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Cambridge HEALTHTECH Institute
25 YEARS
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16th Annual

WPC WORLD PRECLINICAL CONGRESS

June 12-16, 2017
The Westin Copley Place, Boston, MA

Where Preclinical Minds Meet Discovery Technologies

EVENT HIGHLIGHTS

- **12 Conferences** focusing on some of the hottest topics in preclinical research
- **8 Short Courses** offering interactive discussions with experts in the field
- **4 Symposia** covering the latest in upcoming areas of research
- **Training Seminar** providing in-depth instructions in specialized areas
- **Interactive Breakout Discussions** on key topics organized in an informal setting
- **Plenary Keynote Presentations** featuring prominent industry thought-leaders who are playing an important role in innovating drug discovery
- **Plenary Keynote Panel** featuring a group of technical experts from life science technology and service companies, who share their perspectives on new trends impacting preclinical research
- Networking opportunities, poster sessions, student fellowships, and much more

PLENARY KEYNOTE PROGRAM

PLENARY KEYNOTE PRESENTATIONS:

Human Organs-On-Chips

Donald E. Ingber, M.D., Ph.D., Founding Director, Wyss Institute for Biologically Inspired Engineering, Harvard University; Judah Folkman Professor of Vascular Biology, Harvard Medical School & Boston Children's Hospital; and Professor of Bioengineering, John A. Paulson School of Engineering & Applied Sciences, Harvard University

Preclinical and Translation Studies to Support the Anti-PD1 Antibody, Keytruda

Michael Rosenzweig, D.V.M., Ph.D., Executive Director, Oncology-Discovery, Merck Research Laboratories

PLENARY KEYNOTE PANEL:

Insights on Innovative Technologies Enabling Preclinical Research

Moderator: *Leigh Zawel, Vice President and Site Head, New York and Boston Centers for Therapeutic Innovation, Pfizer*

Panelists:

Matt Gevaert, Ph.D., CEO and Co-Founder, KIYATEC

Pradip Majumder, Ph.D., CSO, Mitra Biotech

David Hutto, Ph.D., DVM, DACVP, CSO, Vium

Brian Bonnell, MBA, Marketplace Director, Scientist

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Conference-at-a-Glance*

Monday, June 12

- New Tools for Disease Modeling*
- iPS Cells for Disease Modeling and Drug Discovery*
- Pre-Conference Short Courses*

Tuesday, June 13

- Mastering Medicinal Chemistry - Part 1
- Blood-Brain Barrier
- Preclinical Models and Tools in Oncology - Part 1
- Cancer Immunotherapy and Combinations
- Phenotypic Screening and Chemical Biology
- CRISPR for Target Discovery
- Predicting Drug Toxicity

Wednesday, June 14

- Mastering Medicinal Chemistry - Part 1
- Blood-Brain Barrier
- Preclinical Models and Tools in Oncology - Part 1
- Cancer Immunotherapy and Combinations
- Phenotypic Screening and Chemical Biology
- CRISPR for Target Discovery
- Predicting Drug Toxicity
- Mastering Medicinal Chemistry - Part 2
- Translational Strategies in CNS
- Tumor Models for Cancer Immunotherapy - Part 2
- Immuno-Oncology Targets
- 3D Cellular Models
- Training Seminar: Applying Pharmacology to New Drug Discovery
- Plenary Keynote Program
- Dinner Short Courses*

Thursday, June 15

- Mastering Medicinal Chemistry - Part 2
- Translational Strategies in CNS
- Tumor Models for Cancer Immunotherapy - Part 2
- Immuno-Oncology Targets
- 3D Cellular Models
- Training Seminar: Applying Pharmacology to New Drug Discovery
- Property-Based Drug Design*
- Nano-Delivery: Nucleic Acids, Cancer Immunotherapy and Beyond*

Friday, June 16

- Property-Based Drug Design*
- Nano-Delivery: Nucleic Acids, Cancer Immunotherapy and Beyond*

Separate registration required for Short Courses and Symposia

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FINAL WEEKS
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COVER
CONFERENCE-AT-A-GLANCE
PLENARY KEYNOTE PROGRAM
MEDICINAL CHEMISTRY
ONCOLOGY
SCREENING
DISCOVERY & DEVELOPMENT
SYMPOSIA
SHORT COURSES
TRAINING SEMINAR
SPONSOR & EXHIBIT OPPORTUNITIES
HOTEL & TRAVEL INFORMATION
REGISTRATION INFORMATION

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Where Preclinical Minds Meet Discovery Technologies

The *16th Annual World Preclinical Congress (WPC)* focuses on the very latest trends and technologies impacting preclinical drug discovery and development. *World Preclinical Congress 2017* offers a unique opportunity for chemists, biologists, pharmacologists and translational scientists in industry and academia to come together with technology providers to network and collaborate. It offers a diverse selection of short courses, symposia, a training seminar and conferences that appeals to newcomers, as well as experts in the field.

Stay Connected

#CHIWPC17

CHI's IntroNet Networking at its Best

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

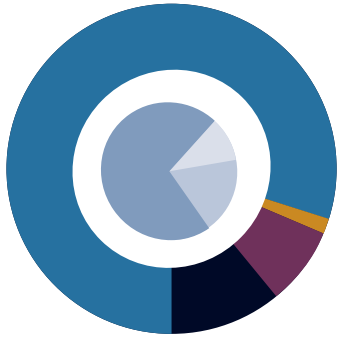
HERE'S WHAT YOU CAN EXPECT IN 2017:

- **12 Conferences** focusing on some of the hottest topics in preclinical research
- **8 Short Courses** offering interactive discussions with experts in the field
- **4 Symposia** covering the latest in upcoming areas of research
- **Training Seminar** providing in-depth instructions in specialized areas
- **Interactive Breakout Discussions** on key topics organized in an informal setting
- **Plenary Keynote Presentations** featuring prominent industry thought-leaders who are playing an important role in innovating drug discovery
- **Plenary Keynote Panel** featuring a group of technical experts from life science technology and service companies, who share their perspectives on new trends impacting preclinical research
- **Exhibit Hall** of 80+ companies offering a glimpse at the latest tools and reagents
- **Poster** sessions featuring cutting-edge, ongoing research
- **1,000+ Attendees:** Networking opportunities to meet with a global gathering of scientists from academia and industry
- Inter-disciplinary forum to meet chemists, biologists, toxicologists and scientists from varied areas of expertise
- **Student Fellowships** to bring together young researchers looking to make a difference
- Exclusive focus on ideas, technologies and interests driving preclinical decision-making
- Sponsored talks by leading technology and service providers showcasing new offerings

HERE'S WHO YOU CAN EXPECT TO MEET IN BOSTON THIS JUNE ...

COMPANY TYPE

Commercial (Biotech & Pharma)	71%
Academic & Government	18%
Healthcare	6%
Services & Societies	4%
Other	1%



GEOGRAPHIC LOCATION

USA*	79%
Europe	11%
Asia	8%
Rest of World	2%

*USA Breakdown:

East Coast	68%
West Coast	18%
Midwest	14%

DELEGATE TITLE

Directors, Executives & Managers	36%
Scientist/Technologist	29%
Sales & Marketing	13%
Professor	12%
Manager	6%
Assistant	4%

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Monday, June 12, 12:00 - 3:00 pm

SC2: Drug Metabolism and Its Impact on Decisions in Lead Discovery - Part 1

This short course will focus on concepts important for those wanting to understand how drug metabolism is applied to drug discovery. Topics will include how drugs are metabolized, what enzymes are involved, common assays for predicting clearance and drug-drug interactions and how drug metabolism concepts are applied during lead optimization. Those scientists involved in medicinal chemistry, pharmacology and drug metabolism will benefit from this overview.

Instructors:

John Erve, Ph.D., Consultant

Adrian J. Fretland, Ph.D., Associate Director, DMPK Oncology iScience, AstraZeneca

Monday, June 12, 3:30 - 6:30 pm

SC3: Drug Metabolism and Its Impact on Decisions in Drug Development - Part 2

This short course will focus on concepts important for those wanting to understand how drug metabolism is applied to drug development. Topics will include how drug metabolites are identified in pre-clinical studies and human clinical trials, the role of bioactivation and the growing importance of transporters in drug disposition and safety. Those scientists involved in medicinal chemistry, pharmacology and drug metabolism will benefit from this overview.

Instructors:

John Erve, Ph.D., Consultant

Mingxiang Liao, Ph.D., Senior Scientist I, DMPK, Takeda Pharmaceutical Intl. Company

SC4: Understanding and Dealing with Drug Disposition in CNS

This course will aim to discuss compound selection in CNS drug discovery by modeling and simulation, factors affecting disposition of biologics, kinetic relationship between systemic circulation and CNS and understanding factors that affect brain ISF/CSF production and clearance and its implications.

Instructor:

Qin Wang, Ph.D., Principal Scientist, Translational Sciences, Biogen

SC5: Convergence of Immunotherapy and Epigenetics for Cancer Treatment

In recent years the understanding of both the immunotherapy and epigenetics of cancer has increased. This course will provide some details of how immunotherapy and epigenetic pathways interact and how they can be exploited to enhance the efficacy of current cancer treatments. The instructors will review recent scientific evidence and pre-clinical data that support the development of combination therapies and offer their perspectives on challenges that may have to be tackled along the way.

Instructors:

Alejandro Villagra, Ph.D., Assistant Professor, Department of Biochemistry and Molecular Medicine, School of Medicine and Health Sciences, The George Washington University

Katherine Bakshian Chiappinelli, Ph.D., Assistant Professor, Department of Microbiology, Immunology, and Tropical Medicine, The George Washington University Cancer Center

Additional Instructors to be Announced

Monday, June 12, 7:00 - 9:30 pm (Dinner Provided)

SC6: How to Best Utilize 3D Spheroids and CRISPR Assays in Oncology

The course will provide an overview of 3D cell culture models, their strengths and weaknesses. The instructors will share their experiences on the challenges they faced from experimental design to data analysis while developing and optimizing these 3D spheroid models for CRISPR-based functional screening. The focus of their presentations will be in the area of oncology research, utilizing either low or high throughput screening approaches.

Instructors:

Madhu Lal-Nag, Ph.D., Group Leader, Trans-NIH RNAi Facility, National Center for Advancing Translational Sciences, National Institutes of Health

Geoffrey Bartholomeusz, Ph.D., Associate Professor and Director, Target Identification and Validation Program, Department of Experimental Therapeutics, Division of Cancer Medicine, The University of Texas M.D. Anderson Cancer Center

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

SC7: Evaluating and Characterizing *in vitro* Models of Drug Toxicity

This short course will focus on ways to evaluate and characterize which *in vitro* model of drug toxicity is best suited to understand the mechanism and extent of drug toxicity involved. Topics will include a general overview of the different types of *in vitro* models available to assess drug toxicity, what are some of their inherent strengths and limitations, and what factors need to be considered when deciding which model to use. Those scientists involved in medicinal chemistry, DMPK, safety pharmacology and toxicology will benefit from this overview by understanding some aspects of how safety assessments are made.

Instructors:

Terry Van Vleet, Ph.D., DABT, Head of Molecular and Computational Toxicology, Department of Preclinical Safety, Abbvie

Will Proctor, Ph.D., Senior Scientist, Head of Investigative Toxicology, Department of Safety Assessment, Genentech

Separate Registration Required.

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DINNER SHORT COURSES

Wednesday, June 14, 7:00 - 9:30 pm

SC8: Applications of Functional Screening Using CRISPR and RNAi

This course will offer details on how the CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)/Cas technology works, how to set up CRISPR-based screens and how to complement it with existing RNAi-based screens using proper analysis and follow-up studies. The instructors will share their experiences on how to go about evaluating reagents/libraries, designing and setting up assays, and interpreting results when dealing with complex biology and informatics. The applications of such functional genomics screens for drug discovery and disease modeling will be discussed, along with design and workflows when working with different model systems. Ideas and best practices will be shared in an informal, interactive setting and attendees will walk away with practical advice and resources.

Instructors:

Jennifer Smith, Ph.D., Assistant Director, ICCB-Longwood Screening Facility, Harvard Medical School

John Doench, Ph.D., Associate Director, Genetic Perturbation Platform, Broad Institute of Harvard and MIT

Roderick Beijersbergen, Ph.D., Group Leader, Netherlands Cancer Institute and Head, NKI Robotics and Screening Center

Michael Bassik, Ph.D., Assistant Professor, Department of Genetics, Stanford University

SC10: Humanized Mouse Models for Preclinical Assessment of Cancer Immunotherapy

The development of severely immunodeficient IL2r null mice that support engraftment of functional human immune systems has enabled the *in vivo* study of human immunity. This presentation will include a general overview of these humanized mouse models, describing currently available strains, the protocols to generate humanized mice, the strengths of each system and a discussion of the application of these models to study human immunology.

Instructor:

Michael Brehm, Ph.D., Associate Professor, The Robert and Sandra Glass Term Chair in Diabetes, Diabetes Center of Excellence, Program in Molecular Medicine, University of Massachusetts Medical School

James Keck, Ph.D., Senior Director, In Vivo Pharmacology, Clinical Lab Services, The Jackson Laboratory

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MEDICINAL CHEMISTRY

The popular 14th Annual Mastering Medicinal Chemistry event brings you the hottest topics in medicinal chemistry from leaders in the pharmaceutical, biotech and academic spaces. We cordially invite you to take part in this must-attend event which aims to showcase the biggest opportunities for small molecules through pre-cutting-edge case studies, panel discussions, poster presentations and breakout discussions. The 2017 event will span over 3 days to feature new research for small molecules in immune-oncology, protein degradation, combination therapies, CNS, kinases, covalent inhibitors, protein-protein interactions, epigenetics and more. It will also host a pre-conference and a post-conference symposium for more in-depth coverage on topics like lead generation and property-based drug design.

June 13-14

Mastering Medicinal Chemistry - Part 1

June 14-15

Mastering Medicinal Chemistry - Part 2

June 15-16

SYMPOSIUM: Property-Based Drug Design

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15th Annual

Mastering Medicinal Chemistry - Part 1

Hot Topics, Emerging Themes, and New Technologies

Recommended Event Package

Conference June 13-14: Mastering Medicinal Chemistry - Part 1

Conference June 14-15: Mastering Medicinal Chemistry - Part 2

Short Course 9 June 14: Importance of Solubility in Drug Discovery and Development Applications

Symposium June 15-16: Property-Based Drug Design

TUESDAY, JUNE 13

7:00 am Registration Open and Morning Coffee

SMALL MOLECULES IN IMMUNE-ONCOLOGY

8:25 Chairperson's Opening Remarks
Lijun Sun, Ph.D., Director, Center for Drug Discovery and Translational Research, Beth Israel Deaconess Medical Center, Harvard Medical School

8:35 Discovery of PF-06840003, a Novel IDO Inhibitor for Cancer Immunotherapy
Stefano Crosignani, Ph.D., Director, Medicinal Chemistry, iTeos Therapeutics
Tumors use Indoleamine 2-3 dioxygenase to induce an immunosuppressive environment by promoting immune tolerance, effector T-cell anergy and enhanced Treg function. We have identified and characterized a new, highly selective, orally bioavailable IDO-1 inhibitor, PF-0684003. PF-0684003 reverses human T-cell anergy *in vitro*. It shows a very favorable ADME profile leading to favorable predicted human pharmacokinetic properties. These studies highlight the strong potential of PF-0684003 as a clinical candidate in immuno-oncology.

9:05 Small Molecule Antagonists of Immune Checkpoint Pathways
Pottayil G. Sasikumar, Ph.D., Associate Research Director, Medicinal Chemistry, Aurigene Discovery Technologies Ltd.
Immune checkpoint antibodies have revolutionized cancer therapy because of their impressive clinical activity. However, they suffer from the shortcomings including the failure to show response in a majority of patients, need to administer by intravenous injection and immune-related adverse events. We are developing small molecule immune checkpoint antagonists that do not exhibit these limitations. CA-170, a candidate from this approach dually targeting PD-L1 and VISTA is now undergoing clinical trials.

9:35 Highly Selective AKR1C3 Inhibitors Significantly Potentiate Antineoplastic Effect of Clinical Chemotherapeutics
Paul Trippier, Ph.D., Assistant Professor, Pharmaceutical Sciences, Texas Tech University Health Sciences Center
AKR1C3 is an enzyme that regulates the production of steroids and prostaglandins implicated in the progression of cancer and plays a role in the metabolism of anticancer agents. Potent and selective AKR1C3 inhibitors act to potentiate the antineoplastic actions of a range of clinically approved chemotherapeutics. Combination treatment of low concentration of AKR1C3 inhibitor and chemotherapeutic provide significant potentiation effect and sensitize resistant cancer cells to the anthracycline drugs.

10:05 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

10:50 Novel IDO1 and TDO2 Selective Inhibitors by *in silico* Screening
Lijun Sun, Ph.D., Director, Center for Drug Discovery and Translational Research, Beth Israel Deaconess Medical Center, Harvard Medical School
We conducted *in silico* screens to identify novel and selective IDO1 and TDO2 inhibitors, respectively. Enzymatic hIDO1 and hTDO2 assays were utilized to confirm inhibitory activity and selectivity. Among the confirmed inhibitors, a series of oxan-4-carboxamides selectively inhibited hIDO1; while a series of substituted 9H-fluorenes were identified as TDO2 selective inhibitors (IC50: 1 μM). In this presentation we will discuss the *in silico* approach and provide updates on characterization data of the inhibitors.

11:20 PANEL DISCUSSION: Challenges and Opportunities in Developing Small Molecule Based Immune-Oncology Therapies
Moderator:
Stephen Young, Ph.D., Vice President, Business Development, Sygnature Discovery Ltd.
Panelists:
Stefano Crosignani, Ph.D., Director, Medicinal Chemistry, iTeos Therapeutics
Paul Trippier, Ph.D., Assistant Professor, Pharmaceutical Sciences, Texas Tech University Health Sciences Center

Pottayil G. Sasikumar, Ph.D., Associate Research Director, Medicinal Chemistry, Aurigene Discovery Technologies Ltd.
Lijun Sun, Ph.D., Director, Center for Drug Discovery and Translational Research, Beth Israel Deaconess Medical Center, Harvard Medical School

11:50 Optimisation of a Series of Potent and Selective Glucocorticoid Receptor Antagonists

Sponsored by SYGNATURE discovery

Stephen Young, Ph.D., Vice President, Business Development, Sygnature Discovery Ltd.

Glucocorticoids regulate a plethora of biological effects via interaction with the ubiquitously expressed glucocorticoid receptor (GR). Excessive glucocorticoid activity leads to a number of adverse effects, including, glucose intolerance, diabetes and abnormal fat distribution. This presentation will describe the continuing optimisation of a series of 1H-pyrazolo[3,4-g]hexahydro-isoquinoline sulphonamides, focusing on efforts to remove off target effects and to maintain a balance of good oral exposure and potent, selective GR antagonism.

12:20 pm Luncheon Presentation: New Strategy to Reduce Hearing Loss Associated with Usher Syndrome

Sponsored by discovery from charles river

Christopher Lock, B.Sc., Ph.D., Senior Scientist, Discovery, Charles River

Usher syndrome type III, characterized by progressive deafness, variable balance disorder and blindness, is caused by destabilizing mutations in the gene encoding the clarin-1 protein (CLRN1). A strategy to identify potential small molecule therapies to mitigate the hearing loss associated with these mutations is demonstrated. This approach can be applied to identify drugs for other protein-destabilizing monogenic disorders. Funded by the Usher III Initiative Research Consortium, the work was carried out by collaborators at Case Western Reserve University, University Hospitals Case Medical Center and Charles River.

12:50 Session Break

NEW TARGETS IN CNS DISEASES, AUTOIMMUNE DISEASES, IMMUNOLOGY AND RARE GENETIC DISEASES

1:40 Chairperson's Remarks

Paul Trippier, Ph.D., Assistant Professor, Pharmaceutical Sciences, Texas Tech University Health Sciences Center

1:50 Discovery of First in Class, Orally Bioavailable P300/CBP HAT Domain Inhibitors

Michael Michaelides, Ph.D., Head, Oncology Chemistry, Senior Research Fellow, AbbVie

The histone acetyltransferases p300/CBP are key transcriptional co-activators that are essential for a multitude of cellular processes and implicated in human pathological conditions, including cancer. Despite their important epigenetic functions, it has been challenging to develop selective and potent p300/CBP inhibitors. Starting with a screening hit identified via virtual ligand screening we have developed and optimized potent and selective inhibitors that exhibit low plasma clearance and high oral bioavailability.

2:20 Huntington's Disease: Challenges in Target Validation and Drug Discovery

Celia Dominguez, Ph.D., Vice President, Chemistry, CHDI Management/CHDI Foundation Inc.

CHDI Foundation is a privately funded nonprofit biopharmaceutical research and development organization that is exclusively dedicated to developing therapies for Huntington's disease (HD), a lethal autosomal dominant neurodegenerative disorder caused by expansion of CAG repeats in the huntingtin (HTT) gene. HD patient brains reveal a devastation of the caudate-putamen, and cortico-striatal-thalamo-cortical circuits seem to be particularly affected. Currently, no disease-modifying therapies are available. Herein will present challenges in target validation and drug discovery in the quest to identify potential therapeutics for HD.

2:50 Design and Synthesis of Novel S-Ribosylhomocysteine Analogues

Christiane Chbib, Pharm.D, Ph.D., Assistant Professor, Pharmaceutical Sciences, College of Pharmacy, Larkin university

New 4-C-Alkyl/aryl-S-ribosylhomocysteine (SRH) analogues and [4-thio]-S-ribosylhomocysteine (SRH) analogues have been designed and synthesized as potential antibacterials. These analogues might impede the S-ribosylhomocysteinase(LuxS)-catalyzed reaction by preventing β-elimination of a homocysteine molecule, and thus depleting the production of quorum sensing signaling molecule AI-2.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:05 Expanding the Capabilities of Current Biophysical Platforms to Support Preclinical Drug Discovery From Hits-to-Lead Through to Lead Optimization

John G. Quinn, Ph.D., Head of Molecular Biophysics & Senior Scientist, Biochemistry & Cellular Pharmacology, Genentech a member of the Roche Group

Real-time biomolecular interaction analysis accelerates preclinical drug discovery by using increasingly versatile SPR instruments for fragments screens, SAR and MoA. Expanding the capabilities of current SPR platforms by developing unconventional assay formats provided effective solutions where alternative functional assays were either unavailable, or lacked the necessary sensitivity, to measure interaction constants of leads. Elucidating the dependence of cellular efficacy on interaction kinetics supports better data-driven decision making within project teams.

