Preclinical Cancer Research: Models and Tools

May 21-23, 2014
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May 21-22

3rd Annual

Tumor Models to Guide Targeted Cancer Therapy and Drug Development

Patient-Derived Xenograft Models and Beyond

5th Annual

Imaging in Preclinical and First-in-Human Clinical Studies in Oncology

Mastering Translational Approach

May 22-23

3rd Annual

Tumor Models for Preclinical Assessment of Cancer Immunotherapy

Applying Novel Immunocompetent Models

3rd Annual

Novel *in vitro* Models of Cancer

Overcoming Challenges of ex vivo Tumor Modeling

Inaugural

New Tools for Epigenetics Screening

Biochemical and Cell-Based Assays for Validating Targets and Leads

Keynote Speaker:

Catalyzing Translational Innovation

Christopher P. Austin, M.D.
Director, National Center for Advancing Translational Sciences, National Institutes of Health

Short Courses:

- Metastatic Mouse Models: Technology and Applications
- How to Best Utilize Organotypic 3D Cell Cultures Assays in Oncology

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Conference-at-a-Glance

Tuesday, May 20	Pre-Conference Short Courses* - Animal Models of Pain: Progress and Challenges - Introduction to Drug Metabolism and Its Role in Drug Toxicity			- Nanotechnology for Enhancing Bioavailability of Poorly Soluble Drugs - Metastatic Tumor Models: Technology and Applications - Safety Testing for Biological Drugs and Vaccines	
Wednesday, May 21	Tumor Models for Targeted Therapy	Imaging in Oncology	Preclinical Drug Safety	Formulation & Drug Delivery	Targeting Pain
	Keynote Speaker: Catalyzing Translational Innovation **Christopher P. Austin, M.D.** *Director, National Center for Advancing Translational Sciences National Institutes of Health*				
Thursday, May 22	Tumor Models for Targeted Therapy	Imaging in Oncology	Preclinical Drug Safety	Formulation & Drug Delivery	Targeting Pain
	Tumor Models for Cancer Immunotherapy	*In vitro* Tumor Models	Epigenetics Screening	Efficient Process Chemistry	
	Dinner Short Courses* - Refining API Process Development for Efficiency			- How To Best Utilize Organotypic 3D Cell Cultures Assays in Oncology - Computational Modeling of Cancer Genomics	
Friday, May 23	Tumor Models for Cancer Immunotherapy	*In vitro* Tumor Models	Epigenetics Screening	Efficient Process Chemistry	

** Separate registration required.*

Five Programs Dedicated to Preclinical Models in Oncology at World Pharma Congress 2014

Despite tremendous progress in our understanding of cancer biology, most novel anticancer therapies fail in Phase III clinical trials. Can we break this paradigm with more predictive preclinical studies? Join pharmaceutical, biotech and academic stakeholders May 21-23 in Boston, for interactive sessions, panel discussions and short courses all geared toward providing opportunities for active networking and collaborating, while gaining strategic insights into solutions for increasing the reproducibility and predictability of preclinical cancer studies.

May 21-22

- Tumor Models for Targeted Therapy
- Imaging in Oncology

May 22-23

- Tumor Models for Cancer Immunotherapy
- *In vitro* Tumor Models
- Epigenetics Screening

Keynote Speaker:

Catalyzing Translational Innovation

Christopher P. Austin, M.D.
Director, National Center for Advancing Translational Sciences
National Institutes of Health

The multi-stage and multifaceted translational spectrum is poorly understood, and the current research ecosystem is operationally not well suited to the distinct needs of translation. As a result, biomedical science is in an era of unprecedented accomplishment without a concomitant improvement in meaningful health outcomes, and this is creating pressures that extend from the scientific to the societal and political. To meet the opportunities and needs of translational science, NCATS was created as NIH's newest component in December 2011, via a concatenation of extant NIH programs previously resident in other components of NIH. NCATS focuses on disease-agnostic issues by acting as a catalyst and bringing together the collaborative teams necessary to develop new technologies and paradigms to improve the efficiency and effectiveness of the translational process. This talk will focus on several programs in the NCATS portfolio that are proving to be successful new models in navigating the translational landscape. The presentation will highlight systems toxicology and preclinical development efforts with a focus on the Tissue Chips for Drug Screening Program and the Tox21 Consortium.

Short Courses*

May 20, 2014 6:00-9:00 pm *(Dinner will be served)*

SC4 - Metastatic Tumor Models: Technology and Applications

Instructors:

Jeffrey E. Green, M.D., Chief, Transgenic Oncogenesis and Genomics Section, Laboratory of Cancer Biology and Genetics, National Cancer Institute

Zoë Weaver Ohler, PH.D., Principal Scientist, Preclinical Evaluation Team Leader, Center for Advanced Preclinical Research, Frederick National Laboratory for Cancer Research (NCI)

Neal Goodwin, Ph.D., Vice President Corporate Research Development, Champions Oncology, Inc.

Bruce R. Zetter, Ph.D., Charles Nowiszewski Professor of Cancer Biology, Department of Surgery, Harvard Medical School

May 22, 2014 6:30-9:30 pm *(Dinner will be served)*

Sponsored by

JSR Life Sciences

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SC7 - How to Best Utilize Organotypic 3D Cell Cultures Assays in Oncology

Instructors:

Arvind Rao, Ph.D., Assistant Professor, Department of Bioinformatics and Computational Biology, The University of Texas MD Anderson Cancer Center

Geoffrey A. Bartholomeusz, Ph.D., Assistant Professor and Director of the siRNA Core Facility, Department of Experimental Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

Lesley Mathews Griner, Ph.D., Research Scientist, Biomolecular Screening and Profiling/Probe Development Group, National Center for Advancing Translational Sciences, NIH

Sophie Lelièvre, DVM, LLM, Ph.D., Associate Professor, Department of Basic Medical Sciences and Associate Director, Discovery Groups, NCI-designated Purdue Center for Cancer Research, Purdue University

The course will provide an overview of the various 3D cell culture models available, their strengths and weaknesses, and where and how these models are being used, specifically for oncology research. The instructors will share their experiences on how they tested and evaluated various cell culture reagents and growth matrices, what worked and what didn't and what you need to consider when setting up low and high throughput screening experiments using 3D cell cultures in your lab. The challenges working with 3D cell cultures, from experimental design to data analysis will be discussed.

**Separate registration required*

> "Great job by short course speakers, good forum, and relaxed atmosphere."
>
> - Senior Principal Scientist, Drug Safety, Pfizer, Inc.

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For questions about the Oncology conferences, please contact:

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For questions about the Epigenetics Screening conference, please contact:

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Tuesday, May 20, 2014 • 9:00am-12:00pm

Genome Editing Technologies and Applications

Targeted Genome and Epigenome Editing Using Engineered CRISPR and TALE Technologies

J. Keith Joung, M.D., Ph.D., Associate Chief of Pathology for Research; Associate Professor of Pathology, The Jim and Ann Orr MGH Research Scholar, Molecular Pathology Unit, Center for Cancer Research, Massachusetts General Hospital

Targeted genome and epigenome editing technologies have recently emerged as important tools for biomedical research and as potential reagents for therapies of gene-based diseases. In this talk, I will present our recent work on the clustered regularly interspaced short palindromic repeat (CRISPR) RNA-guided nuclease platform for introducing targeted genome sequence alterations, including discussion about the latest specificity improvements developed by our group. I will also describe the creation and validation of new technologies for modifying specific epigenomic marks on histones and DNA that can be used to induce targeted alterations in endogenous human gene expression. Taken together, these methodologies provide transformative tools for understanding human biology and offer promising pathways forward for developing therapies based on targeted alterations of gene sequence and expression.

Novel Tools for Cell-Based Screening With Mixed Populations of Isogenic Wild-Type and Mutant Cell Populations

Ranjit S. Bindra, M.D., Ph.D., Assistant Professor, Departments of Therapeutic Radiology & Experimental Pathology, Yale School of Medicine

Cell-based screening is now a common approach to identify novel compounds and genes which regulate key biologic processes in cells. Live cell growth tracking is an especially useful tool for synthetic lethal screens, although current approaches are limited by the requirement for cell lysis, fixation and/or highly specialized imaging techniques. We recently developed a novel system to fluorescently label cell lines for use in screening assays. High expression levels of many fluorescent proteins without nuclear localization can be toxic in cells, and it can adversely affect the ability of automated cell identification programs to discriminate individual cells. To address these two potential issues, we engineered fusion fluorescent proteins which contain modified FK506- and rapamycin-binding protein (FKBP12) destabilizing domains (dd) on their N-termini, and nuclear localization signals (NLSs) on their C-termini. The FKBP12 dd is unstable in the absence of high-affinity ligands, such as rapamycin and a biologically inert derivative, Shield1. The addition of Shield1 blocks the destabilizing effect of the N-terminal domain dd. Thus, fluorescent protein expression can be induced at specific times by the addition of ligand. Fluorescence is localized to the nucleus by the NLS, which facilitates the identification of individual cells using imaging algorithms. We created fusion proteins for blue, yellow, and red fluorescent proteins (referred to as ddBFPnls, ddYFPnls and ddRFPnls, respectively).We chose to modify these specific fluorescent proteins because they have minimally overlapping fluorescence excitation and emission spectra. This particular feature makes them amenable for use in combination to identify and track multiple unique cell populations. We confirmed that multiple cell lines stably expressing ddBFPnls, ddYFPnls and ddRFPnls could be identified and counted in 384- and 96-well microplates, at a range of cell densities and timepoints, using several different imaging platforms. In addition, mixed populations of isogenic cell lines harboring key mutations were obtained from Horizon Discovery and tested with our fluorescent marking system. These fluorescent marking tools will be useful for researchers interested in cell-based screens, and they likely can be used for simultaneous cell tracking of multiple unique populations *in vivo*.

X-MAN Cell Lines – Enabling Translational Research

Chris Lowe, Ph.D., Director, R&D, Cell Line Engineering, Horizon Discovery

Technological advances continue to improve the affordability of whole-genome sequencing and drive the recent successes in human genetics, identifying genes responsible for Mendelian diseases and unraveling the mutations that predispose individuals to common complex diseases. However, identifying the associated mutations is only the first step in the therapeutic pathway. Understanding the involvement of a mutation in a disease or therapeutic pathway remains a challenge and has been hampered by the lack of suitable *in vitro* tools.

