

11:00 AM-1:00 PM **Educational Session 1:
Functional and Molecular Imaging**
Grand Ballroom East

Chairperson: Brian D. Ross, University of Michigan, Ann Arbor, MI

Development and validation of functional and molecular imaging approaches for applications to the pre-clinical and clinical drug development process are ongoing. For example, molecular imaging reporters can be developed to image the activity of specific oncogenic signaling molecules in cell and animal tumor models. This can provide for cell-based high throughput screening assays and *in vivo* PK/PD evaluation of lead compounds. In addition, incorporation of imaging into clinical trials provides for opportunities to gain early and specific insights into drug effects that would not be possible using conventional anatomical imaging approaches. This session will highlight various applications in which imaging technologies can be used within the context of the drug discovery and drug development processes.

[18F]-alpha-V-beta-3 Integrin PET Imaging as a Biomarker of Clinical Angiogenesis

Pamela S. Cohen, GE Healthcare, Princeton, NJ

Individualizing Cancer Therapies Using PET Imaging*

Richard L. Wahl, Johns Hopkins University, Baltimore, MD

Evaluation of Response to Systemic Therapy for Brain Metastases: Challenges and Opportunities

Nancy U. Lin, Dana-Farber Cancer Institute, Boston, MA

Application of Molecular Imaging in Cancer Drug Development and Clinical Trials

Brian D. Ross

11:00 AM-1:00 PM **Educational Session 2:
Nucleic Acid Research**
Grand Salon E

Co-Chairpersons: Joseph A. Califano, Johns Hopkins University School of Medicine, Baltimore, MD, and **Christoph Plass**, Ohio State University, Columbus, OH

This Session will address the role of emerging nucleic acid based technologies in molecular diagnostics and drug development. These new techniques will be key to identifying new targets for therapy and profiling patient tumors in the era of personalized medicine. The detection of mutations, changes in DNA structure, and epigenetic modifications, in tumors as well as body fluids, will be explored. The promise of these advances is clear, yet many hurdles remain and will be discussed.

High Quality Copy Number and Genotype from FFPE Samples Using Molecular Inversion Probes (MIP)*

Malek Faham, Affymetrix, South San Francisco, CA

Mitochondrial Dysregulation and Molecular Diagnostics
Joseph A. Califano

Synthetic Lethal Approaches to the Treatment of Cancers with DNA Repair Defects*

Alan Ashworth, Breakthrough Breast Cancer Research Centre, London, United Kingdom

Epigenetic Contributions to Human Malignancies
Christoph Plass

1:00 PM-2:00 PM **Break**

2:00 PM-4:00 PM **Educational Session 3:
Integration of Biomarkers
into Clinical Trials**
Grand Ballroom East

Chairperson: Thomas G. Roberts, Noonday Asset Management, LP, Charlotte, NC

Cancer drug development has entered a particularly dynamic period in its history: there are more drugs in development, a broader range of targets under investigation, and greater interest from the biopharmaceutical industry than ever before. Yet multiple challenges remain. The success rate of agents entering phase 1 clinical trials is below 10 percent; more than 50 percent of agents in phase 3 trials fail to improve upon a reference regimen; and the therapeutic index of even the newer molecularly-targeted agents remains below what is achieved in other area of medicine. There is widespread optimism that successful integration of biomarkers into clinical development may boost success rates, obviate late-stage failures, and help select subsets of patients who are most likely to receive a clinical benefit from targeted agents.

The Use of Biomarkers in Early Clinical Trials at the NCI
Joseph E. Tomaszewski, National Cancer Institute, Bethesda, MD

Evaluating When a Diagnostic Test or Biomarker Is Informative
Gregory Campbell, Center for Devices and Radiological Health, FDA, Rockville, MD

Translational Use of Imaging in Early Drug Development*
Susan M. Galbraith, Bristol-Myers Squibb Company, Princeton, NJ

Econogenomics 2007: When Does the Inclusion of Biomarkers in Oncology Drug Development Make Economic Sense?*

Thomas G. Roberts

*An extended abstract for this presentation is available in the Invited Abstracts section of the *Proceedings*.

