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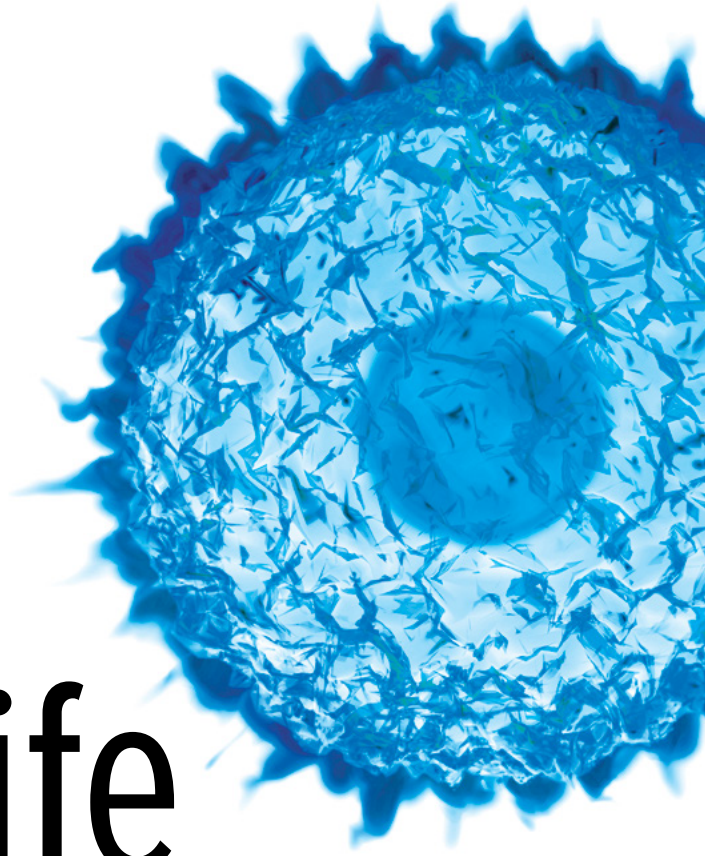

Diagnostics

Technologies, Translation, Trends, and Adoption of Molecular Diagnostics

Drug Discovery & Development

Advancing Drugs for Development: Chemistry to Clinic

Informatics

Knowledge Management, Open Collaboration, Web Service Technologies, and Scalable IT

Biologics

Biotherapeutics for Oncology and Regenerative Medicine

Cancer

Exploring Cancer Targets and the Latest Research Trends

a life changing event

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2011
Conference-at-a-Glance

Monday, February 21

8:00am	Registration and Coffee at the InterContinental Hotel
9:00-5:00pm	Early Oncology Partnering Forum

Tuesday, February 22

Event at InterContinental Hotel

9:00-5:00pm	Early Oncology Partnering Forum

Events at Moscone North Convention Center

8:00am	Short Course Registration and Coffee
9:00-12:00pm	Morning Short Courses (SC 1-5)
12:00pm	Lunch on Your Own
2:00-5:00	Afternoon Short Courses (SC 6-12)

Wednesday, February 23

7:00am	Registration and Morning Coffee
8:00-9:40	**Plenary Keynotes**
9:40-11:00	Grand Opening Refreshment Break in the Exhibit Hall
11:00-12:40pm	Concurrent Programs
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 Programs
4:20-5:20	Reception in the Exhibit Hall
5:20-6:20	Breakout Discussions

Thursday, February 24

8:25-10:30am	Concurrent Programs
10:30-11:30	Refreshment Break in the Exhibit Hall
11:30-12:30pm	Concurrent Programs
12:30-1:45	Sponsored Luncheon Presentations or Lunch on Your Own
1:45-2:15	Ice Cream Refreshment Break in the Exhibit Hall
2:15-3:50	Concurrent Programs
3:50-4:30	Refreshment Break and Poster Awards in the Exhibit Hall
4:30-6:00	Concurrent Programs

Friday, February 25

8:30-10:20am	Concurrent Programs
10:20-11:00	Coffee Break
11:00-12:00pm	Concurrent Programs
12:00-1:30	Sponsored Luncheon Presentations or Lunch on Your Own
1:30-3:35	Concurrent Programs
3:35	Close of Conference

Plenary
Keynote Speakers

Deconstructing the Drug Development Process: The New Face of Innovation

Kenneth Kaitin, Ph.D., Director, Tufts Center for Study of Drug Development

For over 30 years, the Center for the Study of Drug Development at Tufts University has documented the increasing challenge of bringing new pharmaceutical products to market. To succeed in today's competitive marketplace, research-based drug and biotech companies must not only maintain their focus on R&D efficiency and output, but they must also be able to adjust to a rapidly changing and highly volatile R&D environment. In this presentation, Dr. Kaitin will use Tufts CSDD data to document the current status of pharmaceutical R&D and explore new models of innovation.

Overcoming Challenges through Innovation

Jonathan M. Rothberg, Ph.D., Founder, CEO and Chairman, Ion Torrent

ION has developed the world's first semiconductor-based DNA sequencing technology, directly translating chemical information into digital data. DNA sequencing is performed with all natural nucleotides on Ion's proprietary semiconductor chips, leveraging a billion years of evolution and a trillion dollars of investment to allow unprecedented scalability, speed, and costs according to Moore's Law.

To the $1,000 Genome — and Beyond

Kevin Davies, Ph.D., Author, The $1,000 Genome; Editor-in-Chief, Bio-IT World

The field of genome analysis has undergone a revolution in recent years. Next-generation sequencing technologies have dropped the cost of sequencing a human genome from about $1 million in 2007 to less than $10,000 in 2010, with new third- and fourth-generation technologies on the horizon. But will the arrival of the $1,000 genome have any meaningful impact on drug development and the practice of medicine? Kevin Davies, author of *The $1,000 Genome*, will share his observations on the landmarks in next-generation sequencing. He will also highlight the challenges that remain in next-gen data generation, analysis and dissemination for the research and medical communities.

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Attend 12 concurrent programs within 5 scientific channels over 3 days.

Program hopping is encouraged during the event!

Concurrent Programs

February 23-25, 2011

Diagnostics Channel

- Molecular Diagnostics
- Personalized Diagnostics
- Cancer Molecular Markers
- Circulating Tumor Cells

Drug Discovery & Development Channel

- Mastering Medicinal Chemistry Summit
- Translational Science
- Strategies for Clinical Oncology Drug Development

Informatics Channel

- Integrated R&D Informatics & Knowledge Management
- Developing Scalable IT to Support Life Science Data
- Pathway-Targeted Therapies in Cancer

Biologics Channel

- Stem Cells
- Cancer Biologics

Cancer Channel

- Cancer Molecular Markers
- Pathway-Targeted Therapies in Cancer
- Cancer Biologics
- Strategies for Clinical Oncology Drug Development
- Circulating Tumor Cells

Early Oncology Partnering Forum

Strategies and Company Showcases

Sponsored by QIAGEN

February 21-22, 2011
Held at the InterContinental Hotel
Immediately prior to CHI's Molecular Med Tri-Con

Improved diagnosis and treatment of cancer continues to be a major challenge, but there is a rich diversity of approaches under development, many of which may offer substantial potential. CHI's Early Oncology Partnering Forum is designed to showcase a number of the more promising examples of innovative approaches by early stage companies, all of which are seeking out partnering collaborations with more established players in the cancer field.

This two day Partnering Forum opens with a series of perspectives from large companies active in partnering and collaboration to set the stage. This will be followed by three sessions of company presentations, organized by topic. At the end of each session of company presentations, the audience will have an opportunity to meet with the presenters to discuss the potential for collaboration. A total of about 50 companies will be featured with company presentations. An initial list of companies that have been confirmed based on the competitive selection process are listed below. Additional company presentations will continue to be added; please visit our website for the most complete list of company presentations: www.TriConference.com/cpr.

Large Molecule Therapeutics (including cancer vaccines, oncolytic viruses, monoclonal antibodies, RNAi and recombinant proteins):

- AbGenomics
- AzGardaBio
- MabVax Therapeutics
- Mirna Therapeutics
- TumorEnd

Small Molecule Therapeutics (including kinase and HDAC inhibitors, compounds targeting cancer stem cells and cancer metabolism, and others):

- Advanced Cancer Therapeutics
- Del Mar Pharmaceuticals
- GLG Pharma
- Pro-Cure Therapeutics
- Progenra
- Senex Biotechnology
- Threshold Pharmaceuticals
- Tragara Pharmaceuticals

Cancer Diagnostics and Other Tools (including cancer biomarkers, diagnostics for screening, early detection and cancer management, targeted drug delivery platforms and other tools):

- Advanced Research Technology
- Biosystems International
- Chronix Biomedical
- Ensysce Biosciences
- Foundation Medicine
- Horizon Discovery
- ImageneDx
- LIFE Biosystems
- Oxford Gene Technology
- T-Ray Science
- Zetiq Technologies

For a limited time, additional proposals will be accepted for review. To submit a proposal, please use our online submission form, found here: www.TriConference.com/cpr

CHI's INTRO-NET Networking at its Best

Maximize Your Experience onsite at the Molecular Medicine Tri-Conference!

The Intro-Net offers you the opportunity to set up meetings with selected attendees before, during and after this conference, allowing you to connect to the key people that you want to meet. This online system was designed with your privacy in mind and is only available to registered session attendees of this event.

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Pre-Conference Short Courses*

Tuesday, February 22

*Separate Registration Required

Morning Courses: 9am-12pm

(SC1) **Finding a Safe Passage through the Quagmire of High Throughput Screening-Based Biomarker Discovery**

- Data quality in high throughput measurements
- Understanding the relevance of noise structure, systematic vs. random
- Understanding the issue of data overfitting
- Identification of robust drug resistance mechanisms
- Using high-throughput measurements to characterize robust, disease related biological processes
- Replacing associative learning with causative learning through appropriate experimental design

Course Instructor:

Zoltan Szallasi, M.D., Professor, Technical University of Denmark and Senior Scientist, Informatics Program, Children's Hospital Boston, Harvard Medical School

(SC2) **Roadmap for Accelerating Commercialization of Molecular Diagnostics**

- Rationale for reimbursement – understanding coverage
- FDA clearance and navigating claims language
- Maximizing clinical study results while addressing costs

Course Instructors:

William Cook, MBA, Principal, Strategy and Business Development, Clinical Diagnostics, WECA

Patrick F. Terry, Principal, Pricing & Market Access Practice, Scientia Advisors

Bruce Quinn, M.D., Ph.D., Senior Health Policy Specialist, Foley Hoag, LLP

(SC3) **Best Practices in Translational & Personalized Medicine**

- Real world solutions currently in place in pharma, research institutions, and academia
- Tools for enabling better and faster clinical research
- Ways to bridge the gap between bench and bedside
- Informatics solutions that link data from the clinic with cutting edge research

Course Instructors:

Kevin Davies, Ph.D., Editor-in-Chief, Bio-IT World

Raymond Ng, CIO, PROOF Centre of Excellence

Jae Chung, Founder & CEO, goBalto

Guochun Xie, Discovery and Preclinical Sciences IT, Merck & Co.

Jian Wang, Founder & CEO, BioFortis

Chris Smith, Co-founder and Technical Director, Distributed Bio

(SC4) **Identification, Characterization and Targeting of Cancer Stem Cells**

- Targeting cancer stem cells with antibodies: New opportunities, approaches, and challenges for cancer drug development
- Reduction in tumor growth and recurrence in pre-clinical models targeting cancer stem cells
- Drug targets for new classes of cancer drugs that fundamentally change the management of prostate cancer
- Identification of Cancer Stem Cells Having an Oncogenic Protein EGFR Receptor Variant
- Targeting Telomerase in Cancer Stem Cells

Course Instructors:

Robert Hollingsworth, Ph.D., Director, Cancer Biology, MedImmune, Inc.

Tim Hoey, Ph.D., SVP, Cancer Biology, Oncomed Pharmaceuticals, Inc.

Norman J. Maitland, Ph.D., CSO, ProCure Therapeutics, Ltd.

Albert J. Wong, Professor, Cancer Biology and Neurosurgery, Stanford University Medical Centre

Stephen Kelsey, M.D., E.V.P. & Chief Medical Officer, Oncology, Geron Corp.

(SC5) **Early Drug Development and First-in-Human Dose Regimen**

For small molecules, biologics and oncology drug candidates:

- Phase I First in Human (FIH) Single Ascending Dose (SAD), Food Effect (EF), Multiple Ascending Dose (MAD)
- Phase IIIa Proof of Concept (POC) studies
- Starting dose calculation, dose escalation scheme (sequential vs alternative), exposure ceiling estimation, dose escalation stopping criteria
- FIH protocol review process

Course Instructor:

Sean Zhang, M.D., Medical Director, Discovery Medicine and Clinical Pharmacology, Bristol-Myers Squibb

Dale E. Johnson, Pharm.D., Ph.D., President & CEO, Emiliem, Inc.

Lori Kunkel, M.D., Chief Medical Officer, ACT Biotech

Afternoon Courses: 2pm-5pm

(SC6) **Applying Next-Generation Sequencing Technologies: 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 Instructors:

Ronald W. Davis, Ph.D., Director, Stanford Genome Technology Center, Stanford University

Jacob Glanville, Bioinformatics Analyst, Pfizer Global R&D

Adam Kraut, Scientific Consultant, BioTeam, Inc.

(SC7) **Future of Point-of-Care Platforms**

- How are Dx POCT markets changing?
- Which platforms will win? What's going to happen to the big box diagnostic companies?
- Where will the new markets be and how will they be organized?
- What strategies make sense for Dx and POCT companies?

Course Instructors:

Keith F. Batchelder, CEO, Genomic Healthcare Strategies

Peter S. Miller, COO, Genomic Healthcare Strategies

(SC8) **Smarter Studies: Designing Efficient and Rigorous Molecular Diagnostics and Biomarker Studies**

- Why study design is decisive for success or failure
- Critical review of examples
- A roadmap to the answers
- The regulatory perspective

Course Instructors:

Terry Speed, Head, Bioinformatics, The Walter & Eliza Hall Institute of Medical Research

Juergen von Frese, Ph.D., Managing Director, Data Analysis Solutions, DA-Sol GmbH

Michael Palmer, President, Adaptive Pharmacogenomics, LLC

(SC9) **Building an Ontological Framework from Drug Discovery to Clinical Data**

- Introduction on designing and using ontologies with other semantic web technologies
- Examples to highlight the use of ontologies for simultaneous access to drug discovery and health care data
- Sharing of data within the industry and between industry and academia in the precompetitive space

Course Instructor: *Elgar Pichler, Ph.D., Computational Biologist, Boston*

(SC10) **Serve, Collaborate, Disintermediate: Business Strategies for Companion Diagnostics**

Mark Trusheim, President, Co-Bio Consulting, LLC; Executive in Residence & Visiting Scientist, MIT; former Special Government Employee, Office of the Commissioner, FDA

- Business strategy challenges in personalized medicine
- Biomarker services
- Companion diagnostic collaborative developments
- Independently marketed tests
- Business model choices and the circumstances suited to each
- Risks and payoffs a diagnostic company can expect

(SC12) **Dealing with the Blood-Brain Barrier**

- The physiological basis for the "barrier" nature of the BBB
- Experimental approaches 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
- Exposure targeting for biomarker studies

Course Instructors:

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

Christopher L. Shaffer, Ph.D., Associate Research Fellow, Pharmacokinetics, Dynamics & Metabolism, Pfizer, Inc.

Travis T. Wager, Ph.D., Senior Principal Scientist, Neurosciences Chemistry, Pfizer, Inc.

Eighth Annual

Molecular Diagnostics

Is NGS Ready for Prime Time in the Clinical Lab?

WEDNESDAY, FEBRUARY 23

7:00 am Registration and Morning Coffee

8:00 Chairperson's Opening Remarks

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

8:05 Plenary Keynotes *(See Page 2 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

» KEYNOTE PRESENTATIONS

11:00 Chairperson's Opening Remarks

11:10 Massively Parallel Sequencing in Clinical Diagnostics

Wayne W. Grody, M.D., Ph.D., Professor, Divisions of Medical Genetics and Molecular Pathology, Departments of Pathology & Laboratory Medicine, Pediatrics, and Human Genetics, UCLA School of Medicine

This presentation will review the many considerations that must be faced in developing, validating, performing and reporting these new genome-wide tests. Also considered will be the ethical dilemmas raised by this new technology, including genetic discrimination and privacy, level of government oversight, gene patent restrictions, and direct-to-consumer testing.

11:40 AdvaMed Dx: An Ally in Your Molecular Diagnostics Company's Future

Andrew Fish, J.D., Executive Director, AdvaMed Dx

AdvaMed Dx is an advocacy organization focused on issues facing in vitro diagnostic (IVD) companies. The membership developed a strategic plan that encompasses global policy initiatives. This talk will cover the highlights of the policy initiatives for all of IVDs and those particularly important to the field of molecular diagnostics.

12:10 Genome-Era Pathology, Precision Diagnostics and Preemptive Care

Jeffrey E. Saffitz, M.D., Ph.D., Mallinckrodt Professor of Pathology, Harvard Medical School; Chairman, Department of Pathology, Beth Israel Deaconess Medical Center

"Medical sequencing" will revolutionize diagnostics as the foundation of personalized medicine. However, medicine lags far behind the technology and business communities in preparing for this change. Genomic testing must be performed by pathologists in CAP-accredited, CLIA-certified laboratories. Toward this end, we have established the first pathology training curriculum in medical genomics, and are developing a national plan to implement standardized genomic diagnostics in clinical practice.

Sponsored by nanoINK Nano BioDiscovery

12:40 Luncheon Presentation: Miniaturized and High Sensitivity Protein Detection Assays Using High Density Multiplex Nanoarrays

Haris Jamil, Ph.D., Vice President, Business Development, Nano BioDiscovery

NanoInk has developed a multiplex protein array technology for the detection and quantification of low abundance biomarkers using small sample volumes. NanoInk's nanoarrays enables assay miniaturization with improved sensitivity. These protein nanoarrays exhibit improved detection levels over conventional assay technologies with sensitivities for target biomarkers down to the femtograms/ml range.

1:10 Luncheon Presentation

Sponsored by THOMSON REUTERS

1:45 Dessert in the Exhibit Hall

TRANSLATING NEXT-GENERATION SEQUENCING INTO THE CLINICAL LABORATORY: RAISING THE BAR

2:15 Chairperson's Remarks

Karl Voelkerding, M.D., Associate Professor, Pathology, University of Utah; Medical Director, Advanced Technology and Bioinformatics, ARUP Laboratories

2:20 Clinical Next-Generation Sequencing for Inherited Cardiomyopathies

Birgit Funke, Ph.D., FACMG , Associate Laboratory Director, Laboratory for Molecular Medicine, Partners HealthCare Center for Personalized Genetic Medicine and Harvard Medical School

Genetic testing for inherited cardiomyopathies has been challenging due to the high level of genetic heterogeneity and high cost of traditional sequencing technologies. Next-Generation Sequencing allows one to maximize the number of genes that can be tested simultaneously while reducing the cost and turnaround time.

2:50 The True Value of Next-Generation Sequencing in a Clinical Diagnostics Laboratory

Madhuri Hegde, Ph.D., Associate Professor, Genetics Laboratory, Senior Director, Emory University

This presentation will discuss test validation, sequence quality, depth, accuracy, cost analysis and discuss the strength and weaknesses in the utilization of next generation sequencing in clinical testing. Examples from clinical testing for three large panels of varying complexity will be presented.

3:20 Bioinformatics for Clinical Next-Generation Sequencing

Karl Voelkerding, M.D., Associate Professor, Pathology, University of Utah; Medical Director, Advanced Technology and Bioinformatics, ARUP Laboratories

Processing, analyzing and interpreting next-generation sequencing data poses multiple challenges for clinical diagnostic implementation. Unique technical and quality monitoring solutions will need to be instituted to successfully translate raw sequence data into a clinical report. This presentation will describe components and examples of bioinformatic pipelines for managing next-generation sequencing data.

Sponsored by NuGEN imagine more from less

3:50 RNA-Seq Studies of Naïve and Memory Human CD4+ T-cells

Steven Head, Director, NGS and Microarray Cores, The Scripps Research Institute

In this study we describe optimized methods for RNA-Seq library preparation using the NuGEN Ovation RNA-Seq System for analysis of memory and naïve human CD4+ T-cells. We will present data describing functional pathways that distinguish memory and naive CD4 T cells in both normal donors and kidney transplant patients and how these molecular pathways reflect the intrinsic differences between these two important CD4 T-cell types in response to antigen challenge.

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

5:20 Breakout Discussions in the Exhibit Hall

The Value of Microarrays in Molecular Diagnostics – Under-Appreciated or Overrated?

Moderator: Shabbir M. Moochhala, Ph.D., Associate Professor, Distinguish Member of the Technical Staff, Defence Medical & Environmental Research Institute, DSO National Laboratories, Singapore

- Microarrays are widely applied today:
  - From human genotyping to small molecule drug screening
  - From expression profiling to high-throughput toxicological assessments
- Can microarrays be applied beyond the laboratory, closer to the point of need?
- Growth areas that leverage on microarray technology
  - Consumer genetics
  - Pharmaceutical drug screening
  - Biomarker discovery
  - Others
- Commercial opportunities, surveying market trends

Project Management in the Development of an *in vitro* Diagnostic in a Changing Global Environment

Moderators: Diane Ward, Ph.D., Senior Director and David Kern, M.B.A., Senior Director, Myraqa, Inc.

- It's not just the science, the process matters
- Managing a system
- Where project management can add value in an IVD environment
- Alliance management and strategic partnerships

Introducing New Technologies to the FDA

Moderators: Mya Thomae, RAC, CQA, Founder and CEO, and Lianne McLean, Senior Director, Myraqa, Inc.

5:20 Breakout Discussions in the Exhibit Hall (continued)

- Is it too early to meet with the FDA to discuss our new technology?
- Intended use statements
- Regulatory strategies: 510(k) vs. PMA?
- Removing the barriers to commercial success

Screening for Mutations in Genes to Predict Age of Onset for Genetic Disorders

Qing Zheng, M.D., Associate Professor, Genetics, Department of Otolaryngology-HNS, Case Western Reserve University

- Can anyone give an example of a genetic mutation that if known, can predict when the disease may happen during the life of that individual?
- There are many factors that influence onset of disease. How do we calibrate these in light of the genetics?
- Complexity and limitations of predictive medicine: complex traits, genetic modifiers –gene interactions, gene-environmental interactions
- Pharmacogenomics, prenatal diagnosis and screening, carrier testing, preconception testing, ethics and law

"Do We Have a 'Business Model Problem" or a "Reimbursement Problem" for High Value Diagnostics?

Moderator Katherine Tynan Ph.D., Tynan Consulting LLC

- What impact does test complexity have on market entry point?
- Which delivery mechanism is best, IVD kit or service?
- What is the most appropriate sales channel, laboratory or treating physicians?
- Who or what are the barriers to adoption?
- How will these business factors impact reimbursement?

Next-Generation Sequencing for Carrier Testing

Moderator: Stephen Kingsmore, M.B., Ch.B., B.A.O., D.Sc., CSO, National Center for Genome Resources

- What is your title and employer name?
- How many diseases do you think should be tested for carrier status in general US populations?
- At what age do you think carrier testing should ideally be performed in general US populations?
- What should be the cost of comprehensive carrier testing?
- What do you think are the principal bottlenecks to implementation of comprehensive carrier testing in general US populations?
- Do you have another question that you would like us to discuss?

Targeted Resequencing versus Whole Genome Sequencing

Moderator: Karl Voelkderding, M.D., Associate Professor, Pathology, University of Utah; Medical Director, Advanced Technology and Bioinformatics, ARUP Laboratories

Next Generation Sequencing is being applied to multi-gene panels, exomes and whole genomes in clinical research and diagnostics. Each strategy has different cost considerations and complexity of data analysis and interpretation.

- What clinical conditions are multi-gene panels being developed for and implemented in clinical laboratories?
- How is exome sequencing being applied to discover causative genes for Mendelian disorders?
- In what clinical scenarios would whole genome sequencing be applied versus whole exome sequencing?
- What consent and counseling approaches should be considered and implemented when using whole exome and genome sequencing in clinical research?

How Will Consumer Products Companies Make Use of Genomics?

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

- Discussion of some early indications from major companies
- Some successes and failures so far
- Discussion of how new markets will be different
- Where will the next entries be?

Emerging Stakeholders in Personalized Diagnostics

Moderator: Harry Glorikian, Managing Partner, Scientia Advisors

- Personalized medicine is becoming a critical component of healthcare delivery
- Current stakeholders are increasingly active and interested in the benefits offered by personalized medicine
- Emerging stakeholders are creating value-driven services that will impact the future direction of personalized medicine

5:20 Breakout Discussions in the Exhibit Hall (continued)

Discussion on Getting Federal Funding to Develop Early Stage Diagnostic Platforms

Mark David Lim, Ph.D., Support to DARPA/Defense Sciences Office, Strategic Analysis, Inc.

- Landscape of federal funding opportunities for developing novel platform biomedical technologies
- Funding mechanisms
- Discussions for engaging program staff

6:20 Close of Day

THURSDAY, FEBRUARY 24

8:25 am Chairperson's Remarks

» 8:30 EXPERT PANEL: Reforming CPT Codes for Molecular Diagnostics: Perspective of Value-Based Reimbursement

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

Panelists:

Jeffrey A. Kant, M.D., Ph.D., FCAP, FAAAS, Professor, Pathology and Human Genetics, Director, Division of Molecular Diagnostics, University of Pittsburgh Medical Center

Bruce Quinn, M.D., Ph.D., Senior Health Policy Specialist, Foley Hoag LLP

Lee N. Newcomer, M.D., Senior Vice President, Oncology, United Healthcare

INNOVATION AND REGULATION: COLLABORATING WITH DARPA AND FDA

9:30 How to Work with DARPA to Develop Novel, Integrated Molecular Diagnostics

Daniel J. Wattendorf, M.D., Lt. Col., USAF, MC; Program Manager, DARPA/DSO

9:45 Working at the Intersections between Innovation and Regulation

Jonathan Sackner-Bernstein, M.D., Associate Center Director, Technology and Innovation, Center for Devices and Radiological Health, FDA

10:00 SAMiRNA, a New Class of RNAi Molecules with Inherent Stability, Low Toxicity and High Knockdown Efficacy in vivo

Sponsored by BIONEER Innovation + Value + Discovery

Vince Prezioso, Ph.D., Vice President, Global Marketing, Bioneer Corporation

SAMiRNA (Self-Assembled-Micelle- interfering-RNA) is a novel class of RNAi nanoparticles developed by Bioneer. This presentation discusses the therapeutic potential of SAMiRNA by virtue of its low toxicity and superb in vivo serum stability and target gene silencing efficiency. In vivo time course and dose/response experiments reveal the efficacy of SAMiRNA in a mouse tumor model. Data examined include knockdown efficiency of up to 60% after a single dose injection of SAMiRNA targeting well-studied cancer-associated gene, survivin. SAMiRNA's therapeutic potential as a delivery platform for a variety of diseases through the use of cell-type specific targeting ligands also will be discussed.

10:15 Integrated Project Management Panel

Panelists: Deborah Neff, CEO and President, Pathwork Diagnostics Inc.

David Jackson, Sr. Director, Companion Diagnostic Partnerships, Qiagen Manchester

10:30 Refreshment Break in the Exhibit Hall

» 11:30 EXPERT REIMBURSEMENT PANEL: Changing Landscape of Valuation and Reimbursement

Moderator: Felix W. Frueh, Ph.D., President, Medco Research Institute, Medco Health Solutions, Inc.

The panel will address the following topics:

- Comparative effectiveness, how does it help to create data for reimbursement decisions?
- Study design: RCT vs observational vs. retrospective data what evidence is needed for decision making?
- How can technology companies bridge the gap to reimbursement?
- Does working with pharma help to get diagnostics to the market and paid for?
- Regulatory environment: how does it affect reimbursement decisions (CMS, FDA) vs LDT?
- Tools for access (e.g. prior authorization): A new way for value
- Coding system
- Will new, costly therapies (e.g. biologics) save the day for Dx?

Panelists:

Leah Sparks, Vice President, Business Development, DNA Direct

Patrick Terry, Principal, Pricing and Market Access Practice, Scientia Advisors LLC

Kristin Ciriello Pothier, Partner, Health Advances, LLC

Paul Billings, M.D., Ph.D., Chief Medical Officer, Life Technologies

12:30 Using IPA to Explore microRNA Impacts on Molecular Mechanisms of Disease

Sponsored by INGENUITY SYSTEMS

Dana Abramovitz, Product Manager, Ingenuity Systems, Inc.

Learn how IPA was used to explore the role of microRNA in diseases. We will show new IPA functions that enable interactive identification, prioritization and analysis of microRNAs and their targets and visual analysis of the resulting interactions.

1:00 Comprehensive Evaluation of Fusion Gene Variants with Quantitative Nuclease Protection Technology

Sponsored by htg The FFPE Gene Expression Company

Bruce Seligmann, Ph.D., Founder, Director, CSO, VP R&D, High Throughput Genomics

The quantitative nuclease protection assay (qNPA™) enables quick and accurate measurement of mRNA and miRNA in virtually any sample, including formalin, fixed paraffin embedded (FFPE) tissue, making it ideal for clinical research. The fast, automated process requires no extraction; cDNA synthesis, amplification, or labeling that have traditionally has been problematic. An overview of the system and data from patient samples with EML4/ALK and BCR/ABL translocations will be shown.

1:45 Ice Cream Refreshment Break in the Exhibit Hall

NEW ANALYTES IN UNCONVENTIONAL PLACES

2:15 Chairperson's Remarks

Jean Amos Wilson, Ph.D., Vice President, Lab Operations, Berkeley HeartLab, Inc.

