture. The parameters may be associated with the host cell line, the culture media, the mode of culture or the specific protein synthesized. It is important to control these parameters in an industrial bioprocess to ensure consistency of the final product and maximum bioactivity. These parameters will be discussed in the context of bioprocesses for the production of highly efficacious biopharmaceuticals with consistent structural profiles.

9:30 Prospects for Generating Cell-Type Specific Immortalized Cells

Dieter C. Gruenert, Ph.D., Professor, Department of Otolaryngology, Head and Neck Surgery, Department of Laboratory Medicine, University of California, San Francisco

Blastocyst and Induced Pulripotent Stem Cells Derived from Sv40-Transformed Tracheal Epithelial Cells by Somatic Cell Nuclear Transfer or Reprogramming. The prospect of using cell models to study disease pathology and develop new therapies has been significantly enhanced by stem cell technology. In particular, somatic cell nuclear transfer (SCNT) and the generation of induced pluripotent stem cells (iPSCs) has opened the door to new opportunities for developing cell-type specific immortalized cell systems. In this context, we have generated blastocysts through SCNT of SV40-transformed rabbit tracheal epithelial cell nuclei and iPSCs through cellular reprogramming for differentiation into cell-type specific immortalized cells. These cells can now be used for evaluating therapeutic interventions in multiple tissue types in the same genetic background and have the potential for developing and optimizing patient specific therapies.

10:00 Networking Coffee Break

OPTIMIZING CLONES

10:30 Differential Growth, Productivity, Metabolism and Responses to Trophic Factors in CHO Cell Clones

Susan Sharfstein, Ph.D., Associate Professor, Nanobioscience, College of Nanoscale Science and Engineering, University at Albany

To evaluate the range of possible responses to changes in process conditions, the growth, metabolism, and productivity of five Chinese hamster ovary (CHO) clones were explored in response to stimulation with insulin (5 mg/L) and LONG®R3IGF-I (20 µg/L or 100 µg/L). All five clones were derived from the same parental CHO cell line (DG44) and produced the same recombinant monoclonal antibody, with varying specific productivities. Overall product titers were affected by variations in both integrated viable cell density (IVCD) and specific productivity. Nutrient uptake and metabolite generation patterns varied strongly between clones and much less with culture conditions. These results point to the need for careful clonal analysis when selecting clones, particularly for platform processes where media and culture conditions are predetermined.

11:00 Fluorescent Labelling in Semi-Solid Medium to Identify High-Expressing Clones for Recombinant Protein Production

Rénald Gilbert, Ph.D., Research Officer, Biotechnology Research Institute, National Research Council Canada

We have optimized a method to identify those valuable but rare supersecretors. It consists of directly labelling small colonies of CHO cells with a fluorescent antibody against the secreted gene product in semi-solid medium. Because a correlation exists between the intensity of the fluorescent signal and the level of secreted protein, the few supersecretors within a pool of transfected cells can be easily identified and isolated using a micromanipulator or an automated cell picker. This method reduces considerably the work load necessary to generate stable high-expressing cell lines, because only a small number of clones need to be subsequently analyzed for protein production and stability.

11:30pm End of The Bioprocessing Summit

Cambridge Healthtech Institute's Fifth Annual

Baculovirus Technology

WEDNESDAY, AUGUST 24

7:30 am Registration & Morning Coffee

UNDERSTANDING BIOLOGICAL PROPERTIES TO OPTIMIZE BACULOVIRAL MECHANISMS

8:25 Chairperson's Remarks

8:30 OPENING KEYNOTE PRESENTATION
Baculovirus Nucleocapsid Transport to the Nucleus and Beyond!

Loy Volkman, Ph.D., Professor Emerita, Plant & Microbial Biology, University of California, Berkeley

Phylogenetic evidence indicates baculoviruses have been tracking their juvenile insect hosts for about 230 million years, since the radiation of the Lepidoptera. Lepidopteran larvae developed a formidable defense against pathogens during this period: an exoskeleton that covers their exterior surfaces including their respiratory tubes, foreguts and hindguts. Baculoviruses have countered this measure by targeting larval midgut columnar epithelial cells via their microvilli, an extraordinary biological feat.

9:00 FEATURED PRESENTATION
Application of the Baculovirus Expression System in Generating Tools for Drug Discovery

Ian Hunt, Ph.D., Associate Director, Discovery Technologies, Novartis Institutes for BioMedical Research, Inc.

