Monday, September 27, 2010

12:00 p.m. - 2:00 p.m.

Educational Session 1A: Emerging Role of Nanotechnology in Molecular Diagnostics

Grand Ballroom 1

Chairperson: Edison T. Liu, Genome Institute of Singapore, Singapore

The nanotechnology of DNA sequencing
Edison T. Liu

Nanotechnology for multiplexed molecular mapping of tumor heterogeneity: New opportunities in cancer diagnostics and individualized therapy
Shuming Nie, Emory University, Atlanta, GA

High-content screening in microfluidic devices as a new diagnostic method for personalized cancer medicine
Andre Levchenko, Johns Hopkins University, Baltimore, MD

Nanotechnology and individualized oncology*
Mauro Ferrari, The Methodist Hospital Research Institute, Houston, TX

12:00 p.m. - 2:00 p.m.

Educational Session 1B: Hurdles to Molecular Diagnostics Development and Application

Grand Ballroom 2

Chairperson: William Pignato, Novartis Molecular Diagnostics, Cambridge, MA

Regulatory opportunities and challenges in drug/diagnostic co-development
William Pignato

Using biomedical informatics to see the forest AND the trees for molecular diagnostics in cancer therapeutic development*
Kenneth H. Buetow, National Cancer Institute, Rockville, MD

The right stuff: The need for standardized human benchmark samples as the yardstick of truth for assay development
Carolyn Compton, National Cancer Institute, Bethesda, MD

Companion diagnostics development and commercialization: The good, the bad, and the ugly*
David Jackson, QIAGEN, Inc., Manchester, UK

2:00 p.m. - 2:15 p.m.

Break

2:15 p.m. - 4:15 p.m.

Educational Session 2A: Molecular Markers and Patient Decisions

Grand Ballroom 1

Chairperson: Jane Perlmutter, Gemini Group, Naperville, IL

The purpose of this session is to explore the impact of molecular biomarkers on patient decision making. The panel will include clinicians, test developers, decision tool designers, and patient advocates. Questions to be addressed include: 1) What cancer risks are high enough to motivate patients to make lifestyle changes; to take risk-reducing drugs or to undergo prophylactic surgery? 2) What recurrent risks are low enough to motivate clinicians to recommend against and/or patients to feel comfortable foregoing adjuvant chemotherapy? 3) How do clinicians and their patients incorporate the use of molecular markers into decision making? What are the individual, socio/cultural and economic factors that impact these decisions? 4) How can biomarker information be optimally presented to clinicians and patients to increase their use in decision making? 5) When do molecular markers help and/or improve decision making; when to they hurt? 6) How do clinicians and their patients deal with the errors inherent in current testing technologies?

Introduction
Jane Perlmutter

Meeting the challenges in patient decision making in molecular markers: Quality, equality, and health literacy
Jennifer J. Griggs, University of Michigan, Ann Arbor, MI

Highly predictive tests for cancer therapy: Status, potential, process and hurdles
David R. Parkinson, Nodality, South San Francisco, CA

Title TBD
Peter M. Ravdin, UT Health Science Center, San Antonio, TX

Title TBD
Steven M. Shak, Genomic Health, Inc., Redwood City, CA

Panel Discussion

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

2:15 p.m. - 4:15 p.m.

Educational Session 2B: Imaging Biomarkers in Therapeutic Trials

Grand Ballroom 2

Chairperson: Peter S. Conti, USC Keck School of Medicine, Los Angeles, CA

Overview of the SNM Clinical Trials Network
Peter S. Conti

Quantitative approaches to improving conventional and novel biomarkers in oncology
Lawrence H. Schwartz, Columbia University, New York, NY

PET and SPECT molecular imaging as biomarkers in cancer therapeutic trials*
Richard L. Wahl, Johns Hopkins University School of Medicine, Baltimore, MD

Clinical trials using novel molecular imaging cancer biomarkers: Current status and future directions*
David A. Mankoff, University of Washington, Seattle, WA

4:15 p.m. - 4:30 p.m.

Break

4:30 p.m. – 6:30 p.m.

