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CYTOKINE-BASED THERAPEUTICS

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PLENARY KEYNOTE SPEAKERS

Diagnosing the Disease: Disruptive Innovation in Healthcare
Clayton M. Christensen, DBA, Robert and Jane Cizik Professor of Business Administration, Harvard Business School

Disruption of the Pharmaceutical Industry: Moving from Products to Solutions
Elizabeth L. Bewley, MBA, Vice President, Strategic Planning, Johnson & Johnson Health Care Systems Inc.

Risk Diagnosis for Disease Prevention
C. Thomas Caskey, M.D., F.A.C.P., Director and Chief Executive Officer, Brown Foundation Institute of Molecular Medicine, University of Texas Health Science Center

SPEAKERS

Linda Burkly, Ph.D., **Biogen Idec**

Israel F. Charo, M.D., Ph.D., **University of California, San Francisco**

Chen Dong, Ph.D., **MD Anderson Cancer Center**

Charles E. Egwuagu, MPH, Ph.D., **National Institutes of Health**

Rafael Fernandez-Botran, Ph.D., **University of Louisville**

Simon Fricker, Ph.D., **Genzyme Corporation**

Iqbal S. Grewal, Ph.D., **Seattle Genetics, Inc.**

Thomas Hamilton, Ph.D., **Cleveland Clinic**

Wayne Hancock, Ph.D., **Children's Hospital of Philadelphia**

Ziwei Huang, Ph.D., **University of California at San Diego**

Sarah Hymowitz, Ph.D., **Genentech**

Sameer Kawatkar, Ph.D., **Chemokine Pharmaceuticals Inc.**

Sanjay Khare, Ph.D., **ImmunGene**

Sergei V. Kotenko, Ph.D., **UMDNJ - New Jersey Medical School**

Xiaoxia Li, Ph.D., **Cleveland Clinic**

Bailin Liang, Ph.D., **Centocor**

Fabienne Mackay, Ph.D., **Garvan Institute of Medical Research**

Christopher Moore, Ph.D., **University of North Carolina at Chapel Hill**

Wei Tong, Ph.D., **University of Pennsylvania School of Medicine**

Matthew Walters, Ph.D., **ChemoCentryx**

SESSIONS

- Targeting Interleukins and Interferons
- Developing Chemokine Antagonists
- Leveraging Technologies for Cytokine-Based Drug Development
- Targeting the TNF Family
- Novel Therapeutic Targets – Processes, Pathways and Networks
- Therapeutic Potential of Cytokine Targets

PANELS

- Drug Discovery Targeting Protein-Protein Interactions
- Cytokine Networks and the Challenge of Targeted Therapies

BREAKOUT DISCUSSIONS

- Targeting Cytokine Interactions
- What are the Limitations of Cytokine-Based Immunotherapies?
- What is the Predictive Value of Cytokine Biomarkers in Autoimmune and Inflammatory Diseases?

TUESDAY, MARCH 25 • PRE-CONFERENCE SHORT COURSES

(SC2) The Challenge of the Blood-Brain Barrier - a Medicinal Chemistry Perspective

(SC5) Immunological Biomarkers: "How to" and Three Case Studies

(SC8) Models for Evaluating Drug-Drug Ineteraction Potential in Preclinical Development

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Tuesday, March 25

7:00am Registration (Open until 5:30pm)

PLENARY KEYNOTE SESSION

8:00 Plenary Keynote Introduction

Harry Glorikian, Managing Partner, Scientia Advisors

8:15 Diagnosing the Disease: Disruptive Innovation in Healthcare

Clayton M. Christensen, DBA, Robert and Jane Cizik Professor of Business Administration, Harvard Business School

In the absence of the ability to precisely define a disease, the care of patients is best undertaken by highly skilled professionals, whose intuition is based on deep experience. This describes the history of health care, and we call this the practice of intuitive medicine. Molecular biology holds the promise of transforming medical practice into a new phase that we call precision medicine. It promises to dramatically reduce cost and increase the predictable effectiveness of therapy.

9:45 Coffee Break

10:15am – 1:15pm Morning Pre-Conference Short Courses*

Recommended Short Courses*

(SC2) THE CHALLENGE OF THE BLOOD-BRAIN BARRIER – A MEDICINAL CHEMISTRY PERSPECTIVE

Douglas K. Spracklin, Ph.D., Senior Principal Scientist, CNS Drug Metabolism, Pfizer Inc.

