

13th Annual

WPC

World Pharma Congress

Tackling Translational Challenges

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

Register by
February 21, 2014
and Save
up to \$400!

May 21-22

- Tumor Models for Targeted Therapy
- Imaging in Oncology
- Preclinical Drug Safety
- Formulation & Drug Delivery
- Targeting Pain

May 22-23

- Tumor Models for Cancer Immunotherapy
- In vitro* Tumor Models
- Epigenetics Screening
- Efficient Process Chemistry

Conference Highlights

- 90+ presentations led by industry experts focusing on preclinical efforts targeted towards drug discovery/delivery, screening, safety and process chemistry
- 450+ International Attendees
- Five Pre-Conference Short Courses
- Expansive Exhibit Hall – 40+ Sponsors & Exhibitors
- Dedicated Poster Viewing, Roundtables and Panel Discussions

Keynote Speaker:



Catalyzing Translational Innovation

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

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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. <i>Director, National Center for Advancing Translational Sciences National Institutes of Health</i>				
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.

Tackling Translational Challenges

In recent years the World Pharma Congress has built its niche in effectively covering the latest preclinical strategies and technologies for driving better predictions early in the drug discovery process. This year the event will continue its coverage on novel preclinical models for tackling oncology and pain, while discussing ways to improve drug safety screening, formulations and drug delivery and process chemistry.

This year we intend to make **"Tackling Translational Challenges"** an underlying theme for all our presentations and discussions and solicit the participation of attendees and exhibitors involved in preclinical work to join forces in identifying what should be done EARLY to ensure success along the drug development pipeline. We invite all scientists- chemists, biologists, pharmacologists, toxicologists and formulation experts- to help turn this event into a collaborative forum where knowledge is shared, ideas exchanged and collaborations cemented. We hope you can join the World Pharma Congress community and help shape the future of preclinical work being done in the pharmaceutical/biotechnology industry.

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

WorldPharmaCongress.com/Tumor-Models

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 8:30-11:30 am

SC1 - Animal Models of Pain: Progress and Challenges

Instructor:

Jeffrey S. Mogil, Ph.D., E.P. Taylor Professor of Pain Studies, McGill University

Many are frustrated with the lack of translational progress in the pain field, in which huge gains in basic science knowledge obtained using animal models have not led to the development of many novel and clinically effective compounds. A careful reexamination of animal models of pain is therefore warranted. This course will describe the current implementation of animal models of pain, discuss a wide range of modulatory factors affecting data obtained within them, lay out the case for the replacement of current models by more sophisticated ones, and describe progress toward that goal.

Topics to be Covered:

- Classical models of acute, tonic and chronic pain
- Limitations of these classical models
- Refinement of classical models via a consideration of modulatory factors (sex, genetics, testing environment, social modulation)
- Development of new animal models (e.g., operant methods, spontaneous behaviors)

May 20, 2014 2:00-5:00 pm

SC2 - Introduction to Drug Metabolism and Its Role in Drug Toxicity

Instructor:

John Erve, Ph.D., D.A.B.T., Jerve Scientific Consulting, Inc.

Topics to be Covered:

- Basic concepts of drug metabolism
- Newer approaches to investigate *in vitro* and *in vivo* drug metabolism
- Biotransformation pathways
- Understanding the role of reactive metabolites in idiosyncratic drug toxicity
- Role of drug transporters in toxicity
- *In silico* tools to aid drug metabolism research

May 20, 2014 2:00-5:00 pm

SC3 - Nanotechnology for Enhancing Bioavailability of Poorly Soluble Drugs

Chair:

Shaukat Ali, Ph.D., Technical Support Manager, BASF Corp.

Instructors:

Navnit Shah, Ph.D., President & CSO, Kashiv Pharma

Lipa Shah, Ph.D., Principal Scientist, Chemical and Pharmaceutical Profiling, Novartis Institutes for BioMedical Research, Inc.

Michael Perlman, Ph.D., Senior Scientist II, Millennium Pharmaceuticals

Salin Gupta Patel, Ph.D., Associate Principal Scientist, Nanoparticles Technology Development Team Lead, Merck Research Labs

A significant number of new chemical entities (NCEs) are practically insoluble and thus, the industry is struggling to find solutions by adapting the non-conventional innovative and cost effective technologies in development of these molecules. This workshop will be aimed at understanding the significance of nanotechnology in formulation development and its role leading to enhance solubility and bioavailability of drug candidates.

Topics to be Covered:

- Amorphous dispersions and polymeric nanoparticulates
- Liquid dispersions, especially, lipid and surfactant based self emulsifying
- Nano-emulsifying systems (SEDDS/SNEDDS)
- Excipients' role in design of robust dispersive systems and maintaining supersaturation
- Effects of particle size on API stability and performance
- Factors influencing the bioavailability of dosages

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

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

Additional Instructors to be Announced

**Separate registration required*

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Short Courses*

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

SC5 - Safety Testing for Biological Drugs and Vaccines

Instructors:

Non-Clinical Clinical Safety Assessment Strategies of Traditional and Non-Traditional Bio-Pharmaceuticals

Joerg Bluemel, Ph.D., Director, Toxicology, Biologics Safety Assessment/Translational Sciences, MedImmune LLC

Considerations in the Design of Safety Studies for Biologics and Vaccines

Lawrence J. Thomas, Ph.D., DABT, Senior Director, Preclinical Research and Development, Celldex Therapeutics, Inc.

This course will provide information on the key differences in non-clinical safety assessment strategies between low molecular weight compounds and bio-pharmaceuticals, as well as between "traditional" (e.g.: monoclonal antibodies) and "advanced" biologics (e.g.: antibody-drug conjugates, bispecifics). Using case studies, the instructors will offer guidance on species selection, dose selection, assessing drug exposure and special endpoints. Regulatory guidelines and safety consideration for vaccines will be discussed as well.

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

SC6 - Refining API Process Development for Efficiency

Instructor:

Neal Anderson, Ph.D., President, Anderson's Process Solutions

This course is intended for both, chemists new to industrial process development, as well as those who would like an update on the latest advances in the field.

Topics to be Covered:

- **Safety considerations to enable process development.** Reactions that are highly exothermic or generate gases can be difficult to scale up safely, but these considerations and others can become driving forces. Some examples, such as cryogenic alkylations and Curtius rearrangements, will be discussed.
- **Tips to anticipate and avoid scale-up problems.** The laboratory is the first place to avoid difficulties that would arise from future scale-up, such as the generation of impurities from extended processing. Some "war stories" from scale-ups will also be discussed.
- **Approaches for controlling genotoxins in APIs.** Functional groups can flag a compound as a potential genotoxic impurity. The ACE approach (Avoid, Control, Eliminate) can be used to address the problem of genotoxic impurities.

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

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

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JSR Life Sciences



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.

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

SC8 - Computational Modeling of Cancer Genomics

Instructors:

Franziska Michor, Ph.D., Associate Professor, Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute, Department of Biostatistics, Harvard School of Public Health

Additional Instructors to be Announced

Recent advances in high-throughput profiling of cancer genomes have enabled the generation of an unprecedented amount of data. The analysis of this data requires the development of novel computational and mathematical modeling approaches. In this workshop, we will discuss state-of-the art modeling methods.

