Cambridge Healthtech Institute's 17th International

Molecular Medicine Tri-Conference 2010

Conference: February 3-5 | Exhibits: February 3-4
Moscone North Convention Center | San Francisco, CA

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DIAGNOSTICS CHANNEL
Molecular Diagnostics
Personalized Diagnostics
Cancer Molecular Markers

CHEMISTRY CHANNEL
Mastering Medicinal Chemistry

INFORMATICS CHANNEL
Adopting R&D Informatics Systems
Cancer Profiling and Pathways

BIOLOGICS CHANNEL
Stem Cells
RNA Interference
Cancer Biologics
Delivery of Biologics

CANCER CHANNEL
Cancer Molecular Markers
Cancer Profiling and Pathways
Cancer Biologics

EXECUTIVE CHANNEL
Translational Medicine

PLENARY KEYNOTES

When Drug Research is Personal
John F. Crowley, Founder,
Novazyme Pharmaceuticals, Inc.

Technology, Aging, and the Brain
Gary W. Small, M.D., Professor,
David Geffen School of Medicine,
University of California,
Los Angeles

Chips, Clones and Living Beyond 100
Paul J.H. Schoemaker, Ph.D., M.B.A., Professor,
Wharton School of Business

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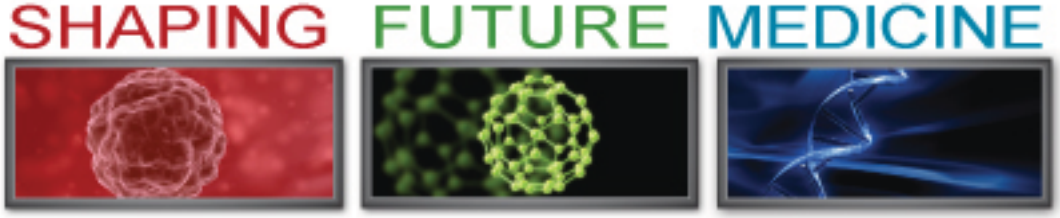

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Tri-Conference.com

Molecular Medicine **Tri-Conference** 2010

CONFERENCE-AT-A-GLANCE

Tuesday, February 2	
8:00 AM	Morning Short Course Registration and Coffee
9:00 - 12:00 PM	**Morning Short Courses (Courses 1-6)**
10:15 - 10:30	Networking Coffee Break
1:00 - 2:00	Afternoon Short Course Registration
2:00 - 5:00	**Afternoon Short Courses (Courses 7-12)**
3:15 - 3:30	Networking Refreshment Break
5:00	Close of Day
Wednesday, February 3	
7:00 AM	Registration and Morning Coffee
8:00 - 9:40	Plenary Keynotes
9:40 - 11:00	Grand Opening Refreshment Break in the Exhibit Hall
11:00 - 12:40 PM	**Concurrent Channels**
12:40 - 1:45	Sponsored Luncheon Presentations or Lunch on Your Own
1:45 - 2:15	Dessert in the Exhibit Hall
2:15 - 4:20	**Concurrent Channels**
4:20 - 5:20	Reception in the Exhibit Hall *(Sponsorship Available)*
5:20 - 6:20	Break-out Discussions
6:20	Close of Day
Thursday, February 4	
8:25 - 10:30 AM	**Concurrent Channels**
10:30 - 11:30	Poster Competition, Refreshment Break & Raffles in the Exhibit Hall
11:30 - 12:30 PM	**Concurrent Channels**
12:30 - 1:45	Sponsored Luncheon Presentations or Lunch on Your Own
1:45 - 2:15	Ice Cream Refreshment Break in the Exhibit Hall
2:15 - 3:05	Plenary Keynote Session
3:05 - 3:45	Refreshment Break in the Exhibit Hall
3:45 - 5:50	**Concurrent Channels**
5:50	Close of Day
Friday, February 5	
8:30 - 10:20 AM	**Concurrent Channels**
10:20 - 11:00	Coffee Break
11:00 - 12:00 PM	**Concurrent Channels**
12:00 - 1:00	Sponsored Luncheon Presentations or Lunch on Your Own
1:00 - 3:05	**Concurrent Channels**
3:05	Close of Conference

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Online: Tri-Conference.com **Email:** reg@healthtech.com **Fax:** 781-972-5425

PRE-CONFERENCE SHORT COURSES*

Tuesday, February 2

*Separate Registration Required

MORNING COURSES: 9AM – 12PM

(SC1) APPLYING NEXT GENERATION SEQUENCING TECHNOLOGIES TO RESEARCH

Introduction to New Technologies and Application in Research

- Technologies for newest platforms for next generation sequencing
- Strategies and tools for managing data
- Demonstration of how tools can be applied to research

Course Moderator:
Stanley Gloss, Founding Partner Managing Director, BioTeam, Inc.
Course Instructors:
Francisco M. De La Vega, D.Sc., Distinguished Scientific Fellow, Computational Genomics Research, Genetics Systems R&D, Life Technologies
Giles Day, Senior Director, BBC Informatics, Pfizer Biotherapeutics & Bioinnovation Center
Ronald W. Davis, Ph.D., Professor, Biochemistry & Genetics, and Director, Stanford Genome Technology Center, Stanford University

(SC2) ONE CASE STUDY IN BREAST CANCER- THREE PERSPECTIVES

Illustrating Current Challenges in Personalized Medicine

- Overview of case study
- Clinical perspective
- Diagnostic and biomarker perspective
- Payer perspective

Course Instructors:
Michael Liebman, Ph.D., Managing Director, Strategic Medicine, Inc.
Laura J. Esserman, Professor, Surgery, University of California, San Francisco Medical Center
Tracey Colpitts, Ph.D., Manager, Abbott Molecular

(SC3) MIGHTY MITOCHONDRIA: Their Relevance to Disease and Translational Medicine

- Mitochondria in disease and drug induced toxicity (James Dykens)
- Assessing mitochondrial function preclinically (Yvonne Will)
- Non-invasive mitochondrial assessment in the clinic (Robert Wiseman)

Course Leader:
Yvonne Will, Ph.D., Compound Safety Prediction- WWMC, Cell Based Assays and Mitochondrial Biology, Pfizer R&D
Course Instructors:
James Dykens, Ph.D., Drug Safety R&D, Pfizer Inc
Yvonne Will, Ph.D., Compound Safety Prediction- WWMC, Cell Based Assays and Mitochondrial Biology, Pfizer R&D
Robert Wiseman, Ph.D., Associate Professor, Department of Physiology, Michigan State University

(SC4) ADDRESSING SAFETY CONCERNS FOR BIOLOGICAL DRUGS

- Overview of challenges pertaining to safety for biologics
- Safety assessments at pre-clinical and clinical stage
- Use of new assays, animal models and biomarkers for early predictions
- Regulatory guidelines and their interpretations

Course Instructors:
Hong Wang, Ph.D., DABT, Safety Assessment, Genentech Inc.
Kathleen Meyer, MPH, Ph.D., DABT, Senior Director, Preclinical Safety Evaluation, XOMA (US) LLC

(SC5) TARGETING CANCER STEM CELLS WITH BIOLOGICS

- Novel nanoparticle fusion proteins, tr1 and tr4, that achieve normal p21 delivery to p53/p21 mutated tumors (tr1) and inhibition of notch signaling (tr4) resulting in tumor eradication
- Differentiation versus self-renewal: changing cancer stem cell fate by targeting stem cell pathways
- Cancer stem-like cells: isolation using biological criteria and use in drug discovery and development
- Cd47: an adverse prognostic factor and therapeutic antibody target on human acute myeloid leukemia stem cells
- Identification of stem cell markers in the normal prostate and prostate cancer

Course Instructors:
Agamemnon Epenetos, Ph.D., FRCP, Chairman, Trojantec Ltd.
Austin Gurney, Ph.D., Vice President, Molecular and Cellular Biology, OncoMed Pharmaceuticals, Inc.
Jennie P. Mather, Ph.D., Senior Vice President, Stem Cell Research, MacroGenics, Inc.
Ravi Majeti M.D., Ph.D., Assistant Professor, Division of Hematology, Stanford Cancer Center, Institute for Stem Cell Biology and Regenerative Medicine
Kevin G. Leong, Ph.D., Scientist, Tumor Biology and Angiogenesis, Genentech, Inc.

(SC6) BLOOD-BRAIN BARRIER

- The physiological basis for the "barrier" nature of the BBB
- Experimental approaches (*in vitro/in vivo*) that are available for screening for brain penetration
- Medicinal Chemistry perspective on *in vitro/in silico* approaches for optimizing CNS penetration
- Multi-parameter optimization (MPO) for CNS penetration
- *In vivo* examples where all these concepts are applied together, e.g., consideration of free fractions in various compartments in relation to *in vitro* pharmacology values
- Projecting human receptor occupancies considering species differences in affinity, free fraction
- Exposure targeting for biomarker studies

Course Instructors:
Christopher L. Shaffer, Ph.D., Associate Research Fellow, Pharmacokinetics, Dynamics & Metabolism, Pfizer, Inc.
Douglas Spracklin, Ph.D., Director, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.
Travis T. Wager, Ph.D. Associate Research Fellow, Neuroscience Discovery, Medicinal Chemistry, Pfizer, Inc.

AFTERNOON COURSES: 2PM – 5PM

(SC7) BEST PRACTICES IN TRANSLATIONAL & PERSONALIZED MEDICINE

- Real world solutions currently in place in pharma, national labs, academia, and industry
- Building collaborations and sharing biological data between Big Pharma
- Bridging the gap between bench and bedside
- Informatics solutions that link data from the clinic with cutting edge research

Course Instructors:
Jeffrey S. Barrett, Ph.D., FCP, Pediatrics Director, Pediatric Pharmacology Research Unit, The Children's Hospital of Philadelphia
Lisa LaLuna, Senior Vice President, Corporate Development & Implementation, ePharmaSolutions
Jeremy Packer, Head, Bioinformatics, Abbott
Faye D. Schilkey, Associate Director, NM Sequencing Center, National Center for Genome Resources

(SC8) STRATEGIES FOR MOLECULAR DIAGNOSTIC COMPANIES

Achieving Success in Rapidly Changing Markets

- Why and how diagnostics markets have changed
- Strategies for success: conventional or new markets?
- Major business model questions including partnering
- How to obtain your next round of funding

Course Instructors:
Keith F. Batchelder, Chief Executive Officer, Genomic Healthcare Strategies
Peter S. Miller, Chief Operating Officer, Genomic Healthcare Strategies

(SC9) FRAGMENT-INSPIRED MEDICINAL CHEMISTRY

- Fragment-based approaches as platforms for medicinal chemistry
- Fragment-based methods that inspire fresh approaches to lead generation
- Optimization of fragment hits
- Combining technology with fragment-based methods to advance medicinal chemistry
- Facing the challenge of applying fragment-based approaches when structural information is not available
- Promises and pitfalls of surface plasmon resonance (SPR) for fragment methods

Course Instructors:
Michelle Arkin, Ph.D., Associate Director, Biology, Small Molecule Discovery Center, Pharmaceutical Chemistry, University of California, San Francisco
Daniel A. Erlanson, Ph.D., Co-founder, Carmot Therapeutics, Inc.

(SC10) TRANSPORTER-MEDIATED DRUG-DRUG INTERACTION POTENTIAL

Strategies for in vitro Characterization

- Clinical relevance of transporter DDI's
- *In vitro*, cell based models for evaluating transporter interactions of substrates and inhibitors
- Case study: minimizing p-glycoprotein interactions as a barrier to CNS penetration

Course Instructors:
Phil Burton, Ph.D., Chief Executive Officer & Chief Scientific Officer, ADMETRx, Inc.
Xingrong Liu, Ph.D., Senior Scientist, DMPK, Genentech, Inc.
Joseph A. Ware, Ph.D., Senior Scientist, Clinical Pharmacokinetics and Pharmacodynamics, Development Sciences, Genentech, Inc.

(SC11) BASIC IMMERSION: CUTTING EDGE SCIENCE & TECHNOLOGY FOR BIOTECH & PHARMA

- Gain a fundamental understanding of the science and technology driving the Biotech/Pharma industry
- Learn basic scientific terminology used by researchers in the life sciences
- Designed for the non-scientist working with or in the biotech/pharma industry
- Immersion course on the biotech basics; Recombinant DNA, Proteins, Stem Cells, Biologics, Drug Discovery and Drug Development

Class Materials Include: The Primer: A Biotechnology Guide for Non-Scientists
Course Instructor:
Karin Lucas, Ph.D., BioTech Primer Instructor and Scientific Advisor

(SC12) DESIGNING RIGOROUS OMICS STUDIES FOR BIOMARKER DISCOVERY AND DEVELOPMENT OF PROGNOSTIC AND PREDICTIVE MOLECULAR DIAGNOSTICS

- Why study design is decisive for success or failure
- Critical review of examples
- Dos and don'ts
- A roadmap to the answers
- Samples: How many are enough?
- Apples and Oranges: Tackling confounding factors
- Companion diagnostics in clinical trials
- The regulatory perspective

Course Instructors:
Terry Speed, Ph.D., Professor, Department of Statistics, University of California, Berkeley
Juergen von Frese, Ph.D., Managing Director, Data Analysis Solutions, DA-Sol GmbH
Donna Roscoe, Ph.D., Senior Reviewer, FDA/OIVD/DIHD

Cambridge Healthtech Institute's Seventh Annual

Molecular Diagnostics:
Next Wave of Personalized Medicine

Industry leader's networking event

WEDNESDAY, FEBRUARY 3

7:00 AM Registration and Morning Coffee

8:00 Plenary Keynote Session *(See Page 26 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

KEYNOTE PRESENTATIONS

11:00 Chairperson's Remarks
Harry Glorikian, Managing Partner, Scientia Advisors

11:05 Molecular Diagnostics as a Value Driver of Pharma/ Pharma as a Value Driver for Molecular Diagnostics
Michael C. Little, Global Head, Diagnostics Development, Novartis Molecular Diagnostics
Molecular Diagnostics is a critical success factor for the future of pharmaceuticals and an essential aspect of the move toward personalized medicine. At the same time, to progress better healthcare and patient outcomes, it is imperative that the pharma industry's understanding of both targeted drug discovery and drug commercialization is fully leveraged to enable innovative diagnostics to be put into clinical practice and influence physician decision-making. The keynote will focus on these elements and discuss 1-2 case studies of how we at Novartis are using our discovery and development approach to work toward bringing innovative companion and stand-alone diagnostic tests to market.

11:40 Building a Successful Diagnostics Business Model in the Era of Personalized Medicine
Richard Ding, CEO, bioTheranostics, a bioMerieux Company Personalized medicine has been generally accepted as an inevitable trend in healthcare. However, much debate is still ongoing related to a sustainable business model for diagnostics companies in this new space. This presentation will identify various challenges, risks and potential returns for diagnostic companies, explore partnership models and propose some basic framework to seize the growth opportunity of personalized medicine.

12:15 PM Personalized Medicine: It Takes a Village
Mark Stevenson, President & COO, Life Technologies Corp.
New technologies, such as next generation sequencing, can be rapidly adopted in the research labs and help breakthroughs in our understanding of disease mechanisms for personalized medicine. But the journey from research technology to diagnostic systems is challenging and slow. As our understanding of disease increases the promise of personalized medicine is coming closer but what will it take to cross the bridge from research tool to routine diagnostics in personalized medicine. The Presentation will focus on the journey Life Technologies has embarked on and the partnerships and collaborations necessary to translate the tools for the research lab into solutions personalized medicine.

12:50 Luncheon Presentation
Information Trends in Biomarker Research
Sponsored by THOMSON REUTERS
Colin Williams, Ph.D., Director, Product Strategy, Thomson Reuters Healthcare and Science
In recent years, the quantity of data published on biomarker research has exploded. The challenge faced by researchers is to find vital, relevant information on the best biomarker quickly and reliably. In this discussion we will introduce BIOMARKERcenter, a comprehensive, fully-indexed biomarker information resource, and through case studies show how it aids the discovery process.

1:45 Dessert in the Exhibit Hall

MOLECULAR DETECTION OF PATHOGENS: MEETING THE NEEDS OF THE COMMUNITY

2:15 Chairperson's Remarks

2:20 Real-time Detection and Characterization of Influenza: The Need for Speed
Karen L. Kaul, M.D., Ph.D., Board of Directors Chair of Molecular Pathology, Director, Molecular Diagnostics Division, Director, Pathology Residency Program, NorthShore University HealthSystem; Clinical Professor of Pathology, University of Chicago Pritzker School of Medicine
The Novel H1N1 Influenza outbreak of 2009 challenged laboratories and hospitals with the need for high volume testing and rapid resulting in order to appropriately treat and isolate infected patients. Molecular approaches offer clear advantages, though no pre-validated assays were available for this unanticipated virus. This presentation will address various assays for detection and differentiation, as well as other laboratory issues, and will review the recent outbreak from the laboratory perspective.

2:50 What Happened with SARS: Lessons Learned and Applied to Influenza
Joseph D. Miller, Ph.D., Chief, Laboratory Preparedness Officer, Influenza Division, Centers for Disease Control and Prevention

3:20 MRSA Surveillance Programs – What Impacts Success?
Lance R. Peterson, M.D., FASCP, FIDSA, Director, Microbiology & Infectious Disease, Evanston Hospital, NorthShore University HealthSystem and University of Chicago
Control of any epidemic relies on detection of those harboring the pathogen (infected and colonized). For any MRSA prevalence, the operational processes most influential are 1) sensitivity of the laboratory methods used, 2) speed at which unknown positive patients are detected, and 3) the selection of who is to undergo screening. The current understanding of these specifics will be presented.

3:50 Real-time Array PCR for Infectious Diseases(RAP-ID): Merging Multiplex PCR and Real-Time Microarray Detection in a Single Tube for Sensitive Parallel Genotyping of Pathogens and Antibiotic Resistances
Sponsored by eppendorf Array Technologies
Wilhelm Pluester, Ph.D., CEO, Eppendorf Array Technologies S.A.
RAP is a novel hybrid technology combining major advantages of microarrays (multiplexing, specificity) and real-time PCR (sensitivity, dynamic range). Target amplification and hybridization of amplicons proceed in a single tube (in the same buffer) resulting in a simplified, automated workflow with minimal hands-on time. First results in multiplex detection of pathogens and antibiotic resistances associated with ventilator-associated pneumonia are presented.

4:05 Platform Genometrica: Novel Instrumentation for Molecular Biology and Medicine
Sponsored by genometrica
Vera Gorfinkel, Ph.D., Associate Professor, SUNY SB, Research consultant, Genometrica Corporation
The technology platform Genometrica aims to develop methods and instruments capable of carrying out on equal footing inexpensive and highly accurate genomic studies including DNA sequencing, hybridization, and quantitative PCR assays. The session will focus on the basic principles, novel engineering solutions, data acquisition/handling methods, and unique research capabilities offered by the Genometrica platform.

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

5:20 BREAK-OUT DISCUSSIONS in the Exhibit Hall

Consumer Diagnostics (Not Just Genomics) – Get Used to It!

Co-Moderators: Peter S. Miller, Chief Operating Officer, and Keith F. Batchelder, Chief Executive Officer, Genomic Healthcare Strategies

- Technology improvements and cost reductions will make genetic, metabolic, and proteomic analysis cheaper
- Consumers will remain interested and companies will develop better ways of reaching the public
- Providers of traditional care will have to come to grips with informed consumers
- How will this happen?

Is Economics Going to Be the Driver of Molecular Diagnostics Adoption?

Moderator: David S. Lester, Ph.D., Vice President, Human Health Solutions, Theranos

- Are molecular diagnostics going to make healthcare cheaper and/or better?
- What are the barriers for adoption of molecular diagnostics?
- Payers: US vs. international challenges.
- How will value of the diagnostic be determined?

Patents and Diagnostics Development: Help or Hindrance?

Moderator: Frances Toneguzzo, Ph.D., Director, Office of Corporate Sponsored Research and Licensing, Massachusetts General Hospital

- Type of patents in the diagnostic space and IP fragmentation
- Other types of intellectual property protection in diagnostics development
- Differentiation in diagnostics and use of patents
- Strategies for effective use of intellectual property to stimulate diagnostic development

Making Molecular Diagnostics Work Now? The Trials and Tribulations of Labs and Money

Moderator: Ian S. Millett, Ph.D., RAC, Senior Consultant, Medical Devices, Biologics Consulting Group, Inc.

- How do you get paid for a molecular diagnostic test?
- Does implementing a molecular diagnostic test in your lab really make sense?
- Life at Ground Zero - The FDA's changing perspective on lab-developed tests
- Pushing and Pulling- Who is your customer and just how Personal can you make that bill?

Strategies for Commercialization of Molecular Diagnostics

Moderator: Harry Glorikian, Managing Partner, Scientia Advisors

6:20 Close of Day

THURSDAY, FEBRUARY 4

HEALTH IT: WHY IS IT SO HARD?

8:25 AM Chairperson's Remarks

Wayne A. Rosenkrans, Jr., Ph.D., Distinguished Fellow, MIT Center for Biomedical Innovation; Program in Ethics and Systems Medicine, Georgetown University; Chairman, Personalized Medicine Coalition; VP, Strategic Consulting, Fuld & Co.; Chief Scientifc Advisor, Expertech Solutions; and Chief Applications Officer, SciTech Strategies

8:30 Keynote Presentation
Ensuring Responsible Testing through Real-Time Collaboration Between Providers, Payors and Labs

Matthew B. Zubiller, VP and General Manager, Advanced Diagnostics Management, McKesson Corp.

As molecular diagnostics proliferate, ensuring responsible testing becomes more complex. This is further complicated by changing reimbursement policies and health care IT reform. Ensuring your lab's success requires technology-enabled collaboration with providers, payors and other labs. This keynote discusses business practices and strategies for labs to offer decision support and access to a broader array of tests to providers, to review payors' reimbursement policies before tests are performed and to build effective lab networks to fulfill orders.

9:15 Keynote Presentation
HIT and PM: Conflict or Convergence

Wayne A. Rosenkrans, Jr., Ph.D., Distinguished Fellow, MIT Center for Biomedical Innovation; Program in Ethics and Systems Medicine, Georgetown University; Chairman, Personalized Medicine Coalition; VP, Strategic Consulting, Fuld & Co.; Chief Scientifc Advisor, Expertech Solutions; and Chief Applications Officer, SciTech Strategies

10:00 The Development of Multigene Prognostic and Predictive Tests in Cancer

Sponsored by ALMAC

Austin Tanney, Ph.D., Scientific Liaison Manager, Almac Diagnostics

The key to the delivery of personalized medicine is the development of molecular diagnostics to improve patient care, from better diagnostic and prognostic tests to companion diagnostics. The use of multigene signatures is increasingly of interest however there are many considerations in developing such signatures from study design to development of deliverable tests. Here we present out experience and perspective.

10:15 Sponsored Presentation *(Sponsorship Opportunity Available)*

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

11:30 Expert Panel
Health IT: What Will Success Look Like?

Moderator: David S. Lester, Ph.D., VP, Human Health Solutions, Theranos

- Reducing healthcare costs
- Facilitating the adoption of molecular diagnostics
- Defining the goals
- Realizing solutions for reaching the goals

Panelists:
Brandon Savage, M.D., Chief Medical Officer, GE Healthcare
Vance Vanier, M.D., Chief Medical Officer, Navigenics, Inc.
Mark N. Blatt, M.D., MBA, Director, Healthcare Industry Solutions, Digital Health Group, Intel Corporation
Jeffrey D. Miller

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

1:45 Ice Cream Refreshment Break in the Exhibit Hall

PLENARY KEYNOTE SESSION

2:15 Plenary Keynote Introduction

2:25 Plenary Keynote Presentation *(See Page 26 for Details)*

3:05 Refreshment Break in the Exhibit Hall

IP ISSUES ON GENE PATENTING: WHAT IS THE SOLUTION?

3:45 Chairperson's Remarks

Jorge A. León, Ph.D., President, Leomics Consulting

3:50 Gene Patents, Perspectives from the Clinical Laboratory

Karen P. Mann, M.D., Ph.D., Associate Professor and Director, Molecular Hematopathology, Department of Pathology and Laboratory Medicine, Emory University Hospital; President Elect, Association of Molecular Pathology

Gene patents are controversial, but are a reality in molecular diagnostics. As a laboratorian who co-directs an active clinical molecular diagnostics laboratory, I will describe how gene patents affect how I practice medicine including the effect of patents on test menus, turnaround times, choice of laboratories for referral testing, and laboratory finance.

4:20 Gene Patents in Molecular Diagnostics: Valuable Assets or Impediments?

Frances Toneguzzo, Ph.D., Director, Office of Corporate Sponsored Research and Licensing, Massachusetts General Hospital

Increasingly, genetic diagnostics are making use of panels of genes/gene fragments for accurate diagnosis of drug responses (toxicity and/or effectiveness and/or dosing) and disease stratification. In a number of situations, the patents covering these genes or their use are held by different owners, including companies, academic institutions and private individuals/foundations. While patents are generally considered valuable in that they provide a period of exclusivity when a company can exclude others from practicing the patented invention and thus protect the investment the company is making in commercializing the invention, this fragmentation of the intellectual property landscape in molecular diagnostics may impede the development of certain tests.

4:50 IP Fragmentation in Genetic Diagnostics
Jorge Goldstein, Director, Biotechnology & Chemical Group, Sterne Kessler Goldstein Fox PLLC
So called "patent thickets" have appeared when multiple patent owners each control one or a few genetic diagnostic correlation patents for one disease, where the multiple patents cover either alterations in one gene or several genes involved in the disease. Such thickets have already resulted in a failure to offer commercial tests for all possible gene alterations, or have generated test designs that are driven primarily by IP concerns. This talk will discuss possible solutions to the problem, including the use of patent pools driven by medical standards.

5:20 Expert Panel: Bioscience Patent Law
- How do IP fragmentation and patent pools affect the clinical labs and end users?
- How do they affect companies that own IP and commercialize IVDs?
- How do they affect companies and academic that discover new markers?
- Why are some licensing models slowing down the advancement of molecular diagnostics?

5:50 Close of Day

FRIDAY, FEBRUARY 5

U.S. UNIVERSAL HEALTH - BREAKING NEWS

8:30 AM Chairperson's Opening Remarks
Brian T. Edmonds, Ph.D., Research Advisor, Global External Research & Development, Lilly Corporate Center

8:35 Regulatory Considerations for Companion Diagnostics and Personalized Medicine
Elizabeth Mansfield, Ph.D., Senior Genomics Advisor, Office of the Chief Scientist; Director, Personalized Medicine, Office of in Vitro Diagnostic Device Evaluation and Safety, Food & Drug Administration
Advances in genomics-based discovery and therapeutic agent targeting have led to greatly increased interest in development of diagnostic/therapeutic combinations that promise to deliver "personalized" therapy to patients. With this vision comes the realization of the importance of the diagnostic test performance upon which the therapeutic safety and efficacy will rest. This presentation of regulatory issues for companion diagnostic devices and codevelopment will address proposed regulatory pathways for the diagnostic device, and emphasize the need for adequate analytical and clinical validation.

9:05 Value Based Laboratory Tests -- What Went Wrong on the Way to the Fair?
Ian S. Millett, Ph.D., RAC, Senior Consultant, Medical Devices, Biologics Consulting Group, Inc.
In spite of tremendous interest, expenditures, and pro-active work by industry, academia, and government, the personalized health care revolution seems to have stalled in the area of new test development and use. This talk will focus on potential reasons for slow uptake of new diagnostic technology, will survey the upcoming landscape, and will remind participants that in the end, it was the tortoise that won the race.