We have used rAAV- mediated homologous recombination, a proprietary part of Horizon's GENESISTM platform (which consists of rAAV, ZFN and CRISPR), to generate suites of isogenic cell lines, carrying specific endogenous mutations in genes such as KRAS, EGFR and PIK3CA, as well as endogenous reporters utilizing NanoLuc luciferase, a small enzyme engineered for optimal performance as a luminescent reporter, to investigate the roles of specific genes and mutations in response to therapeutic agents and demonstrate their utility in functional genomics and high-throughput screening.

For more information on this FREE event please click here.

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3rd Annual

Tumor Models to Guide Targeted Cancer Therapy and Drug Development

Patient-Derived Xenograft Models and Beyond

WEDNESDAY, MAY 21

7:00 am Registration and Morning Coffee

DECISION-MAKING STRATEGIES AND PDX MODELS

8:00 Chairperson's Opening Remarks

Terry A. Van Dyke, Ph.D., Head, Mouse Cancer Genetics Program; Program Director, Cancer Pathways and Mechanisms, National Cancer Institute

8:05 FEATURED PRESENTATION: Making Decisions with Cell Line and Patient-Derived Xenograft Models in Drug Discovery and Development

Anderson Clark, Ph.D., Director, In vivo Pharmacology, Oncology, EMD Serono Research & Development Institute

The focus of this presentation will be around the ways in which we place different types of *in vivo* cancer models within the contexts of drug discovery and development at EMD Serono. Cell line xenograft models will be considered, but the emphasis will be on the use of patient-derived tumor models -- when and how do we use them, how do we interpret the data and how do we translate those data for clinical decision-making.

8:35 FEATURED PRESENTATION: Computational Modeling of Cancer Genomics

Dr. Franziska Michor, Associate Professor, Biostatistics & Computational Biology Dana Farber Cancer Institute

BRaf inhibitors are a clinically-validated targeted cancer therapy. Primary human tumorgraft models of melanoma and colorectal cancer with BRaf mutations were utilized to characterize and differentiate CEP-32496, a novel and selective dual BRaf-EGFR inhibitor on the basis of its efficacy and tolerability profiles, from FDA-approved competitor BRaf inhibitors and define a new therapeutic opportunity for the treatment of B-Raf mutated colorectal cancers.

9:05 Tumorgraft Avatar Platform for Clinical Advancement

Sponsored by CHAMPIONS ONCOLOGY

Neal Goodwin, Ph.D., Vice President, Corporate Research Development, Champions Oncology, Inc.

A patient-derived xenograft (TumorGraft) platform has been established where patient tumors are engrafted to form mouse-avatar TumorGraft models for translational and clinical studies. Therapeutic treatment responses in these mouse avatars are being used prospectively to guide patient treatment and the avatar-directed treatment outcomes correlated with patient treatment outcomes.

9:35 Coffee Break in the Exhibit Hall with Poster Viewing

IMPROVING PREDICTIVE VALUE OF PRECLINICAL STUDIES

10:15 Chairperson's Opening Remarks

Neal Goodwin, Ph.D., Vice President, Corporate Research Development, Champions Oncology, Inc.

10:20 FEATURED PRESENTATION: Preclinical Evaluation in Engineered Cancer Models: A Path to Accelerated Clinical Development?

Terry A. Van Dyke, Ph.D., Head, Mouse Cancer Genetics Program; Program Director, Cancer Pathways and Mechanisms, National Cancer Institute

Progress in the emerging area of human-predictive preclinical animal model platforms will be overviewed. Our work in this arena is carried out at the NCI Center for Advanced Preclinical Research (NCI-CAPR), a novel initiative developed by the Center for Cancer Research (CCR, NCI). CAPR achieves its mission to develop efficient and predictive preclinical strategies through extensive internal and collaborative partnerships. Recent and ongoing studies in one or more of the following areas will be discussed: pancreatic cancer, glioblastoma, lung adenocarcinoma, melanoma and/or serous ovarian cancer.

10:50 Modeling Tumor Cell Dormancy in the Mouse

Jeffrey E. Green, M.D., Chief, Transgenic Oncogenesis and Genomics Section, Laboratory of Cancer Biology and Genetics, National Cancer Institute

Tumor recurrence may occur from the reactivation of dormant tumor cells into clinically manifest metastatic disease, which is a major cause of patient morbidity and mortality. The use of *in vitro* and *in vivo* models to decipher mechanisms of tumor cell dormancy and their use for preclinical testing will be presented. Translating these findings may greatly improve patient outcome.

11:20 Tumor Models Facing New Challenges

Sponsored by oncotest

Sabine Gorynia, Ph.D., Project Manager, Project Management, Oncotest GmbH

Advances in our understanding of the complexity of cancer-including tumor heterogeneity, the role of the tumor micro-environment and the ability of tumors to evolve under therapy- present increasing challenges to the models used to support the discovery and preclinical development of anti-tumor therapies. Oncotest, as pioneers in the field of Patient Derived Xenografts, are continuously developing and adapting their modelling system to help clients better address these challenges.

11:50 The Co-Clinical Trial Paradigm: Improving Predictive Value of Preclinical Studies

Andrew L. Kung, M.D., Ph.D., Director, Pediatric Hematology, Oncology and Stem Cell Transplantation, New York-Presbyterian Morgan Stanley Children's Hospital, Columbia University Medical Center

Conventional mouse studies are poor predictors of efficacy in human clinical trials. The predictive value of preclinical studies may be improved by utilizing newer models that recapitulate the complexity of human disease, along with response criteria that are better aligned with clinical measures of success. The use of genetically engineered mouse models, patient-derived xenografts, and molecular imaging will be reviewed in the context of the co-clinical trial paradigm.

12:20 pm Use of PDX-BL0293, a Patient Derived Xenograft Model of Bladder Cancer, to Test Drug Efficacy

Cedo Bagi, M.D., Ph.D., Senior Research Fellow, Worldwide Comparative Medicine, Global Science & Technology, Pfizer Global R&D

Axl is a receptor tyrosine kinase that is expressed in various human cancers and is associated with invasiveness and metastasis. Pfizer's Axl-inhibitor compound was tested in a patient-derived xenograft (PDX) model of bladder cancer against standard of care.

12:50 LUNCHEON PRESENTATION I: Using Populations of Patient Derived Engraft Models to Support Preclinical Trials of Oncology Therapeutics

Sponsored by MOLECULAR RESPONSE

Thomas B. Broudy, Ph.D., CSO, Molecular Response LLC

The depth and breadth of the Molecular Response tumor bank (144k specimens, 76 clinical diagnoses) enables broad-based PDX studies in patient populations meeting specific inclusion/exclusion criteria, such as: mutational status, failed prior therapy or metastatic lesions. By approximating clinical trials in the preclinical setting, we help our partners to establish more confident clinical development strategies–responsive patient populations, effective combination agents, predictive diagnostic tests, and strategies to delay resistance.

1:20 Session Break

3rd Annual

Tumor Models to Guide Targeted Cancer Therapy and Drug Development

Patient-Derived Xenograft Models and Beyond

MOLECULAR IMAGING BIOMARKERS AND END POINTS

(Shared Session between Tumor Models for Targeted Therapy and Imaging in Oncology)

2:00 Chairperson's Opening Remarks

Paul Acton, Scientific Director and Janssen Fellow, Global Head, Molecular Imaging, Johnson & Johnson

2:05 Translatability of Preclinical Modeling: Case Study of Development of a Targeted Therapeutic with an Imaging Companion Diagnostic

Ingrid Joseph, D.V.M., Ph.D., Senior. Director, Pharmacology, Agensys, an affiliate of Astellas Pharma, Inc.

Traditional xenograft models utilize immortalized cancer cells grown on plastic that exhibit a genetic drift. Therefore, they do not represent the total genetic/epigenetic heterogeneity of the original cancers. Despite demonstrating efficacy in these models, a majority of cancer therapeutics fail in the clinic. Patient derived tumors grown as xenografts (PDXs) appear to maintain the histopathology/molecular characteristic of the original tumor. A case study utilizing PDX models better suited for targeted therapy will be discussed.

2:35 Molecular Imaging for Patient Selection and Predicting Treatment Response

Paul Acton, Scientific Director and Janssen Fellow, Global Head, Molecular Imaging, Johnson & Johnson

Personalized medicine would provide the key diagnostics required to deliver more effective targeted therapies, avoiding unnecessary or ineffective treatments, and reducing side effects. This presentation will outline several approaches to developing predictive imaging biomarkers, including imaging of labeled drugs, and a novel approach to tagging biologics which allows each drug to become its own companion diagnostic.

3:05 Heparin-Reactive Peptides Preferentially Co-Localize *in vivo* with Extracellular Melanin – A Novel Biomarker in Metastatic Melanoma Tumors

Jonathan Wall, Ph.D., Professor of Medicine, Human Immunology and Cancer Program; Director, Amyloid and Preclinical Molecular Imaging Laboratory, University of Tennessee Graduate School of Medicine

Melanoma is the most deadly form of skin cancer with >70,000 individuals diagnosed in 2011 in the USA. During a routine histochemical screen of biotinylated heparin-reactive peptides with a tumor tissue array, we identified certain reagents that preferentially bound melanocytic melanoma tumors. We have now demonstrated peptide reactivity, by using SPECT/CT imaging, co-localization of the peptides with B16F10 murine "metastatic" melanoma tumors within the mouse lung.

3:35 Preclinical and Clinical Applications of Patient Derived Xenograft (PDX) Models

Sponsored by The Jackson Laboratory — Leading the search for tomorrow's cures

Yan Yang, Director, Lab Operations in vivo Services, The Jackson Laboratory

The Jackson Laboratory has established a unique collaboration with over 20 clinical centers to advance cancer treatment. Patient tumors transplanted into the NSG mouse are being screened with SOC and experimental therapeutics for preclinical research or the refinement of patient treatment regimens.

4:05 Modeling Human Cancer: A Multifaceted Approach to Pre-Clinical Development

Sponsored by Biomodels — FAST. INNOVATIVE. PREDICTIVE.

Maria L. Mancini, Ph.D., Principal Investigator, Biomodels, LLC

There are a number of key points to consider when designing therapeutics for the treatment of human cancers. Tumor heterogeneity, stromal contribution, immune response, and treatment resistant sub-populations are all potential confounds that complicate the assessment of novel therapeutic strategies in a pre-clinical setting. Only recently have efforts been directed at treating resistant cell populations (often termed cancer stem cells). In order to study these populations, Biomodels developed a multi-faceted approach to evaluate novel therapeutics.

