Cambridge Healthtech Institute’s

BIOMARKER DISCOVERY SUMMIT 2008

Bridging the Silos in Biomarker Discovery and Validation

September 29 - October 1, 2008 • Loews Philadelphia Hotel • Philadelphia, Pennsylvania

FEATURED SPEAKERS:
• Felix Frueh, Medco
• Sudhir Srivastava, NCI
• Richard Beger, FDA
• Michael Shi, Novartis
• Mark Gerstein, Yale
• Ruth March, AstraZeneca
• Prahlad T. Ram, M.D. Anderson
• Joyce Hernandez, Merck
• Samir Hanash, Fred Hutchinson
• Christopher Newgard, Duke
...plus 70 more...

CORPORATE SPONSORS:

AFFYMETRIX
ALMAC Diagnostics
INGENIUTY SYSTEMS
Mess Scale Discovery
NEXTBIO

FOUR TRACKS:

Fourth Annual Genomic Biomarkers
Delivering on the Promise of Personalized Medicine

Sixth Annual Protein Biomarkers
The Translational Challenge

Ninth Annual Metabolic Biomarkers
Clinical Metabolomics for Drug and Diagnostic Development

Second Annual Biomarker Data Analysis
Systems Biology Approach to Integrate Biomarker Data and Establish Biological and Clinical Relevance

Pre-Conference Events:
• Fit-for-Purpose Biomarker Assay Development and Validation
• Novel Approaches to Cancer Biomarkers
• microRNA as Cancer Biomarkers
• Technology Advances for Protein Biomarker Discovery

EVENT FEATURES:
• Network with 400+ delegates
• Get access to four established meetings and 70+ presentations under one roof
• Choose from a greater selection of pre-conference workshops
• Learn about new tools at the expanded exhibit hall and new technology showcase

Lead Sponsoring Publications:

www.BiomarkerDiscoverySummit.com

Register by July 11th and SAVE up to $350!
Distinguished Faculty

- Jonas S. Almeida, Ph.D., Abell-Hanger Distinguished Professor, Department of Bioinformatics and Computational Biology, The University of Texas, M.D. Anderson Cancer Center
- Gil Alterovitz, Ph.D., Research Fellow, Children’s Hospital Informatics Program, Harvard/Massachusetts Institute of Technology, Division of Health Sciences and Technology, Research Affiliate, MIT Computer Science & Artificial Intelligence Laboratory
- Syltie Bourdeau, Ph.D., Senior Scientist, Asuagen, Inc.
- Richard Beger, Ph.D., Branch Chief, Center for Metabolomics, Division of Systems Toxicology, National Center for Toxicological Research, U.S. Food and Drug Administration
- Christoph Borchers, Ph.D., Associate Professor, Biochemistry & Microbiology, University of Victoria; Director, U Vic–Genome BC Proteomics Centre
- Lucio G. Borus, M.D., Associate Professor of Pediatrics, University of California Los Angeles; Co-Director, Stable Isotope Research Laboratory, Harbor-UCLA Medical Center; Chief Scientific Advisor, SIDMAP, LLC
- Alexander Buko, Ph.D., Director, Analytical Biochemistry and Proteomics, Biogen Idec
- George A. Calm, M.D., Ph.D., Associate Professor, Experimental Therapeutics & Cancer Genetics, The University of Texas, M.D. Anderson Cancer Center
- Mark R. Chance, Ph.D., Director, Center for Proteomics: Director, Center for Synchrontron Biosciences; Professor, Department of Physiology & Biophysics, Case Western Reserve University
- Jake Chen, Ph.D., Assistant Professor, Informatics, Indiana University; Computer Science, Purdue University; Director, Indiana Center for Systems Biology and Personalized Medicine; Founder and Chief Executive Officer, Medeolinx, LLC
- Thomas P. Conrads, Ph.D., Associate Professor, Department of Pharmacology & Chemical Biology; Co-Director, Clinical Proteomics Facility, University of Pittsburgh Cancer Institute, Mage-Women’s Research Institute
- A. Jamie Cuticchia, Ph.D., Director, Duke Bioinformatics, Duke Institute for Genome Sciences & Policy, Duke University Comprehensive Cancer Center
- Frank Diehl, Ph.D., Research Fellow, The Ludwig Center for Cancer Genomics and Therapeutics, Howard Hughes Medical Institute and The Johns Hopkins Medical Institutions
- Visvanath Desanvaram, Ph.D., Director, Statistics, Biomarker Research, Abbott Laboratories
- Bruno Domon, Ph.D., Group Leader, Institute of Molecular Systems Biology, Swiss Federal Institute of Technology, Zurich
- Keith Elliotson, Ph.D., President & Chief Executive Officer, Genmustrct, Inc.
- Mark T. Esser, Ph.D., Senior Research Fellow, Vaccines and Biologics Research, Merck Research Laboratories
- Eric R. Fedk, Ph.D., Head, Inflammation Biology & Immunotoxicology, Non-Clinical Development Sciences, Millennium Pharmaceuticals Inc.
- Dean W. Fehlser, M.D., Ph.D., Associate Professor, Division of Oncology, Stanford University
- James Flynn, Ph.D., Field Application Scientist, NextBio
- Felix Frank, Ph.D., Vice President, Research & Development, Personalized Medicine, Genentech
- Ying Ge, Ph.D., Director of Mass Spectrometry, Human Proteomics Program, School of Medicine and Public Health, University of Wisconsin-Madison
- Mark Gerstein, Ph.D., Albert L. Williams Professor of Biomedical Informatics, Molecular Biophysics and Biochemistry, Computer Science, Yale University
- Sajoy Ghosh, Ph.D., Advisor, Metabolic Diseases, Center of Excellence for Drug Discovery, Clinical Pharmacology & Therapeutics, Medicine, GlaxoSmithKline
- Iris L. Goldknopf, Ph.D., Director, Proteomics, Power3 Medical Products, Inc.
- Dave Goodlett, Ph.D., Associate Professor, Medicinal Chemistry, University of Washington
- G.A. Nagana Gowda, Ph.D., Research Scientist, Department of Chemistry, Purdue University
- David F. Grant, Ph.D., Associate Professor of Toxicology, Co-Head, Mass Spectrometry Facility, Department of Pharmaceutical Sciences, University of Connecticut
- Martin Girovicz, Ph.D., Head of Bioinformatics, Nestle Research Center
- Andrew Grpka, Ph.D., Senior Director, Pharmacogenomics; Director, CNS Research, Celera
- Rebekah Gundy, Ph.D., Biological Chemistry & Biomedical Engineering, Johns Hopkins University
- Alberto Gutierrez, Ph.D., Deputy Director, New Product Evaluation, Office of In Vitro Diagnostic Device Evaluation and Safety, Center for Devices and Radiological Health, U.S. Food and Drug Administration
- Samir Hanash, Ph.D., Program Head, Molecular Diagnostics, Public Health Sciences, Fred Hutchinson Cancer Research Center
- Joyce Hernandez, Ph.D., Manager, Global Data and Information Standards, Merck Research Labs
- Colin Hill, Ph.D., Chief Executive Officer and President, Gene Network Sciences
- Joanna Hunter, Ph.D., Director, Protein Analysis, Capron Proteomics
- Saeed A. Jortani, M.D., Ph.D., Director, Toxicology, University of Louisville Hospital Laboratory; Associate Professor, Pathology and Laboratory Medicine, University of Louisville School of Medicine
- Ananth Kadambi, Ph.D., Senior Scientist, Entelos, Inc.
- Rimaa Kaddarah-Darouk, Ph.D., Associate Professor, Department of Psychiatry and Behavioral Sciences, Duke University Medical Center
- Joshua Latker, M.D., Ph.D., Director, Institute of Proteomics, Harvard Medical School
- Andrew N. Lane, Ph.D., J.G. Brown Chair of Structural Biology, Associate Director (NMR development) CREAM, J.G. Brown Cancer Center and Department of Chemistry, University of Louisville
- Martin D. Leach, Ph.D., Executive Director, Basic Research & Biomarker IT, Merck & Co., Inc.
- Jean Lee, Ph.D., Scientific Director, PKDM, Amgen Inc.
- Michael N. Liebman, Ph.D., Senior Institute Fellow, Winnblad Research Institute; Managing Director, Strategic Medicine, Inc.
- Johan Lindberg, Ph.D., Principal Scientist, Molecular Toxicology, Safety Assessment, AstraZeneca
- James Lyons-Weiler, Ph.D., Director, Bioinformatics Analysis Core, Genomics and Proteomics Core Laboratories, Department of Biomedical Informatics, Department of Pathology, University of Pittsburgh Cancer Institute
- Ruth E. March, Ph.D., Director, Personalized Healthcare Science and Technology; Lead, Personalized Healthcare Team, AstraZeneca
- Prashad T. Ram, Ph.D., Assistant Professor, Department of Systems Biology, The University of Texas, M.D. Anderson Cancer Center
- Suren Moller, Ph.D., Chief Science Officer, Vice President, Research & Development, Exagen AS
- Stephen Naylor, Ph.D., Chief Executive Officer & Chairman, PPM, Inc.
- Randall W. Nelson, Ph.D., Research Professor, Director of the Molecular Biosignatures Analysis Unit, The Biodesign Institute, Arizona State University
- Alexey I. Nerseskov, Ph.D., Assistant Professor, Department of Pathology, University of Michigan Medical School
- Christopher B. Newton, Ph.D., Professor of Pharmacology and Cancer Biology, Professor of Internal Medicine, W. David and Sarah W. Stedman Distinguished Professor; Director, Sarah W. Stedman Nutrition and Metabolism Center, Duke University Medical Center
- Stevens M. Patric, Ph.D., Assistant Professor, Division of Translational Research, Department of Internal Medicine, University of Texas-Southwestern Medical Center
- Shannon Payne, Ph.D., Senior Scientist, Epigenomics, Inc.
- Istvan Pelczer, Ph.D., Lecturer, Senior NMR Spectroscopist, Department of Chemistry, Frick Lab, Princeton University
- Emanual F. Petriccini, Ph.D., Co-Director, Center for Applied Proteomics and Molecular Medicine, Professor of Life Sciences, George Mason University
- Robert Pflum, Ph.D., Senior Applications Manager, Pharmaceutical Business Operations, Waters Corporation
- Philip M. Pochon, Ph.D., Enterprise Information Architect, Covance, Inc.
- Zhenhao Qv, Ph.D., Senior Principal Scientist, Translational Sciences, Boehringer Ingelheim Pharmaceuticals, Inc.
- Mitch Rapoport, Ph.D., Principal Research Scientist, Biomarkers, Centocor Research & Development
- Lisa Roberts Rapp, Research Cell Molecular Biological, GPRD, Advanced Technologies Gene Expression Analysis, Abbott Molecular, Inc.
- Nandini Raghavan, Ph.D., Principal Biostatistician, Non-Clinical Biostatistics, Johnson & Johnson Pharmaceutical Research & Development
- Karin Roiland, Ph.D., Science Lead for NIH Programs, Pacific Northwest National Laboratory
- Henry Rodriguez, Ph.D., M.B.A., Director, Clinical Proteomic Technologies for Cancer, Office of Technology and Industrial Relations, Office of the Director, National Cancer Institute
- Guatherto Rucho, M.D., Ph.D., President and Chief Executive Officer, Genomas, Inc.; Director, Genetics Research, Hartford Hospital
- Jean-Charles Sanchez, Ph.D., Head, Biomedical Proteomics Group, Faculty of Medicine, Geneva University
- Jan E. Schulanz, M.D., Scientific Director, Professor of Cellular & Molecular Biology, Director of Vascular Biology & Angiogenesis Program, Sidney Kimmel Cancer Center
- O. John Semmes, Ph.D., Anthem Professor for Cancer Research; Director, Center for Biomedical Proteomics, Eastern Virginia Medical School
- Natalie S. Serkova, Ph.D., Associate Professor of Anesthesiology and Radiology; Director, Biomedical MRIPET CT Cancer Center Core, University of Colorado Health Sciences Center
- Michael Shi, M.D., Ph.D., Director, Biomarker Project Leader, Exploratory Oncology Development, Novartis Pharmaceuticals Corp.
- Vladimir Shulave, Ph.D., Associate Professor, Virginia Polytechnic Institute & State University, Biomathematics Institute
- Ray Somporaj, Ph.D., Head, Biomedical Informatics, Institute for Biodiagnostics, National Research Council Canada
- Sadhir Srivastava, Ph.D., Chief, Cancer Biomarkers Research Group, NIH National Cancer Institute
- Judd Staples, Director, Translational Initiatives, Corporate and Venture Development, Institute for Genome Sciences & Policy, Duke University
- Paul Tempst, Ph.D., Director, Protein Center, Member, Molecular Biology Program, Memorial Sloan-Kettering Cancer Center
- Vladimir Tolstikov, Ph.D., Metabolomics Core Manager, The University of California Davis Genome Center
- Zenta Tsuakida, Ph.D., Group Leader, Oncology Clinical Biomarker, Discovery Medicine and Clinical Pharmacology, Bristol-Myers Squibb Co.
- Vishal V. Vaidya, Ph.D., Instructor in Medicine, Brigham & Women’s Hospital, Harvard Medical School
- Scott A. Waldman, M.D., Ph.D., Chair, Department of Pharmacology and Experimental Therapeutics; Director, Gastrointestinal Malignancies Program, Kimmel Cancer Center, Thomas Jefferson University
- William Wilkoff, Ph.D., Research Associate, Center for Mass Spectrometry, Scripps Research Institute
- David Wishart, Ph.D., Professor, Departments of Computing Science and Biological Sciences, Alberta Innovates-Technology Futures
- Tanfika Islam Williams, Ph.D., Research Assistant Professor, W.M. Keck FT-ICR Mass Spectrometry Laboratory, Department of Chemistry, North Carolina State University
- Xiang Zhang, Ph.D., Associate Professor, Analytical Chemistry, University of Louisville
CONFERENCE-AT-A-GLANCE