**2:00 PM-4:00 PM Educational Session 4:
Proteomics and Other "-Omics"**
Grand Salon E

Chairperson: Samir M. Hanash, Fred Hutchinson Cancer Research Center, Seattle, WA

This session will review some of the current issues and opportunities in molecular diagnostics related to global profiling. Opportunities stem from the ability to interrogate the genome and other "-omes" with technologies that deliver quantifiable measures. Challenges include developing a mechanistic understanding, not only statistical correlations, from such interrogations and implementing strategies that allow integration of multiple, diverse datasets. Specific topics to be covered include the contributions of proteomics to molecular diagnostics, the emergence of glycomics to profile tumors and biological fluids, and the use of metabolomics to complement genomic-based approaches.

Folate in Cancer Treatment and Prognosis: A Multi"-Omic" Approach*

Cornelia M. Ulrich, Fred Hutchinson Cancer Research Center, Seattle, WA

Anti-Glycan Autoantibody Signatures of Malignancy Status: Applications of Printed Glycan Array in Cancer Diagnostics and Discovery of Therapeutic Targets*

Margaret E. Huflejt, GlycoMedical Research Institute, La Jolla, CA

Development and Implementation of Reverse Phase Protein Microarrays for Patient Tailored Therapies

Emmanuel F. Petricoin, George Mason University, Manassas, VA

Innovative Approaches to Cancer Biomarker Discovery
Samir M. Hanash

4:00 PM-4:15 PM Break

**4:15 PM-5:45 PM Educational Session 5:
Regulatory Challenges to
Biomarker Development**
Grand Salon C

Chairperson: Steven I. Gutman, Food and Drug Administration, Rockville, MD

With completion of the human genome map and the introduction of numerous and refined new molecular diagnostic techniques (multiple tests, microarrays, bioinformatic systems), there has been a wide and growing interest in finding new technology to allow for more cost

effective and personalized diagnostic decision making. With initiation of NIH and FDA programs, namely the NIH Roadmap and the FDA Critical Path Initiative, attention has been placed on the use of biomarkers for broader purposes including for making more directed treatment discovery choices and providing shorter scientific, regulatory and reimbursement paths to market. To date, there has been a surprising paucity of new diagnostic tools for routine clinical use.

Panelists in this educational session will briefly describe some of the challenges facing new biomarker technology on its way to the medical marketplace. Then for the majority of this session, the panelists will answer questions from the audience.

Panelists

Doing the Math – How to Create Least Burdensome Designs in Establishing Performance for New Biomarkers
Gregory Campbell, Center for Devices and Radiological Health, FDA, Rockville, MD

Making the Critical Path a Yellow Brick Road
Samir N. Khleif, National Cancer Institute, Bethesda, MD

Teaching Old Docs New Tricks: What Questions Should Be Asked Before Introducing New Biomarkers into the Clinical Laboratory
Lee N. Newcomer, UnitedHealth Group, Hopkins, MN

Evaluating the Evidence for New Technology
Margaret A. Piper, Blue Cross Blue Shield Association, Atlanta, GA

7:00 PM-8:30 PM Opening Session
Grand Ballroom East

Welcome

Margaret Foti, American Association for Cancer Research, Philadelphia, PA

Introductory Remarks

David Sidransky, Johns Hopkins University, Baltimore, MD

Keynote Address

Blueprint of the Breast and Colorectal Cancer Genomes*
Victor E. Velculescu, Johns Hopkins Kimmel Cancer Center, Baltimore, MD

8:30 PM-9:30 PM Opening Reception

Grand Ballroom West
All registrants are invited to attend.

*An extended abstract for this presentation is available in the Invited Abstracts section of the *Proceedings*.