9:30 Protein Glycosylation in the Baculovirus-Insect Cell System

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

The baculovirus-insect cell system is widely used to produce recombinant glycoproteins. However, the N-glycosylation patterns of these products typically differ from those of their native, mammalian cell-derived counterparts. For the past 15 years, my lab group has focused on insect cell glycoengineering to address this problem. This presentation will focus on our ongoing efforts to humanize protein N-glycosylation in the baculovirus-insect cell system.

10:00 Networking Coffee Break with Exhibit and Poster Viewing

VECTOR ENGINEERING

10:45 Baculoviral Vectors for Gene Editing of Human Stem Cells

Pin Wang, Ph.D., Associate Professor, Chemical Engineering, Biomedical Engineering, Pharmacy and Pharmaceutical Sciences, University of Southern California

We will describe our success of using a baculoviral vector (BV) system carrying zinc finger nucleases (ZFNs) for site-specific modification of cell genome. We observed that BV-mediated transient expression of ZFNs specifically disrupted the desired locus in transduced cells. When BV was engineered to deliver both ZFNs and donor DNA, permanent site-specific gene addition could be achieved.

11:15 Enabling Complex Protein Production in Academic and Industrial R&D

Imre Berger, Ph.D., Group Leader, Structural Biology Unit, EMBL Grenoble

Complex proteins, involved in disease causing processes, are entering center-stage as key drug targets of the future. The baculovirus/insect cell expression system is particularly useful for producing such protein targets, biologics and multicomponent assemblies, for many applications. We have developed MultiBac, a BEVS designed for high-quality multiprotein complex production, and have installed MultiBac as a platform technology at the Eukaryotic Expression Facility (EEF) at the EMBL. Our MultiBac system and several of its successful applications, in academic and industrial R&D, will be presented.

11:45 Enhancements to Baculovirus Expression Technology

Sponsored by
Blue Sky BioServices
Pathways to Productivity

Norman Garceau, Ph.D., President & CSO, Blue Sky Biotech

12:00 pm Sponsored Presentation (Opportunity Available)

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

FOCUS ON BacMam

1:55 Chairperson's Remarks

2:00 BacMam Gene Delivery in Drug Discovery

Robert Ames, Ph.D., Director, Cellular Targets, Biological Reagents and Assay Development, GlaxoSmithKline

BacMam gene delivery has gained prominence for the development of cell-based drug discovery assays due to the short cycle time for reagent generation but more importantly because of the unparalleled experimental flexibility offered by the technology. Rather than stable cell lines we instead generate recombinant BacMam viruses containing the cDNA of interest and use these virus preparations to transduce the target cells of interest. The presentation will highlight the versatility of the technology and how we have optimized and implemented it across drug discovery.

2:30 BacMam-Mediated Recombinant Protein Expression for Cell-Based Reagents

Kim Stutzman-Engwall, Ph.D., Associate Research Fellow, Pfizer Global R&D Groton Labs

Expression of recombinant protein in mammalian cells is a key step in the drug discovery process. Key advantages of recombinant expression in mammalian cells, include the appropriate signal transduction machinery and native glycosylation profiles. These cells are routinely used for cell-based screening assays, binding assays, and selectivity assays. There are several options available for generating mammalian cells expressing recombinant proteins, including transient transfection, generation of stable cell lines and viral transduction using adenoviral, lentiviral, retroviral, or BacMam systems. While each option has advantages and disadvantages and a range of flexible options is desirable, we have recently focused

our efforts on BacMam. Our investigations into the use of BacMam for mammalian cell transductions and the development of novel vectors have enabled us to efficiently optimize expression of poorly expressed proteins, as well as rapidly generate multiple isoforms of GPCRs for selectivity screening. Other key advantages of BacMam are the ability to 'dial-in' the desired level of recombinant protein expression as well as co-express multiple genes simultaneously. We have developed BacMam protocols to optimized large scale protein production using Wave Bioreactors. Several case studies using BacMam technology will be presented.