GENOMIC BIOMARKERS

Monday, September 29

7:30-12:00pm Registration for Pre-Conference Events
8:00-11:00 Tutorial: Fit-for-Purpose Biomarker Assay Development and Validation
8:00-11:00 Workshop: miRNA as Cancer Biomarkers
8:00-3:00 Workshop: Technology Advances for Protein Biomarker Discovery
12:00-3:00 Workshop: Novel Approaches to Cancer Biomarkers
3:00-4:00 Conference Registration
4:00-5:30 Establishing Biomarker Utility
5:30-6:30 Opening Reception in the Exhibit Hall (Sponsorship Available)

Tuesday, September 30

7:00 Registration Open
7:30-8:15 Morning Coffee or Technology Workshops (Sponsorship Available)
8:30-10:15 Gene Expression Profiling of Health and Disease: Bridging Statistics and Biology
8:30-10:15 Translation of Protein Biomarkers to Clinical Practice
8:30-10:15 Metabolomics to Assess Drug Response
8:30-10:15 Gene Expression Profiling of Health and Disease: Bridging Statistics and Biology

10:15-11:10 Networking Coffee Break with Poster and Exhibit Viewing
11:10-12:00 Molecular Diagnostics: Translation to the Clinic
11:10-12:00 Clinical Proteomics: Translation to Molecular Diagnostics
11:10-12:00 Clinical Metabolomics
11:10-12:00 Bridging Omic and Clinical Data

12:00-1:40 Technology Showcases (Sponsorship Available)
1:40-3:00 Personalized Medicine: Translation to Clinical Practice (continued)
1:40-3:00 Protein Biomarkers to Assess Drug Toxicity and Efficacy
1:40-3:00 Cancer Metabolomics
1:40-3:00 Systems Biology Approaches to Biomarker Discovery

3:00-4:00 Networking Refreshment Break with Poster and Exhibit Viewing

Wednesday, October 1

7:00 Registration Open
7:30-8:15 Morning Coffee or Technology Workshops (Sponsorship Available)
8:30-9:50 Genomic Biomarkers in Clinical Pharmacology
8:30-9:50 Post-Translational Modifications as Biomarkers
8:30-9:50 Technology Advances for Metabolic Profiling
8:30-9:50 Integrating Semantic and Omic Approaches for Biomarker Discovery

9:50-10:50 Networking Coffee Break with Poster and Exhibit Viewing
10:50-11:40 Development Considerations for Single-Analyte Markers, Panels, and Profiles
11:40-1:10 Luncheon Technology Workshops
1:10-3:00 Bridging Silos: Integrating Omic Data
3:00 Close of Conference

SPONSORSHIPS AND EXHIBITS

Brand your company as a thought leader in the global biomarker community by participating as an active Sponsor. Showcasing your technologies, services and solutions to our highly targeted audience can significantly impact their buying decisions and help you achieve your sales and business development objectives.

SPONSORSHIP OPPORTUNITIES INCLUDE:
- Technology Showcase – Includes 20-minute presentation within main scientific agenda
- VIP Dinner: Invitation-only dinner for 15+ select delegates
- Breakfast Technology Workshop – Includes 20-minute presentation and 10 minutes of Q&A

Sponsorship packages can be customized to best suit your company’s strategic sales and business development goals.

EXHIBITING

Exhibiting allows your company to differentiate your technologies, services or solutions from competitors and demonstrate its commitment to this science. Exhibitors will enjoy facilitated networking opportunities with 400+ qualified delegates, making it a perfect platform to launch a new product, collect feedback and generate new leads.

PROMOTIONAL PROGRAMS

Reinforce your branding messages, or enhance your booth presence with promotional opportunities such as tote bag, tote bag inserts, session room literature drops and more!

For more information, or to contract your sponsorship or exhibit space today, please contact:

Iilana Schwartz, Manager, Business Development, 781-972-5457 or ischwartz@healthtech.com

www.BiomarkerDiscoverySummit.com
8:00-11:00 Pre-conference tutorial* (*Separate Registration Required)

Instructors: Jean Lee, Ph.D., Scientific Director, PKDM; Amarin Inc.; and Visvanath Desanarayan, Ph.D., Director, Statistics, Biomarker Research, Abbott Laboratories

This tutorial will provide recommendations on the “fit-for-purpose” best practices in the development and validation of biomarker assays and sample analyses. Special emphasis will be on assays where a reference standard material for the biomarker analyte is available. We will provide an overview of the key elements in the broad roadmap to method development and validation for the intended exploratory or advanced biomarker applications. The special challenges in protein biomarker assays will be discussed, including sample stability and collection integrity, validation and QC samples, validity of reference standards, calibration and quantifying methods, method optimization and method feasibility studies. Strategies for moving from biomarker panels in the exploratory phase to the markers chosen to support clinical trials will then be discussed from the analytical perspective. Finally, the recommendations for pre-study and in-study validation will be provided with brief illustrations.

Outline:
1. Introduction - Nomenclature, types of biomarker methods/assays, biomarker method development & validation roadmap, fundamental validity, similarity and differences from PK assays & diagnostic application.
2. Pre-analytical and Bioanalytical elements: Target range, standards, validation & QC samples, stability, matrix effect, and relative selectivity.
3. Calibration curve model selection, evaluation, and weighting.
5. Evaluation of some pre-study validation characteristics such as precision, bias, sensitivity and quantification limits.
6. Illustrations of some analytical issues in pre-study validation and sample analysis.

8:00-11:00 Pre-Conference Workshop* (*Separate Registration Required)

**microRNA as Cancer Biomarkers**

8:00-8:30 Non-Coding RNAs as Cancer Biomarkers
George A. Calin, M.D., Ph.D., Associate Professor, Experimental Therapeutics & Cancer Genetics, The University of Texas, M. D. Anderson Cancer Center

MicroRNAs were linked to the progression of all types of human tumors that were investigated to date. The main molecular alterations are represented by variations in gene expression, usually mild and with consequences for a vast number of target protein coding genes. Recent studies proved that miRNAs are main candidates for the elusive class of cancer predisposing genes and that other types of non-coding RNAs participate in the genetic puzzle giving rise to the malignant phenotype. These discoveries could be exploited for the development of useful markers for diagnosis and prognosis, as well as for the development of new RNA-based cancer therapies.

8:30-9:00 miRNAs as Novel Biomarkers for Detecting Cervical Cancer Lymph Node Metastasis
Sylvie Beaudenon, Ph.D., Senior Scientist, Asuragen, Inc.

miRNA expression profiles can distinguish between lymph nodes, normal cervix and cervical squamous cell carcinomas. miRNAs are differentially expressed between cancer-positive and cancer-negative inguinal lymph nodes from cervical cancer patients. We have identified a subset of seven miRNAs that can distinguish positive from negative lymph nodes from cervical cancer patients. These miRNAs may represent new diagnostic markers for the detection of lymph node metastases in cervical cancer patients.

9:00-9:30 Discovery of miRNA-Based Biomarkers for Cancer
Sam Moyer, Ph.D., Chief Science Officer, Vice President, Research & Development, Exiqon A/S

Abnormal expression of microRNAs (miRNAs) in cancer implies that these small ~22-nucleotide molecules play a role in oncogenesis. Therefore miRNAs may comprise a novel class of diagnostic and prognostic signatures. This talk will focus on examples of using microRNA for cancer classification, prognosis and treatment selection.

9:30-10:00 Coffee Break

10:00-10:30 Her2/neu, microRNAs and Herceptin
Michael N. Liebman, Ph.D., Senior Institute Fellow, Windber Research Institute; Managing Director, Strategic Medicine, Inc.

Herceptin treatment in breast cancer requires the observance of overexpression of Her2/neu in the patient, as measured by FISH and/or IHC. Only 25% of all patients overexpress Her2/neu, and only 40% of these patients respond to Herceptin. In collaboration with BIOBASE, we have pursued upstream analysis of the observed gene expression differences in patients where FISH and IHC present different results and have determined that microRNA appears to function as a switch in determining the different response. This has been analyzed in terms of its potential use as a diagnostic and/or therapeutic target to improve decision-making for treatment in breast cancer patients.