4:35 The Biologist-Med Chemist Interface in Drug Discovery: The Importance of the Assay in Fitting Data to Models to Determine Mechanism of Action

Terry Kenakin, Ph.D., Professor, Department of Pharmacology, University of North Carolina School of Medicine

The muscarinic receptor Gq protein activation profiles of five exemplar molecules (slow binding agonists, partial agonists, inverse agonists, PAM-Agonists and Beta-PAMs) will be compared in calcium and IP1 assays to illustrate how quantitative comparisons to pharmacological models can both identify mechanisms of action and also convert descriptive to predict data for therapeutic systems. The optimal use of these models allow the identification of consistent and simple scales of activity that can guide medicinal chemistry in lead optimization.

5:05 Extended Q&A with Session Speakers

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PLENARY KEYNOTE PROGRAM

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5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

WEDNESDAY, JUNE 14

7:00 am Registration Open

7:30 Interactive Breakout Discussion Groups with Continental Breakfast
This session features various discussion groups that are led by a moderator/s who ensures focused conversations around the key issues listed. Attendees choose to join a specific group and the small, informal setting facilitates sharing of ideas and active networking. Continental breakfast is available for all participants. Details on the topics and moderators are available on the conference website.

DNA-ENCODED LIBRARIES AND NEW CHEMISTRY TECHNOLOGIES

8:35 Chairperson's Remarks
Graham Smith, Ph.D., Senior Medicinal Chemist, AstraZeneca

8:45 Non-Coding RNA as a Small Molecule Druggable Target
Graham Smith, Ph.D., Senior Medicinal Chemist, AstraZeneca
The human proteome consists of some 25,000 gene targets from which most current drug discovery efforts are based. However, in recent years it has become clear that the human transcriptome contains a similar number of gene targets whose RNA does not code for any protein. The role of these transcribed but non-coding RNA (ncRNA) targets is the subject of much active research. Their genetic linkage to diseases and traits is both numerically and statistically the same as that for the protein coding RNA when using SNPs and GWAS analysis.

9:15 PROTACs: Inducing Protein Degradation as a Therapeutic Strategy
George M. Burslem, Ph.D., Research Associate, Molecular, Cellular and Developmental Biology, Yale University
The Crews lab has focused on developing Proteolysis Targeting Chimera (PROTAC), a technology that overcomes the limitations of the current inhibitor pharmacological paradigm. PROTACs offer a mechanism to irreversibly inhibit protein function by destruction of the target proteins. This approach employs heterobifunctional molecules to recruit target proteins to the cellular quality control machinery, thus leading to their degradation. We have demonstrated the ability to degrade a wide variety of targets.

9:45 Structure-Based Optimization of Non-Natural Peptidic Mcl-1 Inhibitors from a DNA-Encoded Library Screen: Macrocyclization, Binding Kinetics, and Nonlinear SAR
Jeffrey Johannes, Ph.D., Associate Principal Scientist, IMED Oncology Medicinal Chemistry, AstraZeneca
Crystallography showed that a non-natural peptidic DNA-encoded library hit bound to Mcl-1 in a β-turn conformation. Linking of the ends of the peptide to form a macrocycle resulted in an approximately 10-fold improvement in binding potency. Further optimization resulted in a nanomolar Mcl-1 inhibitor that is selective against Bcl-2 and Bcl-xL and able to induce cleaved caspase 3 in MV4-11 cells with an IC50 of 4 μM at 6 hours.

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

11:00 Application of Sulfonyl Fluorides in Drug Discovery
Ariamala Gopalsamy, Ph.D., Associate Research Fellow, Medicine Design, Pfizer, Inc.
Phase II attrition poses a formidable challenge to the pharmaceutical drug development process. There is a need to address this challenge during the pre-clinical discovery phase to build confidence in translation. Chemical probes are highly valuable in this regard during the early discovery phase to identify, validate and assess coverage of molecular targets. Sulfonyl fluorides are proven chemical biology tools and provide a means to interrogate targets even in the absence of reactive cysteine or lysine. Select case studies will be presented to highlight the utility of sulfonyl fluoride probes in the early discovery process.

11:30 Strategic Considerations for the Preparation of Functionalizable Heterocycles
Andrew Flick, Ph.D., Senior Principal Scientist, Global R&D, Pfizer, Inc.
Densely packed arrangements of heteroatoms and stereogenic centers constituting the heterocyclic motifs challenge the limits of current technology, prompting the need for new strategies for the synthesis of these systems. Novel approaches which have demonstrated our access to these challenging molecular architectures will be presented--a ruthenium-catalyzed hydrogen transfer of 1,3-diols in the presence of alkyl hydrazines to furnish 1,4-disubstituted pyrazoles and a versatile approach to 5,6-fused heteroaromatics will be described which involves the conjugate addition of a metallated 2-fluoropyridine to substituted nitroolefins followed by a tractable 3-step sequence capable of furnishing these highly important bicyclic arrays.

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

12:30 Session Break

1:00 Coffee and Dessert in the Exhibit Hall with Poster Viewing

1:30 PLENARY KEYNOTE SESSION (click here for details)

3:30 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Close of Conference

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Mastering Medicinal Chemistry - Part 2

Case Studies and Highlights from Industry

Recommended Event Package

Conference June 13-14:Mastering Medicinal Chemistry - Part 1

Conference June 14-15: Mastering Medicinal Chemistry - Part 2

Short Course 9 June 14: Importance of Solubility in Drug Discovery and Development Applications

Symposium June 15-16: Property-Based Drug Design

WEDNESDAY, JUNE 14

11:00 am Registration

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

12:30 Session Break

1:00 Coffee and Dessert in the Exhibit Hall with Poster Viewing

1:30 PLENARY KEYNOTE SESSION (click here for details)

3:30 Refreshment Break in the Exhibit Hall with Poster Viewing

CHEMICAL BIOLOGY, TARGET VALIDATION AND ACTIVITY-BASED PROFILING

4:15 Chairperson's Opening Remarks
Henning Stockmann, Ph.D., Senior Scientist, Chemical Biology, AbbVie Inc.

4:25 FEATURED PRESENTATION: Ligand-Induced Kinase Degradation
Lyn H. Jones, Vice President, Chemical Biology, Jnana Therapeutics
We have discovered a pan-JAK ATP-competitive inhibitor that causes selective degradation of JAK2 and JAK3 in human primary cells at low concentrations. This work suggests that ligand-induced kinase degradation warrants further investigation as it may hold significant promise as a useful therapeutic modality.

4:55 VX-787 (JNJ872): Phenotypic Screen & Target Identification for a First-in-Class, Orally Bioavailable Inhibitor of Influenza PB2
Michael P. Clark, Director, Department of Chemistry, Vertex Pharmaceuticals Inc.
A phenotypic screening approach utilizing a cell protection assay identified a series of azaindole based inhibitors of the cap-snatching function of the PB2 subunit of the influenza A viral polymerase complex. This class of inhibitors was optimized using a bDNA viral replication assay to afford VX-787 (JNJ872). VX-787 represents a first-in-class, orally bioavailable, novel compound that offers unparalleled potential for the treatment of both pandemic and seasonal influenza.

5:25 Integrating Data and Design to Target High Quality Compounds
Tamsin Mansley, Ph.D., Head of North American Operations, Optibrium
A high-quality drug must exhibit a balance of many properties, including potency, ADME and safety. In this presentation, we'll discuss Multi-parameter Optimization (MPO) methods that guide the selection and design of compounds with the highest chance of success, while minimizing opportunities missed by inappropriately rejecting compounds. This will be demonstrated with an application that seamlessly integrates data visualisation, MPO and design, in the context of an example project.

5:55 New Chemical Biology Technologies for Target Identification and High-Throughput Screening: Chemical Glycobiology and Beyond
Henning Stockmann, Ph.D., Senior Scientist, Chemical Biology, AbbVie Inc.
Improved strategies for reliable drug target identification and target engagement studies are urgently needed, whereby cell-surface receptors present particular challenges. We have developed new chemical biology approaches to link probes and reporters to cell-surface receptors and cytosolic proteins in live cells. Our sugar-based cell-surface engineering methods not only enable receptor visualization, isolation, and proteomics-based characterization, but also facilitate target engagement studies and high-throughput ligand binding assays in intact cells.

6:25 Close of Day

6:30 Dinner Short Course Registration
Click here for details on short courses offered.

THURSDAY, JUNE 15

7:15 am Registration Open and Morning Coffee

7:30 Interactive Breakout Discussion Groups with Continental Breakfast
This session features various discussion groups that are led by a moderator/s who ensures focused conversations around the key issues listed. Attendees choose to join a specific group and the small, informal setting facilitates sharing of ideas and active networking. Continental breakfast is available for all participants. Details on the topics and moderators are available on the conference website.

GPCRS, COVALENT INHIBITORS, DEHYDROGENASES AND KINASES: CASE STUDIES & UPDATES

8:35 Chairperson's Remarks
Lieven Meerpoel, Ph.D., Senior Director, Janssen Lead Discovery, Janssen R&D

8:45 KEYNOTE PRESENTATION: Exploring the Pluridimensionality of G Protein-Coupled Receptor Signaling Efficacy; Potential Impacts for Drug Discovery
Michel Bouvier, Ph.D., Professor/General Director, Biochemistry and Molecular Medicine/Institute for Research in Immunology and Cancer, Université de Montréal
It is now clear that G protein-coupled receptors can engage signaling pathways in a ligand-specific manner. Using BRET-based biosensors detecting the activity of multiple signaling pathways in living cells we characterized compounds based on multi-parametric analysis of their efficacy. Such pluridimensional description of compounds allows correlating signaling signatures to specific biological outcomes. Combined with structural analyses of the receptors, it also provides insights into the molecular basis of functional selectivity paving the way for the development of rationally designed biased ligands.

9:15 Discovery of Novel Macrocyclic Inhibitors of Elongation Factor-2 Kinase as Anti-Cancer Agents
Lieven Meerpoel, Ph.D., Senior Director, Janssen Lead Discovery, Janssen R&D
Macroclyclic EF2k inhibitors were designed that inhibit phosphorylation of EF2 at nM concentrations in metabolically stressed MCF10A cells. Minor modifications on the macroclyclic linker, including introduction of chirality, had major effects on EF2K activity, kinase selectivity, ADME and *in vivo* PK properties. Genetic and proteomic enabled deconvolution of potent EF2K versus VPS34 inhibitors. Tumor cell line profiling did not reveal intrinsic sensitivity to EF2K inhibition. Vps34 inhibition abrogates autophagy flux, and is anti-proliferative in a subset of tumor cell lines.

9:45 Selected Poster Presentation: Applying Nature-Inspired 3D-Fragments Towards the Discovery of nM Inhibitors of Cyclophilin D
Eric A. Jamois, Ph.D., Head of US Business Operations, Edelris SAS
Cyclophilins are folding helper enzymes of the Peptidyl Proline Isomerases (PPI) superfamily with a strong reputation as extremely challenging targets. Our research focused on the identification of non-immunosuppressive Cyclophilin D (CypD) inhibitors and their potential implication in mitochondrial function. We will discuss the results obtained in a collaborative FBDD program with Merck Serono, culminating in the identification of a highly potent (nM) inhibitor of Cyclophilin D.

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

11:00 Investigating Small Molecules to Inhibit GLK/MAP4K3 and Prevent PKCp Phosphorylation Potential Therapy to Modulate T Cell Dependent Effector Functions
Tricia May-Dracka, Ph.D., Scientist II, Chemistry and Molecular Therapeutics, Biogen
Germinal center kinase-like kinase (GLK) has been hypothesized to have an effect on key cellular activities, including inflammatory responses. GLK is required for activation of protein kinase C-p (PKCp in T cells. Controlling T helper cell responses would be valuable for treatment for autoimmune diseases. I will disclose for the first time our efforts to identify a potent and selective GLK inhibitor, aided by the first crystal structure of GLK.

11:30 Phenotypes of a Novel Series of 3-Phosphoglycerate Dehydrogenase Inhibitors
Nello Mainolfi, Ph.D., Senior Director, Head of Drug Discovery, Raze Therapeutics
PHGDH (3-phosphoglycerate dehydrogenase) is the first enzyme branching from glycolysis into the serine synthetic pathway. Increases in PHGDH expression (mRNA and protein levels) have been observed in nearly 70% of estrogen receptor-negative breast cancers. We have been able to successfully identify first in class small molecule inhibitors with nanomolar cellular potency, high degree of selectivity and oral bioavailability

12:00 pm Covalent Inhibitors for Glycan-Modifying Enzymes
Gerd Wagner, Ph.D., Reader in Medicinal Chemistry, Department of Chemistry, King's College London
Inhibitors and chemical probes for glycosidases and glycosyltransferases enzymes are of great interest for chemical biology and drug discovery in areas such as infection, inflammation and cancer. However, the development of such inhibitors with drug-like properties remains a formidable challenge, in particular for glycosyltransferases. The presentation will demonstrate how principles of covalent inhibitor discovery can be harnessed to address this challenge, focusing in particular on bacterial enzymes.

12:30 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:00 Session Break

PROTEIN-PROTEIN INTERACTIONS

1:30 Chairperson's Remarks
Salvador Ventura, Ph.D., Professor/Group Leader, Deptartment of Biochemistry and Molecular Biology, Institute of Biotechnology and Biomedicine, Autonomous University of Barcelona

1:35 Development of Protein-Protein Interaction Inhibitors and Use of Biophysical Screening

Kevin Lumb, Ph.D., Global Head of Screening, Discovery Sciences, The Janssen Pharmaceutical Companies of Johnson & Johnson

2:05 Interdiction at a Protein-Protein Interface: Structure-Based Design of Mcl-1 Inhibitors

Sean P. Brown, Ph.D., Principal Scientist, Medicinal Chemistry, Amgen

Although compelling, targeting disruption of Mcl-1's protein–protein interaction to induce tumor cell death was previously thought to be "un-druggable" due to the high affinities of Mcl-1 to the pro-apoptotic Bcl-2 proteins and lack of a small molecule binding pocket. This presentation will describe the convergence of structural information and small molecule conformational analysis applied to the optimization of small molecule high-throughput screening hit to this now "druggable" target.

2:35 Coffee and Dessert Break in the Exhibit Hall. Last Chance for Poster Viewing.

3:20 Targeted Protein Degradation

Andrew J. Phillips, Ph.D., President and CSO, C4 Therapeutics

Emerging capabilities and concepts in targeted protein degradation will be described with a special focus on (i) the discovery and optimization of potent degraders of chromatin reader proteins, and (ii) the degradation of transmembrane proteins.

IMMUNO-ONCOLOGY & FUTURE DIRECTIONS IN MEDICINAL CHEMISTRY

3:50 Repositioning Tolcapone as a Potent Inhibitor of Transthyretin Amyloidogenesis and Associated Cellular Toxicity

Salvador Ventura, Ph.D., Professor/Group Leader, Department of Biochemistry and Molecular Biology, Institute of Biotechnology and Biomedicine, Autonomous University of Barcelona

Transthyretin (TTR) is implicated in fatal systemic amyloidoses. Here we repurpose tolcapone, an FDA-approved molecule for Parkinson's disease, as a very potent TTR aggregation inhibitor. Tolcapone binds specifically to TTR in human plasma, stabilizes the native tetramer in humans and inhibits TTR cytotoxicity. This converts tolcapone in a strong candidate for therapeutic intervention in these diseases, including those affecting the central nervous system, for which no small molecule therapy exists.

4:20 Close of Conference

5:00 Symposia Registration

Click here for details

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ONCOLOGY

With immunotherapy and combination therapy becoming the major focus of oncology research over the last several years, World Preclinical Congress has strengthened and expanded its cancer coverage. Translational strategies, novel preclinical models, combination therapy design, new immuno-oncology targets, cell analysis technologies, nano-delivery methods are the key topics that will be discussed at the event. Join pharmaceutical, biotech, and academic stakeholders for interactive sessions, panel discussions, and short courses, all of which are geared toward providing opportunities for active networking and collaboration. By attending you will be able to gain strategic insight into solutions for increasing the predictability of preclinical cancer studies and accelerating translation in oncology in general and immuno-oncology in particular.

June 12

SYMPOSIUM: New Tools for Disease Modeling

June 13-14

Preclinical Models and Tools in Oncology - Part 1

Cancer Immunotherapy and Combinations

June 14-15

Tumor Models for Cancer Immunotherapy - Part 2

Immuno-Oncology Targets

June 15-16

SYMPOSIUM: Nano-Delivery: Nucleic Acids, Cancer Immunotherapy and Beyond

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6th Annual

Preclinical Models and Tools in Oncology - Part 1

Advancing Translational Oncology and Immuno-Oncology with Novel Models, Tools and Approaches

Recommended Event Package

Symposium June 12: New Tools for Disease Modeling

Conference June 13-14: Preclinical Models and Tools in Oncology - Part 1

Conference June 14-15: Tumor Models for Cancer Immunotherapy - Part 2

Short Course 10 June 14: Humanized Mouse Models for Preclinical Assessment of Cancer Immunotherapy

Symposium June 15-16: Nano-Delivery: Nucleic Acids, Cancer Immunotherapy and Beyond

TUESDAY, JUNE 13

7:00 am Registration Open and Morning Coffee

KEYNOTE SESSION: STRATEGY AND SCIENCE TO ADVANCE TRANSLATIONAL ONCOLOGY

8:25 Chairperson's Opening Remarks
Mario Perro, Ph.D., Group Leader, Pharmacology, Oncology, Roche

8:35 Translational Research in Oncology and Immuno-Oncology
Peter Hammerman M.D., Ph.D., Global Head, Translational Research, Oncology, Novartis
Drug development in oncology has advanced over the past decade with the demonstration of the effectiveness of both targeted and immunotherapy approaches in patients with a diverse array of cancer types. Going forward it will be essential to nominate and understand therapeutic combinations to achieve high degrees of clinical efficacy while minimizing toxicity. In this presentation I will discuss approaches to biomarker identification to guide the use of small molecules and biologics in the context of an integrated translational research program.

9:05 Non-Clinical Approaches to Predict Single Agent vs. Combination Value and Clinical Development Strategies for Emerging Cancer Immunotherapies
James Smothers, Ph.D., Senior Director & Head, Discovery, Immuno-Oncology & Combinations DPU, GlaxoSmithKline
Non-clinical research studies historically support preclinical development and regulatory submission satisfaction and provide critical support of early clinical development hypotheses and clinical trial design including managing expectations of single agent efficacy or setting strategic vision for combination value through biology synergies. Moreover, following early clinical development milestones, an experimental medicine requires ongoing translational review of the clinical readouts beyond efficacy which in turn requires additional non-clinical analyses and experimental execution to drive results-based decision making and data-informed design of late stage clinical trials in anticipation and hope of drug approvals. Examples of non-clinical studies to support all of these activities will be reviewed including choice of experimental models and design.

9:35 Stress, Death, Immunity and Cancer Therapy
Lorenzo Galluzzi, Ph.D., Assistant Professor of Cell Biology Research, Radiation Oncology, Weill Cornell, Weill Cornell Medical College
Some anticancer agents trigger a form of cell death that can elicit an adaptive immune response. Such an "immunogenic cell death" relies on the activation of key stress responses in dying cells, and the consequent emission of danger signals that alert the organism of a threat. Unfortunately, this process is frequently suboptimal, calling for combinatorial strategies that attempt to restore the full-blown immunogenicity of cell death for therapeutic purposes.

10:05 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

TARGETING TUMOR MICROENVIRONMENT: APPROACHES AND TOOLS

10:50 Visualizing Human Immune-System within the Tumor Micro-Environment: Preclinical Imaging of Humanized Animal Models
Mario Perro, Ph.D., Group Leader, Pharmacology, Oncology, Roche
In this talk I will discuss the establishment of humanized mice for cancer immune-

therapy and optical imaging of human mirco-environment within humanized mice. I will also discuss approaches and parameters to study cancer immune-therapies within microscopy.

11:20 Understanding the Tumor Microenvironment to Guide Decisions in the Clinic

Svetlana Sadekova, Ph.D., Senior Principal Scientist, Head of Translational Pathology Group, Merck

Nowadays, it is widely believed that tumor microenvironment is a key player in tumor progression and response to treatment. In this study, we will review the strategy and technology for preclinical and translational research of tumor microenvironment.

11:50 Isolation and Analysis of Tumor-Infiltrating Immune Cell Subpopulations

Sponsored by MACS Miltenyi Biotec

Olaf Hardt, Manager, Research & Development, Oncology, Miltenyi Biotec GmbH

Tumor-infiltrating leukocytes (TILs) constitute a fraction of highly complex and variable cell types inside the tumor tissue, complicating the analysis of individual subpopulations. In particular, the reliable detection of rare subpopulations is hampered by the detection limits of downstream assays. By combining optimized and automated tissue dissociation with specific pre-enrichment of TILs, we significantly increased the quality of data obtained from TIL characterization while reducing the overall time of analysis.

12:05 pm Tiny Bugs, Big Impact - The Microbiome Mediates Immunotherapy Efficacy - Using GF/ Gnotobiotic Models to Predict Response

Sponsored by Biomodels FAST. INNOVATIVE. PREDICTIVE.

Benjamin G. Cuiffo, Ph.D., Scientist, Biomodels, LLC

12:20 Luncheon Presentation: From Syngeneic to Humanized Mouse Models: Addressing the Needs for Novel Immunotherapies

Sponsored by Oncodesign BIOTECHNOLOGY

Jean-Francois Mirjolet, Ph.D., Technology Director, Oncodesign

Case studies will be presented: efficacy of surrogate immune checkpoint modulators, their combination in syngeneic models with biomarker study using intratumoral immune cell phenotyping and cytokine profile analysis as well as efficacy of bispecific antibodies or toxicity analyses and sorafenib metabolism using immune and liver humanized mouse models, respectively. Efficacy of human PD-1 targeting antibody evaluated in humanized mouse models will also be described.