2:20 Advances in Prenatal Diagnosis Involving Circulating Cell-Free Fetal Nucleic Acid

Roger R. Lenke, M.D., Medical Director, Indiana Center for Prenatal Diagnosis

This talk will explore answers to the following questions: What is Circulating Cell-Free Fetal Nucleic Acid? How is it currently used in fetal Rh typing and fetal sex determination? What is its future potential in fetal Down syndrome screening and other potential uses?

2:50 Personalized Genomic Analyses of Human Cancer

Victor E. Velculescu, M.D., Ph.D., Associate Professor, Oncology; Director, Cancer Genetics, Ludwig Center at Johns Hopkins; Co-Director, Cancer Biology, Johns Hopkins Kimmel Cancer Center

It is generally accepted that cancer is a disease caused by accumulation of mutations in specific genes. These tumor-specific mutations provide insights to the cellular processes underlying tumorigenesis and have proven useful for diagnostic and therapeutic purposes. We and others have begun to systematically study the cancer genome through analysis of the majority of protein coding genes in a variety of tumor types, including breast, colorectal, pancreatic, ovarian and brain cancers. These analyses have led to the development of new genome-wide methods for detecting circulating tumor DNA in cancer patients using next generation sequencing approaches. These studies open the door to personalized genomic analyses of cancer patients for therapeutic stratification, prognosis and tumor monitoring.

3:20 A Window into the Brain: New Insights into Schizophrenia Pathophysiology Revealed by Analyses of Brain Transcripts

Nora Perrone-Bizzozero, Ph.D., Professor, Neurosciences, University of New Mexico School of Medicine

Emerging evidence indicates that alterations in brain macro- and micro-circuitry contribute to the development of schizophrenia. A variety of approaches were used for gene expression studies of human post-mortem tissue: from qRT-PCR to DNA microarrays and next generation sequencing. Our results demonstrate that the levels of several neurotransmission-associated transcripts are altered in cerebellar tissue from patients, indicating that brain transcript analyses are very useful tools to study schizophrenia.

3:50 Refreshment Break & Poster Awards in the Exhibit Hall

» KEYNOTE SESSION: REGULATION OF MOLECULAR DIAGNOSTIC TESTING: THREE POINTS OF VIEW

4:25 Chairperson's Remarks

Harry Glorikian, Managing Partner, Scientia Advisors

4:30 Regulation of Molecular Diagnostics

Alberto Gutierrez, Ph.D., Deputy Director, Office of in vitro Diagnostic Device Evaluation and Safety, Food & Drug Administration

5:00 Genomic Medicine: The Pathway from Biobanks to Clinical Practice

Timothy J. O'Leary, M.D., Ph.D., President-Elect, Association for Molecular Pathology;

Deputy Chief Officer, Research & Development Office; Director, Biomedical Laboratory and Clinical Science Research & Development Service, Veterans Health Administration

In spite of abundant information relating gene sequence variation to disease, the clinical impact of molecular diagnosis is largely confined to "traditional" hereditary diseases and cancer. This talk provides a framework for improving linkage between new genetic findings their clinical implementation, using the VA health system as a model.

5:30 Is the Past Prologue – Will Proposed Changes Really Result in Dramatic Changes in the Regulation of Testing?

Stephen P. Day, Ph.D., Director, Medical Affairs, Hologic, Inc.

The partnerships between the FDA and manufacturers and between manufacturers and clinical laboratories has always been dynamic. How the proposed changes in LDT regulation and other changes in FDA policy may potentially benefit and hurt these dynamics will be examined.

6:00 Close of Day

FRIDAY, FEBRUARY 25

HIGHLY MULTIPLEXED CARRIER SCREENING TESTS

8:30 am Chairperson's Remarks

Stephen F. Kingsmore, M.B., Ch.B., B.A.O., D.Sc., CSO, National Center for Genome Resources

8:35 Comprehensive Carrier Screening for Severe Recessive Diseases by Next-Generation Sequencing

Stephen F. Kingsmore, M.B., Ch.B., B.A.O, D.Sc., CSO, National Center for Genome Resources

Next-generation sequencing is transforming genetic research by enabling high throughput analyses of genomes and exomes. We have developed a carrier screening test for almost 500 severe childhood recessive diseases based on target enrichment, next-generation sequencing and bioinformatic analysis. I will describe the test workflow, results from evaluation of over 100 individuals and remaining challenges for implementing next-generation sequencing for molecular diagnostic or carrier testing.

9:05 Comprehensive Mutation and Carrier Screening in X-Linked Disorders

Hans-Hilger Ropers, M.D., Ph.D., Professor, Department of Human Genetics, Humboldt University; Director, Max Planck Institute for Molecular Genetics

Most mutations causing severe X-linked disorders are unique, which poses particular problems for their detection. We have employed genome partitioning and next-generation sequencing to screen the exome of nearly 800 protein-coding genes on the X in 250 families with X-linked mental retardation. This test should be suitable for mutation detection and carrier screening in the 273 X-linked diseases known to date.

9:35 Expanded Diagnostic Gene Panels in Hereditary Colon Cancer: Is More Better?

Matthew J. Ferber, Ph.D., DABMG (Clinical Molecular Genetics),Co-Director, Molecular Genetics Laboratory, Department of Laboratory Medicine and Pathology, Mayo Clinic

Inexpensive and high output DNA sequencing is creating new opportunities for diagnostic laboratories. However, more data means more novel discoveries, many with unknown consequences. Reporting unknown variants, which is the current accepted practice, makes it difficult for physicians to accurately assess a patient's risk for developing disease. How do we balance benefits with risks in this new era?

10:05 Sponsored Presentation *(Opportunity Available)*

10:20 Coffee Break

MULTIPLEXED CLINICAL ASSAYS: THE KRAS STORY WHAT HAVE WE LEARNED?

10:55 Chairperson's Remarks

Eric H. Lai, Senior Vice President, Research & Development, Gen-Probe, Inc.

11:00 KRAS Testing: Comparison of Assays and Formats

Steven M. Anderson, Ph.D., CSO, Genetics and Oncology, Laboratory Corporation of America

The importance of the accurate determination of gene mutation status is becoming increasingly important in solid tumors because of the linkage to specific targeted therapies. In this presentation, different methods of mutational analysis for solid tumors will be discussed using KRAS as an example.

11:30 The Path to the Elucidation of KRAS as a Negative Selection Biomarker

Scott D. Patterson, Ph.D., Executive Director, Medical Sciences, Amgen, Inc.

This presentation will describe the path that led to the qualification of KRAS as a negative selection biomarker for anti-EGFR therapy in metastatic colorectal cancer and the levels of evidence that we attribute to this process.

12:00 pm Automation of Molecular Diagnostics for the Core Clinical Laboratory

Robin A. Felder, Ph.D., Professor, Pathology; Associate Director Clinical Chemistry, The University of Virginia

The increasing demand for molecular testing coupled with financial pressures to reduce the cost of performing these tests has resulted in the need for automation, especially for infectious disease assays which routinely have high sample volumes and can be processed in batches. New analytical systems are now available that will enable molecular diagnostic integration into the core laboratory integrate sample extraction, nucleic acid amplification, and detection either on one instrumented platform or in a multi-instrument modular format. This presentation will review current offerings and future directions for improved process automation as well as simplified integration and operation.

1:35 Detection of Lung Cancer Molecular Subtypes by Gene Expression Arrays, Protein Immunohistochemistry and PCR from Paraffin Based Assays

David Neil Hayes, M.D., M.P.H., Assistant Professor, Clinical Research, Hematology/Oncology, University of North Carolina, Chapel Hill

Gene expression profiling has revealed reproducible subtypes of lung cancer not detectable by routine clinical diagnostic methods. We investigate the nature of the tumor subtypes in terms of clinical relevance and biologic underpinnings such as associated mutations and potential cell of origin. We further investigate a range of issues related to sample quality as they impact different measures of subtype detection.

2:05 Implementing Molecular Testing: A Comparison of Different Formats and Their Adoption

Kenneth J. Bloom, CMO, Clarient, Inc.

2:35 Technology Innovation Enabling Proactive Medicine

Jay Wohlgemuth, M.D., Vice President, Science and Innovation, Quest Diagnostics

Novel gene based, small molecule and protein assay technologies have rapidly advanced over recent years. These technologies enable more sensitive, specific and reproducible measurements of disease associated biomarkers. Over the past 5 years the pace of translation of these markers to clinically valuable diagnostics has begun to accelerate. I will describe the requirements for successful translation and use recent examples across disease areas where the stars have aligned to enable value for patients.

3:05 Intervene XRT: A Genomic-Based Signature to Predict Response to Radiation Therapy

Javier Torres-Roca, M.D., CSO, Cvergenx, Inc.

Intervene XRT comprises a novel patient-specific testing platform for predicting a patient's sensitivity to radiation therapy. This technology has been independently validated in three disease sites and its currently undergoing prospective validation in an NCI-sponsored clinical trial.

3:35 Close of Conference

Second Annual

Personalized Diagnostics

Technologies for Molecular Assays

WEDNESDAY, FEBRUARY 23

7:00 am Registration and Morning Coffee

8:00 Plenary Keynotes *(See Page 2 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

» KEYNOTE PRESENTATIONS

11:00 Chairperson's Opening Remarks

11:10 Massively Parallel Sequencing in Clinical Diagnostics

Wayne W. Grody, M.D., Ph.D., Professor, Divisions of Medical Genetics and Molecular Pathology, Departments of Pathology & Laboratory Medicine, Pediatrics, and Human Genetics, UCLA School of Medicine

This presentation will review the many considerations that must be faced in developing, validating, performing and reporting these new genome-wide tests. Also considered will be the ethical dilemmas raised by this new technology, including genetic discrimination and privacy, level of government oversight, gene patent restrictions, and direct-to-consumer testing.

11:40 AdvaMed Dx: An Ally in Your Molecular Diagnostics Company's Future

Andrew Fish, J.D., Executive Director, AdvaMed Dx

AdvaMed Dx is an advocacy organization focused on issues facing *in vitro* diagnostic (IVD) companies. The membership developed a strategic plan that encompasses global policy initiatives. This talk will cover the highlights of the policy initiatives for all of IVDs and those particularly important to the field of molecular diagnostics.

12:10pm Genome-Era Pathology, Precision Diagnostics and Preemptive Care

Jeffrey E. Saffitz, M.D., Ph.D., Mallinckrodt Professor of Pathology, Harvard Medical School; Chairman, Department of Pathology, Beth Israel Deaconess Medical Center

"Medical sequencing" will revolutionize diagnostics as the foundation of personalized medicine. However, medicine lags far behind the technology and business communities in preparing for this change. Genomic testing must be performed by pathologists in CAP-accredited, CLIA-certified laboratories. Toward this end, we have established the first pathology training curriculum in medical genomics, and are developing a national plan to implement standardized genomic diagnostics in clinical practice.

12:40 Luncheon Presentation
Miniaturized and High Sensitivity Protein Detection Assays Using High Density Multiplex Nanoarrays

Sponsored by NanoInk Nano BioDiscovery

Haris Jamil, Ph.D., Vice President, Business Development, Nano BioDiscovery

NanoInk has developed a multiplex protein array technology for the detection and quantification of low abundance biomarkers using small sample volumes. NanoInk's nanoarrays enable assay miniaturization with improved sensitivity. These protein nanoarrays exhibit improved detection levels over conventional assay technologies with sensitivities for target biomarkers down to the femtograms/ml range.

1:10 Luncheon Presentation

Sponsored by Thomson Reuters

Speaker to be Announced

1:45 Dessert in the Exhibit Hall

SOLID TUMORS: LESSONS FOR BIOMARKER VALIDATION?

2:15 Chairperson's Remarks

Josip Blonder, M.D., SAIC-Frederick, NCI-Frederick

2:20 Solid Tumor Heterogeneity: From Tissue Proteomics to Personalized Medicine

Donald J. Johann, Jr., M.D., Associate Investigator, Center for Cancer Research, National Cancer Institute, National Institutes of Health

Solid tumor heterogeneity is a perplexing scientific and clinical problem. Tissue based proteomic approaches utilizing identity-based mass spectrometry and laser capture microdissection, may serve as a platform allowing enhanced molecular profiling, and the revealing of subtle solid tumor phenotypes.

2:50 Proteomic Profiling of Clinical Specimens in the Context of Cancer Biomarker Discovery and Validation

Josip Blonder, M.D., Senior Research Scientist, Head, Clinical Proteomics, Laboratory of Proteomics and Analytical Technologies, SAIC-Frederick, Inc., NCI-Frederick

Solid tumors undergo tremendous change due to improved understanding of their biology as well as an abundance of new therapeutic agents (i.e., small molecules and monoclonal antibodies) recently approved by FDA. Certainly, clinical proteomics based cancer biomarker discovery could assist tremendously for individual-based treatment assignments, as well as toxicity monitoring. This presentation will highlight a variety of technological approaches utilized in clinical proteomics of renal cell carcinoma (RCC) and summarize respective biological findings in the context of RCC biomarker discovery and validation.

3:20 Clinical Application of Tumor Genotyping to Drive Clincal Trials and Translational Research

Leif Ellisen, M.D., Ph.D., Co-Executive Director, Massachusetts General Hospital Cancer Center, Translational Research Laboratory; Associate Professor of Medicine, Harvard Medical School

Analysis of tumor somatic genetic abnormalities has provided key insights into cancer pathogenesis, signaling, and oncogene dependence. We describe the development and validation of a prospective (pre-treatment), broad-based solid tumor mutation detection platform and its application for clinical decision making, clinical trial enrollment and translational research.

3:50 Sponsored Panel Discussion
Overcoming the Challenges and Issues with FDA Approved IVD Tests

Sponsored by IPM Integrated Project Management

Moderator: Mally Arad, Manager, Integrated Project Management Company, Inc. (IPM)

4:05 "So Many Markers, So Little Tissue": The Layered IHC Solution for Personalized Medicine

Sponsored by 20/20 GeneSystems

Michael S. Lebowitz, Ph.D., Director of R & D, 20/20 GeneSystems, Inc.

L-IHC detects multiple biomarkers in histological (FFPE) samples. From one 5µm tissue section >10 protein biomarkers can be probed enabling pathway profiling in limiting samples (e.g. core needle biopsies) supporting the development of new diagnostic tests.

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

5:20 - 6:20 Breakout Discussions in the Exhibit Hall
Personalized Medicine Partnerships: Emerging Industry Models

Mollie Roth, Esq., Chief Operating Officer, Diaceutics

- The current disconnect between the business models in the pharmaceutical and diagnostic industries
- Why does PM require a new business model?
- What changes are required to move from the current supplier/buyer paradigm into a true partnership?
- What does a truly effective partnership in the PM space look like?
- An overview of the emerging models

Project Management in the Development of an *in vitro* Diagnostic in a Changing Global Environment

Moderators: Diane Ward, Ph.D., Senior Director and David Kern, M.B.A., Senior Director, Myraqa, Inc.

- It's not just the science, the process matters
- Managing a system
- Where project management can add value in an IVD environment
- Alliance management and strategic partnerships

5:20 - 6:20 Breakout Discussions in the Exhibit Hall (continued)

Introducing New Technologies to the FDA

Moderators: Mya Thomae, RAC, CQA, Founder and CEO, and Lianne McLean, Senior Director, Myraqa, Inc.

- Is it too early to meet with the FDA to discuss our new technology?
- Intended use statements
- Regulatory strategies: 510(k) vs. PMA?
- Removing the barriers to commercial success

Proteomic Profiling of Clinical Specimens

Moderator: Josip Blonder, M.D., Senior Research Scientist, Head, Clinical Proteomics, Laboratory of Proteomics and Analytical Technologies, SAIC-Frederick, Inc., NCI-Frederick

- Selection, evaluation, and translation of proteomic technologies for cancer biomarker discovery using analysis of clinical specimens.
- Future prospects of analyzing tissues and body fluids using proteomics: complementing and enhancing MS-based proteomic assays to conventional molecular diagnostics.
- What improvements would facilitate translation of proteomic technologies into the clinical laboratory for quantitative assaying of clinical specimens?

microRNAs for Cancer Treatment Decision Making

Moderator: Glen Weiss, M.D., Director, Thoracic Oncology, VGPCC, Scottsdale Healthcare; Co-Head, Lung Cancer Unit, TGen

- What are the first clinical applications that microRNAs will be used for?
- What barriers need to be overcome to more widely implement microRNAs for cancer treatment decision making?
- Can biofluids supplant tumor tissue derived microRNAs for treatment decision making?
- Could microRNAs be used for both cancer treatment decision making and treatment?

Screening for Mutations in Genes to Predict Age of Onset for Genetic Disorders

Qing Zheng, M.D., Associate Professor, Genetics, Department of Otolaryngology-HNS, Case Western Reserve University

- Can anyone give an example of a genetic mutation that if known, can predict when the disease may happen during the life of that individual?
- There are many factors that influence onset of disease. How do we calibrate these in light of the genetics?
- Complexity and limitations of predictive medicine: complex traits, genetic modifiers –gene interactions, gene-environmental interactions
- Pharmacogenomics, prenatal diagnosis and screening, carrier testing, preconception testing, ethics and law

Emerging Stakeholders in Personalized Diagnostics

Moderator: Harry Glorikian, Managing Partner, Scientia Advisors

- Personalized medicine is becoming a critical component of healthcare delivery
- Current stakeholders are increasingly active and interested in the benefits offered by personalized medicine
- Emerging stakeholders are creating value-driven services that will impact the future direction of personalized medicine

6:20 Close of Day

THURSDAY, FEBRUARY 24

USING microRNA SIGNATURES FOR DIAGNOSTICS AND PROGNOSTICS

8:25 am Chairperson's Remarks

Dalia Cohen, Ph.D., Chief Scientific Officer, Asterand and Bernard Andruss, Ph.D., Director, Collaborations & Business Development, Asuragen, Inc.

8:30 microRNAs: Novel Biomarkers and Targets for Cancer Therapy

Glen Weiss, M.D., Director, Thoracic Oncology VGPCC, Scottsdale Healthcare; Co-Head, Lung Cancer Unit, TGen

Recent studies have uncovered broad implications of microRNAs, demonstrating that a single microRNA can impact hundreds of targets and can affect pathways controllingoncogenic processes. Data will be presented illustrating how using microRNA can impact cancer treatment decision making, validated microRNAs associated with resistance and/or sensitivity to chemotherapy and targeted therapy, and how microRNAs could be used as therapeutics.

9:00 microRNA Gene Regulatory Networks in Sarcomas

Subbaya Subramanian, Ph.D., Assistant Professor, Surgery, University of Minnesota

Deregulation of miRNA mediated gene regulatory networks may play a central role in the pathogenesis of tumors. A systematic analysis of miRNA, mRNA and DNA copy number aberrations can provide insights into the deregulation of fundamental gene regulatory networks involving miRNAs. This talk will cover diverse aspects of miRNA networks in childhood cancers such as osteosarcoma and other cancer types.

9:30 Secretory microRNAs in Cancer Development and Diagnosis

Takahiro Ochiya, Ph.D., Head, Section for Studies on Metastasis, National Cancer Center Research Institute, Tokyo

The physiological role of microRNAs (miRNAs) is widely appreciated as a fine-tuner of multiple genes in the cells of origin. Currently, miRNAs have received greater attention in cancer research. Aberrant miRNA expression is correlated with development and progression of cancer. Furthermore, cellular microRNAs as well as extracellular miRNAs could be used for cancer biomarkers for diagnosis and prognosis.

10:00 Signature Validation and Analysis of Fusion Gene Variants with the nCounter Analysis System *Sponsored by* nanoString TECHNOLOGIES

Sean Ferree, NanoString Technologies

The nCounter Analysis System is a fully-automated, digital, mid-plex genomic analysis platform that is ideal for a broad range of cancer research applications. We will present an overview of the system and data demonstrating the system's utility in expression profile signature validation, analysis of fusion genes, and analysis FFPE samples (with and without RNA purification).

10:30 Refreshment Break in the Exhibit Hall

11:30 Molecular Biomarkers of Cancer: miRNAs and Beyond

Muller Fabbri, M.D., Molecular Virology, Immunology and Medical Genetics, The Ohio State University Comprehensive Cancer Center

While the role of miRNAs as molecular biomarkers for cancer is being supported by an increasing number of studies, also other non-coding RNAs are de-regulated in a cancer-specific fashion and can be part of signatures which harbor prognostic implications for cancer patients. This talk will explain what is currently known about the role of miRNAs and other non-coding RNAs as biological markers in cancer.

12:00 pm Circulating microRNAs as Cancer Biomarkers

Muneesh Tewari, M.D., Ph.D., Human Biology, Fred Hutchinson Cancer Research Center

MicroRNAs have been found to circulate in the bloodstream in a highly stable form and are being investigated as blood-based biomarkers for cancer and other diseases. Results of circulating miRNA studies will be presented, and issues important for developing this class of biomarkers for clinical application will be discussed.

12:30 Development of Mutiplexed Immunoassays for Personalized Medicine *Sponsored by* MSD Meso Scale Discovery

Pankaj Oberoi, Ph.D., Director, Research and Development, Meso Scale Discovery

Meso Scale Discovery® offers a high throughput, sensitive platform allowing for the quantification of biomarkers that can vary over a wide range of concentrations in single or multiplexed format. Early stages of biomarker screening require examination of a broad panel of markers. A focused subset of markers (typically 2-10) emerges from the screen and the immunoassays used to measure them require a greater degree of analyticity and longevity. In this presentation, case studies involving the development and qualification of multiplexed protein biomarker assays for different stages of personalized medicine biomarker applications using Meso Scale Discovery's plate based electrochemiluminescent platform will be presented.

1:45 Ice Cream Refreshment Break in the Exhibit Hall

MINING THE WHOLE GENOME FOR PERSONALIZED MEDICINE

2:15 Chairperson's Remarks

German Pihan, M.D., Chief, Hematopathology Service, Beth Israel Deaconess Medical Center; Director, Hematopathology Fellowship Site Director, HMS Molecular Genetic Pathology Fellowship; Assistant Professor of Pathology, Harvard Medical School

2:20 Cancer 'omics': Lessons Learned from Whole Genome and Transcriptome Sequencing of Non-Hodgkin Lymphomas

Andrew J. Mungall, Ph.D., Staff Scientist, Genome Sciences Centre

Patients with the two most common types of non-Hodgkin lymphoma (NHL): diffuse large B-cell lymphoma and follicular lymphoma show substantial differences in response to treatment and disease outcome, suggesting that molecular subtyping is an important prognostic indicator and that each subtype may benefit from a distinct treatment regimen. Using whole genome and transcriptome

sequencing of NHL tumours we have identified recurrent somatic mutations, improving our understanding of NHL pathogenesis and providing novel targets for pharmacological intervention.

2:50 Genome Redux for Hematologists: Graphical User Interfaces for Visualizing and Reducing Genome-Wide Data Sets into Clinically Actionable Information

German Pihan, M.D., Chief, Hematopathology Service, Beth Israel Deaconess Medical Center; Director, Hematopathology Fellowship Site Director, HMS Molecular Genetic Pathology Fellowship; Assistant Professor of Pathology, Harvard Medical School

3:20 PANEL DISCUSSION: Whole-genome Sequencing Applied to Clinical Diagnostics – Views from the Industry

Sponsored by GenomeQuest

Moderator: Kevin Davies, Ph.D., Author, The $1000 Genome and Editor-in-Chief, Bio-IT World

Whole-genome sequencing applied to diagnostics holds great promise for health care. Globally, the world spends about $5T on health care and about 65% of therapy decisions are based on the results of diagnostics tests. With the precipitous fall in the cost of sequencing, whole-genome sequencing may soon become practical – even common -- for reporting on patient susceptibility, diagnosis, and treatment of genetic disorders. Benefits of this advance include: higher precision, ability to detect complex/multi-gene conditions, far lower long-term costs for patient, economies of scale for instrument manufacturers, higher quality/repeatability for laboratories, and faster delivery/approval of research discoveries. Included is a demonstration of a newly released capability to analyze/report on a patient's disease susceptibility, diagnosis, and treatment on over 2000 disorders from a single whole-genome sequence.

- What are recent research and technological advances in this area?
- What are real examples of benefits to patient care?
- How will this start and expand? What timeframe?
- Will this advance cause market disruption to the health care industry and how?
- What does this mean for researchers and diagnostic companies? For regulators?

Panelists:

Jeffrey E. Saffitz, M.D., Ph.D., Mallinckrodt Professor of Pathology, Harvard Medical School; Chairman, Pathology, Beth Israel Deaconess Medical Center

Richard J Resnick, CEO, GenomeQuest, Inc.

Roberta A. Pagon, M.D., Professor, Pediatrics, University of Washington and Children's Hospital & Regional Medical Center and Editor-in-Chief, GeneReviews (invited)

3:50 Refreshment Break & Poster Awards in the Exhibit Hall

» KEYNOTE SESSION: REGULATION OF MOLECULAR DIAGNOSTIC TESTING: THREE POINTS OF VIEW

4:25 Chairperson's Remarks

Harry Glorikian, Managing Partner, Scientia Advisors

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Alberto Gutierrez, Ph.D., Deputy Director, Office of in vitro Diagnostic Device Evaluation and Safety, Food & Drug Administration

5:00 Genomic Medicine: The Pathway from Biobanks to Clinical Practice

Timothy J. O'Leary, M.D., Ph.D., President-Elect, Association for Molecular Pathology;

Deputy Chief Officer, Research & Development Office; Director, Biomedical Laboratory and Clinical Science Research & Development Service, Veterans Health Administration

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6:00 Close of Day

FRIDAY, FEBRUARY 25

GROWTH IN PERSONALIZED CANCER DIAGNOSTICS

8:30 am Chairperson's Remarks

Matthew Lorence, Ph.D., M.B.A., Vice President, Marketing and Sales, Tessarae, LLC

8:35 Gene Expression Assays and Personalized Cancer Care: Tissue of Origin Test

Federico A. Monzon, M.D., Medical Director, Molecular Diagnostics, The Methodist Hospital; Assistant Professor, Pathology, Weill Cornell Medical College

Gene expression microarray-based assays for tumor tissue of origin determination are now clinically available. This session will review the development and validation of the Pathwork Tissue of Origin Test and its use for personalized diagnostics in patients with tumors of unknown origin.

9:05 SNP Array Karyotyping for Clinical Cancer Applications

Jill Hagenkord, M.D., Director of Molecular Pathology and Clinical Genomics, Creighton Medical Laboratories; Assistant Professor of Pathology, Creighton University School of Medicine

SNP array karyotyping is a novel technique for evaluating cancer chromosomes. SNP array karyotypes offer dramatically higher resolution, do not require culture, perform well on paraffin embedded samples, and can detect clinically relevant abnormalities missed by current clinical techniques. Examples of the clinical utility and impact of SNP array karyotyping will be presented.

9:35 Monoclonal Antibody Proteomics: Discovery and Validation of New Lung Cancer Biomarkers in the Blood

Laszlo Takacs, M.D., Ph.D., Chief Scientific Officer, Biosystems International SAS

Biosystems International's mAb based proteomics technology generates large mAB libraries directed against the natural plasma proteome. Here we show the discovery of 13 mABs that specifically detect stage I non small cell lung cancer from plasma samples. An antibody panel has been validated on multiple cohorts. We will present the development of an IVD test and our initial clinical results.

10:05 Advancing Model Selection for Predictive and Prognostic Signatures

Sponsored by ALMAC

Max Bylesjo, Ph.D., Bioinformatics Team Leader, Almac Diagnostics, UK

This presentation outlines alternative methods to select predictive/prognostic gene signatures for patient risk stratification based on e.g. biological enrichment and independence to clinical covariates, exemplified by data from the MAQC-II project.

10:20 Coffee Break

» 11:00 EXPERT PANEL: Planning for a Biomarker Strategy in All Phases of Drug Development: Advantages of a Translational Approach

Moderator: Brandon W. Higgs, Ph.D., Translational Sciences, MedImmune

Discussion points:

- Biomarker identification efforts in early drug development for companion diagnostics
- The challenges in the identification of a robust surrogate endpoint
- A comparison between laboratory-developed tests (LDTs) vs. FDA approved *in vitro* diagnostic (IVDs): should these be more aligned with respect to FDA oversight?

Panelists:

Suso Platero, Ph.D., Director, Oncology Biomarkers, Centocor R&D, Inc., a Johnson & Johnson Company

Rakesh Sindhi, M.D., FACS, Co-Director, Pediatric Transplantation, University of Pittsburgh

Michael Elashoff, Ph.D., Director, Biostatistics, CardioDx

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

» 1:35 EXPERT PANEL: INTERCONNECTEDNESS IN COMPANION DIAGNOSTICS: How do Technologies, Business Models, and Regulatory Aspects Interrelate?

Moderator: Stephen Naylor, Ph.D., Chairman and CSO, Predictive Physiology and Medicine, Inc.

Discussion Points:

- Which business models work for personalized medicine?
- Considerations when choosing an assay
- Considerations when choosing a partner

Panelists

Brian T. Edmonds, Ph.D., Research Advisor, Global External Research & Development, Lilly Corporate Center

Andrea H. Lauber, Ph.D., Head, Technology Transactions for Clinical Biomarkers & Pharmacodiagnostics Strategic Transactions Group, Bristol-Myers Squibb

Rosanne Welcher, Ph.D., MBA, Vice President, R&D, and General Manager, Dako North America

Mya Thomae, RAC, CAQ, Founder and CEO, Myraqa, Inc.

AUTOMATED SYSTEMS FOR PROTEOMICS

2:30 Chairperson's Remarks

Mya Thomae, RAC, CAQ, Founder and CEO, Myraqa, Inc.