3:00 Baculoviruses for Lentivirus Generation

Kari Airenne, Ph.D., Professor, Biotechnology and Molecular Medicine, A.I. Virtanen Institute, University of Kuopio

We have studied possibility to produce lentiviruses by baculovirus technology. Our results show that safe 3rd generation lentiviruses can be produced by hybrid baculoviruses in adherent and suspension cells. High-titer LV stocks were readily gained in 293T cells and the viruses performed similarly as the LVs produced by conventional means in vitro and in vivo. A scalable and cost-effective capture purification step was also set up based on a DEAE monolithic column enabling of 65% recovery of highly purified lentiviruses.

3:30 Networking Refreshment Break with Exhibit and Poster Viewing

VACCINE DEVELOPMENT

4:15 Application of Baculovirus Technology in the Development of Sipuleucel-T, an Active Cellular Immunotherapy for the Treatment of Asymptomatic or Minimally Symptomatic Metastatic Hormone Refractory Prostate Cancer

Samuel Li, Ph.D., Associate Director, Pre-Clinical Discovery, Dendreon Corporation

Sipuleucel-T (PROVENGE®) is an FDA-approved autologous cellular immunotherapy for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer. This presentation will present the data on the clinical development of sipuleucel-T, and on our Antigen Delivery Cassette™ technology platform in general. Engineering and production of protein antigen PA2024 by the BEVS technology and sipuleucel-T manufacturing are also briefly described.

4:45 Production of Norovirus Virus-Like Particles in the Baculovirus Expression System from Benchtop to GMP Manufacturing

Ross Taylor, Ph.D., Director, Process Development, LigoCyte Pharmaceuticals, Inc.

The baculovirus expression system has been used in both Wave and stirred-tank bioreactor systems for production of two distinct norovirus virus-like particles (VLP). Emphasis has been placed on employing single-use technologies including disposable bags for media storage and sample collection, disposable bioreactors for VLP production, capsule filters for VLP harvest, and membrane chromatography for VLP capture. LigoCyte's VLP manufacturing process results in gram quantities of highly purified VLP which are currently being used in Phase I/II clinical trials.

5:15 Networking Reception, Last Chance for Poster and Exhibit Viewing

6:45 End of Day

THURSDAY, AUGUST 25

7:30 am Breakfast Presentation (Sponsorship Opportunity Available) **or Morning Coffee**

PROTEIN EXPRESSION

8:25 Chairperson's Remarks

8:30 FEATURED PRESENTATION: Virion-Free Protein Production from Baculovirus-Infected Insect Cells

Just M. Vlak, Ph.D., Professor, Vice-Dean and Member Academic Board, Laboratory of Virology, Wageningen University

A novel genetic strategy has been developed to manufacture biopharmaceuticals in insect cells with baculovirus vectors, but without the presence of contaminating baculovirus particles (virions). Rigorous purification procedures are often needed to remove or eliminate particles from the biopharmaceutical products. This novel strategy greatly simplifies the downstream processing of biopharmaceuticals produced in insect cells, hence reduces production costs and enhances the safety of baculovirus-insect cell produced biopharmaceuticals for vaccines and gene therapy.

9:00 Tools for Improving Protein Production in the Baculovirus System

Dominic Esposito, Ph.D., Principal Scientist, Protein Expression Laboratory, SAIC-Frederick, Inc.

Our lab has developed a robust microscale protein production platform which allows us to rapidly analyze a large number of variables to optimize protein expression. Utilizing this system for baculovirus expression, we have been able to improve our chances of successful protein production using a combination of promoters, fusion tags, strains, and expression conditions. The platform technology and its application to the BEVS will be discussed and results of a number of experimental tests of the system will be presented.

9:30 Optimizing Efficiency and Effectiveness when Producing Proteins with the Baculovirus Expression Vector System

Krista Bowman, Ph.D., Senior Scientific Manager, Structural Biology, Genentech, Inc.

We have implemented a fairly high-throughput generic approach to increase not only our efficiency but also our effectiveness in successfully producing proteins with the baculovirus expression vector system. We have combined techniques such as small scale baculovirus infections in multiwell blocks, analysis of expression level following single affinity capture and elution from Ni-NTA Phytips, and analytical fluorescent size exclusion chromatography to gain insight into protein aggregation, multimerization, or complexation. Combining these semi-quantitative and qualitative approaches, we can more rapidly prioritize constructs for further characterization and production.

10:00 Networking Coffee Break

PROTEIN PRODUCTION

10:30 Production of Recombinant Human Multi-Protein Transcription Factor Complexes

Arnaud Poterszman, Ph.D., Research Director, Integrated Structural Biology, IGBMC CNRS/Inserm/Universite de Strasbourg

We present here our strategies for the production of multi-subunit human transcription factors using the baculovirus expression system.