Ellen Q. Wang, Ph.D., Senior Principal Scientist, Pharmacokinetics, Dynamics and Metabolism, Pfizer Global Research and Development

In this course you will learn…

- An introduction to the physiology of the blood-brain barrier
- *In vitro* methods for predicting BBB permeability
- *In vivo* methods for measuring brain exposure and/or target occupancy
- Case studies & applications

(SC5) IMMUNOLOGICAL BIOMARKERS: "HOW TO" AND THREE CASE STUDIES

Moderator: Eric Wakshull, Ph.D., Senior Scientist/Group Leader, Development Sciences, Genentech, Inc.

Immunological Biomarkers and Methods

Annie De Groot, M.D., Chief Executive Officer, EpiVax, Inc. and Brown University

Case Study: GDNF

Michael Moxness, Ph.D., Principal Scientist Clinical Immunology, Amgen Inc.

Case Study: DR 0701

Karin Cederbrandt, Ph.D., Molecular Toxicology, AstraZeneca

Case Study: Alpha-interferon

Maxygen (invited)

Panel Discussion with Q&A

*Separate Registration Required

1:15 Lunch on Your Own

2:30 - 5:30 Afternoon Pre-Conference Short Courses*

Recommended Short Course*

(SC8) MODELS FOR EVALUATING DRUG-DRUG INTERACTION POTENTIAL IN PRECLINICAL DEVELOPMENT

Joseph Ware, Ph.D., Senior. Scientist, Late Stage PK/PD, Genentech, Inc.

James McKim, Ph.D., DABT, President & Chief Scientific Officer, CeeTox, Inc.

Philip S. Burton, Ph.D., Chief Executive & Scientific Officer, ADMETRx, Inc.

This course will cover:

- An overview of drug-drug interactions from the clinical perspective, withdrawn drugs and the overall impact on development
- CYP inhibition and induction methods and *in vitro/ in vivo* correlations
- Transporter models and *in vitro/in vivo* correlationst

*Separate Registration Required

For a complete list of Short Courses, visit Tri-Conference.com

Cover Photo Credit: Dr. Walid Khaled, University of Cambridge

Wednesday, March 26

7:00am Registration (Open until 5:30pm)

PLENARY KEYNOTE SESSION

8:00 Plenary Keynote Introduction

Edward G. Heidig, General Counsel and Deputy Secretary, Business, Transportation and Housing Agency

8:10 Risk Diagnosis for Disease Prevention

C. Thomas Caskey, M.D., F.A.C.P., Director and Chief Executive Officer, Brown Foundation Institute of Molecular Medicine, University of Texas Health Science Center

There are an increasing number of presymtomatic diagnostic options which include: genetic, imaging, and analyte technology. Examples of linking a specifi c diagnostic to a therapeutic decision and FDA approval have fueled the activity for personalized medicine. It must be appreciated that diagnostic capacity emerges far more rapidly than an approved safe therapeutic. Thus the personalized medicine goal has a bottle neck for broad utility. A strategy of studying approved drugs for maximal effi cacy is realistic and reasonable toward that goal since it is estimated that many approved drugs are effective in less than 50% of patients. These approaches will be discussed.

8:55 Disruption of the Pharmaceutical Industry: Moving from Products to Solutions

Elizabeth L. Bewley, MBA, Vice President, Strategic Planning, Johnson & Johnson Health Care Systems Inc.

The pharmaceutical industry is bracing itself for a period of unprecedented challenges. This new era for our industry is being brought on by the confluence of several environmental factors, both internal and external to the industry, including; 1) non-sustainable increases in healthcare expenditures, 2) spiraling costs and decreasing productivity of R&D, 3) reimbursement driven by medical and economic outcomes, and 4) the proliferation and redistribution of healthcare outcomes information. Although all of these factors threaten to disrupt our industry, it is the evolving transparency in healthcare outcomes information that represents the most unsettling threat to our current business model, as well as the largest opportunity to transform our industry. For this transformation to take place, it is imperative that we change from an industry in which the sole mission is to provide products to one that provides broader, cost-effective solutions to areas of major healthcare needs.

9:40 Grand Opening Refreshment Break in the Exhibit Hall

TARGETING INTERLEUKINS AND INTERFERONS

11:00 Chairperson's Remarks

Charles E. Egwuagu, MPH, Ph.D., Chief, Section on Molecular Immunology, Laboratory of Immunology, National Eye Institute, National Institutes of Health

11:10 IFNs and IFN Antagonists in Disease and Clinical Applications

Sergei V. Kotenko, Ph.D., Associate Professor, Department of Biochemistry & Molecular Biology, University Hospital Cancer Center, UMDNJ - New Jersey Medical School

The IFN family consists of three types of IFNs that signal through distinct receptor complexes to coordinately stimulate a variety of innate and adaptive immune mechanisms that contribute to eliminating viral infections and tumor recognition. At the same time, the potency and pleiotropic effects of IFNs require that their expression must be tightly regulated; and IFNs are suspected to be involved in the pathogenesis of some autoimmune diseases. Therefore, there are clinical situations when inhibition of IFNs seems to be desirable. We recently discovered a secreted viral glycoprotein with unexpected ability to inhibit simultaneously both type I (IFN-α/β) and recently identified type III IFNs (IFN-λs). Thus, new members of the IFN family, as well as their antagonists, represent novel therapeutics with diverse clinical applications that will be discussed.