12:50 Session Break

CASE STUDIES

1:40 Chairperson's Remarks

Serena Silver, Ph.D., Senior Investigator, Group Leader, Molecular Pharmacology, Novartis Institutes for BioMedical Research

1:50 Preclinical Development of a Novel Antibody-Directed Nanotherapeutic for Treatment of Solid Tumors

Vasileios Askoxylakis, M.D., Ph.D., Medical Director, Merrimack Pharmaceuticals

Liposomal nanotherapeutics offer several advantages over conventional anti-cancer drugs. Nanotherapeutics are characterized by a prolonged circulation time that leads to higher intratumoral accumulation of their cytotoxic payload and reduced toxicity. MM-310, is an antibody-directed nanotherapeutic designed to exploit the overexpression of EphA2 in tumors in order to deliver a highly effective chemotherapeutic to EphA2-overexpressing cancers.

2:20 Discovery and Characterization of HKT288, a Novel ADC Targeting CDH6 for the Treatment of Ovarian and Renal Cancer

Scott Collins, Ph.D., Scientist, Novartis Institutes for BioMedical Research, Inc

This presentation will discuss preclinical and translational efforts associated with an ADC program. The discovery and characterization of a novel ADC targeting CDH6 for the treatment of ovarian and renal cancer will be featured in this case study.

2:50 Challenges and Solutions in Subcutaneous Tumor Measurements Studies

Sponsored by Biopticon Discovery through imaging

Cem Girit, Ph.D., CEO, Biopticon Corporation

Accurate measurement of subcutaneous tumor volume, shape and color often depend on user technique and assumptions about shape. Generally caliper measurements rely on an over-simplistic shape model and a subjective decision of boundary location, which can lead to a more than 40% over-estimation of volume. We present an alternative methodology that circumvents these issues, handles irregularly shaped tumors and yields more information for future studies.

3:05 Initial Results from the Reproducibility Project Cancer Biology

Sponsored by Science EXCHANGE

Rachel Tsui, Staff Scientist, Science Exchange

The Reproducibility Project Cancer Biology is a collaboration between Science Exchange and the Center for Open Science (COS) to independently replicate key experiments from high-impact published cancer biology studies. The project was initiated in response to multiple reports published from the pharmaceutical industry indicating that more than 70% of published findings could not be reproduced.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

EX VIVO MODELS TO COMPLEMENT OR REPLACE *IN VIVO* MODELING

4:05 Novel Approaches to Cancer Cell Lines Design and Applications

Serena Silver, Ph.D., Senior Investigator, Group Leader, Molecular Pharmacology, Novartis Institutes for BioMedical Research

Growth of cancer cells in 2D format has been a workhorse of the cancer research world, enabling high throughput biology endeavors to identify new targets and new drugs. However, it is clear that we are sampling only a subset of cancer complexity in these models, for example by comparison of genomic characterization between primary tumors, xenografts, and cell lines grown in 2D. I will discuss our efforts to use methods such as co-culture and high content imaging of cells grown in 3D systems to assess if these can indeed "fill the gap" and advance oncology drug discovery.

4:35 A Predictive *in vitro* Preclinical Package to Assess Safety and Efficacy of ImmTAC™ molecules

Luise U. Weigand, Ph.D., Team Leader, Cell Biology, Immunocore, Ltd.

ImmTAC molecules are bispecific molecules comprising a pico-molar affinity T cell receptor fused to an anti-CD3 specific scFv that re-direct a potent T cell response towards target cells. Here we present our *in vitro* approach for preclinical assessment. The full *in vitro* package is used to evaluate safety and efficacy of ImmTAC molecules. The predictability of this process for our most advanced molecule IMCgp100, currently in a Phase I/II study, is discussed.

5:05 A Microfluidic Model for Lymphocyte-Tumor Interactions

Jeffrey Borenstein, Ph.D., Laboratory Technical Staff, Biomedical Microsystems, Draper

Here we describe a multiplex microfluidic chip that sustains tumor samples for periods of days to weeks in a microenvironment that provides precision dynamic control over oxygen gradients, temperature, and lymphocyte concentration. We demonstrate this system in the absence and the presence of compounds known to influence interactions between lymphocytes and tumors, toward application of the technology as a tool for the development of new immunotherapies and ultimately personalized cancer treatments.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

WEDNESDAY, JUNE 14

7:00 am Registration Open

7:30 Interactive Breakout Discussion Groups with Continental Breakfast

This session features various discussion groups that are led by a moderator/s who ensures focused conversations around the key issues listed. Attendees choose to join a specific group and the small, informal setting facilitates sharing of ideas and active networking. Continental breakfast is available for all participants. Details on the topics and moderators are available on the conference website.

CRISPR FOR ONCOLOGY DRUG DISCOVERY

8:35 Chairperson's Remarks

Danilo Maddalo, Ph.D., Lab Head, ONC Pharmacology, Novartis Institutes for BioMedical Research, Novartis Pharma AG

8:45 *In vivo* Generation of Oncogenic Signatures with the CRISPR/Cas9 System

Danilo Maddalo, Ph.D., Lab Head, ONC Pharmacology, Novartis Institutes for BioMedical Research, Novartis Pharma AG

Precise genomic editing leading to cancer formation represents a powerful tool in preclinical research. Generation of signatures resulting in cancer development/ resistance can be investigated and identified by *in vivo* delivery of the CRISPR/ Cas9 system. In this talk I will discuss the methods for generating preclinical animal models, the impact the 'genome editing revolution' has had, and the future applications for drug discovery and target identification.

9:15 Genome Editing and Gene Silencing in 3D Tumor Models: Opportunities for Overlap

Madhu Lal-Nag, Ph.D., Group Leader, Trans-NIH RNAi Facility, National Center for Advancing Translational Sciences, National Institutes of Health

The development of our 3D oncology RNAi and CRISPR/Cas9 screening platform is a step towards understanding the contribution of the tumor microenvironment to cancer cell viability. Our work aims to study and understand the role of tumor heterogeneity, clonal evolution, dormancy and cell death and in doing so, to bring forth some novel mechanisms of action that will help uncover novel druggable targets.

9:45 Engineered Swine Models of Cancer

Sponsored by Surrogen

Adrienne Watson, Ph.D., Senior Research Scientist, Surrogen, A Recombinetics Company

Huge advancements in technology to engineer genetically modified swine, who share immense genetic and physiological similarity to humans, have enabled the development of swine models of human cancer. We describe the latest innovations in cancer modeling in swine, including Recombinetics' model of Neurofibromatosis Type 1, to show the benefits of using swine as a large animal model in research and the vast applications and opportunities of swine models of cancer.

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

ADVANCING TRANSLATIONAL ONCOLOGY AND IMMUNO-ONCOLOGY WITH INDUSTRY-ACADEMIA COLLABORATION

11:00 Industry-Academia Collaboration in the Area of Tumor Models

Dana Cullen, Ph.D., Research Liaison, International Immuno-Oncology Network, Bristol-Myers Squibb

Collaboration is not an option but a necessity if the collective "we" desire to evolve our understanding of immuno-oncology to ultimately improve patient outcomes. Collaboration in preclinical science means greater transparency and sharing of translational tools and data collaborations with academia, federal and industry to further advance innovation in drug discovery and development.

11:30 CTI: Leveraging the Best of Industry and Academia to Create New Medicines

Leigh Zawel, Vice President and Site Head, New York and Boston Centers for Therapeutic Innovation, Pfizer

Pfizer's Centers for Therapeutic Innovation (CTI) were created 5 years ago to marry cutting edge drug discovery technology with innovative academic research with the goal of bringing new medicines to patients. This new model for developing drugs is now fully formed with a robust preclinical pipeline and multiple clinical programs. The underlying principles of how the model works will be reviewed as will a case study featuring a former collaboration.

12:00 pm Bridging Luncheon Presentation: Combination Immune Checkpoint Inhibitors for the Treatment of Solid Tumors in Humanized Mouse Models

Sponsored by discovery from charles river

Paula Miliani de Marval, Ph.D., Research Associate Director, Charles River

The increasing success and interest in cancer immunotherapy, there is a growing need for relevant preclinical models. Our studies with syngeneic tumors, using immune checkpoint inhibitors targeting CTLA-4 and PD-1, showed differential responses across

tumor types. We have evaluated the efficacy of these inhibitors on human tumor xenograft models implanted in CD34+ and PBMC humanized mice. Results from these studies shows significant tumor growth inhibition associated with T cell activation.

12:30 **Session Break**

1:00 **Coffee and Dessert in the Exhibit Hall with Poster Viewing**

1:30 **PLENARY KEYNOTE SESSION (click here for details)**

3:30 **Refreshment Break in the Exhibit Hall with Poster Viewing**

4:15 **Close of Conference**

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4th Annual

Tumor Models for Cancer Immunotherapy - Part 2

Assessing Antitumor Activity and Safety of Immunotherapy Programs

Recommended Event Package

Symposium June 12: New Tools for Disease Modeling

Conference June 13-14: Preclinical Models and Tools in Oncology - Part 1

Conference June 14-15: Tumor Models for Cancer Immunotherapy - Part 2

Short Course 10 June 14: Humanized Mouse Models for Preclinical Assessment of Cancer Immunotherapy

Symposium June 15-16: Nano-Delivery: Nucleic Acids, Cancer Immunotherapy and Beyond

WEDNESDAY, JUNE 14

11:00 am Registration

12:00 pm Bridging Luncheon Presentation: Combination Immune Checkpoint Inhibitors for the Treatment of Solid Tumors in Humanized Mouse Models

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12:30 Session Break

1:00 Coffee and Dessert in the Exhibit Hall with Poster Viewing

1:30 PLENARY KEYNOTE SESSION (click here for details)

3:30 Refreshment Break in the Exhibit Hall with Poster Viewing

PRECLINICAL STRATEGIES TO ADVANCE COMBINATION THERAPY

4:15 Chairperson's Opening Remarks

Gary C. Starling, Ph.D., Associate Vice President, MRL Biologics and Vaccines Discovery, Merck

4:25 KEYNOTE PRESENTATION: Increasing the Efficacy of Immunotherapy with Combinatorial Approaches

Gary C. Starling, Ph.D., Associate Vice President, MRL Biologics and Vaccines Discovery, Merck

Immunotherapy using monoclonal antibodies against the checkpoint inhibitors CTLA-4 and PD-1 have shown dramatic clinical success. To increase therapeutic efficacy in sensitive tumor types or to treat tumors that are resistant to targeting single immune check point inhibitors, combinations of agents are being evaluated. The rationale behind the selection of combination agents will be discussed along with examples of the impact of these combinations.

4:55 Strategic Approaches to Tackle Tumors That are Resistant to Immune Checkpoint Blockade

Brian B. Haines, Ph.D., Principal Scientist, Pharmacology, Merck

The success of immune checkpoint therapies such as CTLA-4 and PD-1 has revolutionized the treatment of many types of cancer. However, not all patients or cancer types respond to these therapies. In this presentation, strategies will be discussed on how to engage both the innate and adaptive arms of the immune response, with the goal to enhance both the breadth and depth of response to checkpoint blockade.

5:25 Novel Humanized Mouse Models in Immuno-Oncology: Applications and Production Consistency

Sponsored by TACONIC

Azusa Tanaka, Ph.D., Product Manager, Precision Research Model, Taconic Biosciences

Humanized mice reconstituted with human hematopoietic stem cells (HSC) mimic human immune responses, supporting translatable research into pathophysiology, immuno-oncology, and novel therapeutic methodologies. Reservations remain regarding reproducibility, HSC sourcing, and the stability of chimeric cells in

humanized mice. To address these concerns, Taconic presents data supporting the consistency, reliability, and chimeric ratios for over 1500 production huNOG (humanized NOG) and over 800 huNOG-EXL (humanized hGM-CSF/hIL-3 NOG) from Taconic production colonies.

5:55 Is Translation Even Necessary? Dose Prediction in the Absence of Validated Preclinical Models
Arijit Chakravarty, Ph.D., CEO, Fractal Therapeutics
This talk will discuss the problem of dose prediction for IO, with broader applicability beyond that.

6:25 Close of Day

6:30 Dinner Short Course Registration
Click here for details on short courses offered.

THURSDAY, JUNE 15

7:15 am Registration Open and Morning Coffee

7:30 Interactive Breakout Discussion Groups with Continental Breakfast
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LEVERAGING IMMUNOPHENOTYPIC FEATURES OF PRECLINICAL MODELS

8:35 Chairperson's Remarks
Zhao Chen, Ph.D., Investigator III, Exploratory Immuno-Oncology, Novartis Institute of Biomedical Research

8:45 Leveraging Immunophenotypic Features of Preclinical Models to Minimize Translational Failures
Mithun Khattar, Ph.D., Immuno-Oncology Lead, Cancer Pharmacology, Takeda Pharmaceuticals International
Syngeneic model systems that provide a wide array of B-cell, Myeloid cell and NK cell mediated tumor-immune milieus with a varying degree of T-cell involvement can help researchers to hone in on the MoA questions. Such a preclinical exploration can then help us with patient selection hypotheses and also potential combination scenarios. The future for IO therapy most likely is going to be targeting multiple facets of immune suppression which could be decided based on prior chemotherapies.

9:15 Genotype, Tissue Type and Tumor Microenvironment
Zhao Chen, Ph.D., Investigator III, Exploratory Immuno-Oncology, Novartis Institute of Biomedical Research
Cancer cells play key roles in shaping up the tumor microenvironment. Cancer genetic studies also tell us that much of the behavior of the tumor is dictated by genetic alterations and tissue origin. However, the link is missing between these tumor cell autonomous traits and their corresponding influence on tumor microenvironment. We are interested in charactering genotype and tissue type dependency of tumor microenvironment, and its relevance to treatment responses.

9:45 3D Spheroid Models of Fresh Patient Tumors: Ex vivo Analysis of Immune Microenvironment and Rational Combination Therapy
Sponsored by NILOGEN ONCOSYSTEMS
Soner Altiok, MD, Ph.D., CSO, Nilogen Oncosystems
Nilogen's 3D-EX℠ immuno-oncology platform utilizes fresh patient tumor tissue with intact tumor immune microenvironment. With the capability to analyze the intimate interactions between the immune system and components of cancer tissue we can accurately assess the therapeutic efficacy of drugs, identify rational drug combinations and develop companion diagnostics to facilitate biomarker-driven drug development efforts and personalized medicine while reducing the cost and risk of bringing a new drug to market.

10:00 Predictive Single-Cell Response Applied to Immuno-Oncology
Sponsored by isoplexis
Sean Mackay, CEO, IsoPlexis
IsoPlexis' technology enables improved targeting of complex immunotherapy treatments to cancer patients. Predictive biomarker data on TCR Engineered T-cell, CAR-T cell, and Checkpoint Inhibitor based therapeutics to detect a multiplexed range of functions from individual patient cells using proprietary bioinformatics will be discussed. These biomarkers indicate which patients will be responders and non-responders providing breakthrough insights for biopharma and translational centers in highly urgent areas of oncology today.

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

MODELING INNATE AND ADAPTIVE IMMUNITY

11:00 Pre-Clinical Models for the Evaluation of Novel Therapies and Anti-Tumor Immune Reponses
Marcus Bosenberg, M.D., Ph.D., Associate Professor of Dermatology and Pathology, Yale University, Co-Leader, Genomics, Genetics and Epigenetics Program, Yale Cancer Center
The success of immune therapies in cancer has underscored the need for accurate pre-clinical models for the evaluation of novel therapies. We have generated a series of genetically diverse syngeneic melanoma cells lines that form tumors following injection into immune competent C57Bl/6J mice. These models represent an ideal set of models for the study of cancer immunology and response to immune therapies.

11:30 Understanding the Biology and Clinical Translation of Syngeneic Mouse Models: What Do They Really Represent?
Elaine Hurt, Ph.D., Senior Scientist, MedImmune
Immune check-point inhibitors are changing the landscape of cancer patient care. While clinical efficacy is apparent, complete understanding of who benefits from IO therapy is still emerging. Preclinical models and the understanding of when these models are predictive of patient responses are evolving as well. I will present the work that MedImmune has conducted to characterize syngeneic models to understand where these particular models fit into the preclinical tool kit.

12:00 pm Preclinical Assessment of Combination of Erdafitinib and αPD-1 Antibody in FGFR2-Driven Genetically Engineered Mouse Model of Lung Cancer

Sangeetha Palakurthi, Ph.D., Head of Cancer Biology and Pharmacology, Belfer Center for Applied Cancer Science, Dana-Farber Cancer Institute

RTK inhibitors have significantly prolonged non-small cell lung cancer patient survival, but the development of resistance limits the durability of clinical response. One potential strategy to enhance the durability of response to targeted therapies, is to couple them with immunotherapy. We hypothesized that the small molecule inhibitor of FGFR, Erdafitinib- mediated tumor cell death and antigen release could prime and activate T-cell responses, and that combination with T-cell directed checkpoint blockade would further enhance antitumor immunity and enhance the durability of response. To test this hypothesis, we evaluated Erdafitinib in combination with αPD-1 antibody in an autochthonous FGFR2K660N/p53 mutant GEMM of lung cancer, in which tumors develop within the context of an intact immune microenvironment. Tumor bearing FGFR2K660N/p53 mutant mice treated with Erdafitinib with or without αPD-1 antibody showed significant tumor regressions compared to control and αPD-1 antibody monotherapy arms. We observed significant survival benefit in the combination group over Erdafitinib monotherapy. Further, immune profiling and biomarker studies suggested that the survival benefit with combination treatment in FGFR-driven lung cancer GEMM may be driven through simultaneous mechanisms of blocking tumor intrinsic FGFR pathway enhancement of anti-tumor immunity. Thus, data presented here provided a rationale for the combined clinical testing of JNJ-493 and PD-1 blockade in patients with FGFR-altered lung cancers.

12:30 Luncheon Presentation: Development of a Novel Phenotypic Platform for Therapy Selection and Understanding Biology of Tumor Immune Response

Sponsored by MITRA BIOTECH

Pradip Majumder, Ph.D., CSO, Mitra Biotech

1:00 Session Break

IMPLEMENTING TRANSLATIONAL APPROACHES

1:30 Chairperson's Remarks

Elaine Hurt, Ph.D., Senior Scientist, MedImmune

1:35 Co-Presentation: Translational Cancer Imaging for Drug Development and Precision Medicine

Quang-Dé Nguyen, Ph.D., Director, Lurie Family Imaging Center, Senior Scientist, Center for Biomedical Imaging in Oncology, Research Associate in Radiology, Harvard Medical School

Annick D. Van Den Abbeele, M.D., Associate Professor, Radiology, Harvard Medical School; Chief, Department of Imaging, Dana-Farber Cancer Institute; Founding Director, Center for Biomedical Imaging in Oncology (CBIO), Imaging, Dana-Farber Cancer Institute

This presentation will discuss several important issues in translational imaging such as Imaging probe developments for immune-oncology applications, imaging co-clinical trials, bidirectional interactions between the mouse hospital and the cancer center, interactions with pharmaceutical companies.

2:05 PANEL DISCUSSION: Mouse Models as a Driver for Translational Immuno-Oncology

Moderator: Elaine Hurt, Ph.D., Senior Scientist, MedImmune

- Modelling toxicity
- The tumour microenvironment
- Immune competency (immunocompromised versus competent models)

2:35 Coffee and Dessert Break in the Exhibit Hall. Last Chance for Poster Viewing.

T CELL THERAPY DEVELOPMENT AND PRECLINICAL ASSESSMENT

3:10 Chairperson's Remarks

Ian McNiece, Ph.D., Executive Consultant, CellMed Consulting

3:20 Preclinical Tumor Models for Evaluating Bispecific Redirected T-Cell Therapeutics

Divya Mathur, Ph.D., Principal Scientist, Pfizer Oncology

Strong evidence exists supporting the important role T-cells play in the immune response against tumors. Still, the ability to initiate tumor-specific immune responses remains a challenge. We have developed a bispecific protein engineered with enhanced pharmacokinetic properties to extend *in vivo* half-life, and designed to engage and activate endogenous polyclonal T cell populations via the CD3 complex in the presence of solid tumors expressing target antigens.

3:50 Modeling for Preclinical Assessment of Treg Adoptive Therapy

Simrit Parmar, M.D., Assistant Professor, Department of Stem Cell Transplantation, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

Tregs are essential for immune homeostasis by maintaining peripheral tolerance and inhibiting autoimmune responses and pathogenic tissue damage. Adoptive therapy with Tregs has been shown to be safe and effective in diseases such as graft vs. host disease, inflammatory bowel disease. The application of Treg adoptive therapy has tremendous promise to combat autoimmune diseases and inflammatory disorders.

4:20 Preclinical Tumor Models to Assess Efficacy of Cellular Immunotherapy Products that Include a Safety or Activation Molecular Switch

Eric Yvon, Ph.D., Director, CAR Program, Research and Development, Bellicum Pharmaceuticals, Inc.

The CID technology platform was designed to address the challenges of current cellular immunotherapies by enabling control over cellular activities and functions. Our CID platform consists of molecular switches triggered inside the patient by infusion of small molecule rimiducid. The "safety switch" is designed to lead to apoptosis, and the "activation switch" is designed to lead to activation and proliferation of immune cells.

4:50 Close of Conference

5:00 Symposia Registration

Click here for details

2nd Annual

Cancer Immunotherapy and Combinations

Next-Generation Agents and Combinations

Recommended Event Package

Conference June 13-14: Cancer Immunotherapy and Combinations

Conference June 14-15: Immuno-Oncology Targets

Symposium June 15-16: Nano-Delivery: Nucleic Acids, Cancer Immunotherapy and Beyond

TUESDAY, JUNE 13

7:00 am Registration Open and Morning Coffee

TARGETING TREGS AS A NOVEL IMMUNOTHERAPY APPROACH

8:25 Chairperson's Opening Remarks
Dario Vignali, Ph.D., Vice Chair and Professor of Immunology, University of Pittsburgh School of Medicine

8:35 Targeting Inhibitory Mechanisms in Cancer
Dario Vignali, Ph.D., Vice Chair and Professor of Immunology, University of Pittsburgh School of Medicine

The relative importance of different Treg suppressive mechanisms remains contentious. The signals that maintain Treg stability and potentiate their function remain obscure. The immune cell surface ligand semaphorin-4a (Sema4a) on conventional T cells and DCs, and the Treg-restricted receptor neuropilin-1 (Nrp1) interact to potentiate Treg function. Nrp1 ligation maintains Treg stability and function in highly inflammatory sites but is dispensable for the maintenance of immune homeostasis, highlighting Nrp1 as a potential immunotherapeutic target in cancer.