10:30-11:00 Evaluation of microRNAs for Diagnosis and Prognosis of Patients with Solid Tumors
Mitch Rapoza, Ph.D., Principal Research Scientist, Biomarkers, Centocor Research & Development

MicroRNAs (miRNAs) are short non-coding RNAs that control the expression of multiple proteins through various mechanisms. It has been shown that miRNAs are differentially expressed in different cancers and limited functional studies have implicated specific miRNAs as either oncogenes or tumor suppressors. Using various expression profiling technologies we have identified and evaluated miRNAs that are potential markers for colorectal cancer (CRC) and squamous cell lung cancer, respectively. In addition, in vitro functional studies of selected miRNAs have provided insight into their biochemical role in CRC. The utility of these analyses compared to previously defined mRNA classifiers will be discussed.
10:30-11:00 MS-Based Quantitative Proteomics for Clinical Diagnosis
Chirag Borchers, Ph.D., Associate Professor, Biochemistry & Microbiology, University of Victoria, Director, UVic-Genome BC Proteomics Centre
A particular focus of our group is the development of MS based techniques such as Multiple Reaction Monitoring (MRM). Our laboratory has developed these assays for simultaneous quantification of the 45 most abundant proteins in blood and cancer-related proteins like EGFR in clinical specimens including biopsy samples.

11:00-11:30 High-Throughput Cell-Based Studies and Protein Microarrays for Biomarker and Target Discovery
Joshua LaBaer, M.D., Ph.D., Director, Institute of Proteomics, Harvard Medical School
We developed a novel form of protein microarrays, called nuclear acid programmable protein array (NAPPA), which can be used to study protein-protein interactions, protein-drug interactions, search for enzyme substrates, and as tools to search for disease biomarkers. In particular, recent experiments have focused on using these protein microarrays to search for autophagy response in cancer patients. Several bona fide autophagy responses, such as responses to p53, have been detected, and a pilot study of responses to 7500 full length human proteins in 50 breast cancer patients and 50 controls has identified over 700 candidate proteins with more frequent responses in patients. These experiments show promise in finding autophagy responses that appear in only cancer patients.

11:30-12:00 Brain Damage Markers: From Discovery in the CSF to Validation in the Plasma
Jean-Charles Sanchez, Ph.D., Head, Biomedical Proteomics Group, Faculty of Medicine, Geneva University
Following any form of brain insult, proteins are released from damaged tissues into the cerebrospinal fluid (CSF). This body fluid is therefore an ideal sample to use in the search for biomarkers of neurodegenerative disorders and brain damage. We used human post-mortem CSF as a model of a massive brain injury and cell death for the identification of such protein markers. Pooled post-mortem CSF samples were analyzed using immunoblot methods that combined immunodepletion of abundant CSF proteins, isotopic mass tagging by the Tandem Mass Tag® (TMT®) technology, 2DLC and protein identification and quantitation by LC-MS/MS. A total of more than 400 proteins were identified, of which 250 proteins were not previously described to be present in CSF. Of these 250 proteins, more than 75% have been described as intracellular proteins suggesting that they were released from damaged cells. From these proteins, five have been further validated as biomarkers in age/exposed European and American cohorts for the early diagnosis of stroke (UFD1, NDRA and DJ1), the thrombotic treatment follow-up-of ischemic stroke (USTP) and the prediction of poor outcome after Subarachnoid Hemorrhage (a panel of markers). Taken together these findings suggest that proteins are differentially expressed by TMT® in post-mortem CSF samples by proteomics approaches demonstrated the value of this concept as a first step toward the discovery of blood markers of brain injury.

12:00-12:45 Lunch on your own

Hotel Break

12:45-13:15 Differential Protein Expression Analysis Using Spectral Count Data in Label-Free Shotgun Proteomics
Alexey I. Nesvizhskii, Ph.D., Associate Professor, Department of Pathology, University of Michigan
Spectral counting has become a popular approach for measuring protein abundance in label-free shotgun proteomics. At the same time, the development of data analysis methods has lagged behind, and previously established methods for gene expression microarray experiments cannot be effectively applied. We present a set of computational tools for statistically robust analysis of spectral count data. We demonstrate that such an approach can be used to discover up-regulated biological functions and pathways in both cell line and patient tissue profiling studies.

13:15-14:45 Mass Informatics of Mass Spectrometry-Based Protein Biomarker Discovery
Xiang Zhang, Ph.D., Associate Professor, Analytical Chemistry, University of Louisville
We have developed the Proteome Discovery Pipeline (PDP), a stand-alone bioinformatics platform used for LC/MS data analysis and biomarker discovery. Data is processed in a series of self-contained analytical steps using modules that are controlled by a graphical user interface. Modules include spectrum deconvolution, alignment, normalization, significance tests, pattern recognition and molecular correlation networks. Modules consist of applications developed in C++ and the MATLAB which are designed for low abundant proteins. We have developed these assays for simultaneous quantification of the 45 most abundant proteins in blood and cancer-related proteins like EGFR in clinical specimens including biopsy samples.

14:45-15:20 Refreshment Break

15:20-16:00 Imaging to Validate Protein Biomarkers
Jan E. Schirmer, M.D., Scientific Director, Professor of Cellular & Molecular Biology, Director of Vascular Biology & Angiogenesis Program, Sidney Kimmel Cancer Center
Enhancing noninvasive imaging and pharmacodelivery by targeting disease biomarkers is challenged by in vivo barriers limiting their access. Blood vessel endothelium prevents tissue penetration of many imaging agents, drugs, nanoparticles and gene vectors. Our discovery and validation strategies integrate tissue subtraction, subtractive proteomics, bioinformatic interrogation, antibody generation, expression profiling, and various imaging modalities to quickly identify the in vivo targetable subset of biomarkers. Magnetic nanoparticle and endothelial cell surfaces in tissue yield novel vascular biomarkers enabling tissue- and disease specific immunotargeting in vivo. This “organellar proteomic imaging of organ and disease biomarker space” creates opportunities for many diseases.

2:30-3:00 The Application of MALDI MS Mass Spectrometry Imaging (MALDI-MSI) to the Clinical Management of Prostate Cancer
O. John Semmes, Ph.D., Professor of Cancer Research; Director, Center for Biomolecular Proteomics, Eastern Virginia Medical School
Diagnosis of prostate cancer is based on pathologic morphologic evaluation. The ability to localize disease-specific molecular changes in tissue would help improve diagnostic accuracy. Direct profiling of proteins in tissue sections using a technology termed MALDI mass spectrometry imaging (MALDI-MSI) provides a more molecular description with possible diagnostic and prognostic implications. We have developed a strategy for the application of MALDI-MSI to the discovery of biomarkers that will improve the clinical management of prostate cancer. Our specific clinical targets are 1) detection of cancer, 2) detection of micrometastatic disease, and 3) detection of insensitive disease. Using tissue samples from approximately 100 tissue sections from strongly defined patient cohorts. We have also begun addressing the issues involved in positioning MALDI-MSI directly in the pathology workflow. Histology guided MS imaging is a promising strategy for identification of prostate cancer specific biomarkers that can be utilized to improve cancer diagnosis and most importantly for individualized and stratified patient risk for micrometastatic disease.

12:00-12:30 Occult Metastases Predict Recurrence Risk in Patients with pN0 Colon Cancer
Scott A. Waldman, M.D., Ph.D., Chair, Department of Pharmacology and Experimental Therapeutics; Director, Gastronemial Maladies Program, Kimmel Cancer Center, Thomas Jefferson University
Patients with stage III (pN0) colon cancer have a 15-20% risk of disease recurrence reflecting under-diagnosis of micrometastases at staging. OCC, selected exclusively by intestinal cells and universally in colon tumors, is a marker of occult metastases in lymph nodes. Here, OCC was quantified by RT-PCR in lymph nodes collected from patients with pN0 colon cancer. Indeed, OCC mRNA identified occult metastases that predicted the risk of disease recurrence in pN0 colorectal cancer. This prospective multicenter trial suggests that OCC is a prognostic and predictive molecular marker, identifying patients at increased risk for disease recurrence who could benefit from adjuvant chemotherapy.

12:30-1:00 Discovery and Validation of DNA Methylation-Based Biomarkers for Early Detection of Colorectal Cancer in Plasma
Shannon Payne, Ph.D., Senior Scientist, Epigenomics, Inc.
Detection of colorectal cancer (CRC) at early stages has been shown to greatly decrease mortality from the disease. Availability of a blood-based test for CRC is expected to improve screening compliance in the general population. Through methylation-sensitive, restriction enzyme based marker discovery we identified a region of theSeptin 9 (SEPT9) gene that is methylated in over 90% of colorectal cancer tissues with little or no methylation in normal colon tissue or other controls. Our process of biomarker development including real-time assay and preanalytics development, and successful application of the SEPT9 methylation biomarker to the specific detection of tumor DNA in multiple studies of CRC patients and controls will be described.

1:00-1:30 A Combinatorial Approach: The Use of MALDI-MS and Nano LC-MS for Early Detection of Colorectal Cancer in Plasma
Taufiqu Islam Williams, Ph.D., Research Assistant Professor, W.M. Keck FT-ICR Mass Spectrometry Laboratory, Department of Chemistry, North Carolina State University
Epithelial ovarian cancer (EOC), the 5th leading cause of cancer deaths among women in the U.S., is characterized by poor survival statistics. Early-stage disease presents with few, if any, symptoms and diagnosis seldom occurs before metastasis has occurred. A 5-year survival rate of only 18% is expected with current case detection methods. For the relatively few cases detected early, 80% of patients reach this survival mark. Insufficient sensitivity and specificity in established diagnostic modules is the primary reason why most patients are diagnosed in advanced disease, when prognosis is decedely poor. We aim to apply MALDI-FT-ICR-MS and nano LC-MS in the investigation of carbohydrates characteristic of tumor including real-time assay and preanalytics development. Preliminary results have demonstrated complimentary glycan information provided by these two technologies.

1:30-2:00 Refreshment Break

2:00-2:30 Overcoming Potential Pitfalls in the Detection of Circulating Tumor Cells in Blood by RT-PCR
Lisa Roberts Rapp, Research Cell/Molecular Biologist, GPRD, Advanced Technologies Gene Expression Analysis, Abbott Molecular, Inc.
Detection of circulating tumor cells (CTC) in the blood of cancer patients may have prognostic and predictive significance. In an effort to detect CTC in breast cancer patients, RT-PCR for Cytokeratin 19 and HER-2 was employed. These two markers are relatively specific for epithelial cells and breast cancer cells, respectively. However, background expression of these tumor specific markers in peripheral blood cells may cause false positives. Our novel method takes advantage of an extremely sensitive technology for the analysis of mutant DNA in plasma samples collected longitudinally from patients with advanced colorectal cancer undergoing different forms of treatments. We found that the amount of circulating mutant DNA reflects the systemic tumor burden and can be used to monitor therapeutic response. This non-invasive approach has the potential to greatly improve patient management and the development of new therapies in the near future.

2:30-3:00 Dynamics of Circulating Tumor DNA in Cancer Patients
Frank Dehl, The Ludwig Center for Cancer Genetics and Therapeutics Howard Hughes Medical Institute and The Johns Hopkins Medical Institutions
The accumulation of somatic mutations is a major mechanism responsible for the development and progression of human cancer. The importance of mutations in tumorigenesis and their irreversible nature make them attractive specific cancer targets. In a preliminary prospective study, we applied an extremely sensitive technology for the analysis of mutant DNA in plasma samples collected longitudinally from patients with advanced colorectal cancer undergoing different forms of treatments. We found that the amount of circulating mutant DNA reflects the systemic tumor burden and can be used to monitor therapeutic response. This non-invasive approach has the potential to greatly improve patient management and the development of new therapies in the near future.