4:20 Refreshment Break in the Exhibit Hall with Poster Viewing

» 5:00 PLENARY KEYNOTE PRESENTATION: Catalyzing Translational Innovation

Christopher P. Austin, M.D., Director, National Center for Advancing, Translational Sciences, National Institutes of Health (Click here for details)

6:00 Welcome Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

3rd Annual

Tumor Models to Guide Targeted Cancer Therapy and Drug Development

Patient-Derived Xenograft Models and Beyond

THURSDAY, MAY 22

7:30 am Interactive Breakout Discussion Groups with Continental Breakfast

CHALLENGING TUMOR HETEROGENEITY

8:35 Chairperson's Remarks

Yan Yang, Director, Lab Operations in vivo Services , The Jackson Laboratory

8:45 Proteomics-Based Analysis of Tumor Models and Its Implication in Combination Therapy

Alex Cao, Ph.D., Director, Oncology Translational Pharmacology, OTM, Novartis Oncology

We have used proteomics to examine broadly the oncogenic receptor tyrosine kinase and key onco-pathway signaling nodes in preclinical tumor models. This approach has facilitated better understanding of tumor signaling in the relevant disease settings. The information has enabled the identification of novel combinations in specific cancer segments.

9:15 Development in the Face of Tumor Heterogeneity

Arijit Chakravarty, Ph.D., Senior Scientist II, Modeling and Simulation, DMPK, Takeda Pharmaceuticals

The promise of the Oncogene Addiction hypothesis was that every tumor in a patient diagnosed with cancer would be driven by a gene (or combination of genes), and that the identification of these genes would provide a predictive biomarker (or a set of biomarkers) that could be used to select the correct therapy for the patient. Almost fifteen years after this concept was proposed, the prospective identification of predictive biomarkers remains elusive as no predictive biomarkers have been successfully identified for any drugs in a prospective manner so far.

9:45 Characterization of Post-Chemotherapy Residual Disease in Triple-Negative Breast Cancer PDX Models

Sponsored by XenTech

Stefano Cairo, Head, Research & Development Laboratory, XenTech

Characterizing and preventing the persistence of post-chemotherapy residual disease is a major challenge for anticancer drug developers. Patient-Derived Xenograft (PDX) models represent an outstanding tool to evaluate this aspect of the pathology. Xentech will present how PDXs may be used to identify residual disease markers and potential new targets.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

GAINING FROM TECHNOLOGICAL ADVANCES

Bridging Session between Four Oncology Tracks**

10:30 Bridging Session Chair

Jonathan Wall, Ph.D., University of Tennessee Graduate School of Medicine

10:35 Targeted NGS Applications for Detection of Somatic Mutations

Oleg Iartchouk, Ph.D., Director, Genomics and Next-Generation Sequencing, Novartis Institutes for Biomedical Research

This talk will give an overview of NGS applications used to discover somatic point mutations and short insertion deletions in different types of cancer samples. Potential promise for some of them in clinical settings will be discussed.

11:05 Accelerating Preclinical Drug Development by *in vivo* and *ex vivo* Imaging in Cancer Models: Optimizing Discovery to Delivery

Werner Scheuer, Research Leader, Pharma Research and Early Development, Discovery Oncology, Roche Diagnostics GmbH

The presentation will discuss the following topics: application of different imaging modalities to monitor the efficacy of compounds on primary tumor growth, metastasis and angiogenesis; simultaneous measurement of Pk and Pd; optimizing application schedules regarding combination therapies; and verification of *in vivo* imaging data by 3-dimensional multispectral fluorescence histology.

11:35 FEATURED PRESENTATION: The Critical Role of Extracellular Matrix and Microenvironment in Metastasis and Dormancy

Mina J. Bissell, Ph.D., Distinguished Scientist, Life Sciences Division, Lawrence Berkeley National Laboratory

I will discuss why and how we developed, and use, 3-dimensional models of normal mammary gland and mammary tumors from both mice and humans to understand breast cancer, and will present recent work, shedding light on why tissue and organ architecture should become also a parameter in cancer research, and how architecture can regulate tissue-specificity as well as the plasticity of tumors. I will also discuss newer and more complex models we have developed to understand metastasis and dormancy and a screen that has allowed us to discover a new class of 'oncogenes' in the EGFR/PI3 Kinase.

12:05 An Integrative Approach to the Evaluation, Selection and Orientation of Novel Cancer Therapeutics

Sponsored by Oncodesign

Jonathan Ewing, Business Development Director, Oncodesign

The challenge in identifying the preclinical activity of cancer therapeutics and orientating their best clinical use is associating relevant in vivo models of human disease with effective pharmacological evaluation and biomarkers. Oncodesign's precision medicine approach to clinical drug candidate selection integrates appropriate in vivo models, extensive pharmacological expertise and pharmaco-imaging tools to provide quantitative, predictive and translational evidence early in drug development.

12:45 Close of Imaging in Preclinical and First-in-Human Clinical Studies in Oncology

**Attendees registered for the following conferences can attend this session:

- Tumor Models to Guide Targeted Cancer Therapy and Drug Development
- Tumor Models for Preclinical Assessment of Cancer Immunotherapy
- Novel *in vitro* Models of Cancer
- Imaging in Preclinical and First in Human Clinical Studies in Oncology

Inaugural

Tumor Models for Preclinical Assessment of Cancer Immunotherapy

Applying Novel Immunocompetent Models

THURSDAY, MAY 22

9:30 am Registration

GAINING FROM TECHNOLOGICAL ADVANCES

Bridging Session between Four Oncology Tracks**

10:30 Bridging Session Chair

Jonathan Wall, Ph.D., University of Tennessee Graduate School of Medicine

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TOP PHARMA STRATEGIES

1:25 Chairperson's Opening Remarks

Debbie Liao, Ph.D., Research Investigator, Oncology Pharmacology, Genomics; Institute of the Novartis Research Foundation

1:30 FEATURED PRESENTATION: Promises and Pitfalls of Preclinical Strategies to Support Development of Cancer Immunotherapies

James F. Smothers, Ph.D., Senior Director & Head, Immuno-Biology, Immuno-Oncology & Combinations DPU, Oncology R&D, GlaxoSmithKline

T cell checkpoint modulation using monoclonal antibodies (mAbs) specific to the CTLA-4, PD-1 / PDL-1 & related pathways is emerging as a powerful strategy to provide significant clinical benefit to cancer patients across several solid tumor indications including melanoma, renal cell carcinoma (RCC) and non-small cell lung cancer (NSCLC). Such clinical successes in immunotherapy for cancer have been greatly dependent upon animal disease model studies to support pre-clinical rationale for their development.

2:00 Choosing the Right Syngeneic Model for Immunotherapy: The "SyngeOmic" Approach

Richard C.A. Sainson, Ph.D., Research Scientist II, Medimmune

With the recent FDA approvals, the modulation of the immune system is now a clinically validated approach to treat cancer. MedImmune continues to develop assets and expertise in Immune Mediated Therapies (IMT). The *in vivo* assessment of IMT molecules is enabled by the use of murine tumours in immunocompetent mice. With the aims of selecting relevant models, we have conducted a detailed genetic and cellular characterization of our models. The resulting dataset will help pre-clinical scientists to refine their *in vivo* plans by testing novel hypothesis in appropriate models.

2:30 Evaluating Immunotherapies Using Preclinical Models

Shailaja Kasibhatla, Ph.D., Associate Director, Oncology Pharmacology, Genomics; Institute of the Novartis Research Foundation

Preclinical modeling for tumor immunotherapy presents unique challenges. Not only is an intact immune system required, but the mechanism of action may be varied and involve multiple cell types across different tissue compartments. We will present some of the approaches we have employed for monitoring immune modulation in pre-clinical murine tumor models.

2:30 Sponsored Presentation *(Opportunity Available)*

3:00 Refreshment Break in the Exhibit Hall with Poster Viewing

MODELING FOR T CELL IMMUNOTHERAPY

3:40 Chairperson's Opening Remarks

Michelle Morrow, Ph.D., Research ScientistII, Medimmune

3:45 FEATURED PRESENTATION: Autochthonous Versus Transplantable Tumor Models For Cancer Immunotherapy: The Importance Of Host/Tumor Interactions

Prof. Benoît Van den Eynde, M.D, Ph.D., Branch Director, Ludwig Institute for Cancer Research, Université Catholique de Louvain, Brussels, Belgium

Most preclinical tumor models use transplantable tumors. Although these have a number of practical advantages, they do not recapitulate the long-term host/tumor interactions that eventually result in immune tolerance of the growing tumor by the host. Autochthonous tumors that can be induced in genetically-modified animals therefore provide better models for cancer immunotherapy. This will be illustrated using an inducible melanoma model.

4:15 Dendritic Cell/Tumor Fusion Vaccination for The Treatment of Hematologic Malignancy

Jacalyn Rosenblatt, M.D., Assistant Professor, Department of Medicine, Harvard Medical School

This presentation will focus on understanding the role of costimulatory molecules in T cell activation *in vivo*. Learning how to manipulate costimulatory pathways may provide new therapeutic approaches for augmenting immunity to microbes and tumor antigens. The approach that her laboratory has taken is to focus on the obligatory *in vivo* functions of costimulatory molecules by using targeted gene disruption to generate mouse strains lacking T cell costimulatory molecules.

4:45 Humanized Mouse Models: Modeling the Human Immune System for Preclinical Safety and Efficacy

Sponsored by Taconic

Michael Seiler, Ph.D., Manager, Scientific Marketing, Taconic

In the preclinical world mice are the most widely used animal models, however 96% of drugs that pass the preclinical drug development phase fail in clinical trials largely due to species-specific differences. To vastly improve predictability a humanized mouse immune system has been developed on the NOD/Shi-scid/IL-2R- null (NOG) base immunodeficient strain.

5:15 ErbB-Targeted CAR T Cell Immunotherapy of Cancer: A Strategy to Maximize the Window of Therapeutic Opportunity

John Maher, M.D., Ph.D., Senior Lecturer in Immunology, NIHR Biomedical, Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London

A CAR-based immunotherapy has been developed to target the extended ErbB family. Efficacy has been demonstrated in xenograft models of several cancers, without toxicity. However, IP delivery promotes cytokine release syndrome via recognition of mouse ErbBs and macrophage activation. To de-risk in man, patients with locally advanced head and neck cancer will receive CAR T cells by intratumoral injection.