Educational Session 3A: From Bench to Bedside

Grand Ballroom 1

Chairperson: Michael K. Samoszuk, Ortho Clinical Diagnostics, Raritan, NJ

The tools of molecular biology have identified many promising biomarkers and molecular signatures that are potentially useful for the detection, diagnosis, and classification of different types of cancer. The purpose of this session will be to focus on case studies from four companies that have begun to commercialize some of these basic science discoveries into clinical diagnostic products that are now being used to manage patients with cancer. The speakers will present background scientific information about the molecular basis of their products and then discuss the opportunities and challenges associated with the translation of basic science discoveries into products. Topics to be discussed include circulating tumor cells, molecular signatures of common solid tumors, characterization of tumors of unknown primary site, genomic profiling of breast cancer, and development of biomarkers for early detection of cancer.

Molecular characterization of cancer: Research tools or clinical diagnostics?*
Yixin Wang, Ortho Clinical Diagnostics, Raritan, NJ

Creating value: The power of molecular diagnostic tests*
W. David Henner, Pathworks Diagnostics, Redwood City, CA

Key principles for establishing the clinical utility of multigene cancer assays: Lessons from Oncotype DX
Steven M. Shak, Genomic Health, Inc., Redwood City, CA

Genetic and epigenetic approaches to cancer diagnostics
Steven Anderson, LabCorp of America, Research Triangle Park, NC

4:30 p.m. – 6:30 p.m.

Educational Session 3B: How Major Ongoing Omics Efforts Will Impact Development and Implementation of Molecular Diagnostics

Grand Ballroom 2

Chairperson: Paul T. Spellman, Lawrence Berkeley National Laboratory, Berkeley, CA

The session will provide an overview of the major systems biology efforts that are underway and will describe how they will impact the deployment and development of new therapies. Molecular classification of tumors into distinct subtypes is moving from a static description of the biological variation found across tumors to a functional dissection of individual cancers that will allow patients to be treated individually. Numerous efforts from NCI and outside groups are pushing personalized medicine forward. Speakers will cover: large-scale genomic screening (TCGA/ICGC), NCI systems biology models (CCSB, Phys-Onc), functional genomics analyses (SU2C, CTD2), and computational resources for analysis (UCSC Cancer Genome Browser). Additionally, there will be clinical perspective on deploying these approaches.

Cancer Genomics and the TCGA project*
David Haussler, University of California, Santa Cruz, Santa Cruz, CA

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Emerging functional genomics strategies for therapeutic development
Thomas F. Westbrook, Baylor College of Medicine, Houston, TX

Computational modeling to personalize therapeutics
Paul T. Spellman

A pathogenetic approach to using next-generation sequencing technologies for biomarker discovery: How small can be beautiful
David G. Huntsman, BC Cancer Agency, Vancouver, Canada

7:30 p.m. - 8:30 p.m.

Opening Session
Grand Ballroom 1

Introductory Remarks
Chairperson: Mehmet Toner, Harvard Medical School, Charlestown, MA

Keynote Address
A systems approach to identification and validation of biomarkers*
Gordon B. Mills, UT M. D. Anderson Cancer Center, Houston, TX

8:30 p.m. – 10:00 p.m.

Opening Reception

Tuesday, September 28, 2010

8:00 a.m. - 10:15 a.m.

Plenary Session 1: Transformative Technology: Large Scale Profiling
Grand Ballroom 1

Chairperson: Jeffrey Settleman, Genentech, Inc., South San Francisco, CA

The efficacy of anticancer drug treatments varies widely across the patient population—largely reflecting the increasingly appreciated extensive genomic heterogeneity that defines this complex disease. This realization has prompted substantial efforts in recent years to explore the relationship between tumor genotypes and the response to oncology drugs, and these efforts are beginning to yield a new paradigm in medical oncology—personalized cancer medicine. To facilitate the discovery of biomarkers that can be used to guide the clinical development of novel therapeutics, a variety of preclinical technologies are now being utilized. These include large-scale profiling of cancer cell line panels, development of novel mouse models of human tumors, and deep analysis of tumor genomes. This session will address the implementation of these new strategies to explore the heterogeneity of cancer genomes and the association of genomic biomarkers with therapeutic efficacy by large-scale modeling.