Tuesday, September 18

7:00 AM-8:00 AM **Continental Breakfast**
Grand Ballroom West

8:00 AM-10:15 AM **Plenary Session 1:
Plasma DNA and Circulating
Tumor Cells**
Grand Ballroom East

Co-Chairpersons: **David Sidransky**, Johns Hopkins University, Baltimore, MD, and **Y. M. Dennis Lo**, The Chinese University of Hong Kong, Hong Kong, SAR, China

The presence of cell-free tumor-derived nucleic acids in the plasma of cancer patients has opened up new possibilities for cancer detection, monitoring and prognostication. Amongst these nucleic acid targets, epigenetic markers targeting DNA methylation alterations in tumor cells hold much promise. Other markers include tumor-associated mutations in plasma, which have also been used to predict response to treatment. One notable development is the detection of epidermal growth factor receptor mutations in serum as a predictor of response to gefitinib in non-small cell lung cancer. For the translation of circulating nucleic acids into clinically applicable tumor markers, highly sensitive methods for their detection and quantitation are necessary. In this regard, the recent development of BEAMing (beads, emulsion, amplification, and magnetics) has offered exciting possibilities for individual plasma DNA molecules to be examined. This session will serve as a forum in which the potential of plasma nucleic acids in cancer diagnostics and management will be explored.

Circulating DNA as a Tumor Biomarker
Dave S. Hoon, John Wayne Cancer Institute,
Santa Monica, CA

Potential of BEAMing Technology to Develop Individualized
Cancer Care
Frank Diehl, Johns Hopkins University, Baltimore, MD

Detection of Epidermal Growth Factor Receptor Mutations in
Serum DNA Using the Scorpion ARMS in Patients with
Advanced Non-small Cell Lung Cancer*
Isamu Okamoto, Kinki University School of Medicine,
Osaka, Japan

Talk from Proffered Papers:
PR-1 Detection and Prognostication of Hepatocellular
Carcinoma by Quantitative Analysis of Aberrantly Methylated
DNA in Serum Using a Non-bisulfite-based Method
K.C. Allen Chan, Chinese University of Hong Kong,
Hong Kong

Summary
David Sidransky and **Y. M. Dennis Lo**

10:15 AM-10:45 AM **Coffee Break**
Grand Ballroom West

10:45 AM-1:00 PM **Plenary Session 2:
Molecular Staging and
Tumor Burden**
Grand Ballroom East

Co-Chairpersons: **George D. Demetri**, Dana-Farber Cancer Institute, Boston, MA, and **Laura J. van 't Veer**, Netherlands Cancer Institute, Amsterdam, The Netherlands

The advent of molecular pathology is leading to more precise characterization and staging of tumors. Markers and screens are currently in development to also identify pre-cancerous lesions and tumors that are pre-metastatic. Such advancements allow researchers to develop the personalized therapies that are revolutionizing patient treatment and prognosis. This session will explore the potential of these emerging technologies, in drug development and patient care.

Intrinsic Tumor Capacity Is Within the Genes
Laura J. van 't Veer

Expansion of Myeloid Immune Suppressor Cells in Tumor-bearing Host Directly Promotes Tumor Angiogenesis, Tumor Growth, and Metastasis*
P. Charles Lin, Vanderbilt University Medical Center,
Nashville, TN

"Being Prepared:" Tissue Conditioning in Forming the Pre-Metastatic Niche
Rosandra N. Kaplan, Memorial Sloan-Kettering Cancer Center, New York, NY

Talk from Proffered Papers:
PR-2 Plasma Is More Sensitive than Cellular Analysis for Detecting JAK2 Mutations and Determining Zygosity
Maher Albitar, Quest Diagnostics Nichols Institute,
San Juan Capistrano, CA

Summary
George D. Demetri and **Laura J. van 't Veer**

1:00 PM-4:30 PM **Exhibits**
Galleria Exhibit Hall South

2:15 PM-4:15 PM **Poster Session A**
Galleria Exhibit Hall South

*An extended abstract for this presentation is available in the Invited Abstracts section of the *Proceedings*.

4:30 PM-6:45 PM **Plenary Session 3:
Tyrosine Kinase Alterations
and Response to Therapy**
Grand Ballroom East

Co-Chairpersons: Sarah S. Bacus, Targeted Molecular Diagnostics, Westmont, IL, and Yosef Yarden, Weizmann Institute of Science, Rehovot, Israel

Mutations or other genetic alterations in genes encoding receptor tyrosine kinases (RTKs) are recognized as common denominators of a wide variety of solid tumors. This session will concentrate on one RTK subtype, namely EGFR and HER2 receptor molecules, which are frequently altered in breast, ovarian, and lung cancer. Both monoclonal anti-RTK antibodies, as well as small molecule kinase inhibitors, have already been developed for clinical use. Moreover, several experimental drugs are in various stages of development. Understanding the ways these receptors interact in the context of a layered signaling network will be highlighted in the session. In addition, the session will concentrate on molecular-based selection of patients for targeted therapy. An emerging clinical issue is the development of secondary (acquired) resistance to therapy. Some mechanisms of drug resistance, as well as the identification of efficacious drug combinations that overcome resistance, will be described in this session.