11:40 CNS Inflammatory Diseases: Development and Regulation by T_H1 and T_H17 Cells

Charles E. Egwuagu, MPH, Ph.D., Chief, Section on Molecular Immunology, Laboratory of Immunology, National Eye Institute, National Institutes of Health

In humans, T_H17 cells increased during active CNS inflammatory disease but decreased following treatment and IL-17-specific antibody treatment reduced disease severity in experimental autoimmune encephalomyelitis and experimental autoimmune uveoretinitis. Interleukin 2, secreted by many T-cell subtypes, promotes T_H17 expansion in patients with uveitis while IFN-g, produced by T_H1 subtype, inhibits T_H17 proliferation by upregulating interleukin-27 in a mouse model of uveitis. Thus, in contrast to T_H17 cells, increase in T_H1 cells correlates with protection from uveitis. This talk will focus on: (i) Our recent experimental findings that provide new perspectives on molecular and cellular mechanisms that regulate development of CNS inflammatory diseases; (ii) Potential therapeutic targets that can be used to mitigate or prevent development of pathogenic autoimmunity; (iii) Mechanistic

explanations for efficacy of Daclizumab therapy in uveitis.

12:10pm IL-6 in Inflammatory Disease

Bailin Liang, Ph.D., Senior Research Scientist, Immunobiology, Centocor

The roles of IL-6 and IL-6 receptor have been actively investigated in inflammatory diseases and cancers. The multiple functions of IL-6 in inflammatory diseases as well as the potential biological therapeutics will be discussed

12:40 Technology Spotlight *(Sponsorship Available)*

1:10 Walk & Talk Luncheon in the Exhibit Hall

DEVELOPING CHEMOKINE ANTAGONISTS

2:15 Chairperson's Remarks

Ziwei Huang, Ph.D., Professor, The Burnham Institute for Medical Research, Professor of Pathology, School of Medicine, University of California at San Diego

2:20 Mechanism of Recognition and Signaling in Chemokine Receptors: Implications for AIDS, Cancer, Immune Diseases and Stem Cell-Based Therapies

Ziwei Huang, Ph.D., Professor, The Burnham Institute for Medical Research, Professor of Pathology, School of Medicine, University of California at San Diego

Chemokines are small chemoattractant cytokines that regulate a wide array of biological and pathological processes. Chemokine receptors have become important and attractive targets for drug discovery. As members of the G protein-coupled receptor (GPCR) superfamily, chemokine receptors are also useful models to study ligand-receptor interactions and signaling mechanisms of GPCRs. Chemokine receptors such as CXCR4 and CCR5 play an important role in HIV-1 pathogenesis, including HIV-associated dementia in the brain. Furthermore, chemokine receptors such as CXCR4 and others mediate a wide variety of physiological and pathological functions including cancer metastasis, autoimmune diseases, transplant rejection, and stem cell migration. Particularly, stem cell migration mediated by chemokines and receptors offers an exciting avenue of developing new stem cell-based regenerative medicine. In collaboration with Chemokine Pharmaceutical Inc., we have recently studied a panel of new synthetic chemokine analogs with very high receptor selectivity and affinity, and much reduced side effect and toxicity. These molecules have been shown to be valuable probes of receptor binding and signaling mechanisms and new therapeutic leads for treating various human diseases mediated by chemokine receptors. In this presentation, we will discuss the latest discovery and application of these novel synthetic molecules for studying the molecular mechanisms of ligand binding and receptor signaling of GPCRs and developing new drugs for AIDS, cancer, autoimmune diseases, and stem cell-based therapies.

2:50 To be Announced

3:20 Targeting CCR9: A Novel Approach to the Treatment of Inflammatory Bowel Disorders

Matthew Walters, Ph.D., Scientist, Biology, ChemoCentryx

ChemoCentryx has developed a potent orally active small molecule inhibitor of CCR9, Traficet-EN.CCR9 is a chemok ine receptor known to play a pivotal role in mediating the migration of T cells to the mucosal surface of the gut. The pathogenicity of CCR9+/CD4+ T-cell is implied by their substantial increase in the circulation of Crohn's Disease patients. Traficet-EN has demonstrated efficacy in preclinical models of IBD and is currently undergoing clinical evaluation in Crohn's Disease patient population.