Selected examples illustrate recent developments and their impact on the structural biology of human protein: (i) HTP mini expression screening, (ii) use of fluorescent proteins as makers and for quality control, (iii) vector development for parallel cloning and (co-) expression of multiple constructs for a single target, (iv) single virus co-expression of multi-subunit complexes.

11:00 Production of Mammalian Vectors in a Non-Mammalian System

Arie van Oorschot, Scientist, Upstream Processing, Process Development, Amsterdam Molecular Therapeutics (AMT)

Potential commercialization of rAAVs produced in mammalian cells is hampered by the inability to produce rAAVs at large scale at acceptable costs. An attractive alternative is the baculovirus expression vector system, a non-mammalian production system by means of baculovirus expression vectors and insect cell suspension cultures. In this scalable production system, the essential components are delivered and assembled into rAAVs using infection of insect cells by three types of baculoviruses.

11:30 Addressing the Scale-Up Problem of Baculovirus Expression

Daniel Fitzgerald, Ph.D., Eclosion SA

We have addressed the "scale-up problem" by developing a novel baculovirus expression system for insect cells, called "iBac", in which recombinant protein expression is turned "off" during scale-up, and is turned "on" only when sufficient recombinant viruses are available for the desired expression scale, resulting in significant improvements in

Cambridge Healthtech Institute's Inaugural

Scaling Up & Down with Optimized Bioreactors + Disposables

WEDNESDAY, AUGUST 24

7:30am Registration & Morning Coffee

REPRESENTATIVE SCALE-DOWN MODELS

8:25 Chairperson's Remarks

8:30 Opening Keynote Presentation

Use of Scale-Down Models to Investigate Raw Material Impact on Process Performance

Gregg Nyberg, Ph.D., Director, Process Development, Amgen, Inc.

Successful scale-up and technology transfer requires process understanding, which is typically achieved through process development and characterization performed in small-scale models. Small-scale models are also important for troubleshooting issues encountered during commercial-scale manufacturing. This case study describes how small-scale models were effectively used to troubleshoot manufacturing issues related to raw material variability.

9:00 Using Small-Scale Studies to Optimize Process Operational Parameters for the Purposes of Scaling the Process to Manufacturing Scale in a Cost and Time-Efficient Manner

Tim Lee, Ph.D., Deputy Director, Industrial Operations, Sanofi Pasteur

This presentation focuses on using microbioreactor technology to determine fermentation conditions without having to perform multiple bioreactor experiments at the 2L to 200 L scale. Small-scale studies include optimizing and finalizing key process parameters like oxygen transfer coefficient, temperature, pH, biomass production during production. Potential PAT applications for controlling and guiding fermentation systems to reach optimum yields are discussed. We have also developed a business case comparison between conventional methods (i.e. centrifugation, microfiltration, ultrafiltration, bead purification) versus newer disposable membrane capture technologies to determine the best route for large-scale manufacturing. Process economics related to the comparison of operational and capital costs are being discussed for large-scale applications.

9:30 Development and Qualification of a Scale-Down Model for a Commercial Cell Culture Process

Bruno Figueroa, Ph.D., Senior Principal Scientist, Bioprocess R&D & Culture Process Development, Pfizer, Inc.

Scale-down models are essential for process characterization and process manufacturing support prior to and during the commercial product life cycle. Development and qualification of a bioreactor scale-down model has become a regulatory expectation. In this case study, we will present how we developed and qualified a scale-down model at 2L scale for a mammalian cell culture process at 12KL scale. Both univariate analysis and multivariate analysis were performed to demonstrate equivalency of cell culture performance and product quality between small scale and commercial scale.

10:00 Networking Coffee Break with Exhibit and Poster Viewing

10:45 Scale-Down Model Assessment for QbD Cell Culture Characterization: A Case Study for a Monoclonal Antibody Production Process

Meg Tung, Senior Research Associate, Late Stage Cell Culture, Pharma Technical Development, Genentech, Inc.