Predicting Clinical Activity to Lapatinib: Beyond ErbB2 (Her2)*

Anne-Marie Martin, GlaxoSmithKline, Collegeville, PA

Personalized Therapy Options for Advanced Non-small Cell Lung Cancer

Roy S. Herbst, UT M. D. Anderson Cancer Center, Houston, TX

A Systems Biology Approach to Molecular Diagnostics in the ErbB-3/HER2 System*

Yosef Yarden

Talk from Proffered Papers:

PR-3 Detection of BCR/ABL T315I Mutations in Cancer and Response to TKI Therapy

David Whitcombe, DxS Ltd, Manchester, United Kingdom

Summary

Sarah S. Bacus and **Yosef Yarden**

Wednesday, September 19

7:00 AM-8:00 AM **Continental Breakfast**
Grand Ballroom West

8:00 AM-10:15 AM **Plenary Session 4:
Signaling Pathway Alterations
and Response to Therapy**
Grand Ballroom East

Co-Chairpersons: Tona M. Gilmer, GlaxoSmithKline, Research Triangle Park, NC, and Judith S. Sebolt-Leopold, JSL Consulting, Ann Arbor, MI

Of the kinase-directed oncologic agents that have thus far gained regulatory approval, the majority are known to target receptor tyrosine kinases either in a highly selective or multi-targeted fashion. On the clinical trial front, the entry of a multitude of small molecule inhibitors of non-receptor kinases would suggest that these agents also hold therapeutic promise. The MEK dependency of BRAF mutated tumors, for instance, points to the utility of downstream inhibitors in the Ras-MAP kinase pathway in the clinical management of this genetically defined tumor population. Other studies with small molecule inhibitors of focal adhesion kinase (FAK) additionally point to their potential clinical utility as a means to target integrin-dependent signaling pathways. This session will also address the therapeutic challenge of treating patients whose tumors are devoid of overexpressed kinase targets, as exemplified by "triple-negative" basal-like breast tumors that are known to be ER-, HER2-, and PR-.

Targeting the Ras/Raf/Map Kinase Signaling Pathway in Advanced Cancer

Neal Rosen, Memorial Sloan-Kettering Cancer Center, New York, NY

Talk from Proffered Papers:

PR-4 Deregulation of the Phosphatidylinositol 3-Kinase Pathway in the Airway Epithelium of Smokers Is Associated with Lung Cancer

Adam M. Gustafson, Boston University, Boston, MA

Invited Talks Continued:

Focal Adhesion Kinase: Targeting Adhesions Signals in Normal and Cancer Cells*

J. Thomas Parsons, University of Virginia Health Sciences Center, Charlottesville, VA

Basal-like Breast Cancer and the Clinical Implications of Biologic Diversity*

Lisa A. Carey, University of North Carolina, Chapel Hill, NC

Summary

Tona M. Gilmer and **Judith S. Sebolt-Leopold**

*An extended abstract for this presentation is available in the Invited Abstracts section of the *Proceedings*.

10:15 AM-10:45 AM **Coffee Break**
Grand Ballroom West

2:15 PM-4:15 PM **Poster Session B**
Galleria Exhibit Hall South

10:45 AM-1:00 PM **Plenary Session 5:
Molecular Classification
of Tumors**
Grand Ballroom East

4:30 PM-6:45 PM **Plenary Session 6:
Angiogenesis and
Determinants of Therapy**
Grand Ballroom East

Co-Chairpersons: **David Paul Carbone**, Vanderbilt-Ingram Cancer Center, Nashville, TN, and **John D. Carpten**, TGen, Phoenix, AZ

Co-Chairpersons: **Heinz-Josef Lenz**, USC/Norris Comprehensive Cancer Center, Los Angeles, CA, and **Judah Folkman**, Harvard Medical School, Boston, MA