Inaugural

Tumor Models for Preclinical Assessment of Cancer Immunotherapy

Applying Novel Immunocompetent Models

5:45 PANEL DISCUSSION: Preclinical Strategies for Cancer Immunotherapy Development

Moderator: John Maher, M.D., Ph.D.,Senior Lecturer in Immunology, King's College London

6:15 Close of Day

FRIDAY, MAY 23

7:30 am Interactive Breakout Discussion Groups with Continental Breakfast

FOSTERING TRANSLATIONAL APPROACHES

8:35 Chairperson's Remarks

Anand Giddabasappa, Ph.D., Principal Scientist, GS & T, Comparative Medicine, Pfizer

8:45 Immunoprevention of Breast Cancer: Preclinical and Clinical Challenges

Vincent K. Tuohy, Ph.D., Mort and Iris November Distinguished Chair in Innovative Breast Cancer Research, Staff, Department of Immunology, Cleveland Clinic

Tissue-specific proteins that are 'retired' from expression in normal tissues as we age but are expressed in emerging tumors may substitute for unavailable pathogens as targets for developing immunoprevention against cancers we confront in our adult years. The challenges involved in preclinical development and clinical trial testing for safety and efficacy of prophylactic vaccination against breast cancer will be discussed.

9:15 FEATURED PRESENTATION: How to Manipulate Costimulatory Pathways to Provide New Therapeutic Approaches for Augmenting Immunity to Tumor Antigens

Arlene H. Sharpe, M.D., Ph.D., Professor, Department of Microbiology and Immunobiology, Harvard Medical School; Co-Director, HITI; Vice Chair for Education, Pathology, Harvard Medical School

This presentation will focus on understanding the role of costimulatory molecules in T cell activation in vivo. Learning how to manipulate costimulatory pathways may provide new therapeutic approaches for augmenting immunity to microbes and tumor antigens. The approach that her laboratory has taken is to focus on the obligatory in vivo functions of costimulatory molecules by using targeted gene disruption to generate mouse strains lacking T cell costimulatory molecules.

9:45 Preclinical Modeling of Human Chimeric Antigen Receptor T Cell Immunotherapy

Saar Gill, M.D., Ph.D., Instructor, Division of Hematology-Oncology, University of Pennsylvania Medical School

Targeted cellular immunotherapy could overcome many limitations of conventional chemotherapy by combining the specificity of antibody therapy with the polyfunctionality of T cells and the capacity for memory induction of vaccine therapy. Chimeric antigen receptor T (CAR) modified T cells have been shown to achieve this goal in mice and in patients. The uses and limitations of models for the preclinical evaluation of CAR T cells will be discussed.

10:15 Boston Tea Party in the Exhibit Hall

MOLECULAR IMAGING FOR CANCER BIOLOGICS DEVELOPMENT

11:00 Using Labeled Antibody-Drug Conjugate Imaging and Mechanistic Modeling to Assess the Therapeutic Potential

Shu Wen Teng, Ph.D., Scientist, DMPK, Takeda Pharmaceutical

The development of antibody-drug conjugates (ADCs) involves a series of design choices that include antibody binding affinity, payload potency, and linker stability. It can be difficult to dissect the contribution of different controllable parameters to the overall efficacy of the ADC. To this end, we have built a mechanistic mathematical model of ADC efficacy, integrating experimental results from ADC imaging studies, *in vitro* viability assays, and *in vivo* xenograft efficacy studies. By combining modeling and imaging based techniques, we can gain insights into the design principles of ADC as well as patient selection criteria, such as the effect of antigen density and tumor vascularity on ADC efficacy.

11:30 Biodistribution of Biologic Drugs Using FMT Imaging

Anand Giddabasappa, Ph.D., Principal Scientist, GS & T, Comparative Medicine, Pfizer, Inc

Pharmacokinetics and the bio-distribution of biologic drugs are typically done by *in vivo* or ex vivo imaging (PET, PET/CT) using radio-labeled molecules. Advances in optical probes and imaging technologies have given us an opportunity to conduct such studies without use of radio-labeled materials. In this presentation I will be discussing the opportunities and challenges of fluorescence molecular tomography (FMT) in biodistribution of biologic drugs.

12:00pm LUNCHEON PRESENTATION: Targeting Epigenetics Using Human Cell Model Systems and Novel *In Vitro* Assays

Sponsored by DiscoveRx

Scott Pattison, Ph.D., Director, Business Development, BioSeek

DiscoveRx's in vitro assays and human model systems enable inhibitor characterization based on target profiles and effects on complex biological systems. Bromodomain inhibitor potency and selectivity was evaluated using BROMOscan™ quantitative binding assays and intracellular target engagement assays. Inhibitors were classified based on their phenotypic impact on primary human cell systems using BioMAP®. These assays can guide compound prioritization, indication selection and highlight potential safety issues to improve clinical success.

OVERCOMING LIMITATIONS OF CONVENTIONAL MODELS

12:55 Chairperson's Opening Remarks

Saar Gill, M.D., Ph.D., Instructor, Division of Hematology-Oncology, University of Pennsylvania Medical School

1:00 Characterizing Immune-Based Mechanisms of Anti-Tumor Activity in Syngeneic Tumor Models

Richard Levenson, M.D., Professor and Vice Chair, Strategic Technologies, Pathology & Laboratory Medicine, University of California, Davis Medical Center

1:30 Tumor Models for Cancer Immunotherapy: Relevance of Tumor Immunogenicity

Alan L. Epstein, M.D., Ph.D., Professor of Pathology, University of Southern California Keck School of Medicine

Seven murine tumors were used to identify key biomarkers that predict successful immunotherapy. For these studies, combination vaccine, antibody targeted LEC chemokine, and low dose chemotherapy to inhibit suppressor cells were used. The results demonstrated that tumor immunogenicity was critical and if low, methods to enhance it are needed in order to provide the proper tumor microenvironment for successful immunotherapy.

2:00 Transnuclear Mice as Models for Anti-Tumor Immunity

Stephanie Dougan, Ph.D., Senior Research Associate, Hidde Ploegh Lab, Whitehead Institute For Biomedical Research

Mice cloned by somatic cell nuclear transfer from the nuclei of antigen-specific lymphocytes can be used as models for studying the immune response to various pathologies. We generated a panel of transnuclear mice from tumor-specific T cells and find that TCR affinity plays little role in the overall response to melanoma. Preliminary findings in pancreatic cancer models suggest that the immune response varies among different tumor types.

2:30 Close of Conference

**Attendees registered for the following conferences can attend this session:

- Tumor Models to Guide Targeted Cancer Therapy and Drug Development
- Tumor Models for Preclinical Assessment of Cancer Immunotherapy
- Novel *in vitro* Models of Cancer
- Imaging in Preclinical and First in Human Clinical Studies in Oncology

5th Annual

Imaging in Preclinical and First in Human Clinical Studies in Oncology

Mastering Translational Approach

WEDNESDAY, MAY 21

7:00 am Registration and Morning Coffee

EMPLOYING VARIOUS MODALITIES AND DEVELOPING NOVEL BIOMARKERS

8:00 Chairperson's Opening Remarks
Erik M. Shapiro, Ph.D., Research Director, Department of Radiology, Michigan State University

8:05 FEATURED PRESENTATION: Image-Guided Surgery and Pathology Using Invisible Near-Infrared Fluorescent Light
John V. Frangioni, M.D., Ph.D., Professor, Department of Medicine and Radiology, Harvard Medical School

Near-infrared light in the wavelength range of 700-900 nm has relatively low attenuation and autofluorescence, permitting interrogation up to 5 mn below the surface of living tissue. In this talk, I will highlight the use of near-infrared fluorescent light for image-guided surgery and automated digital pathology, and review the clinical studies to date in the field.

8:35 Advances in Molecular and Cellular MRI
Erik M. Shapiro, Ph.D., Research Director, Department of Radiology, Michigan State University

This presentation will cover: MRI contrast agents for Molecular and Cellular MRI; Strategies for using targeted contrast agents for Molecular MRI of cancer and other pathologies; Magnetic cell labeling and MRI-based cell tracking; Quantification schemes for Molecular and Cellular MRI; A path towards clinical translation for experimental Molecular and Cellular MRI paradigms

9:05 PET/CT Imaging of Inhaled Biologics for Treatment of Disease in the Lungs
Vania Kenanova, Ph.D., Head, Preclinical PET/SPECT/CT Laboratory, Novartis Institute for Biomedical Research

The goal of this study was to answer if molecular weight plays a role in retention of antibodies or antibody fragments in rat lungs after intranasal delivery to the lungs. Serial PET/CT imaging of rats administered intranasally with [Zr-89] labeled Xolair (intact IgG) or anti-human FceRI Fab (antibody fragment) was utilized to generate the lung activity curves for each agent. Biodistribution and gamma counting was used to validate the imaging results. This talk will go over the study details, results and conclusions in terms of the impact that these findings may have on treatment of lung disease.

9:35 Coffee Break in the Exhibit Hall with Poster Viewing

10:20 Preclinical Ultrasound Imaging for Oncology Models
Terri A. Swanson, MA, LATg, PMP, Preclinical Ultrasound, Global Science & Technology Worldwide Comparative Medicine, Pfizer

High frequency ultrasound imaging (>20MHz) can provide anatomical, functional (flow), physiological and molecular data for *in vivo*, non-invasive, longitudinal studies of xenograft and orthotopic tumors in rodents. It is a translational imaging technique and when combined with ultrasound contrast agents allows for micro-perfusion imaging which can be used to monitor the efficacy of anti-angiogenic compounds and for targeted imaging which can quantify vascular endothelial surface markers such as VEGFR2. These applications and their use in preclinical drug discovery programs for oncology will be discussed.

10:50 Molecular Cancer Imaging and Theranostic Probe: Toward Clinical Translation
Hisataka Kobayashi, M.D., Ph.D., Chief Scientist, Molecular Imaging Program, National Cancer Institute

I will focus on a clinically-feasible example of "activatable" optical imaging probe, a sprayable gamma-glutamyltransferase probe, for assisting cancer detection during surgical or endoscopic procedures. Additionally, our newly developed target cancer cell-specific theranostic technology, photoimmunotherapy, which evolved from the similar concepts to imaging probe development, showed unique features including super-selective cytotoxicity, rapidly induced necrosis, that also leads super-enhanced nano-drug delivery.

11:20 Utilizing Micro-Ultrasound Imaging to Assess Effects of VEGF Blockade in Tumors
Sponsored by VISUALSONICS

Alexandra Eichten, Ph.D., Senior Staff Scientist, Oncology & Angiogenesis, Regeneron Pharmaceuticals

Biomarkers predicting efficacy of anti-VEGF therapies as well as effects of continued anti-VEGF blockade on tumor behavior are only partly understood. We utilized micro-ultrasound imaging to (1) investigate early perfusion changes as indicators of response and (2) use image-guided implantation to establish and study an 'orthotopic' CRC liver metastasis model.