2:35 Clinical Proteomics Technology Assessment: Next Generation Instrumentation, Multiplexing, Molecular Diversity, and the FDA

Fred E. Regnier, Ph.D., J. H. Law Distinguished Professor, Analytical Chemistry, Purdue University

Cell lysates, blood, and most biological fluids have a high level of molecular complexity, ranging up to a hundred thousand components with 10-50 isoforms of each in the case of many proteins. Moreover, these isoforms often vary in their connection to disease as a result of structure alterations, post-translational modifications, and splice variations. Measuring these differences will be a critical component of clinical diagnostics in the future, the question is how.

It is widely understood that orthogonal, multi-dimensional analyses are necessary to deal with levels of complexity this high. Antibodies have the enormous advantage of producing thousands of fold purification with ten fold or more enrichment in minutes in initial sample treatment but surprisingly are not as useful in subsequent steps of analysis. Chromatography and mass spectrometry provide much higher levels of orthogonality, selectivity, speed, and multiplexing capability beyond initial immunoselection. This presentation will examine the potential of new instrumentation systems to provide five or more orthogonal dimensions of discrimination within 30-60 minutes with 10-100 analyte multiplexing at a 10 pg/mL limit of detection.

Clearly regulatory issues surrounding next generation assay technology will be very different than today. For one, it will be necessary to demonstrate that analytical methods are discriminating between isoforms of an analyte, particularly when they differ in activity. As a second, it will be necessary to show what antibodies actually capture along with the degree to which they cross-react. Third, the robustness of new instrumentation systems to provide consistent results over long periods of use must be established. Finally, the prospect of using istopically coded internal standards in quantification may increase expectations in terms of analytical accuracy.

3:05 Methods for Low Cost Proteomic Arrays

Jane P. Bearinger, Ph.D., Medical Countermeasures Group Leader, Senior Scientist, Physics, Lawrence Livermore National Laboratory

As cost is a barrier to adoption of molecular diagnostics, cost-cutting through novel engineering approaches have the potential to greatly impact the field. Surface chemistry methods that address sample, sensitivity and signal to noise constraints to facilitate array development will be presented.

3:35 Close of Conference

Cancer Molecular Markers

Critical Strategies for Personalized Treatment

WEDNESDAY, FEBRUARY 23

7:00 am Registration and Morning Coffee

8:00 Plenary Keynotes *(See Page 2 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

» KEYNOTE PRESENTATIONS: Key Pathways in Cancer

11:00 Chairperson's Opening Remarks

11:10 The Paradigm of Targeted Drugs for the Treatment of Cancer: Inhibiting the BCR-ABL Pathway in Chronic Myeloid Leukemia

Paul W. Manley, Ph.D., Executive Director, Oncology Department, Novartis Institutes for Biomedical Research

In the 10 years that imatinib has been approved for the treatment of CML, the natural history of the disease has been transformed and we have learned much about targeting the BCR-ABL oncogenic signaling pathway that has also been translatable to other malignancies.

11:40 Future of Pathway-Driven Therapies

Neil W. Gibson, Ph.D., CSO, Pfizer Oncology

12:10 pm Personalizing Cancer Care – In Search of Durable Responses

David C. Heimbrook, Ph.D., Head, Discovery, Oncology Discovery and Translational Area, Roche

The recent successes of targeted therapies highlight both the opportunities and the challenges of personalizing cancer care. The combination of diagnostic tools with targeted agents can provide dramatic patient benefits, but improving the durability of clinical responses requires juxtaposition of clinical and pre-clinical studies to address the underlying disease biology. The opportunity provided by this paradigm is exemplified by our ongoing studies with RG7204, an inhibitor of V600E-BRAF.

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

1:45 Dessert in the Exhibit Hall

SOLID TUMORS: LESSONS FOR BIOMARKER VALIDATION?

2:15 Chairperson's Remarks

Josip Blonder, M.D., SAIC-Frederick, INC, NCI-Frederick

2:20 Solid Tumor Heterogeneity: From Tissue Proteomics to Personalized Medicine

Donald J. Johann, Jr., M.D., Associate Investigator, Center for Cancer Research, National Cancer Institute, National Institutes of Health

Solid tumor heterogeneity is a perplexing scientific and clinical problem. Tissue based proteomic approaches utilizing identity-based mass spectrometry and laser capture microdissection, may serve as a platform allowing enhanced molecular profiling, and the revealing of subtle solid tumor phenotypes.

2:50 Proteomic Profiling of Clinical Specimens in the Context of Cancer Biomarker Discovery and Validation

Josip Blonder, M.D., Senior Research Scientist, Head, Clinical Proteomics, Laboratory of Proteomics and Analytical Technologies, SAIC-Frederick, Inc., NCI-Frederick

This presentation will highlight a variety of technological approaches utilized in clinical proteomics of renal cell carcinoma (RCC) and summarize respective biological findings in the context of RCC biomarker discovery and validation.

3:20 Clinical Application of Tumor Genotyping to Drive Clinical Trials and Translational Research

Leif Ellisen, M.D., Ph.D., Co-Executive Director, MGH Cancer Center, Translational Research Laboratory; Associate Professor, Medicine, Harvard Medical School

Analysis of tumor somatic genetic abnormalities has provided key insights into cancer pathogenesis, signaling, and oncogene dependence. We describe the development and validation of a prospective (pre-treatment), broad-based solid tumor mutation detection platform and its application for clinical decision making, clinical trial enrollment and translational research.

3:50 Sponsored Panel Discussion *Sponsored by* IPM
Overcoming the Challenges and Issues with FDA Approved IVD Tests

Moderator: Mally Arad, Manager, Integrated Project Management Company, Inc. (IPM)

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

5:20 - 6:20 Breakout Discussions in the Exhibit Hall

THURSDAY, FEBRUARY 24

USING microRNA SIGNATURES FOR DIAGNOSTICS AND PROGNOSTICS

8:25 am Co-Chairperson's Remarks

Dalia Cohen, Ph.D., Chief Scientific Officer, Asterand and Bernard Andruss, Ph.D., Director, Collaborations & Business Development, Asuragen, Inc.

8:30 microRNAs: Novel Biomarkers and Targets for Cancer Therapy

Glen Weiss, M.D., Director, Thoracic Oncology VGPCC, Scottsdale Healthcare; Co-Head, Lung Cancer Unit, TGen, Oncology, Scottsdale Healthcare and TGen

Recent studies have uncovered broad implications of microRNAs, demonstrating that a single microRNA can impact hundreds of targets and can affect pathways controllingoncogenic processes. Data will be presented illustrating how using microRNA can impact cancer treatment decision making, validated microRNAs associated with resistance and/or sensitivity to chemotherapy and targeted therapy, and how microRNAs could be used as therapeutics.

9:00 microRNA Gene Regulatory Networks in Sarcomas

Subbaya Subramanian, Ph.D., Assistant Professor, Surgery, University of Minnesota

Deregulation of miRNA mediated gene regulatory networks may play a central role in the pathogenesis of tumors. A systematic analysis of miRNA, mRNA and DNA copy number aberrations can provide insights into the deregulation of fundamental gene regulatory networks involving miRNAs. This talk will cover diverse aspects of miRNA networks in childhood cancers such as osteosarcoma and other cancer types.

9:30 Secretory microRNAs in Cancer Development and Diagnosis

Takahiro Ochiya, Ph.D., Head, Section for Studies on Metastasis, National Cancer Center Research Institute, Tokyo

The physiological role of microRNAs (miRNAs) is widely appreciated as a fine-tuner of multiple genes in the cells of origin. Currently, miRNAs have received greater attention in cancer research. Aberrant miRNA expression is correlated with development and progression of cancer. Furthermore, cellular microRNAs as well as extracellular miRNAs could be used for cancer biomarkers for diagnosis and prognosis.

10:00 Signature Validation and Analysis of Fusion Gene Variants with the nCounter Analysis System *Sponsored by* nanoString TECHNOLOGIES

Sean Ferree, NanoString Technologies

The nCounter Analysis System is a fully-automated, digital, mid-plex genomic analysis platform that is ideal for a broad range of cancer research applications. We will present an overview of the system and data demonstrating the system's utility in expression profile signature validation, analysis of fusion genes, and analysis FFPE samples (with and without RNA purification).

10:30 Refreshment Break in the Exhibit Hall

» 11:30 KEYNOTE PRESENTATION

Novel Technology Approaches to Circulating Tumor Cell Capture, Detection and Characterization

Richard Cote, M.D., FRCPath, Professor and Chair, Pathology; Director, University of Miami Biomedical Nanoscience Institute, University of Miami Miller School of Medicine

Detecting and characterizing circulating tumor cells (CTC) can allow an effective cancer patient management. The available approaches for CTC detection are curtailed by difficulties with sensitivity, specificity, efficiency, and high costs. Further, most of these technologies have only a limited ability to perform downstream molecular characterization of CTC. The presentation will describe our development of a parylene-based precision-engineered microfilter to capture CTC in blood, its functional comparison with the current FDA-approved platform, and our data with various cellular and molecular studies of CTC.

NOVEL TECHNOLOGIES FOR THE ISOLATION, DETECTION AND CHARACTERIZATION OF CTC

Chairperson: Stefanie Jeffrey, M.D., Stanford University

12:00 pm Multiplex Analysis of CTC

Stefanie Jeffrey, M.D., Chief, Surgical Oncology Research, Stanford University

12:30 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:45 Ice Cream Refreshment Break in the Exhibit Hall

2:20 Identification and Characterization of Circulating Tumor Cells with the CellSearch System

Leon W.M.M. Terstappen, M.D., Ph.D., Chair, Medical Cell BioPhysics, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente

In this presentation the choices made during the development of the CellSearch system will be reviewed as well as the results of the validation studies and the three separate prospective multi-center registration studies involving patients with metastatic breast, colorectal and prostate cancer.

2:50 Cell Magnetophoresis and Separation in Applications to CTC Isolation

Maciej Zborowski, Ph.D., Staff, Department of Biomedical Engineering, Associate Professor of Molecular Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University

We quantitatively measure cell magnetophoretic mobility as a guiding parameter for the design of magnetic flow sorters and determination of cell magnetic susceptibility changes due to iron uptake. These approaches are applied to CTC separation from blood samples from cancer patients, including patients with head and neck squamous cell carcinoma and metastatic breast cancer.

3:20 Clinical Microfluidics and Molecular Analysis of CTCs

Shannon Stott, Ph.D., Research Associate, BioMEMS Resource Center / MGH Cancer Center, Massachusetts General Hospital, Harvard Medical School

Viable tumor-derived circulating tumor cells (CTCs) have been identified in peripheral blood from cancer patients and are the origin of intractable metastatic disease. We have developed a microchip based on a high-throughput microfluidic mixing approach for the isolation of extremely rare CTCs in blood and showed clinical utility in cancer patients.

3:50 Refreshment Break & Poster Awards in the Exhibit Hall

CTCs IN THE CLINIC

4:25 Chairperson's Remarks

Shivaani Kummar, M.D., Head, Early Clinical Trials Development, Office of the Director, Division of Cancer Treatment and Diagnosis, National Cancer Institute

4:30 Role of Circulating Tumor Cells in Clinical Development of Novel Cancer Therapeutics

Shivaani Kummar, M.D., Head, Early Clinical Trials Development, Office of the Director, Division of Cancer Treatment and Diagnosis, National Cancer Institute

5:00 Circulating Tumor Cells in Drug Development: From Enumeration to Characterization

Marielena Mata, Ph.D., Principal Research Scientist, Oncology Biomarkers, Ortho Biotech Oncology R&D

5:30 Application of Circulating Tumor Cells in Early Stage Clinical Trials

Robert J. Kinders, Ph.D., Head, Pharmacodynamic Assay Development Section, Laboratory of Human Toxicology and Pharmacology, Applied/Developmental Research Directorate, SAIC-Frederick, Inc., NCI-Frederick

Work in our laboratory centers on evaluating the potential of CTCs to replace biopsies in certain clinical trials. Our ultimate goal is to generate a PD response curve analogous to a PK curve, measuring effect over time and relative to dose on the specific molecular target of the new agent under investigation.

6:00 Implementing Quantitative CTC Counts in the Management of Metastatic Breast Cancer: From Observational to Current Interventional Studies

Francois-Clement Bidard, M.D., Ph.D., Assistant Professor, Medical Oncology, Institut Curie, Paris, France

The recently reported Institut Curie (IC) 2006-04 study included 267 first-line metastatic breast cancer patients and confirmed several, but not all, results reported previously in smaller observational studies. Quantitative CTC counts must further demonstrate a clinical and/or a medico-economic improvement to be implemented in the everyday clinical management. The currently ongoing SWOG0500 (USA) and CirCe01 (France) randomized interventional trials have been specifically designed to demonstrate the usefulness of quantitative CTC counts.

6:15 Clinical Importance of the PCR-based Detection of CTCs in Prostate Cancer

Athanasios Armakola, Ph.D., Experimental Physiology Laboratory, University of Athens Medical School, Greece

6:30 Panel Discussion: Evaluating New Technologies for CTC Diagnostic Purposes in the Clinic

Moderator: Shivaani Kummar, M.D., Head, Early Clinical Trials Development, Office of the Director, Division of Cancer Treatment and Diagnosis, National Cancer Institute

7:00 Close of Day

FRIDAY, FEBRUARY 25

GROWTH IN PERSONALIZED CANCER DIAGNOSTICS

8:30 am Chairperson's Remarks

Matthew Lorence, Ph.D., M.B.A., Vice President, Marketing and Sales, Tessarae, LLC

8:35 Gene Expression Assays Personalized Cancer Care: Tissue of Origin Test

Federico A. Monzon, M.D., Medical Director, Molecular Diagnostics, The Methodist Hospital; Assistant Professor, Pathology, Weill Cornell Medical College

Gene expression microarray-based assays for tumor tissue of origin determination are now clinically available. This session will review the development and validation of the Pathwork Tissue of Origin Test and its use for personalized diagnostics in patients with tumors of unknown origin.

9:05 SNP Array Karyotyping for Clinical Cancer Applications

Jill Hagenkord, M.D., Director of Molecular Pathology and Clinical Genomics, Creighton Medical Laboratories; Assistant Professor of Pathology, Creighton University School of Medicine

SNP array karyotyping is a novel technique for evaluating cancer chromosomes. SNP array karyotypes offer dramatically higher resolution, do not require culture, perform well on paraffin embedded samples, and can detect clinically relevant abnormalities missed by current clinical techniques. Examples of the clinical utility and impact of SNP array karyotyping will be presented.

9:35 Monoclonal Antibody Proteomics: Discovery and Validation of New Lung Cancer Biomarkers in the Blood

Laszlo Takacs, M.D., Ph.D., CSO, Biosystems International SAS

Biosystems International's mAb based proteomics technology generates large mAB libraries directed against the natural plasma proteome. Here we show the discovery of 13 mABs that specifically detect stage I non small cell lung cancer from plasma samples. An antibody panel has been validated on multiple cohorts. We will present the development of an IVD test and our initial clinical results.

10:05 Sponsored Presentation *(Opportunity Available)*

10:20 Coffee Break

HOT PATHWAYS IN CANCER STEM CELLS: ULTRA-MALIGNANT CELLS

10:55 Chairperson's Remarks

Enal Razvi, Ph.D., Systems Biosciences SBI

11:00 Targeting Cancer Stem Cell Self Renewal

Austin Gurney, Ph.D., Senior Vice President, Molecular and Cellular Biology, OncoMed Pharmaceuticals

Stem cell pathways such as Notch and Wnt have long been implicated in cancer. A new generation of therapeutics designed to modulate these pathways demonstrates remarkable ability to reduce the tumorigenicity of a broad range of tumor types by forcing cancer stem cell differentiation.

11:30 Regulation of Self-Renewal in Cancer Stem Cells

Pier Giuseppe Pelicci, M.D., Ph.D., Chairman, Department of Experimental Oncology, European Institute of Oncology, Milan, Italy

Our findings suggest that asymmetric divisions of stem cells function as a mechanism of tumor suppression, that CSC quiescence is critical to the maintenance of the transformed clone and that symmetric divisions of CSCs permits its geometric expansion. I will discuss the implications of these findings for the mechanisms regulating checkpoint activation in normal tissue SCs and DNA damage response.

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

1:35 Non-Hierarchical Heterogeneity in Melanoma

Elsa Quintana, Ph.D., Postdoctoral Fellow, Life Sciences Institute, Department of Internal Medicine and Center for Stem Cell Biology, University of Michigan

In cancers that follow a stem cell model, phenotypically distinct tumorigenic cells give rise to diverse non-tumorigenic progeny in a hierarchical process similar to differentiation. In contrast to this model our results indicate that melanoma has many phenotypically diverse tumorigenic cells that undergo reversible changes in phenotype over time.

2:05 VEGF-Dependent and –Independent Angiogenesis Pathways

Napoleone Ferrara, Ph.D., Fellow, Tumor Biology & Angiogenesis, Genentech, Inc.

2:35 Identifying Novel microRNA-Gene Networks in Colon Cancer Stem Cells

Dimitrios Iliopoulos, Ph.D., Assistant Professor, Cancer Immunology & AIDS, Dana-Farber Cancer Institute/Harvard Medical School

We have identified the gene networks involved in colon cancer stem cell formation and maintenance and novel drugs that target these networks and inhibit colon cancer tumor growth and prolong remission *in vivo*.

3:05 Panel Discussion: Emerging Themes in Cancer Stem Cells (CSCs)

In this panel, we will explore the nature of cancer stem cells, and seek to understand their biology. There is much uncertainty as to the identity of CSCs *in vivo* and their roles in the primary tumor versus in metastases. This panel discussion will complement the presentations in this session to provide the delegates a balanced perspective on the current state of this field and outlook for the future, especially as it relates to cancer therapeutics.

Major Topics to be Discussed at the Panel Discussion:

- Evidence for the Existence of CSCs in Various Cancers
- Molecular Identity of CSCs
- Targeting CSCs as Therapeutic Modalities

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

Additional Panelist: Gang Li, Ph.D., Senior Stem Cell Research Scientist, System Biosciences SBI

3:35 Close of Conference

Inaugural

Circulating Tumor Cells

For Cancer Detection, Diagnosis, Prognosis, and Treatment

WEDNESDAY, FEBRUARY 23

7:00 am Registration and Morning Coffee

8:00 Plenary Keynotes *(See Page 2 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

BIOLOGY AND MOLECULAR CHARACTERIZATION OF CTC

11:00 Chairperson's Opening Remarks

Leon W.M.M. Terstappen, M.D., Ph.D., Chair, Medical Cell BioPhysics, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente

» KEYNOTE PRESENTATION

11:10 Biology and Clinical Relevance of Circulating Tumor Cells (CTC)

Klaus Pantel, M.D, Ph.D., Director, Institute of Tumor Biology, UKE, Hamburg, Germany

Detection and molecular characterization of circulating tumor cells (CTC) in the peripheral blood provide new insights into the complex biology of metastasis in cancer patients. This information can be used for (a) estimation of the risk for metastatic relapse or metastatic progression (prognostic information), (b) stratification and real-time monitoring of systemic therapies, and (c) identification of therapeutic taargets and resistance mechanisms.

11:40 High Yield Isolation of Circulating Tumor Cells (CTC) and Protocols for Molecular Diagnosis

Marek Malecki, M.D., Ph.D., Associate Professor, Genetics, Genomics, and Gene Therapy; Director, Biotechnology Program, Western University of Health Sciences

For evaluation of cancer progression, remission, or relapse, molecular imaging and serum analysis are the main clinical pursuits. However, they are often insufficient. Diagnostic analysis of circulating tumor cells (CTC) may provide important insights into the ever changing immunological and genomic profiles of metastasizing cancer cells. To address this problem, we have developed a nanotechnology, based upon genetically engineered single chain variable fragments, to attain the high yield purification of CTC from the cancer patients' blood and refined protocols for the characterization of their genomic and proteomic profiles.

12:10 pm Epithelial-to-Mesenchymal Transitions and Circulating Tumor Cells

Christine Gilles, Ph.D., Laboratory of Tumor and Developmental Biology, Liège University

Epithelial-to-mesenchymal (EMT) processes endow epithelial tumor cells with enhanced migratory/invasive properties and are therefore likely to contribute to the generation of circulating tumor cells (CTCs). We will review data validating the implication of EMT processes in CTC formation and will present animal models with transplantable human breast tumor cells to help characterizing EMT/CTC relationships.

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

1:45 Dessert in the Exhibit Hall

2:20 Morphologic and Morphometric Characterization of Circulating Tumor Cells in Carcinoma Patients

Peter Kuhn, Ph.D., Scripps Physics Oncology Center, The Scripps Research Institute

We use the HD-CTC assay technique and report on the use of this methodology to characterize the incidence of HD-CTCs in peripheral blood samples from a small cohort of metastatic cancer patients, including those with prostate cancer, breast cancer, pancreatic cancer, along with set of normal controls.

ISOLATION AND CHARACTERIZATION OF CTCS FROM PATIENTS WITH LOCALIZED AND METASTATIC CANCER

2:45 Chairperson's Remarks

Leon W.M.M. Terstappen, M.D., Ph.D., Chair, Medical Cell BioPhysics, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente

2:50 Circulating Tumor Cells in Patients Undergoing Surgery for Hepatic Metastases from Colorectal Cancer

Pavlos Papavasiliou, M.D., Surgical Oncology Fellow, Department of Surgical Oncology, Fox Chase Cancer Center

Circulating tumor cells (CTCs) are detectable using a commercially available assay in patients with hepatic metastases from colorectal cancer. CTC levels vary during the course of a patient's treatment and these quantities may correlate with prognosis.

3:20 Circulating Tumor Cells as a Means to Identify Curable Patients with Metastatic Cancer

Daniel Boffa, M.D., Assistant Professor, Yale University School of Medicine, Section of Thoracic Surgery

Subsets of patients with metastastatic cancer may be cured with aggressive therapy. Circulating tumors may identify patients most likely to be cured, as well as patients with a propensity for systemic failure. This information may be used to match patients with the most appropriate treatment strategy including combinations of local and systemic therapy.

3:50 Recent Advances in the Field of Molecular Characterization of CTCs

Siegfried Hauch, Chief Scientific Officer, AdnaGen

Sponsored by Alere

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

5:20 - 6:20 Breakout Discussions in the Exhibit Hall

Techniques for Characterization of CTCs

Moderator: Richard Cote, M.D., FRCPath, Professor and Chair, Pathology; Directory , University of Miami Biomedical Nanoscience Institute, University of Miami Miller School of Medicine

- What are the current challenges and opportunities in techniques for characterizing CTC?
- What are the critical characteristics needed for characterizing circulating tumor cells?
- How should CTC characterization be included in designing clinical trials?

Molecular Profiling of CTCs

Moderator: Dave S. B. Hoon, Ph.D., Director, Molecular Oncology, John Wayne Cancer Institute

- CTC Isolation approaches for quality and consistent detailed analysis of molecular phenotypes
- How representative are the CTCs to patients' tumor burden?
- How relevant are the CTC profile to patient disease outcome and clinical stage?
- Techniques useful for amplying DNA/RNA for small number of CTC.
- When is the most relevant period during patient treatment should we profile CTCs?

Techniques for Characterization of CTCs

Moderator: Klaus Pantel, M.D., Ph.D., Director, Institute of Tumor Biology, UKE, Hamburg, Germany

- Proteins (Multiple immunostainings, EpiSpot)
- RNA (RT-PCR, expression profiling)
- DNA (FISH, PCR, whole genome amplification, array-CGH)

Microfluidics for Selection and Enumeration of CTCs

Moderator: Steven Soper, Ph.D., Chemistry and Mechanical Engineering, Center for BioModular Multi-Scale Systems, Louisiana State University

- Are the enumeration numbers from the Veridex CellSearch System actually the "TRUE" numbers of CTC frequencies found in peripheral blood of cancer patients?

5:20 - 6:20 Breakout Discussions in the Exhibit Hall (continued)

- What is the GOLD STANDARD; while the FDA has approved the Veridex System, does this really supply the actual numbers of CTCs found in patients?
- Is seeding cell lines into "normal" blood viewed as a good standard for evaluating the development/performance of new technologies?
- Is there a need to interrogate larger input volumes, especially if the Veridex System significantly underestimates the "TRUE" number of CTCs in a patient?
- If no GOLD standards exists for CTC enumeration, how are new technologies going to make it through the FDA approval process?
- If the actual CTC numbers are higher than those set by the Veridex system, then is it reasonable to consider using CTCs as a diagnostic marker as well?
- Morphological investigation of the CTCs may be important as well as looking for expression levels of certain markers to distinguish them from interfering cells (normal epithelial cells or WBCs). How can this be done without requiring sophisticated imaging equipment needed for imaging the entire selection bed?
- What about the ability to culture the recovered CTCs for doing follow-up discovery-based investigations (do the cells remain viable following microfluidic selection)?

- Costs of CTC recovery and enumeration per assay; what can/should microfluidics do to address this issue?
  - If the microfluidic is to be used for large-scale screening or monitoring for disease recurrence, the cost of the chip must be reduced to make this feasible. What is a viable cost per assay and what about the supporting peripherals to expand the utility of using this biomarker in the clinic?
  - For diagnostics and prognostics, one-time use devices are critical; should this guide the engineering of the microfluidic system?
  - What are important metrics for guiding the development and marketing new technologies; recovery (in a variety of different scenarios), simplicity of use, cost, or functionality (do more than just enumerate the CTCs)?
- What about the recovery and enumeration of cancer stem cells?
  - Markers (positive selection), size selection, abundance, etc?
  - Utility of collecting cancer stem cells.
- Transitioning these new microfluidic technologies (for rare cell selection) into other target areas.
  - Fetal nucleated red blood cells for molecular profiling unborn fetuses.
  - Bacterial infections.

6:20 Close of Day

THURSDAY, FEBRUARY 24

NOVEL TECHNOLOGIES FOR THE ISOLATION, DETECTION AND CHARACTERIZATION OF CTCS

8:25 am Chairperson's Remarks

Stefanie Jeffrey, M.D., Chief, Surgical Oncology Research, Stanford University

8:30 Location and Phenotypic Characterization of Circulating Tumor Cells for Therapy Selection

Richard Bruce, Ph.D, Manager, Biomedical Engineering, Palo Alto Research Center

Metastatic breast cancer can be optimally treated with targeted therapy selected by the presence of specific phenotypes on tumor tissue. Here a method to locate circulating tumor cells that does not require enrichment is used to locate circulating tumor cells and multiplex assays are used to assess the expression of three biomarkers that are predictive of therapeutic efficacy.

9:00 Polymer-Based Microfluidics for the Efficient Selection and Enumeration of Circulating Tumor Cells (CTCs) and Their Subsequent Molecular Profiling

Steve Soper, Ph.D., Department of Chemistry; Department of Mechanical Engineering; Center for BioModular Multi-Scale Systems; Louisiana State University

The enumeration of CTCs can only provide a limited amount of clinical data; genotyping the CTCs can also help guide therapeutic treatment for a variety of cancers, such as colorectal cancer (CRC). In this presentation, a polymer-based modular microfluidic system will be discussed for securing genotype information from genomic DNA harvested from CTCs launched into peripheral blood.

9:30 Geometrically Enhanced Differential Immunocapture (GEDI) CTCs in Castrate-Resistant Prostate Cancer Patients

Brian J. Kirby, Ph.D., Assistant Professor, Mechanical and Aerospace Engineering, Cornell University

We have developed a design methodology to create high-performance microdevices for circulating tumor cell capture. We present results for CTC capture, analysis, and evaluation of drug-target interaction in castrate-resistant prostate cancer patients.

Sponsored by VERIDEX

10:00 The Present Challenges of Our Future Needs

Mark C. Connelly, Ph.D., Director of Cellular Research and Site Director, Veridex, LLC

10:30 Refreshment Break in the Exhibit Hall

Chairperson: Stefanie Jeffrey, M.D., Stanford University

» 11:30 KEYNOTE PRESENTATION

Novel Technology Approaches to Circulating Tumor Cell Capture, Detection and Characterization

Richard Cote, M.D., FRCPath, Professor and Chair, Pathology; Director, University of Miami Biomedical Nanoscience Institute, University of Miami Miller School of Medicine

Detecting and characterizing circulating tumor cells (CTC) can allow an effective cancer patient management. The available approaches for CTC detection are curtailed by difficulties with sensitivity, specificity, efficiency, and high costs. Further, most of these technologies have only a limited ability to perform downstream molecular characterization of CTC. The presentation will describe our development of a parylene-based precision-engineered microfilter to capture CTC in blood, its functional comparison with the current FDA-approved platform, and our data with various cellular and molecular studies of CTC.

NOVEL TECHNOLOGIES FOR THE ISOLATION, DETECTION AND CHARACTERIZATION OF CTC

Chairperson: Stefanie Jeffrey, M.D., Stanford University

12:00 pm Multiplex Analysis of CTC

Stefanie Jeffrey, M.D., Chief, Surgical Oncology Research, Stanford University

12:30 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:45 Ice Cream Refreshment Break in the Exhibit Hall

2:20 Identification and Characterization of Circulating Tumor Cells with the CellSearch System

Leon W.M.M. Terstappen, M.D., Ph.D., Chair, Medical Cell BioPhysics, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente

In this presentation the choices made during the development of the CellSearch system will be reviewed as well as the results of the validation studies and the three separate prospective multi-center registration studies involving patients with metastatic breast, colorectal and prostate cancer.

2:50 Cell Magnetophoresis and Separation in Applications to CTC Isolation

Maciej Zborowski, Ph.D., Staff, Department of Biomedical Engineering, Associate Professor of Molecular Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University

We quantitatively measure cell magnetophoretic mobility as a guiding parameter for the design of magnetic flow sorters and determination of cell magnetic susceptibility changes due to iron uptake. These approaches are applied to CTC separation from blood samples from cancer patients, including patients with head and neck squamous cell carcinoma and metastatic breast cancer.