9:05 Dominant Antibody Antagonists: A Novel Immunotherapy Approach Targeting the TNFR2 Receptor for Direct Oncogene-Targeted Cancer Killing and Selective Tumor Treg Killing
Denise Faustman, M.D., Ph.D., Director, Immunobiology & Associate Professor, Medicine, Immunobiology, Massachusetts General Hospital, Harvard Medical School

Tumor necrosis factor receptor 2 (TNFR2) is a target protein with restricted expression on the most potent Tregs of the tumor infiltrate. We characterized the effect of TNFR2 antibody antagonists via TNFR2 in human samples from ovarian ascites compared to healthy controls, finding that dominant TNFR2 antagonists demonstrate tumor-specific Treg depletion. Further, blocking TNFR2 signaling with antagonist antibodies also creates a novel tool to possibly eliminate tumors expressing the TNFR2 oncogene and to more potently suppress Tregs.

9:35 KEYNOTE PRESENTATION: Instability of Helios-Deficient Tregs Is Associated with Conversion to a T-Effector Phenotype and Enhanced Antitumor Immunity
Harvey Cantor, M.D., Baruj Benacerraf Professor, Microbiology & Immunobiology; Chairman, Department of Cancer Immunology & Virology, Dana-Farber Cancer Institute

Here we report that selective Helios deficiency within CD4 Tregs leads to enhanced antitumor immunity through induction of an unstable phenotype and conversion of intratumoral Tregs into T effector cells within the tumor microenvironment. Induction of an unstable Treg phenotype is associated with enhanced production of proinflammatory cytokines by tumor-infiltrating but not systemic Tregs and significantly delayed tumor growth. Ab-dependent engagement of Treg surface receptors that result in Helios down-regulation also promotes conversion of intratumoral but not systemic Tregs into T effector cells and leads to enhanced antitumor immunity.

10:05 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

TOWARDS DISCOVERY OF NEW CHECKPOINT INHIBITORS

10:50 Development, Discovery and Details of the Oral Small Molecule Checkpoint Inhibitors, CA170 and CA327
David Tuck, M.D., CMO, Curis, Inc.

CA-170 is a first-in-class, orally-available, small molecule antagonist of the immune checkpoints PD-L1 and VISTA. CA-170 is currently undergoing investigation in a Phase I clinical trial in patients with advanced solid tumors and lymphoma. CA-327 is a first-in-class, orally-available, small molecule antagonist of the immune checkpoints PD-L1 and TIM3. CA-327 is currently undergoing IND-enabling studies, and the company expects to file an IND and initiate clinical testing of CA-327 in 2017.

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11:20 Profiling the Human Tumor Immune Landscape by Flow Cytometry and Gene Expression Analysis

Douglas Wilson, Ph.D., Associate Principal Scientist, Merck

The landscape of immune cells in human solid tumors is markedly heterogeneous. Tumor infiltrating lymphocyte-focused and tumor myeloid cell-focused immunophenotyping panels were developed to quantify the expression of immuno-modulatory receptors (IMRs) on the major human intratumoral immune cell populations by flow cytometry. The major cell populations were also sorted to confirm expression of IMRs by quantitative PCR. A profile of IMR expression in tumors of different origins will be presented.

11:50 Immunotherapy Potency Analysis Using Cellular Impedance

Sponsored by ACEA Biosciences, Inc.

Brandon Lamarche, Ph.D., Research Scientist, ACEA Biosciences

The kinetics of cancer cell destruction by diverse immunotherapies (NK cells, T cells, CARTs, oncolytic viruses, checkpoint inhibitors, bispecific antibodies, BiTEs, combination therapies) can be monitored quantitatively, automatically, and in a label-free manner using the impedance-based xCELLigence instruments. Examples of using this technology to analyze potency and serial killing capacity, and to optimize constructs/conditions for treating both liquid and solid tumor targets will be provided.

12:20 Enjoy Lunch on Your Own

12:50 Session Break

ADVANCES IN TARGETING AGONISTS AND THE TCR COMPLEX

1:40 Chairperson's Remarks

Shane Olwill, Ph.D., Vice President, Head of Development & Immuno-Oncology, Pieris Pharmaceuticals

1:50 Costimulatory T-Cell Engagement by PRS-343, a CD137 (4-1BB)/HER2 Bispecific, Leads to Tumor Growth Inhibition and TIL Expansion in Humanized Mouse Model

Shane Olwill, Ph.D., Vice President, Head of Development & Immuno-Oncology, Pieris Pharmaceuticals

We report potent costimulatory T-cell engagement of the immunoreceptor CD137 in a HER2-dependent manner, utilizing the CD137/HER2 bispecific PRS-343. In a humanized mouse model, PRS-343 displays dual activity based on monospecific HER2-targeting and bispecific, tumor-localized costimulation of CD137. Compared to known CD137-targeting antibodies in clinical development, this approach has the potential to provide a more localized activation of the immune system with higher efficacy and reduced peripheral toxicity.

2:20 TRuC™-T Cells: A Novel Kind of Engineered T Cells for Solid Tumors Exploiting the Signaling Power of the Complete T Cell Receptor

Robert Hofmeister, Ph.D., CSO, TCR² Therapeutics, Inc.

T cells expressing chimeric antigen receptors (CARs) have demonstrated impressive clinical benefit in certain hematological malignancies, but so far struggled in treating solid tumors. Here, we present a novel, non-MHC restricted therapeutic platform for engineering T cells (TRuC™) that is based on the direct fusion of antigen binding domains to subunits of the T cell receptor (TCR) complex. Unlike CARs, which do not integrate into the TCR, TRuC™ variants become part of the TCR and power T cells through the complex signaling cascade of the TCR. TRuC™-T cells potently killed tumor cells *in vitro* and thereby released less cytokines than respective CAR-T cells. In a Raji xenograft model, treatment with CD19-specific TRuC™ T cells was more efficacious than by 28zeta or 4-1BB CD19 CAR-T cells. Likewise, mesothelin-specific TRuC™-T cells were more potent than CAR-T cells. They uniquely eradicated solid tumors and protected mice from a later re-challenge. Our TRuC™ technology appears to be superior over CARs because it relies on the signaling power of the complete TCR.

2:50 Immuno-Oncology Trials - Next Generation Immune Monitoring Tools as a Way Forward

Thomas Oliver Kleen, Ph.D., Executive Vice President, Immune Monitoring, Epiontis GmbH

Monitoring both systemic changes in the blood and intra-tumoral leukocyte subpopulations will be crucial for identifying potential early surrogate markers of immunotherapy treatment success, ultimately paving the way to acceptable secondary endpoints for future Immuno-Oncology trials. Logistics, sample requirements, stability of cells in blood samples and tissue and cost considerations often preclude the use of standard monitoring assays. Novel technologies allow precise and robust quantitation of immune cells in all human samples from only small amounts of blood or tissue.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

TARGETED THERAPY AND CANCER IMMUNOTHERAPY COMBINATIONS

4:05 Epigenetic Priming with HDAC Inhibitor Resminostat Sensitizes Cancer to NK Cell-Based Immunotherapy

Svetlana Hamm, Ph.D., Head, Translational Pharmacology, 4SC Group

The initiation and progression of cancer is controlled by both genetic and epigenetic events. Since epigenetic processes concurrently and concertedly regulate many cellular processes, their deregulation can contribute to a significant part of cancer hallmarks, including the capacity to avoid recognition and elimination by the immune system. Epigenetic drugs were shown to increase immunogenicity and recognizability of tumors by immune cells, and there is growing evidence that combination of epigenetic modulators with different cancer immunotherapies results in increased clinical benefit. Here, I will focus on the combination of epigenetic modulation with NK cell-based immunotherapies by demonstrating that HDAC inhibitor resminostat sensitizes tumor cells to NK cell attack and increases anti-tumoral NK cell response *in vitro* as well as *in vivo*.

4:35 Covalent Irreversible USP7 Inhibitors for Cancer Immunotherapy

Suresh Kumar, Ph.D., Director, R&D, Progenra, Inc.

Tumors employ diverse strategies to suppress and evade the immune system's ability to recognize and destroy tumor cells. Presence of immune suppressive Foxp3+ regulatory T cells (Tregs) in the tumor microenvironment correlate with poor prognosis. Therefore, selective depletion of Tregs or impairment of Treg function is considered an attractive cancer immunotherapy approach. The deubiquitylase (DUB) USP7, a critical node in several cancer signaling pathways, is also essential for maintaining Treg functions. USP7 controls Treg function largely by regulating post-translational modification of Foxp3 and TIP60. Treg specific deletion of USP7 results in impairment of Treg functions and lethal autoimmunity in mice. Progenra has developed potent, selective covalent irreversible USP7 inhibitors that impair Treg functions *ex vivo* and *in vivo*. Most importantly, USP7 inhibitors exhibit powerful anti-tumor activity against

variety of syngeneic solid tumor models in immunocompetent mice. In addition, Progenra's USP7 inhibitors enhances the efficacy of anti-PD1 antibody and cancer vaccines. Along with the already established direct anti-tumor activities of USP7 inhibitors, these studies strongly suggest that USP7 inhibitors alone or in combination can improve the efficacy and expand the scope of cancer immunotherapy.

5:05 Inhibition of Kinase-Mediated Signaling in Myeloid Cells Suppresses Peritumoral Immune Suppression in Pancreas Cancer
Michael Burnet, Ph.D., Managing Director, Oncology Discovery, Synovo GmbH
We have identified small molecule kinase inhibitors that act on myeloid cells infiltrating tumors. These compounds promote the tumor-specific local secretion of interferon gamma leading to activation of CD8+ and NK cells. Tumor specificity appears to be due to a reliance on tumor co-signalling for target pathways to be expressed. The agents have safety margins in the range of 15-30x and are effective in very low doses in mice in the order of 3 to 5 mg/kg/day. The compounds synergize both cytotoxic agents and checkpoint antibodies.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

WEDNESDAY, JUNE 14

7:00 am Registration Open

7:30 Interactive Breakout Discussion Groups with Continental Breakfast
This session features various discussion groups that are led by a moderator/s who ensures focused conversations around the key issues listed. Attendees choose to join a specific group and the small, informal setting facilitates sharing of ideas and active networking. Continental breakfast is available for all participants. Details on the topics and moderators are available on the conference website.

NEXT-GENERATION CANCER VACCINES

8:35 Chairperson's Remarks
Brian Czerniecki, M.D., Ph.D., Chair and Senior Member, Department of Breast Oncology, Moffitt Cancer Center

8:45 Dendritic Cell Vaccination Enhances Immune Responses and Induces Regression of HER2pos DCIS Independent of Route
Brian Czerniecki, M.D., Ph.D., Chair and Senior Member, Department of Breast Oncology, Moffitt Cancer Center
Vaccination with HER2 peptide-pulsed DC1s stimulates a HER2 specific T-cell response. Anti-HER2 DC1 vaccination is a safe and immunogenic treatment to induce tumor-specific T-cell responses in HER2pos patients; immune and clinical responses were similar independent of vaccination route. The immune response in the sentinel lymph nodes, rather than in the peripheral blood, may serve as an endpoint more reflective of anti-tumor activity.

9:15 Optimal Vaccine Clinical Trial Design Incorporating Biologically Relevant Prognostic Markers
Christopher Heery, M.D., CMO, Bavarian Nordic
Therapeutic cancer vaccine development has suffered main failures over the years attributable to poor clinical trial design, poor patient selection, use of ineffective vaccines, and lack of agents to overcome resistance to T-cell-mediated tumor killing. The current landscape of immune-oncology offers the opportunity to overcome all of these factors. This talk will highlight opportunities in combinations with vaccines and one example selection of an ideal patient population based on a validated prognostic marker with mechanistic rationale for clinical evaluation of vaccine.

9:45 Shifting the Immune Balance in the Tumor Microenvironment with Antibody Blockade of Semaphorin 4D Enhances Immune Checkpoint Blockade
Elizabeth Evans, Ph.D., Vice President, Preclinical Research, Vaccinex
The protein Semaphorin 4D (SEMA4D) is highly expressed at the growing invasive margins of tumors, where it restricts the infiltration and migration of anti-tumor immune cells, such as antigen presenting cells and T lymphocytes, into the tumor microenvironment, indicating its role in promoting tumor growth. Antibody blockade reverses this effect, resulting in a shift in the immune balance and inhibition of tumor growth. Preclinical data supporting the combination of anti-semaphorin 4D (SEMA4D) with ipilimumab (anti-CTLA-4) or anti-PD-1/PD-L1 agents will be presented. The humanized IgG4 anti-SEMA4D was well tolerated in Phase I trials of patients with advanced refractory solid tumors, and Phase Ib/II studies of anti-SEMA4D in combination with immune checkpoint for the treatment of lung cancer and melanoma will be discussed.

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

RADIOTHERAPY, CHEMOTHERAPY AND IMMUNOTHERAPY COMBINATIONS

11:00 Rational Development of Combinations of Antiangiogenic Therapy with Immune Checkpoint Blockers Using Mouse Models of HCC and Cirrhosis
Kohei Shigeta, M.D., Ph.D., Research Fellow, Duda Lab, Steele Laboratories for Tumor Biology, Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School
Immunotherapies targeting the programmed death 1 (PD-1) co-inhibitory receptor have shown promise in hepatocellular carcinoma. One challenge will be incorporation of checkpoint blockade with existing, standard anti-angiogenic therapy. I will discuss several strategies addressing this important issue in liver cancer treatment using preclinical models.

11:30 Priming the Immune Microenvironment Using Neoadjuvant Therapy
Osama Rahma, M.D., Assistant Professor, Medicine, Center for Immuno-Oncology, Gastrointestinal Cancer Center, Dana-Farber Cancer Institute, Harvard Medical School
The effect of immune checkpoint inhibitors in combination with other modalities on the tumor immune microenvironment is a key component to understand their mechanism of action and resistance. We are currently investigating the combination of anti-PD-1 antibodies and chemoradiation therapy (CRT) in patients with pancreatic and rectal cancer. Testing this combined modality in the neoadjuvant setting will allow us to study the safety of this approach and its effect on the tumor microenvironment by comparing TILs and other effectors and suppressor immune cells and receptors pre- and post-treatment. In addition, we will study the correlation between these immune biomarkers and clinical outcomes.

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

12:30 Session Break

1:00 Coffee and Dessert in the Exhibit Hall with Poster Viewing

1:30 PLENARY KEYNOTE SESSION (click here for details)

3:30 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Close of Conference

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Inaugural

Immuno-Oncology Targets

Emerging Targets and Pathways for Cancer Immunotherapy and Combinations

Recommended Event Package

Short Course 5 June 12: Convergence of Immunotherapy and Epigenetics for Cancer Treatment

Conference June 13-14: Cancer Immunotherapy and Combinations

Conference June 14-15: Immuno-Oncology Targets

Short Course 10 June 14: Humanized Mouse Models for Preclinical Assessment of Cancer Immunotherapy

Symposium June 15-16: Nano-Delivery: Nucleic Acids, Cancer Immunotherapy and Beyond

WEDNESDAY, JUNE 14

11:00 am Registration

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

12:30 Session Break

1:00 Coffee and Dessert in the Exhibit Hall with Poster Viewing

1:30 PLENARY KEYNOTE SESSION (click here for details)

3:30 Refreshment Break in the Exhibit Hall with Poster Viewing

IMMUNE CHECKPOINT INHIBITORS: BEYOND PD-L1

4:15 Chairperson's Opening Remarks
Angie Inkyung Park, Ph.D., Senior Director, Immunotherapy and Stem Cells, OncoMed Pharmaceuticals

4:25 KEYNOTE PRESENTATION: The Selective IDO1 Inhibitor PF-06840003 Synergizes with Immune Checkpoint Blockade
Manfred Kraus, Ph.D., Director, In vivo Pharmacology, Tumor Cell Biology, Pfizer Oncology

4:55 Induction of Anti-Tumor Immunity by Targeting TIGIT in Solid Cancer
Angie Inkyung Park, Ph.D., Senior Director, Immunotherapy and Stem Cells, OncoMed Pharmaceuticals
Using OncoMed's rabbit MAP Trap platform, we have developed antibodies against checkpoint inhibitor TIGIT. Anti-TIGIT antibodies can block PVR ligand binding and inhibit TIGIT signaling. Anti-TIGIT antibody induced tumor specific T-cell responses, particularly of the Th1 type, increased antigen-specific CD8 response, and promoted a reduction in Treg-mediated immune-suppressive activity, leading to tumor growth suppression and generation of long-term immunological memory against tumors.

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5:25 State-of-the-Art Tissue Expression Analysis Platform for Multiplexed Immuno-Oncology Target and Biomarker Development
Christopher Bunker, Ph.D., Vice President, Business Development, Advanced Cell Diagnostics, Inc.
RNAscope is clinically validated and enables multiplexed tissue analysis of I-O, checkpoint and immune cell markers in human and animal tissues. RNAscope is the most sensitive platform for tissue-based expression analysis. There are 14,000 assays in use and 4 oncology CDx in development. The following applications will be discussed: detection of any mRNA in FFPE tissues; multiplexing to 4-plex; isoform-specific detection; point mutations and CRISPR edit validation; CAR-T lentiviral detection.

5:55 The Third Group of the B7-CD28 Immune Checkpoint Family
Xingxing Zang, Ph.D., Associate Professor, Microbiology and Immunology & Medicine, Albert Einstein College of Medicine
CTLA-4 and the PD-1/PD-L1 pathway are current focuses in cancer immunotherapy. This presentation will discuss other new immune checkpoints for future human cancer immunotherapy.

6:25 Close of Day

6:30 Dinner Short Course Registration
Click here for details on short courses offered.

THURSDAY, JUNE 15

7:15 am Registration Open and Morning Coffee

7:30 Interactive Breakout Discussion Groups with Continental Breakfast
This session features various discussion groups that are led by a moderator/s who ensures focused conversations around the key issues listed. Attendees choose to join a specific group and the small, informal setting facilitates sharing of ideas and active networking. Continental breakfast is available for all participants. Details on the topics and moderators are available on the conference website.

IMMUNOMODULATORY AGONIST TARGETS

8:35 Chairperson's Remarks
Mary Woodall-Jappe, Ph.D., Director, US Discovery Biology-Oncology, Eisai

8:45 EP4 Antagonism in Combination Immuno-Oncology Therapeutic Approaches
Mary Woodall-Jappe, Ph.D., Director, US Discovery Biology-Oncology, Eisai
PGE2 in the tumor microenvironment contributes to the accumulation of immunosuppressive myeloid cells by interacting with the EP4 receptor on newly arriving monocytes, skewing their development into MDSCs and TAMs. The EP4 antagonist E7046, now in Phase I/Ib trials, inhibits this interaction and enhances formation of a more favorable anti-tumor immune milieu. This approach combines well pre-clinically with T cell-directed immunotherapies such as checkpoint inhibitors in boosting anti-tumor immunity.

9:15 Activation of Myeloid IL-27 Production Initiates 4-1BB Agonist Hepatotoxicity
Michael A. Curran, Ph.D., Assistant Professor, Immunology, The University of Texas MD Anderson Cancer Center
Despite impressive efficacy against both hematologic and solid tumors and an ability to suppress adverse events associated with checkpoint blockade, the development of 4-1BB agonist antibodies has been stymied by dose-limiting liver toxicity. We have defined the precise cellular and molecular mechanisms driving 4-1BB agonist hepatotoxicity, and, in so doing, have revealed multiple potential approaches to separate off-target liver toxicity from on-target anti-tumor immunity.

9:45 *In vitro* Characterization and *in vivo* Anti-Tumor Efficacy of a Novel STING Agonist, MK-1454
Saso Cemerski, Ph.D., Principal Scientist, Merck Research Labs

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

RATIONAL COMBINATION IMMUNOTHERAPY

11:00 Exploring Combinations for Anti-PD-1 Cancer Therapy
Jürgen Moll, Ph.D., Director, Pharmacology and Translational Research, Boehringer Ingelheim
The checkpoint signaling pathway involving the PD-1 and PD-L1/2 axis has been critical in advancing cancer immunotherapy. However, many patients do not benefit from checkpoint modulator monotherapy. Hence, combinations with other anticancer drugs have the potential to improve response rates. We explored the combination of anti-PD-1 antibodies with molecular targeted therapies in syngeneic tumor models, and examples are shown of how compounds, expected to be rather tumor targeting, can modulate the immune response and work synergistically with PD-1 antibodies.

11:30 Enhanced Anti-Tumor Effect of Combination Therapy with NHS-muIL12 and Anti-PD-L1 Antibody (Avelumab) in a Preclinical Cancer Model
Chunxiao Xu, Ph.D., Principal Scientist, Immuno-Pharmacology and Immuno-Oncology, EMD Serono
NHS-IL12 is an immunocytokine designed to target tumor necrotic regions to deliver IL12 into the tumor microenvironment. Avelumab, a fully human anti-PD-L1 monoclonal antibody, has shown anti-tumor activity in various malignancies in clinical trials. In the preclinical studies, combination treatment with NHS-muIL12 and avelumab generated an enhanced anti-tumor effect relative to either monotherapy, indicating combination of therapies that target distinct immune pathways may be a promising strategy to improve anti-tumor efficacy.

12:00 pm NKTR-214 plus NKTR-262, a Scientifically-Guided Rational Combination Approach for Immune Oncology
Jonathan Zalevsky, Ph.D., Vice President, Biology & Preclinical Development, Nektar Therapeutics
NKTR-214 is an experimental therapy designed to stimulate cancer-killing lymphocytes in the body by biased cytokine signaling through CD122 receptors found on the surface of CD8+ effector T cells and Natural Killer (NK) cells. NKTR-262 is a novel chemical agent that targets the myeloid immune compartment. The combination of these two agents provides a rational comprehensive approach to engage multiple immune pathways to create an optimal immune oncology therapy.