Modeling drug sensitivity and resistance in human tumor-derived cell lines*
Jeffrey Settleman

An *in vitro* system to model therapeutic response in breast cancer
Joe W. Gray, Lawrence Berkeley National Laboratory, Berkeley, CA

The complex mutation spectrum of lung cancer samples revealed by whole genome sequencing
Zemin Zhang, Genentech, Inc., South San Francisco, CA

Population-based engineered tumor models as a platform for biomarker discovery in cancer**
Murray O. Robinson, AVEO Pharmaceuticals, Cambridge, MA

Prediction of drug response using genomic signatures from the Cancer Cell Line Encyclopedia**
Kavitha Venkatesan, Novartis Institutes for BioMedical Research, Cambridge, MA

10:15 a.m. - 10:45 a.m.

Break

10:45 a.m. - 1:00 p.m.

Plenary Session 2: Minimally Invasive Access to Tumors
Grand Ballroom 1

Chairperson: Peter Kuhn, The Scripps Research Institute, La Jolla, CA

The fluid phase of solid tumors is a critical third microenvironment in the development and progression

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of carcinomas. Cells originating from primary or secondary sites travel through the blood circulatory system to either get cleared out or initiate new tumor growth. Translational research efforts are attempting to identify the various subtypes of circulating tumor cells (CTCs), their origins, their destinations and their impact on the disease. Understanding and characterizing CTCs is a first step towards utilizing them as both biopsy material and directly as a biomarker. It requires approaches of subtyping CTCs and characterizing them at the single cell level. While new technologies are being developed constantly, even early approaches show uses of certain CTCs as a biomarker. New correlations can be established between CTCs and other fluid phase materials. This session will discuss considerations at the translational interface of utilizing both solid and fluid phase biopsy material for cancer research at the single cell level.

Tissue issues: Clinical and research implications of diagnostic biopsy practices*
Kelly J. Bethel, The Scripps Research Institute, La Jolla, CA

Fluid phase of solid tumors, circulating tumor cells in high definition*
Peter Kuhn

Transcriptomics from single cells*
Roger S. Lasken, J. Craig Venter Institute, San Diego, CA

Molecular biomarker analyses using circulating tumor cells**
Siminder Kaur Atwal, Genentech, Inc., South San Francisco, CA

Circulating free DNA as a surrogate for tumor material for EGFR and KRAS analysis**
Gillian Ellison, AstraZeneca, Macclesfield, Cheshire, United Kingdom

1:00 p.m. – 2:15 p.m.

Break

2:15 p.m. - 4:15 p.m.

Poster Session A

North Convention Lobby

4:30 p.m. – 6:45 p.m.

Plenary Session 3: Effect of Intratumoral and Environment Heterogeneity on Identification and Implementation of Molecular Diagnostics

Grand Ballroom 1

Chairperson: Jonathan A. Fletcher, Brigham and Women's Hospital, Boston, MA

The profound genomic heterogeneity in most cancers creates challenges for implementation of molecular diagnostics, and for genomic discovery methods, particularly next-generation sequencing. The many thousands of nonessential passenger mutations, and even functionally important driver mutations, can vary in different aspects of a single cancer. This genomic complexity and heterogeneity is further complicated by post-genomic events, including oncogene alternative splicing and trans-splicing. This session will serve as a forum in which mechanisms, manifestations, and therapeutic relevance of intratumoral heterogeneity are discussed. Examples will include intratumoral heterogeneity in breast cancer, polyclonal genomic resistance to targeted therapies, and post-genomic oncogene rearrangements. Novel approaches to studying intratumoral heterogeneity will also be discussed.

Implications of trans-splicing of RNA for tumor diagnosis and detection*
Jeffrey Sklar, Yale University School of Medicine, New Haven, CT

Integrative molecular profiling: Identification of recurrent, functionally important genomic mechanisms in triple-negative breast cancers
Jorge Reis-Filho, Institute of Cancer Research, London, United Kingdom

Molecular heterogeneity of clinical resistance to kinase inhibitor therapies
Jonathan A. Fletcher

Single cell network profiling by flow cytometry as a platform to reveal pathway signatures and drug response profiles for use in personalized medicine**
Todd Covey, Nodality, Inc., South San Francisco, CA

Nanoscale approaches to define biologic signatures and measure proteomic response to targeted therapies in hematologic and solid tumors**
Alice C. Fan, Stanford Cancer Center, Stanford, CA

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Wednesday, September 29, 2010

8:00 a.m. - 10:15 a.m.