11:35 Applications of Novel Compact, High-Performance MRI Platform for Pre-Clinical Phenotyping and Drug Development
Sponsored by aspectimaging

Tonya Coulthard, Applications and Product Specialist, Aspect Imaging

11:50 Centyrins, a Protein Scaffold with Ideal Properties for Molecular Imaging Applications
Jeannie Rojas, Ph.D., Director, Janssen R&D

The small size of the Centyrin molecule combined with its physical stability enables the Centyrins to be subjected to alternative delivery methods and these methods may allow for high concentrations of Centyrin molecules at the site of disease, while simultaneously lowering toxicity to non-target organs. In addition, due to the small size, Centryins may penetrate further into tissues resulting in higher sensitivity for imaging applications. In this presentation, both *in vivo* and *in vitro* data will be presented to showcase the highly desirable biophysical properties of biophysical properties of the Centyrin molecule, which make this platform ideal for imaging applications.

12:20 pm Non-Invasive *in vivo* Imaging of Transferrin in Breast Cancer Xenografts Using Fluorescence Lifetime FRET: Implications in the Development of Targeted Therapy
Margarida Barroso, Ph.D., Assistant Professor, Cardiovascular Sciences, Albany Medical College

Receptor-mediated uptake of transferrin (Tfn) into human breast xenograft tumors has been demonstrated using near-infrared Förster resonance energy transfer fluorescence lifetime (FRET-FL) imaging in live mice. Near-infrared FRET-FL discriminates between soluble extracellular Tfn and receptor-bound Tfn (intracellular), increasing tumor/blood and non-tumor tissues ratio. Our data supports the quantitative accuracy and sensitivity of NIR FRET-FL imaging to be used non-invasively in live small animal models and for increasing the delivery/residency of Tfn-drug conjugates at the target site.

12:50 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

1:30 Session Break

MOLECULAR IMAGING BIOMARKERS AND END POINTS

(Shared Session between Tumor Models for Targeted Therapy and Imaging in Oncology)

2:00 Chairperson's Opening Remarks
Paul Acton, Scientific Director and Janssen Fellow, Global Head, Molecular Imaging, Johnson & Johnson

2:05 Translatability of Preclinical Modeling: Case Study of Development of a Targeted Therapeutic with an Imaging Companion Diagnostic
Ingrid Joseph, D.V.M., Ph.D., Senior. Director, Pharmacology, Agensys, an affiliate of Astellas Pharma, Inc.

Traditional xenograft models utilize immortalized cancer cells grown on plastic that exhibit a genetic drift. Therefore, they do not represent the total genetic/epigenetic heterogeneity of the original cancers. Despite demonstrating efficacy in these models, a majority of cancer therapeutics fail in the clinic. Patient derived tumors grown as xenografts (PDXs) appear to maintain the histopathology/molecular characteristic of the original tumor. A case study utilizing PDX models better suited for targeted therapy will be discussed.

5th Annual

Imaging in Preclinical and First in Human Clinical Studies in Oncology

Mastering Translational Approach

2:35 Molecular Imaging for Patient Selection and Predicting Treatment Response

Paul Acton, Scientific Director and Janssen Fellow, Global Head, Molecular Imaging, Johnson & Johnson

Personalized medicine would provide the key diagnostics required to deliver more effective targeted therapies, avoiding unnecessary or ineffective treatments, and reducing side effects. This presentation will outline several approaches to developing predictive imaging biomarkers, including imaging of labeled drugs, and a novel approach to tagging biologics which allows each drug to become its own companion diagnostic.

3:05 Heparin-Reactive Peptides Preferentially Co-Localize *in vivo* with Extracellular Melanin – A Novel Biomarker in Metastatic Melanoma Tumors

Jonathan Wall, Ph.D., Professor of Medicine, Human Immunology and Cancer Program; Director, Amyloid and Preclinical Molecular Imaging Laboratory, University of Tennessee Graduate School of Medicine

Melanoma is the most deadly form of skin cancer with >70,000 individuals diagnosed in 2011 in the USA. During a routine histochemical screen of biotinylated heparin-reactive peptides with a tumor tissue array, we identified certain reagents that preferentially bound melanocytic melanoma tumors. We have now demonstrated peptide reactivity, by using SPECT/CT imaging, co-localization of the peptides with B16F10 murine "metastatic" melanoma tumors within the mouse lung.

3:35 Preclinical and Clinical Applications of Patient Derived Xenograft (PDX) Models

Sponsored by The Jackson Laboratory — Leading the search for tomorrow's cures

Yan Yang, Director, Lab Operations in vivo Services, The Jackson Laboratory

The Jackson Laboratory has established a unique collaboration with over 20 clinical centers to advance cancer treatment. Patient tumors transplanted into the NSG mouse are being screened with SOC and experimental therapeutics for preclinical research or the refinement of patient treatment regimens.

4:05 Modeling Human Cancer: A Multifaceted Approach to Pre-Clinical Development

Maria L. Mancini, Ph.D., Principal Investigator, Biomodels, LLC

There are a number of key points to consider when designing therapeutics for the treatment of human cancers. Tumor heterogeneity, stromal contribution, immune response, and treatment resistant sub-populations are all potential confounds that complicate the assessment of novel therapeutic strategies in a pre-clinical setting. Only recently have efforts been directed at treating resistant cell populations (often termed cancer stem cells). In order to study these populations, Biomodels developed a multi-faceted approach to evaluate novel therapeutics.

» 5:00 PLENARY KEYNOTE PRESENTATION: Catalyzing Translational Innovation

Christopher P. Austin, M.D., Director, National Center for Advancing, Translational Sciences, National Institutes of Health (Click here for details)

6:00 Welcome Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

THURSDAY, MAY 22

7:30 am Interactive Breakout Discussion Groups with Continental Breakfast

THERANOSTIC IMAGING

8:35 Chairperson's Opening Remarks

Thomas Reiner, Ph.D., Weill Cornell Medical College

8:45 Poly [ADP-Ribose] Polymerase 1: Imaging of a Nuclear Tumor Marker *in vivo*

Thomas Reiner, Ph.D., Assistant Member, Memorial Sloan-Kettering Cancer Center; Assistant Attending Chemist, Radiochemistry & Imaging Sciences Service; Assistant Professor, Weill Cornell Medical College

The enzyme PARP1 and its function have long been in the focus of medical research due to its key position in the repair of DNA. Here, we report on the design and application of a PARP1 imaging agent, which we showed to have superior pharmacological properties and selectivity *in vivo*, and discuss its potential impact on future clinical research.

9:15 siRNA and miRNA Theranostic Nanoprobes for Oncology

Anna Moore, Ph.D., Associate Professor in Radiology, Harvard Medical School

Molecular imaging technologies have recently undergone massive expansion and are now posed to play crucial role in clinical oncology. Theranostic nanoprobes offer great potential for delivery of therapy and for monitoring of this delivery *in vivo*. This presentation will focus on the overall concept and step-by-step development of targeted "theranostic probes" for delivery of oligonucleotides for siRNA and microRNA therapies.

9:45 Sponsored Presentation *(Opportunity Available)*

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

GAINING FROM TECHNOLOGICAL ADVANCES

Bridging Session between Four Oncology Tracks**

10:30 Bridging Session Chair

Jonathan Wall, Ph.D., University of Tennessee Graduate School of Medicine

10:35 Targeted NGS Applications for Detection of Somatic Mutations

Oleg Iartchouk, Ph.D., Director, Genomics and Next-Generation Sequencing, Novartis Institutes for Biomedical Research

This talk will give an overview of NGS applications used to discover somatic point mutations and short insertion deletions in different types of cancer samples. Potential promise for some of them in clinical settings will be discussed.

11:05 Accelerating Preclinical Drug Development by *in vivo* and *ex vivo* Imaging in Cancer Models: Optimizing Discovery to Delivery

Werner Scheuer, Research Leader, Pharma Research and Early Development, Discovery Oncology, Roche Diagnostics GmbH

The presentation will discuss the following topics: application of different imaging modalities to monitor the efficacy of compounds on primary tumor growth, metastasis and angiogenesis; simultaneous measurement of Pk and Pd; optimizing application schedules regarding combination therapies; and verification of *in vivo* imaging data by 3-dimensional multispectral fluorescence histology.

11:35 FEATURED PRESENTATION: The Critical Role of Extracellular Matrix and Microenvironment in Metastasis and Dormancy

Mina J. Bissell, Ph.D., Distinguished Scientist, Life Sciences Division, Lawrence Berkeley National Laboratory

12:05 An Integrative Approach to the Evaluation, Selection and Orientation of Novel Cancer Therapeutics

Sponsored by Oncodesign Biotechnology

Jonathan Ewing, Business Development Director, Oncodesign

The challenge in identifying the preclinical activity of cancer therapeutics and orientating their best clinical use is associating relevant in vivo models of human disease with effective pharmacological evaluation and biomarkers. Oncodesign's precision medicine approach to clinical drug candidate selection integrates appropriate in vivo models, extensive pharmacological expertise and pharmaco-imaging tools to provide quantitative, predictive and translational evidence early in drug development.

12:35 Close of Imaging in Preclinical and First-in-Human Clinical Studies in Oncology

**Attendees registered for the following conferences can attend this session:

- Tumor Models to Guide Targeted Cancer Therapy and Drug Development
- Tumor Models for Preclinical Assessment of Cancer Immunotherapy
- Novel *in vitro* Models of Cancer
- Imaging in Preclinical and First in Human Clinical Studies in Oncology

Inaugural

Novel *in vitro* Models of Cancer

Overcoming Challenges of ex vivo Tumor Modeling

THURSDAY, MAY 22

9:30 am Registration

GAINING FROM TECHNOLOGICAL ADVANCES

Bridging Session between Four Oncology Tracks**

10:30 Bridging Session Chair

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Sponsored by DiscoveRx

Scott Pattison, Ph.D., Director, Business Development, BioSeek

DiscoveRx's in vitro assays and human model systems enable inhibitor characterization based on target profiles and effects on complex biological systems. Bromodomain inhibitor potency and selectivity was evaluated using BROMOscan™ quantitative binding assays and intracellular target engagement assays. Inhibitors were classified based on their phenotypic impact on primary human cell systems using BioMAP®. These assays can guide compound prioritization, indication selection and highlight potential safety issues to improve clinical success.

1:25 pm Chairperson's Opening Remarks

Alan Wells, M.D., Ph.D., Associate Chair, Pathology, University of Pittsburgh Medical Center

1:30 FEATURED PRESNTATION: An All-Human Microphysiologic Liver System for Carcinoma Metastasis

Alan Wells, M.D., Ph.D., Associate Chair, Pathology, University of Pittsburgh Medical Center

Metastases kill patients, but disseminated cancers are resistant to therapies. The tumor biological events behind this are unknown due to lack of relevant model systems. Further, humans metabolize agents and present toxicities uniquely, hampering drug development. We have developed an all-human microphysiological system of the liver to study both tumor behavior in the common metastatic site, and drug metabolism/efficacy in the main metabolizing organ.