3:50 Plerixafor: A Selective CXCR4 Antagonist for Hematopoietic Stem Cell Mobilization

Simon P. Fricker, Ph.D., Distinguished Scientific Fellow, Genzyme Corporation

Plerixafor (AMD3100) a selective antagonist of the chemokine receptor CXCR4, is currently being developed for the mobilization of haematopoietic stem cells (HSC) for stem cell transplantation. CXCR4, and its ligand SDF-1, have a central role in haematopoiesis, lymphocyte trafficking and homing, and embryonal and neonatal development. The CXCR4/SDF-1 interaction is a key component of the mechanism of HSC homing and retention in the bone marrow, and disruption of this interaction by plerixafor results in the mobilization of HSC into the peripheral circulation. The molecular and in vivo pharmacology of plerixafor will be described from the perspective of its discovery, properties and mechanism of HSC mobilization, and clinical development.

4:20 Reception in the Exhibit Hall *(Sponsorship Available)*

5:00 - 6:00pm Break-out Discussions in the Exhibit Hall

Expanding the Horizons of Ready-to-Go Cell-Based Assays

Moderator: Jaleel Shujath, PBL Biomedical Laboratories

Targeting Cytokine Interactions

Moderator: Rafael Fernandez-Botran, Ph.D., Associate Professor, Department of Pathology & Laboratory Medicine University of Louisville

What is the Predictive Value of Cytokine Biomarkers in Autoimmune and Inflammatory Diseases?

Moderator: Sandip Ray, Co-founder & Chief Scientific Officer, KidsDx

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Thursday, March 27

LEVERAGING TECHNOLOGIES FOR CYTOKINE-BASED DRUG DEVELOPMENT

8:25 am Chairperson's Remarks

Ziwei Huang, Ph.D., Professor, The Burnham Institute for Medical Research, Professor of Pathology, School of Medicine, University of California at San Diego

8:30 Chemokines and Chemokine Receptors: Novel Targets in Atherosclerosis, Multiple Sclerosis and Insulin Resistance

Israel F. Charo, M.D., Ph.D., Associate Director, Gladstone Institute of Cardiovascular Disease, Professor of Medicine, University of California, San Francisco

This presentation will focus on chemokine biology, results from preclinical work in small animals, and an update on the status of chemokine receptor antagonists in human clinical trials.

9:00 New Integrated Technologies Based on Receptor Structural Prediction and Target-Directed Chemistry to Develop Cytokine-Based Therapeutics

Sameer Kawatkar, Ph.D., Senior Scientist, Drug Discovery, Chemokine Pharmaceuticals Inc.

In this presentation, we will describe the recent development and application of our company's proprietary technologies combining computational modeling of receptor structure and target orientated synthetic chemistry to design and develop novel therapeutics targeting cytokines and receptors. Specifically, examples will be given for using our technologies for drug discovery targeting chemokines, which are small chemoattractant cytokines that regulate a wide array of biological and pathological processes. Chemokine receptors, members of the G protein-coupled receptor (GPCR) superfamily, are involved in a wide variety of physiological and pathological functions including viral infection, cancer metastasis, autoimmune diseases, transplant rejection, and stem cell migration. The general utility of our technologies for drug discovery targeting chemokines and receptors will be discussed.

9:30 Targeting CCR7 to Regulate T Cell-Dependent Immune Responses

Wayne Hancock, M.D., Ph.D., Professor of Pathology and Laboratory Medicine, Children's Hospital of Philadelphia and the University of Pennsylvania School of Medicine

The activation of cognate T cells by antigen-presenting dendritic cells is the key event in cellular immunology. This event requires the trafficking of antigen-bearing dendritic cells to draining lymph nodes, as well as the ceaseless migration of T cells across high-endothelial venules and passage to T cell-rich areas in lymph nodes, and both types of trafficking are regulated by CCR7. We have used genetically targeted knockout mice, fusion proteins and monoclonal antibodies to dissect the importance of this pathway in host T cell responses. We report that in those situations in which draining lymph nodes are the key site of antigen presentation, targeting of the CCR7 pathway can have profound therapeutic consequences. Basic science and practical therapeutic aspects of these data will be presented.

10:00 Technology Spotlight *Sponsored by* ProtAffin

Modifying Chemokines Towards Anti-Inflammatory Activity: The CellJammerR Technology

Prof. Andreas Kungl, Ph.D.Chief Scientific Officer, Protaffin Biotechnologie AG

The interaction of chemokines and glycosaminoglycans (GAGs) on endothelial surfaces is crucial for functional presentation of chemokines to their GPCRs. ProtAffin uses its CellJammer®discovery technology to create unique protein-based GAG antagonists. Following rational design, our therapeutic chemokine mutants exhibit strongly enhanced GAG-binding affinity as well as knocked-out GPCR activity. Our lead compound, PA401, is based on human IL-8 and has shown strong efficacy in a number of in vivo models of inflammatory diseases.