Plenary Session 4: Hurdles to Molecular Diagnostics Development and Implementation

Grand Ballroom 1

Chairperson: Mehmet Toner, Harvard Medical School, Charlestown, MA

Moving a proteomic diagnostic from a clinical need to post-marketing validation*
David Paul Carbone, Vanderbilt-Ingram Cancer Center, Nashville, TN

Cancer research in Asia: Challenges and opportunities*
John E. L. Wong, National University of Singapore, Singapore

From heat maps to clinical tests: Why so many biomarkers and so few companion diagnostic tests?*
Nicholas C. Dracopoli, Centocor, Inc., Radnor, PA

Diagnostics and therapeutic applications of nanotechnology
Jennifer West, Rice University, Houston, TX

10:15 a.m. - 10:45 a.m.

Break

10:45 a.m. – 1:00 p.m.

Plenary Session 5: Molecular Prediction, Classification, and Prognostic Markers

Grand Ballroom 1

Chairperson: Stephen J. Chanock, National Cancer Institute, Bethesda, MA

The advent of large-scale genome-wide association analyses of common germline variants has accelerated the discovery of common genetic variants that confer risk for different types of cancer. Currently, the discovery of new regions has generated a large set of markers, most which have not been adequately explored to investigate the underlying biology of the susceptibility alleles. Still, the opportunity to begin to develop sets of variants, not only SNPs but less common and rare mutations has generated extensive interest in exploring the already identified variants in distinct genetic models. While the preliminary work is promising, the catalog of variants is incomplete and the interaction between genetic variants and environmental exposures represent substantive challenges that will require further discovery and better strategies to validate promising findings.

The transition from discovery by genome-wide association studies to validation of clinical risk models: Where are we, what will it take, and when can we expect to be there?
Stephen J. Chanock

Prediction of disease risk using common genetic variants*
David J. Hunter, Harvard School of Public Health, Boston, MA

Potential clinical utilities of prostate cancer risk-associated SNPs*
Jianfeng Xu, Wake Forest University School of Medicine, Winston-Salem, NC

A prospective trial of plasma EBV DNA for the screening of nasopharyngeal carcinoma**
K.C. Allen Chan, The Chinese University of Hong Kong, Hong Kong, China

Exome sequencing of multiple metastases from a lethal prostate cancer reveals BRCA1 deficiency and additional somatic alterations which suggest alternate therapeutic options**
Michael L. Nickerson, National Cancer Institute, Frederick, MD

1:00 p.m. - 2:15 p.m.

Break

2:15 p.m. - 4:15 p.m.

Poster Session B

North Convention Lobby

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4:30 p.m. – 6:45 p.m.

Plenary Session 6: Pharmacodynamic Markers

Grand Ballroom 1

Chairperson: Chris H. Takimoto, Ortho Biotech, Inc., Radnor, PA

Pharmacodynamic and mechanism of action (PD/MofA) biomarkers are key tools in the early stages of drug development. Correlative laboratory studies examining a drug's effects on the molecular target are now a standard component of first-in-human phase 0 and phase I trials in oncology. Such assays may involve the assessment of the effects of an agent on a specific molecular target or target pathway, or its effects on related biological processes. Typically, these studies require invasive biopsies to collect tumor and/or normal tissues. More recent noninvasive techniques for PD readouts in early clinical trials include the characterization of drug effects in circulating tumor cells or functional imaging modalities such as DCE-MRI and specialized PET scans. Despite large infrastructure investments in biomarkers and translational research by industry and academic cancer centers, well-defined examples of rational decision making guided by biomarker endpoints are relatively rare. This session will focus on the optimal integration of PD/MofA biomarker correlative endpoints for dose, schedule and indication selection and on new paradigms for developing integrated strategies for the clinical development of targeted oncology agents. Presentations will include descriptions of biomarker enriched early clinical trials and a discussion on the state of the art of molecular characterization of circulating tumor cells.