The goal of using a QbD approach for cell culture process characterization is to gain overall process understanding, with the final outcomes being both univariate and multivariate acceptable ranges for each parameter tested, and a design space which ensures acceptable process performance and product quality. Due to the sheer number of studies required, the use of scale-down models makes such characterization effort possible. However, the applicability of the QbD characterization study results to the full scale depends on the validity of the scale-down models that are used. This case study will present the scale-down model comparison approach and the strategy that is used to allow meaningful translation of the scale-down QbD study results to the full scale.

11:15 Ensuring Predictability for Scale-Up & Scale-Down by Defining an Engineering Design Space

José Gomes, Principal Scientist & Manager, Bioreactor Process Development, Pfizer, Inc.

11:45 Sponsored Presentations (Opportunities Available)

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

OPTIMIZING PROCESSES WITH SINGLE-USE TECHNOLOGIES

1:55 Chairperson's Remarks

2:00 Single-Use Bioreactor Design

David M. Marks, President and Senior Consultant, DME Alliance Incorporated

This presentation will discuss the challenges and key considerations for the design and scale-up of single-use cell culture bioreactors. A performance comparison with traditional stainless steel bioreactors will be provided, along with a summary of the relative advantages and disadvantages of disposable systems for upstream biologics manufacturing. Discussion will focus on points to consider when selecting disposable bioreactor technology.

2:30 Shaken not Stirred - Single Use Optimum Growth 5L Flasks with Data from Insect Cells, CHO, Hybridoma, HEK293 Cell Lines

Sponsored by THOMSON Solutions™ At Work INSTRUMENT COMPANY

Sam A. Ellis, Vice President, Cell Line Development Products, Thomson Instrument Company

Optimum Growth Flasks (patented) give excellent growth with space saving capability. Optimum Growth Flasks users are able to to grow 2.5L/Flask of Cell Culture, up to 17.5L per shaker, and 52.5L in a triple stack shaker. The Optimum Growth Flasks allow for more protein, and cell growth in studies versus Wave® Bags. Data will be presented on Insect Cells, CHO, Hybridoma, HEK293 Cell Lines.

3:00 Key Considerations during the Scale-Up of a Fully Disposable Perfusion Bioreactor System

Jin Yin, Ph.D., Principal Bioengineer, Cell Culture, Shire Human Genetic Therapies

To support the production of therapeutic proteins, a fully disposable perfusion bioreactor system has been developed. The system consists of a disposable bioreactor and a disposable centrifugation cell retention device, which has been successfully scaled-up to 2000 L scale. Challenges such as mass transfer, mixing, shear stress and centrifuge perfusion capacity during the scale-up of the system will be discussed. The approaches to address these scale-up related challenges will also be presented.

3:30 Networking Refreshment Break with Exhibit and Poster Viewing

MINI/MICRO BIOREACTORS

4:15 Rapid Bioprocess Development Using Miniature Bioreactor Technologies

Frank Baganz, Ph.D., Senior Lecturer, Biochemical Engineering, University College London

The need for greater speed and efficiency during the development of fermentation and cell culture processes has led to the development and application of miniaturised bioreactor technologies. This presentation will focus on shaken microwell-based systems and miniature stirred tank reactors and will cover the engineering characterisation in terms of power input, liquid phase mixing and oxygen mass transfer. Furthermore, examples will be given for the application of these technologies in fermentation and cell culture process development. The application of single-use bioreactor technologies will also discussed.

4:45 Successful Scale-Up of Bioprocesses from Shaken 500 µl Microfluidic Micro-Bioreactors with Fed-Batch Operation, pH Control and Full Online Monitoring Capabilities

Jochen Büchs, Ph.D., Professor and Chair, Biochemical Engineering, Aachen University of Technology

A 500 µL micro-bioreactor system was developed based on the 48 well microtiter plate format. The shape of the wells was designed such that oxygen transfer is enhanced to meet the demand even of fast growing cultures. The ground plate of the micro-bioreactors contains a set of microfluidic valves and pumps. These allow dosing of very small amounts of liquid in the nL-range into the bulk liquid of the shaken micro-bioreactors. Different fed-batch and pH-controlled fermentations were conducted in the 500 µL micro-bioreactor system. Almost the same fermentation kinetics were obtained in 500 µL scale as well as in 1 L scale, demonstrating the usefulness of the developed micro-bioreactor and of the scale-up procedure.