Topics to be Covered:

- Mathematical modeling of cancer initiation and progression
- Treatment response and resistance
- Evolution of genomic aberrations

**Separate registration required*

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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

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: The Application of Primary Tumorgraft Models of B-Raf Mutated Melanoma and Colorectal Cancer to Support the Clinical Development of a CEP-32496, a Potent and Selective Dual Orally-Active Inhibitor of B-Raf and EGFR

Bruce Ruggeri, Ph.D., Senior Director, Oncology Discovery Research, Global R&D, Teva Pharmaceuticals, Inc

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

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

A patient-derived xenograft (Tumorigraft) platform has been established where patient tumors are engrafted to form mouse-avatar Tumorigraft 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

10:20 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

Thomas Metcalfe, Managing Director, 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.

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oncotest
patient derived xenograft

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 Efficacy Axl-Inhibitor on PDX Model of Bladder Cancer (PDX-BL0293)

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

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.

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MOLECULAR RESPONSE

1:20 LUNCHEON PRESENTATION II (Sponsorship Opportunity Available)

1:50 Session Break

MOLECULAR IMAGING BIOMARKERS AND END POINTS

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

2:00 Chairperson's Remarks

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



Tumor Models to Guide Targeted Cancer Therapy and Drug Development

Patient-Derived Xenograft Models and Beyond

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

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.

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4:05 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 (see [page 2](#) 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

CHALLENGING TUMOR HETEROGENEITY

8:35 Chairperson's Remarks

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

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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**

10:45 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.

11:15 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.

11:45 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.

12:15 pm LUNCHEON PRESENTATION (Sponsorship Opportunity Available)

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



Tumor Models for Preclinical Assessment of Cancer Immunotherapy

Applying Novel Immunocompetent Models

THURSDAY, MAY 22

9:30 am Registration

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12:15 pm LUNCHEON PRESENTATION (Sponsorship Opportunity Available)

TOP PHARMA STRATEGIES

12:50 Chairperson's Opening Remarks

1:00 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.

1:30 Choosing the Right Syngeneic Model for Immunotherapy: The "Syngeneic" 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.

2:00 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 Modeling Human Cancer: A Multifaceted Approach to Pre-Clinical Development

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

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2:45 Sponsored Presentation (Opportunity Available)

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

MODELING FOR CELL IMMUNOTHERAPY

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 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.

4:45 Sponsored Presentation

Leon Hall, Ph.D., Associate Director, Preclinical Models, Taconic

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5:15 ErbB-Targeted CART 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 CART cells by intratumoral injection.

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

Panelists: Speakers of the Session

6:15 Close of Day



Tumor Models for Preclinical Assessment of Cancer Immunotherapy

Applying Novel Immunocompetent Models

FRIDAY, MAY 23

7:30 am Interactive Breakout Discussion Groups with Continental Breakfast

FOSTERING TRANSLATIONAL APPROACHES

8:35 Chairperson's Remarks

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

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

A major area of research interest lies in developing cellular immunotherapeutic approaches that may elicit a tumor specific immune response. Critical aspects to consider in designing a tumor vaccine include effectively presenting tumor-associated antigens in the context of necessary co-stimulation, overcoming the immunosuppressive milieu that is characteristic of patients with malignancy, preventing the re-establishment of tolerance, and targeting tumor heterogeneity.

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 CART cells will be discussed.

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

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.

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

12:30 Session Break

OVERCOMING LIMITATIONS OF CONVENTIONAL MODELS

12:55 Chairperson's Opening Remarks

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

Robert Tighe, Associate Director, ImmunoOncology, ImmunoPharmacology, EMD Serono

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



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

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 mm 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 FcεRI 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 Sponsored Presentation

Speaker to be Announced

11:35 Sponsored Presentation (Opportunity Available)

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, Centyrins 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 Remarks

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.

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Imaging in Preclinical and First in Human Clinical Studies in Oncology

Mastering Translational Approach

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 Sponsored Presentations (Opportunities Available)

4:05 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 (see [page 2](#) 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 Remarks

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 poised 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**

10:45 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.

11:15 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.

11:45 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.

12:15 pm LUNCHEON PRESENTATION (Sponsorship Opportunity Available)

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

“ Good opportunity to interact with industry. ”

- Graduate Student, Texas A&M University



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**

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12:15 pm LUNCHEON PRESENTATION (Sponsorship Opportunity Available)

12:50 pm Chairperson's Opening Remarks

1:00 FEATURED PRESENTATION: 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.

1:30 *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.

2:00 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.

2:30 Sponsored Presentations (Opportunities Available)

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

SCREENING FOR EFFICACY AND RESISTANCE

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 Sponsored Presentations (Opportunities Available)

5:15 A Novel Approach to Overcome Oncogenic Addiction via 3D Model Systems

Hakim Djaballah, Ph.D., Director, HTS Core Facility, Molecular Pharmacology and Chemistry Program, Memorial Sloan Kettering Cancer Center

Classical drug discovery approaches for oncology have relied heavily on killing cancer cells; they have worked very well in some cases but not as good as predicted in others with many failures reported the clinic. We have taken an opportunistic approach looking for small molecules which would selectively revert the addictive state of the cancer cell yielding a vulnerable phenotype. I will describe the approach and discuss our findings thus far with the ultimate goal of progression to the clinical.

5:30 PANEL DISCUSSION: Increasing Predictability of *in vitro* Tumor Models

Panelists: Speakers of the Day

6:15 Close of Day



Novel *in vitro* Models of Cancer

Overcoming Challenges of *ex vivo* Tumor Modeling

FRIDAY, MAY 23

7:30 am Interactive Breakout Discussion Groups with Continental Breakfast

ADVANCING 3D TISSUE MODELS

8:35 Chairperson's Remarks

8:45 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.

9:15 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.

9:45 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- κ B 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- κ B pathway and SOX9 play a crucial role in CSCs. Additionally, we found the NF- κ B subunit p65 positively regulates SOX9 expression by binding to its promoter directly. Thus, our work establishes a link between the NF- κ B pathway and epigenetic regulation of SOX9 in pancreatic CSCs.

2:30 Close of Conference

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Functional Screening for Drug Safety Testing

New Models, Markers and Tools for Early Safety Predictions

WEDNESDAY, MAY 21

7:00 am Registration and Morning Coffee

IN VITRO ASSAYS FOR SAFETY TESTING

8:00 Chairperson's Opening Remarks

8:05 *In vitro* Cardiac Safety: Current Issues and Emerging Challenges

Bernard Fermini, Ph.D., Associate Research Fellow, Global Safety Pharmacology, Pfizer Global Research & Development

Following the adoption of the S7B guidance document (2005), pharma has invested significant resources in establishing strategies to identify compounds that may cause prolongation of the QT interval. However, with increasing diversity of the portfolio, current strategies often fail to address emerging non-QT related issues, such as hypertrophy and heart failure. In this presentation we review current and future strategies to address these safety issues.

8:35 Drug Cardiotoxicity Screening by Microelectrode Arrays

Sonia Grego, Ph.D., Senior Research Scientist, Research Triangle Institute (RTI) International

Driven by rapid advancement in stem cell technologies and measurement techniques, *in vitro* cardiotoxicity assays are under intense development. We have carried out functional screenings of iPS cardiomyocytes by a multiwell microelectrode array (MEA) system. Results will be presented of a customized analysis of the rich dataset produced by MEA for reliable extraction of multiple drug response parameters.