**Biomarkers have been flouted as a next frontier in the realm of personalized medicine. However, one has to be specific and clear about its intended use: Diagnostic, Prognostic, or Predictive? Each type has a different purpose. Each has to meet certain criteria to be fit for the purpose. Therefore, when discussing biomarkers, one must clearly state its targeted goal and population.**

5:05-5:30 **Building a Biomarker Information Pipeline and Enabling Translational and Personalized Medicine: Leveraging Industry Standards to Bring Omics Closer to Medicine**

Martin D. Leach, Ph.D., Executive Director, Basic Research & Biomarker IT, Merck & Co Inc.

5:30-6:30 Opening in the Exhibit Hall

---

**Wednesday, September 30**

**GENOMIC BIOMARKERS**

7:00 **Registration Open**

7:30-8:15 **Morning Coffee or Technology Workshops: Biological Variation Based Data Interpretation. Why Can This be of Value?**

Gordon F. Kaple, Ph.D., Senior Director of Biomarker Services, Covance Central Laboratory Services

**Four major GI regions considered. Fourteen had never been described in the GI tract, and six were novel genes. This work offers a perspective on nutrition-specific biomarkers discovery programs. It shows such studies to be complementary to typical drug development programs focusing on disease-specific biomarkers, rather than on the molecular signatures of health.**

8:30-8:50 **Gene Expression Profiling of Health and Disease: Bridging Statistics and Biology**

(Shared session between Genomic Biomarkers and Biomarker Data Analysis)

8:30-8:35 **Chairperson’s Opening Remarks**

8:35-9:00 **Biomarkers: Understanding the Disease Process**

Michael N. Lieberman, Ph.D., Senior Institute Fellow, Weather Research Institute; and Managing Director, Strategic Medicine, Inc.

**Measurement of gene expression data presents an opportunity to further classify patients and their disease using biological specimens, robust experimental methods and statistical analysis to enhance clinical decision making. It is critical, however, to appropriately evaluate this perspective on patient and/or disease stratification in terms of the complexity of the disease process and clinical need, rather than solely on the concept of a disease state. This presentation will describe both the conceptual framework for understanding the relationship between biomarkers and the disease process and results from its application in breast cancer.**

9:00-9:25 **Biomarkers for Metabolic Disease: Predicting Weight Loss From Serotranscriptomics**

Sajobi Ghosh, Ph.D., Advisor, Metabolic Diseases, Center of Excellence for Drug Discovery, Clinical Pharmacology & Discovery Medicine, GlassMedLine

**Serotranscriptomics refers to the study of gene expression in blood samples. We have examined gene expression profiles in whole blood from obese subjects who lost weight significantly different rates in response to a fixed, low calorie diet. Gene expression profiles were analyzed to identify biological pathways that discriminate between obese and lean subjects and between obese, diet-sensitive (ODS) and obese, diet-resistant (ODR) subjects. Additionally, candidate biomarkers of the rate of weight loss were identified and confirmed by quantitative real-time PCR. This approach qualifies whole-blood transcriptome analysis for unraveling the biology underlying obesity and weight-loss. Blood-based biomarkers predictive of the rate of weight loss also opens a promising avenue for individualizing weight-loss therapy by caloric restriction alone or in combination with pharmacotherapy.**

9:25-9:50 **Ingenuity Pathways Analysis: Prioritization of Biomarker Candidates from Omics Data Based on Phenotypic Association**

Deborah Ridley, Ph.D., Senior Application Scientist, Ingenuity Systems

**As gene expression profiling has matured to become a common component of biomarker discovery programs, the challenge has shifted to translating large scale datasets into biomarkers that can be used to diagnose disease and predict patient response to treatment. Prioritization of biomarker candidates – at a practical level - can be achieved by using the phenomenology of the disease to help predict individual responses. Our goal is to develop an approach that can help prioritize biomarker candidates and elucidate the molecular mechanisms connecting those markers to disease phenotypes and pathways.**

9:50-10:15 **Defining Health at the Molecular Level**

Martin Grigorov, Ph.D., Head of Bioinformatics, Nestle Research Center

**The challenge for the Life Sciences in the new century resides in promoting health and in preventing disease. In order to meet this challenge, knowledge should be built to define and better understand the function of the molecular markers which define the healthy status of a biological system. The aim of the present study was to generate a map of gene expression patterns along the human healthy adult gastrointestinal tract in order to use such sets of biomarkers as references when screening for pathological deviations.**

---

**PROTEIN BIOMARKERS**

8:30-8:35 **Chairperson’s Opening Remarks**

8:35-9:00 **Targeted Discovery: From Troponin I to Albumin as Markers**

Rebekah Gandry, Ph.D., Biological Chemistry & Biomedical Engineering, Johns Hopkins University

**To be Announced**

9:00-9:25 **Creating a Reliable Proteomics Pipeline by Identifying and Addressing Roadblocks to the Clinic: The NCI Perspective**

Henry Rodriguez, Ph.D., M.B.A., Director, Clinical Proteomic Technologies for Cancer, Office of Technology and Industrial Relations, Office of the Director, National Cancer Institute

**Although proteomics technologies could address important problems in clinical cancer research, attempts to use proteomics approaches to discover cancer biomarkers in blood and tissues have been largely unsuccessful and have engendered considerable skepticism. The NCI’s Clinical Proteomic Technologies for Cancer initiative (http://proteomics.cancer.gov) is designed to accelerate the transition of proteomics technologies from basic research tools to reliable and robust clinical research platforms. This presentation outlines a strategy for the advancement of clinical proteomic technologies that perform consistently across platforms, instruments and laboratories to facilitate biomarker discovery.**

9:25-9:50 **In Search for Proteomic Biomarkers of Multiple Sclerosis: The Challenges of Translating Early Candidate Discovery to a Panel of Validated Markers**

Alexander Buko, Ph.D., Director, Analytical Biochemistry and Proteomics, Biogen Idec

**Biomarkers for a neurodegenerative disease, such as Multiple Sclerosis (MS), should reflect the pathogenic processes of the disease. However, the identification of relevant biomarkers for MS poses unique challenges. These challenges include a lack of availability of relevant tissues and animal models, the complexity and heterogeneity of the disease, and a lack of pathways for functional validation of candidate biomarkers.**

**Mass-spectra based proteomic profiling has received widespread attention as a tool for biomarker discovery. Proteomics is especially well suited for discovery of biomarkers in cerebrospinal fluid, brain, spinal column and plasma, tissues which one expects to see proteomic changes in MS. A major data-analytical challenge is evolving, which is the extremely high dimensionality of proteomic data from a variety of sample types, exacerbated when the sample size is small. Here, the unique challenges that neurological disorders such as MS introduce to biomarker discovery are described and how technological advances in proteomic methods, sample prep and bioinformatics are overcoming some of these obstacles and are driving the discovery of novel biomarkers.**

9:50-10:15 **Panel Discussion: Translational Challenge**

---

8:00-8:30 Networking Coffee Break with Poster and Exhibit Viewing

**www.BiomarkerDiscoverySummit.com**
Drug-induced liver injury has often been associated with the generation of reactive metabolites, which are primarily detoxified via glutathione conjugation. Since S-adenosylmethionine (SAMe) is the primary source of the sulfur atom in glutathione, SAMe was shown to be significantly reduced following toxic dosing in day 1 and day 2 urine samples. N-methylhydroxycitrate, which is a byproduct of the conversion of S-adenosylmethionine (SAMe) to S-adenosylhomocysteine (SAH), was also shown to be significantly decreased in day 1 and day 2 urine samples following toxic dosing. In order to further validate the results from the metabolomic studies, the Gene Expression Omnibus (GEO) database was used to obtain microarray data from the rat liver treated by liver toxicants. Some genes involved in trans-sulfuration pathway, including glycine-N-methyltransferase and betaine-homocysteine methyltransferase (GNMT and Bhtmt, respectively), were found to be significantly decreased in the toxic compounds compared with the control groups. The metabolic and transcriptomic results show that N-methylhydroxycitrate is a potential non-invasive preclinical biomarker of toxicity that is related to SAMe and glutathione depletion for detoxification of reactive drug metabolites.

9:00-9:25 Metabolomics/Proteomics: Tools for Biomarker Discovery Within Safety Assessment

Johan Lindberg, Ph.D., Principal Scientist, Molecular Toxicology, Safety Assessment, AstraZeneca

Metabolite and protein profiling are methods used for discovery of new safety biomarkers and toxicity problem solving. Examples from the area of liver toxicology and thalidomide will be used to describe the biomarker discovery process. Key components are analytical platforms, bio-statistics, biological contextualization and early biomarker qualification. In addition a novel data reduction tool, Tramasm, for LC-MS data reduction will be described.

9:25-9:50 Metabolomics: A Global Biochemical Approach to the Study of Human Disease and Drug Effects

Bina Kaddurah-Daouk, Ph.D., Associate Professor, Department of Psychiatry and Behavioral Sciences, Duke University Medical Center

We have developed and used sophisticated metabolomics analytical platforms and informatics tools to define initial metabolic signatures for several central nervous system (CNS) diseases and for drugs used to treat these diseases. We will share our experience and early findings from the study of schizophrenia and depression and steps we have taken towards defining biomarkers for disease and response to therapy. We will also highlight the “National Metabolomics Network for Drug Response Phenotypes” a consortium funded by NIH and that brings metabolomics and pharmacogenomic approaches towards providing insights into the underlying basis for individual variation to drug response. Such knowledge could enhance significantly our effort for developing biomarkers that can predict drug response outcomes.

9:50-10:15 Tracer Substrate Derived Metabolite Profiles in Combination with Principal Component Analysis To Assess Drug Response and Toxicity

Lazard G. Borou, M.D., Associate Professor of Pediatrics, University of California Los Angeles; Co-Director, Stable Isotope Research Laboratory, Harbor-UCLA Medical Center; Chief Scientific Advisor, SiDMAP, LLC

Altered structural and intermediary metabolism synthesis as revealed by stable isotope labeled tracer substrates enhances flux studies for the identification of biomarker products for the purpose of assessing drug response in vitro and in vivo. First order kinetics of labeling from a tracer substrate to its numerous products in healthy individuals establishes the strong dependence of product formation in many biochemical reactions for a single substrate, which, in turn, can be used to evaluate drug response using Principal Component Analysis in the large data sets obtained by pathway specific positional 13C labeling. Valproic acid treatment, for example, decreases liver and brain cell glycogen and RNA turnover, while the severe decrease in 13C glucose labeling to cholesterol serves as an early and easy to obtain plasma marker to assess valproic acid action on glucose homoeostasis, limited acetyl formation and sterol synthesis. The severe inhibition of glycogen and RNA turnover, as well as fatty acid and cholesterol syntheses as shown by Principal Component Analysis, which are critical fluxes in liver cells, by a single valproate dose reveals the severe impairment of liver function with permanent cell damage and liver toxicity to follow if valproate treatment continues in a susceptible individual.