9:35 Medco Personalized Medicine: Advancing Healthcare
Lon Castle, M.D., Senior Director, Personalized Medicine, Medco Health Solutions, Inc.
Pharmacogenomic tests bring a new level of precision to pharmaceutical care, enabling treatment that is targeted to the unique genetic characteristics of individual patients. These tests are becoming the standard of care in many therapeutic areas, as physicians and payers become more conversant with the value of testing. Medco's Personalized Medicine healthcare can improve outcomes and reduce the overall costs of care.

10:05 Innovations in Molecular Diagnostics and SamplePreparation Methods: Accelerating Sample-to-Result Diagnostics
Sponsored by Akonni Biosystems
Kevin Banks, Ph.D., Head of Marketing and Sales, Akonni Biosystems
Akonni Biosystems (Frederick, MD) was founded in 2003 and has over 20 patents with 13 others pending. The company's core platform utilizes a gel-drop array technology optimized for developing medical applications, with an emphasis on greatly accelerating the time from sample to result. This session will provide an introduction and overview of the technology and platform. Preliminary results with a number of clinical applications will be discussed.

10:20 Coffee Break

11:00 Economics of Having Diagnostics Reimbursed and the Practical Challenges in Getting Reimbursement
Philip C.M. Ma, Ph.D., Director, McKinsey & Company, Inc.
The impact of diagnostics in influencing care continues to grow with technology advancements in clinical genomics and other molecular markers. In spite of this, the current reimbursement system in the U.S. does not appropriate incentives for effective use - both over and underuse of diagnostics can result. This talk will review how mis-aligned incentives can result from the under-lying micro-economics of different stakeholders (physicians, patients, payors, and diagnostic manufacturers), and will suggest a few ways to improve the micro-economic situation.

11:30 Panel Discussion: Personalized Medicine and Challenges for Implementation
- How will universal healthcare impact your business?
- How will it impact molecular diagnostics adoption?

12:00 PM Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

1:00 Chairperson's Remarks

VALUE OF CONSUMER BASED GENOMICS: WHAT IS THE CONSUMER GOING TO DO WITH IT?

- How good is the information delivered by these tests?
- How well can people understand the results?
- How effectively can they help people manage their health?

1:05 Consumers and Their Genomes
Brian Naughton, Ph.D., Founding Scientist, 23andMe
Over 30,000 individuals now have access to their personal genetic information through 23andMe's web-based services. Consumers sign up for these services to learn about their disease risk or carrier status, to discover their ancestral roots, to find new relatives, or to participate in research on a particular disease such as Parkinson's. This presentation will discuss the ongoing studies that are beginning to reveal how people respond to their personal genetic information.

1:35 Talk Title to be Announced
Patrick F. Terry, CEO, Technic Solutions, LLC; Acting CEO, Grand Therapeutics, Inc.

2:05 Drinking from the Fire Hose: Are Consumers Ready?
Sharon Terry, MA, President and CEO, Genetic Alliance

2:35 Panel Discussion and Q&A with Audience

3:05 Close of Conference

3:50 Presentation *Sponsored by* Proteome Sciences

Isotopic Mass Tags for the Facilitated Development of Multiplex SRM Mass Spectrometric Assays for Protein and Peptide Biomarkers

Helen Byers, Ph.D., Principal Research Scientist, Proteome Sciences plc, UK

Fit-for-purpose assays are essential for biomarker qualification. Selected Reaction Monitoring (SRM) is increasingly used for the quantitation of peptides and proteins, but is limited by expense and delay connected with synthesis of isotope-doped standard peptides and the difficulty to synthesize more complex standards (e.g. with post-translational modifications). Proteome Sciences has developed isotopic versions of its proprietary tandem mass tag (TMT) reagents to differently label sample and standard allowing to establish TMT-SRM, a method that allows the use of synthetic or natural reference standards to establish assays for any peptide or protein in any given sample material..

- Criteria

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

5:20 BREAK-OUT DISCUSSIONS in the Exhibit Hall

Personalized Medicine: Commercial Hurdles to Adoption in an Era of Evidence Based Medicine

Moderator: Katherine Tynan Ph.D., Business Development & Strategic Consulting for Diagnostics Companies, Tynan Consulting LLC

- The evidence required for each of the stakeholders: analytical performance and clinical validity for the FDA, clinical utility for physicians, and medical necessity for payers.
- The strategic importance of "intended use statements" in guiding product/test development
- The opportunities and challenges with reimbursement

Development and Application of Assays in the 3D Format

Moderator: Ray Mattingly, Ph.D., Associate Professor, Pharmacology, Wayne State University

- Challenges in standardization and feasibility of 3D cultures
- Development of 3D format for high-throughput assays
- Protocols for drug screening in 3D culture format
- Advanced 3D co-culture approaches to model tissues

How Innovative Technologies Are Selected, Evaluated, and Translated for Application in Diagnostics for Personalized Medicine to Enhance or Replace Conventional Diagnostics

Moderator: Kewal K. Jain, M.D., Professor, CEO, Jain PharmaBiotech

- The ideal molecular diagnostics laboratory for personalized medicine
- Selection, evaluation, and translation of new diagnostic technologies for personalized medicine
- Role of sequencing
- Future prospects of diagnostics for personalized medicine: supplementing, enhancing or replacing conventional diagnostics

Biomarkers of Efficacy

Moderator: Tracey Colpitts, Ph.D., Business Development, Companion Products, Abbott Molecular

- How does mechanism of action hypotheses translate to population science?
- When and how do we gather prevalence data?
- What priorities should we be making?

Next Generation Sequencing in the Clinical Diagnostics Laboratory

Moderator: Karl V. Voelkerding, M.D., Associate Professor of Pathology, University of Utah and Medical Director for Advanced Technology, ARUP Laboratories

- What are the first diagnostic applications that next generation sequencing will be used for?
- What improvements would facilitate translation of the technology into the clinical laboratory?
- How will laboratories process and interpret the large amounts of data generated?

6:20 Close of Day

THURSDAY, FEBRUARY 4

PERSONALIZING THERAPY: SERUM BIOMARKERS

8:25 AM Chairperson's Remarks

Josip Blonder, M.D., Sr Research Scientist, Head, Quantitative Proteomics, NCI, Frederick

8:30 Personalized Oncoproteomics for Cancer Biomarker Discovery: Application to Renal Cell Carcinoma

Josip Blonder, M.D., Sr. Research Scientist, Head, Quantitative Proteomics, NCI

Discovery of diagnostic, therapeutic and prognostic markers is central to personalized treatment of cancer. Thus, proteomic approaches capable of characterizing the patient's tumor phenotype using clinically relevant specimens are critically needed. A method that relies on tissue-directed oncoproteomics is described and applied for cancer biomarker discovery in the plasma of a patient diagnosed with renal cell carcinoma.

9:00 Protein Quantification Through Targeted Mass Spectrometry: The Way Out of Biomarker Purgatory?

Steven A. Carr, Ph.D., Director, Proteomics, The Broad Institute of MIT and Harvard

Immunoassays are widely used to measure protein biomarkers in patient blood, but useful antibody reagents do not exist for the vast majority of proteins. We are addressing this serious barrier by developing targeted assay methods employing mass spectrometry to screen and quantify low abundance proteins in plasma. This presentation will focus on the latest developments and applications of these technologies.

9:30 Mass Spec for Prostate Biomarkers, Assessing Aggressive vs. Non-Aggressive Prostate Cancer

Jianfeng Xu, M.D., Ph.D., Professor, Epidemiology, Prevention and Cancer Biology, Director, Ctrr for Cancer Genomics, Wake Forest University School of Medicine

Three types of prostate cancer related genetic variants have been found from genome-wide association studies, including those associated with overall prostate cancer risk, aggressive prostate cancer risk, and higher baseline PSA levels. These genetic variants may have potential clinical utility. However, further studies are needed to assess their clinical validity and clinical utility.

10:00 A Novel Tool for Non-Invasive Disease Detection

Sponsored by febit

Jack Leonard, Ph.D., Vice President of Technology Commercialization, febit Inc.

We developed a novel non-invasive diagnostic assay based on microRNAs. Our Biomarker Signature assay has shown an outstanding performance for the integrative detection of a broad panel of diseases and is well suited for high sample throughput at low cost since for each test less than one minute hands-on time is required. Moreover, our approach stands-out by high reproducibility and sensitivity while test-to-test variations are minimal.

10:15 Metabolite Profiling: Opportunities for Identification and Validation of Novel Biomarkers

Sponsored By metanomicshealth

Hajo Schiewe, Ph.D., Senior Manager, Business Development, Metanomics Health

Metabolite profiling is the parallel measurement of a broad range of endogeneous and xenobiotic metabolites in a given biological sample. The metabolome reflects internal or external influences on the pathophysiology of an organism including drug treatment and disease status. Metanomics Health uses mass spectroscopy based metabolite profiling to identify and validate novel metabolite biomarkers for a range of applications in pre-clinical and clinical drug development, disease diagnostics and progression. The analysis and interpretation of metabolite changes can increase the mechanistic understanding of diseases, drugs and other influences on an organism.

Cambridge Healthtech Institute's Inaugural

Personalized Diagnostics:

"Under the Hood" Technologies for Molecular Diagnostics

WEDNESDAY, FEBRUARY 3

7:00 AM Registration and Morning Coffee

8:00 Plenary Keynote Session *(See Page 26 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

KEYNOTE PRESENTATIONS

11:00 Chairperson's Remarks
Harry Glorikian, Managing Partner, Scientia Advisors

11:05 Molecular Diagnostics as a Value Driver of Pharma/ Pharma as a Value Driver for Molecular Diagnostics
Michael C. Little, Global Head, Diagnostics Development, Novartis Molecular Diagnostics
Molecular Diagnostics is a critical success factor for the future of pharmaceuticals and an essential aspect of the move toward personalized medicine. At the same time, to progress better healthcare and patient outcomes, it is imperative that the pharma industry's understanding of both targeted drug discovery and drug commercialization is fully leveraged to enable innovative diagnostics to be put into clinical practice and influence physician decision-making. The keynote will focus on these elements and discuss 1-2 case studies of how we at Novartis are using our discovery and development approach to work toward bringing innovative companion and stand-alone diagnostic tests to market.

11:40 Building a Successful Diagnostics Business Model in the Era of Personalized Medicine
Richard Ding, CEO, bioTheranostics, a bioMerieux Company Personalized medicine has been generally accepted as an inevitable trend in healthcare. However, much debate is still ongoing related to a sustainable business model for diagnostics companies in this new space. This presentation will identify various challenges, risks and potential returns for diagnostic companies, explore partnership models and propose some basic framework to seize the growth opportunity of personalized medicine.

12:15 PM Personalized Medicine: It Takes a Village
Mark Stevenson, President & COO, Life Technologies Corp.
New technologies, such as next generation sequencing, can be rapidly adopted in the research labs and help breakthroughs in our understanding of disease mechanisms for personalized medicine. But the journey from research technology to diagnostic systems is challenging and slow. As our understanding of disease increases the promise of personalized medicine is coming closer but what will it take to cross the bridge from research tool to routine diagnostics in personalized medicine. The Presentation will focus on the journey Life Technologies has embarked on and the partnerships and collaborations necessary to translate the tools for the research lab into solutions personalized medicine.

12:50 Luncheon Presentation
Sponsored by THOMSON REUTERS
Information Trends in Biomarker Research
Colin Williams, Ph.D., Director, Product Strategy, Thomson Reuters Healthcare and Science
In recent years, the quantity of data published on biomarker research has exploded. The challenge faced by researchers is to find vital, relevant information on the best biomarker quickly and reliably. In this discussion we will introduce BIOMARKERcenter, a comprehensive, fully-indexed biomarker information resource, and through case studies show how it aids the discovery process.

1:45 Dessert in the Exhibit Hall

PERSONALIZING THERAPY: TISSUE BIOMARKERS

2:15 Chairperson's Remarks
Linda McAllister, M.D., Ph.D.

2:20 Relating Biomarkers to Efficacy: The Efficacy Curve
Tracey Colpitts, Ph.D., Manager, Abbott Molecular
A method of predicting response in a subgroup defined by a biomarker will be discussed and demonstrated using data from therapeutic trials involving EGFR inhibitors in lung, colon, and breast cancer. Biomarkers that aid in selecting subgroups of patients of response were analyzed and compared. Striking similarities between the different cancers, therapies, and subgroups reveals a relationship between biomarkers and efficacy, which is visualized in the efficacy curve.

2:50 Network and Pathway Analysis of a Novel 3D Breast Carcinoma Model by Both Digital Gene Expression (DGE) and Whole Genome Array Analyses
Ray Mattingly, Ph.D., Associate Professor, Pharmacology, Wayne State University
We have developed a tractable, *in vitro* model of ductal carcinoma *in situ* (DCIS) based on 3D overlay culture in reconstituted basement membrane (rBM). We have applied and cross-validated whole genome microarray (Affymetrix) and digital gene expression (DGE) analyses (Illumina/Solexa) to explore the networks and pathways that underlie DCIS. DGE analysis revealed a broad range of products that are transcribed outside of standard (NCBI 36.3) genes models. These transcripts suggest truncations and changes in anti-sense driven regulatory pathways in DCIS.

3:20 Population Based *in vivo* Biomarker Discovery Using Engineered Human Tumors
Min Wu, Ph.D., Principal Scientist, Translational Research, AVEO Pharmaceuticals, Inc.
Human tumor populations exhibit significant inter-tumor variation, where each tumor harbors a unique set of genetic alterations that impact prognosis and response to treatment. Unfortunately, this variation results in low response rates in the clinic and creates significant challenges for drugs to meet regulatory endpoints. Cancer cell line based xenografts have traditionally been the preclinical model of choice to assess the efficacy of clinical compounds, however, such models exhibit inherent artifacts due to long term in vitro culture, and are unable to adequately capture natural variation seen in human tumor populations. To address this challenge, we have created a population based tumor model system based on Human-in-Mouse tissue transgenic human tumors that feature naturally occurring tumor variation akin to that observed in human tumor populations. Each tumor of the population has been comprehensively characterized at the RNA and DNA level, and the population has been adapted to conduct quantitative efficacy studies of anti-cancer agents and combinations, enabling correlations between response and the genetic context of the tumors. This platform enables us to identify and validate biomarkers of therapeutic response in an in vivo human tumor system.

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

11:20 Metabolomic Analysis of Prostate Cancer Progression
Arun Sreekumar, Ph.D., Molecular Oncology Program, Genomics/Epigenomics, Medical College of Georgia

Prostate cancer is the second most common cause of cancer-related death in men in the United States and afflicts one out of nine of those over the age of 65. There is an urgent need to develop biomarkers that can supplement PSA and increase its specificity for prostate cancer. The advent of high throughput profiling strategies has allowed scientists to look at global changes in genome, proteome and metabolome. Metabolomics, unlike genomics and proteomics, is a young science that has the potential to radically alter the future of healthcare, drug discovery, and drug delivery. It is the single best window into the cellular state discovered to date. Like the other omics-style sciences, where genomics is best understood as defining the genetic potential, transcriptomics is a window into the future (desired) direction of the cellular activity, and proteomics is a window to the functional potential of the cell; metabolomics, the omics science of metabolism, is the only window into the current and actual state of the cell (or by extension, organism) at a specific point in time.

Recently we have profiled the metabolome in prostate cancer progression using a combination of GC and LC chromatography. Our study quantified the levels of >1000 metabolites across 250 biospecimens. Results of the profiling study revealed elevated levels of sarcosine or N-methyl glycine to be associated with advanced prostate cancer. Importantly components of sarcosine pathway were found to regulate prostate cancer aggressivity. In addition to sarcosine we have defined additional metabolites that are being characterized in the context of prostate cancer progression. Our long term objective is to define a multiplex panel of metabolomic markers for prostate cancer progression.

11:45 Circulating Tumor Cells: From Enumeration to Comprehensive Characterization
Nicholas C. Dracopoli, Ph.D., VP, Biomarkers, Centocor R&D, Inc., Johnson & Johnson

Circulating tumor cells (CTC) are very rare and consist of about 1 in 108 or 109 cells in blood drawn from some patients with metastatic cancer. Enumeration of CTCs has been shown to have prognostic value for patients with metastatic breast prostate and colorectal cancer, and is being evaluated to determine if a treatment-related reduction in CTC counts is predictive of therapeutic response. Comprehensive characterization (DNA, RNA and protein) of CTCs will significantly add to the value of CTC enumeration tests, and enable serial monitoring of CTCs for molecular changes occurring during disease progression and as a response to therapy. This presentation will review new approaches for the isolation and characterization of CTCs, and discuss how CTC-derived biomarkers will become a critical factor in the development of personalized treatment strategies in oncology.

12:10 PM Progress in Noninvasive Detection of Nucleic Acid Biomarkers
Charles R. Cantor, Ph.D., CSO, Sequenom, Inc.

Procedures have been developed to enhance the collection of RNA and DNA fragments that enter the peripheral circulation as a result of apoptosis. These include optimized methods of recovering small fragments, amplifying them and then detecting and quantifying sequence characteristics by nucleic acid mass spectrometry. The methods show promise in noninvasive prenatal diagnostics, tumor detection and characterization, and infectious disease agent identification. The overall process is considerably more sensitive and precise than commonly used alternatives.

12:35 Luncheon Presentation I *Sponsored by* nanoINK Nano BioDiscovery

Enhanced Sensitivity of Biomarker Detection and Identification Using Nano-scale Protein Arrays
Jennifer Ohayon, Ph.D., BioDiscovery Project Leader, NanoInk, Inc.

Nanoscale protein arrays will become an essential technology in the pursuit of personalized medicine. NanoInk has developed several DipPen Nanolithography (DPN) platforms, providing a direct write spotting technique capable of generating sub-micron sized features of biomolecules on solid surfaces. The resultant enhancement in biomarker sensitivity will provide a more complete understanding of human disease from a systems biology approach.

1:05 Luncheon Presentation II *(Sponsorship Opportunity Available)*

1:45 Ice Cream Refreshment Break in the Exhibit Hall

PLENARY KEYNOTE SESSION

2:15 Plenary Keynote Introduction

2:25 Plenary Keynote Presentation *(See Page 26 for Details)*

3:05 Refreshment Break in the Exhibit Hall

NEXTGEN SEQUENCING AS A CLINICAL TOOL

3:45 Chairperson's Remarks
German Pihan, M.D., Dpt. of Pathology, Beth Israel Deaconess Medical Center

3:50 Enabling Personalized Medicine: The Growing Role of Next Generation Sequencing
German Pihan, M.D., Department of Pathology, Beth Israel Deaconess Medical Center

Ready access to the genome sequence of a patient is arguably the single most important factor in the implementation of personalized medicine. The recent development of massive parallel sequencing technologies promise to make personalized medicine soon a reality. Here I review the technological state-of-the-art as well as the clinical areas where massive parallel sequencing may have the greatest and most immediate impact.

4:20 Keynote Presentation

HLA Typing by High Resolution Technology
Henry A. Erlich, Ph.D., VP, Discovery Research, Human Genetics, Roche Molecular Systems, Inc.

4:50 Next Generation Sequencing for Hypertrophic Cardiomyopathy Diagnostics
Karl V. Voelkerding, M.D., Associate Professor of Pathology, University of Utah and Medical Director for Advanced Technology, ARUP Laboratories

Hypertrophic cardiomyopathy is an autosomal dominant disorder of cardiac sarcomere structure and function leading to multiple cardiac conditions. At least 16 genes with over 450 mutations have been implicated in HCM. We have currently designed and tested a next generation sequencing approach for the analysis of this multi-gene disorder and are refining our approach for diagnostic application.

5:20 HIV Dynamics Taught by Sequencing
Ramy Arnaout, M.D., DPhil., Associate Director, Clinical Microbiology, BIDMC Staff Pathologist, Department of Pathology, BIDMC and Harvard Medical School, Beth Israel Deaconess Medical Center

High-throughput sequencing platforms provide an approach for detecting rare HIV-1 variants and documenting more fully quasispecies diversity. We applied this technology to understand viral dynamics at the sequence level associated with antiviral treatment failure. Failure was associated with extreme, rapid shifts in population frequencies toward specific resistant forms, and deep sequencing provided a detailed view of the rapid evolutionary impact of selection.

5:50 Close of Day

FRIDAY, FEBRUARY 5

MICRORNA DIAGNOSTICS FOR CANCER: TRANSLATING INFORMATION TO PRACTICAL USE

8:30 AM Chairperson's Opening Remarks
Dalia Cohen, Ph.D., CSO, Rosetta Genomics, Inc.

8:35 Keynote Presentation
Causes and Consequences of microRNA Dysregulation in Cancer
Carlo M. Croce, M.D., Professor, Internal Medicine, College of Medicine & Public Health, The Ohio State University

During the past several years it has become clear that alterations in the expression of microRNA genes contribute to the pathogenesis of most, perhaps all, human malignancies. These alterations can be caused by a variety of mechanisms, including deletions, amplifications or mutations involving microRNA loci, by epigenetic silencing or by dysregulation of transcription factors targeting specific microRNAs. Since malignant cells show dependence on the dysregulated expression of microRNA genes, which in turn control or are controlled by dysregulation of multiple protein coding oncogenes or tumor suppressor genes, these small RNAs provide important opportunities for development of future microRNA based therapies.

9:05 microRNA Polymorphisms and the Future of Personalized Medicine

Prasun J. Mishra, Ph.D., Laboratory of Cancer Biology & Genetics, National Cancer Institute, NIH

Referred to as the micromanagers of gene expression, microRNAs are evolutionarily conserved small non-coding RNAs. Polymorphisms in the microRNA pathway can influence gene regulation and are emerging as powerful tools to study the biology of diseases. Detection of microRNA-polymorphisms can potentially improve diagnosis, treatment and prognosis in patients and has profound implications in the fields of pharmacogenomics and personalized medicine.

9:30 Living in a Sequen-omics World: Data Integration Issues and Challenges

David Sugarbaker, M.D., Chief, Thoracic Surgery, Brigham and Women's Hospital

DNA sequencing and other "-omics" platforms (e.g., mRNA, microRNA, CGH, exon, SNP, and other arrays) have experienced a technological revolution in throughput and scale over the preceding decade that shows no sign of slowing. However, data storage and processing advances have outpaced the ability to fully integrate the resulting massive quantities of data into biologically meaningful and predictive models to apply to risk estimation, prevention, and cure of human diseases, most notably cancer. In addition, further technological innovation will continue to drive down costs which will exacerbate the problem in the near-term but over the long-term will bring more resources to bear in solving these issues and challenges. This session will provide a comprehensive view of the sequen-omics landscape and identify the key issues that will need to be addressed in the future for these platforms to positively affect human health.

We performed the first miRNAome-wide evaluation of specific miRNA expression in dried, forensically relevant biological fluids (blood, semen, saliva, vaginal secretions and menstrual blood). A panel of nine differentially expressed miRNAs was identified that permit the identification of the body fluid using 50pg of total RNA. miRNA profiling provides a promising alternative approach to body fluid identification for forensic casework.

10:05 10:05 LNA™ based Universal RT microRNA PCR System. A new Generation High Throughput QPCR Platform Optimized for Development microRNA based Molecular Diagnostic Assays on Clinical FFPE and Blood Serum and Plasma

Sponsored by EXIQON Seek Find Verify

Jacob Ulrik Fog, Ph.D., Scientific Manager, Diagnostic Product Development Division, Exiqon A/S

Usi ng a Locked Nucleic Acid (LNA™) based miRNA detection technology we have developed a high throughput QPCR system for detection of miRNAs in clinical paraffin-embedded tissue as well as blood derived plasma or serum. The use of the LNA™ bases adds critical specificity and sensitivity creating a more robust system for more rapid assay development in the clinical and diagnostic assay development.

10:20 Coffee Break

11:00 The Onco-SNP and Cancer Risk: microRNA Binding Site Polymorphisms as Biomarkers

Joanne B. Weidhaas, Ph.D., Assistant Professor, Therapeutic Radiology, Yale University

Since microRNAs are global regulators, small aberrations such as SNPs that disrupt their coding sequences or their target binding sites can alter cellular homeostasis and enhance cancer risk. MicroRNA binding site polymorphisms have turned out to be some of the strongest biomarkers of cancer risk, can act as biomarkers of outcome, and may be future targets for therapy.

11:30 Role of microRNA Based Profiling in Determining Tissue of Origin for Carcinoma of Unknown Primary

Gauri Varadhachary, M.D., Associate Professor of Medicine, Department of G.I. Medical Oncology, M.D. Anderson Cancer Center

Carcinoma of unknown primary (CUP) is a heterogenous disease where a patient presents with metastases without an identifiable primary. As more effective cytotoxic and targeted therapies emerge for additional known cancers, accurate identification of CUP subtypes will become increasingly important to the appropriate care of these patients. MicroRNA expression profiling is an emerging tool to help with identification of tissue of origin in patients with CUP.

12:00 PM Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

INNOVATIVE DIAGNOSTICS FOR PERSONALIZED MEDICINE

1:00 Chairperson's Remarks

Kewal K. Jain, M.D., Professor, CEO, Jain PharmaBiotech

1:05 Introduction to the Technologies and their Significance/ Relevance for Personalized Medicine

Kewal K. Jain, M.D., Professor, CEO, Jain PharmaBiotech

1:35 A Low Cost Instrument for Microbead-Based Quantitative End-Point PCR and DNA Sequencing

Vera Gorfinkel, Ph.D., Associate Professor, Stony Brook University

We present a novel, low cost instrument which performs microbead-based quantitative end-point PCR and CE based DNA sequencing. The instrument employs ultra fast, single photon sensitive detection of fluorescent signals in capillaries and operates as a module of the hardware/software suite GENOMETRICA - a novel, universal technology platform for molecular biology and medicine.

2:05 CNV Studies in Autism and other Neurological Disorders

Jim Chinitz, Chief Executive Officer, Population Diagnostics, Inc.

Historically, patients having a common complex disease have been lumped together and considered homogeneous according to phenotype. Population Diagnostics ("PDx") has led a paradigm shift where appreciation is gaining for the heterogeneity of common disease which is likely caused by highly penetrant rare variants which are multi-genic and independently capable of generating the common phenotype. It is necessary to dissect phenotypes into genotypic differences to understand common disease and to personalize medicine. Beyond SNPs, there is a surprising abundance of structural variation in the genome called Copy Number Variants (CNVs), much of it occurring de novo. Recent studies have revealed "causative" rare CNV associations in autism, schizophrenia and ALS. In these models, the metrics that define the level of clinical relevance (i.e. odds ratios) of the rare variants is unprecedented, making them ideal candidates as novel biomarkers for predictive tests and beacons for molecular pathways. PDx is discovering and using a new standard of "causative" biomarkers and is paving the way for a next generation of diagnostic, personalized medicine and drug discovery applications.

2:35 Blood-based Diagnostics of Brain Injuries

Uwe R. Müller, Ph.D., VP, Product Development, Banyan Biomarkers, Inc.

Currently no FDA cleared lab tests exist for TBI and the diagnosis is based on complicated and expensive neurological and radio-imaging tests. Banyan has developed novel biomarkers for detection of TBI in the blood of patients within 2 hours of injury. We will present the results of our ongoing clinical studies, and our progress in the development of appropriate assay systems.