10:15 Technology Spotlight *Sponsored by* RBM

ILCS®: Cytokine Therapy or Cytokine Storm

Ralph L. McDade, Ph.D., Strategic Development Officer, Rules-Based Medicine, Inc.

Instant Leukocyte Culture System (ILCS®) is the first standardized whole blood culture system that provides reproducible leukocyte stimulation without the need of a tissue culture facility or specially trained personnel. Coupled with a 47-plex panel of cytokines, the RBM-ILCS test is the most comprehensive and informative in the immuno-modulation/toxicity industry. Results of a case study discerning a "TeGenero-like cytokine storm" will be presented.

10:30 Poster Competition & Refreshment Break in the Exhibit Hall

PANEL DISCUSSION

11:30 Drug Discovery Targeting Protein-Protein Interactions

- Protein targets in cytokine networks and pathways – new technologies and concepts
- Case studies – success stories and lessons learned
- Current and future trends – using small molecules and synthetic protein- or peptide-based analogs, medicinal chemistry and cytokine biology

Chairperson:

Ziwei Huang, Ph.D., Professor, The Burnham Institute for Medical Research, Professor of Pathology, School of Medicine, University of California at San Diego

Panelists:

Harsukh Gevariya, Ph.D., Senior Scientist, Drug Discovery, Raylight Corp.

Israel F. Charo, M.D., Ph.D., Associate Director, Gladstone Institute of Cardiovascular Disease, Professor of Medicine, University of California, San Francisco

Wayne Hancock, M.D., Ph.D., Professor of Pathology and Laboratory Medicine, Children's Hospital of Philadelphia and the University of Pennsylvania School of Medicine

Simon Fricker, Ph.D., Distinguished Scientific Fellow, Genzyme Corporation

12:30pm Luncheon Workshop *(Sponsorship Available)* **or Lunch on Your Own**

1:30 Break

TARGETING THE TNF FAMILY

1:45 Chairperson's Remarks

Iqbal S. Grewal, Ph.D., FRCPath, Vice President, Preclinical Therapeutics, Seattle Genetics, Inc.

1:50 CD70 as a Target for Antibody-Based Therapeutics

Iqbal S. Grewal, Ph.D., FRCPath, Vice President of Preclinical Therapeutics, Seattle Genetics, Inc.

CD70 is preferentially expressed on activated B and T cells and play an important role in the immune system. In addition, CD70 is abundantly expressed in multiple malignancies. Humanized anti-CD70 monoclonal antibodies as naked antibodies or conjugated to a potent toxic drug, an auristatin derivative, demonstrate significant activity in xenograft models of cancers. An antibody against mouse anti-CD70 also shows beneficial effects in animal models of autoimmunity. In summary, our studies reveal the potential of CD70 as a novel target for antibody-based therapeutics in variety of cancer indications and autoimmunity.

2:20 Preclinical Studies of Anti-OX40L in TH2-driven Diseases

Sarah Hymowitz, Ph.D., Scientist, Protein Engineering, Genentech

OX40L is a critical *in vivo* mediator of TSLP-mediated Th2 responses. Blocking anti-OX40L antibodies significantly inhibit *in vivo* Th2 inflammatory infiltrate, cytokine secretion and IgE induced by TSLP in the lung and skin. Anti-OX40L antibodies are also efficacious in inhibiting antigen-driven Th2 inflammation in mouse and non-human primate models of asthma. Blocking anti-OX40L monoclonal antibodies present a promising strategy for the treatment of human allergic diseases associated with pathologic Th2 immune responses.

2:50 TWEAKing Inflammatory Disease by a Multifunctional Cytokine

Linda Burkly, Ph.D., Distinguished Investigator, Immunology, Biogen Idec

TWEAK (TNF-like weak inducer of apoptosis) is a relatively new member of the TNF family first discovered in macrophages. Similar to other members, TWEAK can act as a soluble cytokine which exerts context-dependent pleiotropic effects on a variety of cell types *in vitro* through its receptor FGF-inducible molecule 14 (Fn14). We have used genetically engineered mice and anti-TWEAK neutralizing mAbs to investigate the biological role of the TWEAK/Fn14 pathway *in vivo*. Our studies demonstrate that TWEAK is a novel pathogenic mediator in autoimmune disease models, suggesting that TWEAK may be a new therapeutic target for the treatment of inflammatory diseases.

3:20 Plenary Keynote Speaker
Ice Bound - A Doctor's Incredible Battle for Survival at the South Pole

Dr. Jerri Nielsen, MD.