9:05 FEATURED PRESENTATION: Patient-Specific iPSCs for Cardiac Safety Assessments

Joseph Wu, M.D., Ph.D., Director, Stanford Cardiovascular Institute; Professor, Department of Medicine and Radiology, Stanford School of Medicine

Cardiac toxicity is a side effect of many pharmaceutical compounds and is a leading cause for drug withdrawal from market because of safety concerns. Current preclinical methods to measure cardiotoxicity are inefficient and rely on genetically altered cell lines, which do not accurately resemble human heart cells. Recent technological advancement has enabled the generation of patient-specific human induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) *in vitro*. The iPSC-CMs generated in this fashion carry all the genetic information from the individuals from whom they are derived. Here I will discuss the generation of iPSC-CMs from patients with cardiovascular diseases. I will also give examples showing how iPSC-CMs can detect drug-induced cardiac toxicity more accurately than the conventional hERG testing used by most pharmaceutical companies. I will also discuss the potential applications of iPSC-CMs for drug discovery.

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

10:20 FEATURED PRESENTATION: Microscale Engineered Liver Tissue for Modeling Human Disease

Sangeeta Bhatia M.D., Ph.D., John J. and Dorothy Wilson Professor of Health Sciences and Technology/Institute for Medical Engineering and Science, and Professor, Electrical Engineering and Computer Science, Massachusetts Institute of Technology

10:50 Contribution of BSEP Inhibition and Mitochondrial Toxicity to Drug Induced Liver Injury - New Assays, New Insights

Yvonne Will, Ph.D., Associate Research Fellow, Compound Safety Prediction, Pfizer Global Research & Development

In this talk I will discuss vesicle-based and cell-based assays for the assessment of BSEP inhibition and the learning's we have had regarding species specificity. In addition, I will speak to the contribution of mitochondrial toxicity to DILI and will provide proof that the dual effect on BSEP and mitochondria will correlate with severe liver injury, whereas BSEP inhibition alone does not lead to liver injury *per se*.

11:20 Multiple Ion Channel Effects (MICE) and the New Era of Safety Pharmacology

Arthur "Buzz" M. Brown, Ph.D., Executive Chairman, CSO, ChanTest Corp.

Sponsored by



EXPLORING RELEVANT *IN VIVO* MODELS

11:50 Systems Level Approaches to Organ Specific Toxicities in Zebrafish

Calum MacRae, M.D., Ph.D., Physician-Scientist, Department of Medicine, Cardiovascular Research Center, Brigham and Women's Hospital; Associate Professor, Harvard Medical School

Many drug effects are a result of complex phenomena that are not recapitulated even in the most sophisticated *in vitro* systems. Using the larval zebrafish, it is possible to model much of drug efficacy and toxicity in a native context and to do this at high throughput. We have exploited a range of assay approaches to move towards a 'TOX' reporter zebrafish line capable of the interrogation of core organ specific toxicities in a manner that ultimately may allow efficacy and toxicity to be balanced in the early phases of drug discovery.

12:20 pm Neurotoxicity and Cardiotoxicity in Zebrafish Embryos: Phenotype-Based Mechanistic Studies for Drug Safety Testing

Jyotshna Kanungo, Ph.D., Senior Investigator, Lead Scientist, Zebrafish HTS Laboratory, National Center for Toxicological Research, U.S. Food and Drug Administration

Manifestations of drug-drug interactions arising from the use of combination drugs could be monitored *in vivo* in zebrafish. Live monitoring of multiple organ/tissue toxicities is an advantage since embryos/larvae express key enzymes involved in drug metabolism including the cytochrome P450 family. Our studies show that the drug effects (alone or in combination with other drugs) in these embryos are similar to those in humans and therefore, provide an excellent platform for mechanistic studies for translatability and therapeutic intervention purposes.

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

1:30 Session Break

EXPLORING RELEVANT *IN VIVO* MODELS

2:00 Chairperson's Remarks

2:05 Application of Knockout Animal Models for Toxicological Safety Assessments

Andrew Olaharski, Ph.D., Associate Director, Toxicology, Agios Pharmaceuticals

Knockout animals are an underutilized model for assessing the safety of pharmacological targets. Despite the inherent caveats, valuable toxicological information can be gleaned from their study. Two case studies exhibiting their utility will be presented: Firstly, a host-resistance study of LRRK2 knockout rats to assess the potential immunological liabilities associated with LRRK2 inhibition and, secondly, the evaluation of selective PLK2 inhibitors in PLK2 knockout mice to assess the impact of pharmacological inhibition on causing genotoxicity.

2:35 Utilizing Mouse Population Models to Understand and Predict Drug Toxicity in Humans

Merrie Mosedale, Ph.D., Research Scientist, Hamner-UNC Institute for Drug Safety Sciences, The Hamner Institutes for Health Sciences

Failure to accurately model clinical drug safety liabilities is, in part, due to a lack of genetic diversity present in traditional nonclinical models. Previous studies have demonstrated the ability of genetically defined mouse populations to more accurately model drug toxicity responses in humans. This presentation will describe recent findings utilizing a Mouse Diversity Panel to investigate mechanisms of drug-induced liver injury and identify risk factors that underlie drug toxicity susceptibility.



Functional Screening for Drug Safety Testing

New Models, Markers and Tools for Early Safety Predictions

3:05 *In vivo* Safety Assessment of Novel Antibody-Drug Conjugates

Joerg Bluemel, Ph.D., Director, Toxicology, Biologics Safety Assessment/Translational Sciences, MedImmune LLC

Antibody-drug conjugates (ADC) are complex molecules composed of a potent cytotoxic low molecular weight drug attached by a chemical linker to an antibody targeting a tumor-associated antigen. The combination of small chemical and large molecule characteristics represent a unique challenge for the design and execution of the nonclinical safety strategy. The presentation will highlight recent experience and challenges for the *in vivo* safety assessment of this new class of highly potent biopharmaceutical drugs.

3:35 Sponsored Presentations (Opportunities Available)

4:05 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 (see [page 2](#) for details)

6:00 Networking 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

OVERCOMING TRANSLATIONAL CHALLENGES

8:35 Chairperson's Remarks

8:45 A Non-Human Primate Model for Investigating Risk of Orthostatic Hypotension – Preclinical Correlate to a Clinical Test

Siddhartha Bhatt, Ph.D., Senior Scientist, Global Safety Pharmacology, Drug Safety Research & Development, Pfizer, Inc.

Drug-induced orthostatic hypotension (OH) is an important clinical concern and could present as an unexpected hurdle for new drug molecules. Thus far, there is a relative paucity of preclinical models for investigating the risk of OH. Herein, we describe development of a preclinical model for assessment of OH using radiotelemetry-transmitter implanted non human primates. The model resembles the clinical test for diagnosing OH and was validated using ganglionic and alpha adrenergic blockers.

9:15 Development of the Liver Toxicity Knowledge Base (LTKB) for Improving the Understanding and Prediction of Drug-Induced Liver Injury (DILI)

Minjun Chen, Ph.D., Principal Investigator, Division of Bioinformatics and Biostatistics, National Center for Toxicological Research, U.S. Food and Drug Administration

The Liver Toxicity Knowledge Base was developed by the FDA's NCTR with the specific aim of improving our understanding and prediction of DILI via integrated analysis of diverse sources of drug-elicited data to achieve an enhanced DILI prediction. In this presentation, we will introduce the current efforts in the LTKB project, including the DILI classifications for drugs based on the FDA-approved drug label and the development of predictive models such as the "Rule-of-Two" and QSAR models.