3:20 Clinical Microfluidics and Molecular Analysis of CTCs

Shannon Stott, Ph.D., Research Associate, BioMEMS Resource Center / MGH Cancer Center, Massachusetts General Hospital, Harvard Medical School

Viable tumor-derived circulating tumor cells (CTCs) have been identified in peripheral blood from cancer patients and are the origin of intractable metastatic disease. We have developed a microchip based on a high-throughput microfluidic mixing approach for the isolation of extremely rare CTCs in blood and showed clinical utility in cancer patients.

3:50 Refreshment Break & Poster Awards in the Exhibit Hall

CTCS IN THE CLINIC

4:25 Chairperson's Remarks

Shivaani Kummar, M.D., Head, Early Clinical Trials Development, Office of the Director, Division of Cancer Treatment and Diagnosis, National Cancer Institute

4:30 Role of Circulating Tumor Cells in Clinical Development of Novel Cancer Therapeutics

Shivaani Kummar, M.D., Head, Early Clinical Trials Development, Office of the Director, Division of Cancer Treatment and Diagnosis, National Cancer Institute

5:00 Circulating Tumor Cells in Drug Development: From Enumeration to Characterization

Marielena Mata, Ph.D., Principal Research Scientist, Oncology Biomarkers, Ortho Biotech Oncology R&D

5:30 Application of Circulating Tumor Cells in Early Stage Clinical Trials

Robert J. Kinders, Ph.D., Head, Pharmacodynamic Assay Development Section, Laboratory of Human Toxicology and Pharmacology, Applied/Developmental Research Directorate, SAIC-Frederick, Inc., NCI-Frederick

Work in our laboratory centers on evaluating the potential of CTCs to replace biopsies in certain clinical trials. Our ultimate goal is to generate a PD response curve analogous to a PK curve, measuring effect over time and relative to dose on the specific molecular target of the new agent under investigation.

6:00 Implementing Quantitative CTC Counts in the Management of Metastatic Breast Cancer: From Observational to Current Interventional Studies

Francois-Clement Bidard, M.D., Ph.D., Assistant Professor, Medical Oncology, Institut Curie, Paris, France

The recently reported Institut Curie (IC) 2006-04 study included 267 first-line metastatic breast cancer patients and confirmed several, but not all, results reported previously in smaller observational studies. Quantitative CTC counts must further demonstrate a clinical and/or a medico-economic improvement to be implemented in the everyday clinical management. The currently ongoing SWOG0500 (USA) and CirCe01 (France) randomized interventional trials have been specifically designed to demonstrate the usefulness of quantitative CTC counts.

6:15 Clinical Importance of the PCR-based Detection of CTCs in Prostate Cancer

Athanasios Armakola, Ph.D., Experimental Physiology Laboratory, University of Athens Medical School, Greece

6:30 Panel Discussion: Evaluating New Technologies for CTC Diagnostic Purposes in the Clinic

Moderator: Shivaani Kummar, M.D., Head, Early Clinical Trials Development, Office of the Director, Division of Cancer Treatment and Diagnosis, National Cancer Institute

7:00 Close of Day

FRIDAY, FEBRUARY 25

FDA REGULATORY ASPECTS OF CTCS: DEVELOPING CLINICAL DIAGNOSTICS

8:30 am Chairperson's Remarks

Avraham Rasooly, Ph.D., Program Director, Cancer Diagnosis Program, NCI

8:35 Regulation of Novel in vitro Diagnostic Devices

Alberto Gutierrez, Ph.D., Deputy Director, New Product Evaluation, Office of in vitro Diagnostic Device Evaluation and Safety, Food and Drug Administration

FUNDING OPPORTUNITIES FOR RESEARCH

9:35 Technology Funding Opportunities at the NationalCancer Institute

Avraham Rasooly, Ph.D., Program Director, Cancer Diagnosis Program, NCI

10:05 Sponsored Presentation (Opportunity Available)

10:20 Coffee Break

CLINICAL IMPLICATIONS OF CTC ANALYSES

10:55 Chairperson's Remarks

Klaus Pantel, M.D, Ph.D., Director, Institute of Tumor Biology, UKE, Hamburg, Germany

» 11:00 KEYNOTE PRESENTATION

Circulating Tumor Cells as Biomarkers: Efficacy-Response and A "Liquid Biopsy" to Predict Drug Sensitivity

Howard Scher, M.D., Chief, Genitourinary Oncology Service, Memorial Sloan-Kettering Cancer Center

Clinically qualified efficacy response (surrogate) biomarkers of survival and predictive biomarkers of drug sensitivity to guide treatment selection are critical unmet needs in prostate cancer drug development and patient management. CTCs have the potential to fulfill these unmet needs. A program to qualify CTC number as a component of an efficacy response biomarker with FDA is ongoing. Separately we are developing assays to profile CTC at the protein, mRNA, and DNA level as predictive markers of sensitivity to androgen receptor signaling inhibitors.

11:30 Circulating Tumor Cells Prognostic Utility Validated in a Prospective International Randomized Clinical Trial

Dave S.B. Hoon, Ph.D., Director, Molecular Oncology, John Wayne Cancer Institute

Our group has developed a multiple mRNA(MM) biomarker RT-qPCR assay to directly assess peripheral blood cells (PBC) in melanoma patients with AJCC stage III and IV disease. We have assessed the MM biomarker platform in several phase II clinical trials. The optimal platform assay was used prospectively to assess the prognostic utility of CTC before and during melanoma active-specific therapy in two phase III international multicenter randomized clinical trials. The analysis demonstrates that CTC can be used as an independent prognostic factor for disease-free survival and overall survival outcomes in both stages of disease. In recent analysis of isolated melanoma CTC we have demonstrated that patients with poor outcome have specific genomic aberrations.

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

1:35 Tailoring Therapy in Breast Cancer Based on Gene Expression Subtypes

Philip Bernard, M.D., Assistant Professor, Pathology, University of Utah, School of Medicine

This talk will discuss the discovery and clinical use of the PAM50 gene set for diagnosing the biologic subtypes of breast cancer commonly referred to as Luminal A, Luminal B, HER2-enriched, and Basal-like. The sensitivities of the different subtypes to standard therapies and investigational drugs will be discussed.

2:05 CTC as a Predictor of Treatment Efficacy in Metastatic Breast Cancer

Minetta C. Liu, M.D., Associate Professor, Medical and Oncology, Georgetown University

2:35 The Role of CTCs in the Adjuvant Treatment of Breast Cancer

Wolfgang Janni, M.D., Ph.D., Professor, Gynecological Clinic, Klinikum der Heinrich-Heine-Universität Düsseldorf

Several trials currently analyze the prognostic relevance of circulating tumor cells (CTC) in peripheral blood in the adjuvant setting. In Germany, CTCs in peripheral blood of breast cancer patients at primary diagnosis and during adjuvant chemotherapy within the SUCCESS-Trial (n=3658 pts) are currently analyzed.

3:05 Molecular Biomarker Analyses Using Circulating Tumor Cells

Elizabeth Punnoose, Ph.D., Scientist, Development Oncology Diagnostics, Genentech

We investigate the technical feasibility of isolating CTCs on different platforms, including CellSearch® and two commercially available CTC-chip platforms, and used the captured CTCs for various downstream molecular analyses used in biomarker assessment. We demonstrate that captured CTCs are amenable to biomarker analyses including HER2 status, qRT-PCR for breast cancer subtype markers, KRAS mutation detection, and EGFR staining by IF.

3:35 Close of Conference

Eighth Annual

Mastering Medicinal Chemistry Summit

Senior Chemists Share Successful Case Studies

WEDNESDAY, FEBRUARY 23

7:00 am Registration and Morning Coffee

8:00 Plenary Keynotes *(See Page 2 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

» KEYNOTE SESSION—Medicinal Chemistry Strategy, Technology and Innovation

11:00 Chairperson's Opening Remarks

Renato Skerlj, Ph.D., Vice President, Medicinal Chemistry, Genzyme Corporation, Drug and Biomaterial R&D

11:10 The Use of Enabling Chemistry Technology to Expedite the Drug Discovery Process

Stevan W. Djuric, Ph.D., Senior Director, Global Pharmaceutical Research & Development, Advanced Technology, Medicinal Chemistry Technologies and Structural Chemistry, Abbott

Gains in efficiency and cycle time with subsequent reduction in overall cost of discovery can be achieved through the judicious use of contemporary enabling chemistry technologies. This talk will highlight developments in compound design and synthesis and new target identification using chemical proteomic approaches.

11:40 Discovery of Sphingosine-1 Phosphate Receptor Modulators: A Case Study in Reverse Pharmacology

Nigel Cooke, Ph.D., Executive Director, Global Discovery Chemistry, Autoimmune, Transplantation and Inflammation, Novartis Institutes for BioMedical Research

Fingolimod (FTY720) is a first in class sphingosine-1 phosphate receptor (S1PR) modulator for the treatment of multiple sclerosis that has demonstrated efficacy and safety in clinical trials. The mechanism of action of S1PR modulators with respect to immune modulation and heart rate regulation will be discussed in the context of designing potential second generation S1PR modulators.

12:10 pm Discovery of Improved Tyrosine Kinase Inhibitors for the Treatment of Chronic Myeloid Leukemia: Nilotinib and Beyond

Paul W. Manley, Ph.D., Executive Director, Oncology Department, Novartis Institutes for BioMedical Research

The introduction of imatinib as a drug targeted towards the BCR-ABL oncoprotein was a great step forward in the treatment of CML, although those patients who develop imatinib-resistance and progress into advanced stage disease still have a poor prognosis. Nilotinib was designed to be a more potent and selective drug that could combat imatinib-resistance in CML.

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

1:45 Dessert in the Exhibit Hall

HOT TOPICS IN MEDICINAL CHEMISTRY

Fragment-Based Discovery and Biophysical Techniques

2:15 Chairperson's Remarks

2:20 Fragment-Based Drug Design

Dean R. Artis, Ph.D., Senior Vice President, Global Research, Elan Pharmaceuticals

2:50 Biophysical Techniques in Medicinal Chemistry Design

Maria M. Flocco, Ph.D., Senior Director & Head, Lead Discovery and Structural Biology & Biophysics, Pfizer Global R&D

Biophysical techniques can provide unique insights into the interactions between small molecules and their biological targets, and have the potential to significantly influence series selection and medicinal chemistry design. Examples of the use of kinetic, thermodynamic, and modality of binding information will be described to illustrate how these data can influence a project's medicinal chemistry strategy.

3:20 nEVOlution: An Integrated Approach to Fragment Screening through a Powerful Combination of Bioassay and Biophysical Technologies

Sponsored by evotec

Steve Courtney, Ph.D., Senior Vice President, Drug Discovery, Evotec (UK) Ltd.

3:50 The Role of Binding Site Water in Determining Affinity, Selectivity, and Kinetics

Sponsored by SCHRÖDINGER.

Chris Higgs, Ph.D., Senior Principal Scientist, Schrodinger

Prediction of relative binding free energies for congeneric molecules remains a computational challenge. There are a number of methods that attempt to predict relative affinities, but these methods lack robustness when applied across different targets. A key feature missing from most methods is the accurate treatment of explicit water molecules in the binding site. To address this, we developed WaterMap, which calculates the locations and displacement free energies of hydration sites. Here, we applied WaterMap to a number of pharmaceutically relevant targets and show that we can accurately explain unintuitive SAR and selectivity profiles.

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

5:20 Breakout Discussions in the Exhibit Hall

Allosteric Modulators and Inhibitors

Moderator: Jeff Reagan, Ph.D., Scientific Director, Department of Metabolic Disorders, Amgen

- HTS methods for allosteric modulators
- Comparison of operation vs mechanistic models
- Allosteric modulation of the beta arrestin pathway
- What parameters can we provide chemists to aid in driving SAR for allosteric modulators

Protein-Protein Interactions

Moderator: Jutta Wanner, Ph.D., Principal Research Scientist, Discovery Chemistry, Roche

- Druggability assessment
- Screening
- Libraries
- Peptidomimetics

Dealing with DMPK

Moderator: Rob Young, Ph.D., CSC, Medicinal Chemistry, GlaxoSmithKline

- Has the industry "cracked" DMPK?
- Have advances in formulation/delivery contributed to the increase in toxicity-related attrition?
- Is the industry too hung up on UID dosing?

6:20 Close of Day

THURSDAY, FEBRUARY 24

Fragment-Based Discovery and Biophysical Techniques (contd)

8:25 Chairperson's Remarks

8:30 Thermodynamics-Based Drug Design: Optimization of Competitive and Allosteric Inhibitors

Ernesto Freire, Ph.D., Professor, Biology, Biophysics & Biophysical Chemistry, John Hopkins University

Traditional drug targets have usually been inhibited in a competitive fashion by small molecular weight compounds. The preferred strategy for targets defined by two interacting proteins may be allosteric rather than competitive inhibitors. A thermodynamic-based approach provides a faster optimization path in both cases. This will be demonstrated with the development of HIV-1 cell entry inhibitors.

9:00 Integration of Fragment-Based Screening, High Throughout Chemistry and uHTS to Identify Inhibitors of MMP-13

Neil Farrow, Ph.D., Senior Principal Scientist, Medicinal Chemistry, Boehringer Ingelheim

This presentation will describe how application of multiple lead identification approaches resulted in three distinct highly potent series of MMP-13 inhibitors. Examples of how structural biology data, novel screening methodologies and high throughput chemistry approaches were used to advance separate chemical series will be given.

9:30 Chemical Biology through Fragment Screening

Sponsored by ANANOSYN Chemistry on Demand Accelerating Drug Discovery

Olga Issakova, Executive Vice President, Nanosyn

This talk will describe a novel approach to fragment screening. It is based on microfluidics technology and allows for rapid generation of ligand efficiency profiles. The results of profiling of over 3,000 fragments across 57 targets will be presented. This systems approach encompasses a broad spectrum of chemistry and biology information and is applicable to the assessment of drugability of targets.

10:00 Balancing Acts: Alignment of Potency, Enthalpy, Entropy and ADME Attributes

Xinjun Hou, Associate Research Fellow & Head, Neuroscience Computational Chemistry, Neuroscience Medicinal Chemistry, Pfizer Worldwide Research and Development

The key strategy of drug discovery is to design molecules that survive to modulate their target and test new concepts in the clinic. A critical role of medicinal chemistry is to balance potency, pharmacokinetics, pharmacodynamics, metabolism, and safety in one molecule. The availability of X-ray crystal structures, computational modeling, high throughput assays and ADME screening data presents the chemist with a plethora of information to digest, to interpret, and to build new hypotheses. This talk will present a case study on how to assemble these data to assess molecules holistically.

10:30 Refreshment Break in the Exhibit Hall

Dealing with Dmpk, Solubility and Blood-Brain Barrier

11:30 Hydrophobicity, Solubility and Aromaticity: New Standards for Drug Discovery

Rob Young, Ph.D., CSC, Medicinal Chemistry, GlaxoSmithKline

Analysis of chromatographically-measured values for 100k GSK compounds has defined a new hydrophobicity standard for contemporary drug discovery. The quality and relevance of this measure (markedly better than octanol-water) and its remarkable impact in resolving developability-related parameters will be presented, including the wide utility of "HydAr" (logD + #Ar) indices.

Imaging in Drug Discovery

12:00 pm Translational Approaches towards the Identification of a Histamine H3 Receptor Antagonist and its' Clinical Evaluation for the Symptomatic Treatment of Allergic Rhinitis

Micahel A. Letavic, Research Fellow, Neuroscience, Johnson & Johnson Pharmaceutical R&D

The characterization of the potent and selective histamine H3 antagonist JNJ-39220675 in several pre-clinical models will be presented, with emphasis on the correlation of receptor occupancy with efficacy, along with details on its clinical evaluation in allergic rhinitis.

12:30 Luncheon Presentation I: Flow Chemistry for the Medicinal Chemist *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

1:00 Luncheon Presentation II: In- and Out-Sourcing of Medicinal Chemistry *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

1:45 Ice Cream Refreshment Break in the Exhibit Hall

TARGETS IN HOT PURSUIT

Targeting Protein-Protein

2:15 Chairperson's Remarks

2:20 Druggability Assessment of Protein-Protein Interfaces (PPIs)

Jutta Wanner, Ph.D., Principal Research Scientist, Discovery Chemistry, Roche

Developing small molecules that modulate protein–protein interactions is difficult but highly desirable. In recent years, numerous computational tools to assess the druggability of PPIs were published. We have evaluated a number of these tools, and will present a comparison of the predicted druggability to the experimental success rates from drug discovery campaigns.

2:50 Discovery and Optimization of Protein-Protein Interaction Modulators via Kinetic Target-Guided Synthesis

Roman Manetsch, Ph.D., Assistant Professor, Chemistry, University of South Florida

Kinetic Target-Guided Synthesis (TGS) is a LCMS-based discovery platform in which the target protein is sampling and assembling reactive fragments into larger inhibitory compounds (JACS 2008, 130(42), 13820). Herein, we will present the use of kinetic TGS for the identification of selective protein-protein interaction modulators (Bcl-xL, Mcl-1, MDM2, and MDMX).

Allosteric Inhibitors & Modulators

3:20 Discovery of a Calcimimetic with Differential Effects upon PTH Secretion and Calcitonin Secretion

Jeff Reagan, Ph.D., Scientific Director, Department of Metabolic Disorders, Amgen

Calcimimetics are positive allosteric modulators of the calcium-sensing receptor (CaSR). We describe a new calcimimetic that effectively reduced PTH levels without promoting CT secretion or hypocalcemia. The new calcimimetic may find use in stage 4 renal disease patients with elevated PTH levels but serum Ca2+ levels within the high normal range.

3:50 Refreshment Break & Poster Awards in the Exhibit Hall

4:30 Hit Identification Strategies for Allosteric Modulators of G Protein-Coupled Receptors

Neil Burford, Ph.D., Senior Research Investigator II, Bristol-Myers Squibb Company

Allosteric modulators of G protein-coupled receptors can have specific advantages over their orthosteric counterparts in terms of receptor subtype specificity, maintainance of the spatial/temporal aspect of signaling, and safety in overdose. It is our goal to develop sensitive, robust, miniaturized and scalable assays for the detection of allosteric modulators from High Throughput Screening.

5:00 Allosteric Regulators of Coagulation Factors

Umesh Desai, Ph.D., Professor, Medicinal Chemistry, Virginia Commonwealth University

Designed sulfated low molecular weight lignins potently and selectively inhibit factors IIa, Xa and XIa through a novel allosteric disruption of enzyme's catalytic apparatus. The molecules are radically different from all the current clinically utilized anticoagulants (heparins, warfarins, hirudins, and peptidomimetics). Small sulfated derivatives have also been designed as regulators of clotting.

5:30 Panel Discussion: Screening for Allosteric Regulators and Modulators

6:00 Close of Day

FRIDAY, FEBRUARY 25

PAIN & ANEMIA

8:30 Chairperson's Remarks

8:35 Discovery of PF-04457845: A Highly Potent, Orally Bioavailable and Irreversible Urea FAAH Inhibitor with Exquisite Selectivity

Douglas S. Johnson, Ph.D., Senior Principal Scientist, Medicinal Chemistry, Pfizer, Inc.

Inactivation of FAAH leads to analgesic and anti-inflammatory phenotypes in rodents without showing the side effects observed with cannabinoid receptor agonists, indicating that FAAH may represent an attractive therapeutic target for the treatment of inflammatory pain. This talk will describe the discovery and characterization of a series of irreversible FAAH piperidine urea inhibitors.

9:05 Lead Optimization Strategies to Identify Potent in vivo Active Hypoxia-Inducible Factor Prolyl Hydroxylase (HIF-PHD) Inhibitors for the Treatment of Anemia

Jennifer Allen, Ph.D., Director, Medicinal Chemistry, Chemistry Research & Discovery, Amgen

Oxygen sensing prolyl hydroxylase domain proteins (PHDs) target hypoxia-inducible factor (HIF) for degredation. Inhibitors of PHDs enhance the transcription factor HIF and its many downstream effects, including the induction of erythropoiesis. This presentation will outline our lead optimization campaign to identify potent HIF-PHD inhibitors that raise erythropoietin (EPO) and hemoglobin (Hb) levels in vivo in pre-clinical species. Inhibitors of HIF-PHDs have shown tractability as a therapeutic approach to treat anemia and related disorders.

9:35 Talk Title to be Announced

Joseph R. Garlich, Ph.D., CSO, Semafore Pharmaceuticals

10:05 Sponsored Presentation *(Opportunity Available)*

10:20 Coffee Break

Oncology

11:00 Minimizing Transporter Efflux to Achieve BBB Penetrant PI3 Kinase Inhibitors

Timothy P. Heffron, Ph.D., Scientist, Discovery Chemistry, Genentech, Inc.

Deregulation of the PI3K/AKT/mTOR pathway has established a desire for PI3K inhibitors with drug-like properties. Our program to identify potent and orally available molecules that selectively inhibit PI3K previously disclosed GDC-0941. This presentation will discuss the evolution of our PI3 kinase inhibitors, highlighting the importance of structure-guided design and optimization of physicochemical properties.

11:30 The Discovery and Clinical Development of TKI258: A Potent, Poly-Targeted Kinase Inhibitor

Paul Renhowe, Ph.D., Director, Novartis Institutes for BioMedical Research

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

1:30 Chairperson's Remarks

1:35 Title to be Announced

Speaker to be Announced

2:05 Potent, Selective, and Orally Bioavailable Inhibitors of mTOR Kinase based on a Quaternary Substituted Tetrahydrofuropyrimidine

Frederick Cohen, Ph.D., Scientist, Discovery Chemistry, Genentech, Inc.

A series of inhibitors of mTOR was designed and synthesized. Compounds in this series were highly selective for mTOR over the closely related PI3 kinases, showed inhibition of the pathway, and anti-proliferative activity in cell-based assays. Furthermore, these compounds had excellent mouse PK, and showed a robust PK/PD relationship in a mouse model of cancer.

2:35 Discovery of Vaniprevir (MK-7009) and MK-5172: Macrocyclic Hepatitis C Virus NS3/4a Protease Inhibitors

John A. McCauley, Ph.D., Senior Research Fellow, Medicinal Chemistry, Merck & Co., Inc.

Vaniprevir is a novel macrocyclic HCV NS3/4a protease inhibitor with an attractive pre-clinical profile, including high *in vitro* potency, significant liver exposure upon oral dosing and efficacy in a chimpanzee model of chronic HCV infection. Phase IIb studies in HCV-infected patients are in progress. The design and discovery of vaniprevir, as well as MK-5172 will be presented.

3:05 Discovery of Small Molecule Antiprion Agents

Adam Renslo, Ph.D., Associate Director, Chemistry, University of California San Francisco

We will describe the discovery of a new class of antiprion small molecules with activity in cell-based assays and in animal models of disease. Whole-body imaging using transgenic animals expressing luciferase under the control of the GFAP promoter has allowed the evaluation of compound efficacy several weeks before animals manifest clinical symptoms of disease.

3:35 Close of Conference

Seventh Annual

Translational Science

Translating Pre-Clinical & Clinical Knowledge to Success

WEDNESDAY, FEBRUARY 23

7:00 am Registration and Morning Coffee

8:00 Plenary Keynotes *(See Page 2 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

» KEYNOTE SESSION: TRANSLATIONAL SCIENCE

11:00 Chairperson's Opening Remarks

11:10 The Role & Promise of the Translational Scientist in Current Drug Development

Michael P. Cooreman, M.D., Vice President Translational Medicine, Biological Sciences, Takeda Global Research and Development Center (Kate will update the CMS)

The Translational Scientist in Drug Research and Development brings together understanding of the biology of human disease, interaction of the investigational compound with target pathways and corresponding relevant animal models of disease into an integrated TM strategy, applying state-of-the art technology and study design, resulting in a mechanism-of-action guided R&D program up to clinical proof on concept, the demonstration of biologically meaningful therapeutic efficacy. In this cross-functional activity, Translational Science/ Medicine has the promise to increase confidence in data and information based decision making for discontinuation or investment in full development. (Kate will update the CMS)

11:40 Translatability Assessment and Proof-of-Concept Planning: Understanding Risks & Opportunities

Martin Wehling, M.D., Managing Director, Institute for Experimental and Clinical Pharmacology and Toxicology, Director, Clinical Pharmacology Mannheim Medical Faculty, Mannheim Ruprecht-Karls-University Heidelberg

'Translational medicine' has the negative connotation of a fashionable phrase. To realize its valuable claims, translational processes need to be based on robust methods regarding biomarker development and predictivity assessment, biostatistical methods, smart and accelerated early human study designs, integration of clinical data and decision algorithms. Systematic translatability assessment increases the reliability of portfolio risk estimates.

12:10 pm How Can We Succeed at Translational Science? A Consideration of Various Strategies

Lucienne Ronco, Ph.D., Global Director, Discovery Medicine/Translational Sciences, Oncology, AstraZeneca

Successful integration of translational science (TS) into drug discovery requires iterative and intimate alignment of drug hunters, clinical disease experts, biomarker and molecular technical experts, and alliance and regulatory partners. Numerous organizational models exist; what works and why? Oncology case studies will be presented illustrating successful incorporation of TS from target selection through to Phase II.

12:40 Luncheon Presentation: Tumor Segregation Panels: FFPE RT-PCR Assays for Molecular Sub-Typing and Rapid Companion Diagnostic Development

Sponsored by compendia bioscience

Daniel R. Rhodes, PhD, CEO and Co-Founder, Compendia Bioscience

Derived from a meta-analysis of more than 25,000 clinical tumor samples and optimized to perform with formalin-fixed specimens, Tumor Segregation Panels™ measure the key molecular variables of 14 major cancer types. This measurement enables correlation with drug response data to identify highly specific companion diagnostics on an existing go-to-market validated platform. During this presentation, case examples from breast cancer and colon cancer will be presented.

1:10 Luncheon Presentation: Strategic Partnering to Increase the Speed and Efficiency of Drug Discovery and Development

Sponsored by COVANCE

Thomas Turi, Ph.D., Vice President Science & Technology, Covance Discovery & Translational Services, Head Biomarker Center of Excellence

Effective discovery and translational medicine strategies require significant investment ranging from experienced staff to appropriate adoption of emerging technologies. Strategic partnering can offer efficiencies in: reduced administrative handling, access to experienced scientists and emerging technologies. This talk will explore the changing landscape and pressures of translational medicine and suggest ways to address the pressures of increased speed and efficiency in drug

1:45 Dessert in the Exhibit Hall

ORGANIZATIONAL MODELS THAT WORK

2:15 Chairperson's Remarks: *Theresa LaVallee, MedImmune*

2:20 Found in Translation – What and How to Establish Effective Science Driven Drug Development

Theresa LaVallee, Ph.D., Director, Research & Development, MedImmune

2:50 An Academic Model of Translational Science

Michael Kalos, Ph.D., Director, Translational and Correlative Studies Laboratory, University of Pennsylvania School of Medicine

It is becoming increasingly apparent that biomarkers drive in a fundamental manner translational and clinical research. Accordingly, the appropriate development of biomarkers is fundamental to the success of the translational studies. In this presentation we will discuss approaches to support the appropriate development of biomarkers, focusing on three elements; 1) quality, 2) comprehensiveness, 3) and integratability of data sets.

3:20 Creating a Translational Science Program: Lessons Learned

Doina Roman, M.D., Senior Medical Director, Translational Medicine,Takeda Global Research & Development Center, Inc.

This talk will describe the journey of Takeda Global Research & Development Center to implement a translational science program into their drug discovery and development. Examples of methodologies & strategies that do and do not work will be presented, as well as the role of the translational science team within an organization.

3:50 Enterprise Translational Medicine: It's a Kind of Magic

Sponsored by idbs

Paul Denny-Gouldson, Ph.D., VP Translational Research, IDBS

The convergence of life science research and medicine is leading to more personalised healthcare. This means organisations need to implement advanced clinical research information systems (ACRIS) that are able to bring together clinical, molecular and imaging data to support translational research. ACRIS architectures typically have a research data repository (RDR) that is separate from medical record systems and is designed to answer scientific questions and assess patient outcomes. Collaborative Web based access to RDR's enable clinical data to be browsed and patient cohorts to be easily created by clinicians and researchers. Critically, sample, molecular and research results also stored in the RDR can be used to stratify the patient cohorts. This presentation will detail key lessons learned in designing and developing ACRIS-type systems for oncology, cardiovascular and neuroscience disease areas; it will also look at technical challenges of clinical data ETL and terminology mapping, pseudonymisation, coping with large data sets such as Next Gen Sequencing (NGS) and cloud based deployment.

4:05 Sponsored Presentation *(Opportunities Available)*

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

5:20 Breakout Discussions in the Exhibit Hall

6:20 Close of Day

STRATEGIES FOR BETTER DRUG DEVELOPMENT

8:25 Chairperson's Remarks: *Francesco Marincola, NIH*

8:30 Immune Responsiveness in Humans & How it Applies to Translational Research

Francesco M. Marincola, Ph.D., Chief, Infectious Disease and Immunogenetics Section (IDIS), Department of Transfusion Medicine, Clinical Center, Associate Director, Trans-NIH Center for Human Immunology, National Institutes of Health

This talk will approach translational science from a new angle: the immune system. How can understanding the immune response in humans help translate to new drug discovery and development? Examples & strategies will be presented.

9:00 Translational Medicine in Practice: Working Across Organizational Divide to Bridge Discovery and Development

Hong I. Wan, Ph.D., Translational Medicine, BioTherapeutics Clinical Programs, Pfizer, Inc.

Translational medicine strategies are becoming increasingly significant and integral parts of today's pharmaceutical development. Pragmatic and appropriate use of biomarkers facilitates clinical decision making. Adequate investment and close collaborations within the organization are critical to the success of biomarker strategy. Public-private partnerships are key drivers to elevate biomarker research in major disease areas.