10:15-11:10 Networking Coffee Break with Poster and Exhibit Viewing

www.BiomarkerDiscoverySummit.com
11:10-11:35: Lost in Translation: Factors Affecting the Clinical Uptake of Molecular Diagnostics

Judd Staples, Director, Translational Initiatives, Corporate and Venture Development, Institute for Genome Sciences & Policy, Duke University

This presentation will explore the barriers to translating new molecular diagnostic discoveries into clinical practice. We will provide a framework to assist researchers in critically evaluating the potential applications of their discoveries and suggest an approach to maximizing the chances that their invention ultimately has an effect in the management of patient care. Topics that will be covered will include assessment of the value of the technology from the perspective of the patient, the healthcare provider, the investor/strategic partner, regulators, and payers.

11:35-12:00: Title to be Announced

Alberto Gutierrez, Ph.D., Deputy Director, New Product Evaluation, Office of In Vitro Diagnostic Device Evaluation and Safety, Center for Devices and Radiological Health, U.S. Food and Drug Administration

12:00-1:40 Lunch Break

1:40-1:45: Chairperson’s Opening Remarks

1:45-2:10: Personalized Healthcare – Where Are We Now?

Ruth E. March, Ph.D., Director, Personalized Healthcare Science and Technology, Lead, Personalized Healthcare Team, AstraZeneca

This talk will examine what Personalized Healthcare (PHC) is, its current state and its main beneficiaries. We will then examine what makes for successful PHC development and what are the main challenges. This will be illustrated by case studies including Iressa®, Exanta™ and products from AstraZeneca’s early development pipeline. The talk will demonstrate that PHC is at an exciting time and depends on all those involved working together to realize the benefits.

2:10-2:35: Biomarker Application in Oncology Clinical Development

Michael Shi, M.D., Ph.D., Director, Biomarker Project Leader, Exploratory Oncology Development, AstraZeneca

This talk will focus on using targeted mass spectrometric immunonassays to investigate human plasma and urinary proteins in healthy and disease cohorts. Results illustrating the ability to detect low level protein variants relevant to type 2 diabetes will be presented, and how these findings are subsequently used to develop advanced assays for disease diagnosis and monitoring.

2:35-3:00: Molecular Biomarkers: Translation to the Clinic

12:00-3:00: Networking Refreshment Break with Poster and Exhibit Viewing

www.BiomarkerDiscoverySummit.com
Clinical Metabolomics

11:10-11:35 Clinical Biomarkers from Biofluid Metabolomics
David Wishart, Ph.D., Professor, Departments of Computing Science and Biological Sciences, University of Alberta

A continuing challenge for metabolomics is having a consolidated resource of “normal” metabolite concentration values to map against in biofluids. Indeed, without a list of normal values, it is very hard to know what is abnormal. In this presentation I will provide an update of our computational and experimental efforts to assemble complete metabolite concentration profiles for most of the commonly relevant biofluids, including cerebrospinal fluid, serum, urine and saliva. I will also briefly survey the knowledge of disease conditions that can be unequivocally characterized by single metabolite biomarkers as well as those conditions that must be characterized by multiple metabolite biomarkers. I will also discuss the need and provide examples of how to develop more sophisticated approaches to using metabolites as disease biomarkers.

11:35-12:00 Global Metabolomics: Navigating from Methods to Biology
William Wilks, Ph.D., Research Associate, Center for Mass Spectrometry, Scripps Research Institute

Human diseases manifest in complex downstream effects, affecting multiple biochemical pathways. We use a non-targeted, mass-spectrometry approach to metabolomics to investigate disease. Plasma samples from patients with inborn errors of metabolism were investigated for validation, and identified additional biomarkers. Investigating the microbiome interaction with the host revealed a surprisingly large effect on plasma biochemistry, and a drug-like response. The neurochemical effect of SIV-infected encephalitis was examined in thymus macaques, addressing problems in central nervous system biochemistry and neurodegenerative disease.

12:00-1:40 Lunch and Technology Showcases

An Automated and Streamlined Solution to Increase Productivity and Confidence in Microarray Studies
Audra A. Logsdon, Affymetrix

This case study highlights the increase in productivity and confidence in microarray results for whole genome expression analysis using a microplate-based high throughput platform. The platform includes automated target preparation, an array processing instrument and complementary reagents that minimize hands-on time. Applications in drug discovery and development will be discussed.

Cancer DSA™: Disease Focused Microarrays: A Platform for Biomarker Discovery and Validation, Optimised for Use with FFPE Tissue
Austen Tanney, Ph.D., Scientific Liaison Manager, Abcam Diagnostics

Searching Large Scale Biological Data for Metabolic Syndrome X Biomarkers
James Flynn, Ph.D., Field Application Scientist, NextBio

NextBio presents the power of Metabolic Syndrome X, one of the most complex and pervasive medical conditions that combines several disorders into one. Patients with Metabolic Syndrome X exhibit classic signs of diabetes, obesity, dyslipidemia, hypertension and heart disease. This fact underscores the need for efficient tools to analyze this complex disease. NextBio is a robust classifier development, and possible aggregation of several classifiers. It recognizes the fact that diabetics suffering from hypertension and heart disease are present in all stages. A classifier method developed for metabolomics data mining in my laboratory. Very high resolution ESI Mass Spectrometry, with the assistance of Metabolite Discovery software (Cerno Bioscience) used for unidentified metabolites elemental composition assignment will be reported. Case studies on Rethor Cell Carcinoma (PDAC) diagnosis test development and Polycystic Kidney Disease (PKD) diagnostic test development will also be presented.

2:10-2:35 Noninvasive Diagnosis of Cancers: A Metabolomics Approach Combining 1H NMR Spectroscopy and a Robust Classification Strategy
Ray Somorjai, Ph.D., Head, Biomedical Informatics, Institute for Bioinformatics, National Research Council Canada

Non-invasively acquired biomedical data tend to be sample poor (sample sizes of 10-100), and initially feature-rich (numbers of features 1,000-10,000). Consequently, they need special considerations before they can be used with confidence as diagnostic/prognostic aids in the clinic. Our statistical classification strategy (SCS) was developed specifically to process and analyze such data. The SCS is a multi-stage interactive approach, consisting of visualization, data preprocessing, best discriminatory feature selection, robust classifier development, and possible aggregation of several classifiers. It recognizes the fact that diagnostic aid methodologies must be robust. Significant attention will be given to the difficulties/pitfalls of biomedical data classification. Of the currently used non-invasive methods (NMR, IR, fluorescence, mass spectrometry and microarrays), I’ll focus on proton NMR spectroscopy and discuss several examples of successfully biomarking common occurring cancers.

2:35-3:00 NMR and MS Based Metabolite Biomarker Discovery for Disease Diagnostics
G.A. Nagana Gowda, Ph.D., Research Scientist, Department of Chemistry, Purdue University

The realization that a large number of small molecular metabolites can be reliably measured under dynamic conditions has led to the exploration of tissue and human body fluid to discover new biomarkers for early detection and treatment of diseases. High resolution analytical methods such as mass spectrometry (MS) and nuclear magnetic resonance (NMR) spectroscopy are the main focus of analysis in the fast developing area of metabolomics. While MS is highly sensitive, NMR spectroscopy provides more reproducible and quantitative data for high throughput analysis. The combination of complementary NMR and MS data has an added benefit of better classification of disease samples. Examples of this approach in several human and animal studies will be highlighted. Currently, the relatively low sensitivity of NMR is one of the bottlenecks for the detection of low concentrated early disease biomarker candidates. To circumvent such problems, we have explored isotopically labeled chemical derivatization methods. These methods, which are based on a class selection of metabolites, enhance sensitivity as well as improve spectral resolution. Advancements in this and other developments will be discussed with emphasis on the studies of human disease.
### Pharmacogenetics Laboratory Test Results into Clinical Action

The emerging use of pharmacogenomic drug metabolism and disease markers in drug development research has sparked considerable interest in the transmission and reporting of pharmacogenomic data. The FDA has recently issued a final guidance on the voluntary submission of pharmacogenomic data, and CDISC and HL7 teams have been actively developing models and vocabularies for this data. This presentation provides an overview of the proposed CDISC/HL7 pharmacogenomic data standards, which include a pharmacogenomic extension to the CDISC/HL7 LAB message, and three new domains within the CDISC SDTM. Example data sets are used to show how the detailed data of the CDISC/HL7LAB-operational standard populates the SDTM biospecimen, pharmacogenomic specimen and pharmacogenomic result domains. Examples of sequence based and gene expression based analyses are shown. A final section discusses proposed pilot projects using the models to submit data under the FDA Voluntary Genomics Data Submission program.

### DNA-Guided Medicine in the Management of Cardiovascular and Psychotropic Drugs

Gualberto Ruatlo, M.D., Ph.D., President and Chief Executive Officer, Genomas Inc.; Director, Genetics Research, Hartford Hospital

Genomas is a biomedical company advancing DNA-Guided medicine with PhysioType™ systems for personalized healthcare. A PhysioType System has 3 components: an ensemble of inherited, stable genetic markers (single nucleotide polymorphisms, SNPs) from various genes, a biostatistical algorithm validated in clinical studies for ascertaining the clinical significance of a patient’s SNPs, and a portal for doctors to select drugs based on an individual's risk of developing side effects. By comparing side effect risks of drugs in a therapeutic class for each patient and by forewarning doctors of adverse responses that will complicate treatment, PhysioType systems substantially enhance patient safety. PhysioType systems in development for statins, atypical antipsychotics, and glitazones will be described.

### Novel Computational Tools for Translating Genomic Biomarkers into Clinical Practice: Case for Warfarin

Saeed A. Jortani, Ph.D., Director, Toxicology, University of Louisville Hospital Laboratory; Associate Professor, Pathology and Laboratory Medicine, University of Louisville School of Medicine

There is a combination of clinical, scientific, and regulatory evidence supporting the adoption of pharmacogenetic-guided dosing for warfarin (Coumadin). This drug is the most commonly used oral anticoagulant medication, currently taken by four million people in the US who are at risk for blood clots and strokes. Because the proper warfarin dose per patient is difficult to assess, most physicians take an educated, ballpark guess, and follow up with a blood test to ensure the medicine is working properly. Confounding this is the fact that therapeutic warfarin doses vary significantly from patient to patient, so that even a “standard dose” can cause life-threatening side effects. By comparing side effect risks of drugs in a therapeutic class for each patient and by forewarning doctors of adverse responses that will complicate treatment, PhysioType systems substantially enhance patient safety. PhysioType systems in development for statins, atypical antipsychotics, and glitazones will be described.