12:30 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:00 Session Break

TARGETING THE TUMOR MICROENVIRONMENT

1:30 Chairperson's Remarks
Daniela Cipolletta, Ph.D., Lab Head, Investigator III, Immuno-Oncology, Novartis Institutes for BioMedical Research

1:35 TME Modulation by Large and Small Molecule: A Lesson from the Anti-PD-1+CSF1R Inhibitor Combination
Daniela Cipolletta, Ph.D., Lab Head, Investigator III, Immuno-Oncology, Novartis Institutes for BioMedical Research
We have used murine models to monitor the immune response upon perturbation of the tumor microenvironment with large and small molecules. This approach has enabled our understanding of tumor-induced immune modulation and the identification of novel combinatorial strategies in specific cancer settings.

2:05 Activation of the STING Pathway to Induce Tumor Immunity
Chudi Ndubaku, Ph.D., Associate Director, Organic Synthetic Chemistry, Aduro Biotech
Production of host type I interferon within the tumor microenvironment, mediated

by the Stimulator of Interferon Genes (STING) pathway, leads to priming of tumor-specific immunity. Therapeutic activation of STING through intratumoral (IT) administration of a novel synthetic CDN derivative (ADU-S100) results in anti-tumor efficacy in mouse syngeneic tumor models. Mechanisms of ADU-S100-induced tumor regression and the design of an ongoing Phase I clinical study with ADU-S100 will be presented.

2:35 Coffee and Dessert Break in the Exhibit Hall. Last Chance for Poster Viewing.

3:20 Co-Cultures of Primary 3D Tumor Spheroids and Immune Cells for Preclinical Efficacy Testing of Cancer Immuno- and Combination Therapy

Christian Schmees, Ph.D., Head of Tumor Biology, Molecular Biology Department, NMI Natural and Medical Sciences Institute at the University of Tübingen

Cellular models closely resembling patient tumors and their interactions with different aspects of the antitumor immune response are highly needed for predicting the efficacy of novel approaches in cancer immunotherapy alone and in combination with other treatments. I will present data from our co-culture model of primary 3D tumor spheroids with T and NK cells allowing for analysis of immune cell infiltration as well as cytotoxicity in response to antigen stimulation and/or compound treatment.

3:50 Profiling the Evolution of Immune Phenotypes in Human Cancer with Low-Input Single-Cell RNA Sequencing

Sanjay Prakadan, Ph.D., The Shalek Lab, MIT Institute for Medical Engineering & Science

Immune cell interactions and phenotypes hold significant diagnostic and prognostic value in the treatment of human cancer. The advent of single-cell technologies affords new opportunities to interrogate these complex biological systems to study these interactions and states with unprecedented resolution. Here, we present a novel platform to perform single-cell RNA sequencing on low-input clinical samples, and demonstrate its utility to infer the cell types, states, and circuits of the immune system in human cancer.

4:20 Close of Conference

5:00 Symposia Registration

Click here for details

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25 YEARS
A Division of Cambridge Innovation Institute

SCREENING

A combination of technical innovation and scientific knowledge has led to the creation of a diverse set of screening tools that can be creatively used for the discovery and validation of novel drug targets and compounds, and for screening adverse drug events. An interesting mix of talks, discussions and courses relating to Phenotypic Screening, Chemical Biology, 3D Cellular Models, CRISPR-based Gene Editing, Disease Modeling and Pluripotent Stem Cells, are being offered at the World Preclinical Congress this year. Join pharmaceutical, biotech, and academic stakeholders to learn from their experiences and expertise on how to best utilize these novel screening technologies.

June 12

SYMPOSIUM: New Tools for Disease Modeling

June 13-14

Phenotypic Screening and Chemical Biology

CRISPR for Target Discovery

June 14-15

3D Cellular Models

FINAL WEEKS
TO REGISTER

COVER
CONFERENCE-AT-A-GLANCE
PLENARY KEYNOTE PROGRAM
MEDICINAL CHEMISTRY
ONCOLOGY
SCREENING
DISCOVERY & DEVELOPMENT
SYMPOSIA
SHORT COURSES
TRAINING SEMINAR
SPONSOR & EXHIBIT OPPORTUNITIES
HOTEL & TRAVEL INFORMATION
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4th Annual

Phenotypic Screening and Chemical Biology

Modern Approaches toward Phenotypic Screening and Targeting Deconvolution

Recommended Event Package

Symposium June 12: iPS Cells for Disease Modeling and Drug Discovery
Conference June 13-14: Phenotypic Screening and Chemical Biology
Conference June 14-15: 3D Cellular Models
Symposium June 15-16: Property-Based Drug Design

TUESDAY, JUNE 13

7:00 am Registration Open and Morning Coffee

MODERN PHENOTYPIC DRUG DISCOVERY

8:25 Chairperson's Opening Remarks
Matt Lucas, Ph.D., Director, Medicinal Chemistry, Yumanity Therapeutics

8:35 Yeast-Based Phenotypic Screening to Identify Brain Penetrant Inhibitors
Matt Lucas, Ph.D., Director, Medicinal Chemistry, Yumanity Therapeutics
Phenotypic screening has undergone a revival in the last decade. In this presentation, I will share some of our learnings from Yumanity's phenotypic screening platform to bias towards the identificatation of scaffolds that are brain penetrant with potential utility to treat protein misfolding diseases.

9:05 Phenotypic Drug Discovery in SMA: Parallel Efforts in Preclinical Development and Target Identification
Atwood Cheung, Ph.D., Investigator III, Global Discovery Chemistry, Novartis Institutes for BioMedical Research, Inc.
Phenotypic drug discovery has been a mainstay of drug development, enabling the discovery of numerous therapeutic molecules. A key challenge, however, has always been the determination of the efficacy target. A recent success story will be presented, where our team progressed a small-molecule preclinical candidate to treat Spinal Muscular Atrophy (SMA) while simultaneously elucidating the molecular mechanism of action.

9:35 Massive Parallelization of Rare Disease Drug Discovery
Ronald Alfa, Ph.D., Director, Translational Biology, Recursion Pharmaceuticals
I will discuss methods to leverage computational biology to perform phenotypic screens in parallel for discovery of therapeutic candidates for dozens of rare genetic diseases.

10:05 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

CHEMOGENOMICS ENABLING PHENOTYPIC DRUG DISCOVERY

10:50 Linking High-Throughput Screens to Identify MOAs and Novel Inhibitors of Mycobacterium Tuberculosis Dihydrofolate Reductase
John Santa Maria, Ph.D., Research Fellow, Cheminformatics, Merck
I describe a framework for joining high-throughput phenotypic and target-based data coupled with machine learning to identify efficacy targets of bioactive compounds. We validate this approach on data from a set of 55,000 compounds in 24 historical Merck antibacterial phenotypic screens and 636 bacterial targets screened in high-throughput biophysical binding assays. Our models revealed relationships between phenotype, target, and chemotype and recapitulated mechanisms for known antibacterials.

11:20 Chemical Biology Informatic Approaches to Enable High-Throughput Screening: Focused Compounds Sets, Target Enrichment, and Hit Expansion
Peter Kutchukian, Ph.D., Associate Principal Scientist, Cheminformatics, Merck
A suite of integrated data repositories and tools have been developed to empower phenotypic screening at our company. A chemogenomics database CHEMGENIE that captures compound-target interactions has been implemented by integrating and harmonizing internal and external data sources, and an algorithm to identify tool compounds has been designed to harness this information. We describe use cases of screening such tools in phenotypic screens, and the ability to identify targets and pathways that perturb a phenotype through "target enrichment".

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Sponsored by Promega

11:50 Kinome-Wide Profiling of Target Engagement and Residence Time in Living Cells Using NanoBRET
Matthew Robers, Senior Research Scientist, Research & Development, Promega Corporation
NanoBRET is the first technology enabling quantitative, real-time assessment of intracellular compound engagement without disruption of cell membrane integrity. NanoBRET enables profiling of intracellular selectivity for clinically relevant kinase inhibitors against >200 selected full-length protein kinases. Of note, residence time analysis via NanoBRET reveals surprisingly durable binding for various tyrosine kinase inhibitors in living cells.

12:20 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:50 Session Break

MOA AND TARGET DECONVOLUTION STRATEGIES

1:40 Chairperson's Remarks
Ceren Korkut, Ph.D., Scientist, Chemical Biology, Biogen

1:50 What Is Your MOA? Target Deconvolution of a Phenotypic Screen
Ceren Korkut, Ph.D., Scientist, Chemical Biology, Biogen
Cellular phenotypic screens are a powerful way to uncover novel biology and discover druggable targets and chemical matter. One of the main bottlenecks for this approach, as opposed to target-based screening, is determining the mechanism of action of lead hits. Our group is developing approaches to determine the MOA of lead hits. These approaches include using proteomics, RNAi, RNA-seq, chemical probes, and *in silico* studies.

2:20 Selective Downregulation of JAK2 and JAK3 by an ATP-Competitive Pan-JAK Inhibitor
Jing (Jeannie) Li, Ph.D., Senior Scientist, Medicinal Chemistry Chemical Biology, Pfizer
PF-956980 has been used previously as a JAK3-selective chemical probe in numerous cell-based experiments. Here, we report that not only is PF-956980 a pan-JAK ATP-competitive inhibitor but it also causes selective reduction of endogenous JAK2 and JAK3 protein levels in human primary immune cells (in a time-dependent manner), leaving the other JAK family members (JAK1 and TYK2) unchanged. We found that PF-956980 selectively downregulated JAK2 and JAK3 mRNA, corresponding to changes observed at the protein level. This work highlights therapeutic opportunities for the development of pharmacological inhibitors that also modulate the expression of their cognate binding proteins.

Sponsored by PsychoGenics

2:50 High Throughput *In Vivo* Phenotypic Drug Discovery
Emer Leahy, Ph.D., President & CEO, PsychoGenics Inc.
PsychoGenics' phenotypic screening approach employs SmartCube®, an *in vivo*, high throughput, behavioral testing platform that combines robotics, computer vision, and machine learning algorithms to capture and analyze data that can be distilled into a "behavioral signature" for a compound. Working in partnership with pharmaceutical/biotech companies, PsychoGenics has been instrumental in identifying therapeutic potential for novel first-in-class compounds resulting in several compounds now in clinical trials or advanced preclinical development.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:05 New Chemical Biology Technologies for Target Identification and High-Throughput Screening: Chemical Glycobiology and Beyond
Henning Stockmann, Ph.D., Senior Scientist, Chemical Biology, AbbVie Inc.
Improved strategies for reliable drug target identification and target engagement studies are urgently needed, whereby cell-surface receptors present particular challenges. We have developed new chemical biology approaches to link probes and reporters to cell-surface receptors and cytosolic proteins in live cells. Our sugar-based cell-surface engineering methods not only enable receptor visualization, isolation, and proteomics-based characterization, but also facilitate target engagement studies and high-throughput ligand binding assays in intact cells.

4:35 Prioritizing Chemical Tool Compounds for Phenotypic Drug Discovery
Yuan Wang, Ph.D., Investigator III, Chemical Biology & Therapeutics, Novartis Institutes for BioMedical Research
The use of potent and selective chemical tools (probes) in phenotypic screens can help drive elucidation of underlying biological processes. The identification of such compounds is nontrivial and biases towards famous compounds should be avoided. Here we investigated large-scale potency data integrated from diverse sources to create a compound tool score, which we used to systematically rank tool compounds.

5:05 Chemical Synthesis of Activity Based Probes and Inhibitors
Ian Foe, Ph.D., Research Scientist, Bogyo Lab, Department of Pathology, Stanford University School of Medicine

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

WEDNESDAY, JUNE 14

7:00 am Registration Open

7:30 Interactive Breakout Discussion Groups with Continental Breakfast
This session features various discussion groups that are led by a moderator/s who ensures focused conversations around the key issues listed. Attendees choose to join a specific group and the small, informal setting facilitates sharing of ideas and active networking. Continental breakfast is available for all participants. Details on the topics and moderators are available on the conference website.

TOOLS AND TECHNIQUES FOR TARGET ID AND VALIDATION

8:35 Chairperson's Remarks
Kieran F. Geoghegan, Ph.D., Research Fellow, Pfizer Worldwide Research

8:45 A Probe-Centered Analysis of γ-Secretase Photolabeling Reveals the Binding Site of Avagacestat

Kieran F. Geoghegan, Ph.D., Research Fellow, Pfizer Worldwide Research

Photoaffinity labeling frequently identifies the protein targets of drugs, but specifying their binding sites by this method is challenging. In photolabeling γ-secretase, a target in Alzheimer's disease, our previous efforts to detect probe-labeled peptides were unsuccessful. Reconsideration of the chromatographic properties of our probes led us to design benzophenone derivatives of the clinical candidate avagacestat incorporating a cleavable link between the photoprobe and biotin. The intention was to minimize the hydrophobicity of labeled peptides. Competition effects showed that γ-secretase was selectively photolabeled, and proteomic LC-MS detected a peptide derivatized at Leu-282 of presenilin-1. The results indicated that avagacestat binds near the enzyme's active site, were supported by results from molecular dynamics, and aligned well with emerging data from cryo-electron microscopy.

9:15 Selected Poster Presentation: HepatoPearls: 3D Liver Micro-Tissues for High-Throughput Drug-Drug Interaction Assays

Raif Eren Ayata, Ph.D., MSc, Topical Drug Delivery/Formulations and Percutaneous Absorption Specialist & Postdoctoral Fellow, Skin/Liver Tissue Engineering, PSL Research University

9:30 Selected Poster Presentation: Validation of a Cellular BRET Platform Using the Bruton's Tyrosine Kinase Model System for High-Throughput Cellular Target

Charu Chaudhry, Ph.D., Senior Research Investigator, Mechanistic Biochemistry, Lead Discovery & Optimization, Bristol-Myers Squibb

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

11:00 Proteomics-Based Methods for In-Depth Analysis of Key Molecular Events in Tumorogenesis

Jarrod Marto, Ph.D., Associate Professor, Department of Biological Chemistry and Molecular Pharmacology, Dana-Farber Cancer Institute

Proteomics-based methods provide a highly parallel readout of multiple biologically relevant events in a single experiment. Collectively, these data provide a detailed view of key molecular mechanisms in cancer initiation and progression and can also facilitate drug target discovery and improved characterization of small molecule-based therapeutics.

11:30 CASE STUDY: Chemical Biology Tools for Target Identification and Target Engagement Studies

Hua Xu, Ph.D., Principal Scientist, Pfizer

Phenotypic screening is a major source for the discovery of first-in-class small molecule drugs, thanks to its 'target agnostic' feature. Recent technology advances and utilization of patient-derived cells have facilitated the design of sophisticated phenotypic assays that recapitulate the disease relevant biology. However, it remains quite challenging to elucidate the mechanism of action and identify the target(s) for compounds of interest from these assays. In this talk, I will present our efforts to use various tools to identify and subsequently validate the target for a phenotypic program.

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

12:30 Session Break

1:00 Coffee and Dessert in the Exhibit Hall with Poster Viewing

1:30 PLENARY KEYNOTE SESSION (click here for details)

3:30 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Close of Conference

3rd Annual

CRISPR for Target Discovery

Exploiting CRISPR/Cas9 for Finding New Targets and Disease Pathways

Recommended Event Package

Short Course 6 June 12: How to Best Utilize 3D Spheroids and CRISPR Assays in Oncology

Conference June 13-14: CRISPR for Target Discovery

Short Course 8 June 14: Applications of Functional Screening Using CRISPR and RNAi

TUESDAY, JUNE 13

7:00 am Registration Open and Morning Coffee

CRISPR-DERIVED CELL LINES AND KNOCK-OUTS FOR DISEASE MODELING

8:25 Chairperson's Opening Remarks
Madhu Lal-Nag, Ph.D., Group Leader, Trans-NIH RNAi Facility, National Center for Advancing Translational Sciences, National Institutes of Health

8:35 Functional Genomics in Dissecting Skin Malignancy
Yejing Ge, Ph.D., Postdoctoral Fellow, Laboratory of Dr. Elaine Fuchs, Department of Mammalian Cell Biology and Development, Rockefeller University
Tissue stem cells govern tissue regeneration and wound-repair. Tumors often hijack normal cellular programs and exploit them for malignancy. Here I use CRIPSR combined with in utero lentiviral injection to knockout candidate genes specifically in the skin epidermis, and interrogate their functions during wounding and tumorigenesis. In doing so, I unravel stem cell plasticity as a molecular mechanism underlying "tumors are wounds that do not heal."

9:05 Using CRISPR/Cas9 to Create a Collection of GFP-tagged Human iPSC Lines to Model Cell Organization and Dynamics
Ru Gunawardane, Ph.D., Director, Stem Cells and Gene Editing, Allen Institute for Cell Science
The Allen Institute for Cell Science is creating a dynamic visual model of hiPSC organization by utilizing the CRISPR/Cas9 system to endogenously label major cellular organelles with a fluorescent protein. We will present the methodologies used for endogenous gene tagging, screening for precise editing, and cell biological and genomic QC. We will also discuss the potential applications of these lines for basic science and disease modeling.

9:35 Modeling Human Pain Using CRISPR/Cas9 Genome Editing
Yung-Chih Cheng, Ph.D., Postdoctoral Research Fellow, F.M. Kirby Neurobiology Center, Boston Children's Hospital, Department of Neurobiology, Harvard Medical School
Pain is a critical sensation allowing people to escape from damage. Scientists have discovered mutations in Nav1.7 channel leads to pathologies associated with exaggerated pain or insensitivity to pain. Here, we use CRISPR technology to generate pathological pain model in mouse and in hiPSC derived sensory neuron based on Nav1.7 channel. These engineered pain models enabled us to mimic the clinical aspects of the genetic forms of pain conditions and provide novel therapeutics for pain disorders in humans.

10:05 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

10:50 Permanent Correction of Diverse Dilated Cardiomyopathy Mutations by Genome Editing
Chengzu Long, Ph.D., Assistant Professor, Division of Cardiology, New York University School of Medicine
Dilated cardiomyopathy (DCM) is one of the most common causes of heart failure, which affects over 38 million patients worldwide. Gene mutations are major causes of idiopathic DCM. To address several challenges for clinical applications of gene editing of DCM *in vivo*, we performed CRISPR/Cas9-mediated gene editing on representative iPSC (induced pluripotent stem cells)-derived cardiomyocytes from multiple DCM patients and restored their function.

11:20 Modeling Endothelial Dysfunction in LMNA-Related Dilated Cardiomyopathy
Nazish Sayed, M.D., Ph.D., Instructor, Cardiovascular Institute, Stanford University School of Medicine
The mechanisms that underlie "cardiolaminopathy" remain elusive. Although LMNA mutations are known to induce endothelial dysfunction, little is known about the EC-specific phenotype. Our data shows that iPSC-ECs derived from LMNA-mutated

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patients exhibit decreased EC functionality. Genome editing of iPSCs enabled us to recapitulate the EC-disease phenotype to dissect the effects of LMNA mutations. This study is a first step towards understanding cardiolaminopathy by modeling endothelial dysfunction.

11:50 Driver-Map™ Genome-Wide Expression Profiling Solution for Biomarker Discovery

Sponsored by CELLECTA Discovery is *Yours*.

Paul Diehl, Ph.D., COO, Cellecta, Inc.

Cellecta's Driver-Map Genome-Wide Expression Profiling assay combines the sensitivity of multiplex PCR with the dynamic range of NGS. The approach achieves 100-fold more sensitivity than RNAseq over a greater dynamic range. Just 10 pg of total RNA shows over 5 orders of magnitude variation in gene expression levels. Applications include analysis of immune cell infiltration, identification of active pathways in tumor and xenograft samples, and profiling of biomarkers from blood.

12:20 pm Luncheon Presentation: High Throughput Screening: Best Technology and Practices

Sponsored by MilliporeSigma

Andrew Ravanelli, Ph.D., Senior Research & Development Scientist, Genome & Epigenome Editing, MilliporeSigma

CRISPR Cas9 nucleases have revolutionized the field of gene editing and high-throughput lentiviral screens continue to hold ever-increasing promise for both basic research and development of future therapies to benefit human health. Even with such powerful technologies at hand, researchers new to the field may find screening of multiple targets to be challenging and time-consuming. MilliporeSigma seeks to share best approaches learned and methods applied over our years of genome editing experience. Here, we will detail the planning steps and workflow overview essential to a successful lentiviral screening experiment. We also present experimental data from the Sanger Wellcome Trust, first of its kind, genome-wide, truly arrayed guide RNA screening libraries for CRISPR-Cas9. Finally, we will compare screening technologies and describe multiple, flexible options for screening gene targets, from small gene panels to entire genomes.

12:50 Session Break

CRISPR FOR FUNCTIONAL AND PHENOTYPIC SCREENS

1:40 Chairperson's Remarks

John Doench, Ph.D., Associate Director, Genetic Perturbation Platform, Broad Institute of Harvard and MIT

1:50 Pooled Screens with CRISPR Technology - Don't Miss Out

John Doench, Ph.D., Associate Director, Genetic Perturbation Platform, Broad Institute of Harvard and MIT

The ease of programming Cas9 with an sgRNA presents an abundance of potential target sites, but the on-target activity and off-target effects of individual sgRNAs can vary. We will discuss improved models that allow for increased on-target efficacy, metrics for understanding potential off-target sites, and how the combination of these findings can be used to design optimal libraries for genetic screens.

2:20 Development of New CRISPR/Cas9-based Tools to Study Drug Interactions Through Knockout and Directed Evolution

Michael Bassik, Ph.D., Assistant Professor, Department of Genetics, Stanford University

We have compared genome-wide shRNA and CRISPR/Cas9 screens to identify novel drug targets, with highly complementary results. By systematic pairwise expression of sgRNAs directed against known drug targets, we identify rare synthetic lethal drug combinations for leukemia in ultra-high-throughput. Finally, we have developed a strategy to use dCas9 to recruit hyperactive AID*Δ, mutagenizing the endogenous target of a drug to map its target binding.

2:50 Arrayed High-Throughput Screening with Synthetic crRNA Libraries

Sponsored by Dharmacon™ part of GE Healthcare

Melissa Kelley, Ph.D., Senior Research & Development Leader, Dharmacon, part of GE Healthcare

In large-scale screening studies, one-well-per-gene arrayed synthetic crRNA libraries have an advantage over pooled CRISPR screens for endpoint assays and high-content imaging. We will describe an arrayed synthetic crRNA library screen in a Cas9-expressing cell cycle reporter cell line where we utilized high-content, multiparametric analysis. The experimental design, assay optimization and analysis employed for hit identification, stratification, and validation to successfully identify cell cycle regulation genes will be described.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:05 Identification of Drug Response Modifiers Using Pooled CRISPR Screening

Roderick Beijersbergen, Ph.D., Group Leader, Netherlands Cancer Institute and Head, NKI Robotics and Screening Center

The CRISPR-Cas9 system has shown to be very efficient in disruption of genes allowing for the comprehensive identification of genes required for cell survival and proliferation. Extending this platform with tools to abrogate the expression of two or more genes simultaneously allows for the identification of genetic interactions associated with synthetic sick of synthetic lethal phenotypes. The identification of genetic interactions in the context of cancer specific genomic alterations will be presented.