3:05 Close of Conference

Cambridge Healthtech Institute's Third Annual

Cancer Molecular Markers

WEDNESDAY, FEBRUARY 3

7:00 AM Registration and Morning Coffee

8:00 Plenary Keynote Session *(See Page 26 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

KEYNOTE PRESENTATIONS

11:00 Chairperson's Remarks
Michael Liebman, Ph.D., Managing Director, Strategic Medicine, Inc.

11:10 Personalizing Medicine: It's a System-Based Challenge
Franklyn G. Prendergast, M.D., Ph.D., Professor, Pharmacology, Biochemistry & Molecular Biology, Director, Center for Personalized Medicine, Mayo Clinic

11:40 Genomic Strategies for Personalized Cancer Treatment
Joseph R. Nevins, Ph.D., Barbara Levine Professor, Duke University
We have made use of expression profiling to develop signatures of oncogenic pathway deregulation that can then be used to profile the state of these pathways within populations of tumors. In addition, the pathway signatures also link the patterns of pathway activation with therapeutics since we have shown that predicting the activation of a pathway also predicts sensitivity to drugs that target the pathway. We have extended this concept to develop more refined signatures that can dissect the complexities of many of the known signaling pathways, providing a more precise capacity to probe the activity or deregulation of the pathway and linking to a broader array of therapeutics.

12:10 PM Panel: Impact of Personalized Medicine on Oncology Drugs and Treatment
Additional Panelist: Mike Boswood, President, CEO, Thomson Reuters

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

1:45 Dessert in the Exhibit Hall

PERSONALIZING THERAPY: TISSUE BIOMARKERS

2:15 Chairperson's Remarks
Tracey Colpitts, Ph.D., Manager, Abbott Molecular

2:20 Relating Biomarkers to Efficacy: The Efficacy Curve
Tracey Colpitts, Ph.D., Manager, Abbott Molecular
A method of predicting response in a subgroup defined by a biomarker will be discussed and demonstrated using data from therapeutic trials involving EGFR inhibitors in lung, colon, and breast cancer. Biomarkers that aid in selecting subgroups of patients of response were analyzed and compared. Striking similarities between the different cancers, therapies, and subgroups reveals a relationship between biomarkers and efficacy, which is visualized in the efficacy curve.

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Ray Mattingly, Ph.D., Associate Professor, Pharmacology, Wayne State University
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3:50 Sponsored Presentation *(Sponsorship Opportunity Available)*

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

5:20 BREAK-OUT DISCUSSIONS in the Exhibit Hall

What is the Forecast for Epigenetics and microRNA?
Moderator: Enal Razvi, Ph.D., System Biosciences SBI
- Status of the microRNA and epigenetics markets
- The research market for microRNA and epigenetics: growth and evolution
- Diagnostics and therapeutics development based on microRNA and epigenetic signatures
- Current challenges and opportunities in these spaces

Challenges to Whole Genome Sequencing
Moderator: s Ng, Ph.D., Assistant Professor, Genomic Medicine, J Craig Venter Institute
- Challenges to whole-genome sequencing
- Identifying de novo and re-current mutations in cancer
- Addressing tumor heterogeneity
- How can we move from characterizing gene variation to utilizing the whole genome
- Sequencing tumors rather than tumor cell lines
- The Complex genomic structure of tumor cells: de novo assembly or strategy to detect structural variants

Are there Cancers of Unknown Primary Tumors?
Moderator: Dalia Cohen, Ph.D., Chief Scientific Officer, Rosetta Genomics, Inc.
- Debate over cancers of unknown primary tumors (CUP)
- Methods to detect CUPs
- Consequences of detection of primary

Gene Signatures in Cancer Diagnostics
Co-Moderators: Gary Geiss, Ph.D., Principal Scientist, NanoString Technologies and David Kern, MBA, Director, MyRaQa
- Developing a gene signature
- Validation of gene signatures
- Regulatory considerations for gene signature diagnostics

Systems Chemical Biology-A New Paradigm
Moderator: Ally Perlina, Senior Application Scientist, GeneGo Inc.
- Utilizing tools for drug repositioning
- Understanding side effects
- Understanding the mechanisms of action for drugs
- Networkable compounds

6:20 Close of Day

THURSDAY, FEBRUARY 4

PERSONALIZING THERAPY: SERUM BIOMARKERS

8:25 AM Chairperson's Remarks
Josip Blonder, M.D., Sr Research Scientist; Head, Quantitative Proteomics, NCI Frederick

8:30 Personalized Oncoproteomics for Cancer Biomarker Discovery: Application to Renal Cell Carcinoma
Josip Blonder, M.D., Sr Research Scientist; Head, Quantitative Proteomics, NCI Frederick
Discovery of diagnostic, therapeutic and prognostic markers is central to personalized treatment of cancer. Thus, proteomic approaches capable of characterizing the patient's tumor phenotype using clinically relevant specimens are critically needed. A method that relies on tissue-directed oncoproteomics is described and applied for cancer biomarker discovery in the plasma of a patient diagnosed with renal cell carcinoma.

9:00 Protein Quantification Through Targeted Mass Spectrometry: The Way Out of Biomarker Purgatory?
Steven A. Carr, Ph.D., Director, Proteomics, The Broad Institute of MIT and Harvard
Immunoassays are widely used to measure protein biomarkers in patient blood, but useful antibody reagents do not exist for the vast majority of proteins. We are addressing this serious barrier by developing targeted assay methods employing mass spectrometry to screen and quantify low abundance proteins in plasma. This presentation will focus on the latest developments and applications of these technologies.

9:30 Mass Spec for Prostate Biomarkers, Assessing Aggressive vs. Non-Aggressive Prostate Cancer
Jianfeng Xu, M.D., Ph.D., Professor, Wake Forest University School of Medicine
Three types of prostate cancer related genetic variants have been found from genome-wide association studies, including those associated with overall prostate cancer risk, aggressive prostate cancer risk, and higher baseline PSA levels. These genetic variants may have potential clinical utility. However, further studies are needed to assess their clinical validity and clinical utility.

10:00 A Novel Tool for Non-Invasive Disease Detection
Sponsored by febit
Jack Leonard, Ph.D., Vice President of Technology Commercialization, febit Inc.
We developed a novel non-invasive diagnostic assay based on microRNAs. Our Biomarker Signature assay has shown an outstanding performance for the integrative detection of a broad panel of diseases and is well suited for high sample throughput at low cost since for each test less than one minute hands-on time is required. Moreover, our approach stands-out by high reproducibility and sensitivity while test-to-test variations are minimal.

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

11:20 Metabolomic Analysis of Prostate Cancer Progression
Arun Sreekumar, Ph.D., Molecular Oncology Program, Medical College of Georgia
Prostate cancer is the second most common cause of cancer-related death in men in the United States and afflicts one out of nine of those over the age of 65. There is an urgent need to develop biomarkers that can supplement PSA and increase its specificity for prostate cancer. The advent of high throughput profiling strategies has allowed scientists to look at global changes in genome, proteome and metabolome. Metabolomics, unlike genomics and proteomics, is a young science that has the potential to radically alter the future of healthcare, drug discovery, and drug delivery. It is the single best window into the cellular state discovered to date. Like the other omics-style sciences, where genomics is best understood as defining the genetic potential, transcriptomics is a window into the future (desired) direction of the cellular activity, and proteomics is a window to the functional potential of the cell; metabolomics, the omics science of metabolism, is the only window into the current and actual state of the cell (or by extension, organism) at a specific point in time.

Recently we have profiled the metabolome in prostate cancer progression using a combination of GC and LC chromatography. Our study quantified the levels of >1000 metabolites across 250 biospecimens. Results of the profiling study revealed elevated levels of sarcosine or N-methyl glycine to be associated with advanced prostate cancer. Importantly components of sarcosine pathway were found to regulate prostate cancer aggressivity. In addition to sarcosine we have defined additional metabolites that are being characterized in the context of prostate cancer progression. Our long term objective is to define a multiplex panel of metabolomic markers for prostate cancer progression.

11:45 Circulating Tumor Cells: From Enumeration to Comprehensive Characterization
Nicholas C. Dracopoli, Ph.D., VP, Biomarkers, Centocor R&D, Inc., Johnson & Johnson
Circulating tumor cells (CTC) are very rare and consist of about 1 in 108 or 109 cells in blood drawn from some patients with metastatic cancer. Enumeration of CTCs has been shown to have prognostic value for patients with metastatic breast prostate and colorectal cancer, and is being evaluated to determine if a treatment-related reduction in CTC counts is predictive of therapeutic response. Comprehensive characterization (DNA, RNA and protein) of CTCs will significantly add to the value of CTC enumeration tests, and enable serial monitoring of CTCs for molecular changes occurring during disease progression and as a response to therapy. This presentation will review new approaches for the isolation and characterization of CTCs, and discuss how CTC-derived biomarkers will become a critical factor in the development of personalized treatment strategies in oncology.

12:10 PM Progress in Noninvasive Detection of Nucleic Acid Biomarkers
Charles R. Cantor, Ph.D., CSO, Sequenom, Inc.
Procedures have been developed to enhance the collection of RNA and DNA fragments that enter the peripheral circulation as a result of apoptosis. These include optimized methods of recovering small fragments, amplifying them and then detecting and quantifying sequence characteristics by nucleic acid mass spectrometry. The methods show promise in noninvasive prenatal diagnostics, tumor detection and characterization, and infectious disease agent identification. The overall process is considerably more sensitive and precise than commonly used alternatives.

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

1:45 Ice Cream Refreshment Break in the Exhibit Hall

PLENARY KEYNOTE SESSION

2:15 Plenary Keynote Introduction

2:25 Plenary Keynote Presentation *(See Page 26 for Details)*

3:05 Refreshment Break in the Exhibit Hall

NEXTGEN SEQUENCING AS A CLINICAL TOOL

3:45 Chairperson's Remarks

3:50 Enabling Personalized Medicine: The Growing Role of Next Generation Sequencing
German Pihan, M.D., Department of Pathology, Beth Israel Deaconess Medical Center
Ready access to the genome sequence of a patient is arguably the single most important factor in the implementation of personalized medicine. The recent development of massive parallel sequencing technologies promise to make personalized medicine soon a reality. Here I review the technological state-of-the-art as well as the clinical areas where massive parallel sequencing may have the greatest and most immediate impact.

4:20 Keynote Presentation

HLA Typing by High Resolution Technology
Henry A. Erlich, Ph.D., VP, Discovery Research, Human Genetics, Roche Molecular Systems, Inc.

4:50 Next Generation Sequencing for Hypertrophic Cardiomyopathy Diagnostics
Karl V. Voelkerding, M.D., Associate Professor of Pathology, University of Utah and Medical Director for Advanced Technology, ARUP Laboratories
Hypertrophic cardiomyopathy is an autosomal dominant disorder of cardiac sarcomere structure and function leading to multiple cardiac conditions. At least 16 genes with over 450 mutations have been implicated in HCM. We have currently designed and tested a next generation sequencing approach for the analysis of this multi-gene disorder and are refining our approach for diagnostic application.

5:20 HIV Dynamics Taught by Sequencing
Ramy Arnaout, M.D., DPhil., Associate Director, Clinical Microbiology, BIDMC Staff Pathologist, Department of Pathology, BIDMC and Harvard Medical School, Beth Israel Deaconess Medical Center
High-throughput sequencing platforms provide an approach for detecting rare HIV-1 variants and documenting more fully quasispecies diversity. We applied this technology to understand viral dynamics at the sequence level associated with antiviral treatment failure. Failure was associated with extreme, rapid shifts in population frequencies toward specific resistant forms, and deep sequencing provided a detailed view of the rapid evolutionary impact of selection.

5:50 Close of Day

FRIDAY, FEBRUARY 5

MICRORNA DIAGNOSTICS FOR CANCER: TRANSLATING INFORMATION TO PRACTICAL USE

8:30 AM Chairperson's Opening Remarks
Dalia Cohen, Ph.D., Chief Scientific Officer, Rosetta Genomics, Inc.

8:35 Keynote Presentation

Causes and Consequences of microRNA Dysregulation in Cancer
Carlo M. Croce, M.D., Professor, Internal Medicine, College of Medicine & Public Health, The Ohio State University
During the past several years it has become clear that alterations in the expression of microRNA genes contribute to the pathogenesis of most, perhaps all, human malignancies. These alterations can be caused by a variety of mechanisms, including deletions, amplifications or mutations involving microRNA loci, by epigenetic silencing or by dysregulation of transcription factors targeting specific microRNAs. Since malignant cells show dependence on the dysregulated expression of microRNA genes, which in turn control or are controlled by dysregulation of multiple protein coding oncogenes or tumor suppressor genes, these small RNAs provide important opportunities for development of future microRNA based therapies.

9:05 microRNA Polymorphisms and the Future of Personalized Medicine
Prasun J. Mishra, Ph.D., Laboratory of Cancer Biology & Genetics, NCI, NIH
Referred to as the micromanagers of gene expression, microRNAs are evolutionarily conserved small non-coding RNAs. Polymorphisms in the microRNA pathway can influence gene regulation and are emerging as powerful tools to study the biology of diseases. Detection of microRNA-polymorphisms can potentially improve diagnosis, treatment and prognosis in patients and has profound implications in the fields of pharmacogenomics and personalized medicine.

9:30 Living in a Sequen-omics World: Data Integration Issues and Challenges
David Sugarbaker, M.D., Chief, Thoracic Surgery, Brigham and Women's Hospital
DNA sequencing and other "-omics" platforms (e.g., mRNA, microRNA, CGH, exon, SNP, and other arrays) have experienced a technological revolution in throughput and scale over the preceding decade that shows no sign of slowing. However, data storage and processing advances have outpaced the ability to fully integrate the resulting massive quantities of data into biologically meaningful and predictive models to apply to risk estimation, prevention, and cure of human diseases, most notably cancer. In addition, further technological innovation will continue to drive down costs which will exacerbate the problem in the near-term but over the long-term will bring more resources to bear in solving these issues and challenges. This session will provide a comprehensive view of the sequen-omics landscape and identify the key issues that will need to be addressed in the future for these platforms to positively affect human health.

10:05 Sponsored Presentation *(Sponsorship Opportunity Available)*

10:20 Coffee Break

11:00 The Onco-SNP and Cancer Risk: microRNA Binding Site Polymorphisms as Biomarkers
Joanne B. Weidhaas, Ph.D., Assistant Professor, Yale University
Since microRNAs are global regulators, small aberrations such as SNPs that disrupt their coding sequences or their target binding sites can alter cellular homeostasis and enhance cancer risk. MicroRNA binding site polymorphisms have turned out to be some of the strongest biomarkers of cancer risk, can act as biomarkers of outcome, and may be future targets for therapy.

11:30 Role of microRNA Based Profiling in Determining Tissue of Origin for Carcinoma of Unknown Primary
Gauri Varadhachary, M.D., Associate Professor of Medicine, Department of G.I. Medical Oncology, M.D. Anderson Cancer Center
Carcinoma of unknown primary (CUP) is a heterogeneous disease where a patient presents with metastases without an identifiable primary. As more effective cytotoxic and targeted therapies emerge for additional known cancers, accurate identification of CUP subtypes will become increasingly important to the appropriate care of these patients. MicroRNA expression profiling is an emerging tool to help with identification of tissue of origin in patients with CUP.

12:00 PM Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

TARGETING CANCER STEM CELLS

1:00 Chairperson's Remarks

1:05 Impact of Antibodies on Cancer Stem Cells: Discovering Underlying Pathways Essential to Cancer Stem Cell Biology
Tim Hoey, Ph.D., VP, Cancer Biology, OncoMed Pharmaceuticals, Inc.
Cancer stem cells are thought to mediate tumor initiation, metastasis, and recurrence. We have isolated and characterized CSCs from a variety of major tumor types and have found that these cells are preferentially resistant to many current therapies. As part of our effort to develop novel agents targeting CSCs, we have developed an anti-DLL4 antibody that blocks Notch signaling. Anti-DLL4 inhibits tumor growth through multiple mechanisms including a reduction in CSC frequency.

1:35 Understanding Tumor Cell Heterogeneity in NSCLC: Contributions to Resistance and Relapse
Erica L. Jackson, Ph.D., Scientist, Genentech, Inc.
Tumors are made up of a heterogeneous mixture of cell types and it is possible that distinct cell populations play unique roles in tumorigenesis. We are studying functionally defined cell populations to determine what distinguishes chemo-resistant cells from bulk tumor cells.

2:05 ABC Transporters' Role in Cancer Stem Cell Drug Resistance
Muhammad Al-Hajj, Ph.D., Director, Stem Cell Discovery Unit, GlaxoSmithKline
One of the mechanisms by which residual disease become chemo-resistant is via the decreased efficiency of chemo-therapeutics through the action of ATP-binding cassette (ABC) proteins that are variably expressed by the tumor cells and tend to be up-regulated in some cancer stem cells. The clinical relevance of the ABC transporters in the context of cancer stem cells is paramount and their application requires better understanding of the role individual transporters play in the mechanism and the development of more specific inhibitors with minimal off target effects. Here we'll discuss the role of two specific transporters in pancreatic and colon cancer stem cells and their value as therapeutic targets.

2:35 New Visions of Cancer Therapy through the Prism of the Cancer Stem Cell Hypothesis
Justin D. Lathia, Ph.D., Research Associate, Department of Stem Cell Biology and Regenerative Medicine, Lerner Research Institute, Cleveland Clinic Foundation
The failure of conventional therapies to fundamentally alter the survival of advanced and metastatic cancers has many causes but one appears to be the striking cellular heterogeneity in most cancers. The cancer stem cell hypothesis posits that tumors contain a cellular hierarchy of differentiation and tumor propagation potential. As studies have demonstrated that cancer stem cells display therapeutic resistance, angiogenic potential, and a propensity towards invasion/metastasis, the identification of signaling pathways and molecular targets in cancer stem cells may yield improved cancer therapies.

3:05 Close of Conference

Cambridge Healthtech Institute's Seventh Annual

Mastering Medicinal Chemistry

The Senior Level Chemist Event

WEDNESDAY, FEBRUARY 3

7:00 AM Registration and Morning Coffee

8:00 Plenary Keynote Presentations *(See Page 26 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

KEYNOTE PRESENTATIONS: RECENT APPROVALS AND CLINICAL CANDIDATES

11:00 Chairperson's Remarks
Hing Sham, Ph.D., Senior Vice President, Chemical Sciences, Elan Pharmaceuticals

11:10 Recent Approval: Mozobil from Development to Approval
Renato Skerlj, Ph.D., VP, Medicinal Chemistry, Genzyme Corporation Drug and Biomaterial R&D
Mozobil™ (plerixafor injection), a first in class small molecule antagonist of the chemokine receptor CXCR4, was granted marketing approval by the FDA in December 2008 and indicated for the mobilization of hematopoietic stem cells to the bloodstream for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma and multiple myeloma.

11:40 Discovery of a State-Dependent Cav2.2 Blocker for the Treatment of Chronic Pain
Scott B. Hoyt, Ph.D., Research Fellow, Department of Basic Chemistry, Merck Research Laboratories
Voltage-gated Cav2.2 calcium channels control the release of neurotransmitter at presynaptic terminals, and thus play a critical role in pain signaling. The state-independent Cav2.2 blocker ziconotide, a peptide that must be administered via intrathecal injection, has demonstrated clinical efficacy in the treatment of severe chronic pain. State-dependent Cav2.2 blockers may likewise provide clinical pain relief without adversely affecting other nerve functions.

12:10 PM Discovery of Lorcaserin: A Selective 5-HT2C Agonist for the Treatment of Obesity
Brian Smith, Ph.D., Director, Medicinal Chemistry, Arena Pharmaceuticals, Inc.
Compelling evidence suggests that drugs which activate the 5-HT2C receptor cause weight loss and thus have potential as anti-obesity agents. Because serotonin elicits a number of biological responses through modulation of other 5HT receptors, selectivity has been a critical challenge. This presentation outlines events, challenges and achievements that led to the discovery and development of lorcaserin.

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

1:45 Dessert in the Exhibit Hall

CASE STUDIES FROM CHEMISTRY TO THE CLINIC

2:15 Chairperson's Remarks

2:20 Discovery of SCH 530348 – A Thrombin Receptor Antagonist with Potent Antiplatelet Effects
Samuel Chackalamannil, Ph.D., Distinguished Research Fellow, Discovery Research, Schering-Plough Research Institute
SCH 530348, a himbacine-based thrombin receptor antagonist (TRA), is currently undergoing Phase-III clinical studies for acute coronary syndrome and secondary prevention of cardiovascular events in high risk patients. In a Phase-II clinical study in PCI patients, SCH 530348 showed no statistically significant increase in major or minor bleeding when added to standard of care, and showed a non-statistically significant reduction in major adverse cardiac events, including periprocedural myocardial infarction.

2:50 Macrocycle-based Drug Discovery: The Ulimorelin Story
Helmut Thomas, Ph.D., Senior Vice President, Research & Preclinical Development, Tranzyme Pharma, Inc.
The discovery and development path leading from a small molecule macrocyclic screening library to the novel ghrelin receptor agonist, ulimorelin (TZP-101), a Phase III product for the treatment of GI hypo-motility disorders, will be presented in detail. The specific attributes of the medicinal chemistry technology (MATCH™) that enabled the rapid progression of these efforts from hit-to-lead-to-clinic will be outlined.

3:20 Executive Panel

Medicinal Chemistry Drivers: Innovation, Technology, Efficiency and Luck
Moderator: *Graeme Semple, Ph.D., Vice President, Discovery Chemistry, Arena Pharmaceuticals, Inc.*
Panelists:
Michael Henning, Ph.D., Vice Director & Head, Discovery Technologies, F. Hoffmann-La Roche Ltd
Kenneth A. Savin, Ph.D., Manager, Global External Research & Development, Eli Lilly & Co.
Gary W. Small, M.D., Parlow-Solomon Professor on Aging, Professor of Psychiatry & Biobehavioral Sciences, Director, UCLA Center on Aging

3:50 Thermodynamic *Sponsored by* SCHRÖDINGER **Contributions of Water Molecules to Ligand-Receptor Binding**
Christopher Higgs, Ph.D., MRSC, Senior Applications Scientist, Schrödinger, LLC
Interpreting structure-activity data is often challenging even with the availability of crystal structures. The role of solvent thermodynamics in protein binding sites is often overlooked but can be important in explaining experimental data. Here, we present a statistical thermodynamic approach to the treatment of binding site water molecules and show that hydration site displacement patterns can be used to explain SAR trends, ligand selectivity, and site-directed mutagenesis. Applications of the method to the A2A adenosine receptor, PDZ domains, a broad range of kinases, and other systems of pharmaceutical interest will be discussed.

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

5:20 BREAK-OUT DISCUSSIONS in the Exhibit Hall

6:20 Close of Day

THURSDAY, FEBRUARY 4

FRAGMENT-INSPIRED AND STRUCTURE-GUIDED MEDICINAL CHEMISTRY

8:25 AM Chairperson's Remarks
Charles Reynolds, Ph.D., Research Fellow, Computer Aided Drug Discovery, Johnson & Johnson

8:30 Drug Discovery Facilitated by Fragment Screening Efforts
Michael Henning, Ph.D., Vice Director & Head, Discovery Technologies, F. Hoffmann-La Roche Ltd
Rapid gain in potency of compounds by structure based drug design together with the high sensitivity of biophysical methods like Surface Plasmon Resonance (SPR) enable the use of fragment molecules to guide drug discovery efforts. The lecture will review the fragment screening efforts at Roche and analyze benefits and challenges of the approach from these experiences. Drug targets like β-secretase or chymase are used as case studies.

9:00 Synthesis, *in vitro* and *in vivo* Evaluation of PI3K Inhibitors
Matthew Burger, Ph.D., Research Investigator II, Global Discovery Chemistry, Novartis Institutes for Biomedical Research
Phosphoinositide-3-Kinase (PI3K) is an important oncology target due to the deregulation of its signaling pathway in a wide variety of human cancers. A lead series from a combinatorial library was identified that potently inhibits PI3K. Using SBDD the lead series was optimized to yield PI3K inhibitors with suitable PK properties to establish a PK/PD-efficacy relationship in a mouse A2780 xenograft model.

9:20 Design, Synthesis and Optimization 2-aminoquinazolines as PDK1 Inhibitors

Savithri Ramurthy, Ph.D., Research Investigator, GDC/ONC, Novartis Institutes of Biomedical Research, Emeryville, CA

Herein, we describe the use of iterative structure-guided design to discover two sets of leads from the series Quinazolines as PDK1 inhibitors. The *in vitro* and *in vivo* activity of potent PDK1 inhibitors will be discussed along with the medicinal chemistry approaches utilized to optimize the chemical series for kinase selectivity, efflux, and hERG.

9:40 Presentation *Sponsored by* evotec www.evotec.com

Fragment Based Drug Discovery at Evotec - Application to the identification of BACE and PDE10a inhibitors

James Madden, Ph.D., Principal Scientist, Evotec (UK) Limited

Evotec's FBDD platform (EVOlutionTM) integrates orthogonal screening technologies, namely; biochemical, NMR and SPR to test fragments in a high throughput, highly sensitive mode. Evotec has successfully applied this technology in a number of programs. This presentation will describe 2 case studies where EVOlutionTM has been used to discover BACE and PDE10a inhibitors.

10:00 Luncheon Presentation *Sponsored by* THOMSON REUTERS

The Role of Medicinal Chemistry in Translational Research

Josep Prous, Jr., Ph.D., MBA, Vice President and Chief Scientific Officer, Thomson Reuters Healthcare & Science

The biomedical community has embraced the translational research approach to finding better and safer medicines. However, to meet the promises of this approach, researchers need a knowledge-based methodology in which the constituent disciplines share data appropriately. This talk will show how medicinal chemistry provides a bridge between early biology findings and clinical application of new molecular entities.

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

11:30 Computing Specific Residue-ligand Interaction Energies using Quantum Mechanical Energy Decomposition: A Tool for Guiding Drug Design

Charles Reynolds, Ph.D., Research Fellow, Computer Aided Drug Discovery, Johnson & Johnson

Quantum methods are just beginning to find wider application in drug discovery. We have used pair-wise decomposition of protein-ligand interaction energies, computed using the DivCon program, to analyze the interactions that drive potency in a series of protein kinase B inhibitors. These computed interaction energies were used to derive two heat maps: (1) an interaction energy map and (2) an SAR map. These interaction energies, and resulting maps, provide detailed information not otherwise available for identifying the residues in an active site that are most critical for ligand binding.

12:00 PM The Emperor's New Crystal: Examples of X-ray Bloopers; a Cautionary Tale

Edward Kesicki, Ph.D., Director, Small Molecule Drug Discovery, Infectious Disease Research Institute

I will give examples of "solved" structures in which incorrect ligands were fitted to the electron density map of a kinase co-crystal, a result of a typographical error in the paperwork sent to the crystallographer. In addition, I will show a class of selective PI3 kinase inhibitors that would have never been discovered using known X-ray crystal structures.