2:00 *Ex vivo* Tumor Tissue Model for Patient-Specific Drug Screens

Geoffrey Bartholomeusz, Ph.D., Assistant Professor, Department of Experimental Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

The inability to replicate tumor heterogeneity utilizing *in vitro* cell culture models have prevented these studies from being successfully translated into clinical practice. Prolonged time, high costs and resource consuming have slowed the development of patient-derived xenograft models. The relevance of an *ex vivo* tumor tissue in identifying a patient specific single agent of drug cocktail will be discussed.

2:30 Phenotypic Profiling of Compound Activity in Cultured Human Tumour Tissues

Leo Price, Ph.D., Principal Investigator, Toxicology, Leiden Amsterdam Center for Drug Research

To bridge the gap between *in vitro* and *in vivo* models for cancer, we developed an ultra-high content screening platform for human tumour tissues. Using 3D tissues cultured from cell lines and patient-derived cancer stem cells, compounds can be profiled in a context that more closely simulates the patient situation. Screening in tissues derived from the same cell lines that will be used in xenograft models is also predicted to improve the concordance of *in vitro* and preclinical data. This approach is expected to significantly reduce the proportion of compounds that fail in pre-clinical studies.

3:00 Refreshment Break in the Exhibit Hall with Poster Viewing

SCREENING FOR EFFICACY AND RESISTANCE

3:40 Chairperson's Opening Remarks

Leo Price, Ph.D., Leiden Amsterdam Center for Drug Research

3:45 Use of Repository and Newly Established Cell Lines to Model Cancer Drug Sensitivity and Resistance

Cyril H. Benes, Ph.D., Principal Investigator and Director, Center for Molecular Therapeutics, Massachusetts General Hospital Cancer Center

I will discuss the use of large cell lines collections to identify candidate biomarkers of therapeutic response and of cell lines newly derived from tumors with acquired resistance to provide valuable insights into the mechanisms underlying resistance and discover novel therapeutic modalities.

4:15 An Evolving View of Cancer: Studying the Emergence of Resistance to Targeted Agents Using Colony Growth Kinetics and a 3D Culture System

Arijit Chakravarty, Ph.D., Senior Scientist II, Modeling and Simulation, DMPK, Takeda Pharmaceuticals

The changing picture of the landscape of carcinogenesis and tumor response to therapy frames cancer as a disease of genomic instability and somatic Darwinian evolution. Developing realistic model systems and methodologies to study heterogeneity and evolution in populations of cancer cells would be the first step in leveraging the emerging picture of cancer in Oncology drug development. In this presentation I will discuss the challenges posed by tumor heterogeneity and evolution, and the methods by which a novel 3D soft agar system allows us to study this process. We extract the growth kinetics of individual colonies via high-content analysis, and then couple this with mathematical modeling, to identify novel insights on the emergence of resistance to targeted agents.

4:45 Determination of Target Engagement on Cancer Targets *in vitro* and *in vivo*

Michael Dabrowski, Ph.D., CEO & Co-Founder, Pelago Bioscience AB

We have developed a generic method for evaluating drug binding to target proteins in cells and tissues (Martinez Molina et al. Science 2013). The CEllular Thermal Shift Assay (CETSA™) is based on the physical phenomenon of ligand-induced thermal stabilization of target proteins. Using this technique, it is possible to quantify physiological relevant drug-target interactions in cells and tissue completely label free. We have validated drug binding in mammalian cancer cell lines for a set of important clinical targets and show that a range of critical factors that are important for drug development can be identified at the target engagement level, including drug transport and activation, off-target effects, drug resistance as well as drug distribution in animal tissues.

5:15 Selected Poster Presentations

3D Bioprinting of Vascularized, Heterogeneous Cell-Laden Tissue Constructs

David Kolesky, Wyss Institute

Culturing Cancer Cells on Myoma Tissue: Development of a Novel Fully Human Organotypic 3D Invasion Model

Katja Fagerlund, Ph.D., Pharmatest Svcs Ltd

Inaugural

Novel *in vitro* Models of Cancer

Overcoming Challenges of ex vivo Tumor Modeling

5:45 PANEL DISCUSSION: Increasing Predictability of *in vitro* Tumor Models
Moderator: Leo Price, Ph.D., Leiden Amsterdam Center for Drug Research

6:15 Close of Day

FRIDAY, MAY 23

7:30 am Interactive Breakout Discussion Groups with Continental Breakfast

ADVANCING 3D TISSUE MODELS

8:25 Chairperson's Opening Remarks
Bumsoo Han, Ph.D., Associate Professor, Mechanical and Biomedical Engineering, Purdue University

8:30 Microscale Tumor and Fibrosis Models
Shuichi Takayama, Ph.D., Professor, Biomedical Engineering, Professor, Macromolecular Science and Engineering, University of Michigan
This presentation will introduce micro-technologies targeted for cell-based assays in cancer and fibrosis. Devices include a microfluidic source-sink chemotaxis analysis system, a 384 hanging drop array for cancer spheroid formation, and a microscale fibroblast-collagen gel contraction assay enabled by aqueous two phase system microdroplets. Comparisons of these assays with conventional platforms for drug testing will also be presented.

9:00 Phenotypic-Based Primary Screen for Angiogenesis Inhibitors
Mohanraj Dhanabal, Ph.D., Group Leader, Lead Discovery Technology, EMD Serono
Angiogenesis, the formation of new blood vessels from the pre-existing microvasculature, is among the key events for many physiological and pathological processes. We describe an angiogenesis assay system, which allows rapid and reliable quantification of three-dimensional vessel formation *in vitro* in a miniaturized format using (BD Matrigel™) onto 384 plates. Such a platform is used for screening compounds in a 384-well plate format to a High Content Screening. Finally, we used this to screen more compounds during the drug discovery and development process, which led us to the identification and prioritization of compounds with potent antiangiogenic activity.

9:30 The Effect of the Tumor Three-Dimensionality and the Metastasis-Associated Stroma on Malignant Cell Response to Antineoplastic Agents: Implications in Anti-Cancer Drug Screening
Eugen Dhimolea, Ph.D., Research Fellow, Medical Oncology, Dana Farber Cancer Institute, Harvard Medical School
We assessed the pathophysiological relevance of heterotypic *in vitro* three-dimensional (3D) tissue cultures, comprised of malignant and non-malignant accessory cells from organs frequently targeted by metastatic disease, by testing the activity of more than 100 FDA-approved antineoplastic drugs. Our 3D co-culture provides a practical and clinically-relevant experimental system to study the mechanisms of metastatic microenvironment-related drug resistance and to screen for biologically active compounds that circumvent it.

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 Tumor-Microenvironment-on-Chip (TMOC)
Bumsoo Han, Ph.D., Associate Professor, Mechanical and Biomedical Engineering, Purdue University
Targeted delivery of therapeutic and imaging agents to tumors without non-specific accumulation at normal tissues can significantly improve the treatment and diagnosis of cancers. Nanotechnology recently enabled various functional nanoparticles as vehicles for targeted delivery. However, it is extremely challenging to optimize their design and configuration using traditional cell culture and animal models. In order to address this challenge, a new *in vitro* model was developed to simulate the complex 3-D tumor microenvironments relevant to the transport of nanoparticles.

11:30 Microengineered Physiological Biomimicry: Human Organ-on-Chips
Dongeun (Dan) Huh, Ph.D., Wilf Family Term Assistant Professor, Bioengineering, UPENN
This talk will present interdisciplinary research efforts focused on leveraging unique capabilities of microfluidics and microfabrication to develop microengineered biomimetic models that reconstitute complex structures, dynamic microenvironments, and physiological functions of human organs. Specifically, I will talk about i) a bioinspired microsystem that mimics the structural and functional complexity of the alveolar-capillary interface in the living human lung and ii) a specialized *in vitro* human disease model that simulates pulmonary edema.

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

12:30 Session Break

MODELS FOR EPIGENETIC DRUG DISCOVERY

(Shared Session between Novel *in vitro* Models of Cancer and Epigenetics Screening)

1:00 Tissue Architecture as the Basis for Target Discovery and Drug Screening in Breast Cancer
Sophie Lelièvre, D.V.M., L.L.M., Ph.D., Associate Professor, Department of Basic Medical Sciences and Associate Director, Discovery Groups, NCI-Designated Purdue Center for Cancer Research, Purdue University
The epigenome is the mirror of tissue phenotypes. Only 3D culture permits the mimicry of complex or subtle phenotypic traits triggered by tissue architecture. I will present how the analysis of the earliest architectural alteration known to be necessary for breast cancer onset, i.e., the loss of apical polarity has led to the discovery of epigenetic modulators involved in breast homeostasis and serves as the basis for high throughput screening of preventive and therapeutic agents.

1:30 Assaying Anticancer Therapeutics in Microfluidic 3D Cell Culture
Amir R. Aref, Ph.D., Department of Cancer Biology & Medical Oncology, Dana-Farber Cancer Institute
Metastasis contributes to over 90% of all cancer-related deaths. Cancer cells breaking free from their neighbors and acquiring the ability to migrate can both occur via a process similar to epithelial-mesenchymal transition (EMT), and represent critical steps in the early stages of metastasis. In addition to cell intrinsic changes, metastasizing carcinoma cells engage in interactions with their microenvironment that facilitate metastatic progression.

2:00 Epigenetic Regulation of SOX9 by the NF-κB Signaling Pathway in Pancreatic Cancer Stem Cells
Lei Sun, Ph.D., Postdoctoral Fellow, Mouse Cancer Genetics Program, Center for Cancer Research, National Cancer Institute, National Institutes of Health
To investigate epigenetic regulation of genes in pancreatic cancer stem cells (CSCs), we compared the global DNA methylation status of CpG promoters in CSCs to non-CSCs. Our results suggested the NF-- B pathway and SOX9 play a crucial role in CSCs. Additionally, we found the NF-- B subunit p65 positively regulates SOX9 expression by binding to its promoter directly. Thus, our work establishes a link between the NF-- B pathway and epigenetic regulation of SOX9 in pancreatic CSCs.