Great progress has been made in defining the genomic changes that drive tumor progression and the signaling pathways that lead to the transformation of normal cells into malignant derivatives and their progression into invasive cancers. Understanding the molecular basis of tumorigenesis has, in recent years, led to the identification of many new targeted cancer therapeutics and, with the aid of new molecular diagnostic technologies, has allowed us to classify tumors based on their genetic, epigenetic, proteomic, and functional profiles. The challenge now lies in harnessing the potential of targeted therapies and these sophisticated new technologies to treat individual tumors and individual patients. This session will focus on understanding new levels of complexity in tumor classification: aberrant splicing, regulatory microRNAs, and epigenetic alterations, and reveal some of the lessons being learned and additional challenges that still lay ahead.

As of August 2007, eight drugs have been approved by the FDA that are solely antiangiogenic or inhibit angiogenesis as one of their activities. More than 20 drugs with antiangiogenic activity are in Phase III clinical trials. Angiogenesis inhibitors have also been approved in more than 30 countries to treat cancer (or macular degeneration). More than 1.2 million patients are currently being treated with this new class of drugs (as determined by physician's prescriptions). Combinations of angiogenesis inhibitors have just recently begun to be introduced into cancer therapy, reflecting a similar evolution that culminated in combination chemotherapy for HIV and for tuberculosis. However, there are as yet no accepted biomarkers that can be used to guide optimum antiangiogenic dosing, determine therapeutic efficacy, or detect ultra-early recurrence of cancer. The need for such biomarkers or other cancer detection methods is becoming urgent, especially because: (i) Angiogenesis inhibitors are relatively less toxic than conventional anti-cancer chemotherapy, precluding "maximum tolerated dose" as a guide to optimum dosing; (ii) Many angiogenesis inhibitors reveal a bi-phasic U-shaped dose-efficacy curve that is not linear like cytotoxic chemotherapy; and (iii) Antiangiogenic therapy is most effective when administered chronically to achieve uninterrupted elevated blood levels over long periods of time (months to years). This session will focus on new basic and applied research in the development of novel angiogenesis based biomarkers, methods for molecular imaging of the microvascular system, and angiogenesis based predictors of disease designed to further enhance the early successes of antiangiogenic cancer therapy.

Microarray Analysis of Aberrant Splicing in Cancer*
John Conboy, Lawrence Berkeley National Laboratory, Berkeley, CA

References:
Davis DW, Herbst RS, Abbruzzese JL. CRC Press 2007.
Folkman J. Nature Reviews Drug Discovery 2007; 6:273-286.
Schultheis AM, et al. Proc ASCO 2006; 24:5017.

Human microRNAs: Powerful Biomarkers for Cancer Diagnostics*
Zvi Bentwich, Rosetta Genomics, Rehovot, Israel

The Elusive Search for Biomarkers of Anti-VEGF Activity*
Lee M. Ellis, UT M. D. Anderson Cancer Center, Houston, TX

Epigenetic Biomarker Discovery and Validation
Mathias Ehrich, Sequenom, Inc., San Diego, CA

Talk from Proffered Papers:
PR-5 An Immune Response Enriched 72-Gene Prognostic Profile for Early Stage Non-small Cell Lung Cancer (NSCLC)
Paul Roepman, Agendia, Amsterdam, The Netherlands

Molecular Imaging with PET to Measure Tumor Vascular Physiology *in vivo* in Man*
Patricia M. Price, Christie Hospital NHS Trust, Manchester, United Kingdom

Summary
David Paul Carbone and **John D. Carpten**

1:00 PM-2:15 PM **Special Session: Professional
Advancement Session for
Young Investigators Meet-The-
Experts Roundtables**
Grand Salon E

1:00 PM-4:30 PM **Exhibits**
Galleria Exhibit Hall South

Can Angiogenesis Regulatory Proteins Guide Ultra-early Detection and Therapy of Recurrent Human Cancer?*

*An extended abstract for this presentation is available in the Invited Abstracts section of the *Proceedings*.