4:35 High Efficiency Synthetic sgRNA for CRISPR

Sponsored by SYNTHEGO

Kevin Holden, Ph.D., Head, Synthetic Biology, Synthego

Synthego demonstrates, through a collaborative effort with key researchers utilizing CRISPR, that synthetic 100-mer sgRNA produces consistent and superior genome editing in a variety of cell types including adherent mammalian cell lines, primary T-cells, iPSCs and model organism embryos. This technology will help to enable successful and consistent genome editing for both basic research models and for sensitive primary human cells to be used for therapeutic applications.

4:50 Technology Panel: Trends in CRISPR Technology and Applications

This panel will bring together 3-5 technical experts from leading technology and service companies to discuss trends and improvements in library design, assay reagents and platforms, and data analysis tools that users can expect to see soon to explore new applications.

Moderator: John Doench, Ph.D., Associate Director, Genetic Perturbation Platform, Broad Institute of Harvard and MIT

Participants: Experts from sponsor companies (Opportunity available)

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

WEDNESDAY, JUNE 14

7:00 am Registration Open

7:30 Interactive Breakout Discussion Groups with Continental Breakfast
This session features various discussion groups that are led by a moderator/s who ensures focused conversations around the key issues listed. Attendees choose to join a specific group and the small, informal setting facilitates sharing of ideas and active networking. Continental breakfast is available for all participants. Details on the topics and moderators are available on the conference website.

CRISPR FOR ONCOLOGY DRUG DISCOVERY

8:35 Chairperson's Remarks
Danilo Maddalo, Ph.D., Lab Head, ONC Pharmacology, Novartis Institutes for BioMedical Research, Novartis Pharma AG

8:45 *In vivo* Generation of Oncogenic Signatures with the CRISPR/Cas9 System
Danilo Maddalo, Ph.D., Lab Head, ONC Pharmacology, Novartis Institutes for BioMedical Research, Novartis Pharma AG
Precise genomic editing leading to cancer formation represents a powerful tool in preclinical research. Generation of signatures resulting in cancer development/resistance can be investigated and identified by *in vivo* delivery of the CRISPR/Cas9 system. In this talk I will discuss the methods for generating preclinical animal models, the impact the 'genome editing revolution' has had, and the future applications for drug discovery and target identification.

9:15 Genome Editing and Gene Silencing in 3D Tumor Models: Opportunities for Overlap
Madhu Lal-Nag, Ph.D., Group Leader, Trans-NIH RNAi Facility, National Center for Advancing Translational Sciences, National Institutes of Health
The development of our 3D oncology RNAi and CRISPR/Cas9 screening platform is a step towards understanding the contribution of the tumor microenvironment to cancer cell viability. Our work aims to study and understand the role of tumor heterogeneity, clonal evolution, dormancy and cell death and in doing so, to bring forth some novel mechanisms of action that will help uncover novel druggable targets.

9:45 Engineered Swine Models of Cancer
Sponsored by Surrogen
Adrienne Watson, Ph.D., Senior Research Scientist, Surrogen, A Recombinetics Company
Huge advancements in technology to engineer genetically modified swine, who share immense genetic and physiological similarity to humans, have enabled the development of swine models of human cancer. We describe the latest innovations in cancer modeling in swine, including Recombinetics' model of Neurofibromatosis Type 1, to show the benefits of using swine as a large animal model in research and the vast applications and opportunities of swine models of cancer.

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

11:00 *In vivo* and *ex vivo* Cancer Engineering via Somatic Genome Editing
Peter Cook, Ph.D., Postdoctoral Researcher, Laboratory of Andrea Ventura, M.D., Ph.D., Cancer Biology and Genetics Program, Memorial Sloan Kettering Cancer Center
Using CRISPR-Cas9 genome editing, we have developed a strategy for modeling cancer-associated genomic rearrangements. An induced chromosomal deletion generating an uncharacterized receptor tyrosine kinase fusion transforms mouse adult neural stem cells, generating brain tumors that are highly similar to human high grade gliomas and respond to a specific kinase inhibitor. This technique holds promise for more accurate modeling of human tumors and targeted therapy development.

11:30 Knocking Out Specific miRNAs Using a Double CRISPR Approach Identifies Their Function During Development: Embryogenesis Recapitulating Tumorigenesis
G. Ian Gallicano Ph.D., Associate Professor, Department of Biochemistry and Molecular & Cellular Biology, and Director, Transgenic Core Facility, Georgetown University Medical Center
My laboratory investigates miRNA mechanisms during development. Knocking out individual miRNAs to study their function has been difficult using homologous recombination technology. However, CRISPR technology has solved this problem. We used a two CRISPR approach to remove individual miRNAs resulting in new embryonic stem cells lines. During development oncogenes are activated and subsequently deactivated, a process that goes awry in many cancers. As a result, CRISPR technology used during development could shed light on understanding tumorigenesis.

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

12:30 Session Break

1:00 Coffee and Dessert in the Exhibit Hall with Poster Viewing

1:30 PLENARY KEYNOTE SESSION (click here for details)

3:30 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Close of Conference

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3rd Annual

3D Cellular Models

Engineering Predictive Preclinical Screening Models

Recommended Event Package

Symposium June 12: iPS Cells for Disease Modeling and Drug Discovery
Conference June 13-14: Phenotypic Screening and Chemical Biology
Conference June 14-15: 3D Cellular Models

WEDNESDAY, JUNE 14

11:00 am Registration

12:00 pm Bridging Luncheon Presentation: 3D Bioprinted Tissue Models for Predictive Toxicology and Disease Modeling

Sponsored by organovo

Jeff Irelan, Ph.D., Director, Scientific Applications, Tissue Operations, Organovo

Translation of preclinical data to clinical outcomes remains a challenge in drug development. Organovo's ExVive™ 3D Bioprinted Human Liver and Kidney Tissues are positioned to bridge the gap by providing tissue-like responses *in vitro* through spatially-controlled, automated deposition of cells. Multicellular tissues preserve native cellular interactions for assessment of biological responses at the biochemical, transcriptional, and histological levels. Examples of toxicological applications and capacity for disease modeling will be discussed.

12:30 Session Break

1:00 Coffee and Dessert in the Exhibit Hall with Poster Viewing

1:30 PLENARY KEYNOTE SESSION (click here for details)

3:30 Refreshment Break in the Exhibit Hall with Poster Viewing

3D MODELS: STEM CELL SOURCES

4:15 Chairperson's Opening Remarks

Claudia McGinnis, Ph.D., Principal Scientist & Group Leader, Pharma Research and Early Development, Pharmaceutical Sciences, Mechanistic Safety, Roche Innovation Center Basel

4:25 Stem Cell-Derived Kidney Models for Drug Discovery

Piyush Bajaj, Ph.D., Senior Scientist, Drug Safety R&D, Investigative Toxicology Group, Pfizer

I discuss the current state of *in vitro* kidney models in support of drug discovery. Advances in both 2D and 3D models – specifically using organoid-based culture and organ-on-a-chip technologies – will be presented. Finally, we highlight ongoing efforts to leverage pluripotent stem cells to develop a physiologically relevant *in vitro* human kidney model that has been characterized in terms of drug transporter function and sensitivity to known nephrotoxicants.

4:55 Modeling Neurological Diseases Using Human-Induced Pluripotent Stem Cells

Shawn Je, Ph.D., Assistant Professor, Program in Neuroscience and Behavioral Disorders, Duke-National University of Singapore Medical School

The ability to make functional neural cells from human pluripotent stem cells (hPSCs) provides a unique opportunity to study human brain development and neurological disorders. I present recent findings from our laboratory – 1) the direct induction and functional maturation of forebrain glutamatergic and GABAergic neurons from hPSCs, 2) the generation of midbrain-like organoids from hPSCs, and 3) their utilities in modeling human neurological disorders.

5:25 Overcoming Barriers to High Throughput Single Cell Clonal Culture

Sponsored by STEMCELL Technologies

Michael Hiatt, Scientist, Research & Development, STEMCELL Technologies, Inc.

Traditional methods of deriving clonal cultures offer a choice between low-throughput techniques, or more rapid methods that may sacrifice true clonality. Ensuring clonality in 3D sphere-forming assays is particularly challenging. We will present a novel workflow for high-throughput clone derivation in non-adherent 3D cultures. This method is ideally suited to gene editing or cancer sphere-forming assay applications.

5:40 Nortis' Organ-on-Chip Technology: Human Tissue Microenvironments for Basic Research, Drug Toxicology & Efficacy Testing

Sponsored by NORTIS

Henning Mann, Ph.D., Scientific Director, Nortis, Inc.

The Nortis system is a novel, commercially available technology allowing to recapitulate units of human organs in microfluidic chips, providing *in-vivo* like cues to guide tissue architecture and function. Developed organ models include vasculature, kidney and liver models for toxicology studies, blood-

brain barrier models for drug transport studies, and vascularized tumor/tissue microenvironment models for drug efficacy studies. Our aim is to substantially improve *in-vitro* predictability of clinical outcome.

5:55 Automated 3D Stem Cell Profiling of Drug Candidates for Identification of Developmental Toxicity
Claudia McGinnis, Ph.D., Principal Scientist & Group Leader, Pharma Research and Early Development, Pharmaceutical Sciences, Mechanistic Safety, Roche Innovation Center Basel
Embryonic stem cells, and their ability to differentiate *in vitro*, are an essential 3D model for *in vitro* developmental toxicity approaches. We routinely use this approach to profile our early drug candidates to deprioritize compounds with the highest risk of *in vivo* findings. We have recently fully automated this 3D assay, which proved to be a highly challenging project, and this presentation will cover the most important milestones and results from this effort.

6:25 Close of Day

6:30 Dinner Short Course Registration
Click here for details on short courses offered.

THURSDAY, JUNE 15

7:15 am Registration Open and Morning Coffee

7:30 Interactive Breakout Discussion Groups with Continental Breakfast
This session features various discussion groups that are led by a moderator/s who ensures focused conversations around the key issues listed. Attendees choose to join a specific group and the small, informal setting facilitates sharing of ideas and active networking. Continental breakfast is available for all participants. Details on the topics and moderators are available on the conference website.

3D MODELS: MICROENGINEERED CHIPS

8:35 Chairperson's Remarks
Jose A. Lebron, Ph.D., Executive Director, Investigative Laboratory Sciences, Safety Assessment & Laboratory Animal Resources, Merck & Co., Inc.

8:45 KEYNOTE PRESENTATION: The Need for Analytical Chemistry and Multi-Omics for Understanding the Physiology and Pathology of 3D Cellular Models: Examples from the Neurovascular Unit/Blood-Brain Barrier
John P. Wikswo, Ph.D., Founding Director, Vanderbilt Institute for Integrative Biosystems Research and Education and Gordon A. Cain University Professor, Vanderbilt University
We review how validation of a microphysiological system (MPS) as an effective recapitulation of the organ it models could affect the design, operation, and testing of organ chips. We consider how MPS validation would benefit from a mouse-on-a-chip, for example by allowing a proteomic, transcriptomic, and metabolomic comparison of a mouse brain with both transwell and microfluidic neurovascular units. These tools can then be applied to assess disease models.

9:15 Bioprinted Renal Tubules on Perfusable Chips
Kimberly Homan, Ph.D., Research Associate, Lewis Research Group, Wyss Institute for Biologically Inspired Engineering, Harvard University
Three-dimensional models of kidney tissue that recapitulate human responses are needed for drug screening, disease modeling, and, ultimately, kidney organ engineering. We present a bioprinting method for creating functional 3D human renal proximal tubules *in vitro*. This *in vitro* model system allows customization by printing perfusable vasculature and multiple cell types in predefined locations, enabling both drug screening and drug toxicity mechanistic studies at user-defined levels of complexity.

9:45 A Microfluidic Model of Transport Tissues for 96-Well Format Screening of Therapeutics
Sponsored by DRAPER
Joseph Charest, Ph.D., Program Manager, Biomedical Solutions, Draper
Preclinical screening for therapeutics will become more predictive when *in vitro* models express organ- or tissue-specific function. Our model uses controlled microfluidic fluid flow, cell-substrate topography, and cell-cell cues to guide cells to form tissue with organ-specific function. A 96-well format scales the model to high levels of throughput and integrated electrical traces provide near real-time data collection of barrier function.

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

11:00 Instrumented Cardiac Microphysiological Devices Fabricated by Multimaterial 3D Printing
Johan Ulrik Lind, Ph.D., Research Associate, Disease Biophysics Group, John A. Paulson School of Engineering and Applied Sciences, Wyss Institute for Biologically Inspired Engineering, Harvard University
Microphysiological systems promise to accelerate biomedical research by providing accurate *in vitro* models of human tissue. However, device instrumentation and fabrication remain severe obstacles. Here, we present a multimaterial 3D printing methodology for fabricating cardiac microphysiological devices with built-in sensors. The platform allows non-invasive and scalable readouts of the contractile stress and beat rate of multiple cardiac microtissues, to support higher throughput drug dose response studies, and long-term experiments.

11:30 KEYNOTE PRESENTATION: The NIH Tissue Chips for Drug Screening Program: Improving Health through Smarter Science
Danilo A. Tagle, Ph.D., MS, Associate Director, Special Initiatives, Office of the Director, National Center for Advancing Translational Sciences (NCATS), NIH
Tissues-on-chips involves the development of 3D platforms engineered to support living human tissues and cells, and are designed as accurate models of the structure and function of human organs, such as the lung, liver and heart. Researchers can use these models to predict whether a candidate drug, vaccine or biologic agent is safe or toxic in humans in a faster and more effective way than current methods.

12:00 pm Making It Biologically Relevant with RAFT™ 3D Cell Culture System

Sponsored by Lonza

Theresa D'Souza, Ph.D., Section Manager, Cell Biology Research & Technology, Lonza Walkersville, Inc.

The environmental cues cells are experiencing in a three-dimensional (3D) cell culture environment bring them closer to their *in vivo* state compared to two-dimensional (2D) culturing surfaces. RAFT™ 3D Cell Culture system allows the creation of tissue-like structures with cells growing within or on top of a compressed, high-density collagen scaffold.

12:15 3D-Culture Using Elplasia Microplates

Sponsored by kuraray

Gonzalo Castillo, Ph.D., Consultant to Elplasia Life Science of Kuraray Co. Ltd., BioEnsis

The use of 3D-cell culture models has been growing steadily in the last few years, because they closely resemble the natural cellular environment. Pharmacology utilizing 3D- cultures allow for more accurate *in vitro* to *in vivo* predictions, thereby preventing costly expenditures in downstream development. Elplasia microplates offer a complete flexible solution that allows for scalable relevant 3D cultures.

12:30 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:00 Session Break

3D MODELS: TAKING SCREENING INTO THE THIRD DIMENSION

1:30 Chairperson's Remarks

Mohammad F. Kiani, Ph.D., FAHA, Professor, Mechanical Engineering, Bioengineering, and Radiation Oncology, Temple University

1:35 A Biomimetic Microfluid Assay for Rapid Screening of Anti-Inflammatory Drugs

Mohammad F. Kiani, Ph.D., FAHA, Professor, Mechanical Engineering, Bioengineering, and Radiation Oncology, Temple University

There is an urgent need for rapid screening of anti-inflammatory drugs before they are tested in human trials. We have developed and validated a novel biomimetic microfluidic assay (bMFA) that reproduces the entire leukocyte adhesion cascade in a physiologically realistic 3D environment and validated it directly against a mouse model of inflammation. We have used bMFA to rapidly screen the potentially therapeutic effects of a novel drug for treating sepsis.

2:05 3D Liver Spheroids for High-Throughput Drug-Drug Interaction Screening

Noushin Dianat, Ph.D., Bioengineering Team Leader, Colloids & Divided Materials Lab, ESPCI Paris

Persisting failures in clinical validation of promising drug candidates due to safety issues reflect the inefficiency of traditional 2D mono-layer models. In order to study DILI due to drug-drug interaction (DDI), we have developed a high-throughput technology of miniaturized 3D spheroid fabrication with primary human hepatocytes. 3D micro-livers were then treated with a panel of drugs and drug-drug interaction risk was evaluated.

2:35 Coffee and Dessert Break in the Exhibit Hall. Last Chance for Poster Viewing.

3:20 A 3D Self-Assembled Neural Spheroid Model for Capillary-Like Network Formation

Diane Hoffman-Kim, Ph.D., Associate Professor, Medical Science and Engineering, Brown University

In vitro models of the specialized neurovascular environment are imperative for advancing understanding of healthy and pathological states, and for developing therapeutics. We have developed a spheroid model to study the formation of capillary-like networks in a three-dimensional environment that incorporates both neuronal and glial cell types, and does not require exogenous vasculogenic growth factors.

3:50 Current and Future Impact of Advanced 2D and 3D Tissue Models on Improving Safety Testing in Early Drug Development

Jose A. Lebron, Ph.D., Executive Director, Investigative Laboratory Sciences, Safety Assessment & Laboratory Animal Resources, Merck & Co., Inc.

Despite multiple advances, preclinical de-risking efforts do not always predict clinical outcomes. Emerging *in vitro* technologies promise to fill some of these de-risking gaps. We characterized two *in vitro* hepatocyte co-culture models – Organovo's 3D BioPrinted ExVive™ Human Liver and Ascendance's Hepatopac® micropatterned hepatocyte-fibroblast models. We review the results of these evaluations and provide perspective on what additional models are needed and how future use of *in vitro* systems could look.

4:20 Organ in a Drop: A 3D Cellular Model Constructed by Droplet-Based Microfluidics

Dong Chen, Ph.D., Professor, Institute of Process Equipment, College of Energy Engineering, Zhejiang University

Developing a 3D model of a human organ that consists of multiple cells embedded in a 3D scaffold and expresses improved functions is practically important for drug developments. We show that droplet-based microfluidics is a powerful technique to construct a 3D cellular model of an organ in a drop, with precise spatial control of different cells in the 3D microenvironment.

4:50 Development of a Human Skin Explant Culture System as an Alternative to Animal Testing

Apostolos Pappas, Ph.D., Research Manager and Fellow, Emerging Science and Innovation, Johnson & Johnson Consumer, Inc.

The talk is around the development of a 3D skin explant system which allows testing of compounds/technologies that could affect all layers of skin (epidermis, dermis, subcutaneous).

5:20 Close of Conference

FINAL WEEKS
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Cambridge HEALTHTECH Institute
25 YEARS
A Division of Cambridge Innovation Institute

DISCOVERY & DEVELOPMENT

The analysis of massive amounts of 'omics data is uncovering remarkable insights into disease biology, creating a wealth of new drug targets, and the potential for the development of novel pharmaceutical agents. Key to efficiently utilizing these new targets is the need for preclinical validation, harnessing new disease models to assess efficacy and toxicity, as well as emerging capabilities of CRISPR, nanoparticle-based delivery, and new methods for tackling the challenging aspects of crossing the blood brain barrier and addressing CNS diseases. Join pharmaceutical, biotech, and academic stakeholders for interactive sessions, panel discussions, and short courses, all of which are geared toward providing opportunities for active networking and collaboration.

June 12

SYMPOSIUM: iPS Cells for Disease Modeling and Drug Discovery

June 13-15

Blood-Brain Barrier

Predicting Drug Toxicity

June 14-15

Translational Strategies in CNS

FINAL WEEKS
TO REGISTER

COVER
CONFERENCE-AT-A-GLANCE
PLENARY KEYNOTE PROGRAM
MEDICINAL CHEMISTRY
ONCOLOGY
SCREENING
DISCOVERY & DEVELOPMENT
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Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

10th Annual

Predicting Drug Toxicity

Discovering New Models and Integrating Innovative Strategies

Recommended Event Package

Short Course 3 June 12: Drug Metabolism and Its Impact on Decisions in Drug Development - Part 2

Short Course 7 June 12: Evaluating and Characterizing *in vitro* Models of Drug Toxicity

Conference June 13-14: Predicting Drug Toxicity

Conference June 14-15: 3D Cellular Models

TUESDAY, JUNE 13

7:00 am Registration Open and Morning Coffee

HOW WELL AND HOW EARLY CAN WE PREDICT DRUG TOXICITIES?

8:25 Chairperson's Opening Remarks
Paul B. Watkins, M.D., Director, Institute for Drug Safety Sciences, Howard Q. Ferguson Distinguished Professor, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill

8:35 KEYNOTE PRESENTATION: Predicting Liver Safety Liabilities in New Drug Candidates: Are We There Yet?
Paul B. Watkins, M.D., Director, Institute for Drug Safety Sciences, Howard Q. Ferguson Distinguished Professor, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill
Drug Induced Liver Injury (DILI) remains a major adverse event leading to termination of drug development programs and regulatory actions. Recent advances in understanding mechanisms that underlie DILI, more complex organotypic liver culture systems, novel mechanistic biomarkers, and quantitative systems toxicology modeling are increasingly impacting decisions made within both industry and regulatory agencies, and should improve the efficiency of drug development in the near future.

9:05 Optimizing Dose Combinations via Simultaneous Toxicity & Antitumor Efficacy Modeling
Dean C. Bottino, Ph.D., Scientific Director, Quantitative Clinical Pharmacology, Takeda Pharmaceuticals International
A key question in early clinical oncology novel-novel combination drug development is: what recommended Phase II dose (RP2D) combination will optimize the efficacy of the combination while avoiding excessive toxicity? We describe a method combining clinical toxicity data, used to derive the maximum tolerated exposure (MTE) combination curve, with preclinical efficacy data, used to determine which point along this curve will provide optimal antitumor effect.