2:30 Close of Conference

**Attendees registered for the following conferences can attend this session:
- Tumor Models to Guide Targeted Cancer Therapy and Drug Development
- Tumor Models for Preclinical Assessment of Cancer Immunotherapy
- Novel *in vitro* Models of Cancer
- Imaging in Preclinical and First in Human Clinical Studies in Oncology

Inaugural

New Tools for Functional Epigenetics Screening

Biochemical and Cell-Based Assays for Validating Targets and Leads

THURSDAY, MAY 22

11:00 am Registration

SAFETY SCREENING FOR EPIGENETIC DRUGS

12:50 pm Chairperson's Opening Remarks

Chair: Jatinder Singh, Ph.D., Principal Scientist, Drug Safety and Metabolism, AstraZeneca Pharmaceuticals

1:00 Safety Considerations for Developing Epigenetic Drugs

Jatinder Singh, Ph.D., Principal Scientist, Drug Safety and Metabolism, AstraZeneca Pharmaceuticals

Pharmacological modulators of epigenetic targets are being evaluated for the treatment of both oncology and non-oncology disease indications. This novel paradigm for drug development is associated with unique safety considerations such as transgenerational effects. These will be discussed in the context of current knowledge of epigenetic modulation. Practical recommendations for preclinical safety strategies for epigenetic drug discovery and development programs will be discussed.

1:30 3D Chromatin Organization as a Novel Indicator in Drug Safety Assessment

Jian Tajbakhsh, Ph.D., Program Leader, Translational Cytomics; Head, Chromatin Biology Laboratory, Cedars-Sinai Medical Center

Off-target global DNA demethylation by epigenetic drugs could lead to unwanted cryptic DNA methylation toxicity and carcinogenesis by influencing chromatin conformation, genome organization and gene expression programs. Utilizing high-content and high-throughput 3D image-cytometry of epigenetic marks, the higher-order chromatin organization can be used as an indicator for the causal assessment of global DNA demethylation and heterochromatin decondensation in drug-treated cells towards associated risks such as cytotoxicity and genomic instability.

2:00 High-Content Phenotypic Screening for Novel Inhibitors of Pathological Cardiac Hypertrophy

Brian G. Reid, Ph.D., Director, High Throughput and High Content Screening Core Facility; Research Assistant Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, Department of Pharmaceutical Sciences, University of Colorado

Cardiomyocyte hypertrophy is a hallmark of diastolic heart failure, also known as heart failure with preserved ejection fraction (HFpEF). There are a host of cellular pathways that can contribute to pathological cardiac hypertrophy, including epigenetic influences such as HDAC activity. We have developed an *in vitro* high-content phenotypic assay for cardiomyocyte hypertrophy in primary myocytes that simultaneously monitors multiple phenotypic parameters in a pathway agnostic approach to the discovery of novel therapeutic strategies for the treatment of HFpEF.

2:30 Preclinical Safety Assessment of Epigenetic Drugs: A Practical Perspective

Paul Vancutsem, D.V.M., Ph.D., Senior Director, Toxicology and DMPK, Constellation Pharmaceuticals

Epigenetic mechanisms are`pivotal to the differentiation of cells during development and adulthood. Therefore, drugs developed in oncology and primary care to target these pathways challenge the toxicologist to re-examine accepted paradigms of risk assessment and management. This talk reviews known phenotypes associated with epigenetic imbalances and the timing of their occurence in the context of current guidelines, accepted preclinical study designs and common clinical precautions.

3:00 Refreshment Break in the Exhibit Hall with Poster Viewing

BIOCHEMICAL ASSAYS & SCREENING PLATFORMS

3:45 Preclinical Safety Assessment of Epigenetic Drugs: A Practical Perspective

Alejandra Raimondi, Associate Director, Lead Discovery Cell-based Assay Group, Epizyme Inc.

EZH2 is a histone methyltransferase implicated in many cancers and with misregulated enzyme activity in a subset of germinal center B cell non-Hodgkin lymphomas (NHL) that provides a clear and promising path for drug development. Results from our high-quality in vitro combination platform performed in mutant bearing EZH2 cells have shown that the single agent activity of our development candidate EPZ-6438 was strongly enhanced when combined with all components of the CHOP chemotherapy regimen. Interestingly the synergistic effect observed with glucocorticoid receptor agonists, prednisolone and dexamethasone, extended to cell lines with wild type EZH2.

4:15 Interrogating the Bromodomain Family through Chemical Biology

Laura Zawadzke, Ph.D., Principal Research Scientist, Constellation Pharmaceuticals

Readers of histone acetylation include the bromodomain family. Proteins which contain bromodomains often include other reader domains or chromatin-modifying enzyme functions. It is hypothesized that selective inhibitors of bromodomains will find utility in not only basic research of this emerging protein/protein interactions class, but also towards disease amelioration. This talk describes a biochemical approach taken by a Constellation and Genentech collaboration towards identifying selective small molecule inhibitors as probe molecules. Through a platform screening approach, potent and selective bromodomain probes have been identified.

4:45 High-Throughput Assays for Readers and Writers of Histone Methylation

Brandi M. Baughman, Ph.D., Postdoctoral Research Associate, Center for Integrative Chemical Biology and Drug Discovery, The University of North Carolina at Chapel Hill

Readers and writers of histone methylation are important regulators of cellular differentiation and development and are increasingly being implicated in numerous disease states. Small molecules that disrupt interactions between these regulators and chromatin would enable a systematic study of histone regulators and could potentially reveal novel targets for drug discovery. Our group implements several high-throughput assays for screening small molecule modulators of histone methylation. These assays span various technologies to target both readers and writers of histone methylation.

5:15 Kinetic Characterization of Inhibition of Histone Deacetylase by Isoform Specific Inhibitors

Yan-Ling Zhang Ph.D., Director, In Vitro Pharmacology Therapeutics Platform, Stanley Center for Psychiatric Research, Broad Institute of Harvard and MIT

Histone deacetylases (HDACs) play a critical role in the modulation of chromatin topology and the regulation of gene transcription. Deregulation of their activity has been implicated in many diseases including cancer, diabetes and psychiatric disorders. Significant efforts have been made to identify selective HDAC inhibitors with unique inhibition kinetics to understand the requirements for on- target efficacy and mitigate side effect. A highly quantitative microfluidic capillary electrophoresis assay was developed to characterize inhibition kinetics and selectivity of newly developed HDAC inhibitors.

5:45 Late Breaking Presentation

6:15 Close of Day

FRIDAY, MAY 23

7:30 am Interactive Breakout Discussion Groups with Continental Breakfast

CELLULAR SYSTEMS FOR STUDYING EPIGENETIC PATHWAYS

8:35 Chairperson's Opening Remarks

Fred Winston, Ph.D., John Emory Andrus Professor of Genetics, Harvard University Medical School

8:45 FEATURED PRESENTATION: Using Yeast to Study Eukaryotic Transcription, Chromatin Structure, and Epigenetics

Fred Winston, Ph.D., John Emory Andrus Professor of Genetics, Harvard University Medical School

Transcription by RNA polymerase II is a highly conserved process, from yeast to humans. Many essential factors required for transcription have been discovered using yeast as a model system. In addition, chromatin remodeling factors, histone chaperones, and histone post-translational modifications were initially discovered by yeast genetics. I will discuss genetic and genomic studies of conserved factors required for these processes and what they suggest regarding genetic and epigenetic control in eukaryotes.

Inaugural

New Tools for Functional Epigenetics Screening

Biochemical and Cell-Based Assays for Validating Targets and Leads

9:15 A Novel Chemical Biology Strategy to Study Epigenetic Regulation Using Phenotypic Screening

Yan Liu, Ph.D., Investigator, R&D Platform Technology & Science, GlaxoSmithKline

At GSK we built a systematically designed chemical probe library, which target 736 unique proteins with multiple maximally selective compounds for each target, to study epigenetic regulation in biological systems, histone modifications in particular. Using a high-content imaging assay to quantify H3K27me3 levels in HCC1806 cellular system, we screened this unique set of biologically diverse, target-annotated chemical compounds. Results from our study revealed novel therapeutically useful pathways and targets of H3K27me3 regulation.

9:45 Discovery of New Epigenetic Pathways by Phenotypic Quantitative Interactome Screening

Xian Chen, Ph.D., Associate Professor, Biochemistry & Biophysics, University of North Carolina at Chapel Hill

We have been pioneering in introducing a variety of quantitative proteomic approaches, amino acid-coded mass tagging (AACT) or SILAC named by others in particular, to profile phenotypic protein-protein interactions (PPIs) in the living stimulated cells. These approaches have led to non-biased dissections of different pathways involved in signal transduction and epigenetic regulation, and more importantly to the identifications of novel pathway components in an interconnected manner. Biological follow-up characterizations of these components then systematically elucidate the pathways or mechanism these components are involved in.

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

MODELS FOR EPIGENETIC DRUG DISCOVERY

10:55 Chairperson's Opening Remarks

11:00 High-Throughput Screening to Identify Inhibitors of JARID1/KDM5 Histone Demethylases

Qin Yan, Ph.D., Assistant Professor, Department of Pathology, School of Medicine, Yale University

Epigenetic aberrations often lead to cancer and other human diseases. The JARID1/KDM5 histone demethylases removes the H3K4me3/2 marks. Since the JARID1A/B demethylases are highly expressed in various cancers and play critical roles in drug resistance and cancer stem cells, they are novel targets for cancer treatment. We showed with genetically engineered mouse cancer models that JARID1A loss suppresses tumor formation in mice. Using AlphaScreen based HTS screen, we identified lead compounds that inhibit JARID1 enzymes.

11:30 Stem Cell and Animal Models for Target Discovery and Validation

Laurie Jackson-Grusby, Ph.D., Assistant Professor, Harvard Medical School; Faculty, Department of Pathology, Boston Children's Hospital and Harvard Stem Cell Institute

12:00 pm Targeting Epigenetics Using Human Cell Model Systems and Novel *In Vitro* Assays

Sponsored by DiscoveRx

Scott Pattison, Ph.D., Director, Business Development, BioSeek

DiscoveRx's *in vitro* assays and human model systems enable inhibitor characterization based on target profiles and effects on complex biological systems. Bromodomain inhibitor potency and selectivity was evaluated using BROMOscan™ quantitative binding assays and intracellular target engagement assays. Inhibitors were classified based on their phenotypic impact on primary human cell systems using BioMAP®. These assays can guide compound prioritization, indication selection and highlight potential safety issues to improve clinical success.