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

1:45 Ice Cream Refreshment Break in the Exhibit Hall

PLENARY KEYNOTE SESSION

2:15 Plenary Keynote Introduction

2:25 Plenary Keynote Presentation *(See Page 26 for Details)*

3:05 Refreshment Break in the Exhibit Hall

TARGETS IN HOT PURSUIT I

3:45 Chairperson's Remarks

Thomas Högberg, Ph.D., Vice President, 7TM Pharma, Hørsholm, Denmark

3:50 Redesign of Arylsulfonamide Gamma Secretase Inhibitors to Achieve Novelty and High *in vivo* Activity

Andrei Konradi, Ph.D., Senior Director, Medicinal Chemistry, Elan Pharmaceuticals

The transformation of known arylsulfonamide Gamma Secretase Inhibitors (GSIs) into Elan's arylsulfonyl pyrazolopiperidine GSIs, using small molecule modeling and pharmacophore hypotheses, will be described. Exploration of analogs to maximize *in vitro* potency, metabolic stability, pharmacokinetics, and *in vivo* activity will be presented. Several novel synthetic methods to prepare the target compounds will be described.

4:20 Discovery of the Nedd-8 Activating Enzyme Inhibitor MLN4924

Steve Langston, Ph.D., Senior Scientist, Millennium Pharmaceuticals, the Takeda Oncology Company

The ubiquitin-proteasome system (UPS) is responsible for the regulated degradation of intracellular proteins with important roles in cellular function including cancer cell growth and survival. NEDD8-activating enzyme (NAE) is an essential component UPS that regulates degradation of a subset of proteins upstream of the proteasome. The discovery of MLN4924, a first in class inhibitor of NAE, will be presented.

4:50 Discovery of the Hedgehog Inhibitor GDC-0449

Michael Koehler, Ph.D., Scientist, Discovery Chemistry, Genentech, Inc.

5:20 Exploration of SAR and optimization of in silico derived CRTH2 antagonists

Thomas Högberg, Ph.D., Vice President, 7TM Pharma, Hørsholm, Denmark

Several chemical series of antagonists for the PGD2 receptor CRTH2 were identified from a small focused library originating from a knowledge-based process using physicogenetic relationships and ligand information. The elucidation of SAR by synthesis of smaller libraries and design of specific target structures led to identification of novel drugable chemotypes.

5:50 Close of Day

FRIDAY, FEBRUARY 5

STRATEGIES FOR EFFECTIVE MEDICINAL CHEMISTRY

8:30 AM Chairperson's Opening Remarks

Kenneth A. Savin, Ph.D., Manager, Global External Research & Development, Eli Lilly & Co.

8:35 A Paradigm Change in the Application of ADME Resources to Early Lead Generation Activities

Kenneth A. Savin, Ph.D., Manager, Global External Research & Development, Eli Lilly & Co.

With the advent of new technology and processes, there are new possibilities for the application of ADME resources to projects at earlier phases in a project's life-cycle. We have been able to change the way ADME supports projects with the hope of improving our ability to come to decision points earlier in lead generation.

9:05 Understanding Structure-Toxicity Relationships as a Guide to Safer Drugs

John C.L. Erve, Ph.D., DABT, Principal Research Scientist II, Drug Safety Metabolism, Wyeth Research

Reactive metabolites are a concern due to their potential role in drug toxicity. Despite our understanding of bioactivation pathways and ability to minimize reactive metabolite formation, toxicity remains a cause of failure during drug development. This talk will review structure-toxicity relationships so that this knowledge can benefit drug discovery.

9:35 Biotransformation to Enable Chemistry SAR

Douglas Spracklin, Ph.D., Director, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

Biotransformation science has evolved well beyond traditional structural elucidation of metabolites. Contemporary biotransformation data is especially well suited to aid chemistry SAR development, i.e., identifying metabolic hot spots, non-obvious metabolic pathways, potential reactive metabolites, etc. Knowledge around these attributes can be extremely helpful in prioritizing chemical series and selecting individual molecules for development.

10:05 Sponsored Presentation *(Sponsorship Opportunity Available)*

10:20 Coffee Break

IMAGING AS AN EXCITING TOOL IN DRUG DISCOVERY

Chair: *Michael A. Letavic, Research Fellow, Neuroscience, Johnson & Johnson Pharmaceutical R&D*

11:00 Imaging Drug Action in the Human Brain

Joanna Fowler, Ph.D., Senior Chemist, Brookhaven National Laboratory

Radiotracers and drug molecules labeled with short-lived positron emitting isotopes such as carbon-11 (t1/2: 20.4 min), fluorine-18 (t1/2: 110 min) or nitrogen-13 (t1/2: 10 min) are unique scientific tools for measuring biochemical transformations and drug pharmacokinetics and pharmacodynamics in the living human and animal body.

11:30 Image Analysis Considerations for Preclinical, *in vivo* Medical Imaging

Matt Silva, Head, Imaging Sciences, Millennium, The Takeda Oncology Company

With the expanding role of preclinical and translational imaging in drug research, it is necessary to consider not only study design and imaging modality but also visualization and image quantification. This presentation will review the role of imaging technologies and show examples of experiments and image analysis procedures, including kinetic analysis of dynamic contrast-enhanced MRI and bone topology analysis from 3D CT data.

12:00 PM Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

TARGETS IN HOT PURSUIT II

1:00 Chairperson's Remarks

Nick Terrett, Ph.D., Chief Scientific Officer, Ensemble Discovery Corp.

1:05 Modulators and Consequences of Hsp90 Regulation by Small Molecules

Brian S. J. Blagg, Ph.D., Associate Professor of Medicinal Chemistry, The University of Kansas; Winner of the 2009 David W. Robertson Award in Medicinal Chemistry

The 90 kDa heat shock proteins (Hsp90) are molecular chaperones required for the refolding of denatured proteins and the maturation of nascent polypeptides into their biologically active, three-dimensional structures. In fact, numerous proteins represented in all six hallmarks of cancer are dependent upon Hsp90 for conformational maturation. Innovative approaches toward C-terminal inhibition of Hsp90 will be discussed.

1:35 Design and Synthesis of RDEA119, a Potent and Orally Bioavailable MEK Inhibitor

Jean-Michel Vernier, Ph.D., VP, Chemistry Discovery, Ardea Biosciences

This presentation will discuss the design, synthesis and structural-activity relationship that led to the discovery of RDEA119, a novel highly potent and selective MEK inhibitor currently in Phase I clinical trial. RDEA119 is being developed under a global license agreement with Bayer HealthCare.

2:05 From a Concept towards a First-In-Class Drug for a Human Amyloid Disease

Jeffery W. Kelly, Ph.D., Chair, Molecular and Experimental Medicine, Lita Annenberg Hazen Professor of Chemistry, The Skaggs Institute, The Scripps Research Institute

The seminar will cover the twenty-one year adventure from our initial demonstration that rate-limiting transthyretin tetramer dissociation and monomer misfolding was sufficient for transthyretin amyloidogenesis linked to neurodegeneration, to the recent clinical trial results of FoldRx demonstrating that a transthyretin kinetic stabilizer halts neurodegeneration in familial amyloid polyneuropathy. This is the first pharmacologic evidence supporting the validity of the amyloid hypothesis.

2:35 DNA-Programmed Chemistry Approach to Macrocyclic Lead Compounds

Nick Terrett, Ph.D., CSO, Ensemble Discovery Corp.

DNA-programmed chemistry is an integrated platform for the synthesis and screening of macrocycles that interact with protein-protein drug discovery targets such as the oncology target, BCL-XL. We have also discovered a series of macrocycles that competitively antagonize the interaction of TNFα with TNF receptors in both biochemical and cell-based assays, and that also have anti-inflammatory activity *in vivo*.

3:05 Close of Conference

Cambridge Healthtech Institute's Second Annual

Adopting R&D Informatics Systems

Data Management, Integration & Knowledge Management

WEDNESDAY, FEBRUARY 3

7:00 AM Registration and Morning Coffee

8:00 Plenary Keynote Session *(See Page 26 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

EXECUTIVE STRATEGIES–INTEGRATED R&D INFORMATICS

11:00 Chairperson's Remarks
David M. Sedlock, Ph.D., Senior Director, Research & Development Systems, Millennium, The Takeda Oncology Company

11:10 Enterprise Scientific Workflow Environment Drives Innovation
Daniel J. Chin, Ph.D., Senior Principal Research Scientist, Roche Palo Alto
Most informatics investments increase the efficiency of drug discovery. The introduction of an enterprise-wide scientific workflow platform enables research informatics organizations to shift their efforts towards scientific innovation. Researchers apply scientific workflows for *in silico* experimentation and exploration, leading to scientific hypotheses and discoveries. Enterprise environments enable researchers to share and evolve their scientific workflows, further increasing research productivity. Examples of scientific workflows and the setting required to run scientific workflow platforms effectively in pharmaceutical research will be discussed.

11:40 The Pistoia Alliance, Inc.–A Construct for Precompetitive Collaboration
Chris Waller, Ph.D., Senior Director, Precompetitive Collaborations, Research, Development & Medical Informatics, Worldwide Technology, Pfizer, Inc.
The Pistoia Alliance has been established to provide the foundation of data standards, ontologies and associated web-services to enable the Pharmaceutical discovery workflow through common business terms, relationships and processes. Current progress, learnings and how companies, academics and others can participate in this approach will be described.

12:10 PM Recent Strategies with Cloud, Wikis, Ontologies and Open Source Data Standards
Giles M. Day, Senior Director, BBC Informatics, Pfizer, Inc.

12:40 Luncheon Presentation I *Sponsored by* Microsoft
**By attending Microsoft's Luncheon presentation you are opting to receive further communications from Microsoft.*
Personalized Medicine: The Missing Pieces
Jim Karkanias, Senior Director of Applied Research & Technology, Microsoft Health Solutions Group
Discoveries to make personalized medicine a reality depend on leveraging the "open universe" of life sciences data. To assist investigators with ad hoc questions, hypothesis generation, and validation, investigators must describe and verify systems about the life science universe. This session will introduce a strongly typed repository of linked data that makes it possible to conceive and deliver game-changing therapies.

1:10pm Luncheon Presentation II *Sponsored by* BioFortis
Empowering Scientists with Hypothesis-Driven Data Exploration
Jian Wang, Ph.D., CEO, BioFortis Inc.
A significant bottleneck on productivity in translational research is the inability for scientists to directly interrogate data by themselves. We present a novel solution & case study to demonstrate how, with the right tools, scientists can be more self-sufficient, efficient and productive, while enabling informatics specialists to focus more on higher value contributions instead of mundane ad hoc data manipulations.

1:45 Dessert in the Exhibit Hall

2:15 Chairperson's Remarks
David M. Sedlock, Ph.D., Senior Director, Research & Development Systems, Millennium, The Takeda Oncology Company

2:20 Integrated Informatics Systems for R&D
Vaibhav A. Narayan, Ph.D., Senior Director, Integrative Neurosciences & Biomarkers, Johnson & Johnson Pharmaceuical Research & Development

2:50 Executive Panel with Q&A

Are We Integrating the Right Data: Extending Beyond Laboratory Data to Decisions Impacting Project Success
Moderator: *David M. Sedlock, Ph.D., Senior Director, Research & Development Systems, Millennium, The Takeda Oncology Company*
- Data Aggregation vs. Data Integration
- Data Management vs. Knowledge Management
- Integrating Data Management Systems across Multiple Sites
- Effective Data Integration in Translational Medicine Research
- Role of Open Source Technology in Systems Design
- Is There a 'Cloud' in Your Future?
- Barriers Sharing Research and Development Data
- Process Management vs. Technology Considerations when Deploying New Systems

Panelists:
Susie Stephens, Director, Biomedical Informatics, Pharmaceutical Research & Development, Johnson & Johnson
Daniel J. Chin, Ph.D., Senior Principal Research Scientist, Roche Palo Alto
Chris Waller, Ph.D., Senior Director, Precompetitive Collaborations, Research, Development & Medical Informatics, Worldwide Technology, Pfizer, Inc.
Giles M. Day, Senior Director, BBC Informatics, Pfizer, Inc.

3:50 Presentation *Sponsored by* accelrys

Workflow based Enterprise Informatics
Frank Brown, Ph.D., Vice President & Chief Scientific Officer, Accelrys
Accelrys is producing a new generation of Enterprise Informatics systems for chemical, biological and image data registration and mining. The new generation features workflow driven application logic and business rules, clients that leverage the latest collaborative environments such as Microsoft SharePoint, and novel storage techniques to handle the complexity and diversity of today's data types.

4:05 Sponsored Presentation *(Sponsorship Opportunity Available)*

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

5:20 BREAK-OUT DISCUSSIONS in the Exhibit Hall

6:20 Close of Day

THURSDAY, FEBRUARY 4

DATA INFORMATION AND KNOWLEDGE MANAGEMENT

8:25 AM Chairperson's Remarks
Thomas P. Hill, Principal, The Leverage Innovation Group; former Director, Learning and Knowledge Management, Genentech

8:30 SparkLab 360 - The Complete System for Managing your Lab Research *Sponsored by*
Roi Paz, Chief Executive Officer, SparkLix Bio-IT
Electronic lab notebooks (ELNs) and laboratory information management systems (LIMS) are essential tools in lab management. SparkLix – an Innovation Award recipient from the Association for Laboratory Automation – developed SparkLab 360, which integrates features from ELNs and LIMS in one user-friendly system. This presentation focuses on how SparkLab enables design, planning, execution and analysis of the entire research process.

9:00 Knowledge for Strategic Advantage: Accelerating the R&D Cycle
Thomas P. Hill, Principal, The Leverage Innovation Group; former Director, Learning and Knowledge Management, Genentech
This presentation focuses on key elements of knowledge leveraged for strategic advantage in the Life Sciences industry, the key challenge of how to accelerate the R&D process by using collaborative informatics technologies and an examination of specific scientific business solution implementations for results. In addition, the key features of a robust collaborative scientific business solution will be identified.

9:30 ASAP-Emphasizing Multidimensional Drug Discovery
W. Patrick Walters, Ph.D., Senior Research Fellow & Group Head, Computational Drug Discovery Technologies, Vertex Pharmaceuticals, Inc.
ASAP is new software platform designed to help drug discovery teams make better decisions. ASAP provides an intuitive overview of the data that also allows scientists to easily "drill down" and examine the details of particular experiments. A combination of "filters" and heat maps allows teams to focus on aspects of the data while remaining aware of the "big picture".

10:00 RISe Architecture – Architectural Aspects of an Integrated Research Informatics Platform *Sponsored by*
Ajay Shah, Ph.D., MBA, PMP, Director of Research Informatics, Elan Pharmaceuticals Inc.
Elan and Infosys are building a research data integration platform called RISe (Research Informatics System at élan). RISe enables registration of biological entities, their inventory, associated workflows, and integration with chemical data utilizing a workflow driven, multi-tiered, SOA based architecture built on the Microsoft.NET platform. To maximize extensibility in a research environment, the database combines Entity-Attribute-Value design for flexible definition of entities, efficiency-prioritized OLTP schema for inventory management, and a planned ETL interface to a semantic database.

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

11:30 Agile Software Development: Meeting the Rapidly Changing Needs in Drug Discovery
Man-Ling Lee, Ph.D., Senior Program Analyst, Discovery Chemistry, Small Molecule Drug Discovery, Genentech, Inc.
To support drug discovery project teams meeting their timelines, the CompChem/ChemInformatics Group at Genentech has established an agile approach to satisfy the changing needs. The basis are two flexible software platforms, AEREA (Aestel Scientific Information) and Pipeline Pilot (Accelrys). The pres entation will discuss the implementation and impact of two applications: one for lead selection and one for DMPK data analysis.

INTEGRATIVE DATA MANAGEMENT THROUGH CLOUD, WIKIS, ONTOLOGIES & SEMANTIC WEB

12:00 PM Application of Translational Informatics in Tailored Therapeutics
Susie Stephens, Director, Biomedical Informatics, Pharmaceutical Research & Development, Johnson & Johnson

12:30 Managing Research Portfolios – Can IT help you? *Sponsored by*
Arvindh Balakrishnan, Vice President Life Sciences, Oracle
Joe Duncan, Chief Executive Officer, Teranode
Research departments work on hundreds of thousands of molecules, markers and targets. How can we simplify information gathering across your scientific community in order make consistent portfolio management decisions? This talk will focus on using Oracle technologies like semantic web; and how portfolios can be reflected in best in class portfolio management tools.

1:00 Luncheon Presentation *Sponsored by*
SOA-based IT Framework for Life Science Research
David A. Medina, Worldwide Life Science and Pharma Segment Executive, Hewlett-Packard Company
This presentation will present a collaborative platform for bioinformatics used in bioresearch based on a scalable, standards-based, easy-to-deploy, SOA-based architecture. This platform will facilitate the integration of intra-organizational research efforts and enable inter-o rganizational R&D collaboration. The platform will also enable pharma R&D organizations to effectively access disparate data sources and facilitate the cross-analysis of genomic, proteomic and clinical data.

1:45 Ice Cream Refreshment Break in the Exhibit Hall

PLENARY KEYNOTE SESSION

2:15 Plenary Keynote Introduction

2:25 Plenary Keynote Presentation *(See Page 26 for Details)*

3:05 Refreshment Break in the Exhibit Hall

INTEGRATIVE DATA MANAGEMENT THROUGH CLOUD, WIKIS, ONTOLOGIES & SEMANTIC WEB CONT.

3:45 Chairperson's Remarks
Susie Stephens, Director, Biomedical Informatics, Pharmaceutical Research & Development, Johnson & Johnson

3:50 Data Integration–What's in it for *Me*?
Randal Chen, Ph.D., Director, Research Informatics, Amgen, South San Francisco

4:20 Semantic Web and Cloud Computing for Integrative Data Management and Analysis Infrastructure
Jonas S. Almeida, Ph.D., Abell-Hanger Distinguished Professor, Bioinformatics and Computational Biology, University of Texas, M.D. Anderson Cancer Center
The systems nature of biological processes and the scalability of cloud computing created an irresistible trend towards distribution of both the data and the ecosystem of applications that analyze them. Accordingly, at M.D. Anderson Cancer Center we are exploring the use of semantic web to render distributed infrastructure manageable and its contents safely discoverable. An open-source prototype was developed, see s3db.org.

4:50 Collaborative Drug Discovery Humanitarian and Commercial Researcher Network Case Studies
Barry A. Bunin, Ph.D., Chief Executive Officer & President, Collaborative Drug Discovery (CDD), Inc.
Collaborative Drug Discovery (CDD) has created a community based platform that combines traditional drug discovery informatics with Web2.0 features to provide the best of both worlds. Recent efforts to selectively arrest TB in the dormant phase working with leading researchers and mining SAR data will be presented. A global community of leading TB researchers supported by leading foundations will be reviewed. Advances from communities working together on commercial

drug discovery bringing together industry, foundations, and academia will also be emphasized.

5:05 Panel: Drug Discovery Collaborations in 2010
Moderator: *Barry A. Bunin, Ph.D., Chief Executive Officer & President, Collaborative Drug Discovery (CDD), Inc.*
- Biopharmaceutical – CRO collaborations
- Virtual Pharmaceutical collaborations
- PPP (academic-industry-foundation) collaborations

Panelists:
Vaibhav A. Narayan, Ph.D., Senior Director, Integrative Neurosciences & Biomarkers, Johnson & Johnson Pharmaceuical Research & Development
Uli Schmitz, Ph.D., Director, Structural Chemistry, Gilead
Adam Renslo, Ph.D., Associate Director, Chemistry, Adjunct Assistant Professor, Pharmaceutical Chemistry

5:50 Close of Day

FRIDAY, FEBRUARY 5

TRANSLATIONAL INFORMATICS– HOW FAR HAVE WE COME?

8:30 AM Chairperson's Opening Remarks
Pearl S. Huang, Ph.D., Integrator, Oncology Franchise, Research & Early Development, Merck & Co.

8:35 Implementing a Translational Biomarker Strategy to Reduce Attrition in Drug Development
Irina Antonijevic, M.D., Ph.D., Director, Translational Research, Biological Research, Lundbeck Research, Inc. USA
Early efforts towards the discovery of molecular biomarkers for CNS disorders are encouraging. However, confirmation, and ultimately validation of such biomarkers is dependent on state-of-the-art bioinformatics analyses as well as assay development. These prerequisites will ensure identification of biomarkers that are reproducible and hence of clinical relevance.

9:05 High Content Mining of Disease Biomarkers
Jake Chen, Ph.D., Assistant Professor, Informatics & Computer Science, Indiana University School of Informatics; Director, Indiana Center for Systems Biology and Personalized Medicine, Indiana University-Purdue University Indianapolis; Founder, MedeoLinx, Inc.
To facilitate the interpretation of raw Omics data into detailed disease-specific knowledge of candidate biomarkers, we developed a "high-content biomarker mining" software system. The system can help manage and correlate molecular functions, molecular connectivity, biological pathways, and literature information. Its application into the current biomarker development process will help improve the success rate and quality of candidate biomarkers.

9:35 Single Molecule Real Time Biology: New technologies Enabling a More Complete Characterization of Disease Biology
Eric Schadt, Ph.D., Chief Scientific Officer, Pacific Biosciences
While there has been an explosion of technologies that enable more comprehensive characterizations of complex biological processes like common human diseases, we are still unable to glimpse a large enough fraction of the biology of these systems to build models that are predictive enough to achieve clinical utility. However, with a new wave of technologies on the horizon, providing for the capability to examine the activity of single molecules real time, we will soon be capable of generating the right scale and diversity of data (DNA sequence, RNA sequence, real time monitoring of mRNA translation, full characterizations of base modifications in genomes and transcriptomes) at low cost to dramatically enhance the construction of models for common human diseases that achieve clinical utility. I will cover the single molecule real time (SMRT) technologies from Pacific Biosciences and how these technologies will revolutionize our ability to characterize living systems, and then present a number of integrative biology approaches to taking the types of data SMRT technologies will generate to get at predictive models of disease that can be used to drive the identification and validation of drug targets and biomarkers.

10:05 Sponsored Presentation *(Sponsorship Opportunity Available)*

10:20 Coffee Break

11:00 Profiling Patients to Drive Biomarker Development
N. R. Nirmala, Ph.D., Director, Biomarker Analysis and Informatics Unit, Translational Sciences, Novartis Institutes of Biomedical Research
Gene expression profiling is one of the key ways in which a genome-wide view of a patient's response to drug treatment can be obtained. Such a molecular level view can provide strategies for customized therapies in many contexts. In this talk, the oppportunities and challenges that this technology presents will be discussed with a couple of case studies. Extension of this approach to other technologies will also be presented in the context of biomarker development.

11:30 Panel: Informatics at R&D Interphases
Moderator: *Pearl S. Huang, Ph.D., Integrator, Oncology Franchise, Research & Early Development, Merck & Co.*
- Linking clinical outcome with molecular data: filling the gaps
- Capturing uniform clinical language for outcomes
- Compatible and user- friendly data systems—can one size fit all?
- Disease cohorts-how many, how big, what is acceptable quality

12:00 PM Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

INTEGRATED GENOMIC, BIOLOGY, AND IMAGE DATA

1:00 Chairperson's Remarks
Ajay Shah, Ph.D., MBA, PMP, Director, Research Informatics, Elan Pharmaceuticals, Inc.

1:05 Image Analysis Considerations for Pre-clinical, *in vivo* Medical Imaging
Matt Silva, Head, Imaging Sciences, Millennium, The Takeda Oncology Company
With the expanding role of preclinical and translational imaging in drug research, it is necessary to consider not only study design and imaging modality but also visualization and image quantification. This presentation will review the role of imaging technologies and show examples of experiments and image analysis procedures, including kinetic analysis of dynamic contrast-enhanced MRI and bone topology analysis from 3D CT data.

1:35 RISe Prowler: A Semantic Web Approach to Integrating External and In-house Biology and Chemistry Information
Ajay Shah, Ph.D., MBA, PMP, Director, Research Informatics, Elan Pharmaceuticals, Inc.

2:05 Development of a Registration System for Biologics in a Collaborative Special Interest Group
Jeremy Packer, Ph.D., Head, Bioinformatics, Abbott

2:35 Development of Combination Therapies for Multiple Sclerosis Using Systems Level Informatics
Frederic S. Young, Ph.D., Chief Scientist, Vicus Therapeutics
We start with a multilevel systems physiology model that combines metabolomic analysis with integrated physiological analysis. The model is used to define a set of systems informatic features of ontogeny, phylogeny, homeostasis, and repair that distinguishes the disease state from homeostasis. We describe our use of this systems informatic signature as an algorithm for the development of combination therapies for multiple sclerosis.

3:05 Close of Conference

Cambridge Healthtech Institute's Sixth Annual

Cancer Profiling and Pathways:

Next Sequence in the War against Cancer

WEDNESDAY, FEBRUARY 3

7:00 AM Registration and Morning Coffee

8:00 Plenary Keynote Session *(See Page 26 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

KEYNOTE PRESENTATIONS

11:00 Chairperson's Remarks
Michael Liebman, Ph.D., Managing Director, Strategic Medicine, Inc.

11:10 Personalizing Medicine: It's a System-Based Challenge
Franklyn G. Prendergast, M.D., Ph.D., Professor, Pharmacology, Biochemistry & Molecular Biology, Director, Center for Personalized Medicine, Mayo Clinic

11:40 Genomic Strategies for Personalized Cancer Treatment
Joseph R. Nevins, Ph.D., Barbara Levine Professor, Breast Cancer Genomics, Center for Applied Genomics & Technology, Duke University

Perhaps the major challenge in developing more effective therapeutic strategies for the treatment of most major cancers is confronting the heterogeneity of the disease, recognizing that most cancers are not one disease but multiple disorders with distinct underlying mechanisms. We have made use of expression profiling to develop signatures of oncogenic pathway deregulation that can then be used to profile the state of these pathways within populations of tumors. In addition, the pathway signatures also link the patterns of pathway activation with therapeutics since we have shown that predicting the activation of a pathway also predicts sensitivity to drugs that target the pathway. We have extended this concept to develop more refined signatures that can dissect the complexities of many of the known signaling pathways, providing a more precise capacity to probe the activity or deregulation of the pathway and linking to a broader array of therapeutics. We suggest that this approach can provide a framework for an overall strategy towards the development of personalized treatment options for the individual patient, including strategies for personalized combination therapy.

12:10 PM Panel: Impact of Personalized Medicine on Oncology Drugs and Treatment
Additional Panelist: Mike Boswood, President, CEO, Thomson Reuters

- How could information about differences of individuals become a way to improve drug discovery rather than reduce ROI?
- How can you change it to bring in new knowledge?
- How do you change perception of culture?
- Is it purely technology that is needed to solve the problem?

12:40 Luncheon Presentation I *Sponsored by* nanoString TECHNOLOGIES

Digital, Multiplexed Measurements of up to 550 mRNAs in Clinically Relevant Sample Types Using the nCounter™ Analysis System
Gary Geiss, Ph.D., Principal Scientist, NanoString Technologies, Inc.

The nCounter Analysis System utilizes color-coded molecular barcodes to digitally count nucleic acid molecules. The system can multiplex 550 targets without enzymatic manipulation. A variety of input samples have been tested, including FFPE and crude cell lysates. The technology has been applied to multi-gene expression cancer signatures and mRNA fusion-transcripts. Products to measure miRNAs and dsDNA are under development.