9:30 What can TM Deliver for Healthcare in 2015...in 2020? How do we Make it Happen?

Christopher Milne, Ph.D., Associate Director, CSDDR; Assistant Professor, Public Health & Community Medicine, Tufts University Medical School

The prospects of a new pathway for the R&D enterprise to achieve a new level of technical, commercial, and scientific productivity entails examining the steps that academia, government and industry must take, both independently and interactively, to enable TM to fulfill its promise.

10:00 A Novel Intracoronary Device to Resolve the Complexity of Atherosclerosis Through Localised Biomarker Data

Sponsored by PLAQUETEC

Richard Owen, Ph.D., Chief Scientific Officer, PlaqueTec Ltd

PlaqueTec's device measures intracoronary biomarker gradients in a manner that negates patient to patient variation thereby offering actionable data for surrogate end points and potential new druggable targets for atherosclerosis and CVD.

10:30 Refreshment Break in the Exhibit Hall

11:30 Biomarkers in Translational Medicine: From Data Points to Decision-Making Tools

Thierry Sornasse, Ph.D., Director, Translational Medicine, Biomarker Integration, Elan Pharmaceuticals, Inc.

Biomarker discovery and development is a crucial component of any therapeutic area's drug development. The role of biomarkers in translational medicine from the information/knowledge management point-of-view will be presented.

12:00 Today's Merck: Driving Innovation and Translational Science Through Successful Partnering

Linda A. Egger, Ph.D., CLP™, Senior Director, Franchise Licensing Integrator, Diabetes & Obesity

Merck's approach to partnering includes a commitment to a strong internal research capability and a continued investment in innovation. We leverage this capability by openly collaborating with the best partners to develop a portfolio of external early-stage partnerships/joint research programs as an integral component of our global research strategy to drive innovation and translational science.

» 12:30 pm EXPERT PANEL: Can the Pharmaceutical Industry Collaborate on Drug Development Like it Has Done in the Field of Pre-Competitive Biomarker Initiatives?

Moderator: Thierry Sornasse, Ph.D., Director, Translational Medicine, Biomarker Integration, Elan Pharmaceuticals, Inc.

1:00 Luncheon Presentation II: In- and Out-Sourcing of Medicinal Chemistry Metabolomics: A Tool for Early Detection of Toxicological Effects and Biology Based Grouping of Chemicals

Sponsored by metanomicshealth

Bennard van Ravenzwaay, Ph.D., Senior Vice President, Experimental Toxicology & Ecology, BASF SE, Metanomics Health GmbH, metanomics GmbH

During a 5 year cooperation we have jointly developed the MetaMap®Tox data base, which contains the metabolome profiles and toxicological information of approximately 500 data rich compounds. These are specific for different toxicological modes of action.

1:45 Ice Cream Refreshment Break in the Exhibit Hall

INFORMATICS FOR TRANSLATIONAL SCIENCE IN THE ERA OF MOLECULAR MEDICINE

2:15 Chairperson's Remarks

2:20 Bringing it All Together so the Sum is Greater than the Parts: Effective Knowledge Management in Translational Medicine

Eric Perakslis, Ph.D., Vice President, R & D IT, Johnson & Johnson

The focus would be the social engineering and leadership capabilities that are essential for successful translational science. These include incentive structures, traversing data domains, hypothesis generation and testing developmental strategies.

2:50 Using Systems Biology to Accelerate Oncology Drug Development

Matthew Onsum, Ph.D., Principal Scientist, Merrimack Pharmaceuticals

A review of how Merrimack used mathematical models of a cancer signaling pathways with biomarker measurements to identify cancer indications that would have a proportion of responders to our lead oncology drug. These simulations were used to prioritize our clinical development plans.

3:20 Sponsored Presentation

Sponsored by RBM

3:35 Highly Multiplexed (>500 protein) Mass Spec-Based MRM Assays

Sponsored by CAPRION PROTEOMICS

Daniel Chelsky, Ph.D., CSO, Caprion Proteomics, Inc.

Quantitative, sensitive, and specific protein assays are now possible on a large scale with MRM mass spectrometry. Assays on this scale open up new possibilities in biomarker discovery and validation in toxicology, disease monitoring and drug efficacy.

3:50 Refreshment Break & Poster Awards in the Exhibit Hall

4:30 Pre-Competitive Translational Informatics—From Theory to Practice

Sandor Szalma, Ph.D., Senior Research Fellow, R&D Informatics, Centocor R&D Inc.

The development of a translational medicine informatics infrastructure has been the underpinning of the translational research strategy of the pharmaceutical companies of Johnson & Johnson. This infrastructure has been built based on open-source platforms and is now forming the basis of pre-competitive sharing and mining of clinical and associated molecular profiling data.

5:00 Data Management Challenges in Translational Medicine

Isobel Anderson, Ph.D., Lead, Global TAU, Discovery Information, AstraZeneca

The integration of clinical and discovery data is key to a successful translation medicine strategy. In addition to the technical challenges there are issues of data sharing, data standardization and consent. Here we discuss the relative merits of different approaches that have been implemented at AstraZeneca to make the right data accessible to all our researchers.

5:30 Building a Translational Informatics Vision

Sorena Nadaf, Director, Translational and Biomedical Informatics, CIO, HDFCCC Translational Informatics, University of California, San Francisco

Dealing with the era of Molecular Medicine requires cutting edge information available at the fingertips of healthcare professionals. Building such a Translational Research environment depends upon an Informatics footprint that can bring these avenues together. Translational Informatics provides the answers.

6:00 Close of Day

TRANSLATIONAL BIOMARKERS: ONCOLOGY

8:30 Chairperson's Remarks: *Chris H. Takimoto, Centocor*

8:35 Translational First in Human Oncology Studies with Biomarker Defined Endpoints: A New Paradigm for Phase I Oncology Trials

Chris H. Takimoto, M.D., Ph.D., Senior Director, Translational Medicine, Ortho Biotech Oncology R&D, Centocor R&D, Inc.

The study designs of the FIH phase 1 trials at Ortho Biotech/Centocor that incorporate the biomarkers and patient selection markers will be discussed.

9:05 Using Biomarker-Based Patient Stratification to Return Elesclomol to the Clinic

Ronald K. Blackman, Ph.D., Director, Translational Biology, Synta Pharmaceuticals

The oncology drug elesclomol failed to meet its primary endpoint in a recent Phase 3 study. Coupling analysis of the trial data with an enhanced understanding of the drug's mechanism of action, we have identified LDH as a biomarker that may predict outcome. Based on this marker, clinical testing is slated to resume.

9:35 Discovery and Translation of Biomarkers for Clinical Trials

Suso Platero, Ph.D., Director, Oncology Biomarkers, Centocor R&D, Inc., a Johnson & Johnson company

Biomarkers can provide a window into the mechanism of action of compounds and help identify the group of patients that will likely respond to treatment. How those biomarkers are found and how they are developed for use in clinical trials will be shown with specific examples in the area of oncology.

10:05 OncoPredictor: A System for Identifying Clinically Relevant Biomarkers from Large Scale Cell Line Profiling

Sponsored by

compendia bioscience

Daniel R. Rhodes, Ph.D., CEO and Co-Founder, Compendia Bioscience

Utilizing drug response data from 240 cancer cell lines, OncoPredictor is a complete system to identify both univariate and multi-variate biomarkers of drug response and resistance and, critically, to characterize the prevalence of the markers in clinical populations and sup-populations using the more than 40,000 clinical genomic profiles in Oncomine™. This presentation will include numerous examples of the identification of both known and novel predictive biomarkers and their potential impact in clinical development strategy and patient treatment.

10:20 Coffee Break

» 11:00 EXPERT PANEL: Planning for a Biomarker Strategy in All Phases of Drug Development: Advantages of a Translational Approach

Moderator:

Brandon W. Higgs, Ph.D., Translational Sciences, MedImmune

Panelists:

Suso Platero, Ph.D., Director, Oncology Biomarkers, Centocor R&D, Inc., a Johnson & Johnson company

Rakesh Sindhi, M.D., FACS, Co-Director, Pediatric Transplantation, University of Pittsburgh

Michael Elashoff, Ph.D., Director, Biostatistics, CardioDx

Discussion points:

- Biomarker identification efforts in early drug development for companion diagnostics
- The challenges in the identification of a robust surrogate endpoint
- A comparison between laboratory-developed tests (LDTs) vs. FDA approved *in vitro* diagnostic (IVDs): should these be more aligned with respect to FDA oversight?

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

CASE STUDIES

1:30 Chairperson's Remarks: *Mark Day, Abbott Laboratories*

1:35 Novel Pathways to Drug Development: Biomarker Impact on Drug Discovery and Development Decision Making

Mark Day, Ph.D., Associate Director, Translational Sciences, Abbott Laboratories

There is a clear need for the development of biomarkers that can improve the congruency of animal studies to clinical outcome; to address target engagement, dose selection, and the translatability of drug effects generated in animal models, new disease model validation, and the identification of pharmacodynamic markers.

2:05 Translating Cell and Gene Therapies to the Clinic: A Practical Approach

David DiGiusto, Ph.D., Director, Hematopioetic Cell Therapies, Virology/ Hematology, City of Hope Medical Center

Translating cell and gene therapies to the clinic requires extensive preclinical development including scale up, materials resourcing, establishing in process and final product assays and release criteria. We will describe our experience in bringing human hematopoietic stem cell and adoptive T-cell gene therapy applications to clinical trials. Information will include product development strategy, device development, reagent qualification and regulatory hurdles encountered and conquered.

2:35 From the Idea to the Patient and to a Pharma Deal: Discovery: Pre-Clinical and Early Clinical Development of Angiotensin Converting Enzyme 2 (ACE2)

Manfred Schuster, Ph.D., COO, APEIRON Biologics AG

Insight into pre-clinical and clinical development strategy of a therapeutic enzyme, new aspects regarding regulation mechanisms of the Renin Angiotensin System and how a company with 12 employees was able to close a 330 million deal with big Pharma.

3:05 Speaker Q&A

3:35 Close of Conference

Inaugural

Strategies for Clinical Oncology Drug Development

Innovations & Ideas that Translate to the Patient

WEDNESDAY, FEBRUARY 23

7:00 am Registration and Morning Coffee

8:00 Plenary Keynotes *(See Page 2 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

VACCINES & IMMUNOTHERAPEUTICS

11:00 Chairperson's Opening Remarks: *James Gulley, NCI/NIH*

11:10 Sipuleucel-T Immunotherapy for Advanced Prostate Cancer

David L. Urdal, Ph.D., Chief Scientific Officer, Dendreon Corporation

Will describe the clinical efficacy and safety data supporting FDA approval of the first autologous cellular immunotherapy approved for the treatment of cancer. Data on immune response, product potency, and correlation of potency measures with clinical outcomes will be described.

11:40 Cancer Vaccines: New Paradigm in Changing Cancer to a Chronic Disease

Helen Sabzevari, Ph.D., Global Head, Oncology-Immunotherapy, EMD-Serono, Inc.

12:10 pm Ipilimumab Development: Contribution to a New Immunotheray Paradigm

Axel Hoos, M.D., Ph.D., Medical Lead, Immunology/Oncology, Bristol-Myers Squibb

Ipilimumab development has contributed valuable lessons to the evolution of a new development paradigm for cancer immunotherapies as spearheaded by the Cancer Immunotherapy Consortium. This new paradigm encompasses new tools and development principles for immuno-oncology. It offers a better defined path for development of new therapies in this space.

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

1:45 Dessert in the Exhibit Hall

2:15 Chairperson's Remarks

2:20 HN1: a Novel Human Monoclonal Antibody Targeting Mesothelin for Cancer Therapy

Mitchell Ho, Ph.D., Head, Antibody Therapy Unit, LMB, National Cancer Institute, National Institutes of Health

We recently generated HN1, a fully human IgG, that binds mesothelin with high affinity. The HN1 epitope is different from that of SS1, a mouse Fv used to develop an immunotoxin (SS1P) and a chimeric antibody (MORAb-009) that are currently in clinical trials. HN1 binds strongly to cell surface-associated mesothelin on mesothelioma, ovarian cancer, lung adenocarcinoma and pancreatic cancer cells. HN1 kills cancer cells with very strong antibody-dependent cell-mediated cytotoxicity and has potential for mesothelin-expressing cancer treatment.

2:50 Initial Experience With Autologous Heat Shock Protein Vaccine for Brain Tumor Patients

Andrew T. Parsa, M.D., Ph.D., Associate Professor in Residence of Neurological Surgery, Reza & Georgianna Khatib Endowed Chair in Skull Based Tumor Surgery; Principal Investigator, Brain Tumor Research Center, University of California, San Francisco

3:20 Genomics-Guided Personalized Immunotherapy of Human Cancers: Rationale & Challenges

Pramod Srivastava, Ph.D., Director, Center for Cancer & Infectious Disease, University of Connecticut

High throughput DNA sequencing, and sophisticated informatics tools provide new opportunities for immunotherapy of human cancer. The scientific and clinical rationale for these opportunities, as well as the novel logistical and regulatory challenges expected of them, shall be discussed.

3:50 Sponsored Presentations *(Opportunities Available)*

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

5:20 Breakout Discussions in the Exhibit Hall

6:20 Close of Day

THURSDAY, FEBRUARY 24

8:25 Chairperson's Remarks:

Peter Choyke, M.D., Chief, Molecular Imaging Program, National Cancer Institute

» 8:30 KEYNOTE PRESENTATION: Innovative and Efficient Drug Development: Endpoints, Biomarkers, Imaging, and Adaptive Designs

Donald Berry, Ph.D., Head, Division of Quantitative Sciences & Chairman, Department of Biostatistics & Frank T. McGraw Memorial Chair of Cancer Research, The University of Texas M.D. Anderson Cancer Center

IMAGING IN THE PATIENT

9:00 Molecular Imaging of Cancer in Clinical Trials: Have Imaging Biomarkers Come of Age?

Peter Choyke, M.D., Chief, Molecular Imaging Program, National Cancer Institute

Unprecedented opportunities now exist for the study of cancer in humans using molecular imaging, particularly PET and Radionuclide imaging. Targeted imaging agents for the major hallmarks of cancer including angiogenesis, growth factors, hypoxia, apoptosis, amino acid transport and proliferation, among others, are now readily available. This presentation will focus on the impact of this diverse group of new radiopharmaceuticals on oncologic drug discovery and development.

9:30 Improving Drug Development with Molecular Imaging

Steven M. Larson, M.D., Chief, Nuclear Medicine Service; Director, Laurent and Alberta Gerschel Positron Emission Tomography Center and Head, Nuclear Medicine Research Laboratory, Memorial Sloan Kettering Cancer Center

10:00 Speaker to be Announced

10:30 Refreshment Break in the Exhibit Hall

11:30 Challenges of Using Imaging as a Biomarker in Clinical Trials

Peter S. Conti, Professor, Biomedical Engineering, Radiology, Pharmacy, University of Southern California

12:00 Imaging Methods and Biomarkers for the Early Assessment of Novel Anti-Angiogenic Therapies

Rikki N. Waterhouse, Ph.D., Senior Group Leader, Cancer Imaging and Radiochemistry, Advanced Technology, Global Pharmaceutical Discovery, Abbott

Tumor reduction as the result of anti-angiogenic therapy occurs relatively late in the course of treatment. Thus, earlier indications of efficacy, especially in the evaluation of novel therepeutic agents, is critical for confirming target engagement and to optimize dose selection. The current imaging and non-imaging biomarkers used for the early detection of efficacy of antiagiogenic drugs, including the advantages and limitations of each, will be presented.

12:30 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:45 Ice Cream Refreshment Break in the Exhibit Hall

HOT TOPICS IN ONCOLOGY CLINICAL RESEARCH

2:15 Chairperson's Remarks: *Jonathan Pachter, OSI Pharmaceuticvals*

2:20 ANA773, a Novel Immunotherapeutic Drug for the Treatment of Cancer

James Appleman, Ph.D., Senior Vice President, Research, Anadys Pharmaceuticals

ANA773 is an oral prodrug of a small-molecule TLR7 agonist. Extensive pre-clinical demonstration of immune induction by this agent both *in vitro* and *in vivo* provided the basis for clinical investigation of ANA773 in the treatment of both cancer and chronic Hepatitis C. Overall development strategy and status will be described.

2:50 Evidence of Early Anti-Tumor Immune Responses in Patients Treated with Cetuximab, Detected by Novel Piezoelectric Biosensors

Hossein Borghaei, D.O., M.S., Medical Oncology, Fox Chase Cancer Center

We can demonstrate induction of host derived anti EGFR-ICD (intracellular domain) antibody responses in patients with metastatic solid tumors treated with cetuximab. Blood samples are collected pre and post treatment and using the piezoelectric biosensors (cantilevers) we are able to show better sensitivity than standard ELISA.

3:20 Epithelial-Mesenchymal Transition (EMT) as a Framework for Selection of Targets, Sensitive Patients & Therapeutic Combinations for Clinical Oncology

Jonathan A. Pachter, Ph.D., Senior Director, Biochemical & Cellular Pharmacology, OSI Pharmaceuticals, Inc.

Pre-clinical and clinical evidence indicate that EMT marker status predicts sensitivity of cancer patients to the EGFR kinase inhibitor erlotinib. The activity of various Molecular Targeted Therapies, including the IGF-1R/IR kinase inhibitor OSI-906 and the mTORC1/2 kinase inhibitor OSI-027 to inhibit tumor cell proliferation as a function of epithelial vs. mesenchymal phenotype will be discussed, and effective combinations will be proposed based on EMT rationale. Both pre-clinical and clinical data will be presented.

3:50 Refreshment Break & Poster Awards in the Exhibit Hall

CTCs IN THE CLINIC

Chairperson's Remarks: *Avraham Rasooly, Ph.D., Program Director, Cancer Diagnosis Program, National Cancer Institute*

4:30 Presentation to be Announced

5:00 Circulating Tumor Cells in Drug Development: From Enumeration to Characterization

Marielena Mata, Ph.D., Principal Research Scientist, Oncology Biomarkers, Centocor R&D, Inc.

5:30 Application of Circulating Tumor Cells in Early Stage Clinical Trials

Robert J. Kinders, Ph.D., Head, Pharmacodynamic Assay Development Section, Laboratory of Human Toxicology and Pharmacology, Applied/Developmental Research Directorate, SAIC-Frederick, Inc., NCI-Frederick

Work in our laboratory centers on evaluating the potential of CTCs to replace biopsies in certain clinical trials. Our ultimate goal is to generate a PD response curve analogous to a PK curve, measuring effect over time and relative to dose on the specific molecular target of the new agent under investigation.

6:00 Implementing Quantitative CTC Counts in the Management of Metastatic Breast Cancer: From Observational to Current Interventional Studies

Francois-Clement Bidard, M.D., Ph.D., Assistant Professor, Medical Oncology, Institut Curie, Paris, France

The recently reported Institut Curie (IC) 2006-04 study included 267 first-line metastatic breast cancer patients and confirmed several, but not all, results reported previously in smaller observational studies. Quantitative CTC counts must further demonstrate a clinical and/or a medico-economic improvement to be implemented in the everyday clinical management. The currently ongoing SWOG0500 (USA) and CirCe01 (France) randomized interventional trials have been specifically designed to demonstrate the usefulness of quantitative CTC counts.

6:15 Clinical Importance of the PCR-based Detection of CTCs in Prostate Cancer

Athanasios Armakola, Ph.D., Experimental Physiology Laboratory, University of Athens Medical School, Greece

6:30 Panel Discussion: Evaluating New Technologies for CTC Diagnostic Purposes in the Clinic

Moderator: Avraham Rasooly, Ph.D., Director, Cancer Diagnosis Program, NCI

Additional Panelist: Mark Carle Connelly, Ph.D., Director, Cellular Research, Veridex, LLC

7:00 Close of Day

FRIDAY, FEBRUARY 25

TRANSLATIONAL BIOMARKERS: ONCOLOGY

8:30 Chairperson's Remarks: *Chris H Takimoto, Centocor*

8:35 Translational First in Human Oncology Studies with Biomarker Defined Endpoints: A New Paradigm for Phase I Oncology Trials

Chris H. Takimoto, M.D., Ph.D., Senior Director, Translational Medicine, Ortho Biotech Oncology R&D/Centocor R&D, Inc.

The study designs of the FIH phase 1 trials at Ortho Biotech/Centocor that incorporate the biomarkers and patient selection markers will be discussed.

9:05 Using Biomarker-Based Patient Stratification to Return Elesclomol to the Clinic

Ronald K. Blackman, Ph.D., Director, Translational Biology, Synta Pharmaceuticals

The oncology drug elesclomol failed to meet its primary endpoint in a recent Phase 3 study. Coupling analysis of the trial data with an enhanced understanding of the drug's mechanism of action, we have identified LDH as a biomarker that may predict outcome. Based on this marker, clinical testing is slated to resume.

9:35 Discovery and Translation of Biomarkers for Clinical Trials

Suso Platero, Ph.D., Director, Oncology Biomarkers, Centocor R&D, Inc., a Johnson & Johnson company

Biomarkers can provide a window into the mechanism of action of compounds and help identify the group of patients that will likely respond to treatment. How those biomarkers are found and how they are developed for use in clinical trials will be shown with specific examples in the area of oncology.

10:05 Sponsored Presentation

Sponsored by

compendia bioscience

OncoPredictor: A System for Identifying Clinically Relevant Biomarkers from Large Scale Cell Line Profiling

Daniel R. Rhodes, Ph.D., CEO and Co-Founder, Compendia Bioscience

Utilizing drug response data from 240 cancer cell lines, OncoPredictor is a complete system to identify both univariate and multi-variate biomarkers of drug response and resistance and, critically, to characterize the prevalence of the markers in clinical populations and sup-populations using the more than 40,000 clinical genomic profiles in Oncomine™. This presentation will include numerous examples of the identification of both known and novel predictive biomarkers and their potential impact in clinical development strategy and patient treatment.

10:20 Coffee Break

ONCOLOGY CLINICAL TRIALS

Chairperson: *James Gulley, NCI/NIH*

11:00 Immunotherapy Clinical Trials are Telling us about Meaningful Endpoints and Appropriate Patient Populations

James L. Gulley, M.D., Ph.D., F.A.C.P., Director, Clinical Trials Group, Laboratory of Tumor Immunology and Biology & Senior Clinician, Medical Oncology Branch Center for Cancer Research, National Cancer Institute National Institutes of Health

Recent clinical data in prostate cancer suggest significantly improved overall survival without any improvement in time to progression. They also suggest that the kinetics of an anti-tumor immune response may favor using the vaccine in an earlier patient population. These data have important implications for trial design

and patient population.

11:30 Fast-Tracking an Orphan Drug Indication within an Oncology Development Project

Dale Johnson, Pharm.D., Ph.D., President & CEO, Emiliem, Inc.; Adjunct Professor, University of California, Berkeley

Drug candidates targeting biological pathways with multiple indications can capitalize on orphan indications while maintaining a separate oncology development strategy. A "Master File" IND with a PK/PD, biomarker-driven approach is utilized. The ideal candidate can be formulated for specialized systemic and/or local delivery. An mTOR pathway inhibitor will be highlighted.

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

1:30 Chairperson's Remarks

1:35 Accelerated Approval in Oncology

Robert Lechleider, M.D., Director, Clinical Development, Oncology, MedImmune

This talk will discuss the regulatory requirements for gaining accelerated approval for new molecular entities and biologics. Case studies of recent accelerated approvals, their role in development, and strategies to gain and secure accelerated approval will be discussed.

2:05 How Do Characteristics of Global Oncology Trials Affect Center Participation in Emerging Regions?

Fabio Thiers, M.D., CEO, VIS Research Institute & Co-Director, Global Clinical Trials Research Program, MIT/NBER

Planners of late-stage global oncology trials need to make sure that their studies can be effectively conducted in emerging regions. We will describe findings of a systematic study designed to determine which disease-specific trial characteristics and patient selection criteria are more likely to affect participation in key emerging regions.

2:35 Population Based Cancer Models for *in vivo* Biomarker Discovery and Validation

Joerg Heyer, Ph.D., Director, Genetic Models, Translational Research, AVEO Pharmaceuticals

Personalized medicine and biomarkers are an integral part of drug discovery. Biomarker discovery traditionally will be initiated during early/mid stage clinical development and thereby limits the impact of biomarkers during later stages. Here we present a novel population based pre-clinical model that enables biomarker identification in early stages of drug discovery and allows for biomarker validation in subsequent clinical trials.

3:05 Speaker Q&A for Clinical Trial Design

Moderator/Chairperson: James Gulley, NCI/NIH

3:35 Close of Conference

Third Annual

Integrated R&D Informatics & Knowledge Management

Integrating Internal and External Data to Impact Drug Discovery and Clinical Development

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9:40 Grand Opening Refreshment Break in the Exhibit Hall

» KEYNOTE SESSION: GETTING MORE VALUE AND GENERATING KNOWLEDGE FROM LARGE VOLUMES OF DATA AND STUDIES

11:00 Chairperson's Opening Remarks

Kevin Davies, Ph.D., Author, The $1,000 Genome; Editor-in-Chief, Bio-IT World

11:10 Generating More Knowledge from Our Data and More Value from Our Studies: The Value of Expert Skills

Anastasia M. Khoury Christianson, Ph.D., Senior Director, Discovery Information, AstraZeneca Pharmaceuticals

A major challenge in translational science is finding the relevant data, information and knowledge to allow meaningful correlation between pre-clinical observations and clinical outcomes. This presentation will concentrate on the key success factors for leveraging information, generating new knowledge and ensuring best informed decisions in our drug projects.

11:40 Burn the Hay or Build a Better Magnet to Find the Needles in our Haystack?

Martin Leach, Ph.D., Executive Director, IT for Discovery & Pre-Clinical Sciences (DPS), Merck

The expense and availability of technology enables compulsive hoarding, but at what cost to research? The ability to find things now relies heavily on search technology, data-mining or semantic-mining techniques that require proper classification of the structured and unstructured data, information, and knowledge. The presentation will explore some of the lessons learned at Merck and other organizations.

12:10 pm From Virtual Machine to Virtual Pharmaceutical Organization: Cloud-Ba sed Translational Informatics for European IMI Projects

Eric Perakslis, Ph.D., Vice President, Research & Development IT, Johnson & Johnson

Anthony Rowe, Ph.D., Department of Computing, Imperial College, London

In this talk, we illustrate the design of the IT infrastructure for collaborative translational research in the UBIOPRED IMI project. The system is based on the Cloud computing infrastructure with a strong focus on supporting open collaborative research. The convergence of the two trends will realize a powerful new generation of IT infrastructure for life science.

12:40 Data: Challenges in Translational and Clinical Informatics

Sponsored by BioFortis

Jian Wang, Ph.D., CEO, BioFortis, Inc.

There are many unique challenges faced by research informatics groups when dealing with complex clinical and translational data sets. These challenges are exacerbated by the fact that researchers are asking increasingly more dynamic and complex questions against these data sets. Traditional BI (business intelligence) methods have their limitations under these conditions. In this presentation, we will describe these unique challenges and BioFortis' innovative approach to help address them, focusing on a repeatable process we developed in data cleaning & standardization, data exploration, and data analysis from working with our partners & clients.

1:45 Dessert in the Exhibit Hall

KNOWLEDGE MANAGEMENT FOR IMPROVED R&D

2:15 Chairperson's Remarks

Michael S. Lajiness, Ph.D., Principal Scientist, Structural & Computational Sciences, Eli Lilly & Co.

2:20 Integrating Knowledge from the Bench, Literature and the Clinic: Successes and Challenges

Bryan Takasaki, Ph.D., IS Informatics Science Director, R&D Information, AstraZeneca

The Knowledge Engineering initiative within AstraZeneca has recently delivered the first version of a platform that integrates internal and external evidence for connections between key concepts such as targets, pathways, compounds, diseases and clinical outcome. This talk will describe the impact of this new platform and lessons learned during its development.

2:50 Integrated Information & Informatics to Drive Drug Discovery

Michael S. Lajiness, Ph.D., Principal Scientist, Structural & Computational Sciences, Eli Lilly & Co.

One of the most important, but often unmet needs in pharmaceutical drug discovery is simple access to data in an integrated and effective manner. This work will describe Mobius, an integrated information system developed internally at Eli Lilly to meet a variety of data delivery needs to support Drug Discovery efforts.

3:20 Implementing a Biomarker Data Mining System

Daniel Ingber, Senior Manager, Research Information Systems, MedImmune

Biomarker Data Mining (BDM) will lead to a better understanding of drug action, an improved ability to understand physiological responses, and better overview of interrelationships between research and clinical data. MedImmune just completed building a BDM and Data Warehouse platform to extract, transform, and load (ETL) data from various disparate storage locations and formats. These include sources such as current databases and spreadsheets, from which are assembled and presented correlated data for exploratory analyses. This talk presents considerations on how to build and manage a system with a flexible data model which supports a scalable, industrial-strength scientific data pipeline.

3:50 The Pipeline Pilot NGS Collection: A New Approach to the Challenges of NGS Data Analysis

Sponsored by accelrys

Clifford Baron, Accelrys

In repeated surveys, scientists using next generation sequencing technologies report that data analysis is their greatest challenge, and the most significant impediment to continued market growth. This is so despite the availability of over a dozen commercial software offerings and literally hundreds of public domain NGS algorithms, with more appearing weekly. The most frequently discussed factor contributing to the data analysis challenge is the sheer volume of data generated. But as significant though less frequently acknowledged is the rapid evolution of available algorithms and attendant computational best practices, and the need for techniques tailored to specific research goals. We discuss how Pipeline Pilot, a widely used commercial software system for the rapid development and deployment of computational pipelines, can be used along with a newly released collection of NGS analysis components to address these fundamental challenges.