In the coldest and most isolated place on earth, Dr. Jerri Nielsen, author of Ice Bound, found the courage to survive. As sole doctor on a 12-month scientific expedition, she diagnosed her own breast cancer. The Antarctic winter made leaving impossibility, thereby forcing Dr. Nielsen and her teammates to use their skills and resourcefulness to treat her illness. This is an incredible story of one women's courage and survival.

4:00 Ice Cream Refreshment Break in the Exhibit Hall with BEST OF SHOW AWARDS

4:45 The Role of BAFF in Autoimmunity is T Cell-Independent but Requires MyD88 Signaling

Professor Fabienne Mackay, Ph.D., Director, Autoimmunity Research Unit, Wellcome Trust Senior Research Fellow, Garvan Institute of Medical Research

The TNF-like ligand BAFF is a fundamental survival factor for B cells, essential during their maturation. However, overproduction of BAFF in transgenic (Tg) mice triggers autoimmune disorders similar to Systemic Lupus Erythematosus (SLE) and Sjögren's syndrome (SS), possibly as the result of abnormal self-reactive B cell survival. Intriguingly, we showed that excess BAFF only mildly affected B cell immune tolerance, could not prevent deletion of high affinity self-reactive B cells but could rescue some low affinity self-reactive B cells, in particular marginal zone (MZ) B cells. As germinal center formation and antibody affinity maturation were not essential for disease in these mice, we questioned the real implication of low affinity autoreactive B cells in driving the disease. Indirect and direct effects of BAFF on T cell activation and expansion of the effector T cell compartment in BAFF Tg mice were then thought to perhaps contribute to nephritis in these animals. Surprisingly, BAFF Tg mice lacking T cells develop the same autoimmune disease as the original BAFF Tg mice. Interestingly, MyD88-/- B cells had impaired autoantibody production in BAFF Tg mice. Thus, this work revealed that autoimmunity in BAFF Tg mice is the result of an abnormal innate B cell response involving the combined effects of excess BAFF and TLR signaling.

5:15 Novel Ways to Target TNF Family Members for Inflammation

Sanjay Khare, Ph.D., President, ImmunGene

Several TNF family members are crucial in health and disease. So far, targeting one pathway provides partial benefit in some patients. Improved methods will be discussed to selectively target these pathways.

5:45 End of Day

Friday, March 28

NOVEL THERAPEUTIC TARGETS – PROCESSES, PATHWAYS AND NETWORKS

8:30am Chairperson's Remarks

Thomas Hamilton, Ph.D., Chairman, Department of Immunology, Lerner Research Institute, Cleveland Clinic; Editor-in-Chief, Journal of Interferon & Cytokine Research

8:35 Post-Transcriptional Controls of Cytokine Expression

Thomas Hamilton, Ph.D.

It is becoming widely recognized that the expression levels of many cytokines (TNF, IL-1, IL-6, chemokines) are determined at post-transcriptional levels including mRNA processing, decay, and translation. The activities that regulate these processes are potential therapeutic targets that may provide more precise modulation of inflammatory activity.

9:05 Regulation and Function of Inflammatory TH17 Cells

Chen Dong, Ph.D., Associate Professor, Department of Immunology, MD Anderson Cancer Center

9:35 The Regulatory Role of SIGIRR in Colonic Epithelial Homeostasis, Inflammation and Tumorigenesis

Xiaoxia Li, Ph.D., Department of Immunology, Lerner Research Institute, Cleveland Clinic

Despite constant contact with the massive population of commensal bacteria, the colonic mucosa is normally hypo-responsive to these potentially proinflammatory threats. Here we report that the single immunoglobulin IL-1 receptor related molecule (SIGIRR), a negative regulator for Toll-IL-1R signaling, plays a critical role in gut homeostasis, intestinal inflammation and colitis-associated tumorigenesis by maintaining the microbial tolerance of the colonic epithelium. SIGIRR-deficient colonic epithelial cells displayed commensal bacteria-dependent intrinsic homeostatic defects, accompanied by constitutive upregulation of inflammatory genes, increased inflammatory responses to DSS challenge and increased AOM+DSS-induced colitis-associated tumorigenesis. The gut-epithelium specific expression of the SIGIRR-transgene in the SIGIRR-deficient background reduced the cell survival of the SIGIRR-deficient colon epithelium, abrogated the hypersensitivity of the SIGIRR-deficient mice to DSS-induced colitis and reduced AOM+DSS-induced tumorigenesis. Taken together, our results indicate that epithelium-derived SIGIRR plays a critical role in controlling the homeostasis and innate immune responses of the colon to enteric microflora.