Sponsored by MatTek CORPORATION

9:35 Organotypic Small Intestinal Tissue Model for Prediction of Adverse Drug Reactions
Seyoum Ayehunie, Ph.D., Vice President, MatTek Corporation
Gastrointestinal adverse drug reactions (ADR) cause health problems and create a burden on the health care system and the pharmaceutical industry. Gastrointestinal ADR often lead to late-stage drug attrition. In this presentation, we will demonstrate the utility of a novel in vitro 3D primary human small intestine based system to identify biomarkers that can better predict human ADR compared to preclinical animal models, and is ideal for therapeutic candidate screening.

10:05 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

10:50 Quantitative Systems Modeling of Tolvaptan-Induced Hepatotoxicity
Sharin Roth, Ph.D., Director, Clinical Pharmacology, Bioanalytical & Biomarkers, Otsuka Pharmaceuticals
Quantitative systems modeling of tolvaptan-induced liver injury was performed using DILIsym®. Toxicity was mechanistically multifactorial in nature according to the simulations, with contributions from both bile acid accumulation and mitochondrial electron transport chain (ETC) inhibition. Predicted risk factors include basal ETC flux, mitochondrial respiratory reserve capacity, and BSEP function. Characteristics related to exposure were less correlated with susceptibility.

FINAL WEEKS
TO REGISTER

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11:20 Strategies for Integration of *in silico* and *in vitro* Data for Off-Target Safety Assessments
Terry Van Vleet, Ph.D., DABT, Head of Molecular and Computational Toxicology, Department of Preclinical Safety, AbbVie
Typically, small molecule compounds are evaluated against a screening panel of potential off-targets to determine if they interact with human proteins of interest that may have consequence for toxicities. However, it is not feasible to screen each compound for all possible off-target interactions. One way to potentially enhance the coverage of *in vitro* screening is with computational methods to predict potential chemical interactions with human protein targets. This strategy may fill gaps in off-target screening that could not be covered routinely with panels.

11:50 Human-Based Phenotypic Profiling Uncovers Mechanisms of Toxicity
Sponsored by DiscoverX
Adam Best, Ph.D., Product Manager, DiscoverX Corporation
Human-based phenotypic profiling is an attractive method for the discovery of chemical toxicity mechanisms. Using a standardized panel of human primary cell and co-culture model systems, BioMAP® Diversity PLUS, a database was generated. We identified a biomarker signature common to skin irritants, which was shared by several reference compounds including a lead compound from a drug discovery program that was terminated due to skin toxicity in primates.

12:20 pm Luncheon Presentation: Preclinical Considerations for Cellular Therapeutic Safety Study Designs
Sponsored by discovery from charles river
Shawna Jackman, Ph.D., DABT, Principal Research Scientist, Photobiology, Charles River Laboratories
Complex and comprehensive preclinical evaluations are essential to assess potential clinical risks and to meet regulatory expectations for cell therapy products and specific intended indication. These design considerations include selection of the appropriate test system, study duration, toxicological endpoints and cell fate criteria. This presentation will address the unique challenges in the design and execution of these safety studies for cellular therapeutics.

12:50 Session Break

HOW GOOD ARE THE NEW *IN VITRO* MODELS FOR EARLY TOXICITY SCREENING?

1:40 Chairperson's Remarks
Mary Ellen Cvijic, Ph.D., Director, Lead Evaluation & Lead Profiling, Department of Lead Discovery and Optimization, Bristol-Myers Squibb

1:50 Human on a Chip Systems as Phenotypic Models for Drug Toxicity and Efficacy Evaluation
James J. Hickman, Ph.D., Professor, Nanoscience Technology, Chemistry, Biomolecular Science, and Electrical Engineering, University of Central Florida
We are establishing functional *in vitro* systems to create organs and subsystems to model organ function and diseases, such as cancer and neurological deficits. The idea is to integrate microsystems fabrication with protein and cellular components, offering biologically, mechanically and electronically interactive functional multi-component systems. Some of the more advanced body-on-a-chip systems being developed will be discussed, as well as the results of workshops held to explore what is needed for validation and qualification of these systems.

2:20 Inotropy and Chronotropy Screens in Human Engineered Myocardium
Malte Tiburcy, M.D., Research Fellow, Institute of Pharmacology and Toxicology, University Medical Center Goettingen
Tissue engineered organ surrogates evolve rapidly as advanced tools for safety and efficacy screens. We developed engineered human myocardium (EHM) from defined cell populations under serum-free culture conditions in collagen type 1-hydrogels for applications in phenotypic drug screens. An automated tissue culture and analysis platform for high throughput screening of inotropic and chronotropic effects is presented. Validation of the EHM screening platform by test compounds with known and unknown pharmacologic profiles is discussed.

2:50 ZeGlobalTox - An Innovative Approach to Address Organ Drug Toxicity using Zebrafish
Sponsored by ZeClinics Drug Discovery Through Zebrafish
Javier Terriente, Ph.D., CSO, Research & Development, ZeClinics
Cardio-, neuro- and hepatotoxicity are major attrition causes during drug development. Drug-induced organ-toxicity can be assessed using zebrafish larvae, which provides high predictivity on possible human drug-induced liabilities; bridging the gap between preclinical *in vitro* safety evaluation and rodent models in a fast and cost-effective manner. ZeGlobalTox is an innovative assay that integrates sequential cardio-, neuro- and hepatotoxicity assessment in the same animal, allowing an strong impact in 3R implementation.

3:20 The Innovation Hub - Simplifying Access to the Latest Models and Innovative Strategies
Sponsored by scientist
Gursatya "Guru" Singh, PSM, Director, Scientific Content, Scientist.com
The Innovation Hub is a dedicated section of the Scientist.com marketplace in which we highlight and provide access to cutting-edge research tools, technologies and services. In the Innovation Hub, you can search for the latest CRISPR/Cas9 gene editing services, find new toxicity assays, browse a growing list of 3D tissues and access the latest *in silico* models of disease.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:05 The Need for Increased Sensitivity in *in vitro* Drug Toxicity Testing
Ian Sweet, Ph.D., Associate Professor, Department of Medicine, University of Washington
In this talk, I will first consider the theoretical underpinnings of the ideal *in vitro* test of drug effects and toxicity. The second half will focus on very sensitive technology we have developed that continuously measures detailed time courses of pharmacologically relevant drug effects on solid tissue samples. The accuracy and throughput positions this technology as an important investigational component of a drug discovery strategy.

4:35 Further Defining the Role of Human Stem Cell Derived Cardiomyocytes to Assess Proarrhythmia
Gary Gintant, Ph.D., Senior Research Fellow, Integrative Pharmacology, Integrated Science and Technology, AbbVie
The availability of human stem cell derived cardiomyocytes (representing normal as well as diseased phenotypes) provides unique opportunities and challenges for evaluating cardiac safety of drug candidates. This presentation describes present and future roles of these cardiomyocytes as an *in vitro* proarrhythmia assay, and

within the Comprehensive *in vitro* Proarrhythmia Assay (CiPA) initiative to guide the efficient development of safe drugs and reshape regulatory expectations.

5:05 High Content Screening for Predictive Safety/Toxicity Assays
Mary Ellen Cvijic, Ph.D., Director, Lead Evaluation & Lead Profiling, Department of Lead Discovery and Optimization, Bristol-Myers Squibb
High content imaging (HCI) is emerging as an important tool for safety and efficacy studies to advance drug discovery efforts. Due to its multi-parametric nature, this technology enables the identification of subtle changes in cell phenotypes which otherwise would be missed by conventional toxicity assay technologies. Here, we present case studies for HCI screening to investigate toxicity targets, mode-of-action and safety biomarkers for organ toxicities.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

WEDNESDAY, JUNE 14

7:00 am Registration Open

7:30 Interactive Breakout Discussion Groups with Continental Breakfast
This session features various discussion groups that are led by a moderator/s who ensures focused conversations around the key issues listed. Attendees choose to join a specific group and the small, informal setting facilitates sharing of ideas and active networking. Continental breakfast is available for all participants. Details on the topics and moderators are available on the conference website.

HOW CAN WE BETTER UNDERSTAND & IDENTIFY DRUG-INDUCED ORGAN TOXICITIES?

8:35 Chairperson's Remarks
Laszlo Urban, M.D., Ph.D., Global Head, Preclinical Secondary Pharmacology, Novartis Institutes for BioMedical Research, Inc.

8:45 Excipient Related Adverse Events
Laszlo Urban, M.D., Ph.D., Global Head, Preclinical Secondary Pharmacology, Novartis Institutes for BioMedical Research, Inc.
While regulatory agencies monitor the use of excipients, there is little knowledge about their broad biological behavior. Sporadic studies have highlighted safety concerns with some excipients, however, no systematic and rigorous safety investigations which are applied to drug candidates are required for these molecules. Here we present data from a broad scale investigation of biological effects of excipients in a variety of *in vitro* assays and possible implications of positive findings.

9:15 Prediction of Metabolism Mediated Drug Toxicity: Where Are We Now?
Jayaprakasam Bolleddula, Ph.D., Senior Scientist II (Associate Director), Drug Metabolism and Pharmacokinetics, Takeda Pharmaceuticals
Idiosyncratic adverse drug reactions (IADRs) are one of the major causes of drug attrition at various stages of development and even after marketing. The mechanisms of IADRs are complex and poorly understood. Circumstantial evidence suggests that most IADRs are due to formation of reactive metabolites through bioactivation of drug molecules and their subsequent covalent binding to biological macromolecules. The current strategies followed across the pharmaceutical industry to mitigate reactive metabolites and future perspectives will be presented.

9:45 Drug-Cytokine Interaction in Idiosyncratic Hepatotoxicity
Patricia Ganey, Ph.D., Professor, Department of Pharmacology and Toxicology, Institute for Integrative Toxicology, Michigan State University
Interaction with cytokines likely contributes to idiosyncratic liver injury from nonsteroidal anti-inflammatory drugs. We found that NSAIDs synergize with tumor necrosis factor (TNF) and interferons (IFN) to cause hepatocellular killing *in vitro*. The kinases JNK and ERK are critical mediators of cell death, but their roles differ depending on NSAID structure. Findings suggest that, even within the same pharmacologic class, synergy with cytokines occurs by different kinase signaling mechanisms.

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

11:00 A Current Industry Perspective on Assessing Hepatotoxicity Risk in Drug Discovery
William Proctor, Ph.D., DABT, Senior Scientist, Head of Investigative Toxicology, Department of Safety Assessment, Genentech, Inc.
Extensive efforts are made to assess hepatotoxicity risk in drug discovery, which is difficult as there is poor concordance of preclinical species to identify human hepatotoxicants. Genentech employs a panel of *in vitro* models to investigate potential DILI risk with additional consideration for indication and projected dose/exposure. This talk will focus on standard and emerging technologies to assess hepatotoxicity risk and will demonstrate through case studies how the data can be used in a weight-of-evidence approach to characterize risk for DILI in small molecules.

11:30 Genetically Heterogeneous Mouse Populations Enable Study of Idiosyncratic Hepatotoxicity
Alison Harrill, Ph.D., Geneticist, National Toxicology Program Division, National Institute for Environmental Health Sciences
Diversity Outbred mice were specially bred to encompass a large degree of well-randomized genetic diversity across individuals, providing an opportunity to model idiosyncratic toxicities and to identify pharmacogenetics risk factors that confer susceptibility. This presentation will demonstrate the utility of Diversity Outbred mice for detection and study of idiosyncratic hepatic adverse reactions, as well as translation of mouse-derived pharmacogenetic risk factors to the clinic.

12:00 pm Bridging Luncheon Presentation: 3D Bioprinted Tissue Models for Predictive Toxicology and Disease Modeling
Sponsored by organovo
Jeff Irelan, Ph.D., Director, Scientific Applications, Tissue Operations, Organovo
Translation of preclinical data to clinical outcomes remains a challenge in drug development. Organovo's ExVive™ 3D Bioprinted Human Liver and Kidney Tissues are positioned to bridge the gap by providing tissue-like responses *in vitro* through spatially-controlled, automated deposition of cells. Multicellular tissues preserve native cellular interactions for assessment of biological responses at the biochemical, transcriptional, and histological levels. Examples of toxicological applications and capacity for disease modeling will be discussed.

12:30 **Session Break**

1:00 **Coffee and Dessert in the Exhibit Hall with Poster Viewing**

1:30 **PLENARY KEYNOTE SESSION (click here for details)**

3:30 **Refreshment Break in the Exhibit Hall with Poster Viewing**

4:15 **Close of Conference**

3rd Annual

Blood-Brain Barrier

New Understanding, Strategies and Tools for Delivering Therapy to the Brain

Recommended Event Package

Short Course 4 June 12: Understanding and Dealing with Drug Disposition in CNS

Conference June 13-14: Blood-Brain Barrier

Conference June 14-15: Translational Strategies in CNS

TUESDAY, JUNE 13

7:00 am Registration Open and Morning Coffee

UNDERSTANDING AND PREDICTION OF BRAIN PENETRATION AND TRANSPORT ACROSS THE BBB

8:25 Chairperson's Opening Remarks
Torben Moos, Ph.D., The Faculty of Medicine, Department of Health Science and Technology, Laboratory of Neurobiology, Aalborg University

8:35 KEYNOTE PRESENTATION: Targeted Uptake and Transport of Nanocarriers at the Blood-Brain Barrier
Torben Moos, Ph.D., The Faculty of Medicine, Department of Health Science and Technology, Laboratory of Neurobiology, Aalborg University
Targeted delivery of immunoliposomes containing oxaliplatin to brain capillary endothelial cells (BCECs) was studied *in vitro* and *in vivo* in the rat with the aim of quantifying nanocarrier and cargo uptake in BCECs and the remainder portion of the CNS. The study provides evidence for a preferential uptake and processing of the targeted liposomes within the BCECs. Studies are undergoing to track down the fate of the liposomes and their cargo.

9:05 Towards High-Relevance Screening: *In Vivo* Microscopy-Based Cell-Phenotype Assays
Leonard Khiroug, Ph.D., CSO, Neurotar Ltd.
Critical bottlenecks of preclinical drug discovery are often addressed with high-content screening (HCS) and, especially for CNS, with phenotypic screening (PS). However, limited relevance of *in vitro* microscopy-based HCS assays, and low resolution of *in vivo* imaging- or behavior-based PS tests, leave room for improvement. Quantitative *in vivo* microscopy can help screen BBB-crossing biologics and small molecules for their effects on cellular phenotypic features (morphology, motility, signaling), possibly emerging as a high-relevance screening (HRS) method of choice.

9:35 But HOW Did It Affect the Brain?
Lois A. Lampson, Ph.D., Associate Professor of Neurosurgery, Brigham & Women's Hospital/Harvard Medical School
Full-sized antibodies, delivered to the blood, can affect the brain. Antibody-mediated reduction of amyloid in animal models of Alzheimer's disease is one example, among others. Even where the effect is well-documented, its basis can be controversial: is the antibody actually working from within the brain? If so, how did it get there? If not, how was its effect on the brain achieved? Specific examples and alternatives will be compared.

10:05 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

NEW IMAGING TECHNIQUES & TOOLS

10:50 Antibody-Based PET Imaging in Mouse Models of Alzheimer's Disease
Dag Sehlin, Ph.D., Researcher, Department of Public Health/Geriatrics, Uppsala University
Due to their high specificity, antibodies are attractive in PET ligand development, but the BBB is an obstacle to antibody-based PET imaging within the CNS. By engineering antibodies in various formats to target the transferrin receptor for active brain delivery, we have enabled specific PET imaging of amyloid-beta pathology in mouse models of Alzheimer's disease. This technique may allow imaging of CNS targets where conventional PET ligands are currently lacking.

11:20 Predicting and Optimizing the Territory of Blood-Brain Barrier Opening by Superselective Intra-Arterial Cerebral Infusion under Dynamic Susceptibility Contrast MRI Guidance
Piotr Walczak, M.D., Ph.D., Associate Professor, Radiology, Johns Hopkins University
Interventional neuroradiology techniques are minimally invasive and allow for superselective drug delivery to specific brain regions. The passage of most agents, however, is impaired by the blood-brain barrier (BBB). Despite its discovery over 40 years ago, hyperosmotic BBB opening (BBBO) remains highly variable, preventing

its widespread implementation. Here, we report on a technique that enables the prediction and optimization of the BBBO territory using real-time MRI guidance.

11:50 A Realistic and Dynamic 3D Tissue Model for Investigation of Blood Brain Barrier Functionality

Sponsored by SynVivo

Prabhakar Pandian, Ph.D., Chief Technology Officer, SynVivo, Inc.

Physiologically relevant 3D blood brain barrier (BBB) model recreates a histological slice of brain tissue in communication with endothelial cells across the BBB. Consistent with *in vivo* phenotype, cells cultured under dynamic flow conditions exhibit tight junction formation and functional responses. Patented architecture allows real time visualization of cellular and barrier functionality. Studies highlighting permeability of small molecules, transporters, inflammation and therapeutic screening including *in vivo* validation will be presented.

12:05 pm Longitudinal Studies of BBB, Cells and Organelles Using a Unique *in vivo* Microscopy Platform

Sponsored by neurotar

Leonard Khiroug, Ph.D., CSO, Neurotar Ltd.

CNS cells and subcellular organelles, such as neuronal dendritic spines or glial fine processes, are best studied in their natural environment, i.e. in the intact brain of a live animal. We shall discuss several preclinical studies performed using our *in vivo* multiphoton imaging platform in combination with Neurotar's proprietary device, Mobile HomeCage, which enables microscopic analysis of (sub)cellular structure and function in the brain of awake, behaving mice.

12:20 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:50 Session Break

NEW IMAGING TECHNIQUES & TOOLS (CONT.)

1:40 Chairperson's Remarks

Robyn S. Klein, M.D., Ph.D., Director, Center for Neuroimmunology & Neuroinfectious Diseases, Department of Internal Medicine, Neurobiology, Pathology & Immunology, Washington University School of Medicine

1:50 Role of Blood-Brain Barrier Function in Alzheimer's Disease Pathogenesis Investigated by Using a 3D Microfluidic Platform

Yoojin Shin, Ph.D., Postdoctoral Fellow, Mechanical Engineering, MIT

We have developed a physiologically relevant three-dimensional (3D) human neural cell culture model of Alzheimer's disease (AD) with a neurovascular unit (blood brain barrier, BBB) in a microfluidic system (3D AD-BBB model). Using this model, we proposed to investigate the impact of the BBB on AD pathogenesis and to explore whether Aβ and/or toxic molecules generated from 3D cultures expressing multiple AD genes disrupt normal BBB function. In this study, we found Aβ disrupts BBB function involving permeability increase. We also found that the presence of the BBB increases cell viability in the 3D cultures, and that Interleukin-8 (IL-8) and IL-6, which are secreted from the BBB, are responsible for increased cell viability in our 3D AD models.

2:20 Development of Highly Efficient BBB Transport of Antibodies to the CNS Using *in vivo* Phage Display with Single Domain VNAR to the Transferrin Receptor

Frank S. Walsh, Ph.D., CEO, Ossianix

Partially enriched phage libraries to TfR1 were injected *in vivo* and isolated from brain parenchyma through 3 enrichment cycles. A number of hits were formatted on a Fc backbone and found to give over one log greater exposure in brain parenchyma than previous hits and produced brain/plasma ratios of over 5% at 18 hours after a single IV injection of 2 mg/kg. These VNARs, which bind with equal affinity to mouse and human TfR1, have now been formatted as bispecific agents with a variety of antibodies and give highly efficient BBB transfer at low therapeutic doses. The VNAR TfR1 panel promises to be a highly efficient method for transfer of therapeutic levels of antibody or other biologics to the CNS.

2:50 Poster Highlight Presentation: Delivery of Therapeutic Peptides Across Cellular Barriers for Type II Diabetes by Fusion to Gangliosides with Varied Acyl Chains

Daniel Chinnapen, Ph.D ., Assistant Professor of Pediatrics, Boston Children's Hospital / Harvard Medical School

Delivery of biologics across highly selective mucosal barriers has been challenging due to their inability to internalize and cross host cells. Based on an understanding of intracellular lipid sorting, we are developing ganglioside(lipid)-fusions for the delivery of therapeutic peptides across intestinal mucosa for oral based treatment of Type II Diabetes. *In vitro* monolayer and *in vivo* mouse studies show that only peptides fused to gangliosides are absorbed and are efficacious.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

THE BLOOD-BRAIN BARRIER AT SITES OF PATHOLOGY

4:05 Viral Sensing at the Blood-Brain Barrier

Robyn S. Klein, M.D., Ph.D., Director, Center for Neuroimmunology & Neuroinfectious Diseases, Department of Internal Medicine, Neurobiology, Pathology & Immunology, Washington University School of Medicine

Arboviruses that infect the CNS include members of the Flaviviridae (e.g., West Nile virus), and Togaviridae (Alphaviruses) families. Mechanisms exist to protect the CNS from infection with neurotropic viruses, including innate immune responses and the BBB. Our research has highlighted various mechanisms by which viruses modulate BBB function. Here we will present new data focused on mechanisms of BBB entry and dysfunction during alphavirus encephalitis.

4:35 Selected Poster Presentation: Impact of Regional Heterogeneity of Blood-Brain Barrier on Drug Transport

Irena Loryan, M.D., Ph.D., Translational PKPD Group, Department of Pharmaceutical Biosciences, Uppsala University, Sweden

Local dissimilarities in blood-brain barrier (BBB) drug transport, due to different expression of active efflux and influx transporters, as well as spatial differences in post-BBB intra-brain distribution are key factors governing the brain regional drug disposition. Using a novel methodology for the assessment of drug transport from blood to the brain regions of interest referred as Combinatory Mapping Approach (CMA-ROI) spatial neuropharmacokinetics of various drugs has been investigated and will be presented.

Selected Poster Presentation: Investigating the Brain in Mouse Models for Duchenne Muscular Dystrophy

Emine Bagdatlioglu, Ph.D. Student, The John Walton Muscular Dystrophy Research Centre, Institute of Genetic Medicine, Newcastle University, UK.

Duchenne muscular dystrophy (DMD) is a muscle wasting disease caused

by mutations in the DMD gene, which encodes the large cytoskeletal protein, dystrophin. Dystrophin's function in the CNS remains unknown but has been associated with the BBB. This study aims to determine if cognitive impairment is progressive by utilising two mouse models for DMD. Quantitative and qualitative MRI, behavioural testing and proteomic profiling were employed to determine how loss of dystrophin affects the brain.