4:05 A Customizable Biomarker Discovery System

Sponsored by ARIADNE

Ilya Mazo, Ph.D., CEO, Ariadne Genomics

Finding all the relevant facts from the vast diversity of published literature on a specific research topic continues to be a time-consuming challenge. Transforming this information into knowledge useable by a diverse set of scientists has lead to large investments in information science. Often these solutions have limited flexibility and extendibility. Ariadne developed a system that capitalizes on knowledge extraction to interpret and integrate information from public and legacy sources including disease associations, druggability, mechanisms of action and toxicity, and experimental data. The system is very flexible and extendable across different domains; Target ID, lead Opt, Preclinical, Clinical development. The customization of this practical knowledge management solution to meet oncology-specific domains will be discussed with the focus on biomarker candidate identification.

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

5:20 - 6:20 Breakout Discussions in the Exhibit Hall

Workflow-Based Informatics

David Sedlock, Ph.D., Senior Director, R&D Systems, Millennium Pharmaceuticals, The Takeda Oncology Company

- How are workflows used in the R&D setting?
- Where do we apply informatics solutions to workflow management?
- What are some of the tools used to manage workflows?
- Do we see process improvements when using these tools?

Building Ontologies

Elgar Pichler, Ph.D., Computational Biologist, Boston

- Do we need ontologies and if so, what are (un)satisfied needs for ontologies in the health care and life sciences space?
- Technological, organizational, and personal problems in collaborative development and sharing of ontologies
- Ontology resources

Clinical Data Integration

Carol Hill, Ph.D., Informatics Project Leader II, Clinical Data Integration, Duke Clinical Research Institute

- What are barriers to integrating and sharing clinical data (cultural, legal/ethical, technical)?
- How do standards help/hinder data integration?
- What tools/strategies are people using to integrate clinical data across studies?
- Challenges/experience in association to clinical information to specimens to results data sets across an enterprise

THURSDAY, FEBRUARY 24

WORKFLOW-BASED INFORMATICS TO INCREASE PRODUCTIVITY IN R&D

8:25 Chairperson's Remarks

David Sedlock, Ph.D., Senior Director, R&D Systems, Millennium Pharmaceuticals, The Takeda Oncology Company

8:30 Development of a Media Request System to Manage Biological Reagent and Media Laboratory Supplies

David Sedlock, Ph.D., Senior Director, R&D Systems, Millennium Pharmaceuticals, The Takeda Oncology Company

Co-Author: Chris Perkins, Millennium Pharmaceuticals, The Takeda Oncology Company

The management of laboratory processes is an important contributor to the successful outcomes of basic and applied pharmaceutical research. We partnered with the Laboratory Operations group at Millennium to develop a structured workflow tool to handle requests and delivery of laboratory media to the scientists.

9:00 Compound Management System: Challenges and Opportunities for Improving Workflow Efficiency

Hongmei Huang, Ph.D., Director & Site Head, NIBR IT, Novartis

Richard Kuo, Ph.D., Lab Head, NIBR Compound Management, Novartis

As business processes mature and technology evolves, there is an increasing demand on IT and logistics teams to upgrade or replace legacy systems, in addition to maintaining the existing systems. We will present a case study of our endeavor to replace a legacy Compound Management request fulfillment system. Through this case study, we will shed light on the challenges, at times interesting dilemmas, and opportunities that upgrading a highly integrated software/hardware landscape presents.

10:00 Closing the Gap Between R&D and Manufacturing: Siemens' Vision on Collaborative Platforms Being Key to Future Pharma Success

Sponsored by SIEMENS

Rebecca Vangenechten, Business Development, Siemens AG, Pharma US

Regulatory developments and technological innovation are opening up new opportunities for companies to use lifecycle collaborative management to bring together parts of the value chain that have traditionally been relatively distant from each other. Collaboration will become increasingly important across the R&D / manufacturing interface and across the pharma / patient interface.

10:15 Generating New Scientific Insights Through Workflow Driven Search and Nonclinical Safety Data Integration

Sponsored by POINT CROSS

Shree Nath, Ph.D., VP, Pharmaceuticals & HLS, PointCross

We have combined parametric and text-based search with statistical indices, ontologies and collaborative workflows to provide scientists with novel ways of exploring safety and efficacy signals across semantically integrated nonclinical data. Techniques for rapidly extracting data and harmonizing both taxonomies and units from LIMS, and legacy paper/PDF reports will be illustrated using case studies from individual companies, and from collaborative consortia.

10:30 Refreshment Break in the Exhibit Hall

11:30 External Request Management System to Enhance Chemical Synthesis Data Management and Communications with CROs

Zhenbin Li, Ph.D., Senior Principal Analyst, Information Technology, Boehringer Ingelheim

With the increasing trend of external collaboration in research and development, a system to effectively manage data, workflows, and communications between pharmaceutical companies and CROs is necessary. ERMS (External Request Management System) is designed to facilitate external request processes for chemical synthesis, and can be extended into other collaborative research activities.

12:00 Talk Title to be Announced

Narayan Desai, Principal Experimental Systems Engineer, Mathematics and Computer Science Division, Argonne National Laboratory

12:30 Luncheon Presentations *(Sponsorship Opportunities Available)* or Lunch on Your Own

1:45 Ice Cream Refreshment Break in the Exhibit Hall

INFORMATICS FOR TRANSLATIONAL SCIENCE IN THE ERA OF MOLECULAR MEDICINE

2:15 Chairperson's Remarks

Matthew Onsum, Ph.D., Principal Scientist, Merrimack Pharmaceuticals

2:20 Bringing it All Together so the Sum is Greater than the Parts: Effective Knowledge Management in Translational Medicine

Eric Perakslis, Ph.D., Vice President, Research & Development IT, Johnson & Johnson

The focus would be the social engineering and leadership capabilities that are essential for successful translational science. These include incentive structures, traversing data domains, hypothesis generation and testing developmental strategies.

2:50 Using Systems Biology to Accelerate Oncology Drug Development

Matthew Onsum, Ph.D., Principal Scientist, Merrimack Pharmaceuticals

A review of how Merrimack used mathematical models of a cancer signaling pathways with biomarker measurements to identify cancer indications that would have a proportion of responders to our lead oncology drug. These simulations were used to prioritize our clinical development plans.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Refreshment Break & Poster Awards in the Exhibit Hall

4:30 Pre-Competitive Translational Informatics—From Theory to Practice

Sandor Szalma, Ph.D., Senior Research Fellow, R&D Informatics, Centocor R&D, Inc

The development of a translational medicine informatics infrastructure has been the underpinning of the translational research strategy of the pharmaceutical companies of Johnson & Johnson. This infrastructure has been built based on open-source platforms and is now forming the basis of pre-competitive sharing and mining of clinical and associated molecular profiling data.

5:00 Data Management Challenges in Translational Medicine

Isobel Anderson, Ph.D., Lead, Global TAU, Discovery Information, AstraZeneca

The integration of clinical and discovery data is key to a successful translation medicine strategy. In addition to the technical challenges, there are issues of data sharing, data standardization and consent. Here we discuss the relative merits of different approaches that have been implemented at AstraZeneca to make the right data accessible to all our researchers.

5:30 Building a Translational Informatics Vision

Sorena Nadaf, Director, Translational and Biomedical Informatics; CIO, HDFCCC Translational Informatics, University of California San Francisco

Dealing with the era of Molecular Medicine requires cutting edge information available at the fingertips of healthcare professionals. Building such a Translational Research environment depends upon an Informatics footprint that can bring these avenues together. Translational Informatics provides the answers.

6:00 Close of Day

FRIDAY, FEBRUARY 25

BUILDING ONTOLOGIES, USING SEMANTIC WEB & WIKIS

8:30 Chairperson's Remarks

Elgar Pichler, Ph.D., Computational Biologist, Boston

8:35 Ontologies for the Masses

Mark Musen, Ph.D., Professor, Stanford University, & The National Center for Biomedical Ontology

The National Center for Biomedical Ontology is creating Web-based information technology to enable distributed authoring and publication of ontologies to drive a wide range of applications. This talk will provide an overview of the Center's Web 2.0 support for management of the ontology life cycle.

9:05 Ontological Realism and the Open Biomedical Ontologies Foundry

Werner Ceusters, M.D., Professor of Psychiatry, Director Ontology Research Group, NYS Center of Excellence in Bioinformatics & Life Sciences, University at Buffalo

'Ontology' is a term which tends to be assigned to knowledge representation artifacts of different sorts, including classifications, controlled vocabularies and formal terminologies. Most artifacts are designed for a specific purpose and optimized for concrete operational goals that often make it difficult to reuse these artifacts in even slightly different contexts.

9:35 The Translational Medicine Ontology: Driving Personalized Medicine by Bridging the Gap from Bedside to Bench

Susie M. Stephens, Ph.D., Director, Biomedical Informatics, Johnson & Johnson Pharmaceutical

The Translational Medicine Ontology provides terminology that bridges diverse areas of translational medicine from bedside to bench. An overview of the ontology will be provided along with a demonstration of its utility through question answering over a prototype knowledge base composed of sample patient data integrated with linked open data.

10:05 Annotating and Interpreting Functional Genomics Datasets

Chris Stoeckert, Ph.D., Research Professor, Department of Genetics, Center for Bioinformatics, University of Pennsylvania

Functional genomics technologies create large datasets plus the ability to create large numbers of datasets. Scalable challenges for microarray and HTS datasets include management in the sense of knowing what specimens were analyzed and with which procedures. Standards and tools have been developed to enable reproducible research with these datasets.

10:35 Coffee Break

INFORMATICS TOOLS TO HANDLE BIOLOGICS SCREENING, ASSAY DATA & REGISTRATION SYSTEMS

11:00 Building a Platform for Integrated Research Informatics–Innovation, Agility and Lessons Learned

Ajay Shah, Ph.D., Director, Research Informatics, Elan Pharmaceuticals

11:30 Biologics Registration–Centocor Case Study

Venkat Koka, Ph.D., P.M.P., Senior Scientist, Immunology Research, Janssen Pharmaceutical Group

Pharmaceuticals are largely of two main categories—small molecules and biologics. Few biologics are amenable to chemical synthesis approaches as they are protein-based; instead, these are engineered using molecular biology techniques. The drug discovery processes are divergent, requiring different approach to data management. The main challenge with biologics data management and workflow enabling solutions is robust registration.

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

CLINICAL DATA INTEGRATION & BIOMARKERS

1:30 Chairperson's Remarks

Carol Hill, Ph.D., Informatics Project Leader II, Clinical Data Integration, Duke Clinical Research Institute

1:35 Fusing Clinical and Omics Data to Facilitate Biomarker Discovery

Victor Lobanov, Director, Informatics & Pharmaceutical R&D, Johnson & Johnson Pharmaceutical

With the decreasing cost of omics platforms, composite biomarkers have been attracting more interest. Ability to fuse clinical data with omics results is at the core of effective development of composite biomarker models. We'll describe an internally developed platform that combines database technology, standard ontologies and a graphical user interface to facilitate biomarker discovery.

2:05 Collaborating Across Divisions to Develop Translational Research and Medicine Informatics and Technologies (TRAM-IT) Roadmaps

Csilla Csank, Ph.D., Millennium: The Takeda Oncology Company

Building an infrastructure to support Translational Research and Medicine into the future is no small voyage. This talk will discuss how multi-disciplinary teams from across divisions and technology groups can effectively work together to define informatics and technologies roadmaps, brainstorm on technologies, select solutions, and define process improvements.

2:35 Application of CDISC and Operational Data Management Support to Biomarker Analysis for Clinical Studies

Carol Hill, Ph.D., Informatics Project Leader II, Clinical Data Integration, Duke Clinical Research Institute

Duke Clinical Research Institute has completed several biomarker studies for planned submission to regulatory agencies. Samples collected were released to research laboratories for biomarker analysis. Activities included defining data elements, supporting laboratory processes, applying data validation rules, and application of metadata for future use.

3:05 Knowledge Representation and Ontology in the Biomedical Domain

Olivier Bodenreider, Ph.D., Staff Scientist, Cognitive Science Branch, Lister Hill National Center for Biomedical Communications

Biomedical ontologies have become central resources to many aspects of life sciences, from the functional annotation of gene products to clinical documentation. Examples of biomedical ontologies will be provided. This talk also explores the role of biomedical ontologies in knowledge management, data integration and decision support.

3:35 Close of Conference

Developing Scalable IT to Support Life Science Data

Data Storage, Data Management and Analytics of Large Datasets

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» KEYNOTE SESSION: GETTING MORE VALUE AND GENERATING KNOWLEDGE FROM LARGE VOLUMES OF DATA AND STUDIES

11:00 Chairperson's Opening Remarks

Kevin Davies, Ph.D., Author, The $1,000 Genome; Editor-in-Chief, Bio-IT World

11:10 Generating More Knowledge from Our Data and More Value from Our Studies: The Value of Expert Skills

Anastasia M. Khoury Christianson, Ph.D., Senior Director, Discovery Information, AstraZeneca Pharmaceuticals

A major challenge in translational science is finding the relevant data, information and knowledge to allow meaningful correlation between pre-clinical observations and clinical outcomes. This presentation will concentrate on the key success factors for leveraging information, generating new knowledge and ensuring best informed decisions in our drug projects.

11:40 Burn the Hay or Build a Better Magnet to Find the Needles in our Haystack?

Martin Leach, Ph.D., Executive Director, IT for Discovery & Pre-Clinical Sciences (DPS), Merck

The expense and availability of technology enables compulsive hoarding, but at what cost to research? The ability to find things now relies heavily on search technology, data-mining or semantic-mining techniques that require proper classification of the structured and unstructured data, information, and knowledge. The presentation will explore some of the lessons learned at Merck and other organizations.

12:10 pm From Virtual Machine to Virtual Pharmaceutical Organization: Cloud-Based Translational Informatics for European IMI Projects

Eric Perakslis, Ph.D., Vice President, Research & Development IT, Johnson & Johnson

Anthony Rowe, Ph.D., Department of Computing, Imperial College, London

In this talk, we illustrate the design of the IT infrastructure for collaborative translational research in the UBIOPRED IMI project. The system is based on the Cloud computing infrastructure with a strong focus on supporting open collaborative research. The convergence of the two trends will realize a powerful new generation of IT infrastructure for life science.

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

1:45 Dessert in the Exhibit Hall

LARGE SCALE DATA STORAGE, RETRIEVAL & ACCESSIBILITY–OMIC DATA

2:15 Chairperson's Remarks

Matthew Trunnell, Manager, Research Computing, Broad Institute

2:20 Challenges in Management and Analysis of Sequencing Data at Large Scale

Matthew Trunnell, Manager, Research Computing, Broad Institute

The Broad's adoption of second-generation sequencing technologies has driven a 40-fold growth in our data repositories. This talk will discuss our ongoing adjustment to working at the multi-petabyte scale with particular emphasis on data storage, support for the analysis of multi-terabyte data sets, and new approaches to the management of unstructured research data.

2:50 From Genomic Data to Personalized Medicine

Karen Eilbeck, Ph.D., Assistant Professor, Human Genetics, & Biomedical Informatics, University of Utah School of Medicine

There are many challenges to managing and utilizing personal genomic data. Using ontologies to describe the reference features, the personal changes and the effect of those changes provides the means for a standard format for storage, exchange and analysis of these data.

3:20 Handling Large Scale Data

Anthony Masiello, Novartis Institutes for BioMedical Research

The past two decades have seen a proliferation of increasingly high throughput molecular biology platforms. Technologies from early microarrays, genotyping, SNP arrays, and now NGS data are giving us experience, but what are we learning from it? We will share case studies covering the evolution of whole genome technologies to highlight the infrastructure and ever changing needs associated with bringing high throughput platforms on-line and making them productive.

3:50 Sponsored Presentations *(Opportunities Available)*

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

5:20 Breakout Discussions in the Exhibit Hall

Proteomic Data Management

Brian Halligan, Ph.D., Scientist, Bioinformatics Research Center, Medical College of Wisconsin

- Acquisition of MS Data
- Analysis of MS Data
- What data to store and for how long?
- Data Storage formats
- Public Deposit of data

Management of Unstructured Data at Large Scale

Matthew Trunnell, Manager, Research Computing, Broad Institute

6:20 Close of Day

THURSDAY, FEBRUARY 24

LARGE SCALE DATA STORAGE, RETRIEVAL & ACCESSIBILITY—OMIC DATA CONTINUED

8:25 Chairperson's Remarks

9:00 Low Cost, Scalable Proteomics Data Analysis Using Amazon's Cloud Computing Services and Open Source Search Algorithms

Brian Halligan, Ph.D., Scientist, Bioinformatics Research Center, Medical College of Wisconsin

One of the major difficulties for many laboratories setting up proteomics programs has been obtaining and maintaining the computational infrastructure required for the analysis of the large flow of proteomics data. We describe a system that combines distributed cloud computing and open source software to allow laboratories to set up scalable virtual proteomics analysis clusters.

9:30 Storage, Analysis, and Visualization: Solutions for NGS Data Analysis

Michael Brudno, Ph.D., Assistant Professor & Canada Research Chair in Computational Biology, University of Toronto

The quantity of next generation sequencing data makes it difficult to transfer to a public cloud, and end users may lack computational facilities for analysis. We present a hybrid solution, where the sequencing centre becomes the provider of a private cloud used for easy data analysis, while visualization is handled with Savant.

10:00 The BioAssay Ontology Project: Novel tools to Query and Analyze Diverse Data

Stephan Schürer, Ph.D., Center for Computational Science, and Department of Pharmacology, Miller School of Medicine, University of Miami

We developed the first BioAssay Ontology (BAO) to organize and formally describe high-throughput and high-content data. BAO and novel software tools that are developed in this project enable querying, browsing and ultimately analysis and integration of diverse data sets. In contrast to established tools, our ontology-driven semantic description of biological screening data enables reasoning and thus can uncover hidden, inferred knowledge that is not explicitly defined in the ontology or the data. Using a large number of annotated assays - primarily derived from PubChem - we show how BAO tools make it easy to ask complex queries and enable intuitive retrieval of results that would otherwise require more complicated searches or could not be asked at all. We also illustrate BAO-facilitated analyses across large number of assays; the results can be useful for to evaluate and follow-up screening hits.

10:30 Refreshment Break in the Exhibit Hall

11:30 NGS Data Management, Analysis, and Visualization

Kip Lord Bodi, Genomics Core Director, Tufts Core Facility, Tufts University School of Medicine

While the amount of data generated by next-generation sequencing increases exponentially, the analysis of that data still represents a bottleneck in NGS workflows. One alternative to commercial software packages is Galaxy, an open source, web-based tool that can help individual researchers make sense of their NGS data.

12:00 pm Breaking Down Sequence Data for Massively Parallel Assembly on the Cloud

C. Titus Brown, Ph.D., Assistant Professor, Computer Science & Engineering and Microbiology and Molecular Genetics, Michigan State University

12:30 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:45 Ice Cream Refreshment Break in the Exhibit Hall

INFORMATICS FOR TRANSLATIONAL SCIENCE IN THE ERA OF MOLECULAR MEDICINE

2:15 Chairperson's Remarks

Matthew Onsum, Ph.D., Principal Scientist, Merrimack Pharmaceuticals

2:20 Bringing it All Together so the Sum is Greater than the Parts: Effective Knowledge Management in Translational Medicine

Eric Perakslis, Ph.D., Vice President, Research & Development IT, Johnson & Johnson

The focus would be the social engineering and leadership capabilities that are essential for successful translational science. These include incentive structures, traversing data domains, hypothesis generation and testing developmental strategies.

2:50 Using Systems Biology to Accelerate Oncology Drug Development

Matthew Onsum, Ph.D., Principal Scientist, Merrimack Pharmaceuticals

A review of how Merrimack used mathematical models of a cancer signaling pathways with biomarker measurements to identify cancer indications that would have a proportion of responders to our lead oncology drug. These simulations were used to prioritize our clinical development plans.

3:20 Sponsored Presentations *(Opportunity Available)*

3:50 Refreshment Break & Poster Awards in the Exhibit Hall

4:30 Pre-Competitive Translational Informatics—From Theory to Practice

Sandor Szalma, Ph.D., Senior Research Fellow, R&D Informatics, Centocor R&D, Inc.

The development of a translational medicine informatics infrastructure has been the underpinning of the translational research strategy of the pharmaceutical companies of Johnson & Johnson. This infrastructure has been built based on open-source platforms and is now forming the basis of pre-competitive sharing and mining of clinical and associated molecular profiling data.

5:00 Data Management Challenges in Translational Medicine

Isobel Anderson, Ph.D., Lead, Global TAU, Discovery Information, AstraZeneca

The integration of clinical and discovery data is key to a successful translation medicine strategy. In addition to the technical challenges, there are issues of data sharing, data standardization and consent. Here we discuss the relative merits of different approaches that have been implemented at AstraZeneca to make the right data accessible to all our researchers.

5:30 Building a Translational Informatics Vision

Sorena Nadaf, Director, Translational and Biomedical Informatics; CIO, HDFCCC Translational Informatics, University of California San Francisco

Dealing with the era of Molecular Medicine requires cutting edge information available at the fingertips of healthcare professionals. Building such a Translational Research environment depends upon an Informatics footprint that can bring these avenues together. Translational Informatics provides the answers.

6:00 Close of Day

FRIDAY, FEBRUARY 25

WORKFLOW-BASED INFORMATICS TO INCREASE PRODUCTIVITY IN R&D

8:25 Chairperson's Remarks

David Sedlock, Ph.D., Senior Director, R&D Systems, Millennium Pharmaceuticals, The Takeda Oncology Company

8:30 Development of a Media Request System to Manage Biological Reagent and Media Laboratory Supplies

David Sedlock, Ph.D., Senior Director, R&D Systems, Millennium Pharmaceuticals, The Takeda Oncology Company

Co-Author: Chris Perkins, Millennium Pharmaceuticals, The Takeda Oncology Company

The management of laboratory processes is an important contributor to the successful outcomes of basic and applied pharmaceutical research. We partnered with the Laboratory Operations group at Millennium to develop a structured workflow tool to handle requests and delivery of laboratory media to the scientists.

9:00 Compound Management System: Challenges and Opportunities for Improving Workflow Efficiency

Hongmei Huang, Ph.D., Director & Site Head, NIBR IT, Novartis

Richard Kuo, Ph.D., Lab Head, NIBR Compound Management, Novartis

As business processes mature and technology evolves, there is an increasing demand on IT and logistics teams to upgrade or replace legacy systems, in addition to maintaining the existing systems. We will present a case study of our endeavor to replace a legacy Compound Management request fulfillment system. Through this case study, we will shed light on the challenges, at times interesting dilemmas, and opportunities that upgrading a highly integrated software/hardware landscape presents.

10:00 Closing the Gap Between R&D and Manufacturing: Siemens' Vision on Collaborative Platforms Being Key to Future Pharma Success

Sponsored by SIEMENS

Rebecca Vangenechten, Business Development, Siemens AG, Pharma US

Regulatory developments and technological innovation are opening up new opportunities for companies to use lifecycle collaborative management to bring together parts of the value chain that have traditionally been relatively distant from each other. Collaboration will become increasingly important across the R&D / manufacturing interface and across the pharma / patient interface.

10:15 Generating New Scientific Insights Through Workflow Driven Search and Nonclinical Safety Data Integration

Sponsored by POINT CROSS

Shree Nath, Ph.D., VP, Pharmaceuticals & HLS, PointCross

We have combined parametric and text-based search with statistical indices, ontologies and collaborative workflows to provide scientists with novel ways of exploring safety and efficacy signals across semantically integrated nonclinical data. Techniques for rapidly extracting data and harmonizing both taxonomies and units from LIMS, and legacy paper/PDF reports will be illustrated using case studies from individual companies, and from collaborative consortia.

10:30 Refreshment Break in the Exhibit Hall

11:30 External Request Management System to Enhance Chemical Synthesis Data Management and Communications with CROs

Zhenbin Li, Ph.D., Senior Principal Analyst, Information Technology, Boehringer Ingelheim

With the increasing trend of external collaboration in research and development, a system to effectively manage data, workflows, and communications between pharmaceutical companies and CROs is necessary. ERMS (External Request Management System) is designed to facilitate external request processes for chemical synthesis, and can be extended into other collaborative research activities.

12:00 Talk Title to be Announced

Narayan Desai, Principal Experimental Systems Engineer, Mathematics and Computer Science Division, Argonne National Laboratory

12:30 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:45 Ice Cream Refreshment Break in the Exhibit Hall

CLINICAL DATA INTEGRATION & BIOMARKERS

1:30 Chairperson's Remarks

Carol Hill, Ph.D., Informatics Project Leader II, Clinical Data Integration, Duke Clinical Research Institute

1:35 Fusing Clinical and Omics Data to Facilitate Biomarker Discovery

Victor Lobanov, Director, Informatics & Pharmaceutical R&D, Johnson & Johnson Pharmaceutical

With the decreasing cost of omics platforms, composite biomarkers have been attracting more interest. Ability to fuse clinical data with omics results is at the core of effective development of composite biomarker models. We'll describe an internally developed platform that combines database technology, standard ontologies and a graphical user interface to facilitate biomarker discovery.

2:05 Collaborating Across Divisions to Develop Translational Research and Medicine Informatics and Technologies (TRAM-IT) Roadmaps

Csilla Csank, Ph.D., Millennium: The Takeda Oncology Company

Building an infrastructure to support Translational Research and Medicine into the future is no small voyage. This talk will discuss how multi-disciplinary teams from across divisions and technology groups can effectively work together to define informatics and technologies roadmaps, brainstorm on technologies, select solutions, and define process improvements.

2:35 Application of CDISC and Operational Data Management Support to Biomarker Analysis for Clinical Studies

Carol Hill, Ph.D., Informatics Project Leader II, Clinical Data Integration, Duke Clinical Research Institute

Duke Clinical Research Institute has completed several biomarker studies for planned submission to regulatory agencies. Samples collected were released to research laboratories for biomarker analysis. Activities included defining data elements, supporting laboratory processes, applying data validation rules, and application of metadata for future use.

3:05 Knowledge Representation and Ontology in the Biomedical Domain

Olivier Bodenreider, Ph.D., Staff Scientist, Cognitive Science Branch, Lister Hill National Center for Biomedical Communications

Biomedical ontologies have become central resources to many aspects of life sciences, from the functional annotation of gene products to clinical documentation. Examples of biomedical ontologies will be provided. This talk also explores the role of biomedical ontologies in knowledge management, data integration and decision support.

3:35 Close of Conference

Seventh Annual

Pathway-Targeted Therapies in Cancer

The Prevailing New Paradigm

WEDNESDAY, FEBRUARY 23

7:00 am Registration and Morning Coffee

8:00 Plenary Keynotes *(See Page 2 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

» KEYNOTE PRESENTATIONS: Key Pathways in Cancer

11:00 Chairperson's Opening Remarks

John McDonald, Ph.D., Professor, Biology, CSO, Ovarian Cancer Institute, Georgia Institute of Technology

11:10 The Paradigm of Targeted Drugs for the Treatment of Cancer: Inhibiting the BCR-ABL Pathway in Chronic Myeloid Leukemia

Paul W. Manley, Ph.D., Executive Director, Oncology Department, Novartis Institutes for Biomedical Research

In the 10 years that imatinib has been approved for the treatment of CML, the natural history of the disease has been transformed and we have learned much about targeting the BCR-ABL oncogenic signaling pathway that has also been translatable to other malignancies.

11:40 Future of Pathway-Driven Therapies

Neil W. Gibson, Ph.D., CSO, Pfizer Oncology

12:10 pm Personalizing Cancer Care – In Search of Durable Responses

David C. Heimbrook, Ph.D., Head of Discovery, Oncology Discovery and Translational Area, Roche

The recent successes of targeted therapies highlight both the opportunities and the challenges of personalizing cancer care. The combination of diagnostic tools with targeted agents can provide dramatic patient benefits, but improving the durability of clinical responses requires juxtaposition of clinical and pre-clinical studies to

12:40 Contextual Drug Discovery and Development via High-Content Analysis of Cellular Networks *Sponsored by* Lonza

John K. Westwick, Ph.D., President and CEO, Odyssey Thera, Inc.

We have developed an integrated paltform comprised of a diverse panel of live cell, protein complex-based high-content signal transduction assays, semi-automated cell culture, automated liquid handling, high throughput automated confocal microscopy, and the requisite automated image analysis, IT infrastructure and data mining capabilities. This platform enables system-wide signaling analysis and definition of compound mechanisms, selectivity and safety. The technology platform has been validated to expedite success rates of preclinical drug discovery and development programs.

1:45 Dessert in the Exhibit Hall

METASTASIS AND EMT: CELL ADHESION MARKERS

2:15 Chairperson's Remarks

2:20 Epithelial-Mesenchymal Transition and Metastasis

George Vande Woude, Ph.D., Director & Distinguished Scientific Investigator, Van Andel Institute

2:50 Modeling and Targeting Mesenchymal-Epithelial-Transition (MET) as an Essential Process for Tumor Re-Initiation and Metastasis

Fredika M. Robertson, Ph.D., Professor, Experimental Therapeutics, Director of Translational Research, The Morgan Welch Inflammatory Breast Cancer Research Program, The University of Texas M.D. Anderson Cancer Center

Inflammatory breast cancer is the most metastatic variant of locally advanced breast cancer, and displays rapid metastasis by cell aggregates defined as tumor emboli. IBC tumor emboli express abundant E-cadherin, and have distinct gene, protein, and microRNA signatures consistent with the process of mesenchymal-epithelial transition (MET), which is a program that supports accelerated metastasis and tumor re-initiation at sites distant from the primary tumor.