9:45 Sponsored Presentation (Opportunity Available)

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

10:45 Translational Qualification of Renal Biomarkers

David Brott, Ph.D., Safety Scientist, Enabling Safety Sciences in Global Regulatory Affairs, Patient Safety and Quality Assurance (GRAPS), AstraZeneca Pharmaceuticals

Several preclinical urinary biomarkers have been qualified and accepted by the health authorities (FDA, EMA and PMDA) for detecting drug-induced kidney injury during preclinical toxicological testing. Validated human assays for many of these biomarkers have become commercially available and this study was designed to characterize some of the novel clinical renal biomarkers. The talk will present current qualification/characterization of clinical renal biomarkers in healthy volunteers as well as type 1 and 2 diabetics with comparison to renal biomarker changes observed in a rat drug-induced type 1 diabetic model. In addition, data comparison of single analyte vs. multiplex kidney biomarker assays will be presented.

11:15 Organs-on-Chips for Predicting Drug Toxicity and Efficacy

Danilo A. Tagle, Ph.D., Associate Director for Special Initiatives, National Center for Advancing Translational Sciences (NCATS), NIH

Organs-on-chips are bio-engineered microdevices that represent functional units of human organs such as, the lung, liver and heart, modeling both cell architecture and physiology. This unique platform could ensure that safe and effective therapeutics are identified sooner, and ineffective or toxic ones are rejected early in the development process. To accomplish this goal, the NIH has partnered with DARPA and FDA to improve the process for predicting whether drugs will be safe in humans.

11:45 Close of Conference

Suggested Event Package:

May 20

Pre-Conference Short Course*

Introduction to Drug Metabolism and Its Role in Drug Toxicity
Safety Testing for Biological Drugs and Vaccines
(See [page 3](#) and [4](#) for details.)

May 21-22

Functional Screening for Drug Safety Testing Conference

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



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

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 Cytoomics; 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 Sponsored Presentations (Opportunities Available)

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

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

4:15 Interrogating the Bromodomain Family through Chemical Biology

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

4:45 Sponsored Presentations (Opportunities Available)

5:15 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.

5:45 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.

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 Remarks



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.

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.

Inaugural



New Tools for Functional Epigenetics Screening

Biochemical and Cell-based Assays for Validating Targets and Leads

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

MODELS FOR EPIGENETIC DRUG DISCOVERY

10:55 Chairperson's 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 Luncheon Presentation (Sponsorship Opportunity Available) or **Lunch on Your Own**

12:30 Session Break

MODELS FOR EPIGENETIC DRUG DISCOVERY CONT'D

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

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; 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-κB pathway and SOX9 play a crucial role in CSCs. Additionally, we found the NF-κB subunit p65 positively regulates SOX9 expression by binding to its promoter directly. Thus, our work establishes a link between the NF-κB pathway and epigenetic regulation of SOX9 in pancreatic CSCs.

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 [page 4](#) for details.)

May 22-23

New Tools for Functional Epigenetics Screening Conference

* *Separate registration required*

“ State of art developments on sciences, great speakers. ”

- Research Scientist, Hamner Institutes for Health Sciences



Formulation and Drug Delivery

Strategies for Enhancing Solubility, Bioavailability and Faster Product Design and Development

WEDNESDAY, MAY 21

7:00 am Registration and Morning Coffee

IMPROVING BIOAVAILABILITY WITH PHARMACEUTICS & FORMULATION STRATEGIES

8:00 Chairperson's Opening Remarks



8:05 FEATURED PRESENTATION: Solithromycin, a Fourth Generation Macrolide, the First Fluoroketolide in Development for Use in Oral and Intravenous Dosing Formulations for Adult and Pediatric Use

Prabhavathi Fernandes, Ph.D., President and CEO, Cempra, Inc.

In the last two decades there has been a focus on developing i.v. antibiotics. Hospitalization is expensive and exposes patients to hospital acquired infections. In many cases, a potent oral antibiotic can allow a patient to be treated as an outpatient. Solithromycin is in Phase 3 clinical development in oral and i.v. dosing formulations. If approved, solithromycin would be the first antibiotic in a generation to be available in oral capsule and suspension and as i.v. formulation to be able to treat all age groups, including young children.

8:35 Impact of BDDCS Compound Classification on Oral Absorption and the Need for Influx Intestinal Transporter: Statins/ACE Inhibitors as a Case Study

Ayman El-Kattan, Ph.D., Associate Research Fellow, Pharmacokinetic Dynamics & Metabolism, Pfizer, Inc.

Some statins/ACE inhibitors have low intestinal permeability with usually poor fraction of absorption ($f_a < 80\%$). Based on BDDCS classification, these compounds are class III and IV. In this presentation, we discuss: 1) The influx intestinal transporters that facilitate the absorption of statins/ACEi including review of structure, SAR/clinical relevance; 2) The impact of food and pharmacogenomics on statins/ACEi absorption; and 3) The use of prodrug as an effective approach to overcome poor oral absorption.

9:05 Simulating the Gastro-Intestinal Tract to Understand Drug Behavior – How Close Do We Need to Go?

Anette Müllertz, Ph.D., Associate Professor, Pharmaceutical Design and Drug Delivery, Department of Pharmacy, University of Copenhagen

Depending on the drug and the dosage form in question, different conditions or events encountered during transit of the gastro-intestinal tract will be determining the absorption of the drug. Therefore one should carefully consider how to develop an *in vitro* assay that will predict the behavior of specific dosage forms. In some cases simulations of the stomach will be of utmost importance, whereas this is not important in other cases. Likewise the digestion processes have to be taken into account for some dosages forms. These factors should be considered when developing an *in vitro* model for development of oral drug products.

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

PREFORMULATION FOR RISK ASSESSMENT & MITIGATION

10:20 Risk-Based Approach to Exploratory Drug Product Development

Madhushree Gokhale, Ph.D., Senior Research Investigator, Drug Product Science & Technology, Bristol-Myers Squibb Co.

An integrated risk-based approach to understand material (form) risks, chemical stability risks, delivery risks and processing risks during early stages of drug product development not only provide a robust design space but also lead to focused drug product development and risk mitigation plans. This talk will highlight use of high-throughput screening techniques, *in vitro*, *in silico*, *in vivo* tools and mini-piloting tools, as well as case studies to showcase integrated risk-based approach in early drug product development.

10:50 What You See May NOT be What You Get – Why Dissolution Testing May be an Unreliable Predictor of *in vivo* Success

Robert A. Bellantone, Ph.D., Associate Professor, Division of Pharmaceutical Sciences, Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Long Island University; President, Physical Pharmaceutical LLC

For poorly soluble drugs and new oral drug delivery strategies, compendial *in vitro* dissolution methods may not provide data relevant for predicting whether a formulation will work successfully *in vivo*. This talk will discuss dissolution-absorption and excipient-solubility relationships, which *in vitro* data are most relevant for different situations, and why existing methods may not provide the needed data. In addition, some new methods to obtain relevant *in vitro* data will be discussed.