1:10-1:40 A Novel Genome-Wide Screening Application Using Pooled Viral miRNA-adapted shRNA (shRNAmir) Libraries *Sponsored by* Thermo SCIENTIFIC

Katie Jansen Spayd, Ph.D., Research Scientist, Thermo Fisher Scientific

Pooled shRNA libraries are powerful genetic discovery tools that allow for high-throughput screening of the entire genome in a cost-effective and less labor-intensive manner. Unlike arrayed shRNA library approaches requiring many multi-well plates, screens using lentiviral shRNA pools can be performed in a single tissue culture plate. Clonal populations of cells expressing an individual shRNA become enriched or depleted in this mixed population in response to a selective pressure. Genes required for cell enrichment or cell depletion can then be deconvoluted by next-generation sequencing or microarrays hybridized with barcode sequences corresponding to each shRNA in the pool. Here, we present a novel pooled shRNA screening approach for identifying regulators of endogenous gene expression. Epithelial cell adhesion molecule (EpCAM), a cell surface receptor that is highly expressed in a variety of tumorigenic cells, promotes cell proliferation and tumor formation via transcriptional activation of mitogenic genes. Thus, EpCAM represents a target for the development of new cancer therapeutics. We performed a whole-genome pooled shRNA screen to identify novel regulators of EpCAM expression. OVCAR8 cells were transduced with the Thermo Fisher Scientific Decode™ RNAi Viral shRNAmir Pools. Following puromycin selection, we used magnetic-activated cell sorting (MACS) to separate cells on the basis of EpCAM protein expression. Genomic DNA was isolated from EpCAM+ and EpCAM- cells and the shRNAs enriched or depleted within each population were identified using custom microarrays. The genes targeted by shRNAs enriched in EpCAM- cells were identified as candidate regulators of EpCAM expression. This work demonstrates that pooled shRNA libraries may be used in a variety of novel screening strategies, including the identification of novel regulators of tumor-associated genes.

1:45 Dessert in the Exhibit Hall

1:45 Dessert in the Exhibit Hall

WORKING BACKWARDS IN CANCER: FROM THE CLINIC TO DISCOVERY

2:15 Chairperson's Remarks
Michael Liebman, Ph.D., Managing Director, Strategic Medicine, Inc.

2:20 Using Drug-Induced Feedback Loops to Identify Indications and Combination Partners
Donald Bergstrom, Director, Experimental Medicine Oncology, Merck
James W. Watters, Associate Director, Molecular Profiling Oncology, Merck

Treatment with molecular targeted agents can result in compensatory feedback regulation as cells respond to inhibition of signaling pathways. We will present clinical evidence that treatment with a small molecule inhibitor of gamma secretase results in pathway modulation and compensatory feedback, and describe pre-clinical experiments designed to leverage this concept for drug response prediction.

2:50 Genomic Solutions to Diagnostic and Prognostic Clinical Predictions in Head and Neck Cancer
Geoffrey Childs, Ph.D., Professor of Pathology, Albert Einstein College of Medicine
Richard V. Smith, M.D., FACS, Professor, Vice-Chair, Department of Otorhinolaryngology-Head and Neck Surgery, Montefiore Medical Center and Albert Einstein College of Medicine

The strategy our group employs is to utilize the data obtained from high throughput assays including gene expression measurements of mRNA and miRNA, global methylation patterns of DNA and global proteomics to develop prognostic and diagnostic signatures to predict outcome, local regional recurrence presence/absence of lymph node metastasis at initial diagnosis and to predict optimal treatment options.

3:20 Moving Research Closer to the Bedside, *in vitro* and *in vivo* Analyses with Primary Tumors
Fred Poordad, M.D., Chief of Hepatology, Liver Disease and Transplant Center, Cedars-Sinai Medical Center, Xin Wei Wang, Ph.D., Senior Investigator Head, Liver Carcinogenesis Section, Laboratory of Human Carcinogenesis, National Cancer Institute, NIH, and Michael R. Briggs, Ph.D., Senior Director, Biology, Vertex Pharmaceuticals, Inc.

The incidence of Primary Liver Cancer is increasing in the west and constitutes a tremendous burden on world health as the third leading cause of cancer deaths worldwide. The 5 year survival rate is a dismal 11 %, due in large part to late diagnosis and limited treatment options. The etiology of this devastating disease as well as current and proposed new therapies wil be discussed. Steps to better diagnose and stratify patients for targeted therapy will be considered as a new and exciting phase of cancer research. Finally, a move toward more relevant research will be presented as an hypothesis that

will be tested in the coming years as more new and current therapies are compared and contrasted to current best practice.

4:05 How do you go from Pathways to Clinical Outcomes?

Sponsored by Biovista

Aris Persidis, Ph.D., President, Biovista, Inc.

In drug discovery and development what what really counts is the clinical outcome, the Benefit/Risk of the drug within the context of its pathway or mechanism of action (MoA). Biovista screens the MoA of any drug or target against the MoA of 8,000 indications and 12,000 adverse events (AEs). This is simultaneous, unbiased indication discovery and AE profiling, and it is unique. It helps to bridge the gap from molecular pathway to clinical outcome in a single step. Case studies in cancer and other diseases will be described.

4:35 Reception in the Exhibit Hall *(Sponsorship Available)*

5:20 BREAK-OUT DISCUSSIONS in the Exhibit Hall

What is the Forecast for Epigenetics and microRNA?

Moderator: Enal Razvi, Ph.D., System Biosciences SBI

- Status of the microRNA and epigenetics markets
- The research market for microRNA and epigenetics: growth and evolution
- Diagnostics and therapeutics development based on microRNA and epigenetic signatures
- Current challenges and opportunities in these spaces

Challenges to Whole Genome Sequencing

Moderator: s Ng, Ph.D., Assistant Professor, Genomic Medicine, J Craig Venter Institute

- Challenges to whole-genome sequencing
- Identifying de novo and re-current mutations in cancer
- Addressing tumor heterogeneity
- How can we move from characterizing gene variation to utilizing the whole genome
- Sequencing tumors rather than tumor cell lines
- The Complex genomic structure of tumor cells: de novo assembly or strategy to detect structural variants

Are there Cancers of Unknown Primary Tumors?

Moderator: Dalia Cohen, Ph.D., Chief Scientific Officer, Rosetta Genomics, Inc.

- Debate over cancers of unknown primary tumors (CUP)
- Methods to detect CUPs
- Consequences of detection of primary

Gene Signatures in Cancer Diagnostics

Co-Moderators: Gary Geiss, Ph.D., Principal Scientist, NanoString Technologies and David Kern, MBA, Director, MyRaQa

- Developing a gene signature
- Validation of gene signatures
- Regulatory considerations for gene signature diagnostics

Systems Chemical Biology-A New Paradigm

Moderator: Ally Perlina, Senior Application Scientist, GeneGo Inc.

- Utilizing tools for drug repositioning
- Understanding side effects
- Understanding the mechanisms of action for drugs
- Networkable compounds

6:20 Close of Day

THURSDAY, FEBRUARY 4

REAL EXAMPLES OF INTEGRATING PATHWAY DATA

8:25 AM Chairperson's Remarks

Megan Laurance, Ph.D., Senior Scientist, Ingenuity Systems, Inc.

8:30 Keynote Presentation

Kenneth H. Buetow, Ph.D., Associate Director, Bioinformatics and Information Technology, National Cancer Institute

9:00 Cooperative and Complementary Genetic Selection in Brain Tumors

Markus Bredel, M.D., Ph.D., Director, Northwestern Brain Tumor Institute Research Program, Assistant Professor, Department of Neurological Surgery, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, and Lurie Center for Cancer Genetics Research and Center for Genetic Medicine

Brain tumors are a disease of the genome. These tumors show recurrent patterns of genetic aberrations. Dissecting which genetic events function cooperatively to deregulate principal signaling pathways in brain tumors and which are complementary to such deregulation will help developing refined therapeutic strategies to treat these complex diseases.

9:30 Expression Based Patient Stratification for Cancer Prognostics

Peter J. van der Spek, Ph.D., Department of Bioinformatics, Erasmus MC - Medical Faculty

Systems biology approaches in life sciences and health open new perspectives for patient stratification. Microarray and next-generation sequencing techniques provide vast volumes of data and detailed information about natural variants vs. mutations in the underlying molecular etiology of the disease. Knowledge bases allow scientists to place their research results in perspective.

10:00 Functional Analysis of Omics Data in Cancer

Sponsored by GeneGo

Yuri Nikolsky, Ph.D., CEO, GeneGo, Inc.

High-throughput assays are indispensable in studies of complex human diseases. Numerous methods have been developed for Omics data analysis. I will describe GeneGo techniques of pathway, network, and interactome analysis, and summarize recent results of our collaborative studies on breast, colorectal, pancreatic, and glial cancers. I will also describe functional analysis of predictive gene signatures developed for FDA's MAQCII project.

10:15 Cellular Target Profiling and Quantitative Phosphoproteomics Reveal Insight into a Drug's Efficiency and Cellular Mode of Action

Sponsored by KINAXO Biotechnologies GmbH

Jutta Fritz, Ph.D., Head of Technology, Kinaxo Biotechnologies

System-wide approaches integrating drug target identification and global phosphoproteomics depict a compound's cellular mode of action and its impact on signal transduction. KINAXO's chemical proteomics and global quantitative phosphoproteomics platform revealed Sorafenib's target profile and allowed quantification of phosphorylation patterns in relation to drug administration, thereby facilitating monitoring of the integration of signaling and pointing at additional therapeutic applications.

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

11:30 microRNA Expression Profiling for the Identification of Forensically Relevant Biological Fluids

Jack Ballantyne, Ph.D., Professor, Department of Chemistry, Associate Director for Research, National Center for Forensic Science, University of Central Florida

We performed the first miRNAome-wide evaluation of specific miRNA expression in dried, forensically relevant biological fluids (blood, semen, saliva, vaginal secretions and menstrual blood). A panel of nine differentially expressed miRNAs was identified that permit the identification of the body fluid using 50pg of total RNA. miRNA profiling provides a promising alternative approach to body fluid identification for forensic casework.

12:00 pm Gene Expression Signatures of Pathway Activity as Biomarkers in Oncology: RAS Pathway Signature

Andrey P. Loboda, Ph.D., Research Fellow, Oncology Molecular Profiling, Merck Research Laboratories

12:30 Luncheon Presentation I

Sponsored by METABOLON

Overview of Metabolomics

John Ryals, Ph.D., Chief Executive Officer, Metabolon, Inc.

Metabolomics is the global profiling of biochemicals and metabolites in biological samples and provides a snapshot of the metabolic state of a biological system. As such, it can rapidly characterize and identify metabolic changes caused by drugs, disease, diet or environment effects. This talk provides an overview of metabolomics and the technology requirements for profiling hundreds of biochemicals. The technology platform deployed at Metabolon involves the separation of analytes on three independent analytical platforms (GC-MS, LC-MS/MS(+), LC-MS/MS(-)). Proprietary software processes the mass spectral data and retention times by matching the run data to a database of biochemical standards. This "chemo-centric" approach results in the positive identification of hundreds of biochemicals in a single sample. Through statistical analysis, the significant changes are identified and mapped onto biochemical pathways. Because biochemicals are closely related to biological phenotype, identification of affected pathways not only provides insight into the biological mechanism but uncovers biomarkers useful in diagnosing and monitoring.

1:00 Luncheon Presentation II *Sponsored by* BIOBASE

Regulatory Network Analysis of Cancer Gene Expression Profiles for Target and Biomarker Discovery Using the ExPlain™ Analysis System

Raymond DiDonato, Ph.D., Product Manager, BIOBASE Corporation

High-throughput gene expression analysis techniques generate large amounts of data, which pose a particular challenge of transforming expression data into meaningful hypotheses for target discovery and candidate biomarker identification. Traditional approaches for interpreting expression data rely on mapping differentially expressed genes to canonical pathways, biological processes, or disease states. However, understanding the transcriptional regulators and upstream signaling events that lead to differential gene expression can help better identify the molecular mechanisms that influence changes in gene expression profiles, facilitating discovery of targets which themselves are not differentially expressed, but which are key to underlying disease mechanisms. In this session we present a case study in which ExPlain™, a tool that employs the BIOBASE Knowledge Library™ for promoter and regulatory network analysis, was used to uncover target and biomarker candidates from a cancer gene expression experiment, by identifying upstream signaling molecules likely involved in the underlying pathways leading to the disease state.

1:45 Ice Cream Refreshment Break in the Exhibit Hall

PLENARY KEYNOTE SESSION

2:15 Plenary Keynote Introduction

2:25 Plenary Keynote Presentation *(See Page 26 for Details)*

3:05 Refreshment Break in the Exhibit Hall

SYSTEMS BASED APPROACHES TO CANCER SEQUENCING: PUTTING TOGETHER A NETWORK OF CHANGES

3:45 Chairperson's Remarks

Robert L. Strausberg, Ph.D., Deputy Director, J. Craig Venter Institute

3:50 Whole Genome Sequencing in Cancer

Gad Getz, Ph.D., Head, Cancer Genome Analysis, The Broad Institute

4:20 Systematic Discovery of Cancer Gene Fusions using Paired End Transcriptome Sequencing

Chandan Kumar, Ph.D., Michigan Center for Translational Pathology, University of Michigan

Gene fusions represent common genetic aberrations in cancers that can serve as specific biomarkers and therapeutic targets. The recent discovery of recurrent gene fusions in prostate and lung cancers portends similar aberrations in other common carcinoma. We employ paired end transcriptome sequencing and customized bioinformatic pipelines to characterize gene fusions and chimeric transcripts in cancer.

4:50 Mapping Cancer Genomics Data to Pathways

David Haussler, Ph.D., Professor & Director, Biomolecular Science & Engineering, University of California, Santa Cruz

It is essential, but challenging to interpret cancer genomics data in terms of biological meaningful perturbations of molecular pathways within tumor cells. I will discuss a new Cancer Genomics Browser, on the web at genome-cancer.ucsc.edu, that accomplishes this through large-scale data analysis and probabilistic modeling. This methodology is currently being used in several large-scale cancer studies, including the ISPY breast cancer trial, the TCGA project and by one of the SU2C Dream Teams.

5:20 Analyzing Coding Variants

Pauline Ng, Ph.D., Senior Scientist, Human Genomic Medicine, J. Craig Venter Institute

Whole genome and whole exome sequencing are identifying a large number of coding variants. Some of these coding variants may have functional consequences that lead to disease. I will discuss the behavior of coding variants and the webtools we have made to analyze them.

5:50 Close of Day

FRIDAY, FEBRUARY 5

MICRORNA DIAGNOSTICS FOR CANCER: TRANSLATING INFORMATION TO PRACTICAL USE

8:30 AM Chairperson's Opening Remarks

Dalia Cohen, Ph.D., Chief Scientific Officer, Rosetta Genomics, Inc.

8:35 Keynote Presentation: Causes and Consequences of microRNA Dysregulation in Cancer

Carlo M. Croce, M.D., Professor, Internal Medicine, College of Medicine & Public Health, The Ohio State University

During the past several years it has become clear that alterations in the expression of microRNA genes contribute to the pathogenesis of most, perhaps all, human malignancies. These alterations can be caused by a variety of mechanisms, including deletions, amplifications or mutations involving microRNA loci, by epigenetic silencing or by dysregulation of transcription factors targeting specific microRNAs. Since malignant cells show dependence on the dysregulated expression of microRNA genes, which in turn control or are controlled by dysregulation of multiple protein coding oncogenes or tumor suppressor genes, these small RNAs provide important opportunities for development of future microRNA based therapies.

9:05 microRNA Polymorphisms and the Future of Personalized Medicine

Prasun J. Mishra, Ph.D., Laboratory of Cancer Biology & Genetics, National Cancer Institute, NIH

Referred to as the micromanagers of gene expression, microRNAs are evolutionarily conserved small non-coding RNAs. Polymorphisms in the microRNA pathway can influence gene regulation and are emerging as powerful tools to study the biology of diseases. Detection of microRNA-polymorphisms can potentially improve diagnosis, treatment and prognosis in patients and has profound implications in the fields of pharmacogenomics and personalized medicine.

9:35 Living in a Sequen-omics World: Data Integration Issues and Challenges

Gavin Gordon, Ph.D. Co-Director, Thoracic Surgery Oncology Lab, Brigham & Womens Hospital

DNA sequencing and other "-omics" platforms (e.g., mRNA, microRNA, CGH, exon, SNP, and other arrays) have experienced a technological revolution in throughput and scale over the preceding decade that shows no sign of slowing. However, data storage and processing advances have outpaced the ability to fully integrate the resulting massive quantities of data into biologically meaningful and predictive models to apply to risk estimation, prevention, and cure of human diseases, most notably cancer. In addition, further technological innovation will continue to drive down costs which will exacerbate the problem in the near-term but over the long-term will bring more resources to bear in solving these issues and challenges. This session will provide a comprehensive view of the sequen-omics landscape and identify the key issues that will need to be addressed in the future for these platforms to positively affect human health.

10:05 Sponsored Presentation *(Sponsorship Opportunity Available)*

10:20 Coffee Break

11:00 The Onco-SNP and Cancer Risk: microRNA Binding Site Polymorphisms as Biomarkers

Joanne B. Weidhaas, Ph.D., Assistant Professor, Therapeutic Radiology, Yale University

Since microRNAs are global regulators, small aberrations such as SNPs that disrupt their coding sequences or their target binding sites can alter cellular homeostasis and enhance cancer risk. MicroRNA binding site polymorphisms have turned out to be some of the strongest biomarkers of cancer risk, can act as biomarkers of outcome, and may be future targets for therapy.

11:30 Role of microRNA Based Profiling in Determining Tissue of Origin for Carcinoma of Unknown Primary

Gauri Varadhachary, M.D., Associate Professor of Medicine, Department of G.I. Medical Oncology, M.D. Anderson Cancer Center

Carcinoma of unknown primary (CUP) is a heterogeneous disease where a patient presents with metastases without an identifiable primary. As more effective cytotoxic and targeted therapies emerge for additional known cancers, accurate identification of CUP subtypes will become increasingly important to the appropriate care of these patients. MicroRNA expression profiling is an emerging tool to help with identification of tissue of origin in patients with CUP.

12:00 PM Luncheon Presentation *(Sponsorship Opportunity Available)*

or Lunch on Your Own

TARGETING CANCER STEM CELLS

1:00 Chairperson's Remarks
Tim Hoey, Ph.D., VP, Cancer Biology, OncoMed Pharmaceuticals, Inc.

1:05 Impact of Antibodies on Cancer Stem Cells: Discovering Underlying Pathways Essential to Cancer Stem Cell Biology
Tim Hoey, Ph.D., VP, Cancer Biology, OncoMed Pharmaceuticals, Inc.
Cancer stem cells are thought to mediate tumor initiation, metastasis, and recurrence. We have isolated and characterized CSCs from a variety of major tumor types and have found that these cells are preferentially resistant to many current therapies. As part of our effort to develop novel agents targeting CSCs, we have developed an anti-DLL4 antibody that blocks Notch signaling. Anti-DLL4 inhibits tumor growth through multiple mechanisms including a reduction in CSC frequency.

1:35 Understanding Tumor Cell Heterogeneity in NSCLC: Contributions to Resistance and Relapse
Erica L. Jackson, Ph.D., Scientist, Department of Tumor Biology and Angiogenesis, Genentech, Inc.
Tumors are made up of a heterogeneous mixture of cell types and it is possible that distinct cell populations play unique roles in tumorigenesis. We are studying functionally defined cell populations to determine what distinguishes chemo-resistant cells from bulk tumor cells.

2:05 New Visions of Cancer Therapy through the Prism of the Cancer Stem Cell Hypothesis
Justin D. Lathia, Ph.D., Research Associate, Department of Stem Cell Biology and Regenerative Medicine, Lerner Research Institute, Cleveland Clinic Foundation
The failure of conventional therapies to fundamentally alter the survival of advanced and metastatic cancers has many causes but one appears to be the striking cellular heterogeneity in most cancers. The cancer stem cell hypothesis posits that tumors contain a cellular hierarchy of differentiation and tumor propagation potential. As studies have demonstrated that cancer stem cells display therapeutic resistance, angiogenic potential, and a propensity towards invasion/metastasis, the identification of signaling pathways and molecular targets in cancer stem cells may yield improved cancer therapies.

2:35 Close of Conference

Cambridge Healthtech Institute's Fifth Annual

Stem Cells

Shaping the Future of Regenerative Medicine

WEDNESDAY, FEBRUARY 3

7:00 AM Registration and Morning Coffee

8:00 Plenary Keynote Session *(See Page 26 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

ADVANCING REGENERATIVE MEDICINE

Addressing the numerous topics central to the theme of regenerative medicine, this meeting assembles prominent researchers, clinicians, businessmen, and regulators who not only are at the cutting edge of their respective fields, but also represent wide areas of expertise. The cross-fertilization of the information presented in the area of stem cell research engineers brainstorming and provides a forum for discussion to enable the rapidly expanding therapeutic potential of regenerative medicine.

11:00 Chairperson's Remarks
Dawn Driscoll, MBA, Ph.D., Principal, DCi

11:10 Keynote Presentation

Stem Cells: Moving from Discovery Towards the Clinic
Alan Trounson, Ph.D., President, California Institute of Regenerative Medicine

11:55 Featured Presentation
Diabetes Under Control
Andrew Rakeman, Ph.D., Scientific Program Manager, Regeneration, Juvenile Diabetes Research Foundation
Diabetes treatments necessitate the replacement or regeneration of pancreatic beta cells to improve glucose control and avoid serious side effects. Replacement of beta cells has attracted considerable attention with the use of cadaveric islets, pig islets and a variety of adult stem cells. It appears that the best source to date is cells obtained from human embryonic stem cells and there is hope that iPS cells may one day also be an appropriate source. More recently, interest has focused on regenerating the pancreas as a result of access to human progenitors as well as a better understanding of cell proliferation and neogenesis will accelerate the development of beta cell regenerative medicines.

12:40 PM Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

1:45 Dessert in the Exhibit Hall

CONSIDERATIONS FOR ADVANCING REGENERATIVE MEDICINE INTO THE CLINIC

2:15 Chairperson's Remarks
Dawn Driscoll, MBA, Ph.D., Principal, DCi Biotech

2:20 hESC-Derived Oligodendrocyte Progenitor Cells-GRNOPC1 for Acute Spinal Cord Injury
Edward Wirth III, M.D., Ph.D., Medical Director, Geron Corporation

2:50 From Tissue Engineering to Regenerative Medicine: An Evolution in Understanding
Damien Bates, M.D., Ph.D., Chief Medical Officer, Organogenesis, Inc.

3:20 MSC-Derived SB623 Cells for Stable Stroke
Casey Case, Ph.D., Vice President of Research, SanBio, Inc.
SB623 cells are derived from bone marrow stromal cells (MSCs). They have shown great potential in models of CNS regeneration. The cells are used allogeneically and implanted directly at the site of injury. Our first clinical application will be in stable ischemic stroke patients. Models of efficacy and safety will be discussed as will issues pertaining to manufacturing and clinical plans.

3:50 Presentation *Sponsored by* Thermo SCIENTIFIC

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

5:20 BREAK-OUT DISCUSSIONS in the Exhibit Hall
Forecasting Cell Therapy Sales - How and Why
Host: Dawn Driscoll, MBA, Ph.D., Principal, DCi Biotech
Investors, Manufacturing, HR, and Management all want to know, "How much of this cell therapy are you really going to sell, and when?" This interactive discussion will address:

- Basics of forecasting for both allogeneic and autologous cell therapies, in order to support decision making for clinical development, investor presentations, and manufacturing capacity;
- Determining realistic patient numbers, the impact of reimbursement on sales, the impact of projected sales on GMP manufacturing capacity;
- Staffing needs to support a given forecast.

6:20 Close of Day

THURSDAY, FEBRUARY 4

ENABLING TECHNOLOGIES FOR REGENERATIVE MEDICINE

8:25 Chairperson's Remarks
Marc Unger, Ph.D., CSO, Fluidigm

8:30 Human Embryonic Stem Cells (hESCs) for Tissue Regeneration: How to Get the Cells We Need
Harold S. Bernstein, M.D., Ph.D., Professor of Pediatrics, Eli and Edythe Broad Center of Regeneration Medicine & StemCell Research, University of California, San Francisco Cardiovascular Research Institute
Cell therapies derived from hESCs have shown promise in animal models of human disease. However in some cases, such as in attempts to augment myocardial tissue, fully differentiated hESC-derived cells may be beyond the ability to fully incorporate into and improve the function of existing tissue. To address this, we have focused on identifying subpopulations of hESCs that preferentially differentiate into specific embryonic germ layers, developing chemical and miRNA-based enrichment strategies for directed differentiation of hESCs, and creating reporter hESC lines and non-integrating molecular beacons that facilitate the selection of precursors committed to specific lineages.

9:00 Engineering the Morphogenesis of Pluripotent Stem Cells
Todd McDevitt, Ph.D., Assistant Professor, Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory

9:30 Improved Culture Conditions for the Growth and Recovery of Cryopreserved Human Pluripotent Stem Cells
Angie Rizzino, Ph.D., Professor, Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center
Poor recovery of cryopreserved hES cells and iPS cells is a significant impediment to progress with pluripotent stem cells. To address this problem, we have determined that Y-27632, a specific inhibitor of Rho kinase (ROCK) activity, significantly enhances recovery of hES cells from cryopreserved stocks when cultured with or without a growth inactivated feeder layer. Remarkably, hES cells that had formed relatively few colonies even seven days after thawing exhibited rapid growth upon addition of Y-27632. Additionally, we determined that Y-27632 significantly improves the recovery of cryopreserved human iPS cells and their growth upon subculture.

10:00 Presentation *Sponsored by* Fluidigm

Programmable, Fully Automated Microfluidic Stem Cell Culture System

Marc A. Unger, Ph.D., CSO, Fluidigm Corporation

Cell reprogramming techniques require treating cells with multiple factors, either for conversion of differentiated cells into induced pluripotent stem (IPS) cells or for conversion of pluripotent cells into a desired type of differentiated cells. Fluidigm is developing a versatile, automated cell culture system which can culture cells, carry out multi-factor dosing experiments, and image the cells in both fluorescence and incident light modes in any desired time sequence. The results of in-chip cell culture and multi-factor dosing experiments will be described and applications discussed.

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

11:30 Integrated Chemical Genomics Reveals Modifiers of Cell Fate in Pluripotent Stem Cells

April Pyle, Ph.D., Assistant Professor, Microbiology, Immunology & Molecular Genetics, Eli and Edythe Broad Center of Regenerative Medicine & Stem Cell Research; Jonsson Comprehensive Cancer Center, University of California, Los Angeles

While hESCs can be maintained *in vitro*, cells grown in continuous culture have been shown to develop cytogenetic and genetic aberrations associated with cancer *in vivo*. Additionally, hESCs exhibit poor survival as single cells following dissociation, which limits the ability to perform genetic manipulation and homogenous differentiation of hESCs. In order to identify pathways involved in regulating self-renewal and survival without instability, we have developed a cell-based high content screening (HCS) assay using small molecules. This method provided a comprehensive approach for studying hESC fate *in vitro* and identified a number of novel regulators of hESC growth.

12:00 PM Biocompatible Grafted Carbon Nanotubes as Scaffolds for Preferential hESC Differentiation

Jennifer Lu, Ph.D., Professor, School of Engineering, University of California, Merced

Presented is our research on using biocompatible grafted carbon nanotubes as scaffolds for preferential neuron cells differentiation from hESCs. It has been found that carbon nanotube-based scaffolds promote the growth factor adsorption, leading to more selective differentiation. It has been observed that surface properties such as hydrophilicity and charge can play important roles in directing hESC differentiation. Novel responsive scaffolds have been synthesized and the potential use of such dynamic scaffolds for cell growth, differentiation and proliferation will be discussed.