12:30 Session Break

MODELS FOR EPIGENETIC DRUG DISCOVERY CONT'D

(Shared Session between Epigenetics Screening and Novel *in vitro* Models of Cancer)

12:55 Chairperson's Opening Remarks

Eugen Dhimolea, Ph.D., Research Fellow, Medical Oncology, Dana Farber Cancer Institute, Harvard Medical School

1:00 Tissue Architecture as the Basis for Target Discovery and Drug Screening in Breast Cancer

Pierre-Alexandre Vidi, Ph.D., Department of Basic Medical Sciences, Purdue University

The epigenome is the mirror of tissue phenotypes. Only 3D culture permits the mimicry of complex or subtle phenotypic traits triggered by tissue architecture. I will present how the analysis of the earliest architectural alteration known to be necessary for breast cancer onset, i.e., the loss of apical polarity has led to the discovery of epigenetic modulators involved in breast homeostasis and serves as the basis for high-throughput screening of preventive and therapeutic agents.

1:30 Assaying Anticancer Therapeutics in Microfluidic 3D Cell Culture

Amir R. Aref, Ph.D., Department of Cancer Biology & Medical Oncology, Dana-Farber Cancer Institute

Metastasis contributes to over 90% of all cancer-related deaths. Cancer cells breaking free from their neighbors and acquiring the ability to migrate can both occur via a process similar to epithelial-mesenchymal transition (EMT), and represent critical steps in the early stages of metastasis. In addition to cell intrinsic changes, metastasizing carcinoma cells engage in interactions with their microenvironment that facilitate metastatic progression.

2:00 Epigenetic Regulation of SOX9 by the NF-κB Signaling Pathway in Pancreatic Cancer Stem Cells

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2:30 Close of Conference

Suggested Event Package:

May 21-22

Functional Screening for Drug Safety Testing Conference

OR

Tumor Models to Guide Targeted Cancer Therapy and Drug Development Conference

May 22

Recommended Dinner Short Course*

How to Best Utilize Organotypic 3D Cell Cultures Assays in Oncology

(See here for details.)

May 22-23

New Tools for Functional Epigenetics Screening Conference

** Separate registration required*

> "This meeting is a great way for a newcomer to this field to get up to date information in a short period of time."
>
> - Assistant Research Professor, University of North Carolina Wilmington

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CHI offers comprehensive sponsorship packages which include presentation opportunities, exhibit space, branding and networking with specific prospects. Sponsorship allows you to achieve your objectives before, during, and long after the event. Any sponsorship can be customized to meet your company's needs and budget. Signing on early will allow you to maximize exposure to qualified decision-makers..

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Showcase your solutions to a guaranteed, targeted audience. Package includes a 15- or 30-minute podium presentation within the scientific agenda, exhibit space, on-site branding, access to cooperative marketing efforts by CHI, and more.

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Opportunity includes a 30-minute podium presentation. Boxed lunches are delivered into the main session room, which guarantees audience attendance and participation. A limited number of presentations are available for sponsorship and they will sell out quickly. Sign on early to secure your talk!

Invitation-Only VIP Dinner/Hospitality Suite

Sponsors will select their top prospects from the conference pre-registration list for an evening of networking at the hotel or at a choice local venue. CHI will extend invitations and deliver prospects, helping you to make the most out of this invaluable opportunity. Evening will be customized according to sponsor's objectives (i.e. purely social, focus group, reception style, plated dinner with specific conversation focus).

Exhibit

Exhibitors will enjoy facilitated networking opportunities with qualified delegates. Speak face-to-face with prospective clients and showcase your latest product, service, or solution.

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Additional branding and sponsorship opportunities available!

For sponsorship and exhibit information, please contact:

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Business Development Manager
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CHI's Lead Generation Programs will help you obtain more targeted, quality leads throughout the year. We will mine our database of 800,000+ life science professionals to your specific needs. We guarantee a minimum of 100 leads per program! Opportunities include:

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

World Pharma Congress Student Fellowship

Full time graduate students and PhD Candidates are encouraged to apply for the World Pharma Congress Student Fellowship. Applications are due by *March 7, 2014*.

- Interested students must complete the application for the 2014 Student Fellowship
- Fellows are required to present a scientific poster. A poster title and abstract are due at the time of the application
- All applications will be reviewed by the scientific review committee and the accepted students will be notified no later than March 14, 2014 if they were accepted for the 2014 Student Fellowship
- Accepted 2014 Student Fellows will receive a discounted conference rate of $195*, which must be paid in full by April 4, 2014
- This fellowship is limited to 10 students and is for the Main Conference Only*
- All accepted 2014 Student Fellows will be asked to help promote the conference onsite at their college, and throughout their social media networks
- Students not accepted for the 2014 Student Fellowship, can register at a discounted rate $295*, and will not be required to present a poster

** This discounted rate cannot be combined with any other discounts for this event. Your discounted rate does not grant access to any of the short courses or pre-conference events. It also does not include hotel, travel or meals*

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 materials, your abstract must be submitted, approved and your registration paid in full by April 4, 2014.

Register online, or by phone, fax or mail. Please indicate that you would like to present a poster. Once your registration has been fully processed, we will send an email with a unique link and instructions for submitting your abstract using our online abstract submission tool. Please see below for more information.

Reasons you should present your research poster at this conference:

- **Your poster will be exposed to our international delegation**
- **Receive $50 off your registration**
- **Your poster abstract will be published in our conference materials**
- **Your research will be seen by leaders from top pharmaceutical, biotech, academic and government institutes**

Hotel & Travel Information

Conference Venue and Host Hotel:

Westin Boston Waterfront
425 Summer St.
Boston, MA 02210
T: 617-532-4600

Room Rate: **$269 s/d**
Reservation Cutoff: **April 23, 2014**

Please visit our conference website to book your reservations online or call the hotel directly to reserve your sleeping accommodations. You will need to identify yourself as a Cambridge Healthtech Institute conference attendee to receive the discounted room rate with the host hotel. 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.

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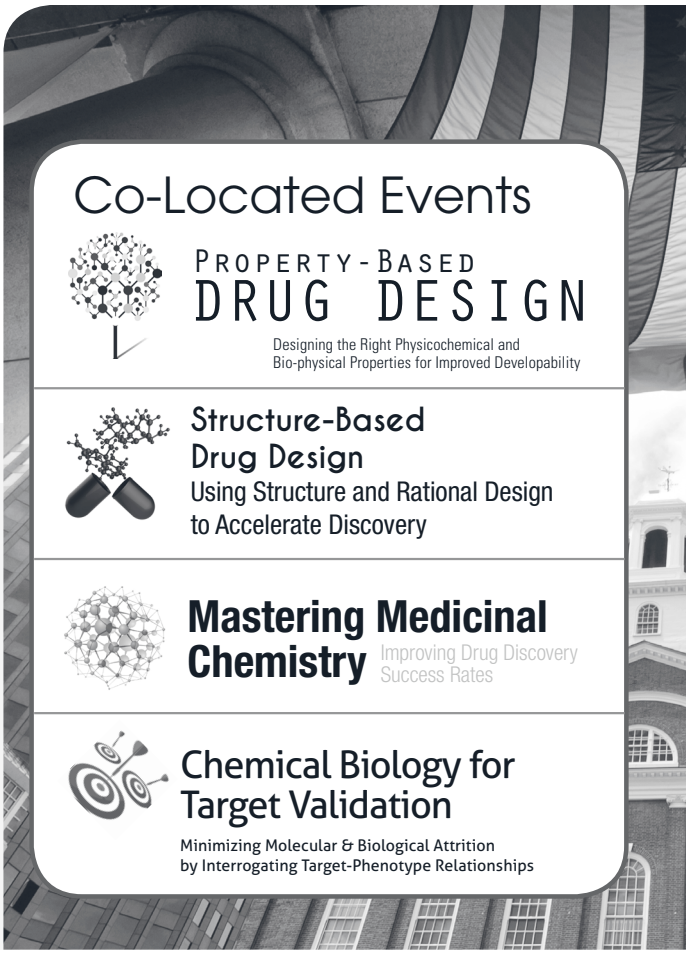
We understand that you have many choices when making your travel arrangements. Please understand that reserving your room in the CHI room block at the conference hotel allows you to take full advantage of the conference sessions, events and networking opportunities, and ensures that our staff will be available to help should you have any issues with your accommodations.



Preclinical Cancer Research: Models and Tools

13th Annual WPC World Pharma Congress

May 21-23, 2014
Westin Boston Waterfront, Boston, MA

Pricing and Registration Information

BEST VALUE! EVENT PRICING

Includes access to 2 conferences, excludes short courses

	Commercial	Academic, Government, Hospital-affiliated
Advance Registration Rate until May 16, 2014	$2,799	$1,249
Registrations After May 16, 2014 and on-site	$2,899	$1,299

SINGLE CONFERENCE PRICING

Includes access to 1 conference, excludes short courses

Advance Registration Rate until May 16, 2014	$1,799	$749
Registrations After May 16, 2014 and on-site	$1,899	$799

Program Selection: When registering please indicate the one conference you will attend:

May 21-22, 2014	May 22-23, 2014
T1 Tumor Models for Targeted Therapy	T6 Tumor Models for Cancer Immunotherapy
T2 Imaging in Oncology	T7 *In vitro* Tumor Models
T3 Preclinical Drug Safety	T8 Epigenetics Screening
T4 Formulation & Drug Delivery	T9 Efficient Process Chemistry
T5 Targeting Pain	

SHORT COURSE PRICING

Single Short Course	$699	$399
Two Short Courses	$999	$699
Three Short Courses	$1,199	$899

May 20, 2014	May 22, 2014 *(Dinner will be served)*
SC1 Animal Models of Pain: Progress and Challenges	SC6 Refining API Process Development for Efficiency (Dinner)
SC2 Introduction to Drug Metabolism and Its Role in Drug Toxicity	SC7 How To Best Utilize Organotypic 3D Cell Cultures Assays in Oncology (Dinner)
SC3 Nanotechnology for Enhancing Bioavailability of Poorly Soluble Drugs	SC8 Computational Modeling of Cancer Genomics (Dinner)
SC4 Metastatic Tumor Models: Technology and Applications (Dinner)	
SC5 Safety Testing for Biological Drugs and Vaccines (Dinner)	

CONFERENCE DISCOUNTS

Alumni Discount	20% Off
Drug Safety Executive Council (DSEC) Members	25% Off
Poster Discount	$50 Off

POSTER DISCOUNT ($50 Off) Poster abstracts are due by April 4, 2014 Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact **jring@healthtech.com**.

* CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

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If you are unable to attend but would like to purchase the World Pharma Congress 2014 CD for $750 (plus shipping), please visit WorldPharmaCongress.com. Massachusetts delivery will include sales tax.

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Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link.

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.

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

How to Register: **WorldPharmaCongress.com**

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Please use keycode **ONC F** when registering!