### Translational Biomarkers for Kidney Toxicity

Viutil S. Vaidya, Ph.D., Instructor in Medicine, Brigham & Women’s Hospital, Harvard Medical School

Drug-induced nephrotoxicity plays a major role in the high incidence and prevalence of kidney injury in both hospitalized and non-hospitalized patients, which in many circumstances can be prevented or at least minimized by effective predictive toxicity screening in preclinical drug development studies. The absence of sensitive, specific, reliable and reproducible renal injury biomarkers affects the evaluation of response to therapy and individual patient safety, especially dose monitoring decisions for important life saving drugs with potential inherent kidney toxicity risk. For the last 100 years there have been no accepted kidney injury biomarkers. The standard metrics such as serum creatinine and blood urea nitrogen are very insensitive and non-specific functional biomarkers. The urine has yielded the most promising markers for the early detection of acute kidney injury (AKI) and further characterization is anticipated, which will qualify these markers as useful tools for the earlier diagnosis, identification of mechanism of injury, and assessment of site and severity of injury. Hopefully, one or more of these biomarkers, either alone or in combination, will prove to be useful in facilitating early diagnosis, guiding targeted intervention and monitoring disease progression and resolution. Translational biomarkers have the potential to not only transform the way we do predictive nephrotoxicity assessment but also the way we diagnose and treat patients with AKI.

### Vaccines, Biomarkers and Correlates of Protection

Mark T. Esser, Ph.D., Senior Research Fellow, Vaccines and Biologics Research, Merck Research Laboratories

Vaccine biomarker assays have been used historically to monitor disease incidence and prevalence, measure immune responses to natural infection or vaccination and to determine the duration of immunity. This talk will discuss how multiplexed antibody biomarker assays are being implemented in the development, licensure and post-licensure surveillance of vaccines with a case study on GAR-DASIL™, Merck’s vaccine for the prevention of cervical cancer.

### Use of Toxicity Biomarkers in Regulatory Review: An FDA Reviewer’s Perspective

Thomas Papoian, Ph.D., D.A.B.T., Pharmacologist/Toxicologist, Division of Cardiovascular and Renal Products, Center for Drug Evaluation and Research, U.S. Food and Drug Administration

During development of drug or biologic therapeutics, toxicities are often seen in treated animals that can have serious implications for human subjects if similar effects were to occur at therapeutic doses. In the majority of cases, such toxicities are clinically monitorable using established assessments, such as clinical signs or standard laboratory tests. However, situations are not uncommon in which the toxicities seen in animals are not easily monitorable in humans. This can occur when there is a lack of an appropriate validated biomarker to monitor a specific toxicity if and when it develops, thus preventing appropriate interventions in patients before serious or irreversible toxicity develops. Availability of validated biomarkers for specific toxicities can greatly assist the safety assessment process by regulatory reviewers, so that development of needed therapeutics can proceed in a safe manner. Potential use of validated biomarkers of toxicity in a regulatory setting will be discussed.

---

**POSTER INFORMATION**

Reasons You Should Present Your Research Poster at the BIOMARKER DISCOVERY SUMMIT 2008:

- Your poster will be exposed to over 400 delegates
- Receive $50 off your registration fee
- Your poster abstract will be published on our conference CD
- Your research will be seen by leaders from top pharmaceutical, biotech, academic and government institutes

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. Please submit your abstract and register for the meeting. To secure a poster board and inclusion in the conference CD, your abstract must be submitted, accepted and registration paid in full by September 8, 2008.

www.BiomarkerDiscoverySummit.com
We have been developing NMR and MS approaches to determining accurate positional and mass isotopomer distributions in a wide variety of metabolites and media and cells exposed to 13C-labeled precursors. The simultaneous acquisition of concentrations and isotopomer information for critical reporter metabolites greatly increases the biochemical information content, and with the aid of simple modeling, provides mechanistic insights into the response of cancer cells and tissues to environmental stress including disease states and response to therapeutic agents. Important biochemical pathways that are presently probed include glycolysis, pentose phosphate pathways, Krebs cycle, anaerobic reactions, nucleotide biosynthesis, redox stress pathways, protein biosynthesis and phospholipid turnover. The pathway information is especially helpful for generating new hypotheses as well as testing current ideas based on other Omics such as gene expression or protein data. The principles will be illustrated with applications in lung and breast cancer.

NMR-Based Metabolomics: Translational Application in Cancer and Anti-Cancer Treatment
Natalie J. Serkova, Ph.D., Associate Professor of Anesthesiology and Radiology, Director, Biomedical MR/PET/CT Cancer Center Core, University of Colorado Health Sciences Center
Cancer cells possess a highly unique metabolic phenotype which is characterized by high glucose uptake, increased glycolytic activity, decreased mitochondrial activity, low biogenic and increased phospholipid turnover. In addition to these general metabolic markers of malignancy, specific endogenous metabolites are implicated in particular tumors, such as N-acetyl aspartate in neuroblastoma, myo-inositol in glioma, citrate in prostate cancer, based on tissue-specific biochemistry. All these metabolic hallmarks can be readily assessed to monitor responsiveness and resistance developments to novel targeted drugs, where specific inhibition of cell proliferation (cytostatic effect) occurs rather than direct induction of cell death (cytotoxicity). Using modern analytical techniques in combination with statistical approaches, “metabolomics”, a global metabolic profile on patient samples can be established and validated for responders and non-responders, providing additional metabolic end-points. This review describes existing nuclear magnetic resonance (NMR)-based approaches for global metabolic profiling in tissue biopsies, body fluids and, finally, non-invasive assessment of metabolic biomarkers using non-invasive radiological techniques. Most recent studies on metabolic response to novel targeted drugs (tyrosine kinase inhibitors, metabolic modulators) are analyzed.

Metabolic Fingerprinting of Breast Cancer Development
Vladimir Shulaev, Ph.D., Associate Professor, Virginia Polytechnic Institute & State University, Bioinformatics Institute
We use metabolomics approaches to study the progression of malignancy in human breast epithelial cells. Weinberg cell model is used to categorize the metabolic changes associated with malignant transformation. We performed the liquid chromatography-mass spectrometry (LC-MS) and gas chromatography-mass spectrometry (GC-MS) based metabolomics analysis followed by multivariate statistical analysis to identify robust molecular signatures that can provide accurate classification of normal and malignant cells.

Institutional Affiliations

Bioinformatics Institute
Vladimir Shulaev, Ph.D., Associate Professor, Virginia Polytechnic Institute & State University, Bioinformatics Institute

4:25-4:50 Using Causal Network Models for Mechanistic Biomarker Discovery and Development
Keith Elliston, Ph.D., President & Chief Executive Officer, Genstruct, Inc.
The development of personalized medicine requires a detailed understanding of the molecular mechanisms of disease, and of drug action. The implementation of personalized healthcare requires the development of mechanistic diagnostics to enable the matching of a patient’s disease to the right therapeutic regimen. To meet this demand, Genstruct has implemented a Causal Network Modeling™ Platform capable of using any Omic data source to develop mechanistic models of disease and drug action, and to define mechanistic biomarkers. Mechanistic Biomarkers are distinct from conventional, correlative biomarkers by their placement within a molecular mechanism explaining how the Mechanistic Biomarker relates to the pathophysiology in question or to the efficacious response triggered by a successful therapeutic. Similarly, mechanistic toxicity biomarkers can measure undesirable molecular networks affected by drug treatment, as applicable. In all cases, a Mechanistic Biomarker research program starts by building Causal Network Models for disease progression and for drug response to map the molecular networks controlling the biological processes relevant to the disease. A data-driven approach to understanding the causal network topology governing a disease state or underlying an efficacious drug response is the critical starting point for the discovery of Mechanistic Biomarkers.

4:50-5:15 Achieving Confidence in Mechanism for Biomarker Discovery and Accelerated Drug Development
Colin Hill, Ph.D., Chief Executive Officer and President, Gene Network Sciences
Despite advances in our powers of observation, the ability to determine biological mechanisms from large-scale multi-omic technologies continues to be a major bottleneck in the discovery of biomarkers of disease progression and drug response. This can be overcome by utilizing computational learning methods that identify directly from the data the circuits and connections between drug-affected molecular constituents and physiological observables. The marriage of multi-omics technologies with reverse engineering approaches can provide missing insights needed to improve drug development success rates.

HOTEL INFORMATION
Loews Philadelphia Hotel
1200 Market Street
Philadelphia, PA 19107
Phone: 215-627-1200  Fax: 215-231-7205
Discounted Room Rate: $189 s/d
Reduced Room Rate Cutoff: September 8, 2008
To reserve your hotel room, please call the hotel directly at 215-627-1200. Identify yourself as a Cambridge Healthtech Institute conference attendee to receive the reduced room 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.

TRAVEL INFORMATION
FLIGHT DISCOUNTS:
To receive a 5% discount on American Airlines, American Eagle and AmericanConnections call and make your flight reservations at 1-800-433-1790 or go online at aa.com. Please refer to the authorization number AN# A2418SS via phone or enter it in the promotion discount box online.

CAR RENTAL DISCOUNTS:
Special discount rentals have been established with AVIS for this conference. Please call AVIS directly at 800-331-1600 and reference the Avis Worldwide Discount (AWD) Number 8868190 or go to avis.com.
and experimental protocols and eventually applicable for regulatory use. Dating and standardizing gene signatures, to make them portable across platforms, technologies in long-term rodent studies, have proven difficult to develop. We also discuss the need for validating biomarkers for predictive toxicology and risk assessment using toxicogenomic technologies.

Pharmaceutical Research & Development
Nandini Raghavan, Ph.D., Principal Biostatistician, Non-Clinical Biostatistics, Johnson & Johnson

9:25-9:50 Noninvasive Safety Biomarkers of Germinal Center Atrophy and Infection
Eric R. Fedyk, Ph.D., Head Inflammation Biology & Immunotoxicology, Non-Clinical Development Sciences, Millennium Pharmaceuticals, Inc.

The pathology of autoimmune disease is characterized by recurrent chronic inflammation. Successful therapeutic intervention requires immunosuppression, however not of a magnitude that predisposes subjects to infection, a current safety risk, particularly in outpatient settings (e.g. rheumatoid arthritis). Dosing patients for "efficacy without infection" is an elusive endeavor with contemporary therapeutics, largely due to inherent heterogeneity among subjects. Recent development of noninvasive, antecedent biomarkers of immunosuppression and infection, in genetically heterogeneous primate models, has the potential to improve dosing of subjects in clinical trials and patients in clinical practice.

9:25-9:50 Genomic Biomarkers for Early Screens for Non-Genotoxic Carcinogenicity
Nandini Kaghavan, Ph.D., Principal Biostatistician, Non-Clinical Biostatistics, Johnson & Johnson Pharmaceutical Research & Development

Genomic drug safety screens will accelerate the process for developing safer drugs and limit the failure of drugs in late stage development due to toxicity issues, by identifying potential toxicity issues early in the development process. As a result, there is now heightened interest in developing biomarkers for predictive toxicology and risk assessment using toxicogenomic technologies from pharmaceutical companies as well as from governmental agencies worldwide. In this talk we describe the development of a gene-expression based signature to predict non-genotoxic carcinogenicity with high accuracy, using 24 hour microarray experiments on rats. This approach is especially useful in the immunology area, as these tissues samples do contain immune cells that are the targets of the drug action. These biomarkers are useful in both understanding the key mechanism of action, as well as optimizing the use of these drugs. A gene expression based 'hypothesis-free' approach complements the more traditional 'hypothesis-driven' biomarker analyses in immunology including flow cytometry and immunohistochemistry, and is especially useful when the detail of the drug action is not well understood.