12:30 Luncheon Presentation *Sponsored by* MSD Meso Scale Discovery

Multiplex Biomarker Assays for Translational Research

Robert Umek, Ph.D., Director of Research, Meso Scale Discovery

1:45 Ice Cream Refreshment Break in the Exhibit Hall

PLENARY KEYNOTE SESSION

2:15 Plenary Keynote Introduction

2:25 Plenary Keynote Presentation *(See Page 26 for Details)*

3:05 Refreshment Break in the Exhibit Hall

IPS CELLS: FROM SCREENING TO THERAPY

Induced pluripotent stem cells (iPS) cells, the most recent advancement in stem cell research, even further widen and generate applications for stem cell research. iPS cells exhibit great promise in drug discovery and screening as well as in regenerative medicine. iPS Cells: From Screening to Therapies not only explores current methods of generating, maintaining, and utilizing iPS cells but will address the shift in using them to contribute to Shaping the Future of Regenerative Medicine.

3:45 Chairperson's Remarks

Bruce Conklin, M.D., Senior Investigator, Gladstone Institute of Cardiovascular Disease, Professor of Medicine, Division of Medical Genetics, University of California, San Francisco

IPS CELLS FOR DISEASE MODELS

3:50 Featured Speaker
Potential Promise of iPS Cells for Understanding Disease Progression

Sheng Ding, Ph.D., Assistant Professor, Chemistry, Scripps Research Institute

4:20 iPS Cells for Cardiovascular Models and Diagnostics

Bruce Conklin, M.D., Senior Investigator, Gladstone Institute of Cardiovascular Disease, Professor of Medicine, Division of Medical Genetics, University of California, San Francisco

Our functional genomic experiments focus on GPCR signaling pathways in pluripotent ES cell-derived cardiac myocytes. We use high-throughput gene inactivation methods, including siRNA and gene trapping in ES cells, and then analyze ES cell-derived cardiomyocytes. Our initial signaling studies focused on mouse ES cells, and ES cell-derived mice. We are using human iPS cells for similar signaling studies and to produce models of human cardiac disease including Long QT syndrome.

4:50 Using iPS Cells to Model Neurological Diseases

Clive N. Svendsen, Ph.D., Professor, Anatomy & Neurology, University of Wisconsin

5:20 Hoseok Song, Ph.D., Professor of Biology, University of California, San Diego

5:50 Close of Day

FRIDAY, FEBRUARY 5

IPS CELLS FOR REGENERATIVE HEALING

8:30 AM Chairperson's Opening Remarks

Timothy J. Kamp, M.D., Ph.D., Professor of Medicine & Physiology; Co-Director Stem Cell and Regenerative Medicine Center, University of Wisconsin

8:35 microRNA-Target Gene Networks as Fundamental Factors in the Next Generation Regenerative Strategies

Preethi H. Gunaratne, Ph.D., Assistant Professor, Department of Biology & Biochemistry, University of Houston

MicroRNAs are small non-coding RNAs that integrate multiple genes within and across biological pathways. LIN28/let-7; c-MYC-E2F/miR-17-92 and Oct4/Sox2/miR-302-cyclin D1 networks have been tightly linked to embryonic (ES) and more recently to iPS cells. We have also uncovered additional miRNAs regulated by Ronin, a non-canonical pluripotency factor that target genes regulating cytoskeletal remodeling and epigenetic silencing. Discussed is the potential role of these key miRNAs in the next generation regenerative strategies.

9:05iPS Cells Offer New Alternative and Early Treatment in Genetic Diseases

Yuet Wai Kan, MB, BS, D.Sc., Professor, Department of Medicine, University of California, San Francisco

Two alternatives are currently available to parents if the prenatal diagnosis of a serious genetic disease is made: to terminate the pregnancy, or to continue it and take care of a seriously ill child. Generation of iPS cells from the amniotic fluid or CVS cells used for the diagnosis, correction of the mutation, and differentiation of the cells into specific tissues may in the future offer a new alternative. In addition, it will allow early treatment of the genetic disease, an important consideration in diseases where organ damage begins early in life.

9:35 Pluripotent Stem Cells Derived from Adult Human Testes

Martin Dym, Ph.D., Professor, Biochemistry & Molecular & Cellular Biology, Georgetown University Medical Center

Male germline stem cells obtained from adult human testes can be reprogrammed spontaneously to generate pluripotent stem cells. The production of these "non-canonical" iPS cells is spontaneous, and do not require the addition of exogenous genes, some of which may be cancer causing. Our results suggest that human spermatogonial stem cells have great potential for cell-based, autologous organ regeneration therapy for various diseases and it is thus possible that in the near future men could be cured of disease with a biopsy of their own testes.

10:05 Poster Presentation: Differentiation of Human Embryonic and Human Induced Pluripotent Stem Cells Along the Otic Lineage

Kinuko Masaki, Stanford University

10:20 Coffee Break

IPS CELLS FOR REGENERATIVE HEALING CONT'D

11:00 Directed Differentiation of Human iPS Cells Generates Active Motor Neurons

William Lowry, Ph.D., Assistant Professor, Department of Molecular, Cell and Developmental Biology, University of California, Los Angeles

A study of gene expression profiles of mouse and human ESCs and iPSCs suggests that, while iPSCs are quite similar to their embryonic counterparts, a recurrent gene expression signature appears in iPSCs regardless of their origin or the method by which they were generated. Shown is how both hESCs and hiPSCs can differentiate to form fully functional differentiated progeny. We are now setting out to understand whether the differentiated progeny of hESCs and hiPSCs share commonalities or differences as was observed in their undifferentiated parent cells in an attempt to make predictions about whether these two types of pluripotent cells have similar potentials in regenerative medicine.

11:30 Functional Cardiomyocytes Derived from Human Induced Pluripotent Stem Cells

Timothy J. Kamp, M.D., Ph.D., Professor of Medicine & Physiology; Co-Director Stem Cell and Regenerative Medicine Center, University of Wisconsin

Human iPS cells hold great promise for cardiovascular research and therapeutic applications, but the ability of human iPS cells to form functional cardiomyocytes requires careful analysis and optimization. We provide electrophysiological, pharmacological, and biochemical evidence that iPS cells can differentiate into the three major types of functional cardiomyocytes which can be used in a variety of applications.

12:00 PM Lunch on Your Own

IPS CELLS FOR DRUG SCREENING

1:00 Chairperson's Remarks

1:05 Featured Speaker
Stem Cells and Drug Discovery: The Beginning of a New Era?

Lee Rubin, Ph.D., Director, Translational Medicine, Harvard Stem Cell Institute

1:35 CATALYST: The Industrialization of Advanced iPSC Technology for Drug Discovery

Sponsored by Fate Therapeutics

Dan Shoemaker, Chief Technology Officer, Fate Therapeutics

CATALYST is designed to accelerate the innovation of induced pluripotent stem cell (iPSC) technology in collaboration with industry to support launching a fully-enabled platform in this new paradigm of drug discovery and development. CATALYST is exploring the creation of iPSC-derived, disease-specific model systems that improve the recapitulation of human physiology and more effectively predict clinical response. CATALYST is committed to developing an iPS cell technology platform to accelerate candidate identification and lead validation for drug discovery and development for pharmaceutical members. This session will discuss:

- The critical elements of industrialization, including cell sourcing, reprogramming, differentiation and commercial supply
- Approaches for creating non-genetically modified iPS cells and mature phenotypes
- Quantitative methods to analyze cell states for high-quality differentiation and disease modeling
- Uses of iPSC technology in drug discovery

1:50 Sponsored Presentation

Sponsored by DV biologics

Targeting Muscular Dystrophy: How do we Mimic the *In Vivo* System?

Lorena Griparic, Ph.D., Research Scientist, DV Biologics

Muscular dystrophy (MD) is a well characterized neuromuscular disorder. Here we show that using cells isolated from different tissues of MD patients and their pedigree is an effective tool for understanding how to treat the disease. Our MD pedigree system is the first commercially available tool allowing the study of this disease and the production of iPS cells.

2:05 iPSC-enabled Drug Discovery: A Paradigm Shift to Increase POS in the Clinic

Sponsored by iPierian

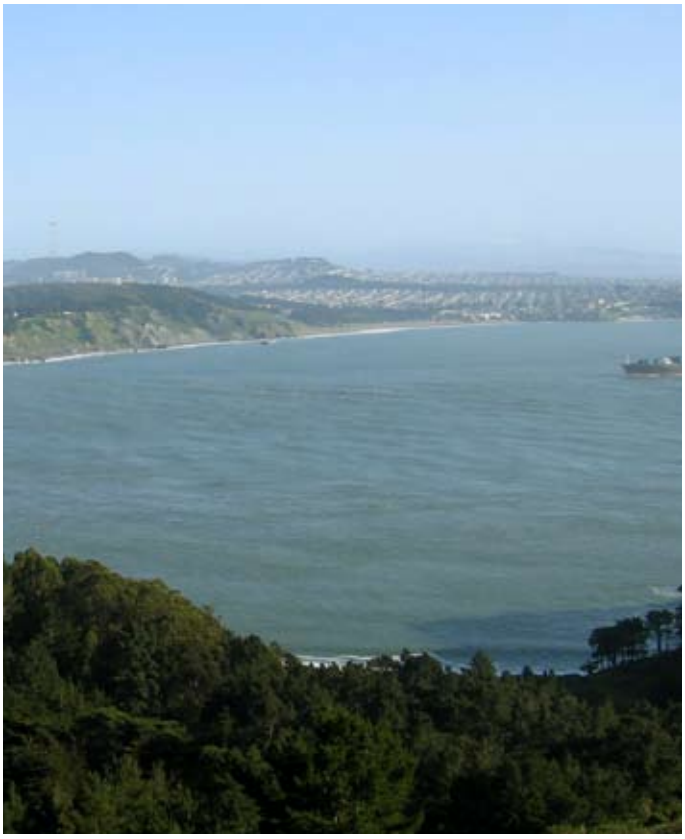
Berta Strulovici, Chief Technology Officer, iPierian

Until recently, human disease specific pluripotent stem cells could be made only by tedious genetic modification of existing hES cells or by generating such cells from embryos with diagnosed monogenic diseases. Recent advances using induced pluripotent stem cells (iPSCs) have enabled the production of unlimited numbers of cells with a very specific genetic background that can be used as models for drug discovery. Coupled with the ability of these cells to be differentiated to virtually "any type of cell in the body", the iPSC technology has the ability to revolutionize the way drug discovery is done today. In my presentation, I will describe the use of human iPSC-based assays for drug discovery in our therapeutic areas of focus.

2:20 iPS Cells Panel of Experts

iPS cells have invigorated and united the stem cell research community and strides continue in efficient re-programming. This is evident through funding and companies investing their future through this revolutionary technology. Hear the experts in the iPS Cells field as they present their latest technology followed by an interactive panel discussion.

3:05 Close of Conference



HOTEL & TRAVEL INFORMATION

Conference Venue
The Moscone North Convention Center
747 Howard Street
San Francisco, CA 94103
www.moscone.com
Host Hotel

Marriott San Francisco Hotel
55 Fourth Street
San Francisco, CA 94103
Discounted Group Rate: $199* s/d
*Room Rate includes
complimentary internet
access in your guestroom
Discounted Room Rate Cut Off Date:
January 6, 2010
(T) 415-896-1600
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Minutes from the Moscone Convention Center, discover the beautiful San Francisco Marriott rising 39 stories high into the city skyline. Just south of Market Street, the hotel is steps away from the city's top attractions, including the Yerba Buena Gardens, world-class shopping on Union Square, and AT&T Park, home of the San Francisco Giants. Enjoy magnificent views of downtown San Francisco.

Please visit the conference website to make your hotel reservation on-line. You may also call the hotel directly to make your reservation by asking for the Cambridge Healthtech and/or Molecular Medicine Tri-Conference group rate. Reservations made after the cut-off date or after the group room block has been filled (whichever comes first) will be accepted on a space and-rate availability basis. Rooms are limited, so please book early.

For additional Travel Information, visit the hotel and travel page of the conference website tri-conference.com.

Reserve your hotel and save $75 off your conference registration.*

*You must book your reservation under the Molecular Medicine Tri-Conference room block for a minimum of three nights at the Marriott San Francisco Hotel.

BIOLOGICS CHANNEL

Cambridge Healthtech Institute's Second Annual

RNA Interference:
From Tools to Therapies

WEDNESDAY, FEBRUARY 3

7:00 AM Registration and Morning Coffee

8:00 Plenary Keynote Session *(See Page 26 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

THE POWER AND POTENTIAL OF WHOLE GENOME RNAi SCREENS

11:00 Chairperson's Remarks
Christophe J. Echeverri, Ph.D., CEO and CSO, Cenix BioScience GmbH

11:10 Genome-wide RNAi Screen in *Drosophila* Cells Identifies G Protein-coupled Receptor Kinase 2 as an Evolutionarily Conserved Regulator of the NFKB Signaling
Mika Rämet, M.D., Ph.D., Professor of Experimental Pediatric Immunology and Infectious Diseases, University of Tampere, Finland
We have carried out an RNA interference-based genome-wide *in vitro* reporter assay screen in *Drosophila* for components of NF-KB pathways. We analyzed 16, 025 dsRNA-treatments and identified ten novel NF-KB regulators. Of these, Gprk2 was shown to be evolutionary conserved regulator of NF-KB signalling. siRNA-silencing of human ortholog GRK5 in HeLa cells impaired NF-KB reporter activity. Morpholino-silencing of zebrafish GRK5 homolog in fish embryos caused impaired IL-1β and TNF-α expression after *E. coli* infection. Gprk2/GRK5 was identified as an evolutionarily conserved modulator of NF-KB signaling.

11:40 *Alexander Bishop, Ph.D., Associate Professor, UT San Antonio*

12:10 PM Generation And Integration of HT-RNAi Screening Data
Pedro Aza-Blanc, Ph.D., Director, Functional Genomics Resources, The Burnham Institute for Medical Research

12:40 Luncheon Presentation I
Using siRNA to Investigate Non-Coding RNA (ncRNA) Function in Control of Mitosis and Apoptosis in Cells
Sponsored by applied biosystems part of life technologies
Susan Magdaleno, Ph.D., Senior Manager, Scientist, RNAi Technologies Research & Development, Applied Biosystems
Long non-coding RNAs (ncRNA) are critical to biology and disease. Life Technologies has now developed a suite of integrated tools and workflows to discover, validate, and knock-down ncRNA which will accelerate understanding of the function of ncRNA in the cell. We will describe the special requirements for using siRNAs to knock down ncRNA and will highlight the application of siRNAs to investigate ncRNA function in regulating mitosis and apoptosis in normal and cancer cells.

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

1:45 Dessert in the Exhibit Hall

EXPLORING HIGH CONTENT RNAI SCREENS

2:15 Chairperson's Remarks
Paul Kassner, Ph.D., Scientific Director, Lead Discovery, Amgen, Inc.

2:20 Use of Fluorescence Microscopy to Track Protein Localization in siRNA Screening
Paul Kassner, Ph.D., Scientific Director, Lead Discovery, Amgen, Inc.

2:50 Comparative Analysis of RNAi Screening Performance Across Multiple Kinase-Focused Libraries: How Good is a Good Kinase Targeting Sequence?
Hakim Djaballah, Ph.D., Director, HTS Core Facility, Memorial Sloan Kettering Cancer Center
We have assembled and obtained several kinase focused libraries for use in the comparative analysis of RNAi knockdown performance. We have performed a systematic RNAi screening of the Kinome represented in several siRNA and shRNA libraries for gene inactivation that modulate apoptotic events in an isogenic pair of cell lines, namely HeLa/B5 and HeLa/N10. HeLa B5 is stably transfected and over expresses Bcl-XL, a member of the anti-apoptotic Bcl-2 family, whereas the HeLa N10 contains an empty expression vector as a control. We have employed a high content assay measuring real time induction of apoptosis in live cells together with an end point measure of nuclear count and morphological changes post fixation and staining. We will present and discuss our findings.

3:20 Speaker to be Announced

3:50 Sponsored Presentation *(Sponsorship Opportunity Available)*

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

5:20 BREAK-OUT DISCUSSIONS in the Exhibit Hall

Design of HT-RNAi Screens for Target Identification and Validation
Moderators: Paul Kassner, Ph.D., Scientific Director, Lead Discovery, Amgen Inc.
Christopher Miller, Ph.D., Group Director, Applied Genomics, Bristol-Myers Squibb Co.
Topics for discussion:
- Choice of screening format, libraries and reagents
- Design of positive and negative controls
- Addressing the issue of off-target effects
- Statistical approaches for prioritizing hits

Perspectives on siRNA Delivery Systems
Moderators: Ian MacLachlan, Ph.D., Chief Scientific Officer, Tekmira Pharmaceuticals Inc.
Antonin de Fougerolles, Ph.D., Vice President, Research, Alnylam Pharmaceuticals Inc.
Topics for discussion:
- Key attributes necessary for delivery
- Pharmaceutical aspects of siRNA formulations
- Formulation-specific safety questions
- Immune activation and RNAi delivery

Progress in Developing RNAi Therapeutics
Moderator: Bob Brown, Ph.D., Senior Vice President, Research, Dicerna Pharmaceuticals Corp.
Topics for discussion:
- Transitioning from the lab to the clinic
- Challenges in the clinic
- RNAi therapies for acute versus chronic conditions
- Lessons learnt from gene therapy and antisense

6:20 Close of Day

THURSDAY, FEBRUARY 4

SCREENING AND VALIDATING DRUG TARGETS USING RNAi SCREENS

8:25 AM Chairperson's Remarks
Christopher Miller, Ph.D., Group Director, Applied Genomics, Bristol-Myers Squibb Co.

8:30 Cancer Target Identification and Validation by siRNA Library Screening
Xiaoyu Lin, Ph.D., Associate Research Investigator, siRNA Therapeutics, Abbott Laboratories
We have been performing large-scale siRNA library screens to identify novel cancer targets. One of the critical aspects of screen data analysis is to discard false positive hits due to siRNA off-target effect. We will discuss several different approaches to confirm on-target effect of siRNA library hits. Using several targets identified in the library screen as examples, we will update on the progress of how RNAi-based technologies have helped target discovery and validation in the oncology area.

9:00 Hitting Cancer Where it Hurts Most: Large Scale RNAi Screens for Cancer Cell Vulnerability
Roderick L. Beijersbergen, Ph.D., Group Leader, Division of Molecular Carcinogenesis, The Netherlands Cancer Institute
Large scale RNAi screens for cancer cell vulnerability RNA interference based technologies allow for the interrogation of the role and phenotype of all individual genes in the human genome. Using these techniques we aim to identify those genes that upon functional inactivation have a causal effect on tumor cell behavior and survival representing novel drug targets.

9:30 Leveraging RNAi and Chemogenomic Screens for Target Identification and Validation
Christopher Miller, Ph.D., Group Director, Applied Genomics, Bristol-Myers Squibb Co.
Libraries of RNAi reagents are being widely used for screening cellular assays for target identification. We are using RNAi libraries in combination with libraries of small molecule tool compounds. Using both types of libraries adds confidence to hits identified from these screens and provides genetic and chemical tools for hit follow up. Examples will be presented to illustrate this approach in target identification and validation.

10:00 Sponsored Presentation *(Sponsorship Opportunity Available)*

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

11:30 Panel: Do's and Don'ts in RNAi Screening
Panelists:
Christophe J. Echeverri, Ph.D., CEO and CSO, Cenix BioScience GmbH
Christopher Miller, Ph.D., Group Director, Applied Genomics, Bristol-Myers Squibb Co.
Hakim Djaballah, Ph.D., Director, HTS Core Facility, Memorial Sloan Kettering Cancer Center
Paul Kassner, Ph.D., Scientific Director, Lead Discovery, Amgen, Inc.

12:30 PM Luncheon Presentation *Sponsored by*
RNAi and KinaseSwitch Technology Platforms
Christine L. Olsson, Ph.D., Taconic
Novel *in vivo* technology platforms have recently been developed that will enable investigators to gain greater insights into drug and target-related disease mechanisms. TaconicArtemis RNAi and KinaseSwitch mouse models are the newest commercially available additions to these technologies. Inducible/reversible RNAi technology enables gene knockdown in all tissues of the body and can be induced and reversed, providing an optimal surrogate for therapeutic drug action. More recently, KinaseSwitch technology, an invaluable tool during key stages of drug development, allows investigators to identify biological roles of a specific kinase and possible side effects that result from its inhibition.

1:45 Ice Cream Refreshment Break in the Exhibit Hall

PLENARY KEYNOTE SESSION

2:15 Plenary Keynote Introduction

2:25 Plenary Keynote Presentation *(See Page 26 for Details)*

3:05 Refreshment Break in the Exhibit Hall

CLINICAL CHALLENGES WITH RNAi THERAPEUTICS

3:45 Chairperson's Remarks
Cristina Rondinone, Ph.D., Director Research, Metabolic Diseases, Hoffmann La Roche Inc.

3:50 LNA Antimirs – Pioneering microRNA Therapeutics
Henrik Orum, M.Sc., Ph.D., VP and CSO, Santaris Pharma
Short, single stranded LNA oligonucleotides delivered systemically as naked molecules are able to potently and safely inhibit therapeutically attractive miRNAs in a range of tissues in experimental animals. The presentation will provide an update on the unique features of LNA oligonucleotides in miRNA therapeutics with particular emphasis on the pre-clinical and clinical development of SPC3649, an LNA AntimiR targeting miRNA-122.

4:20 Pre-clinical and Clinical Development of Atu027 (siRNA-lipoplex/AtuPLEX) for Oncology
Ansgar Santel, Ph.D., Senior Scientist, Silence Therapeutics plc
Atu027 refers to a liposomally formulated siRNA targeting PKN3 expression in the vascular endothelium. Pre-clinical studies in rodents and non-human primates demonstrated that intravenous administration is well tolerated and gives rise to RNAi-mediated suppression of PKN3 gene expression. Various proof-of-concept experiments on mouse tumor xenografts suggest profound inhibition of tumor progression and particularly of metastasis, which laid the foundation for therapeutic application in oncology. Atu027 is currently tested in a Phase-I clinical trial on subjects with advanced solid cancers. Pre-clinical data emphasizing pharmacological activity in mouse models and an update on the current Phase-I study will be discussed.

4:50 Talk Title to be Announced

5:20 Talk Title to be Announced
Bob D. Brown, Ph.D., Senior Vice President, Research, Dicerna Pharmaceuticals Corp.

5:50 Close of Day

FRIDAY, FEBRUARY 5

NOVEL FORMULATIONS FOR RNAi DELIVERY

8:30 AM Chairperson's Opening Remarks
Bob D. Brown, Ph.D., Senior Vice President, Research, Dicerna Pharmaceuticals, Corp.

8:35 Therapeutic siRNA Delivery: Tackling the 800 Pound Gorilla
Steven F. Dowdy, Ph.D., Investigator, Howard Hughes Medical Institute; Professor, Department of Cellular & Molecular Medicine, University of California, San Diego School of Medicine
To date, siRNA delivery remains the rate-limiting step for RNAi therapeutics development. We developed a Peptide Transduction Domain-dsRNA Binding Domain (PTD-DRBD) fusion protein siRNA delivery approach. PTD-DRBD delivered siRNAs induced RNAi responses in the entire population of all cell types assayed (primary and tumorigenic) in a non-cytotoxic fashion. PTD-DRBD combinatorial *in vivo* delivery of EGFR and Akt2 siRNAs induced a synthetic lethal response that significantly increased survival of intracerebral glioblastoma pre-clinical models. These observations demonstrate the ability of PTD-DRBD to efficiently delivery siRNAs *in vivo*.

9:05 Induction of Therapeutic Gene Silencing in Leukocyte-Implicated Diseases by Targeted and Stabilized Nanoparticles

Dan Peer, Ph.D., Head, Laboratory of Nanomedicine, Department of Cell Research and Immunology and the Center for Nanoscience and Nanotechnology, Tel Aviv University

Leukocytes are among the most difficult cells to transduce with RNAi. We developed a strategy that can target different subsets of leukocytes and selectively silence genes *in vivo* using targeted, stabilized nanoparticles (tsNPs). These carriers do not induce lymphocyte activation, interferon responses or release liver enzymes and are fully degradable. Three pre-clinical examples inflammatory bowel disease (IBD), blood cancer and viral infection will be discussed. We will show that tsNPs can be used for *in vivo* validation of new drug targets, for prevention of viral infection and for inducing therapeutic gene silencing in a preclinical setting.

9:35 Characterization of Immune Responses to tkRNAi Therapeutics

Johannes Fruehauf, M.D., Ph.D., VP, Research, Cequent Pharmaceuticals, Inc.

Transkingdom RNA interference (tkRNAi) describes a novel method for delivery of therapeutic RNA interference into gastrointestinal tissues using engineered bacteria which produce and deliver mediators of RNAi. Clinical trials are about to begin for the prevention of colon Polyposis, and for the treatment of Inflammatory Bowel Disease (IBD). Here we demonstrate recent results from large screening efforts characterizing the effects of tkRNAi on cytokine profiles and innate immunity.

10:05 Sponsored Presentation *(Sponsorship Opportunity Available)*

10:20 Coffee Break

11:00 Panel: Do We Understand the Challenges We Face With RNAi Therapeutics?

Panelists:
Bob D. Brown, Ph.D., Senior Vice President, Research, Dicerna Pharmaceuticals Corp.
Ian MacLachlan, Ph.D., CSO, Tekmira Pharmaceuticals
John Rossi, Ph.D., Professor and Chair, Molecular Biology, Beckman Research Institute of the City of Hope
Steven Highlander, Ph.D., Partner, Intellectual Property, Fulbright & Jaworski, L.L.P.

12:00 PM Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

NOVEL APPROACHES FOR TARGETED DELIVERY

1:00 Chairperson's Remarks

John Rossi, Ph.D., Professor and Chair, Molecular Biology, Beckman Research Institute of the City of Hope

1:05 *In vivo* delivery of Dicer substrate RNAs for treatment of HIV infection

John Rossi, Ph.D., Professor and Chair, Molecular Biology, Beckman Research Institute of the City of Hope

The application of RNAi for treatment of HIV infection has many advantages over conventional drugs. The inhibitors can be rapidly changed according to the viruses ability to mutate. This presentation will discuss the use of aptamers and dendrimers to deliver Dicer substrate RNAs *in vivo*. The results obtained demonstrate that Dicer substrate siRNAs can be delivered in a cell type specific manner with an aptamer, and can be generally delivered with dendrimers to effectively inhibit HIV replication in a humanized mouse model.

1:35 Targeted RNA-based Cancer Therapies

Paloma H. Giangrande, Ph.D., Assistant Professor, Department of Internal Medicine, University of Iowa

A major hurdle for the clinical translation of siRNAs into effective therapies is delivery. We describe an RNA aptamer-based approach for the targeted delivery of siRNAs to prostate cancer (PC) cells. The aptamer-siRNA reagent (chimera) is effective when administered systemically and is suitable for efficient chemical synthesis. When administered systemically to mice bearing PSMA-positive tumors, the RNA chimera triggered tumor regression without affecting normal tissues. This work is the first description of *in vivo* efficacy following systemic administration of an aptamer-siRNA chimera and thus represents a milestone for this platform technology.