10:05 Technology Spotlight *(Sponsorship Available)*

10:20 Coffee Break in the Foyer

PANEL DISCUSSION

11:00 Cytokine Networks and the Challenge of Targeted Therapies

Chairperson:

Chen Dong, Ph.D., Associate Professor, Department of Immunology, MD Anderson Cancer Center

Panelists:

Linda Burkly, Ph.D., Distinguished Investigator, Immunology, Biogen Idec

Thomas Hamilton, Ph.D., Chairman, Department of Immunology, Lerner Research Institute, Cleveland Clinic; Editor-in-Chief, Journal of Interferon & Cytokine Research

Iqbal S. Grewal, Ph.D., FRCPath, Vice President, Preclinical Therapeutics, Seattle Genetics, Inc.

12:00pm Luncheon Workshop *(Sponsorship Available)*
or Lunch on Your Own

THERAPEUTIC POTENTIAL OF CYTOKINE TARGETS

1:00 Chairperson's Remarks

Rafael Fernandez-Botran, Ph.D., Associate Professor, Department of Pathology & Laboratory Medicine University of Louisville

1:05 Targeting Cytokine Interactions with Glycosaminoglycans to Modulate Inflammation

Rafael Fernandez-Botran, Ph.D., Associate Professor, Department of Pathology & Laboratory Medicine University of Louisville

Many cytokines and chemokines are able to interact with cell surface and matrix glycosaminoglycans (GAGs). These cell- or tissue-bound mediators accumulate near the site of secretion and function to promote cell recruitment and inflammation. Disruption of cytokine-GAG interactions by means of binding inhibitors would then have a potential to interfere with leukocyte recruitment and activation, thus inhibiting inflammation. Supporting evidence will be presented and discussed.

1:35 Cytokine Receptor Signaling in Hematopoietic Stem Cells and Myeloprolferative Diseases

Wei Tong, Ph.D., Assistant Professor, Hematology Division, Department of Pediatrics, Children's Hospital of Philadelphia (CHOP), University of Pennsylvania School of Medicine (U PENN)

This presentation will aim to elucidate the molecular mechanisms by which the adaptor protein, Lnk, downregulates cytokine receptor and JAK2 pathways in controlling hematopoietic stem cell (HSC) activity as well as the potential involvement of Lnk dysfunction in hematologic malignancies.

2:05 Title to Be Determined

2:35 NLRX1: A Novel Inhibitor of Mitochondrial Antiviral Signaling and Type 1 Interferon

Christopher Moore, Ph.D., Jenny Ting Lab, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill

NLRX1 is a novel highly conserved member of the NLR protein family. This protein functions as a constitutive inhibitor of MAVS-mediated antviral responses from within the mitochondria. Overexpression of NLRX1 is inhibitory while siRNA-mediated reduction of NLRX1 results in the enhanced production of virally-mediated type 1 interferon production. Discovery of the function of this protein represents the intersection of three ancient cellular processes-NLR protein signaling, the intracellular detection of virus, and the role of the mitochondria as a platform for cell signaling.

3:05 Close of Conference

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Cambridge Healthtech Institute (CHI) appreciates your past participation at the Molecular Medicine Tri-Conference. Through loyalty like yours, CHI has been able to build this event into a must attend for senior level decision-makers. As a result of the great loyalty you have shown us, we are pleased to extend to you the exclusive opportunity to save an additional 25% off the registration rate. Just check off the box marked Alumni Discount on the registration form to receive the discount!

Please note: Our records must indicate you were an attendee of the Tri-Conference event in the past in order to qualify.

Sponsoring Publications

BENTHAM SCIENCE · BIOPHOTONICS INTERNATIONAL · Current Medicinal Chemistry · Current Topics in Medicinal Chemistry · DRUG DISCOVERY NEWS · Future Pharmaceuticals · Genome Technology

Web Partners

BioSpace · CanBiotech Biotechnology Portal & B2B Marketplace · genomeweb · hum-molgen.org central gateway to HUMan MOLecular GENetics · SelectScience.net The Scientists' Choice

Supporting Organization

BAYBIO

YES! Register me for CYTOKINE-BASED THERAPEUTICS, *Part of Molecular Medicine Tri-Conference* **CYA F**

1. REGISTRATION INFORMATION:

❒ Mr. ❒ Ms. ❒ Mrs. ❒ Dr. ❒ Prof.

Name

Job Title Div./Dept.