Blazing the pharmacologic audit trail: Pharmacodynamic biomarkers in early drug development*
Chris H. Takimoto

Circulating tumor cells: Potential uses, pitfalls and challenges in their use as pharmacodynamic markers
Gerhardt Attard, Royal Marsden Hospital, Sutton, United Kingdom

Biomarkers in early clinical trials: Too much too soon?
Patricia M. LoRusso, Karmanos Cancer Center, Detroit, MI

Imaging endpoints to predict response to IGF1R/IR inhibition in CRC models**
Natalie J. Serkova, University of Colorado Cancer Center, Aurora, CO

The quantitative analysis of epidermal growth factor receptor (EGFR) mutations in non-small cell lung cancer (NSCLC) and its correlation with response rate of EGFR tyrosine kinase inhibitors (TKI)**
Junpu Xu, Beijing ACCB Biotech Ltd., Beijing, China

Thursday, September 30, 2010

8:00 a.m. - 10:15 a.m.

Plenary Session 7: Tumor Microenvironment

Grand Ballroom 1

Chairperson: Adriana Albini, IRCCS Multimedica, Milan, Italy

The tumor microenvironment plays a crucial role in the determination of the fate of both normal and cancer cells. It is represented by a complex society of many cell types and the extracellular matrix elaborated by them. Not just an innocent bystander, the microenvironment has been recognized to extensively cooperate in cancer, though inflammation, reactive stroma, responses to hypoxia, and contribution to anaerobic glycolysis. Therefore, it is mandatory in the era of molecular therapy and diagnostics, to dissect the mechanism of microenvironment-driven malignancy. In this session, different targets within the microenvironment that can be addressed for therapeutic approaches will be illustrated. First of all, tumor progression requires the formation of new blood vessels. On the basis of this observation, histopathological and molecular diagnostic tools to detect angiogenesis have been developed and led to the antiangiogenic approach to cancer therapy. However, after a very exciting time, recently failures and pitfalls using antiangiogenesis have emerged, indicating that we need to rethink and improve this strategy.

Integrins are the key adhesion molecules connecting cancer cells to the tumor extracellular matrix; and are involved in collective invasion. Anti-integrin agents could

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increase tumor sensitivity to irradiation, due to enhanced oxygenation of the tissue. In the session, targeting an embryonic signaling pathway to suppress the metastatic phenotype is also approached; the hESCs (human embrionic stem cells) microenvironment is able to reprogram the aggressive phenotype of cancer cells to a less aggressive one. In hypoxic microenvironments, especially in cancer, the sonic hedgehog pathway has been found to be upregulated, suggesting it may be a possible molecular diagnostic tool and a target for treatment. Glycogen metabolism provides nutritional support to cancer cells and could represent a marker of response to antiangiogenic therapy.

The data presented in this session strengthen the concept that the tumor microenvironment will be a powerful source of novel markers and innovative therapies targeted to host tumor-associated cells.

Deep collective cancer invasion: Breaking radioresistance by anti-integrin therapy*
Peter Friedl, Radboud University, Nihjmegen Medical Center, Nijmegen, The Netherlands

Angiogenesis success and pitfall in diagnosis, therapy, and cancer prevention*
Adriana Albini

Targeting an embryonic signaling pathway to suppress the metastatic phenotype*
Mary J. C. Hendrix, Children's Memorial Research Center, Chicago, IL

Hedgehog signaling and desmoplasia are regulated by hypoxia in pancreatic cancer**
Taly Spivak-Kroizman, UT M. D. Anderson Cancer Center, Houston, TX

Glycogen metabolism provides nutritional support to renal cancer cells under conditions of stress and may serve as a marker of response to antiangiogenic therapy with bevacizumab**
Dimitra Tsavachidou, UT M. D. Anderson Cancer Center, Houston, TX

10:15 a.m. - 10:45 a.m.

Break

10:45 a.m. – 1:00 p.m.

Plenary Session 8: Molecular Marker Trial Design

Grand Ballroom 1

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

Personalized approaches for advanced non-small cell lung cancer: The M. D. Anderson BATTLE programs
Roy S. Herbst

Clinical application of genomic profiling in breast cancer and the TAILORx trial*
Joseph Sparano, Albert Einstein College of Medicine, Bronx, NY

How to design molecular markers-based clinical trials: Are they doable?
Ana Maria Gonzales-Angulo, UT M. D. Anderson Cancer Center, Houston, TX

Oncogene mutations and fusions as molecular biomarkers and targets in advanced lung adenocarcinomas*
Paul A. Bunn, Jr., University of Colorado, Denver, CO

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