9:50-10:50 Networking Coffee Break with Poster and Exhibit Viewing
**Technology Advances for Metabolic Profiling**

8:30-8:35 Chairperson’s Opening Remarks
8:35-9:00 NMR-Based In-Situ Metabolic Profiling of the Life Cycle of Malaria Parasite P. falciparum With High Temporal Resolution
Jovan Peclet, Ph.D., Lecturer, Senior NMR Spectroscopist, Department of Chemistry, Frick Lab, Princeton University

Metabolic mixture analysis can be most efficient when using unbiased and quantitative analytical methods, such as NMR spectroscopy, and sophisticated statistical techniques. In addition, keeping the sample in its native condition can be an essential benefit. We have been studying the 48 hour life cycle synchronization of malaria parasites, P. falciparum, in red blood cell (RBC) cultures. The current research to be discussed in this talk has been focusing on in-situ media analysis of the cell culture following temporal changes with high resolution. Metabolic changes in the media present a sensitive and very informative reflection of the metabolism over the various stages of the parasitic infection and development. We have been able to characterize this process with both accessible and the combination of NMR and statistical analysis follow the high temporal resolution kinetics of metabolic changes in the media, and screen the effects of known antimalarial drugs and anticipated drug candidates.

9:00-9:25 Mass Spectral Metabonomics Beyond Elemental Formula: Chemical Database Querying by Matching Experimental with Computational Fragmentation Spectra
David F. Grant, Ph.D., Associate Professor of Toxicology, Co-Head, Mass Spectrometry Facility, Department of Pharmaceutical Sciences, University of Connecticut
Despite recent advances in NMR and mass spectrometry, the structural identification of organic compounds in complex biofluids remains a significant analytical challenge. For mass spectrometry applications in toxicology, the goal is usually limited to determination of elemental formula. Here we test the hypothesis that unknown chemical structures can be determined by matching their experimental collision induced dissociation (CID) fragmentation spectra with computational fragmentation spectra of compounds retrieved from chemical databases. The monoisotopic molecular weights (MMW + 10 ppm) of 102 “test” compounds were used to download 102 “bins” from the PubChem database. Each bin contained the corresponding test compound and, on average, 272 other candidate compounds, including 158 compounds having the same elemental formula as the test compound. Commercially available software was used to generate fragmentation spectra for all compounds in each of the 102 bins. Experimental CID spectra for each of the 102 test compounds were then compared to the computational spectra in order to rank candidate compounds based on number of fragment MMW matches. This method returned the test compound as the highest ranking (or tied with the highest ranking) compound for 65 of the 102 bins. The test compound was ranked within the top 20 candidate compounds for 87 bins. In addition, the correct elemental formula was ranked first for 96 of 102 bins. Thus, matching experimental with computational fragmentation spectra is a valid method for rapidly discriminating among compounds having the same elemental formula and provides a novel approach for querying chemical databases for structural information.

9:25-9:50 Addressing the Analytical Problems of Global Systems Biology Using Ultra High Resolution LC and Exact Mass MS/MS
Robert Plumb, Ph.D., Senior Applications Manager, Pharmaceutical Business Operations, Waters Corporation
The analytical challenges that face global systems biology in an animal study or a human population environment are many fold. These include the detection of all of the analytes in the samples, the accurate measurement of their relative concentrations, data reduction, the identification of critical biological pathways, and, in many cases, the need for high throughput and rapid the processing of thousands of samples. The detection of endogenous metabolites requires a high resolution, high sensitivity instrumentation such as chromatography and mass spectrometry system. This is especially true in biological samples such as plasma, urine, and bile, where the matrix is particularly complicated. Reversed-phase liquid chromatography coupled to electrospray mass spectrometry is particularly suited to this task as it is compatible with the biological matrix; more recently the use of sub 2μm particles operated at higher temperatures has been demonstrated to give increased LC performance. In this presentation we will illustrate the benefits of this technique for the metabolicomics, and show how the use of higher operating temperatures and longer columns can generate very high resolution chromatograms with peak capacities of 1000 in just 1 hour with peak widths of less than 1 second. Reference will be made to the effect of these narrow peak widths on MS data capture rates and mass accuracy. We will demonstrate how this approach has been used to analyze samples from a toxicity study to elucidate the effects of the gut microflora play in controlling drug metabolism and metabolic response to a toxicological insult. We will also show how this approach has been used to process samples from a human metabolomics study with a very short analysis time to elucidate the effected biological pathways via the identification of putative biomarkers by exact mass hybrid quadrupole TOF MS/MS.

**Biomarker Data Analysis**

8:30:8:35 Chairperson’s Opening Remarks
8:35-9:00 MOA Biomarker Discovery for IKKb Inhibition Program: An Interdisciplinary Approach
Zhenhao Qi, Ph.D., Senior Principal Scientist, Translational Sciences, Boehringer Ingelheim Pharmaceuticals, Inc.
There is increasing demand for Mechanism of Action (MOA) biomarker(s) in Phase I clinical trials to demonstrate compound hits the target is in vivo, thus allowing better decision making at early phase. In this IKK beta inhibition MOA biomarker program, we employed an interdisciplinary approach to combine statistical genome-wide search on in-house established gene expression database and literature/text mining to narrow down to a set of biologically relevant genes. Our statistics-driven in vivo LPS whole blood assay allowed us to find optimal inhibition window for IKK beta-selective inhibitor; we were able to identify 2 high potential biomarkers whose responses were statistically significant at their EC50 concentrations in the gene (Tasman) and protein (ELISA) expression experiments with a full dose range of inhibitor, these 2 genes will serve as ex vivo predictive MOA biomarkers in the Phase 1 trial.

9:00-9:25 Semantic Web Abstractions for Biomedical Informatics: A Better Foundation for Integrating Sensitive Heterogenous Data Sources
Jovan S. Almeida, Ph.D., Abell-Hanger Distinguished Professor, Department of Bioinformatics and Computational Biology, The University of Texas, M.D. Anderson Cancer Center
The maturation of semantic web technologies (SW) offers a more generic foundation to weave integrated data management systems than the relational and object oriented approaches that precede it. With the deceptively simple claim of taking a step back to the foundations of Entity-Relationship-Entity models, SW enables evolvable knowledge representation and inference systems that can cope with the system approach of modern biomedical research and its translation into personalized medicine. Because the meaning of data changes with the analysis that its representation enables, data management and data analysis can no longer be treated as separate components of knowledge engineering for the Life Sciences. The same applies to security and privacy issues intrinsic to biomarker discovery initiatives. The more generic nature of SW abstractions enables the incorporation of access permission in the data model such that permission to access travels with the data rather than staying at the point of access to the data store.

9:25-9:50 Using Networks to Integrate Omic and Semantic Data: Towards Understanding Protein Function on a Genome Scale
Mark Gerstein, Ph.D., Albert L. Williams Professor of Biomedical Informatics, Molecular Biophysics and Biochemistry, Computer Science, Yale University
My talk will be concerned with topics in proteomics, in particular predicting protein function on a genomic scale. We approach this through the prediction and analysis of biological networks, focusing on protein-protein interaction and transcription-factor-target ones. I will describe how these networks can be determined through integration of many genomic features (including those derived from using the semantic web and text mining) and how they can be analyzed in terms of various simple topological statistics. In particular, I will discuss: (1) Integrating gene expression data with the regulatory network illuminates transient hubs; (2) Integration of the protein interaction network with 3D molecular structures reveals different types of hubs, depending on the number of interfaces involved in interactions (one or many); (3) Analysis of betweenness in biological networks; (4) Analysis of structure of the regulatory network shows that it has a hierarchical layout with the “middle-managers” acting as information bottlenecks; (5) Development of useful web-based tools for the analysis of networks, PubMed and tYNA; (6) Using known semantic web relationships as training sets to improve biological query applications; and (7) Using literature data to predict protein interactions.
Development Considerations for Single-Analyte Markers, Panels, and Profiles

10:50-11:15  Optimal Biomarker Approach: Data Analysis Considerations of Individual, Panel or Profile
Stephen Needor, Ph.D., Chief Executive Officer & Chairman, PPM Inc.
The advent of relatively high throughput and broad analyte coverage analysis in “omic” measurements has reignited a debate about what constitutes the optimal biomarker solution. Is it a single analyte per biological event, or a panel (3-10 analytes) or even a profile (>20 analytes)? This will be discussed in the context of statistical and data analysis as well as data mining characteristics.

11:15-11:40  Panel Discussion

11:40-1:10  Luncheon Technology Workshop

Enabling Drug Development Through Multiplexed Assays
Pankaj Oberoi, Ph.D., Director, Scientific Services, Meso Scale Discovery
Meso Scale Discovery (MSD) has an electrochemiluminescence platform that is fast (1-3 minutes per plate independent of plate density), robust (non-fluidics instrument), radioactive free, sensitive (detection limits near 1 attomole) and has a wide dynamic range (5 log) with multiplexing capabilities. The performance (sensitivity, reproducibility, and ease of use) of multiplexing cytokines, cell signaling pathways, and multiplexed toxicology biomarkers assays will be presented. Development of multiplex panels for complex matrices is challenging because of varying levels of biomarkers, interfering substances in the sample, and interactions between proteins measured. The platform allows for simple assay development that can greatly reduce the amount of time to develop novel assays. The combined properties of the system provide both a cost and time savings with a highly quantitative assay format while improving productivity.

1:10-1:15  Chairperson’s Opening Remarks

1:15-1:40  Integration of Metabolic and Transcriptomic Profiling for Understanding of Diabetes and Obesity Mechanisms
Christopher B. Newgard, Ph.D., Director, Sarah W. Stedman Nutrition and Metabolism Center, Duke University Medical Center
Type 2 diabetes is a disease that occurs as a result of metabolic dysfunction in multiple tissues, including most prominently liver, skeletal muscle, and the pancreatic islets of Langerhans. An understanding of the transcriptional and metabolic networks that control normal functions in these tissues, and identification of the network elements that are perturbed during development of type 2 diabetes, are essential steps in the development of new therapies for the disease. The value of targeted mass spectrometry-based profiling of key clusters of intermediary metabolites for identifying specific network perturbations will be highlighted, as will recent examples of integration of metabolomic and transcriptomic profiling for identifying heretofore unrecognized regulatory pathways.

1:40-2:05  Integrating Gene and Protein Expression Biomarkers in a Systems Biology Approach to Colon Cancer
Mark R. Chance, Ph.D., Director, Case Center for Proteomics; Director, Center for Synchrotron Biosciences; Professor, Department of Physiology & Biophysics, Case Western Reserve University
Protein interaction networks are at the heart of functional control of human disease. Network and pathway modeling driven by Omics-based approaches are increasingly important to our understanding of disease progression and drug responses. However, deriving and validating network models are complex research problems requiring integration of multiple types of high-throughput data. We have recently employed a systems biology approach to find small networks of proteins discriminative of late stage human colorectal cancer (CRC). Expression proteomics studies were initially used to identify proteins differentially regulated when comparing normal and late stage tumor tissues obtained from adequately sized cohorts of human patients. Proteins identified by these experiments were used to seed a search for protein-protein interaction networks selective for biological relevance to the human colon. We chose four significant networks returned by this search and illustrated using measures of mutual information, calculated using gene expression data, that certain protein “signatures” within each network are highly discriminative of late stage cancer versus control. These signatures would not have been discovered using only proteomic data, or by merely clustering the gene expression data. Expanding these signatures by a single hop generated four sub-networks, which were analyzed for biological relevance to human CRC. A number of the proteins in these sub-networks have been shown to be critically involved in the progression of CRC. Others have been recently identified as potential markers of CRC, and still others merit follow-on experimental validation for biological significance in this disease. This general approach can be applied to network modeling for a number of diseases.