Company

Address

City/State/Postal Code

Country

Telephone

Would you like to receive event updates via fax ❒ Yes ❒ No Fax

Email*

**Email is not a mandatory field. However, by excluding your email you will not receive notification about online access to pre-conference presenter materials, conference updates and networking opportunities.*

2. PRICING INFORMATION:

PRE-CONFERENCE EVENTS (MARCH 25)

❒ $995 **The Biotech Pharma Partnership**

Choose 1 Short Course:
❒ $695 Commercial
❒ $345 Academic, Government, Hospital-Affiliated

Choose 2 Short Courses:
❒ $995 Commercial
❒ $595 Academic, Government, Hospital-Affiliated

Best Value

MORNING SHORT COURSES:
❒ (SC1) Biomarkers Are Us
❒ **(SC2) Blood-Brain Barrier**
❒ (SC3) ADMET
❒ (SC4) The Epigenetics Stem Cell Signature
❒ **(SC5) Immunological Biomarkers**

AFTERNOON SHORT COURSES:
❒ (SC6) Circulating Tumor Cells
❒ (SC7) Cancer Stem Cells
❒ **(SC8) Drug-Drug Interactions**
❒ (SC10) Navigating Through Indian Regulatory Terra Incognita

	Commercial	Academic, Government, Hospital-Affiliate
Track Pricing (March 26-28)		
Access to 250+ Presentations Covering 11 Tracks, CHI's Intro-Net, Scientific Posters and more!		
Early Registration until January 11, 2008	❒ $1545	❒ $845
Advance Registration until February 22, 2008	❒ $1695	❒ $995
Registration after February 22, 2008	❒ $1895	❒ $1045

Track Selection: (REQUIRED)
CHOOSE ONE: Please indicate the ONE track you are most likely to attend.

❒ Track 1: Molecular Diagnostics
❒ Track 2: Mastering Medicinal Chemistry
❒ Track 3: Pathway Analysis
❒ Track 4: Stem Cells Congress
❒ Track 5: R&D Risk Mitigation
❒ Track 6: Clinical Trials Asia
❒ Track 7: Preclinical Development
❒ Track 8: Translational Medicine
❒ **Track 9: Cytokine-Based Therapeutics**
❒ Track 10: Cancer Molecular Markers
❒ Track 11: Trends in Drug Safety

❒ Yes, I will attend Clayton Christensen's Keynote presentation (March 25)

Discounts*
❒ Poster ($50 off) ❒ Alumni (25% off) ❒ BayBio Member (25% off)
** (See page 2 for Alumni details • Alumni and Bay Bio Discount cannot be combined • Discounts not applicable on Pre-Conference Events only registrations)*

❒ Yes, I want to take advantage of the hotel incentive offer* at $75 off
My confirmation number is _____ ❒ InterContinental San Francisco Hotel or ❒ Westin Market Street Hotel
* Must be under the Molecular Medicine Tri-Conference room block for a minimum of three nights.

Purchase presentation materials for the entire event for only $750.
CD Includes presentation material from all eleven tracks, poster abstracts and more.
❒ I cannot attend but would like to purchase the event CD for $750 (plus shipping) (Massachusetts delivery will include 5% sales tax).

3. PAYMENT INFORMATION:

❒ Enclosed is a check or money order payable to Cambridge Healthtech Institute, drawn on a U.S. bank, in U.S. currency.
❒ Invoice me, but reserve my space with credit card information listed below.
Invoices unpaid two weeks prior to conference will be billed to credit card at full registration rate. Invoices must be paid in full and checks received by the deadline date to retain registration discount. If you plan to register on site, please check with CHI beforehand for space availability.
❒ Please charge: ❒ AMEX (15 digits) ❒ Visa (13-16 digits) ❒ MasterCard (16 digits) ❒ Diners Club (14 digits)

Card # Exp. Date

Cardholder

Signature

Cardholder's Address (if different from above)

City/State/Postal Code

Country

Please refer to the Registration Code below:

REGISTER 3 – 4th IS FREE
Individuals must register for the same conference or conference combination and submit completed registration forms together for discount to apply. Please reproduce this registration form as needed

PRESENT A POSTER AND SAVE $50
Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference CD, your abstract must be submitted, accepted and registration paid in full by **February 12, 2008**. Register online to use the Poster Abstract Submission form or, if you register by phone, fax, or mail, you will receive Poster Abstract Submission guidelines via email.
(Please Note: Registration must be paid in full to present a poster.)
Title _____

Yes! I would like to receive a FREE subscription to:

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

ADDITIONAL REGISTRATION DETAILS
Each registration includes all conference sessions, posters and exhibits, food functions, and a copy of the conference CD.

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

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

SUBSTITUTION/CANCELLATION POLICY
In the event that you need to cancel a registration, you may:
- Transfer your registration to a colleague within your organization
- Credit your registration to another Cambridge Healthtech Institute program
- Request a refund minus a $100 processing fee per conference
- Request a refund minus the cost ($750) of ordering a copy of the CD

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

Program and speakers are subject to change.

Video /audio recording of any kind is prohibited onsite.

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