Talk from Proffered Papers:
PR-6 Non-Invasive Imaging of Barriers to Drug Delivery in Tumors: Monitoring Changes in Interstitial Fluid Pressure
Yaron Hassid, Weizmann Institute of Science, Rehovot, Israel

Summary
Heinz-Josef Lenz and **Judah Folkman**

Federico Innocenti, University of Chicago, Chicago, IL

Talk from Proffered Papers:
PR-7 An Exploratory Analysis of the R250W Polymorphism in the KLK2 Gene as a Prognostic Marker in Prostate Cancer
Manish Kohli, University of Rochester, Rochester, NY

Summary
Margaret R. Spitz and **Olufunmilayo I. Olopade**

7:00 PM-9:00 PM **Conference Networking Reception and Dinner**
 Grand Ballroom West

10:15 AM-10:45 AM **Coffee Break**
 Grand Ballroom West

10:45 AM-1:00 PM **Plenary Session 8: Integrating Biomarkers and Drug Development**
 Grand Ballroom East

Thursday, September 20

7:00 AM-8:00 AM **Continental Breakfast**
 Grand Ballroom West

8:00 AM-10:15 AM **Plenary Session 7: Germline Molecular Determinants**
 Grand Ballroom East

Co-Chairpersons: **Margaret R. Spitz**, UT M. D. Anderson Cancer Center, Houston, TX, and **Olufunmilayo I. Olopade**, University of Chicago Medical Center, Chicago, IL

Interindividual variation in response to cancer drug therapy can be explained in part by common variants in specific genes that influence the absorption, metabolism, or disposition of drugs or are in the target cellular pathway. Such variants might also influence an individual's cancer risk. Therefore, by correlating gene expression or germline single-nucleotide polymorphisms with a drug's efficacy or toxicity we can generate a "personalized molecular medicine" profile, or pharmacogenetic profile that can be used to individualize treatment. This is the promise and potential of pharmacogenetic in which drugs and drug combinations can be optimized for each individual's unique genetic makeup by selecting drugs likely to be most effective and least toxic for each patient. This session will highlight the potential applications and future challenges in pharmacogenetic research relating to cancer therapeutics and risk assessment.

Molecular Mechanisms of Resistance to Anti-VEGF Therapies: IL-8 and Its Receptors
Heinz-Josef Lenz, USC/Norris Comprehensive Cancer Center, Los Angeles, CA

Germline Predictors of Outcome in Non-small Cell Lung Cancer*
Xifeng Wu, UT M. D. Anderson Cancer Center, Houston, TX

Application of UGT1A1 Genetic Testing in Patients Treated with Irinotecan*

Co-Chairpersons: **Nicholas C. Dracopoli**, Bristol-Myers Squibb Company, Princeton, NJ, and **Patricia M. Price**, Christie Hospital NHS Trust, Manchester, United Kingdom

Biomarkers are being increasingly used throughout the cancer drug development process. In early clinical studies, pharmacodynamic markers are used to evaluate the relationship of drug exposure and biological effect on the target and downstream pathways, confirm mechanism of action, and to identify the optimal dose and schedule for a new drugs and drug combinations. In later clinical studies, biomarkers are being used to predict drug response and disease prognosis and to change the benefit:risk ratio for patients. This session will discuss innovative approaches for the development of biomarkers for identifying optimal drug combinations, predicting resistance to therapy, and for the use of imaging tools as pharmacodynamic markers in cancer drug development.

Cellular Pharmacogenetics to Discover Cancer Drug Combinations
Spyro Mousses, TGen, Phoenix, AZ

Elucidating Mechanisms of Sensitivity and Resistance to EGFR Tyrosine Kinase Inhibitors in Lung Cancer*
William Pao, Memorial Sloan-Kettering Cancer Center, New York, NY

Identification of Biomarkers that Predict Resistance to Therapy
René Bernards, The Netherlands Cancer Institute, Amsterdam, The Netherlands

Speaker to be announced

Summary
Nicholas C. Dracopoli and **Patricia M. Price**

1:00 PM-1:15 PM **Closing Remarks**
 Grand Ballroom East

David Sidransky, Johns Hopkins University, Baltimore, MD

*An extended abstract for this presentation is available in the Invited Abstracts section of the *Proceedings*.