2:05 Development of Novel Therapeutic RNAi Compounds and Effective *in vivo* Delivery Approaches

Joanne Kamens, Ph.D., Senior Director of Research Collaboration Management, RXi Pharmaceuticals

RNA interference (RNAi) offers a novel approach to the drug development process, because RNAi compounds can potentially be designed to target any one of the genes in the human genome. Other potential advantages of RNAi therapeutics include, rapid development of lead compounds, high selectivity for the target gene, high potency (low dose) and low toxicity due to natural mechanism of action. We will introduce unique single-oligo (rxRNA^{solo}) and short-duplex (rxRNA^{nano}) RNAi compounds, as well as novel *in vivo* delivery approaches, including self-delivering rxRNA molecules (*sd*-rxRNA) for local and systemic delivery, and targeted delivery to phagocytic immune cells using.

2:35 Development of RNA Interference Therapeutics

Antonin De Fougerolles, VP, Research, Alnylam Pharmaceuticals

Novel therapies based on short interfering RNA (siRNA) duplexes have tremendous potential to treat diseases by silencing the expression of otherwise non-druggable proteins. Development of therapeutics using siRNA has advanced rapidly, with multiple different clinical trials ongoing and several more poised to enter the clinic in the coming years. Although challenges remain, delivery represents the main hurdle for faster and broader development of siRNA therapeutics. A summary of the advances made around siRNA delivery will be presented.

3:05 Close of Conference

Cambridge Healthtech Institute's Inaugural

Cancer Biologics

WEDNESDAY, FEBRUARY 3

7:00 AM Registration and Morning Coffee

8:00 Plenary Keynote Session *(See Page 26 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

DELIVERY OF CANCER BIOLOGICS PENETRATION AND DISTRIBUTION

11:00 Introduction and Welcome

Gregory P. Adams, Ph.D., Co-Leader, Molecular and Translational Medicine Program, Fox Chase Cancer Center

11:10 Tumor Penetration of Therapeutic Antibodies -The Impact of Size and Exposure Time on Distribution

David Blakey, Ph.D., Chief Scientist, Cancer and Infection Research Area, AstraZeneca

The ability of intact antibodies and fragments to access tumor cells distant from the tumor blood supply is an important therapeutic consideration for antibody based oncology drugs. Pre-clinical and clinical data will be reviewed regarding the impact of size and exposure time on antibody distribution within tumors.

11:40 Anti-tumor Efficacy Maximization through Blocking Multiple Targets of Angiogenesis

Dana Hu-Lowe, Ph.D., Group Leader, Associate Research Fellow, Cancer Biology, Pfizer, Inc., PGRD-La Jolla

Vascular normalization and adaptivety potentially contribute to resistance to anti-VEGF/VEGFR therapies in the clinic. Other targets, including the Activin receptor Like Kinase 1 (ALK-1), also play a role in promoting tumor angiogenesis. A fully human mAb against ALK-1 was generated. The differential and complimentary outcome of anti-ALK-1 and anti-VEGF will be discussed.

12:10 PM Optimizing Targeting of Anti-tumor Antibodies

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We have found that anti-HER2 scFv molecules penetrate and localize in a solid tumors less efficiently with increasing affinity. We will describe studies performed with anti-HER2 human IgGs molecules that demonstrate that affinity also impacts the targeting of intact antibodies. Studies examining the roles of affinity on *in vitro* ADCC and internalization into tumor cells will also be discussed.

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

1:45 Dessert in the Exhibit Hall

SELECTIVE TARGETING OF TUMORS

2:15 Chairperson's Remarks

Matthew K. Robinson, Ph.D., Assistant Professor, Molecular and Translational Medicine Program, Fox Chase Cancer Center

2:20 Bispecific Antibodies: An Approach to Enhance Targeting Selectivity and Efficacy

Matthew K. Robinson, Ph.D., Assistant Professor, Molecular and Translational Medicine Program, Fox Chase Cancer Center

Work will be presented on our efforts to develop and optimize the targeting selectivity of bispecific antibodies that co-target two distinct tumor associated antigens. We hypothesize that the targeting selectivity afforded by these molecules can potentially be leveraged for the development of new immunodrug conjugates.

2:50 Selective Penetration and Targeting of Tumors

Tapas K. Das Gupta, M.D., Ph.D., D.Sc., Professor and Head, Surgical Oncology, University of Illinois Chicago; Co-founder, CDG Therapeutics, Inc.

CDG Therapeutics has developed a cell penetrating peptide (28aa) from azurin, a redox protein secreted by Pseudomonas aeruginosa. p28 preferentially enters cancer cells, localizes in the nucleus and stabilizes p53 inducing cell cycle arrest and apoptosis in a series of solid tumors. p28 is stable, nontoxic and currently in a Phase I clinical trial.

3:20 A Systems Biology Approach to Engineering Therapeutic Antibodies: Development of an ErbB2/ErbB3 Bispecific Antibody

Alexandra Huhalov, Ph.D., Principal Scientist, Merrimack Pharmaceuticals

Using quantitative biological datasets of cell signaling we have generated computational models of the ErbB signaling network and identified ErbB3 as a promising target. The application of these models to guide the design of MM-111, a bispecific antibody-based therapeutic targeting the ErbB2/ErbB3 heterodimer, and its antitumor activity will be discussed.

3:50 Large Volume Subcutaneous Delivery: Challenges and Opportunities

Robin Hwang, Ph.D., Executive Director, Halozyme

There are many monoclonal antibodies (mAbs) in development for cancer therapeutics. Generally, mAbs require a higher dosage than the typical protein therapeutics. It has been shown clinically that the "standard" subcutaneous injection can go up to 1.5 mL, beyond which skin distortion and pain can occur. As a result, most biotech companies spend much effort in concentrating MAbs to ≈100 mg/mL and then trying to stabilize these formulations to avoid aggregates and particulates. Halozyme's Enhanze™ Technology permits the large volume subcutaneous (SC) dosing, with corresponding lower protein concentration which was not previously feasible. Bypassing high-concentration formulation challenges has the potential to accelerate the timeline to bring a product to the clinic, enables an IV-SC switch, in some cases improves bioavailability, and improve patient convenience and compliance. In this talk, large volume SC delivery and device options will be presented.

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

5:20 BREAK-OUT DISCUSSIONS in the Exhibit Hall

6:20 Close of Day

THURSDAY, FEBRUARY 4

ENGINEERING FOR DELIVERY

8:25 AM Chairperson's Remarks

Tugrul Kararli, Ph.D., President & Founder, Pharmacircle

8:30 Tumor Targeting Theory-Kinetic & Diffusive Processes that Determine Antibody Macro & Microdistribution

K. Dane Wittrup, Ph.D., C.P. Dubbs Professor, Chemical Engineering & Biological Engineering, Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

A diverse array of tumor targeting agents ranging in size from peptides to nanoparticles is currently under development for applications in cancer imaging and therapy. However, it remains largely unclear how size differences among these molecules influence their targeting properties. Here

we develop a simple, mechanistic model that can be used to understand and predict the complex interplay between molecular size, affinity, and tumor uptake.

9:00 Nanoparticle Agents for Tumor Targeting and Penetration

Shuming Nie, Ph.D., Wallace H. Coulter Distinguished Faculty Chair in Biomedical Engineering, Director of Emory-Georgia Tech Cancer Nanotechnology Center, Professor of BME. Chemistry, Materials Science and Engineering, and Hematology and Oncology, Emory University and Georgia Institute of Technology

Nanoparticles have functional and structural properties not available from discrete molecules or bulk materials. When conjugated with monoclonal antibodies, peptides or small molecules, nanoparticles can be used to target malignant tumors with high specificity and affinity. We developed a new class of biocompatible and nontoxic nanoparticles for *in vivo* tumor targeting and detection based on self-assembled nanostructures and pegylated colloidal gold.

9:30 Delivery of Antibodies – Market Analysis & Overview

Tugrul Kararli, Ph.D., President & Founder, Pharmacircle

10:00 Sponsored Presentation *(Sponsorship Opportunity Available)*

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

DELIVERY OF ANTIBODIES

11:30 Engineered Antibodies for Molecular Imaging of Cancer

Anna M. Wu, Ph.D., Professor, David Geffen School of Medicine at UCLA

Cancer-targeting antibodies have been optimized for *in vivo* imaging by conversion into fragments such as diabodies, minibodies, and scFv-Fc. Recombinant fragments recognizing a variety of cell-surface markers have been labeled with positron-emitting radionuclides (I-124, Cu-64, F-18) for positron-emission tomography (PET) detection of tumors in preclinical models. ImmunoPET represents a broad platform for conducting "immunohistochemistry *in vivo*" to address biological questions in living organisms, including target expression, target coverage, and response to therapy.

12:00 Advanced Polymer Conjugate Technology for Optimization of Cancer Therapeutics

Christine Loehrlein, Ph.D., A.D., New Products and Technology Strategy Research, Nektar Therapeutics

Conjugation of a therapeutic agent to polyethylene glycol and other polymers is a general strategy that can be used to optimize pharmacological parameters of that drug, with the ability to affect both its efficacy and side effect profile. Nektar's Advanced Polymer Conjugate Technology platform can be used to enable a wide range of molecules, including proteins, peptides, small molecule oral and parenteral drugs, and antibody fragments. Nektar is currently using this approach to develop advanced oncolytics with sustained exposure to tumor cells, and exploring opportunities to extend this technology to other cancer therapeutics.

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

1:45 Ice Cream Refreshment Break in the Exhibit Hall

PLENARY KEYNOTE SESSION

2:15 Plenary Keynote Introduction

2:25 Plenary Kenynote Presentation *(See Page 26 for Details)*

3:05 Refreshment Break in the Exhibit Hall

NOVEL MODES OF ACTION FOR CANCER BIOTHERAPEUTICS
BI- AND TRI-SPECIFIC ANTIBODIES

3:45 Chairperson's Remarks

Stefan Dübel, Ph.D., Director, Biotechnology, Technische Universität Braunschweig, Germany

3:50 Mode of BiTE Antibody Action in Cancer Therapy

Patrick Baeuerle, Ph.D., CSO and Senior Vice President, Research & Development, Micromet AG

BiTE (bispecific T cell engager) antibody blinatumumab targets CD19 on B cell malignancies and has provided clinical proof of concept in phases 1 and 2. We will discuss the mode of BiTE antibody action in inducing highly efficient cancer cells lysis, and provide background on how BiTE antibodies are produced, are administered in the clinic, and have been pre-clinically developed.

4:20 Catumaxomab (Removab), the First EC-approved Trifunctional Bispecific Antibody: The Road from Pre-clinical Development to Approval and Beyond

Diane Seimetz, Ph.D., M.D.R.A., CSO and Executive Vice President, Fresenius Biotech GmbH

Catumaxomab, a targeted therapy for intraperitoneal treatment of malignant ascites, targets the epithelial cell-adhesion molecule (EpCAM) and CD3 evoking T-cell cytotoxicity on EpCAM-expressing tumor cells. The Fc-region of catumaxomab provides a third functional binding site, which binds and activates Fcγ-receptor-positive accessory cells. The development rationale, pre-clinical and clinical data, approval process and preparations for further clinical development will be presented.

4:50 Bispecific EGFR-IGF1R Program

Eric Furfine, Ph.D., Senior Vice President, Research and Pre-clinical Development, Adnexus Therapeutics, a Bristol-Myers Squibb R&D Company

Adnectins offer several potential advantages compared to traditional targeted biologics, including speed of discovery, efficient manufacturing, and the ability to create multi-functional targeted products. We are currently advancing products combining two Adnectins to enable modulation of two distinct targets. We will present methods to engineer and optimize multi-specific Adnectins, and pre-clinical data on a bispecific Adnectin to EGFR and IGF1R.

5:20 Multi-specific Antibody by Design

Changshou Gao, Ph.D., Principal Scientist, Antibody Discovery and Protein Engineering, MedImmune LLC

We'll discuss efforts to engineer and optimize multispecific antibody formats to address the challenges pertaining to bispecific and multispecific molecules, and provide data of our multispecific constructs with excellent expression level, great biophysical stability, good *in vitro* and *in vivo* activities, and potential manufacturing feasibility. Our multispecific constructs retain similar *in vivo* half-life and effector functions to their parental antibodies.

5:50 Close of Day

FRIDAY, FEBRUARY 5

ADVANCES IN ANTIBODY-DRUG CONJUGATES

8:30 AM Chairperson's Opening Remarks
Hans-Peter Gerber, Ph.D., Senior Director, Tumor Therapies, Wyeth Oncology Discovery

8:35 A Novel Minor Groove Binding Alkylating Agent for Antibody Targeted Chemotherapy of CD70 Expressing Cancers
Nils Lonberg, Ph.D., Senior Vice President and Scientific Director, Medarex, Inc.
An antibody drug conjugate comprising a CD70 targeting monoclonal antibody and a novel alkylating agent is now in Phase I clinical development for kidney cancer and lymphoma. The mechanism of action of this novel therapeutic, activated through a multistep mechanism including esterase mediated removal of a blocking group and protease mediated release of the cytotoxic drug, will be discussed.

9:05 Pre-clinical and Clinical Development of Calicheamicin Derivatives Conjugated to Monoclonal Antibodies
Hans-Peter Gerber, Ph.D., Senior Director, Tumor Therapies, Wyeth Oncology Discovery
Gemtuzumab ozogamicin (Mylotarg), a semi-synthetic derivative of calicheamicin linked to a humanized anti-CD33 monoclonal antibody, is approved for the treatment of AML. CMC-544 (inotuzumab ozogamicin), an anti-CD22 immuno-conjugate of calicheamicin, is currently being evaluated in B-cell non-Hodgkin's lymphoma (B-NHL) patients. I will describe the mechanism of action and the pharmacology of calicheamicin conjugates and provide an overview of clinical trials.

9:35 Antibody-Maytansinoid Conjugates: Demonstrating Benefit in the Treatment of Solid and Liquid Tumors
John M. Lambert, Ph.D., Executive Vice President and CSO, ImmunoGen, Inc.
Several new highly potent cell-killing agents such as derivatives of the anti-mitotic microtubule agent, maytansine, are currently being utilized in ADCs to achieve effective, well tolerated anticancer drugs. Several AMCs show encouraging efficacy in clinical trials, including T-DM1, currently being developed by Genentech using ImmunoGen's maytansinoid technology. New payloads for ADCs are realizing the promise of antibody-mediated delivery in cancer.

10:05 Broad Application of Scaffold Antibodies for Targeted Tumor Therapy
Gary Woodnutt, Ph.D., Vice President,Biology, CovX Research, A Pfizer organization
The progression of novel cancer therapeutics that have the potential of truly impacting disease requires the identification of targets that affect tumor growth combined with a modality capable of rapid exploitation of those targets either as monotherapy or in combination. We will describe how the use of bioconjugation to a proprietary scaffold antibody allows us to develop these therapeutics rapidly and effectively.

10:20 Coffee Break

EMERGING NEW TECHNOLOGIES

11:00 Bi-specific, High Affinity T Cell Receptor Fusions as Anti-Cancer Therapeutics
Rebecca Ashfield, D.Phil., Senior Research Project Manager, Immunocore Ltd
Bi-specific TCRs, consisting of high affinity T cell receptors fused to an anti-CD3 scFv, are being developed for the treatment of several tumor types. The presentation will cover engineering of these reagents, demonstration of efficacy including animal models, and a discussion of the planned first-in-man clinical trial including toxicity testing, a challenge since the molecules are entirely human specific.

11:30 Chemosensitization of Cancer Cells by siRNA Using Targeted Nanogel Delivery
John F. McDonald, Professor and Director, Integrated Cancer Research Center, School of Biology, Georgia Institute of Technology
Targeted cancer therapy by RNA interference (RNAi) is a promising approach to silence genes *in vivo*. Delivery is a major hurdle for the development of RNAi therapeutics. We report on the successful use of hydrogel nanoparticles (nanogels) functionalized with peptides that specially target the EphA2 receptor to deliver small interfering RNAs (siRNAs) targeting EGFR to increase sensitivity to Taxane therapy.

12:00 PM Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

EFFECTOR-ENHANCED BIOTHERAPEUTICS

1:00 Chairperson's Remarks
John F. McDonald, Professor and Director, Integrated Cancer Research Center, School of Biology, Georgia Institute of Technology

1:05 Human RNase Fusion Proteins for Tumor Therapy
Stefan Dübel, Ph.D., Director, Biotechnology, Technische Universität Braunschweig, Germany
RNases are non-toxic while in circulation but highly effective in cell killing after targeted internalization. An entirely human immunoenzyme against CD30+ lymphomas was constructed from a human scFv-Fc antibody fragment and a human RNase. It did not affect the human embryonlal kidney used for its production but strongly inhibited proliferation of CD30+ lymphoma cells.

1:35 Glycoengineering for the Enhancement of Antibody Activity
Dennis Benjamin, Ph.D., Senior Director, Antibody Technologies, Seattle Genetics, Inc.

2:05 Antibody Fc Engineering to Enhance Cytotoxicity, Pharmacokinetics, and Pharmacodynamics
John R. Desjarlais, Ph.D., VP, Research, Xencor, Inc.
We have engineered the antibody Fc domain to enhance its affinity for Fc receptors, leading to a set of variants that confer high ADCC activity onto antibodies targeting a wide range of tumor targets. These variants also enhance anti-tumor activity in mouse models and cynomolgus monkeys. A phase I trial is underway to determine their effects in humans.

2:35 Arzerra™ (ofatumumab), a Novel Human Therapeutic CD20-Antibody: Mechanisms of Action and Efficacy in B-CLL
Frank Beurskens Ph.D., Senior Scientist, Strategic Research, Genmab, B.V.
We developed a unique human monoclonal CD20 antibody, ofatumumab, that targets a distinct epitope encompassing both the small and large extracellular loops of the CD20 molecule and displays an exceptional efficacy in inducing complement dependent cell lysis (CDC). Novel insights into the mechanisms of tumor cell killing by ofatumumab and its efficacy in clinical trials in B-CLL will be discussed.

3:05 Close of Conference

Cambridge Healthtech Institute's Inaugural

Delivery of Biologics

WEDNESDAY, FEBRUARY 3

7:00 AM Registration and Morning Coffee

8:00 Plenary Keynote Session *(See Page 26 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

PENETRATION AND DISTRIBUTION

11:00 Introduction and Welcome

Gregory P. Adams, Ph.D., Co-Leader, Molecular and Translational Medicine Program, Fox Chase Cancer Center

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

5:20 BREAK-OUT DISCUSSIONS in the Exhibit Hall

6:20 Close of Day

THURSDAY, FEBRUARY 4

ENGINEERING FOR DELIVERY

8:25 AM Chairperson's Remarks

Tugrul Kararli, Ph.D., President & Founder, Pharmacircle

8:30 Tumor Targeting Theory-Kinetic & Diffusive Processes that Determine Antibody Macro & Microdistribution

K. Dane Wittrup, Ph.D., C.P. Dubbs Professor, Chemical Engineering & Biological Engineering, Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

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9:00 Nanoparticle Agents for Tumor Targeting and Penetration

Shuming Nie, Ph.D., Wallace H. Coulter Distinguished Faculty Chair in Biomedical Engineering, Director of Emory-Georgia Tech Cancer Nanotechnology Center, Professor of BME. Chemistry, Materials Science and Engineering, and Hematology and Oncology, Emory University and Georgia Institute of Technology

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9:30 Delivery of Antibodies – Market Analysis & Overview
Tugrul Kararli, Ph.D., President & Founder, Pharmacircle

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

DELIVERY OF ANTIBODIES

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12:00 Advanced Polymer Conjugate Technology for Optimization of Cancer Therapeutics
Christine Loehrlein, Ph.D., A.D., New Products and Technology Strategy Research, Nektar Therapeutics

Conjugation of a therapeutic agent to polyethylene glycol and other polymers is a general strategy that can be used to optimize pharmacological parameters of that drug, with the ability to affect both its efficacy and side effect profile. Nektar's Advanced Polymer Conjugate Technology platform can be used to enable a wide range of molecules, including proteins, peptides, small molecule oral and parenteral drugs, and antibody fragments. Nektar is currently using this approach to develop advanced oncolytics with sustained exposure to tumor cells, and exploring opportunities to extend this technology to other cancer therapeutics.

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

1:45 Ice Cream Refreshment Break in the Exhibit Hall

PLENARY KEYNOTE SESSION

2:15 Plenary Keynote Introduction

2:25 Plenary Kenynote Presentation *(See Page 26 for Details)*

3:05 Refreshment Break in the Exhibit Hall

CLINICAL CHALLENGES WITH RNAI THERAPEUTICS

3:45 Chairperson's Remarks
Bob D. Brown, Ph.D., Senior Vice President, Research, Dicerna Pharmaceuticals Corp.

3:50 LNA Antimirs – Pioneering microRNA Therapeutics
Henrik Orum, M.Sc., Ph.D., VP and CSO, Santaris Pharma

Short, single stranded LNA oligonucleotides delivered systemically as naked molecules are able to potently and safely inhibit therapeutically attractive miRNAs in a range of tissues in experimental animals. The presentation will provide an update on the unique features of LNA oligonucleotides in miRNA therapeutics with particular emphasis on the pre-clinical and clinical development of SPC3649, an LNA AntimiR targeting miRNA-122.

4:20 Pre-clinical and Clinical Development of Atu027 (siRNA-lipoplex/AtuPLEX) for Oncology
Klaus Giese, Ph.D., CSO, Silence Therapeutics plc

Atu027 refers to a liposomally formulated siRNA targeting PKN3 expression in the vascular endothelium. Pre-clinical studies in rodents and non-human primates demonstrated that intravenous administration is well tolerated and gives rise to RNAi-mediated suppression of PKN3 gene expression. Various proof-of-concept experiments on mouse tumor xenografts suggest profound inhibition of tumor progression and particularly of metastasis, which laid the foundation for therapeutic application in oncology. Atu027 is currently tested in a Phase-I clinical trial on subjects with advanced solid cancers. Pre-clinical data emphasizing pharmacological activity in mouse models and an update on the current Phase-I study will be discussed.

4:50 Talk Title to be Announced
Ian MacLachlan, Ph.D., CSO, Tekmira Pharmaceuticals

5:20 Talk Title to be Announced
Bob D. Brown, Ph.D., Senior Vice President, Research, Dicerna Pharmaceuticals Corp.

5:50 Close of Day

FRIDAY, FEBRUARY 5

NOVEL FORMULATIONS FOR RNAI DELIVERY

8:30 AM Chairperson's Opening Remarks
C. Satishchandran, Ph.D., Chief Technology Officer, Research Technology Center, Pfizer, Inc.

8:35 Therapeutic siRNA Delivery: Tackling the 800 Pound Gorilla
Steven F. Dowdy, Ph.D., Investigator, Howard Hughes Medical Institute; Professor, Department of Cellular & Molecular Medicine, University of California, San Diego School of Medicine

To date, siRNA delivery remains the rate-limiting step for RNAi therapeutics development. We developed a Peptide Transduction Domain-dsRNA Binding Domain (PTD-DRBD) fusion protein siRNA delivery approach. PTD-DRBD delivered siRNAs induced RNAi responses in the entire population of all cell types assayed (primary and tumorigenic) in a non-cytotoxic fashion. PTD-DRBD combinatorial delivery of EGFR and Akt2 siRNAs induced a synthetic lethal response that significantly increased survival of intracerebral glioblastoma pre-clinical models. These observations demonstrate the ability of PTD-DRBD to efficiently delivery siRNAs.

9:05 Induction of Therapeutic Gene Silencing in Leukocyte-Implicated Diseases by Targeted and Stabilized Nanoparticles
Dan Peer, Ph.D., Head, Laboratory of Nanomedicine, Department of Cell Research and Immunology and the Center for Nanoscience and Nanotechnology, Tel Aviv University

Leukocytes are among the most difficult cells to transduce with RNAi. We developed a strategy that can target different subsets of leukocytes and selectively silence genes *in vivo* using targeted, stabilized nanoparticles (tsNPs). These carriers do not induce lymphocyte activation, interferon responses or release liver enzymes and are fully degradable. Three preclinical examples inflammatory bowel disease (IBD), blood cancer and viral infection will be discussed. We will show that tsNPs can be used for *in vivo* validation of new drug targets, for prevention of viral infection and for inducing therapeutic gene silencing in a preclinical setting.

9:35 Characterization of Immune Responses to tkRNAi Therapeutics

Johannes Fruehauf, M.D., Ph.D., VP, Research, Cequent Pharmaceuticals, Inc.

Transkingdom RNA interference (tkRNAi) describes a novel method for delivery of therapeutic RNA interference into gastrointestinal tissues using engineered bacteria which produce and deliver mediators of RNAi. Clinical trials are about to begin for the prevention of colon Polyposis, and for the treatment of Inflammatory Bowel Disease (IBD). Here we demonstrate recent results from large screening efforts characterizing the effects of tkRNAi on cytokine profiles and innate immunity.

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10:20 Coffee Break

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Panelists:
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Ian MacLachlan, Ph.D., CSO, Tekmira Pharmaceuticals
John Rossi, Ph.D., Professor and Chair, Molecular Biology, Beckman Research Institute of the City of Hope
Steven Highlander, Ph.D., Partner, Intellectual Property, Fulbright & Jaworski, L.L.P.

12:00 PM Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

NOVEL APPROACHES FOR TARGETED DELIVERY

1:00 Chairperson's Remarks

John Rossi, Ph.D., Professor and Chair, Molecular Biology, Beckman Research Institute of the City of Hope

1:05 *In vivo* delivery of Dicer substrate RNAs for treatment of HIV infection

John Rossi, Ph.D., Professor and Chair, Molecular Biology, Beckman Research Institute of the City of Hope

The application of RNAi for treatment of HIV infection has many advantages over conventional drugs. The inhibitors can be rapidly changed according to the viruses ability to mutate. This presentation will discuss the use of aptamers and dendrimers to deliver Dicer substrate RNAs *in vivo*. The results obtained demonstrate that Dicer substrate siRNAs can be delivered in a cell type specific manner with an aptamer, and can be generally delivered with dendrimers to effectively inhibit HIV replication in a humanized mouse model.

1:35 Targeted RNA-based Cancer Therapies

Paloma H. Giangrande, Ph.D., Assistant Professor, Department of Internal Medicine, University of Iowa

A major hurdle for the clinical translation of siRNAs into effective therapies is delivery. We describe an RNA aptamer-based approach for the targeted delivery of siRNAs to prostate cancer (PC) cells. The aptamer-siRNA reagent (chimera) is effective when administered systemically and is suitable for efficient chemical synthesis. When administered systemically to mice bearing PSMA-positive tumors, the RNA chimera triggered tumor regression without affecting normal tissues. This work is the first description of *in vivo* efficacy following systemic administration of an aptamer-siRNA chimera and thus represents a milestone for this platform technology.

2:05 Development of Novel Therapeutic RNAi Compounds and Effective *in vivo* Delivery Approaches

Dmitry Samarsky, Ph.D., VP, Technology Development, RXi Pharmaceuticals

RNA interference (RNAi) offers a novel approach to the drug development process, because RNAi compounds can potentially be designed to target any one of the genes in the human genome. Other potential advantages of RNAi therapeutics include, rapid development of lead compounds, high selectivity for the target gene, high potency (low dose) and low toxicity due to natural mechanism of action. We will introduce unique single-oligo (rxRNA^{solo}) and short-duplex (rxRNA^{nano}) RNAi compounds, as well as novel *in vivo* delivery approaches, including self-delivering rxRNA molecules (*sd*-rxRNA) for local and systemic delivery, and targeted delivery to phagocytic immune cells using.