11:20 Disadvantaged Drugs Turned into Super APIs with Expanded Clinical Utility

Gabor Heltovics, CEO, DRGT

The continuous flow Super-API technology delivers significant pharmacological improvements for compounds where earlier t_{max} , higher C_{max} and higher exposure can lead to clinically meaningful benefit. Disadvantageous food effect can also be reduced or eliminated by the technology due to the novel structure of the developed Super-APIs.

Sponsored by



11:35 Sponsored Presentation (Opportunity Available)

11:50 How HIGH Can You Get? – The Use of *in vitro* Data to Reduce Animal Experiments

Geeti Gangal, Ph.D., Principal Scientist, Chemical and Pharmaceutical Profiling, Novartis Institutes for Biomedical Research, Inc.

Cocrystals, nanosuspension, microemulsion and amorphous Solid dispersion are the various techniques that are commonly utilized to manage solubility issues of the poorly water soluble drugs. *In vitro* tools like pBDDCS, Q-plus and Gastroplus have been used in the literature for the compound classification and assessing the risk associated in the development. However, together these *in vitro* tools can be used as powerful guidance to pick the best formulation that would work for your compound and can lead to reducing animal experiments.

12:20 pm Is it Crystal Clear? Stability and Performance Prediction for Amorphous Pharmaceuticals

Sunny P. Bhardwaj, Ph.D., Senior Scientist, Basic Pharmaceutical Sciences, Merck & Co.

Majority of new drug candidates under development are poorly water-soluble. The amorphous state is of considerable interest since it confers higher apparent solubility and faster dissolution than its crystalline counterpart. However, being the thermodynamically unstable form, it runs the risk of crystallization leading to the loss of solubility advantage. In this presentation, we will discuss different approaches to predict the solid-state and solution state physical stability of the amorphous state with case studies.

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

1:30 Session Break

ENABLING TECHNOLOGIES FOR ENHANCING SOLUBILITY AND DELIVERY

2:00 Chairperson's Remarks

2:05 Novel Approach of IV Formulation Development of Solithromycin, a Fourth Generation Macrolide Antibiotic

Sara Wu, Ph.D., Director, Product Development, Cempra, Inc.

Solithromycin is a fourth generation macrolide, the first fluoroketolide antibiotic in Phase III clinical trials for Community Acquired Bacterial Pneumonia. The challenges faced during the development of the intravenous formulation of solithromycin will be presented. Optimization of the intravenous formulation to achieve the dosing goal while providing acceptable solubility and local site tolerance relied on an *in vitro* dynamic precipitation model, rabbit ear-vein irritation model and the Phase I clinical results on local tolerance.

2:35 Targeted Delivery of Prolyl Hydroxylase Inhibitors as a Therapeutic Strategy for Treatment of Ulcerative Colitis

Murtaza Tambuwala, Ph.D., Lecturer in Pharmacy, School of Pharmacy and Pharmaceutical Sciences, University of Ulster

This talk will highlight a new strategy for effective management and treatment of ulcerative colitis using targeted drug delivery technology which will allow the use of low dose thus reducing drug related side effects and increase in drug efficacy.



Formulation and Drug Delivery

Strategies for Enhancing Solubility, Bioavailability and Faster Product Design and Development

This research involves the use of novel drug delivery system used to deliver drugs locally to the colon. Using transgenic mice we have shown for the first time that genetic loss of Prolyl hydroxylase-1 is protective in colitis, via epithelial barrier function enhancement.

3:05 Nano Suspension: Why, How & the “Golden Syringe”

Lieyu (Richard) Hu, Ph.D., Scientist, Pharmaceutical Sciences, Cubist Pharmaceuticals, Inc.

A major challenge hindering the development of new chemical entities is low aqueous solubility, limiting formulation and delivery options, in particular intravenous administration. Nanosuspensions, which consist of pure crystalline drug particles stabilized with surface modifier(s) in aqueous media, offer an attractive means of addressing such development challenges. Nanosuspensions can be tailored to enable drug release in a controlled fashion to meet the needs of patients. This talk describes the preparation, characterization, and applications of such nanosuspensions.

3:35 Sponsored Presentations (Opportunities Available)

4:05 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 (see [page 2](#) 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

Topic 1: Why Can't We Bring More Solid Dispersions to Market?

Robert A. Bellantone, Ph.D., Associate Professor, Division of Pharmaceutical Sciences, Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Long Island University; President, Physical Pharmaceutical LLC

- We have been studying solid dispersions for approximately five decades, why do we still not know how to control them?
- What do we need to learn before we can make these systems work for more drugs?
- Is there a knowledge gap between the solid state stability and dissolution performance?

FORMULATION & PROCESS DEVELOPMENT STRATEGIES

8:35 Chairperson's Remarks

8:45 Formulation and Process Strategies for Preventing Form Conversion in Wet Granulation

Ajit S. Narang, Ph.D., Senior Research Investigator, Drug Product Science & Technology, Bristol-Myers Squibb Co.

Form conversions that are associated with hydration state change may be difficult to control during drug product processing and storage. In this presentation, a case study discussing the thermodynamic driver for form conversion would be presented. In addition, formulation and process strategies, such as the use of a hydrophilic polymer and control of processing conditions, to mitigate form conversion during processing would be discussed with a case study.

9:15 Optimizing Granulating Fluid Levels in High Shear Wet Granulation Using Wet Mass Rheology

Rahul R. Gandhi, Ph.D., Principal Scientist, Process Engineering Formulations, Dr. Reddys Laboratories Ltd.

This work demonstrates the use of wet mass rheology to optimize granulating fluid level (GFL) during high shear wet granulation (HSWG) of a formulation containing 90% API. Rheology is correlated with compactibility of final blends and dissolution rates of the tablet. This work is important to formulations with high API content that demonstrate

lot-to-lot variability in material attributes. The use of wet mass rheology to optimize granulating fluid levels for processability and product performance is demonstrated.

9:45 Sponsored Presentation (Opportunity Available)

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



10:45 FEATURED PRESENTATION: Cohesion Reduction of Fine Pharmaceutical Powders via Surface Modification

Rajesh N. Davé, Ph.D., Distinguished Professor of Chemical, Biological and Pharmaceutical Engineering; Site Director, NSF-ERC on Structured Organic Particulate Systems, New Jersey Institute of Technology

Fine powders due to high cohesion pose great challenge to pharmaceutical industry because of problems such as, agglomeration, poor flowability, electrostatic charging and low bulk density. Dry coating based surface modification as a predictive, model-based approach is presented to mitigate these problems, leading to the improvements in flow, fluidization, dispersion, and bulk density. A bulk property based 2-D phase-map is also proposed to help make manufacturing decisions regarding the formulation strategy for solid pharmaceutical dosages.

11:15 Optimizing Physical Properties by Forming Co-Crystals for Pharmaceutical Development

Dedong Wu, Ph.D., Senior Scientist, Pharmaceutical Development, AstraZeneca

The presentation will introduce pharmaceutical cocrystal approach and discuss opportunities and challenges of cocrystal applications in drug development. Cases studies from on-going projects will demonstrate how to use cocrystals to optimize important physical properties of drug candidates, including solubility, physical stability and solid-state property (e.g. melting point), thus enhancing drug developability in terms of quality, cost and time.

11:45 Luncheon Presentation (Sponsorship Opportunity Available) or Lunch on Your Own

FORMULATION/PROCESS CHEMISTRY SHARED PRESENTATION

12:50 pm Chairperson's Opening Remarks

1:00 Bridging Drug Substance and Drug Product Development: The Role of Solid State Chemistry in an API Process R&D Organization

Shuang Chen, Ph.D., Senior Scientist, Process R&D, AbbVie, Inc.