3:20 Overexpression of miR-429 Induces Mesenchymal-to-Epithelial Transition (MET) in Metastatic Ovarian Cancer Cells

John McDonald, Ph.D., Professor, Biology, CSO, Ovarian Cancer Institute, Georgia Institute of Technology

Molecular profiling of ovarian cancer (OC) cells with differing metastatic potentials identified significant differences in epithelial/mesenchymal cell biomarkers. Overexpression of miR-429 in mesenchymal ovarian cancer cells, resulted in reversal of the mesenchymal phenotype. Our results indicate that miR-429 may not only be a useful biomarker of EMT in ovarian cancer, but also of potential therapeutic value in reducing OC metastasis.

3:50 Translating Biomarker Discovery to Clinical Utility: A Case Study on Prostate Cancer *Sponsored by* ARIADNE

Elena Schwartz, Ph.D., Lead Scientist, Translational Medicine, Ariadne Genomics

Many potential cancer biomarkers are discovered daily, but only a handful ever makes it through clinical validation. A fast, efficient and accurate bioinformatics method, developed by Ariadne, establishes a much-needed bridge between biomarker theory and practice. To illustrate this powerful integrative knowledge-based approach, an analysis of prostate cancer literature and omics datasets are used to define prostate cancer pathways that can enrich the current understanding of disease mechanism and quickly focus research efforts on identifying potential biomarkers with clinical utility.

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

5:20 - 6:20 Breakout Discussions in the Exhibit Hall

Reactive Oxygen Species (ROS) and Cancer Progression

Hirak S. Basu, Ph.D., CSO, Colby Pharmaceuticals

- Targeting ROS to prevent prostate cancer progression
- Role of ROS in sugar metabolism in cancer vs. normal cells
- Targeting hypoxia induced ROS to develop novel cancer therapies
- Targeting radiation induced ROS to develop chemo-radiation sensitizers

Imaging Methods in Drug Development

Mehdi Adineh, Ph.D., Scientific Director, Core Laboratory, ACR

- Challenges of integrating imaging in clinical trials
- Using imaging as a window of drug action mechanism
- Role of an imaging CRO

Modeling and Targeting of the Mesenchymal –Epitheilal Transition (MET) & EMT

Moderator: Fredika M. Robertson, PhD., Professor, Experimental Therapeutics; Director, Translational Research, The Morgan Welch Inflammatory Breast Cancer Research Program, The University of Texas M.D., Anderson Cancer Center

- Signatures of EMT, MET, and Tumor Plasticity
- Approaches to Block Metastasis by Targeting EMT and MET
- MicroRNAs regulating EMT and MET: Potential uses as biomarkers and therapeutics
- Challenges in Identifying Targeted Therapeutics to Block MET vs EMT

HCA of Cellular Networks – Ready for Prime Time?

Moderator: John K. Westwick, Ph.D., President and CEO, Odyssey Thera, Inc.

- What is the "wish list" for an optimal merging of HCA and systems analysis?
- Key Challenges
  - Complexity is both the engine and the challenge
  - Descriptive/functional data –sets can lack mechanistic definition
  - Cell types for analysis
  - Standardization
  - Merging divergent data sets
- Key opportunities and applications

5:20 - 6:20 Breakout Discussions in the Exhibit Hall (continued)

- Systems-based discovery
- Defining target and drug mechanisms, selectivity
- Toxicology
- Expediting preclinical development
- Drug re-positioning
- Biomarkers

Personalizing Cancer Care – In Search of Durable Responses

Moderator: David C. Heimbrook, Ph.D., Global Head, Discovery Oncology, Pharma Research and Early Development, Roche

- Access to patient samples – role of mandatory biopsies?
- Selection of appropriate combinations of targeted therapies – complexity of preclinical modeling
- Polypharmacy of targeted agents– variable or fixed-dose combinations
- Regulatory and safety issues – combinations of unregistered drugs
- Focus on tumor profiling – are we missing opportunities in the tumor stroma?

Label-free Biosensors in Biochemical Assays for Signaling Research: Present and Future

Sriram Kumaraswamy, Ph. D., Product Manager, ForteBio, Inc.

- Biosensors for monitoring protein-protein interactions – technology round-up
- Label-free assays on the benchtop vs. in a core facility
- Microfluidics vs. Microplate-based: What lies ahead for label-free biosensors?

6:20 Close of Day

THURSDAY, FEBRUARY 24

CLINICAL UTILITY OF FINDING RELEVANT PATHWAYS

8:25 am Chairperson's Remarks

Zoltan Szallasi, M.D., Professor, Technical University of Denmark; Senior Scientist, Informatics Program, Children's Hospital Boston, Harvard Medical School

8:30 An Individualized Genomic Strategy Predicts Sensitivity of Aggressive Breast Cancers to HDAC Inhibitors

Andrea H. Bild, Ph.D., Assistant Professor, Department of Pharmacology and Toxicology, University of Utah

Treating unselected cancer patients dilutes proof of drug efficacy when a minority of patients respond to therapy. We present an efficient method using genomically derived drug response signatures to predict an individual tumor's sensitivity to a particular drug, offering a proof of concept with valproic acid (VPA).

9:00 RasPathway Signature in Breast and Other Types of Cancer

Tan Ince, M.D., Ph.D., Assistant Professor of Pathology, Director, Tumor Stem Cell Division, Interdisciplinary Stem Cell Institute, University of Miami Miller School of Medicine Biomedical Research

9:30 Genome Integrity Checkpoints as Functionally Defined Cancer Pathways with a Proven Potential to Personalize Cancer Treatment

Zoltan Szallasi, M.D., Professor, Technical University of Denmark and Senior Scientist, Informatics Program, Children's Hospital Boston, Harvard Medical School

In this talk we will use the actual measured activity or lack thereof of the various genome integrity checkpoints to produce a functional definition of cancer relevant pathways. We will demonstrate how the quantification of those predicts response to specific chemotherapeutic agents with remarkable accuracy.

10:00 Structural Basis of Shh Regulation by Neutralizing Antibody 5E1 and Hedgehog-Interacting Protein: Role of the Shh Pseudo-Active Site in Signaling

Henry R. Maun, Ph.D., Senior Research Associate, Genentech, Inc.

10:30 Refreshment Break in the Exhibit Hall

NOVEL TECHNOLOGIES FOR THE ISOLATION, DETECTION AND CHARACTERIZATION OF CTC

Chairperson: *Stefanie Jeffrey, M.D., Stanford University*

» 11:30 KEYNOTE PRESENTATION

Novel Technology Approaches to Circulating Tumor Cell Capture, Detection and Characterization

Richard Cote, M.D., FRCPath, Professor and Chair, Pathology; Director, University of Miami Biomedical Nanoscience Institute, University of Miami Miller School of Medicine

Detecting and characterizing circulating tumor cells (CTC) can allow an effective cancer patient management. The available approaches for CTC detection are curtailed by difficulties with sensitivity, specificity, efficiency, and high costs. Further, most of these technologies have only a limited ability to perform downstream molecular characterization of CTC. The presentation will describe our development of a parylene-based precision-engineered microfilter to capture CTC in blood, its functional comparison with the current FDA-approved platform, and our data with various cellular and molecular studies of CTC.

12:00 pm Multiplex Analysis of CTC

Stefanie Jeffrey, M.D., Chief, Surgical Oncology Research, Stanford University

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

1:45 Ice Cream Refreshment Break in the Exhibit Hall

2:20 Identification and Characterization of Circulating Tumor Cells with the CellSearch System

Leon W.M.M. Terstappen, M.D., Ph.D., Chair, Medical Cell BioPhysics, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente

In this presentation the choices made during the development of the CellSearch system will be reviewed as well as the results of the validation studies and the three separate prospective multi-center registration studies involving patients with metastatic breast, colorectal and prostate cancer.

2:50 Cell Magnetophoresis and Separation in Applications to CTC Isolation

Maciej Zborowski, Ph.D., Staff, Biomedical Engineering, Associate Professor, Molecular Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University

We quantitatively measure cell magnetophoretic mobility as a guiding parameter for the design of magnetic flow sorters and determination of cell magnetic susceptibility changes due to iron uptake. These approaches are applied to CTC separation from blood samples from cancer patients, including patients with head and neck squamous cell carcinoma and metastatic breast cancer.

3:20 Clinical Microfluidics and Molecular Analysis of CTCs

Shannon Stott, Ph.D., Research Associate, BioMEMS Resource Center / MGH Cancer Center, Massachusetts General Hospital, Harvard Medical School

Viable tumor-derived circulating tumor cells (CTCs) have been identified in peripheral blood from cancer patients and are the origin of intractable metastatic disease. We have developed a microchip based on a high-throughput microfluidic mixing approach for the isolation of extremely rare CTCs in blood and showed clinical utility in cancer patients.

3:50 Refreshment Break & Poster Awards in the Exhibit Hall

CLINICAL UTILITY OF FINDING RELEVANT PATHWAYS

4:30 The Cancer Genome Atlas: An Integrated Genomic Analysis Identifies Clinically Relevant Subtypes of Glioblastoma

David Neil Hayes, M.D., M.P.H., Assistant Professor, Clinical Research, Hematology/Oncology, University of North Carolina, Chapel Hill

Recent work by the Cancer Genome Atlas has catalogued a set of molecular alterations in high grade malignant gliomas. I will describe the manner in which the catalogue of mutations and other genomic aberrations coordinate in human tumors and how these might be exploited for therapeutic benefit.

5:00 Network-Based, Integrative Identification of Biological Pathways that Drive Breast Cancer Clinical Subtypes

Gábor Balázsi, Ph.D., Assistant Professor, Systems Biology, The University of Texas, M.D. Anderson Cancer Center

We identified "driver networks" for various breast cancer subtypes that were more reproducible across independent data sets than gene lists obtained by either standard gene expression analysis, or solely gene expression-based network analysis. The functional relevance of a subset of driver genes could be confirmed by siRNA experiments *in vitro*.

5:30 A Phenotypic Drug Discovery Approach to Discover Novel Inhibitors of Tumor Angiogenesis

Mark T. Uhlik, Ph.D., Senior Research Scientist, Angiogenesis & Tumor Microenvironment Biology, Eli Lilly & Company

6:00 Close of Day

FRIDAY, FEBRUARY 25

BRINGING PATHWAYS TO PATIENTS

8:30 am Chairperson's Remarks

Michael R. Briggs, Ph.D., Sr. Director, Head, Biology, Vertex Pharmaceuticals, Inc.

8:35 Pathways and Translational Medicine, Pre-Clinical to Clinical Activities

Michael R. Briggs, Ph.D., Sr. Director, Head, Biology, Vertex Pharmaceuticals, Inc.

9:05 Molecular Profiling of Tumor to Select Therapy in Clinical Trials of Pancreatic Cancer

Ramesh K. Ramanathan, M.D., Medical Director, TGen Clinical Research Services, Scottsdale Health Care; Clinical Professor of Medicine, University of Arizona, College of Medicine, Phoenix

Advanced pancreatic cancer has a very poor prognosis and molecular prognostic factors of therapy have not been identified. This talk will focus on the use of molecular profiling of patients' tumors to select target based therapy in clinical trials.

9:35 Translating Gene Expression into Clinical Care: Sarcomas as a Paradigm

Robert B. West, M.D., Ph.D., Associate Professor, Department of Pathology, Stanford University Medical Center

Sarcomas include many subtypes with specific underlying molecular events driving oncogenesis. Gene expression profiling and other molecular studies have identified oncogenic pathways of particular importance in sarcomas which can be targeted by investigational drugs.

10:05 Sponsored Presentation *(Opportunity Available)*

10:20 Coffee Break

HOT PATHWAYS IN CANCER STEM CELLS: ULTRA-MALIGNANT CELLS

10:55 Chairperson's Remarks

Enal Razvi, Ph.D., Systems Biosciences SBI

11:00 Targeting Cancer Stem Cell Self Renewal

Austin Gurney, Ph.D., Senior Vice President, Molecular and Cellular Biology, OncoMed Pharmaceuticals

Stem cell pathways such as Notch and Wnt have long been implicated in cancer. A new generation of therapeutics designed to modulate these pathways demonstrates remarkable ability to reduce the tumorigenicity of a broad range of tumor types by forcing cancer stem cell differentiation.

11:30 Regulation of Self-Renewal in Cancer Stem Cells

Pier Giuseppe Pelicci, M.D., Ph.D., Chairman, Department of Experimental Oncology, European Institute of Oncology, Milan, Italy

Our findings suggest that asymmetric divisions of stem cells function as a mechanism of tumor suppression, that CSC quiescence is critical to the maintenance of the transformed clone and that symmetric divisions of CSCs permits its geometric expansion. I will discuss the implications of these findings for the mechanisms regulating checkpoint activation in normal tissue SCs and DNA damage response.

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

1:35 Non-Hierarchical Heterogeneity in Melanoma

Elsa Quintana, Ph.D., Postdoctoral Fellow, Life Sciences Institute, Department of Internal Medicine and Center for Stem Cell Biology, University of Michigan

In cancers that follow a stem cell model, phenotypically distinct tumorigenic cells give rise to diverse non-tumorigenic progeny in a hierarchical process similar to differentiation. In contrast to this model our results indicate that melanoma has many phenotypically diverse tumorigenic cells that undergo reversible changes in phenotype over time.

2:05 VEGF-Dependent and –Independent Angiogenesis Pathways

Napoleone Ferrara, Ph.D., Fellow, Tumor Biology & Angiogenesis, Genentech, Inc.

2:35 Identifying Novel microRNA-Gene Networks in Colon Cancer Stem Cells

Dimitrios Iliopoulos, Ph.D., Assistant Professor, Cancer Immunology & AIDS, Dana-Farber Cancer Institute/Harvard Medical School

We have identified the gene networks involved in colon cancer stem cell formation and maintenance and novel drugs that target these networks and inhibit colon cancer tumor growth and prolong remission *in vivo*.

3:05 Panel Discussion: Emerging Themes in Cancer Stem Cells (CSCs)

In this panel, we will explore the nature of cancer stem cells, and seek to understand their biology. There is much uncertainty as to the identity of CSCs *in vivo* and their roles in the primary tumor versus in metastases. This panel discussion will complement the presentations in this session to provide the delegates a balanced perspective on the current state of this field and outlook for the future, especially as it relates to cancer therapeutics.

Major Topics to be Discussed at the Panel Discussion:

- Evidence for the Existence of CSCs in Various Cancers
- Molecular Identity of CSCs
- Targeting CSCs as Therapeutic Modalities

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

Additional Panelist: Gang Li, Ph.D., Senior Stem Cell Research Scientist, System Biosciences SBI

3:35 Close of Conference

WEDNESDAY, FEBRUARY 23

7:00 am Registration and Morning Coffee

8:00 Plenary Keynotes *(See Page 2 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

STEM CELLS: ADVANCING REGENERATIVE MEDICINE

11:00 Chairperson's Opening Remarks
Todd McDevitt, Ph.D., Associate Professor, Biomedical Engineering, Georgia Institute of Technology

» KEYNOTE PRESENTATION:

11:10 Novel Approaches to Stem Cell Based Lung, Kidney, Pancreatic and Intestinal Regenerative Therapies
David Warburton, M.D., D.Sc., Professor, Director, Developmental Biology & Regenerative Medicine, Children's Hospital Los Angeles, University of Southern California
Amniotic fluid is a novel, ethically neutral and scalable source of stem cells, capable of contributing to tissues in all three germ layers. Applications of this approach to lung, kidney and pancreatic regenerative therapies include stem cell based tissue engineering of hollow viscuses such as bronchus, intestine and the genitourinary tract.

11:40 Engineering Stem Cell Microenvironments for Directed Differentiation
Todd McDevitt, Ph.D., Associate Professor, Biomedical Engineering, Georgia Institute of Technology
Stem cell phenotype is directly related to the summation of environmental cues capable of influencing cell fate decisions. Thus, integrating control of environmental factors via different types of engineering approaches enables new routes to direct differentiation of stem cells in more efficient, robust and scalable manners.

12:10 pm Differentiating Cardiac Cells for Regenerative Therapy
Kathryn Ivey, Ph.D., Staff Research Investigator, Stem Cell Core Director, Gladstone Institute of Cardiovascular Disease
We have been exploring the use of microRNAs to direct differentiation of mouse or human ES cells into the cardiac lineage. More recently, we have identified factors that can directly program cardiac fibroblasts into functional cardiac muscle cells. These types of approaches will impact the future of regenerative cardiac therapies.

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

1:45 Dessert in the Exhibit Hall

2:15 Chairperson's Remarks
Paul J. Turek, M.D., FACS, FRSM, President, American Society of Andrology; Director, The Turek Clinic

2:20 Effects of Long Term Culture on Human Embryonic Stem Cell Aging
Andrew Lee, Ph.D. Candidate, Medicine, Radiology, Stanford University
Challenges that prevent safe and efficacious translation of stem cell therapies to the clinic include prolonged *in vitro* culture of pluripotent stem cell lines, failure of therapeutic derivatives to engraft following *in vivo* transplantation, and potential for teratoma formation. This talk will summarize progress in addressing these issues for future clinical application.

2:50 Combinatorial Development of Biomaterials for Tissue Engineering and Drug Delivery
Daniel G. Anderson, Ph.D., Professor, Chemical Engineering, Harvard-MIT Division of Health Sciences & Technology, David H. Koch Institute for Integrative Cancer Research
We have developed automated methods which have been applied towards the development of new methods to control stem cell behavior, as well as vehicles for drug delivery. In particular, these combinatorial libraries of different biomaterials have enabled new methods for microparticulate drug delivery, non-viral gene therapy, siRNA delivery, and vaccines.

3:20 Using Testicular Germline Stem Cells for an *in vitro* Human Reproductive Toxicology Assay
Paul J. Turek, M.D., President, American Society of Andrology; Director, The Turek Clinic
Cell based *in vitro* bioassays could streamline drug development by eliminating costly animal studies currently employed in drug testing paradigms. This lecture presents the biological rationale for, and feasibility of, a germline stem cell based model of human spermatogenesis.

3:50 Sponsored Presentations *(Opportunities Available)*

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

5:20 Breakout Discussions in the Exhibit Hall

6:20 Close of Day

THURSDAY, FEBRUARY 24

IPS CELLS: REALIZING PERSONALIZED THERAPIES

8:55 Chairperson's Remarks
Larry A. Couture, Ph.D., Senior Vice President, Center for Applied Technology Development, Beckman Research Institute of City of Hope

9:00 Comparison of Human Pluripotent Stem Cells
Kiichiro Tomoda, Ph.D., Research Scientist, Gladstone Institute of Cardiovascular Disease, The Gladstone Institute, University of California, San Francisco
Human Pluripotent stem cells (human embryonic stem cells (hESCs) and human induced pluripotent stem cells (hiPSCs) which can differentiate into cell types of the three germ layers in vitro and in vivo, are attractive sources for human cell replacement therapies; however, we still do not fully understand many properties of hiPSCs. To gain insight into hiPSCs, we have been comparing several hiPSCs with hESCs lines in terms of gene expression profile, proliferation and differentiation potentials. Our latest results from the comparison will be discussed in the meeting.

9:30 Challenges for Efficient Production of Human iPS cells
Bonnie Barrilleaux, Ph.D., Postdoctoral Fellow, CIRM Stem Cell Training Program, Department of Cell Biology and Human Anatomy, School of Medicine, University of California, Davis
Viral gene delivery is currently the most reliable option for delivering reprogramming genes to produce human induced pluripotent stem cells (hiPSCs). Using amphotropic virus, we have generated and characterized three hiPSC lines. However, commonly used pluripotency-inducing genes (including c-Myc, Oct4, SOX2, and KLF4) all have known links to cancer, necessitating higher biosafety level handling requirements when producing pantropic lentivirus encoding these genes. To address these biosafety issues, we describe the use of ecotropic lentivirus for overexpression of oncogenes in human cells, as well as polymer complexation to enhance transduction while avoiding aerosol-forming centrifugation of viral particles.

10:00 The Road to Translation of iPS Cells
Marie Csete, M.D., Ph.D., Executive Vice President, Research & Development, Organovo, Inc.
The lecture will review promising (closest to clinic) potential applications for iPS cells, with emphasis on the bottlenecks. The lecture will review the importance of iPS cells in drug discovery, with emphasis on the need for three-dimensional in vitro tissue culture models.

10:30 Refreshment Break in the Exhibit Hall

11:30 Regulatory and Manufacturing Considerations for the Development of Autologous Induced Pluripotent Stem Cell Therapies

Larry A. Couture, Ph.D., Senior Vice President, Center for Applied Technology Development, Beckman Research Institute of City of Hope

Perhaps the most important potential application for induced pluripotent stem cells (iPSC) is their use as autologous cell therapeutics. While human embryonic stem cells (hESC) and iPSC are treated by the FDA according to established regulations for cell therapeutics, the application of these regulations in establishing safety and manufacturing reproducibility of an autologous cell therapy will be a significant regulatory and manufacturing challenge. We will consider the nature of these challenges and discuss possible approaches to overcoming them.

12:00 pm Panel Discussion with Morning Speakers

12:30 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:45 Ice Cream Refreshment Break in the Exhibit Hall

2:15 Chairperson's Remarks

Gay M. Crooks, Professor, Pathology & Laboratory Medicine, University of California, Los Angeles

2:20 Mesoderm Commitment and Blood Formation from Human Pluripotent Stem Cells

Gay M. Crooks, Professor, Pathology & Laboratory Medicine, University of California, Los Angeles

CD34+ cells produced from hPSC harbor intrinsic, functional differences from the "adult" CD34+ cells used in clinical transplantation. By identifying the earliest stage of mesoderm commitment from hPSC, we can understand and manipulate the process by which blood formation from hPSC is regulated.

2:50 Therapeutic Human Pluripotent Stem Cell-Derived Cells to Treat Cancer and HIV/AIDS

Dan S. Kaufman, M.D., Ph.D., Associate Professor, Medicine, Division of Hematology, Oncology, and Transplantation; Associate Director, Stem Cell Institute; University of Minnesota

hESC and iPSC-derived NK cells can preferentially kill HIV-infected cells. We aim to use human pluripotent stem cells as a resource for new clinical immunotherapeutic applications against various diseases. Separate studies by our group have derived vascular cells and osteogenic cells from hESCs and iPSCs suitable for regenerative medicine therapies.

3:20 Novel microRNAs in hESC and Pluripotent Cells

Ronald P. Hart, Ph.D., Cell Biology & Neuroscience, Rutgers Stem Cell Research Center, Rutgers University

Using deep sequencing of small RNAs, we identified novel candidate microRNA genes in human embryonic stem cells and early neuronal precursor cells. Since a large number of differentiation mechanisms require microRNAs, we propose that these novel microRNAs serve to establish phenotypic stability during commitment to new cell types.

3:50 Refreshment Break and Poster Awards in the Exhibit Hall

4:30 Generation of Functional Dopaminergic Neurons from Human iPSCs under Xeno-Free Defined Conditions for Treating Parkinson's Disease

Xianmin Zeng, Ph.D., Associate Professor and Director, CIRM Shared Research Laboratory for Stem Cells & Aging, Buck Institute for Age Research

Neural and dopaminergic differentiation measured by various molecular and cellular methods in iPSCs is efficient and similar to in hESCs using a scalable defined cultured system readily transferable to a GMP facility. Importantly, iPSC-derived dopaminergic neurons could improve symptoms of PD in a pre-clinical rodent model, and be genetically modified efficiently.

5:00 Reprogramming Tumor-Specific T Cells Using iPS Technology for the Treatment of Patients with Cancer

Nicholas P. Restifo, M.D., Principal Investigator, National Cancer Institute

Anti-tumor T cells can induce long-lasting disappearance of metastatic cancer, but terminal differentiation, exhaustion and senescence of these T cells can hamper their effectiveness. Our laboratory and clinical teams at the NIH Clinical Center seek academic and industrial partners to rapidly translate iPS technology into new clinical cancer immunotherapy trials.

5:30 Panel Discussion with Afternoon Speakers

6:00 Close of Day

RIDAY, FEBRUARY 25

TRANSLATION: BASIC STEM CELL RESEARCH TO CLINICAL APPLICATIONS

8:30 Chairperson's Remarks

Greg Bonfiglio, Managing Partner, Proteus Venture Partners

8:35 Translating Stem Cell Research: Challenges at the Research Frontier

David Magnus, Ph.D., Director, Stanford Center for Biomedical Ethics; Professor, Medicine & Biomedical Ethics, Pediatrics, Stanford University

The tremendous public expectations placed upon stem cell research means that the public and many patients are impatient for treatments. The combination of hype and failure to swiftly deliver on promises of treatment is a potential land mine for the field of stem cell research. This talk will discuss the challenges of stem cell research and clinical trials.

9:05 Commercialization of Regenerative Medicine: Translating Great Science into Successful Business

Greg Bonfiglio, Managing Partner, Proteus Venture Partners

The presentation will address moving Regenerative Medicine from bench to bedside. We will review the market for Regenerative Medicine Companies, discuss the current funding environment, and examine the venture process. Ultimately, we will outline a new capital efficient model for the development of Regenerative Medicine technologies.

9:35 Clinically-Compliant Differentiation of hESCs for the Treatment of Spinal Cord Injury and Disease

Hans S. Keirstead, Ph.D., Associate Professor, Anatomy and Neurobiology, University of California, Irvine

Human cell-based therapies require well defined, high purity populations of cells. We have generated FDA-compliant human embryonic stem cell derivates suitable for addressing clinical indications. Pre-clinical data supporting a clinical trial will be reviewed, with an emphasis on the common themes pertinent to human embryonic stem cell translation.

10:05 Sponsored Presentation *(Opportunity Available)*

10:20 Coffee Break

11:00 Challenges and Opportunities in Characterization of Cell-Based Therapies

Malcolm Moos Jr., M.D., Ph.D., Medical Officer, Cell and Tissue Therapy Branch, Cellular and Gene Therapies, FDA CBER

11:30 Hematopoietic Stem Cell Transplantation for Autoimmune Diseases

Richard Burt, M.D., Associate Professor, Division of Immunotherapy, Northwestern University Feinberg School of Medicine

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

1:30 Chairperson's Remarks

Robert J. Deans, Senior Vice President, Regenerative Medicine, Athersys, Inc.

1:35 GRNCM1: Human Embryonic Stem Cell-Derived Cardiomyocytes for the Treatment of Heart Failure

Katharine Spink, Ph.D., Vice President of Operations and RegMed Programs, Geron Corporation

This presentation will discuss Geron's GRNCM1 program, in which we are developing hESC-derived cardiomyocytes for the treatment of heart failure, including methods for high efficiency differentiation of cardiomyocytes from hESCs, characterization of the resulting cell population, pre-clinical data on cellular function, and steps for the development of this product towards the clinic.

2:05 Brain and Spinal Cord Injury: Mechanistic Pathways by which Adherent Stem Cells Modulate Inflammation and Mediate Recovery

Robert J. Deans, Senior Vice President, Regenerative Medicine, Athersys, Inc.

2:35 Immune Targeting of Glioblastoma Cancer Stem Cells

John S. Yu, M.D., Professor and Vice-Chair, Neurosurgery, Cedars-Sinai Medical Center; Chairman and CSO, Immunocellular Therapeutics, Ltd. (IMUC)

In order to target cancer stem cells, we utilized a dendritic cell vaccine strategy to target tumor specific antigens what are overexpressed on glioblastoma cancer stem cells. Of 17 glioblastoma patients treated in this phase 1 trial, 41 percent of patients developed an antigen specific interferon gamma response after vaccination. The median progression free survival was 17.7 months and the median survival was not reached to date. Given these findings, a multi-institutional randomized phase 2 trial has been initiated.

3:05 Close of Conference

WEDNESDAY, FEBRUARY 23

7:00 am Registration and Morning Coffee

8:00 Plenary Keynotes *(See Page 2 for Details)*

9:40 Grand Opening Refreshment Break in the Exhibit Hall

PENETRATION & DISTRIBUTION OF SOLID TUMORS

11:00 Chairperson's Opening Remarks

Gregory P. Adams, Ph.D., Co-Leader, Developmental Therapeutics Program, Fox Chase Cancer Center

11:10 Tumor Penetration of Therapeutic Antibodies–Implications for Cancer Therapy

David Blakey, Ph.D., Chief Scientist, Oncology Discovery, 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 on antibody distribution within tumors will be reviewed and the implications for therapy will be discussed.

11:40 The Influence of Affinity and Internalization on Tumor Targeting and Penetration of Antibodies

Gregory P. Adams, Ph.D., Co-Leader, Developmental Therapeutics Program, Fox Chase Cancer Center

While a number of antibodies have been licensed for the treatment of cancer, the affinity associated with optimal targeting and penetration of solid tumors has yet to be determined. We will present our studies employing a panel of anti-HER2 human IgG molecules that bind over a range of affinities to the identical epitope on HER2 and discuss the impact of affinity and antigen-mediated internalization on targeting and penetration.

NANOPARTICLES FOR TARGETED DELIVERY

12:10 pm Opportunities and Challenges in the Development of Targeted Nanomedicines

Theresa M. Allen, Ph.D., Division Chair, Drug Delivery, Centre for Drug Research & Development; Professor Emeritus, Pharmacology & Oncology, University of Alberta

Ligand-targeted nanomedicines (LTN) that deliver drugs, including siRNAs, selectively to target cells may, or may not, improve therapeutic responses versus passively targeted nanomedicines. Improvements in outcomes for LTN must be of sufficient magnitude to compensate for the additional complexities (equals increased costs) involved in their development.

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

1:45 Dessert in the Exhibit Hall

2:15 Chairperson's Remarks

Theresa M. Allen, Ph.D., Division Chair, Drug Delivery, Centre for Drug Research & Development; Professor Emeritus, Pharmacology & Oncology, University of Alberta

2:20 Therapeutic Cell Engineering Using Cell Surface-Conjugated Synthetic Nanoparticles

Darrell J. Irvine, Associate Professor, Massachusetts Institute of Technology

An approach to enhance adoptive T-cell therapy of cancer and other cell therapies will be described, based on the direct conjugation of drug-loaded nanoparticles to the surface of therapeutic cells. We show how this approach dramatically enhances the potency of cytokine or small-molecule adjuvant drugs, using dosages that have no effect when given by traditional systemic routes.