5:15 Networking Reception, Last Chance for Poster and Exhibit Viewing

6:45 End of Day

THURSDAY, AUGUST 25

7:30 am Breakfast Presentation (Sponsorship Opportunity Available) or Morning Coffee

OPTIMIZING BIOPROCESSES

8:25 Chairperson's Remarks

8:30 Stability Studies to Support Comparability Studies

Nanda K. Subbarao, Ph.D., Senior Consultant, Biologics Consulting Group, Inc.

Stability testing is a cornerstone of comparability demonstration and Stability Studies are required as part of testing to show comparability of pre and post change lots. Current regulatory expectations for performing such stability studies will be discussed. Studies at the long term storage condition required to evaluate the whether the shelf life and impurities of the DS or DP pre and post change are acceptable. Stability studies under accelerated and stress conditions are very useful to provide a quick evaluation of the absence of differences in the fragility of the product before and after the change and to detect any new degradation pathways. Differences between comparability studies for products during clinical studies and post approval will be discussed.

9:00 DOE 101: The Basic Principles of Design of Experiments

Martin Kane, Associate Director, Process Statistics, Human Genome Sciences, Inc.

Design of Experiments (DOE's) are tests or series of tests in which purposeful changes are made to the input variables of a process or system so that we may observe, learn, and identify the reasons for changes in the output response(s). This talk is an introduction to design of experiments with an emphasis on basic principles. Benefits of DOE include: cost savings, determination of the interdependency between variables, hidden replication, predictive capability, optimal setting of specifications and key quality characteristics.

9:30 Platform Development Strategy for the Production of Monoclonal Antibodies by Glycoengineered Yeast

Jeffrey Ly, Staff Biochemical Engineer, Biologics New & Enabling Technologies, Merck & Co., Inc.

An alternative to mammalian cell culture being investigated is the use of faster growing microbial systems which offer the ability to reduce development timelines and production costs. The use of glycoengineered ***Pichia pastoris*** libraries, that replicate the most essential glycosylation pathways found in mammals, is now becoming a viable option. Glycoengineering offers the unique advantage of producing more homogeneous glycosylation patterns, as opposed to the large heterogeneity of glycan moieties found in mammalian cells. Examples will be presented where antibody titers > 1g/L are expressed in large scale cultivations with uniform human N-linked glycans. Optimization of process conditions through statistical design of experiments, molecular profiling and metabolite analysis enabled the development of a commercially viable & robust platform process that yields consistent productivity and product quality.

10:00 Networking Coffee Break

INNOVATING BIOREACTOR USE & DESIGN

10:30 Advances in Simulation Methods for Predicting Mass Transfer in Gas-Sparged Bioreactors

Chris Antoniou, Principal Project Engineer, Global Engineering & Technology, Biogen Idec

This talk will review computational fluid dynamics (CFD) simulation methods for designing and optimizing bioreactors. In particular, two different approaches (Lagrangian particle tracking and Eulerian population balance) for modeling gas sparging are discussed. These approaches are applied to a commercial mammalian cell culture bioreactor. Different sparger configurations are analyzed to understand effect of geometrical changes. The talk summarizes results of the two approaches and provides guidelines for simulations.

11:00 An Automated, Sensorized Scalable Bioreactor for 3D Perfusion Cell Seeding and Culture, Within Multiple Independent Chambers

Stefania Adele Riboldi, Ph.D., Co-Founder and CEO, SKE Advanced Therapies

Bioreactors, as a means to generate and maintain a controlled culture environment and enable directed tissue growth could represent the key element for the development of automated, standardized, traceable, and safe manufacturing processes for engineered tissues for clinical applications. To this purpose, an automated, scalable device capable of online, real-time monitoring of critical culture parameters will be presented, representing a step forward towards a reliable, safe and automated manufacturing of biological tissues.

11:30 Plastic Bioreactors: Smart & Cheap, Not Disposable

Wayne Curtis, Ph.D., Professor, Chemical Engineering, Penn State University

We developed and patented a simple plastic bioreactor for the purpose of enabling lower-value bioproducts production (not the alternative paradigm of convenience and disposability). Cost reduction is also achieved by avoiding instrumentation in favor of smart, feed-forward control. We have demonstrated these to 100-L scale with plant tissue culture performance comparable to traditional cell culture reactors. Ongoing work includes development for cellulosic biomass, autotrophic fermentations plant propagation and microbial waste-to-value bioprocesses.

12:00 pm End of The Bioprocessing Summit

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