This presentation provides an overview on the important role solid state chemistry plays throughout the development of drug candidates. Case studies are presented to highlight some of the benefits of having a dedicated solid state chemistry group within an API organization that effectively bridges between API and DP developments resulting in robust processes, manufacturing efficiencies, and improved timelines.

1:30 Close of Conference

Suggested Event Package:

May 20

Pre-Conference Short Course*

Nanotechnology for Enhancing Bioavailability of Poorly Soluble Drugs (See [page 3](#) for details)

May 21-22

Formulation and Drug Delivery Conference

May 22

Recommended Dinner Short Course* (Dinner will be served)

Current Trends in Crystallization and Polymorphism: Experiment and Prediction (Part of Property-Based Drug Design Conference)

May 22-23

Efficient Process Chemistry Conference*

Property-Based Drug Design Conference* (See [page 26](#) for details)

*Separate registration required



Efficient Process Chemistry

Successes and Challenges in API Development

THURSDAY, MAY 22

11:00 am Registration

FORMULATIONS/PROCESS CHEMISTRY SHARED PRESENTATION

11:15 Optimizing Physical Properties by Forming Co-Crystals for Pharmaceutical Development

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11:45 Luncheon Presentation (Sponsorship Opportunity Available) or Lunch on Your Own

MULTI-DISCIPLINE PROCESS R&D

12:50 pm Chairperson's Opening Remarks

Neelakandha S. Mani, Ph.D., Scientific Director, & Fellow, Discovery Sciences, J&J PRD

1:00 Bridging Drug Substance and Drug Product Development: the Role of Solid State Chemistry in an API Process R&D Organization

Shuang Chen, Ph.D., Senior Scientist, Process R&D, AbbVie, Inc.

This presentation provides an overview on the important role solid state chemistry plays throughout the development of drug candidates. Case studies are presented to highlight some of the benefits of having a dedicated solid state chemistry group within an API organization that effectively bridges between API and DP developments resulting in robust processes, manufacturing efficiencies, and improved timelines.

1:30 Investigative and Engineering Approaches in Chemical Process Development

Apurva Chaudhary, Ph.D., Principal Fellow, Project Leader, Chemical Development, Novartis US

Enhanced process understanding based on scale-up experiences and engineering approaches have been used to understand the mechanisms of reactions and then develop new large scale processes by minimizing by-products and enhancing yields.

2:00 Incorporating Continuous Flow Technology in Exploratory Process Development

Bryan Li, Ph.D., Associate Research Fellow, Chemical R&D, Pfizer Pharmaceutical Science

Continuous flow technology offers many advantages over batch methods, including precise control of stoichiometry, reaction time and temperature, high reproducibility, and often better reaction profile. While flow chemistry has been used widely in the fine chemicals arena, it has not been widely adopted in the pharmaceutical industry, especially in the early development stage. This presentation will discuss efforts and examples how flow technology is implemented in Pfizer's exploratory development portfolio.

2:30 Managing and Controlling the Life Cycle of Impurities in Drug Development

Ryan Sasaki, Director, Global Strategy, ACD/Labs

Based on scale-up priorities (cost-effectiveness, safety, practicality, etc.), the synthetic route of a drug will be altered, changed, and optimized throughout the drug development cycle. Managing the life cycle of this process, the fate of relevant impurities, along with all the associated data is a major challenge. This presentation will highlight a novel approach for Impurity Resolution Management to help better manage process knowledge.

Sponsored by



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

THINKING AHEAD IN ROUTE DEVELOPMENT

3:45 Organo-Catalysis for Industrial Set Up: Development of a Green, Cost-Efficient Process for the Manufacture of (S)-Pregabalin

Mauro Adamo, Ph.D., Professor of Organic and Medicinal Chemistry, Centre for Synthesis of Chemical Biology (CSCB), Royal College of Surgeons in Ireland

This talk deals with the development of a new process for the manufacture of (S)-Pregabalin. The presentation will highlight the crucial elements of synthetic planning adopted and will provide an example of process development in terms of cost efficiency and E factor. We show that it is possible to redesign the synthesis of a large volume API using only cheap, readily available and recyclable catalysts that can be prepared from natural sources.

4:15 Practical Asymmetric Syntheses of Challenging Drug Candidates

Joerg Deerberg, Ph.D., Senior Research Investigator, Chemical Development, Bristol-Myers Squibb Co.

The manufacture of Active Pharmaceutical Ingredients (APIs) of increasing structural complexity, particularly those possessing multiple centers of asymmetry, requires practical chemical tools capable of sustaining the rigors of efficiency, robustness, and isomeric purity control. This presentation will summarize recent efforts at Bristol-Myers Squibb on a series of challenging drug molecules, each of which incorporates the above design principles, resulting in concise bulk syntheses with a high degree of efficiency and stereo control.

4:45 Sponsored Presentations (Opportunities Available)

5:15 Exploring and Optimizing Cost-Effective Route toward DPP-IV Inhibitor Compounds

Nhut Diep, Ph.D., Principal Scientist, Chemical Development, Forest Laboratories

This presentation describes the efforts around optimization methods for preparing DPP-IV inhibitor compounds. We will illustrate the extensive exploration synthetic strategies that were developed for cost-effective, novel streamline process, temporary protection-deprotection sequence, and scalable process toward Dutogliptin. Efforts to identify a scalable process led to the discovery of several useful transformations, including the asymmetric lithiation-boronation of the Boc-pyrrolidine that provided a single compound; the development of a streamline-telescope coupling reaction and workup which led to a robust crystallization/purification method.

5:45 Staying Off the Critical Path: Delivery of Pre-IND/Phase I API Supplies

Scott Duncan, Ph.D., Senior Staff Scientist, Chemical Development, Alkermes, Inc.

The first case study will illustrate an approach in which aggressive timelines were met while balancing the long term considerations of the non clinical program. The second case study will describe an approach to mitigate risk scaling up an "undeveloped" process to deliver material for IND enabling non clinical studies and then to deliver Phase I clinical supplies in the face of a "morphing" clinical program.

6:15 Close of Day



Efficient Process Chemistry

Successes and Challenges in API Development

FRIDAY, MAY 23

7:30 am Interactive Breakout Discussion Groups with Continental Breakfast

PROCESS DEVELOPMENT AND SCALE-UP CONSIDERATIONS

8:35 Chairperson's Remarks

Neal Anderson, Ph.D., President, Anderson Process Solutions



8:45 FEATURED PRESENTATION: Telaprevir Route Development Retrospective

Gerald Joseph Tanoury, Ph.D., Senior Scientific Fellow, Process Chemistry, Vertex Pharmaceuticals

Telaprevir is a protease inhibitor approved for the treatment of Hepatitis C. This talk will highlight the efforts toward developing a cost-effective process for the manufacture of Telaprevir, with a focus on the chemical processes for two chiral intermediates which were cost drivers for the manufacture of drug substance.

9:15 Step Economy Considerations in Route Development and Scale-Up of Drug Candidates

Neelakandha Mani, Ph.D., Scientific Director and Fellow, Discovery Sciences, Janssen Pharma R&D

The number of steps used to synthesize a drug molecule represents the single most significant component that impacts the manufacturing cost of an API. Step economy is equally important in early development, where, while the cost of API is not critical, the speed of synthesis plays perhaps the biggest role in fast tracking early clinical development. Examples of strategies for step economy in the scale-up synthesis of multiple candidate molecules will be presented.