2:50 Understanding Key Delivery Aspects Controlling the Therapeutic Window of MM-302: HER2-Targeted Liposomal Doxorubicin

Bart Hendriks, Ph.D., Associate Director and Research Team Leader, MM-302, Merrimack Pharmaceuticals

MM-302 is the first of a new class of nanoparticle drugs that is designed to deliver the cytotoxic drug, doxorubicin, specifically to tumor types that over-express the Her2 receptor. Pre-clinical data and mathematical modeling approaches have been used to demonstrate how HER2 levels and vascular parameters are key factors that control the delivery of MM-302 to target and non-target cells.

3:20 POSTER SPOTLIGHT: Targeting the Transforming Growth Factor-Beta (TGF-Beta) Family: A New Generation of Cancer Therapeutic

John Zwaagstra, National Research Council of Canada

3:50 Sponsored Presentations *(Opportunities Available)*

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

5:20 Breakout Discussions in the Exhibit Hall

Clinical and Regulatory Strategies to Optimize the Development Process for Cancer Biotherapeutics

Moderator: To be Announced

- Ideal patient population for immunotherapeutics
- Adaptive trial designs
- Challenges with toxicity and safety
- Regulatory considerations

Challenges of Developing Antibody-Drug Conjugates

Moderator: Hans-Peter Gerber, Ph.D., Senior Director, BioConjugate/Vascular Biology Group, Center for Integrative Biology and Biotherapeutics (CIBB), Pfizer Biotherapeutics

- Selecting the size/PK balance for optimal tumor penetration and reduced clearance
- Strategies to identify " cleaner" targets
- How the target biology impacts on the type of linker and product selected
- Issues regarding selection of payloads
- Issues regarding the safety profile and minimizing liver toxicity

Challenges of Targeting Cancer Stem Cells

Moderator: Norman J. Maitland, Ph.D., CSO, Procure Therapeutics Ltd.

- Approaches to the identification and evaluation of new cancer stem cell targets
- Payloads that overcome the enhanced resistance of cancer stem cells
- Potential safety issues
- Strategy for entering clinical trials

Cost/Benefit Ratio of New Treatments for Cancer

Moderator: Theresa M. Allen, Ph.D., Division Chair, Drug Delivery, Centre for Drug Research & Development; Professor Emeritus, Pharmacology & Oncology, University of Alberta

- Are the costs beginning to exceed the benefits? Are these costs limiting access? Will this prevent their approval or sales in countries other than the USA?
- What would be an appropriate balance between the costs and benefits of new therapies: Are there guidelines for this? Should there be guidelines?
- Improved quality of life is often not incorporated into cost/benefit analyses. How could this be approached?

Antibodies versus Alternative Scaffolds: Pros and Cons

Moderators: David Blakey, Ph.D., Chief Scientist, Oncology Discovery, AstraZeneca
Josefin-Beate (Josi) Holz, Ph.D., CMO, Drug Development, Ablynx NV

- Focus on tumor penetration, specificity, half-life and toxic load
- Weighing up Fc-effector function versus immunological side effects
- Small immunoglobulin fragments versus alternative scaffolds
- Challenges with manufacturing and intellectual property

6:20 Close of Day

THURSDAY, FEBRUARY 24

BIOMARKERS FOR PATIENT SELECTION, SAFETY & TREATMENT

8:25 Chairperson's Remarks

Michael Kalos, Ph.D., Director, Translational and Correlative Studies Laboratory, University of Pennsylvania School of Medicine

8:30 Translational Sciences in Oncology: A Risk Mitigation Strategy

Theresa LaVallee, Ph.D., Director, Translational Sciences Oncology, MedImmune

Oncology drug development has a low success rate in the industry. Given the heterogeneity of tumors and multiple lines of therapy, odds are against having the handful of phase 2 trials most drugs are evaluated in being the successful ones. The basis of translational sciences is to have a data rich development plan that enables decisions about clinical trial design and internal development decisions.

9:00 The Roles of IGFBPs in Both Mechanisms of Action and Mechanisms of Resistance for Trastuzumab-Mediated Cancer Growth Inhibition

Wen Jin Wu, M.D., Ph.D., Principal Investigator, Division of Monoclonal Antibodies, Food and Drug Administration (tentative)

We found that trastuzumab induced secretion of insulin-like growth factor binding protein-3 (IGFBP3), an inhibitory factor of breast cancers, in trastuzumab-sensitive breast cancer cells, indicating that IGFBP3 may serve as a predictive biomarker for determining therapeutic response. We also found that high levels of IGFBP-2 contribute to the trastuzumab-resistance, suggesting IGFBP2 may be used as a therapeutic target.

9:30 Translation of Imaging Based Biomarkers from Research to Clinical Drug Trials

Nicholas Van Bruggen, Ph.D., Head, Biomedical Imaging, Genentech

Imaging based biomarkers can influence drug developers decisions by providing early evidence of biological activity. The choice of the imaging biomarker is often selected from understanding the MoA as determined from nonclinical imaging studies, and ideally should reflect its efficacy. This presentation will highlight several examples of the translation of imaging based biomarker from research to clinical drug trials.

10:00 Development of OncologyMAP™: A Public-Private Partnership Dedicated to Providing a Powerful New Tool for Discovery of Biomarker Patterns in Cancer

Sponsored by RBM RULES•BASED MEDICINE

Ralph McDade, Ph.D., VP & Strategic Development Officer, Rules Based Medicine

OncologyMAP is the newest service offering in Rules-Based Medicine's portfolio of Multi-Analyte Profiles (MAPs). Developed in partnership with the National Cancer Institute's Proteomics Initiative, OncologyMAP contains 101 quantitative, multiplexed immunoassays for measuring cancer-related proteins in serum, plasma or tissue extracts. This novel tool offers an unparalleled platform to aid in the discovery and development of novel therapies and diagnostics in oncology. The OncologyMAP is powered by RBM's data-driven approach to efficiently and cost-effectively discover useful biomarker patterns.

10:15 Layered-Immunohistochemistry: A Novel Platform for Predictive and Prognostic Diagnostics for Personalized Medicine

Sponsored by 20/20 GENESYSTEMS

Michael S. Lebowitz, Ph.D., Director of R & D, 20/20 GeneSystems, Inc.

L-IHC is a technology for detection of >10 protein biomarkers in standard histological (FFPE) samples of only 5µm. L-IHC allows for complete pathway profiling and determination of pathway activation status enabling development of companion diagnostic tests.

10:30 Refreshment Break in the Exhibit Hall

RATIONAL DESIGN FOR MORE EFFECTIVE MOLECULES

11:30 Rational Design Approaches to Improve Bispecific Antibodies

Matthew K. Robinson , Ph.D., Assistant Professor, Developmental Therapeutics Program, Fox Chase Cancer Center

Increased emphasis is being placed on the development of bispecific antibodies for the treatment of cancer. Work will be presented on our efforts to improve the efficacy of bispecific-scFv antibodies by incorporating rational design approaches into the development and construction process.

12:00 pm Rational Engineering of Antibody-Like Molecules for Therapeutic Use

Neeraj Kohli, Protein Expression Group Leader, Therapeutic Design, Merrimack Pharmaceuticals, Inc.

Multispecific antibody-like molecules targeting growth factor receptor signaling pathways comprise a promising new class of anti-cancer agents. We use systems biology approaches to identify design characteristics and rational antibody engineering techniques to construct molecules that have these optimal avidities, affinities, and robust pharmaceutical properties. Application of this approach to a bispecific molecule targeting two receptor tyrosine kinases will be presented.

12:30 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

1:45 Ice Cream Refreshment Break in the Exhibit Hall

2:15 Chairperson's Remarks

Alan L. Epstein, M.D., Ph.D., Professor, Pathology, University of Southern California Keck School of Medicine

DEVELOPMENTS WITH ANTIBODY DRUG CONJUGATES

» 2:20 KEYNOTE PRESENTATION: Clinical Trial Results of Trastuzumab-DM1, a First-in-Class HER2 Antibody Drug Conjugate, in Patients with HER2+ Metastatic Breast Cancer

Yu-Waye Chu, M.D., Product Development, Oncology, Genentech, Inc.

A single-arm, Phase II study (TDM4374g) showed an objective response of 32.7% in 110 patients. Preliminary results of a randomized Phase II study (TDM4450g) demonstrate favorable safety and efficacy. Phase III trials of T-DM1 and T-DM1 plus pertuzumab are ongoing in the first line setting and in previously treated patients.

2:50 Calicheamicin Antibody-Drug Conjugates and Beyond

Puja Sapra, Ph.D., Director Bioconjugates, Oncology Research Unit Pfizer, Inc.

Differences in the mechanism of action between calicheamicin (DNA double strand break inducing) and tubulin inhibitor based antibody drug conjugates will be reviewed. The development of novel antibody drug conjugates targeting cancer stem cells and novel strategies to identify novel drug linker compounds with selectivity for tumor cells will be discussed.

3:20 Early Stage Antibody Drug Conjugate Development: Preparations for the Clinic

Dowdy Jackson, Scientist, Oncology, MedImmune, Inc.

Our presentation will cover the following topics: An overview of the ADC development process at MedImmune; Examining antibody internalization and intracellular localization; Analyzing challenges associated with ADC development.

3:50 Refreshment Break & Poster Awards in the Exhibit Hall

4:30 Development of Antibody-Drug Conjugates (ADCs) as Novel Cancer Therapeutics

Jonathan G. Drachman, M.D., Senior Vice President, Research & Translational Medicine, Seattle Genetics, Inc.

Antibody-drug conjugates represent an important and rapidly expanding class of empowered antibodies for the treatment of cancer. This presentation will focus on the pre-clinical and clinical development of ADCs utilizing the potent auristatin class of antimitotic drugs. Data from brentuximab vedotin (SGN-35), SGN-75, and other pipeline programs at Seattle Genetics will be discussed.

5:00 The Impact of Linker on the Biodistribution and Metabolism of Antibody-Maytansinoid Conjugates

Hans Erickson, Ph.D., Principal Scientist, Biochemistry, ImmunoGen, Inc.

Several antibody-maytansinoid conjugates (AMCs) are being evaluated in clinical

trials. The most advanced AMC, Trastuzumab-DM1 (T-DM1), utilizes an uncleavable thioether-based linker. How the choice of cleavable disulfide based linkers and uncleavable thioether based linkers influence the pre-clinical efficacy, tumor localization and activation, and clearance of AMCs will be discussed.

5:30 Discovering and Designing Immunotoxins for the Treatment of Solid Cancers

Glen MacDonald, Ph.D., CSO and Vice President, Operations, Viventia Biotechnologies, Inc.

Conventional antibody-based biologics have resulted in modest clinical benefit for solid cancers. We have engineered antibody-toxin fusion proteins to create a pipeline of highly potent anti-cancer agents designed for use against solid cancers. Our unique discovery approach, molecular design rationale, biological characterization and clinical experience with these molecules are presented.

6:00 Nanobodies as Novel Therapeutic Approaches Targeting Cancer Epitopes

Josefin-Beate (Josi) Holz, Ph.D., CMO, Drug Development, Ablynx nv

This talk will describe the discovery of Nanobodies targeting cancer epitopes including GPCRs, and present a case study of the stem cell mobilizing Nanobody development candidate from bench to bedside. Challenges experienced and opportunities in translational research will be included.

6:30 Close of Day

FRIDAY, FEBRUARY 25

ADVANCES WITH BI- AND TRI-SPECIFIC ANTIBODIES

8:30 Chairperson's Remarks

Tobias Raum, Ph.D., Senior Director, Discovery, Micromet, Inc.

8:35 A Bispecific T Cell-Engaging Antibody for Therapy of Leukemia and Lymphoma

Tobias Raum, Ph.D., Senior Director, Discovery, Micromet, Inc.

The CD19/CD3-bispecific BiTE antibody blinatumomab has commenced a pivotal study in patients with B-lineage acute lymphoblastic leukemia, and a clinical Phase 1 study in patients with non-Hodgkin's lymphoma is ongoing. Pre-clinical and clinical data will be reviewed showing a high potency and specificity of blinatumomab. A pipeline of BiTE antibodies for treatment of solid tumor indications is emerging and an update will be given on recent progress.

9:05 Pre-Clinical Development of a Bi-Specific TandAb for Treating Hodgkin´s Lymphoma

Melvyn Little, Ph.D., CSO, Affimed Therapeutics AG

This bispecific (CD30/CD16A) tetravalent TandAb (MW 105kDa) successfully completed an extensive toxicology program. No adverse clinical events and no measurable amounts of anti-drug antibodies were observed. No loss of activity occurred after storage in its lyophilised formulation at 40degC for one year. IND and IMPD approval obtained for clinical studies..

9:35 MM-111: A Novel Bi-Specific Inhibitor of the ErbB2/ErbB3 Oncogenic Unit: Safety and Tolerability in Patients with Refractory HER2-positive Cancers

Charlotte McDonagh, Ph.D., Director, MM-111 Project Leader, Merrimack Pharmaceuticals, Inc.

MM-111, a novel bi-specific antibody that specifically inhibits the ErbB2/ErbB3 heterodimer, is currently under investigation in a first-in-human phase 1-2 study to evaluate safety and tolerability and provide preliminary efficacy data in HER-2+ advanced breast cancer. The rational design and characteristics of MM-111 and preliminary clinical properties will be discussed.

10:05 HGF-Autocrine Loop Predicts Glioblastoma Sensitivity to MET Inhibition

Qian Xie, Ph.D., Senior Research Scientist, Laboratory of Molecular Oncology, Van Andel Research Institute

Due to its invasive nature, glioblastoma (GBM) is the most aggressive brain cancer. Hepatocyte growth factor (HGF) binds to MET tyrosine kinase receptor and induces invasive tumor growth. As MET inhibitors are entering clinical trials against several types of cancer, including GBM, it is compelling to identify therapeutic determinants that could indicate which patient subsets are suitable for this therapy. We investigated three types of GBM models in vivo for their sensitivity to MET or EGFR inhibitors and will discuss our findings.

10:20 Coffee Break

EMERGING NEW TECHNOLOGIES

11:00 Pre-Clinical and Interim Phase I Results of PRS050 - A Unique and Novel Non-Fc Domain Biobetter VEGFA Antagonist for the Treatment of Solid Tumors

Laurent Audoly, Ph.D., CSO, Pieris AG

This Anticalin, PRS050, a novel protein scaffold lacking an Fc domain, has been characterized in multiple preclinical disease models to evaluate its potency, efficacy, and unique differentiating features. PRS050 is being dosed in an open Phase I clinical trial in patients with solid tumors. Results from this ongoing clinical trial will be presented.

11:30 Pre-Clinical and Phase One Clinical Progress with a Novel Single-Chain Mono-Specific Polypeptide Protein Drug

Paul A. Algate, Ph.D., Director, Research, Trubion Pharmaceuticals, Inc.

TRU-016 is a novel humanized anti-CD37 SMIPTM protein that mediates direct and indirect killing of normal and malignant B-cells. Pre-clinical data will be presented demonstrating mechanisms of action and combinatorial activity with other therapeutics. Updated clinical studies investigating the therapeutic potential of TRU-016 against B-cell malignancies will be presented.

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

NEW AND INTERESTING APPROACHES

1:30 Chairperson's Remarks

Melvyn Little, Ph.D., CSO, Affimed Therapeutics AG

1:35 Pre-Clinical and Clinical Development of an Immunocytokine Targeting CD20 (DI-Leu16-IL2)

Stephen D. Gillies, Ph.D., President, CEO, Provenance Biopharmaceuticals Corp.

Pre-clinical studies in SCID mouse models of human lymphoma suggest that DI-Leu16-IL2, an anti-CD20 immunocytokine, has a unique mechanism(s) of action. Monkey safety studies have been completed, including pilot studies showing that subcutaneous dosing is better tolerated and more efficacious than intravenous dosing. Early clinical development strategies will be discussed.

2:05 Identification, Pre-Clinical and Clinical Development of FP-1039 (FGFR1:Fc), A Novel Antagonist of Multiple Fibroblast Growth Factor (FGF) Ligands

W. Michael Kavanaugh, M.D., Senior VP & Head, R&D, Five Prime Therapeutics, Inc.

FP-1039 is a fusion protein consisting of the extracellular domain of FGFR1 linked to the IgG1 Fc domain. FP-1039 binds multiple FGFs and prevents them from activating multiple FGF receptors. Pre-clinical and Phase 1 Clinical Trial Results of FP-1039 in patients with advanced solid tumor malignancies will be presented.

2:35 Delivering Effective Blockade of Immunosupression to Enhance Tumour Rejection: Monoclonal Antibody Discovery and Pre-Clinical Development

Ross Stewart, Ph.D., Scientist, Oncology, MedImmune Ltd.

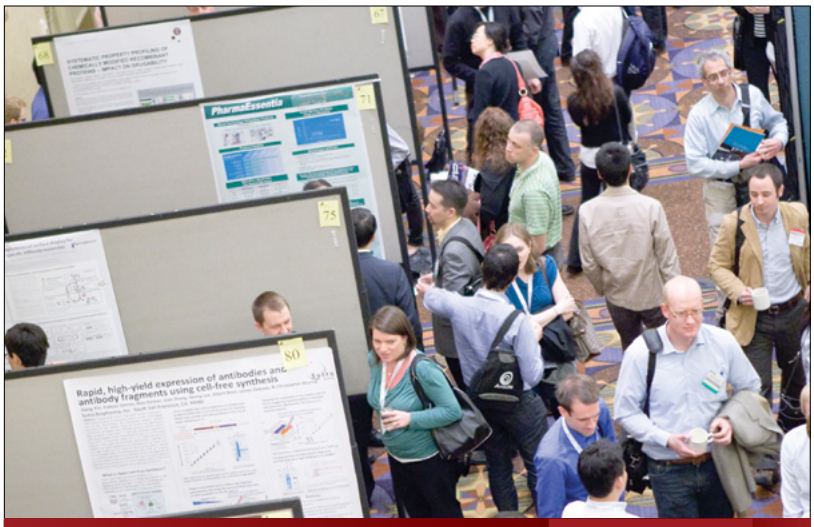
Using our state of the art antibody drug discovery platforms, we have identified an antibody directed against a well characterized T-cell inhibitory ligand expressed on the surface of tumors, and have gone on to characterize its safety profile and anti-tumor activity in a series of pre-clinical models.

3:05 Two Components for the Immunotherapy of Cancer

Alan L. Epstein, M.D., Ph.D., Professor, Pathology, University of Southern California Keck School of Medicine

Cancer immunotherapy may revolutionize the diagnosis and treatment of cancer patients. Studies show that both immune activation and the reversal of immunosuppression are required for successful immunotherapy. Murine tumor models displaying a variety of immune escape mechanisms may be useful to hasten the translation of these studies to man.

3:35 Close of Conference



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Current Medicinal Chemistry
Current Pharmacogenomics and Personalized Medicine
Current Stem Cell Research & Therapy
ddn Drug Discovery News
drug discovery world DDW
ESC & iPSC NEWS
Expert Reviews Clinical Immunology
Expert Reviews Clinical Pharmacology
Expert Review of Molecular Diagnostics
Expert Review of Proteomics
Expert Reviews Anti-infective Therapy
Expert Review of Vaccines
future ONCOLOGY
GEN Genetic Engineering & Biotechnology News
Genome Technology
genomeweb
Hematopoiesis News
Immunotherapy
International DrugDiscovery
IOS Press
Mesenchymal Cell News
nature
Personalized Medicine Quarterly Review Journal
Pharmacogenomics
Science AAAS
TheScientist Magazine of the Life Sciences

Hotel and Travel Information

Conference Venue

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

Host Hotel

InterContinental San Francisco Hotel
888 Howard Street
San Francisco, CA 94103
(T) 415-616-6500
(F) 415-616-6581

Discounted Group Rate: $199* s/d
Discounted Rate Cut-Off Date:
January 28, 2011
*Room Rate includes complimentary internet access in your guestroom

Please visit TriConference.com to make your hotel reservation

You can also make your hotel reservations at ANY of the recommended hotels by calling the hotel directly and asking for the Molecular Med Tri-Conference and/or the Cambridge Healthtech 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.

Reserve your hotel and **SAVE $75 OFF** your conference registration*

*You must book your reservation under the Tri-Conference room block for a minimum of 2 nights at the Intercontinental Hotel

Travel Information

For additional travel information please visit www.TriConference.com

Alumni Discount

Receive **20%** Off Your Registration!

Cambridge Healthtech Institute (CHI) appreciates your past participation at the Molecular Med TRI-CON. Through loyalty like yours, CHI has been able to build this event into a must attend for senior level decision-makers. As a result of the great loyalty you have shown us, we are pleased to extend to you the exclusive opportunity to save an additional 20% off the registration rate. Just check off the box marked Alumni Discount on the registration form to receive the discount! *Please note: Our records must indicate you were an attendee of the Tri-Conference event in the past in order to qualify.*

Sponsorship and Exhibit Opportunities

Sponsorship Opportunities include:

Podium Presentations

Present your solution for 15 or 30 minutes in the session room during lunch or as part of the main conference program. These presentations allow you to speak to our captive, end-user audience about your latest technology. Agenda presentation sponsorships include a **15 or 30-minute podium presentation** within the scientific agenda of your choice, as well as exhibit space, onsite branding and access to the conference delegate lists.

Invitation-Only VIP Dinner/Hospitality Suite

Sponsor will select invitees from the conference pre-registration list for an evening of networking at the host hotel or a top local venue. CHI will extend invitations, conduct follow-up and monitor responses. Reminder cards will be placed in the badges of those delegates who will be attending.

Exclusive Cocktail Receptions (Program-specific)

CHI will invite all delegates from a specific conference program to your private reception at the host hotel. Cocktails and hors d'oeuvres will be served in a setting conducive to networking. These receptions are available on a first-come, first-served basis.

Exhibiting

Exhibiting allows you to meet and speak with your prospects and customers face-to-face. Traffic building programs will be in place to ensure traffic on the expo floor.

The expo floor will include: refreshment breaks, vendor theatre presentations, an evening networking reception, and the New Product Pavilion. To increase traffic, CHI promotes exhibit & keynote passes to the local biotech community

New Product Pavilion

Once again, the Molecular Med Tri-Conference will feature a New Product Pavilion located on the exhibit floor. The New Product Pavilion is the place for exhibitors to introduce and promote your new product to conference attendees. CHI will promote the New Product Pavilion in our pre-show promotions, on our website, as well as on on-site.

Other Promotional Opportunities

- Conference Tote Bags
- Tote Bag Inserts
- Badge Lanyards
- Refreshment Breaks
- Program Guide Event Directory Sponsorship
- Poster Abstract Book
- Poster Award Sponsorship
- Corporate Branding Packages
- and more…

For sponsorship & exhibits information, please contact:

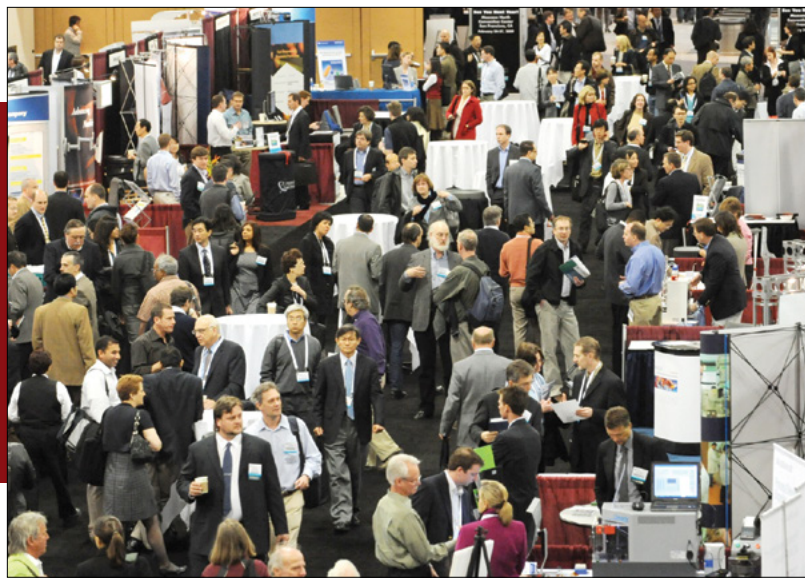
Carol Dinerstein
Director, Business Development
Phone: 781-972-5471
dinerstein@healthtech.com

Jon Stroup
Manager, Business Development
Phone: 781-972-5483
jstroup@healthtech.com

triconference.com/sponsorship

2011 Sponsor/Exhibitors (As of 9/29/2010)

Accelrys
Adis (a Wolters Kluwer Business)
Almac Diagnostics
Ambry Genetics
Analytical Biological Services
Analyticon Discovery GmbH
ApoCell
Aragen Bioscience
Asuragen
Aurigene Discovery Technologies
Axxin
Bioneer, Inc.
Bright Star Research - Quantalife
CambridgeSoft Corporation
ChemBridge Corporation
Chemical Computing Group
DOCRO, Inc.
Dualsystems Biotech
DxS
Enamine
Esoterix Clinical Trials Services
Evotec
ForteBio
Future Science Group
GeneGo
IDBS
Ingenuity Systems, Inc.
Integrated Project Management Company, Inc.
InterMed Discovery
Kalexsyn
Linguamatics
Marken
Medical Device Consultants, Inc.
Metanomics Health
Miltenyi Biotec
MitoProd SA
NanoInk
NanoString Technologies
Nanosyn
Novartis Molecular Diagnostics
Optibrium
Parthys Reverse Informatics
Pharmacore
PreClinOmics
Rules Based Medicine
Sequenom
ShanghaiBio Corp.
Simulations Plus, Inc.
Taconic
Teledyne Isco
The Jackson Laboratory
Thomson Reuters
Transgenomic
TriLink BioTechnologies
TTP Labtech Ltd.
Veridex
World Courier, Inc.
Zeptosens



Pricing and Registration Information

PRE-CONFERENCE EVENTS

Early Oncology Partnering Forum (February 21-22 at the InterContinental Hotel)

Non-Conference Attendee Rate $1395
Conference Attendee Rate..... $795

Short Courses (February 22)

Choose 1 Short Course
Commercial $695
Academic, Gov't, Hospital Affiliated.....$345

Choose 2 Short Courses
Commercial $995
Academic, Gov't, Hospital Affiliated $595

Morning Short Courses

(SC1) HTS-Based Biomarker Discovery
(SC2) Commercialization of Molecular Diagnostics
(SC3) Best Practices in Translational & Personalized Medicine
(SC4) Identification, Characterization, and Targeting of Stem Cells
(SC5) Early Drug Development & FIH Dose Regimen

Afternoon Short Courses

(SC6) Next Generation Sequencing Technologies
(SC7) Future of POC Platforms
(SC8) Designing Molecular Diagnostics & Biomarker Studies
(SC9) Building an Ontological Framework
(SC10) Molecular Technologies for Infectious Disease
(SC12) Blood-Brain Barrier

PROGRAM PRICING (February 23-25)

Access to 250+ Presentations Across 12 Programs, CHI's Intro-Net, Scientific Posters and more!

	Commercial	Academic, Government, Hospital-Affiliated
Registration after January 21, 2011	$2050	$1155

Program Selection
When registering, please indicate the ONE program you are most likely to attend. Program hopping is encouraged during the event.

DIAGNOSTICS CHANNEL

Molecular Diagnostics
Personalized Diagnostics
Cancer Molecular Markers
Circulating Tumor Cells

DRUG DISCOVERY & DEVELOPMENT CHANNEL

Mastering Medicinal Chemistry Summit
Translational Science
Strategies for Clinical Oncology Drug Development

INFORMATICS CHANNEL

Integrated R&D Informatics & Knowledge Management
Developing Scalable IT to Support Life Science Data
Pathway-Targeted Therapies in Cancer

BIOLOGICS CHANNEL

Stem Cells
Cancer Biologics

CANCER CHANNEL

Cancer Molecular Markers
Pathway-Targeted Therapies in Cancer
Cancer Biologics
Strategies for Clinical Oncology Drug Development
Circulating Tumor Cells

How to Register: TriConference.com

T: 781.972.5400 or Toll-free in the U.S. 888.999.6288 | reg@healthtech.com

Please use keycode TRI F when registering

Please refer to the Registration Code below:

CONFERENCE DISCOUNTS

- Poster Discount ($50 Off)
- Alumni Discount (20% Off)
- BayBio Discount (20% Off)
- Hotel Discount ($75 Off) *See page 30 for details.*

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

For Poster Information, visit the TriConference website or Click Here. Deadline to submit is January 14th.

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 Available! Special rates are available for multiple attendees from the same organization. For more information on group discounts contact David Cunningham at +1-781-972-5472

Alumni Discount SAVE 20%: We appreciate your past participation at the Molecular Med Tri-Con. Through loyalty like yours, this event has become a must-attend for senior level decision makers. As a result of your great loyalty, we are pleased to extend this exclusive opportunity to save an additional 20% off the registration rate. Simply select the "Alumni Discount" option on the online registration form to take advantage of this special offer. Please note: In order to quality, our records must indicate you are a past attendee of the Molecular Med Tri-Con event.

ADDITIONAL REGISTRATION DETAILS

Each registration includes all conference sessions, posters and exhibits, food functions, and a copy of the conference proceedings link.
To view our handicap information and our substitutions/cancellations policy, go to http://www.healthtech.com/regdetails
Video and/or audio recording of any kind is prohibited onsite at all CHI events. To purchase conference proceedings visit TriConference.com.

Molecular Med TRI-CON 2011

February 23-25 | Moscone North Convention Center | San Francisco, CA