2:05-2:30  A Systems Biology Approach to Biomarker Discovery
Karen Rodland, Ph.D., Science Lead for NIH Programs, Pacific Northwest National Laboratory
Efforts to identify biomarkers for early diagnosis or prognosis of cancer and other diseases have often focused on a singular molecular species, with preference given to mRNA, microRNA, proteins, autoantibodies or metabolites based on available technologies and model systems. Each one of these measurements provides a snapshot of cell function, but a dynamic understanding of disease processes really requires the integration of all these modalities to the extent possible. Particularly in the context of using biomarkers to guide therapeutic interventions, it is necessary to understand the relationship between changes in expression, and changes in function. One aspect of systems biology is the integration of heterogeneous datasets to define relationships that predict function. This talk will describe the application of this approach to model chronic obstructive pulmonary disease.

2:30-2:55  Connecting the Biomarker Dots in Cancer and Neurodegenerative Diseases
Ira L. Goldberg, Ph.D., Director, Proteomics, Power3 Medical Products, Inc.
The application of fundamental principles to Omic integration to address unmet clinical needs will be illustrated with examples from cancer and neurodegenerative diseases. The integrations relate analytical with clinical validation across different analytical processes and platforms; clinical diagnostics with assessment of severity, disease progression, and efficacy; and data analysis integrating proteomic and genomic biomarkers, post-translational modifications, and protein isoforms. The clinical applications cover testing of blood serum for early detection of breast cancer as well as for early differential diagnosis and monitoring of the neurodegenerative diseases. The attainment of biological significance in terms of monitoring mechanisms of disease through blood testing as well as practical clinical diagnostic applications of such testing will also be discussed.

3:00  Close of Conference
The following companies participated in the 2007 Biomarker Discovery Summit

Abbott Labs
ADLYFE Inc
Agilent Technologies
Amgen Inc
Amylin Pharmaceuticals Inc
Annamalai Univ
Aspreva Pharmaceuticals
Astellas Pharma Inc
AstraZeneca Pharmaceuticals Inc
Asuragen Inc
Avalon Pharmaceuticals Inc
Axela Biosensors
BD Diagnostics
Bio Rad Labs
BioFortis Inc
Boehringer Ingelheim Pharma
Bristol Myers Squibb Co
BT Luke & Associates
Caprion Proteomics
Carestream Health
Case Western Reserve Univ
Celera Diagnostics
Centocor R&D Inc
Central Connecticut State Univ
Cogenics
CompanionDx Consulting
Conservant Healthcare Systems
Corning Inc
Correlogic Systems Inc
Covance Lab
Critical Path Institute
Crossover EOOD
Dako Denmark AS
Dankook Univ
Decision Biomarkers Inc
Diamics Inc
Digilab BioVision GmbH
DSM Food Specialties
Duke Univ
Edgewood Chemical Biological Ctr
Eli Lilly & Co
EMD Biosciences Inc
EMD Lexingen Research Ctr
Exiqon AS
Expression Pathology Inc
FDA
FDA CDER
Fox Chase Cancer Ctr
Frantz BioMarkers
Genoptix Inc
GenTel BioSciences Inc
Genzyme Corp
George Mason Univ
GlaxoSmithKline
Global Alliance for TB Drug Development
Grifols USA
Hallym Univ
Hills Pet Nutrition
HistoRx Inc
Immunicon Corp
Informa Healthcare
Institute for BioAnalytics
IO Informatics Inc
Johnson & Johnson
London Genetics Ltd
MD Anderson Cancer Ctr
Medicines Co
MedImmune Inc
Merck & Co
Meso Scale Discovery
Miami Univ
Millipore Corp
Mitsubishi Chemical Corp
Monarch Life Sciences
Nagoya Univ
NASA Ames Research Ctr
Nastech Pharmaceutical Co Inc
Natl Ctr for Toxicological Research
Neural Diagnostics Pty Ltd
NIH NCI
NIH NEI
NIH NIA
Northeastern Univ
Novartis Horsham Research Ctr
Novartis Institutes for BioMedical Research Inc
Novartis Pharmaceuticals
Novo Nordisk USA
Novovax Inc
Open Biosystems
Paterson Institute for Cancer Research
Pathwork Diagnostics
Pfizer Global R&D Groton Labs
Pfizer Ltd
Philips Research Asia
PrecisionMed
Predictive Biosciences
Predictive Physiology & Medicine Inc
Pressure BioSciences Inc
Pronota NV
Proteome Sciences Plc
Purdue Univ
Renovar Inc
Roche Labs Inc
Roche Palo Alto
Rosetta BioSoftware
Rosetta Genomics Inc
Rosetta Inpharmatics
Rules Based Medicine Inc
Sandia Natl Labs
Sartorius Stedim Biotech
Schering Plough Research Institute
Seoul Natl Univ
Seoul Natl Univ Hospital
Sepracor Inc
SIDMAP
Siemens AG Medical Solutions
Sirtris Pharmaceuticals Inc
Strategic Diagnostics Inc
Taipei Veterans General Hospital
Tandem Labs
TAP Pharmaceuticals Inc
Theranostics Health
Thermo Fisher Scientific Inc
Thomas Jefferson Univ
Thompson Scientific
Tulip BioLabs Inc
UMDNJ
Univ Hospital
Univ of California Davis
Univ Of Colorado Denver
Univ Of Florida Gainesville
Univ Of Pennsylvania
Univ Of Queensland
Univ of Texas Dallas
Univ of Vienna
Univ of Virginia
Univ Of Wisconsin Madison
Vanderbilt Univ
Veeda Clinical Research UK
Viventia Biotech
Washington Univ
Wyeth Pharmaceuticals
Wyeth Research Labs
Xceed Molecular
Zoegen Corp

www.BiomarkerDiscoverySummit.com
BIOMARKER DISCOVERY SUMMIT 2008

September 29 - October 1, 2008 • Loews Philadelphia Hotel • Philadelphia, PA

[YES! Register me for BIOMARKER DISCOVERY SUMMIT 2008]

REGISTRATION INFORMATION

REGISTER 3 — 4th IS FREE

Individuals must register for the same conference or conference combination and submit completed registration forms together for discount to apply. Please reproduce this registration form as needed.

Name
Job Title
Company
Address
City/State/Postal Code
Country
Phone
Fax
Email

Would you like to receive event updates via fax? YES  NO

Present a Poster and Save $50

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference CD, your abstract must be submitted, accepted and registration paid in full by September 8, 2008. Register online to use the Poster Submission form or, if you register by phone, fax, or mail, you will receive Poster Abstract Submission guidelines via email. I am interested in presenting a poster at:

Biomarker Discovery Summit 2008

Please send information about related CHI conferences:

Biomarkers Europe
Biomarker Assay Development
Biomarker World Congress

CHI INSIGHT PHARMA REPORTS

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

ADDITIONAL REGISTRATION DETAILS

Each registration includes all conference sessions, posters and exhibits, food functions, and a copy of the conference CD. For a list of reports, visit InsightPharmaReports.com, or contact Rose LaRaia at rlaraia@healthtech.com, 781-972-5444

ADDITIoNAL REgISTRATIoN DETAILS

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

GROUP DISCOUNTS

Special rates are available for multiple attendees from the same organization. Contact David Cunningham at 781-972-5444

HANDICAPPED EQUAL ACCESS

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

Substitution/Cancellation Policy

In the event that you need to cancel a registration, you may:

• Transfer your registration to a colleague within your organization;
• Credit your registration to another Cambridge Healthtech Institute program;
• Request a refund minus a $100 processing fee per conference;
• Request a refund minus the cost ($500) of ordering a copy of the CD.

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

Program and speakers are subject to change. Video and audio recording of any kind is prohibited onsite at all CHI events.

FAX or MAIL your registration to:

Cambridge Healthtech Institute
250 First Avenue, Suite 300, Needham, Massachusetts 02494
T. 781-972-5400 or toll-free in the U.S. 888-999-6288
F. 781-972-5425 • www.healthtech.com

Present a Poster and Save $50

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference CD, your abstract must be submitted, accepted and registration paid in full by September 8, 2008. Register online to use the Poster Submission form or, if you register by phone, fax, or mail, you will receive Poster Abstract Submission guidelines via email. I am interested in presenting a poster at:

Biomarker Discovery Summit 2008

Please send information about related CHI conferences:

Biomarkers Europe
Biomarker Assay Development
Biomarker World Congress

CHI INSIGHT PHARMA REPORTS

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

ADDITIONAL REGISTRATION DETAILS

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

GROUP DISCOUNTS

Special rates are available for multiple attendees from the same organization. Contact David Cunningham at 781-972-5444

HANDICAPPED EQUAL ACCESS

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

Substitution/Cancellation Policy

In the event that you need to cancel a registration, you may:

• Transfer your registration to a colleague within your organization;
• Credit your registration to another Cambridge Healthtech Institute program;
• Request a refund minus a $100 processing fee per conference;
• Request a refund minus the cost ($500) of ordering a copy of the CD.

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

Program and speakers are subject to change. Video and audio recording of any kind is prohibited onsite at all CHI events.

FAX or MAIL your registration to:

Cambridge Healthtech Institute
250 First Avenue, Suite 300, Needham, Massachusetts 02494
T. 781-972-5400 or toll-free in the U.S. 888-999-6288
F. 781-972-5425 • www.healthtech.com

Present a Poster and Save $50

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference CD, your abstract must be submitted, accepted and registration paid in full by September 8, 2008. Register online to use the Poster Submission form or, if you register by phone, fax, or mail, you will receive Poster Abstract Submission guidelines via email. I am interested in presenting a poster at:

Biomarker Discovery Summit 2008

Please send information about related CHI conferences:

Biomarkers Europe
Biomarker Assay Development
Biomarker World Congress

CHI INSIGHT PHARMA REPORTS

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

ADDITIONAL REGISTRATION DETAILS

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

GROUP DISCOUNTS

Special rates are available for multiple attendees from the same organization. Contact David Cunningham at 781-972-5444

HANDICAPPED EQUAL ACCESS

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

Substitution/Cancellation Policy

In the event that you need to cancel a registration, you may:

• Transfer your registration to a colleague within your organization;
• Credit your registration to another Cambridge Healthtech Institute program;
• Request a refund minus a $100 processing fee per conference;
• Request a refund minus the cost ($500) of ordering a copy of the CD.

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

Program and speakers are subject to change. Video and audio recording of any kind is prohibited onsite at all CHI events.

FAX or MAIL your registration to:

Cambridge Healthtech Institute
250 First Avenue, Suite 300, Needham, Massachusetts 02494
T. 781-972-5400 or toll-free in the U.S. 888-999-6288
F. 781-972-5425 • www.healthtech.com