9:45 Development of Efficient Asymmetric Propargylations and Application on Pilot Plant Scale

Daniel Fandrick, Ph.D., Principal Scientist, Chemical Development, Boehringer Ingelheim

The development of general and operationally simple stereoselective propargylations utilizing a metallo-boron exchange with a propargyl boronate is presented. Application of our methodology provided a sustainable process towards the potent azaindole glucocorticoid agonist BI 653048 on a pilot plant scale. Development of a continuous flow process to prepare the key propargyl boronate reagent on 0.8 metric ton scale is also presented.

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

11:00 Belviq (lorcaserin): From Process Chemistry to Commercial Manufacture

Antonio Garrido Montalban, Ph.D., Senior Director, Chemical R&D, Arena Pharmaceuticals, Inc.

11:30 Talk Title to be Announced

Roger Bakale, Ph.D., Senior Director, Worldwide Chemical Process R&D, Teva

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

12:30 Session Break

MORE PROCESS CHEMISTRY CASE STUDIES

12:55 Chairperson's Opening Remarks

Mahavir Prashad, Ph.D., Head, Chemical Development Unit US, Novartis Pharmaceuticals Corporation

1:00 Process Research and Kilogram Synthesis of TAK-733, an Investigational, Potent MEK Inhibitor

Yuxin (Marilyn) Zhao, Ph.D., Senior Scientist, Process Chemistry Group, Takeda California, Inc.

1:30 Incorporating Flow Chemistry

Timothy Braden, Process Chemistry Group, Chemical Product R&D, Eli Lilly and Company

2:30 Case Study

Neil Langille, Ph.D., Senior Scientist, Process R&D, Amgen

3:00 Close of Conference

Suggested Event Package:

May 21-22

Formulation & Drug Delivery Conference

May 22-23

Efficient Process Chemistry Conference

May 22

Recommended Dinner Short Course*

Refining API Process Development for Efficiency (see [page 4](#) for details)

* Separate registration required.

“A focused group with a diversified background. The interaction among the attendees was superb.”

Senior Principal Scientist, Chemical R&D, Pfizer



PAIN: Novel Drug Targets and Screening Tools

Exploring Cellular Pathways and Validating Targets for Improved Pain Therapeutics

WEDNESDAY, MAY 21

7:00 am Registration and Morning Coffee

TARGETING MEMBRANE RECEPTORS & ION CHANNELS

8:00 Chairperson's Opening Remarks

8:05 New Approaches to NMDA Receptor Modulation: Glycine Site Functional Partial Agonists are Efficacious and Do Not Cause Psychotomimetic Effects

Ronald Burch, M.D., Ph.D., CMO, Research & Development, Naurex, Inc.

GLYX-13 and NRX-1074 are NMDA receptor Glycine Site Functional Partial Agonists. These agents both inhibit neuropathic pain (e.g. Chung model). In clinical trials, these agents do not cause psychotomimetic side effects, unlike previously studied agents such as ketamine that completely block the NMDA receptor ion channel. Dosing for 12 weeks in patients is not associated with reduction in efficacy. In animals, neither NMDA receptor glycine site functional partial agonist substituted for ketamine in drug discrimination trials.

8:35 Amelioration of Neuropathic, Inflammatory and Cancer Pain in Rodent Models With a Novel Brain-Penetrant Peptide-Neurotensin Conjugate

Jean Lachowicz, Ph.D., CSO, R&D, Angiochem, Inc.

The analgesic properties of neurotensin have been recognized for decades, but because the peptide does not cross the blood-brain barrier, its therapeutic utility is limited. We have created a conjugate of neurotensin and Angiopep-2, which is recognized by a receptor that mediates transcytosis across the blood-brain barrier. This An2-Neurotensin shows efficacy in rodent models of multiple types of pain when administered systemically.

9:05 CGRP Receptor Antagonists for the Treatment of Migraine

Ian Bell, Ph.D., Principal Scientist, Discovery Chemistry, Merck Research Laboratories

Calcitonin gene-related peptide receptor antagonists (CGRP-RAs) have demonstrated clinical efficacy for acute treatment of migraine. In general, these agents have shown similar clinical responses to triptans with a reduced incidence of adverse events. Interestingly, the precise mechanism of action of CGRP-RAs, in particular whether they act centrally or peripherally, continues to be a matter of debate. Our program to develop novel, orally bioavailable CGRP-RAs and our efforts to elucidate their site of action will be discussed.

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

10:20 Angiotensin II Type 2 Receptor (AT2R) Antagonists as Novel Analgesics for Relief of Neuropathic Pain

Maree Smith, Ph.D., Executive Director, Centre for Integrated Preclinical Drug Development (CIPDD) & Professor of Pharmacy, The University of Queensland, Australia

Highly selective small molecule AT2R antagonists produce dose-dependent analgesia in rodent models of neuropathic pain, with analgesia abolished by genetic deletion of the AT2R. The analgesic mode of action involves attenuation of augmented angiotensin II/AT2R signaling in the dorsal root ganglia (DRGs) to block p38 MAPK and p44/p42 MAPK activation that are key enzymes in the phosphorylation of Nav1.7, Nav1.8, Cav2.2 and TRPV1, that are expressed in DRG neurons and are implicated in neuropathic pain.

10:50 The Role of Acid Sensing Ion Channels (ASICs) in Pain and Inflammation

Kathleen Sluka, Ph.D., Professor, Department of Physical Therapy and Rehabilitation Science, University of Iowa

Acid sensing ion channels (ASICs) are activated by decreased extracellular pH and are the primary acid-sensors in the nervous system. ASICs are found in nociceptors and play a significant role in inflammatory and non-inflammatory muscle pain. ASICs are also expressed on synoviocytes and regulate inflammation. The role of ASICs on nociceptors in transmitting inflammatory and non-inflammatory muscle pain, as well as the role of ASICs on synoviocytes in the regulation of inflammation will be presented.

11:20 Qube - High Throughput Screening with Genuine Electrophysiology

Richard Kondo, Ph.D., Head, Sales, North America, Sophion Bioscience

The Qube is a 384 channel, gigaohm-seal based automated patch clamp instrument for recordings from voltage-gated and ligand-gated ion channels. It offers the capability to screen large compound libraries for ion channel block or modulation. Data are obtained with a throughput of more than 30,000 wells tested per 24 hours.

11:35 Case Study Presentation by Collectricon

Speaker to be Announced

Sponsored by



USE OF IMAGING AS A TRANSLATIONAL TOOL

12:05 Longitudinal MRI Studies in Rats: Mechanisms of Ongoing Pain and Development of Chronic Pain

David A. Seminowicz, Ph.D., Assistant Professor, Department of Neural & Pain Sciences, University of Maryland School of Dentistry

Studies using functional and structural MRI in rats can provide information about mechanisms of acute and chronic pain that cannot be easily assessed in humans. In this talk, I will describe our studies involving the longitudinal analysis of brain changes in central and peripheral neuropathic pain models in rats. In combination with longitudinal studies in humans, these designs can potentially be used to monitor the efficacy of various pain interventions.