2:35 Talk Title to be Announced

C. Satishchandran, Ph.D., Chief Technology Officer, Research Technology Center, Pfizer, Inc.

3:05 Close of Conference

Translational Medicine

Completing the Circle: Bedside Back to Bench

WEDNESDAY, FEBRUARY 3

7:00 AM Registration and Morning Coffee

8:00 Plenary Keynote Session *(See Page 26 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

TRENDS IN TRANSLATIONAL MEDICINE

11:00 Chairperson's Remarks

Christina M. Coughlin, M.D., Ph.D.; Medical Director, Oncology; Clinical Research and Development; Pfizer Oncology

11:10 Translational Approach to Studying Stroke

Giora Z. Feuerstein, M.D., Assistant VP, Discovery Translational Medicine, Wyeth Research Labs

To improve success of clinical trials and speed drug development, departments of Translational Medicine in pharma have formed to figure out the which molecular, biochemical and physiological biomarkers can best substitute for the absence of cinical outcome studies. My presentation will illustrate how we've applied a translational approach to develop better therapies for stroke. Specifically we've focused on reducing attrition rate of compounds/biologicals by optimizing 1. Target Validation; 2. Compound -Target interaction; 3. innovative Pharmacokinetic-Pharmacodynamic and proof of Mechanism of Action (MoA); 4. disease biomarkers; 5. Patient selections for clinical trials based on evidence for likelihood to respond to treatment.

11:40 Contribution of Translational Approaches to Recent Advances in Immuno-therapeutics, Immuno-rejection and Beyond

Francesco Marincola, M.D., Chief, Infectious Disease and Immunogenetics Section, NIH; Editor in Chief, Journal of Translational Medicine

The complexity underlying a pathological process does not necessarily require complex solutions. The biology determining allograft or cancer rejection, autoimmunity or tissue damage during pathogen infections is complex; however, common patterns are emerging that lead to a common final outcome: tissue destruction with resolution of the pathogenic process (cancer, infection) or tissue damage and organ failure (allograft rejection, autoimmunity). Human observations based on transcriptional profiling converge into an "immunological constant of rejection" that signals such occurrences. This constant includes the coordinate activation of interferon stimulated genes (ISGs) and immune effector functions (IEFs). Understanding this final effector pathway may suggest novel strategies for the induction or inhibition of tissue-specific destruction with therapeutic intent in cancer and other immune pathologies. This presentation will discuss how vaccines may play a role in tissue-specific destruction and use this as a model to demonstrate how to understand the dynamics of therapeutics by studying target tissues in real time .

12:10 PM Panel: Practical Translational Medicine

Moderator: Vivek Kadambi, Ph.D., Senior Director, Millenium Pharmaceuticals

- When to use biomarkers for go/no-go decisions on proceeding with development of a clinical compound
- How has translational medicine changed over the past 5 years?
- Fostering partnerships between industry, academics and government granting institutions
- How are pharmaco-dynamic and predictive markers being used right now in clinical development?

Panelists: Giora Z. Feuerstein, M.D., Assistant Vice President and Head, Discovery Translational Medicine, Wyeth Research Labs
Lise Kjems, M.D., Ph.D., Executive Director, Global Program DiagnosticDirector, Molecular Diagnostics Novartis Francesco Marincola, M.D., Chief, Infectious Disease and Immunogenetics Section, NIH; Editor-in-Chief, Journal of Translational MedicineWilliam B. Mattes, PhD, DABT, PharmPoint Consulting, Former Executive Director, Predictive Safety Testing Consortium
Yali Fu, Ph.D., Program Director, Grants and Contracts Operations Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute
Hans Winkler, Ph.D., Senior Director, Global Head Oncology Biomarkers, Johnson & Johnson

12:40 Luncheon Presentation I *Sponsored by* PreClinOmics adding value to research

ZDSD Rat: A Model for Diabetes, Metabolic Syndrome, and Obesity without Leptin or Leptin Receptor Mutations

Richard G. Peterson, Ph.D.; Executive VP Research & Development, PreClinOmics, Inc.

- The ZDSD rat is a model for obesity, insulin resistance, metabolic syndrome and diabetes with a normal leptin axis.
- The disease conditions expressed in the ZDSD more closely resemble the human situation when compared to other animal models.
- The obesity and diabetes in the ZDSD rat can be modulated with diet.
- The obesity and diabetes in the ZDSD rat can be treated with standard pharmaceuticals.
- The ZDSD rat expresses the bone, renal and other complications seen in diabetes.

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

1:45 Dessert in the Exhibit Hall

WORKING BACKWARDS IN CANCER: FROM THE CLINIC TO DISCOVERY

2:15 Chairperson's Remarks

Michael Liebman, Ph.D., Managing Director, Strategic Medicine, Inc.

2:20 Using Drug-Induced Feedback Loops to Identify Indications and Combination Partners

Donald Bergstrom, Ph.D., Director, Experimental Medicine Oncology, Merck
James W. Watters, Ph.D., Associate Director, Molecular Profiling Oncology, Merck

Treatment with molecular targeted agents can result in compensatory feedback regulation as cells respond to inhibition of signaling pathways. We will present clinical evidence that treatment with a small molecule inhibitor of gamma secretase results in pathway modulation and compensatory feedback, and describe pre-clinical experiments designed to leverage this concept for drug response prediction.

3:00 Moving Research Closer to the Bedside, *in vitro* and *in vivo* Analyses with Primary Tumors

Fred Poordad, M.D., Chief of Hepatology, Liver Disease and Transplant Center, Cedars-Sinai Medical Center, Xin Wei Wang, Ph.D., Senior Investigator Head, Liver Carcinogenesis Section, Laboratory of Human Carcinogenesis, National Cancer Institute, NIH, and Michael R. Briggs, Ph.D., Senior Director, Biology, Vertex Pharmaceuticals, Inc.

The incidence of Primary Liver Cancer is increasing in the west and constitutes a tremendous burden on world health as the third leading cause of cancer deaths worldwide. The 5 year survival rate is a dismal 11 %, due in large part to late diagnosis and limited treatment options. The etiology of this devastating disease as well as current and proposed new therapies wil be discussed. Steps to better diagnose and stratify patients for targeted therapy will be considered as a new and exciting phase of cancer research. Finally, a move toward more relevant research will be presented as an hypothesis that will be tested in the coming years as more new and current therapies are compared and contrasted to current best practice.

4:05 How do you go from Pathways to Clinical Outcomes? *Sponsored by* Biovista

Aris Persidis, Ph.D., President, Biovista, Inc.

In drug discovery and development what what really counts is the clinical outcome, the Benefit/Risk of the drug within the context of its pathway or mechanism of action (MoA). Biovista screens the MoA of any drug or target against the MoA of 8,000 indications and 12,000 adverse events (AEs). This is simultaneous, unbiased indication discovery and AE profiling, and it is unique. It helps to bridge the gap from molecular pathway to clinical outcome in a single step. Case studies in cancer and other diseases will be described.

4:35 Reception in the Exhibit Hall *(Sponsorship Available)l*

5:20 BREAK-OUT DISCUSSIONS in the Exhibit Hall

1. Novel Imaging Biomarkers in Drug Development

Moderator: Jingsong Wang, M.D., Director of Immunology, Discovery Medicine & Clinical Pharmacology, Bristol-Myers Squibb, Co.

- The distinct advantage and unique challenges in applying imaging biomarkers in drug development
- The most promising novel imaging biomarkers for drug development, and which therapeutic areas will benefit the most from using imaging biomarker
- The role of pharmaceutical company, CRO, academia and regulatory agency in the discovery, development and qualification of imaging biomarkers

2. Biomarkers in Translational Medicine

Co-Moderators:
Christina M. Coughlin, M.D., Ph.D.; Medical Director, Oncology; Clinical Research and Development; Pfizer Oncology
Hans Winkler, Ph.D., Senior Director, Global Head Oncology Biomarkers, Johnson & Johnson

- Which type of biomarkers will speed drug development the most?
- Predictive marker clinical validation: retrospective vs. prospective trial requirements
- Do we still need phamaco dynamic analysis in Phase II?

3. New Funding Opportunities for Biotechs

Moderator:
Yali Fu, Ph.D., Program Director, Grants and Contracts Operations Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute

- Understand NIH Enhanced Peer Review
- NCI's new initiatives on SBIR funding
- Phase II Bridge awards to help biotechs further develop their technologies

4. New Animal Models in Translational Medicine

- Ideal characteristics for new animal models
- Advantages of new animal models
- Designing studies and using new animal models in discovery research

Co-Moderators:
Richard G. Peterson, Ph.D., Professor Emeritus, Indiana University School of Medicine and EVP, Research and Development PreClinOmics, Inc.
Troy A. Gobbett, MS, Director, Sales & Marketing for PreClinOmics,Inc.

6:20 Close of Day

THURSDAY, FEBRUARY 4

IMAGING: CLINICAL TO PRE-CLINICAL

8:25 AM Chairperson's Remarks

Jingsong Wang, M.D., Director, Immunology, Discovery Medicine & Clinical Pharmacology, Bristol-Myers Squibb, Co.

8:30 Assessing Mechanism of Action of Anticancer Agents using Functional Imaging in Oncology Drug Development

Dana Hu-Lowe, Ph.D., Group Leader, Associate Research Fellow, Cancer Biology, Pfizer, Inc., PGRD-La Jolla

Multiple imaging modalities have helped us to gain a deeper understanding of the mechanism of action of drug candidates beyond conventional pharmacological end points used in nonclinical and clinical settings. More importantly, functional imaging modalities are providing in-depth information on the modes of action of various anti-angiogenesis agents. These learnings are vital for improving efficiency in drug development.

9:00 Animal Imaging for Translational Approaches to CNS Drug Discovery

Rudy Schreiber, Ph.D., Senior Director, Pharmacology, Discovery and Early Clinical Research

In this presentation, I demonstrate how Sepracor's translational medicine approach for CNS drug discovery using emerging imaging methods and collaborative approaches such as cooperative technology development within a pain consortium. I'll present animal SPECT data for our inhibitors of monoamine neurotransmitter transporters (serotonin, noradrenaline and dopamine) in rodents and non human primates (with one example of human PET): I will include also brain microdialysis data in rodents where we measured all 3 neurotransmitters, and share human data generated in a fMRI pain imaging consortium.

9:30 Image Analysis Considerations for Pre-clinical, *in vivo* Medical Imaging

Matthew Silva, Ph.D., Head, Imaging Sciences, Millennium, The Takeda Oncology Company

10:00 Standardized Solutions for Non-Invasive Imaging of Cell Trafficking *Sponsored by* Celsense

Eric T. Ahrens, Ph.D., Founder and Chief Scientific Officer, Celsense, Inc.

A limiting factor in the development of new therapies is an inability to non-invasively assay cell trafficking in vivo. In this talk Dr. Eric Ahrens will describe a unique non-invasive imaging platform for visualizing and quantifying cells *in vivo* using magnetic resonance techniques. Applications include visualization and quantification of transplanted cells in immunotherapy and regenerative medicine and monitoring of inflammatory processes.

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

CHALLENGES IN TRANSLATIONAL BIOMARKER DEVELOPMENT

11:30 Biomarkers for Proof of Concept and Patient Selection

Hans Winkler, Ph.D., Senior Director, Global Head Oncology Biomarkers, Johnson & Johnson

The talk will comprise a discussion about the value of pharmacodynamic markers for proof of principle and decision making in PhaseI/II. Furthermore, the necessity and utility of predictive markers that can be applied for patient selection will be discussed.

12:00 PM Patient Selection Biomarker Approaches in Oncology

Daniel S. Johnston, Ph.D., Principal Research Scientist II, Pfizer Research and Development

This presentation will focus on the current strategies to identify patient selection biomakers in oncology. Both clinical and preclinical approaches will be discussed.

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

1:45 Ice Cream Refreshment Break in the Exhibit Hall

PLENARY KEYNOTE SESSION

2:15 Plenary Keynote Introduction

2:25 Plenary Keynote Presentation *(See Page 26 for Details)*

3:05 Refreshment Break in the Exhibit Hall

REDESIGNED ANIMAL MODELS

3:45 Chairperson's Remarks

Alain Stricker-Krongrad, Ph.D., Senior Scientific Adviser, Global Business Development, Charles River

3:50 An Animal Model of Parkinson's Disease Psychosis: Assessing Potential Therapeutic Efficacy of 5-HT2A Inverse Agonists

Krista McFarland, Ph.D., Team Leader, In Vivo Pharmacology, ACADIA Pharmaceuticals, Inc.

Available antipsychotic drugs do not provide an ideal treatment for psychosis in Parkinson's disease (PDP) because their blockade of dopamine receptors counteracts the dopamine replacement therapy used to alleviate the motor symptoms of PD. Development of alternate pharmacotherapies is limited by the lack of an animal model. Recent efforts to develop such a model and assess the potential therapeutic efficacy of 5-HT2A inverse agonists for the treatment of PDP will be discussed.

4:20 Engineered Human-In-Mouse Tumors for Population Based *in vivo* Biomarker Discovery

Min Wu, Ph.D., Principal Scientist, Translational Research, AVEO Pharmaceuticals, Inc.

I will present a NEW population-based tumor model system using Human-in-Mouse tissue transgenic human tumors that feature naturally occurring tumor variation akin to that observed in human tumor populations. The goal is to identify and validate biomarkers that ultimately predict responsive versus non-responsive patient populations to guide clinical development.

4:50 Appropriate Animals Models for Safety Assessment of Biologics

Timothy MacLachlan, Ph.D., Associate Director of Nonclinical Safety Assessment, Genzyme Corporation

The proper safety assessment of biopharmaceuticals has been an evolving process. While the paradigm set for small molecules was applied early, and some aspects have remained the same, other areas have required modification. The specificity of some biologics like monoclonal antibodies has necessitated study in higher order species. However, alternatives such as mice transgenic for the human target have proved useful, and at times, more accurate in risk assessment. Examples of these approaches will be discussed.

5:20 Comparative Oncology Drug Development

Melissa C. Paoloni, DVM, DACVIM, Director, Comparative Oncology Program, National Institutes of Health, National Cancer Institute

Comparative oncology is a model system to evaluate novel drugs, devices, biologics and imaging strategies in pet dogs with cancer to help inform their development for human cancer patients. Although much of this effort is preclinical, it also applies to agents that are already "first in man." The goal behind it is to garner information to help make informed go and no-go decisions to drive human oncology clinical trial design by answering questions about PK, PD, schedule, regime, dose, toxicity and clinical outcome (to just name a few). It has been well recognized and utilized by many within the pharmaceutical industry. It also has the ability to pilot personalized medicine approaches-a key to the future of oncology drug development.

5:50 Close of Day

FRIDAY, FEBRUARY 5

TRANSLATIONAL INFORMATICS – HOW FAR HAVE WE COME?

8:30 AM Chairperson's Opening Remarks

Pearl S. Huang, Ph.D., Integrator, Oncology Franchise, Research & Early Development, Merck & Co.

8:35 Implementing a Translational Biomarker Strategy to Reduce Attrition in Drug Development

Irina Antonijevic, M.D. Ph.D., Director, Translational Research, Biological Research, Lundbeck Research, Inc. USA

Early efforts towards the discovery of molecular biomarkers for CNS disorders are encouraging. However, confirmation, and ultimately validation of such biomarkers is dependent on state-of-the-art bioinformatics analyses as well as assay development. These prerequisites will ensure identification of biomarkers that are reproducible and hence of clinical relevance.

9:05 High Content Mining of Disease Biomarkers

Jake Chen, Ph.D., Assistant Professor, Informatics & Computer Science, Indiana University School of Informatics; Director, Indiana Center for Systems Biology and Personalized Medicine, Indiana University - Purdue University Indianapolis; Founder, MedeoLinx, Inc.

To facilitate the interpretation of raw Omics data into detailed disease-specific knowledge of candidate biomarkers, we developed a "high-content biomarker mining" software system. The system can help manage and correlate molecular functions, molecular connectivity, biological pathways, and literature information. Its application into the current biomarker development process will help improve the success rate and quality of candidate biomarkers.

9:35 Single Molecule Real Time Biology: New technologies Enabling a More Complete Characterization of Disease Biology

Eric Schadt, Ph.D., Chief Scientific Officer, Pacific Biosciences

While there has been an explosion of technologies that enable more comprehensive characterizations of complex biological processes like common human diseases, we are still unable to glimpse a large enough fraction of the biology of these systems to build models that are predictive enough to achieve clinical utility. However, with a new wave of technologies on the horizon, providing for the capability to examine the activity of single molecules real time, we will soon be capable of generating the right scale and diversity of data (DNA sequence, RNA sequence, real time monitoring of mRNA translation, full characterizations of base modifications in genomes and transcriptomes) at low cost to dramatically enhance the construction of models for common human diseases that achieve clinical utility. I will cover the single molecule real time (SMRT) technologies from Pacific Biosciences and how these technologies will revolutionize our ability to characterize living systems, and then present a number of integrative biology approaches to taking the types of data SMRT technologies will generate to get at predictive models of disease that can be used to drive the identification and validation of drug targets and biomarkers.

10:05 Automating Biomarker Discovery and Qualification; Capturing Hypothesis, Analysis and IP

Sponsored by idbs

Jonathan Sheldon, Ph.D., Director of Translational Medicine, IDBS

Long lists of un-annotated proteins and genes are not a sufficient end point for 'omics analysis, they need to be annotated with data from many public and proprietary sources. IDBS provide solutions to not only automate the discovery and subsequent annotation of biomarker results, but to capture each step of the experimental set up, data capture, and analysis in a compliant manner.

10:20 Coffee Break

TRANSLATIONAL INFORMATICS – HOW FAR HAVE WE COME? (CONTINUED)

11:00 Profiling Patients to Drive Biomarker Development

N. R. Nirmala, Ph.D.,Director, Biomarker Analysis and Informatics Unit, Translational Sciences, Novartis Institutes of Biomedical Research

Gene expression profiling is one of the key ways in which a genome-wide view of a patient's response to drug treatment can be obtained. Such a molecular level view can provide strategies for customized therapies in many contexts. In this talk, the oppportunities and challenges that this technology presents will be discussed with a couple of case studies. Extension of this approach to other technologies will also be presented in the context of biomarker development.

11:30 Panel: Informatics at R&D Interphases

Moderator: Pearl S. Huang, Ph.D., Integrator, Oncology Franchise, Research & Early Development, Merck & Co.

- Linking clinical outcome with molecular data: filling the gaps
- Capturing uniform clinical language for outcomes
- Compatible and user- friendly data systems—can one size fit all?
- Disease cohorts-how many, how big, what is acceptable quality

12:00 PM Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

CASE STUDIES ON SUCCESSFUL ORGANIZATIONAL COLLABORATIONS AND SYSTEM APPROACHES

1:00 Chairperson's Remarks

William B. Mattes, Ph.D., DABT; Former Executive Director, Predictive Safety Testing Consortium, Critical Path Institute

1:05 Taking personalized medicine to the next level- The critical Interface between Translational Medicine and Molecular Diagnostics

Lise Kjems, M.D. Ph.D., Executive Director, Global Program DiagnosticDirector, Molecular Diagnostics Novartis

Translational Medicine has reformed our drug development paradigm. Early clinical profiling of New Molecular Entities can enable identification of subsets of patients with a unique risk/benefit profile. In this talk, the opportunities and challenges related to this identification will be discussed. The role of Molecular Diagnostics is critical in developing and integrating novel patient treatment algorithms

1:35 Fostering Collaborations between Biotech and Academics to Speed Translational Medicine

Thomas Ichim, Ph.D., CEO, MediStem Labs, Inc.

2:05 Commercial Collaborations and other Approaches to Direct Academic Cancer Research towards Clinical Outcomes

Clive Stanway, Ph.D., CSO, Cancer Research Technology Ltd., Wolfson Institute for Biomedical Research

Cancer Research Technology (CRT) is the development and commercialization arm of Cancer Research UK (CR-UK) which has an annual science spend in excess of $500M.CRT works with CR-UK through multiple tracks to drive translational research including dedicated industry experienced, peer-reviewed funding for managed research in the PI's laboratory or in collaboration with focused drug discovery research groups around the UK. Specific examples and outcomes of this strategy will be presented with some discussion of CRT's flexible and creative approach to partnerships.

2:35 Development of Combination Therapies for Multiple Sclerosis Using Systems Level Informatics

Frederic S. Young, Ph.D., Chief Scientist, Vicus Therapeutics

We start with a multilevel systems physiology model that combines metabolomic analysis with integrated physiological analysis. The model is used to define a set of systems informatic features of ontogeny, phylogeny, homeostasis, and repair that distinguishes the disease state from homeostasis. We describe our use of this systems informatic signature as an algorithm for the development of combination therapies for multiple sclerosis.

3:05 Close of Conference

PLENARY KEYNOTE PRESENTATIONS

WEDNESDAY, FEBRUARY 3

8:10 - 8:55 am When Drug Research is Personal

John F. Crowley, Founder, Novazyme Pharmaceuticals, Inc.

Mr. Crowley's emotion-packed presentation will focus on his personal struggle to find a cure for Pompe disease, a rare and fatal illness that is caused by a defective or missing enzyme. Pompe disease affects fewer than 10,000 people world-wide, including Mr. Crowley's two small children.

Mr. Crowley, a Harvard educated businessman, created and built a pharmaceutical company devoted expressly to finding a cure for the disease. He will detail his journey through the labyrinth of scientific and business fronts, which lead up to a first-round clinical trial.

8:55 – 9:40 am Technology, Aging, and the Brain

Gary W. Small, M.D., Parlow-Solomon Professor on Aging, Professor of Psychiatry & Biobehavioral Sciences, Director, UCLA Center on Aging, Director, Memory & Aging Research Center, Director, Geriatric Psychiatry Division, Semel Institute for Neuroscience & Human Behavior, David Geffen School of Medicine at UCLA

New neuroimaging and other technologies are teaching us about how the brain ages and what we can do about it. Although memory declines as we age, medical and non-pharmacological strategies may protect brain health and improve memory performance. At the same time, innovation in digital technology is not only changing the way we live and communicate, it appears to be altering how our brains function. As a consequence of this high-tech stimulation, we are witnessing the beginning of a new form of the generation gap – a *brain gap* dividing younger digital natives, immersed in the technology early in life, from older *digital immigrants*, who adapt to the new technology more reluctantly. This lecture will describe this current pivotal point in brain evolution and how we can harness the new technology and lifestyle choices to improve memory and brain function so we can live better and longer.

THURSDAY, FEBRUARY 4

2:25 – 3:05 pm Chips, Clones and Living Beyond 100

Paul J.H. Schoemaker, Ph.D., M.B.A., Chairman and Chief Executive Officer, Decision Strategies International, Inc.; Research Director, Mack Center for Technological Innovation, The Wharton School; Adjunct Professor of Marketing, The Wharton School Adjunct Professor, WhartonSchool of Business

As information technologies and life sciences continue to converge, new business opportunities and challenges will arise for the field of diagnostics and beyond. This keynote reviews the deeper forces shaping the future of the biosciences, from social and economic to technological and political, including the stresses they will introduce for existing business models and healthcare. Not only will bio-convergence introduce new products, services and competitors, it may create entirely new industries on a scale larger than the computer revolution has to date. Several broad scenarios will be painted for the state of the biosciences in 2025 and the forces that might take us there, summarizing a multi-year strategy study conducted and supervised by the speaker at the Wharton school.

EXHIBIT AND SPONSORSHIP INFORMATION

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New Product Showcase Pavilion

For the first time ever, the Molecular Medicine Tri-Conference will feature a New Product Showcase Pavilion. The New Product Showcase Pavilion is the place for exhibitors to introduce and promote their new product to conference attendees. CHI will promote the New Product Showcase Pavilion in our pre-show promotions, on our website, as well as on-site.

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- ❑ SC3 Mighty Mitochondria: Their Relevance to Disease and Translational Medicine
- ❑ SC4 Addressing Safety Concerns For Biological Drugs
- ❑ SC5 Targeting Cancer Stem Cells With Biologics
- ❑ SC6 Blood-Brain Barrier

AFTERNOON SHORT COURSES:

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- ❑ SC8 Strategies for Molecular Diagnostic Companies
- ❑ SC9 Fragment - Inspired Medicinal Chemistry
- ❑ SC10 Transporter-Mediated Drug-Drug Interaction Potential
- ❑ SC11 Basic Immersion: Cutting Edge Science & Technology for Biotech & Pharma
- ❑ SC12 Designing Rigorous Omics Studies

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PROGRAM SELECTION: *(REQUIRED)* Please indicate the ONE program you are most likely to attend.

DIAGNOSTICS CHANNEL
❑ Molecular Diagnostics ❑ Cancer Molecular Markers
❑ Personalized Diagnostics

CHEMISTRY CHANNEL
❑ Mastering Medicinal Chemistry

INFORMATICS CHANNEL
❑ Adopting R&D Informatics Systems
❑ Cancer Profiling and Pathways

BIOLOGICS CHANNEL
❑ Stem Cells ❑ Cancer Biologics
❑ RNA Interference ❑ Delivery of Biologics

CANCER CHANNEL
❑ Cancer Biologics ❑ Cancer Profiling and Pathways
❑ Cancer Molecular Markers

EXECUTIVE CHANNEL
❑ Translational Medicine

DISCOUNTS*
❑ Poster ($50 off) ❑ Alumni (20% off) ❑ BayBio (10% off) ❑ Hotel ($75 off) see pg 18 for details
Hotel Confirmation number is _____

*Alumni and Bay Bio Discount cannot be combined. Discounts not applicable on Pre-Conference Events, (Conference registrations only)

❑ I cannot attend but would like to purchase the Molecular Medicine Tri-Conference CD for $750 (plus shipping). Massachusetts delivery will include sales tax

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)

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Signature _____

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Present a Poster and Save $50!

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

Special poster deadlines apply. To secure a poster board and inclusion in specific conference materials, your abstract must be submitted, approved and your registration paid in full by the following deadlines:

December 23, 2009
Poster abstracts submitted and approved by December 23, 2009 will be included in the Program Guide and Conference Proceedings Link.

January 8, 2010
Poster abstracts submitted and approved between December 24, 2009 and January 8, 2010 will not be included in the Program Guide, but instead will be included in the Program Addendum and Conference Proceedings Link.

All poster abstracts are due no later than January 8, 2010. Register online, or by phone, fax or mail. Indicate that you would like to present a poster and you will receive abstract submission instructions via email.

❑ Yes, I am interested in presenting a poster at:
Molecular Medicine Tri-Conference

Please refer to the Registration Code below:

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

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

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

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

Substitution/Cancellation Policy
In the event that you need to cancel a registration, you may:

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

NOTE: Cancellations will only be accepted up to two weeks prior to the conference. Program and speakers are subject to change.

CHI Insight Pharma Reports
A series of diverse reports designed to keep life science professionals informed of the salient trends in pharmaceutical technology, business, clinical development, and therapeutic disease markets. For a detailed list of reports, visit **InsightPharmaReports.com**, or contact Rose LaRaia, rlaraia@healthtech.com, 781-972-5444.

Barnett Educational Services
Barnett is a recognized leader in clinical education, training, and reference guides for life science professionals involved in the drug development process. For more information, visit **www.barnettinternational.com**.

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