12:35 pm Imaging Pain in Awake Rats: Applications in Preclinical Drug Discovery

Craig Ferris, Ph.D., Professor, Department of Psychology and Pharmaceutical Sciences, Director, Center for Translational Neuroimaging, Northeastern University

Functional Magnetic Resonance Imaging (fMRI) is a powerful and translatable technology used to study brain function and activity. In addition, the identification of imaging biomarkers independent of behavioral assays can be used to as an indication of pharmacodynamics and efficacy in the research and development of novel analgesics. We have employed the use of functional MRI in awake rats to assess changes in brain activity following challenge with a variety of pain stimuli in wild-type and transgenic rats with and without drug treatment.

1:05 Luncheon Presentation (Sponsorship Opportunity Available) or Lunch on Your Own

1:35 Session Break



PAIN: Novel Drug Targets and Screening Tools

Exploring Cellular Pathways and Validating Targets for Improved Pain Therapeutics

VALIDATING ANIMAL MODELS: WHERE ARE THE GAPS?

2:00 Chairperson's Remarks

2:05 Are We Making Progress in Developing and Validating Preclinical Animal Models of Pain and Analgesia?

Edward Bilsky, Ph.D., Professor of Pharmacology; Vice President for Research and Scholarship, University of New England

Significant attention has been focused on preclinical animal models, their use in understanding the neurobiology of human pain, and in their ability to predict analgesic efficacy in pharmaceutical drug development process. This session will examine the progress made to date in refining the models and how we measure the different components of pain and pain relief in animals, and how we can use these approaches to improve the drug development process.

2:35 A Novel Procedure for Research on Pain-Related Depression in Rats

S. Stevens Negus, Ph.D., Professor, Department of Pharmacology and Toxicology, Virginia Commonwealth University

Pain is often associated with depression of behavior and mood, and relief of pain-related depression is a common goal of treatment. We have developed a novel preclinical assay of pain-depressed behavior in rats, and we have used this procedure to examine expression, neurobiology and treatment of pain-related behavioral depression. Data will be presented to suggest a role for dysregulated mesolimbic dopamine signaling as a mediator of pain-depressed behavior and a target for treatment.

3:05 Animal Models of Pain for Drug Discovery

Kirsten Raeal, Ph.D., Senior Research Investigator, Discovery Research, Purdue Pharma, L.P.

3:35 Sponsored Presentations (Opportunities Available)

4:05 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 (see [page 2](#) for details)

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

7:00 Close of Day



Nice and informative meeting with high level presentations ”

- Scientist, BIND Therapeutics

THURSDAY, MAY 22

7:30 am Interactive Breakout Discussion Groups with Continental Breakfast

GENETIC & EPIGENETIC TARGETS OF PAIN

8:35 Chairperson's Remarks

8:45 How Do We Produce a Step Change in the Discovery of New Analgesics?

Chas Bountra, Ph.D., Professor, Translational Medicine & Head, Structural Genomics Consortium, University of Oxford

Three issues that will play an important role in the discovery and development of new analgesics will be discussed during this talk: 1. Epigenetic proteins as fundamental mediators of chronic pain pathology; 2. Critical role of open partnerships between academia and industry in early discovery; and 3. Likelihood of *in vitro* clinical assays being more predictive of activity in patients.

9:15 A Long Non-Coding RNA, a New Player in Neuropathic Pain

Yuan-Xiang Tao, Ph.D., M.D., Professor and Vice Chair of Research, Department of Anesthesiology, Rutgers, The State University of New Jersey, New Jersey Medical School

Neuropathic pain is a common clinical condition. Current treatments are often inadequate or ineffective owing to our incomplete understanding of the mechanisms that underlie the genesis of neuropathic pain. We recently identified a long non-coding RNA, which is up-regulated in the injured primary sensory neurons following nerve injury. Evidence indicates that it may be an endogenous trigger in neuropathic pain development and maintenance and could be a new target for preventing and/or treating this disorder.

9:45 Sponsored Presentation (Opportunity Available)

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

10:45 Speaker to be Announced

11:15 Targeting Transient Receptor Potential (TRP) Channels for Pain Relief: Of Mice and Men (Or Only Mice?)

Arpad Szallasi, M.D., Ph.D., Medical Director for the Transfusion Services, Monmouth Medical Center, NJ, and Adjunct Professor of Pathology, Drexel University College of Medicine

Over the past 30 years, TRP channels have evolved from a somewhat obscure observation on how fruit flies detect light to become the center of drug discovery efforts. At present, site-specific resiniferatoxin (a TRPV1 agonist) injections are being evaluated as "molecular scalpels" to achieve permanent analgesia in cancer patients with chronic, intractable pain. Small molecule TRPV1, TRPV3 and TRPA1 antagonists have also been advanced into clinical trials. This talk will discuss the promise and challenges of developing TRP channel antagonists as a new generation of pain therapeutics.

11:45 Close of Conference

Suggested Event Package:

May 20

Recommended Short Course*

Animal Models of Pain: Progress and Challenges
(see [page 3](#) for Short Course details)

May 21-22

PAIN: Novel Drug Targets and Screening Tools Conference

* Separate registration required.

Sponsor & Exhibit Opportunities

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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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!

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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).

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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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ACD/Labs	Druggability Technologies	Molecular Imaging, Inc.	Stemgent-Asterand
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Biomodels, LLC	EMD Millipore	Oncotest GmbH	VisualSonics
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Additional branding and sponsorship opportunities available!

For sponsorship and exhibit information, please contact:

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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*



Hotel & Travel Information

Conference Venue and Host Hotel:

Westin Boston Waterfront
425 Summer St.
Boston, MA 02210
T: 617-532-4600
[Hotel Website](#)

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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Car Rental Discounts:

Special discount rentals have been established with Hertz for this conference.

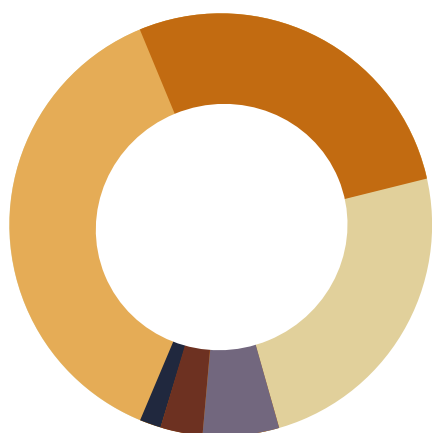
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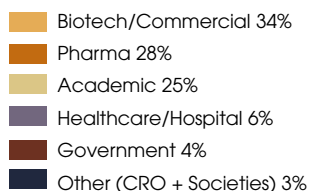
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2013 Attendee Demographics



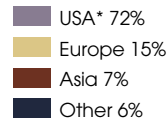
COMPANY TYPE



COMPANY TITLE



GEOGRAPHIC LOCATION



*USA Breakdown:

East Coast 72%

West Coast 15%

Midwest 13%

“ WPC was a highly-focused meeting with a great mixture of attendees from scientist to key leaders present. ”

Director of Business Development, Biomodels, LLC

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Pricing and Registration Information

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Early Registration until February 21, 2014	\$2,499	\$1,099
Advance Registration until April 4, 2014	\$2,699	\$1,199
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Advance Registration until April 4, 2014	\$1,699	\$729
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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 <i>In vitro</i> 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 (<i>Dinner will be served</i>)
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)	

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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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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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