DRUG DELIVERY &TRANSPORT ACROSS BBB: UPDATES FROM THE INDUSTRY

5:05 Engineered Protein Capsules for Targeted Delivery to the Brain

Axel H. Meyer, Ph.D., Head of Brain Delivery, Neuroscience Discovery, AbbVie GmbH & Co. KG

Virus-like particles (VLPs) have been studied as therapeutic or diagnostic tools as they can be loaded with various drugs. In this presentation we describe Engineered Protein Capsules (EPCs) which are VLPs consisting of genome-free components of the native John Cunningham (JC) virus. These particles can be produced in a recombinant system, filled with different cargos from nucleic acids to proteins and used for targeted delivery to the brain.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

WEDNESDAY, JUNE 14

7:00 am Registration Open

7:30 Interactive Breakout Discussion Groups with Continental Breakfast

This session features various discussion groups that are led by a moderator/s who ensures focused conversations around the key issues listed. Attendees choose to join a specific group and the small, informal setting facilitates sharing of ideas and active networking. Continental breakfast is available for all participants. Details on the topics and moderators are available on the conference website.

DRUG DELIVERY &TRANSPORT ACROSS BBB: UPDATES FROM THE INDUSTRY(CONT.)

8:35 Chairperson's Remarks

Danica Stanimirovic, M.D., Ph.D., Director, Translational Bioscience Department, Human Health Therapeutics Portfolio, National Research Council of Canada

8:45 Development of the BBB-Crossing, Amyloid-ß Oligomer-Targeting Therapeutic for Alzheimer's Disease

Balu Chakravarthy, Ph.D., Senior Research Officer, National Research Council Canada

An amyloid-ß (Aß) oligomer-binding peptide (ABP) was engineered to cross the blood-brain barrier using a single-domain antibody, FC5. FC5-ABP demonstrated dose- and time-dependent increase in CSF and brain exposure in mice, rats and dogs, compared to ABP alone. In AD-transgenic mice and rats, systemic injection caused an accelerated (within 4 weeks) reduction of Aß levels in CSF and brain parenchyma, illustrating importance of cross-BBB delivery of the Aß–targeting therapeutic.

9:15 Efficient Delivery of Biologics across BBB for Neurological Diseases

Denise Karaoglu Hanzatian, Ph.D., Principal Research Scientist, Biologics Discovery, AbbVie Bioresearch Center, AbbVie

9:45 Blood-Brain Barrier Carta Project: Novel Targets and BBB-Crossing Single-Domain Antibodies

Danica Stanimirovic, M.D., Ph.D., Director, Translational Bioscience Department, Human Health Therapeutics Portfolio, National Research Council of Canada

BBB Carta project is a comprehensive molecular 'map' of BBB cells, brain vessels and neurovascular unit. BBB Carta was used to select novel BBB-selective targets that undergo a receptor-mediated transcytosis. Single domain antibodies raised against these targets were evaluated as potential novel BBB carriers in models *in vitro*, and in animal studies. Some of these antibodies showed enhanced brain penetration and ability to induce central pharmacological responses after systemic exposure.

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

11:00 Treatment of Human Lysosomal Storage Disorders with Blood-Brain Barrier Penetrating IgG-Fusion Proteins

Ruben Boado, Ph.D., Vice President, Research & Development/Co-Founder, ArmaGen, Inc.

Protein therapeutics can be re-engineered as brain penetrating IgG-fusion proteins for the CNS treatment of rare disorders, like Lysosomal Storage Disorders (LSD). The IgG domain targets a specific endogenous receptor-mediated transporter system within the blood-brain barrier (BBB), such as the human insulin receptor (HIR). The protein therapeutic domain of the fusion protein exerts the pharmacological effect in brain once across the BBB. Several brain penetrating enzyme fusion proteins have been engineered for LSD. First in human Phase I/II clinical trials are in progress.

11:30 FEATURED PRESENTATION: Tackle One of the Toughest Problems in Medicine: Delivery of Biologics Across the Blood-Brain Barrier

Per-Ola Freskgard, Ph.D., Vice Director and Senior Leader, Neuroscience, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd.

This presentation will provide a short overview of the progresses that were made over the last 5 years to identify novel antibody engineering platforms that utilizes receptor-mediated transcytosis to cross the blood-brain barrier (BBB). With focus on understanding BBB cell biology, receptor trafficking and key properties of an efficient transport vector

12:00 pm Bridging Luncheon Presentation: Disruptive and Novel Regulatory Therapeutic Strategy for Treatment of Neurodegenerative Diseases by Neuronal Peptide GM6

Sponsored by GENERVON

Winston Ko, CEO, Genervon Biopharmaceuticals, LLC

GM6 showed neuroprotection in neurodegenerative disease rodent models. Using DNA microarrays, Genervon identified 1259 genes altered ≥ 2-fold in SH-5YSY cells, including 89, 48, 46 and 9 genes associated with ALS, AD, PD and MS, respectively, suggesting repression of apoptotic pathway and stimulation of mitotic/proliferation pathways. Phase 1 and 2A trials demonstrated safety of GM6 and observed favorable shifts in biomarkers and improved functional measures. Planning Phase 3 trials.

12:30 **Session Break**

1:00 **Coffee and Dessert in the Exhibit Hall with Poster Viewing**

1:30 **PLENARY KEYNOTE SESSION (click here for details)**

3:30 **Refreshment Break in the Exhibit Hall with Poster Viewing**

4:15 **Close of Conference**

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Inaugural

Translational Strategies in CNS

Bridging the CNS Preclinical to Clinical Gap

Recommended Event Package

Symposium June 12: iPS Cells for Disease Modeling and Drug Discovery

Short Course 4 June 12: Understanding and Dealing with Drug Disposition in CNS

Conference June 13-14: Blood-Brain Barrier

Conference June 14-15: Translational Strategies in CNS

Short Course 10 June 14: Humanized Mouse Models for Preclinical Assessment of Cancer Immunotherapy

WEDNESDAY, JUNE 14

11:00 am Registration

12:00 pm Bridging Luncheon Presentation: Disruptive and Novel Regulatory Therapeutic Strategy for Treatment of Neurodegenerative Diseases by Neuronal Peptide GM6

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12:30 Session Break

1:00 Coffee and Dessert in the Exhibit Hall with Poster Viewing

1:30 PLENARY KEYNOTE SESSION (click here for details)

3:30 Refreshment Break in the Exhibit Hall with Poster Viewing

CURRENT CHALLENGES AND OPPORTUNITIES IN CNS DRUG DEVELOPMENT

4:15 Chairperson's Opening Remarks

Murali Gopalakrishnan, Ph.D., Senior Director, Head Search & Evaluation Neuroscience, AbbVie

4:25 Current Challenges and Opportunities in CNS Drug Development

Murali Gopalakrishnan, Ph.D., Senior Director, Head Search & Evaluation Neuroscience, AbbVie

CNS drug development represents an exciting area, particularly for neurodegenerative indications. This presentation details current understanding of CNS-related disease biology, emerging targets, new technologies and the major hurdles facing developers bringing CNS therapies to market.

4:55 Developing Novel CNS Therapies at Yumanity

Kenneth Rhodes, Ph.D., CSO, Yumanity Therapeutics

Yumanity Therapeutics is working to fill a critical need in drug discovery by identifying novel targets, pathways and drug candidate molecules for diseases caused by protein misfolding. This presentation will cover Yumanity's three integrated discovery platforms and their productivity in the context of target and molecule discovery for neurodegenerative diseases including Parkinson's disease, Alzheimer's disease and ALS.

5:25 Identification of Relevant Physiological Readouts for CNS Drug Development

Sponsored by NeuCyte Translatable Neuroscience

Daniel Haag, Ph.D., CSO, NeuCyte

High attrition rates of novel CNS drugs indicate that current preclinical testing fail to meet the unmet needs of patients. NeuCyte supports the early phases of CNS drug discovery programs for Lead Compound Optimization. Based on our SynFire™ technology, NeuCyte's human neural *in vitro* platforms are uniquely suited for assessing relevant higher order electrophysiology readouts allowing for a more reliable predictor of drug efficacy and potential CNS Safety/Toxicology.

5:55 CT-526: A Peptide Targeting CDK5 in Neurodegenerative Disease

Kent Werner, M.D., Ph.D., Co-Founder and CEO, Cogentis Therapeutics; Johns Hopkins Neurology Adjunct Faculty

In Alzheimer's disease, CDK-5 is one of the two major kinases to phosphorylate tau and is found to be 10x more active than in cognitively normal controls - largely

due to p25. Previous efforts to target CDK5 were toxic and unsuccessful. CT-526 is a peptide targeting p25 and exhibiting zero toxicity at 100x the effective dose. In multiple models, CT-526 reduces tau hyperphosphorylation, amyloid plaque formation, neuroinflammation and rescues phenotype.

6:25 Close of Day

6:30 Dinner Short Course Registration
Click here for details on short courses offered.

THURSDAY, JUNE 15

7:15 am Registration Open and Morning Coffee

7:30 Interactive Breakout Discussion Groups with Continental Breakfast
This session features various discussion groups that are led by a moderator/s who ensures focused conversations around the key issues listed. Attendees choose to join a specific group and the small, informal setting facilitates sharing of ideas and active networking. Continental breakfast is available for all participants. Details on the topics and moderators are available on the conference website.

IMPLEMENTING SUCCESSFUL TRANSLATIONAL STRATEGIES

8:35 Chairperson's Remarks
Antti Nurmi, Ph.D., Managing Director, Discovery, Charles River

8:45 Translatability of Early Development Proof of Principle Trials in Neurology
Johan Luthman, Ph.D., Vice President, Neuroscience Clinical Development, Neurology Business Group, Eisai, Inc.
Biomarkers are gaining importance as predictive biomarkers to supplement clinical outcome measures, although validation of biomarkers as surrogate outcome measures still remains a high hurdle. Alzheimer's disease (AD) is a clear illustration of the introduction of biomarkers has entirely changed the way drug R&D is executed, but also shows the challenges of addressing remaining hurdles.

9:15 Incorporating Biomarker Endpoints in Early Clinical Development to Enable the Successful Development of Novel Neurodegenerative Therapies
Danielle Graham, Ph.D., Director, Neurodegenerative Disease, Biomarker Discovery and Development, Biogen
This presentation will focus on preclinical discovery biomarker strategies designed to increase the successful transition of biomarkers from preclinical discovery to clinical development. As one example, the presentation will highlight studies conducted in cynomolgus monkey with BIIB076, a pan tau antibody, and the CSF pharmacokinetic and pharmacodynamic biomarker data generated. These data were critical for dose selection and sampling times in our ongoing Phase I with BIIB076.

9:45 Translational Validation of Preclinical Models of Neurological Disease
Sponsored by discovery from charles river
Antti Nurmi, Ph.D., Managing Director, Discovery, Charles River
Charles River offers early discovery phase efficacy testing for novel therapies aimed at neurological and psychiatric conditions. Using a full range of different animal models, we use translational methods including *in vitro* assays, behavioral and cognitive testing and imaging to accelerate the development of novel CNS and neurological disease related therapies. Multi-modal study designs are essential for robust preclinical data that translate to success in the clinic.

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

11:00 Preclinical to Clinical Translation for Tau-Directed Therapeutics
Michael K. Ahlijanian, Ph.D., Director, Discovery Biology and Head, Clinical Biomarkers, Bristol-Myers Squibb
Halting the progression of tau pathology is an important therapeutic target in neurodegenerative diseases. This talk will review different therapeutic modalities that target tau and the preclinical data sets that can be generated to inform dose selection and provide target engagement and proof of pharmacology endpoints in clinical studies. Specific case studies will be used as examples.

11:30 Preclinical Development of NPT088: Translation of a Novel Finding into an Alzheimer's Drug Candidate
Jonathan Levenson, Ph.D., Senior Director, Preclinical Research and Development, Proclara Biosciences
An unexpected discovery revealed that a minor capsid protein from filamentous bacteriophage M13 selectively binds to and remodels misfolded proteins with an amyloid conformation, such as those found in AD. Here we describe the preclinical development of NPT088, a novel Ig fusion protein and therapeutic approach, for the treatment of AD and other neurodegenerative disorders.

12:00 pm Validation of Animal Models and Understanding Animal Model MOA
Manuela Polydoro, Ph.D., Investigator II, Neuroscience, Novartis Institutes for BioMedical Research, Inc.
Despite large financial investment in drug development, the clinical development success rate of most programs remains low. One explanation is imperfect preclinical research, in which the use and outcome of animal models is pivotal to bridge the translational gap to the clinic. The selection of validated and predictive models is essential to address clinical questions. The translational value of animal models could be further enhanced when combined with novel translational approaches.

12:30 Luncheon Presentation: Accelerating Drug Discovery and Development for Huntington's Disease
Sponsored by discovery from charles river
Larry Park, Ph.D., Director, In Vivo Research, CHDI
CHDI Foundation is a nonprofit biomedical research organization focused on developing therapies for Huntington's disease. CHDI's activities extend from exploratory biology to the identification and validation of therapeutic targets, and from drug discovery to clinical studies and trials. CHDI manages a diverse portfolio of research projects through a novel virtual model that encourages scientific collaboration to more directly connect academic research, drug discovery and clinical development.

1:00 Session Break

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BIOMARKERS, IMAGING AND NOVEL PRECLINICAL MODELS

1:30 Chairperson's Remarks
Tricia A. Thornton-Wells, Ph.D., Investigator III / Clinical Genetics Expert, Neuroscience Disease Area Portfolio Leader, Novartis Institutes for BioMedical Research

1:35 Non-Invasive Epigenetic Neuroimaging
Changning Wang, Ph. D., Instructor, Martinos Center, Massachusetts General Hospital
The epigenetic neuroimaging is expected to usher in a new area of human epigenetic research. Brain imaging studies will provide valuable information to study the causes and epigenetic mechanisms of human disease, especially on neurodegenerative diseases and substance use disorders.

2:05 Translational Strategies in Psychiatry
Gopi Shanker, Ph.D., Head of Psychiatry, Neuroscience Department, Novartis Institutes for Biomedical Research (NIBR)

2:35 Coffee and Dessert Break in the Exhibit Hall. Last Chance for Poster Viewing.

3:20 Using MRI to Identify Sex Differences in the APOE4 Rat
Craig Ferris, Ph.D., Professor, Psychology and Pharmaceutical Sciences, Director, Center for Translational NeuroImaging, Northeastern University
With MRI, we characterized the brain and cognitive development of young male and female APOE Ɛ4 knock-in rats, a preclinical model of Alzheimer's disease. Male APOE4 rats show a deficit in cognitive function, altered microarchitecture and functional connectivity with elevated oxidative stress. Female APOE4 rats show normal cognitive function, functional connectivity and microarchitecture. Does the APOE4 isoform confer some benefit to healthy adult females while they are still reproductively active?

3:50 Developing Biomarkers for the Frontotemporal Disorders
Nadine Tatton, Ph.D., Scientific Director, The Association for Frontotemporal Degeneration
Biomarkers that enable clinicians and researchers to accurately diagnose FTD and monitor disease progression are critical to both clinical practice and drug development. However, such biomarkers are currently unavailable, resulting in diagnostic delays or errors and impeding the search for effective treatments. In 2016, the AFTD launched a global request for proposals that would accelerate the discovery of biomarkers across the spectrum of frontotemporal disorders.

4:20 Minimally Invasive Biomarkers of General Anesthetic-Induced Developmental Neurotoxicity
Xuan Zhang, M.D., Ph.D., Division of NeuroToxicology, National Center for Toxicological Research, FDA
The association of general anesthesia with developmental neurotoxicity is demonstrable in a variety of animal models from rodents to nonhuman primates. Nearly all general anesthetics tested have been shown to cause abnormal brain cell death in animals when administered during periods of rapid brain growth. Minimally-invasive procedures, such as microPET, provide the opportunity to bridge the preclinical/clinical gap and translate findings from the animal laboratory to the human clinic.

4:50 Functional Brain Measures (fMRI and EEG) to Characterize an Awake Individual Using Either Resting or Task Based Data
William Z. Potter, M.D., Ph.D., Senior Advisor, National Institute of Mental Health
NIMH follows a target validation approach whereby studies of any putative drug include direct evidence of a functional brain effect related to its primary biochemical action(s). Such evidence includes both exposure/response studies on degree of receptor occupancy and downstream functional consequences measured by fMRI, EEG and/or MRS. Data from efforts to validate or reject therapeutic hypotheses about mGluR2/3 agonists, Kappa selective opiate antagonists and GABA subtype selective agonists utilizing agents developed at Lilly and AstraZeneca will be presented.

5:20 Close of Conference

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SYMPOSIA

June 12

iPS Cells for Disease Modeling and Drug Discovery

New Tools for Disease Modeling

Phenotypic and Genotypic Cell Analysis in Immuno-Oncology

June 15-16

Nano-Delivery: Nucleic Acids, Cancer Immunotherapy and Beyond

Property-Based Drug Design

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2nd Annual

iPS Cells for Disease Modeling and Drug Discovery

Disease Modeling and Screening in Neuroscience and Other TAs

Recommended Event Package

Symposium June 12: iPS Cells for Disease Modeling and Drug Discovery
Conference June 13-14: CRISPR for Target Discovery
Conference June 14-15: Translational Strategies in CNS

MONDAY, JUNE 12

7:00 am Registration Open and Morning Coffee

KEYNOTE SESSION: MODELING COMPLEX DISEASES TO IDENTIFY NOVEL THERAPIES

9:00 Chairperson's Opening Remarks
Ulrich Broeckel, M.D., Professor of Pediatrics, Medicine and Physiology, Pediatrics, Medical College of Wisconsin

9:10 Using Induced Pluripotent Stem Cells for Drug Development in Neurology and Psychiatry
Ricardo Dolmetsch, Ph.D., Global Head, Neuroscience, Novartis Institutes for Biomedical Research
This presentation will explain how iPSC-based experimental approaches are being used to address the biological mechanisms underlying psychiatric and neurodegenerative disorders and are helping to inform drug development.

9:40 iPSC-Based Screening Strategy to Identify Novel Drug Candidates
Christoph Patsch, Ph.D., Principle Scientist, Team Lead, Stem Cell Assays, Roche Innovation Center
In preclinical drug discovery, there is an unmet need for novel disease relevant cell-based assays. iPSC technologies offer new opportunities in disease modeling. Here, we present a drug discovery strategy based on primate neuronal cell models that are derived from patient and Cynomolgus monkey iPSCs.

10:10 Coffee Break

PATIENT-DERIVED STEM CELL MODELS FOR PERSONALIZED TREATMENT DEVELOPMENT

10:40 Patient-Derived Stem Cells for *in vitro* Modeling of Parkinson's Disease
Birgitt Schuele, M.D., Director for Gene Discovery and Stem Cell Modeling, Translational Sciences, Parkinson's Institute and Clinical Center
A critical need to advance the field presents the differentiation of Lewy body Parkinson's disease from other non-Lewy body forms of parkinsonism. This is important because the underlying molecular pathomechanisms, and hence potential therapeutic targets, are unlikely to be similar for both. IPSC technology utilizing donors with high-quality and comprehensive clinical data and eventually with confirmative neuropathology at autopsy is the key for successful interpretation of findings and clinical translation.

11:10 Induced Pluripotent Stem Cell-Derived Cardiomyocytes to Predict Patient-Specific Responses to Drug Treatments
Ulrich Broeckel, M.D., Professor of Pediatrics, Medicine and Physiology, Pediatrics, Medical College of Wisconsin
We will discuss the underlying concepts of phenotypic variation and the impact of genomic variation on common, complex phenotypes in iPSCs. To demonstrate this, we have established 250 iPSC cell lines from the NHLBI HyperGen study. This study represents a bi-racial cohort with extensive data on cardiovascular disease and associated risk factors. We will discuss our approach to analyzing disease phenotypes on a molecular level using iPSC-derived cardiomyocytes.

11:40 Sponsored Presentation *(Opportunity Available)*

12:10 pm Enjoy Lunch on Your Own

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MODELS FOR STUDYING NEUROLOGIC AND NEURODEGENERATIVE DISORDERS

1:40 Chairperson's Remarks
James Kasuboski, Ph.D., Postdoctoral Fellow, Neuroscience, Pfizer

1:50 KEYNOTE PRESENTATION: Learning about Neurodegenerative Disease Using Human Stem Cell-Derived Neurons
Lee Rubin, Ph.D., Professor, Stem Cell & Regenerative Medicine, Harvard University; Director, Translational Medicine, HSCI
A growing body of work suggests that human diseased neurons produced from pluripotent stem cells can reproduce known features of certain neurodegenerative diseases. I will describe work demonstrating that studies using pluripotent cells also have predictive value: they can reveal previously unknown, but important, aspects of the disease process.

2:20 Rapid and Efficient Inducible Neuron Differentiation for High Throughput Pharmaceutical Screening
James Kasuboski, Ph.D., Postdoctoral Fellow, Neuroscience, Pfizer
Recent iPSC advances have allowed for the generation of human neurons for use in assay development and drug discovery. Though various lengthy multi-step methods have been developed to generate neurons, they are too burdensome and inconsistent for effective screening. Our group has generated an inducible one step system to generate homogenous cultures from iPSC lines in a fourth of the time and provide a feasible and affect screening tool.

2:50 Novel Insights into Alzheimer's Disease Pathogenesis through the Use of iPSC Technology
Tracy L. Young-Pearse, Ph.D., Assistant Professor, Neurology, Brigham and Women's Hospital and Harvard Medical School
The ability to accurately and systematically evaluate the cellular mechanisms underlying human neurodegenerative disorders such as Alzheimer's disease (AD) should lead to advancements in therapeutics. Recent developments in human iPSC technology has afforded the opportunity to use human neurons and glia to study cellular changes involved in neurological diseases. Using iPSCs from sporadic and late-onset patients, we have identified candidate signaling pathways contributing to AD pathology.

3:20 Refreshment Break

3:50 Three Dimensional iPSC-Derived Neuronal Model for Alzheimer's Disease
Weiming Xia, Ph.D., Acting Associate Director of Research, Geriatric Research Education Clinical Center, Bedford VA Hospital
Efforts to model the physiological environment of the Alzheimer's disease (AD) brain are facilitated by combining two cutting edge technologies to generate three-dimensional (3D) human neuronal culture from induced pluripotent stem cells (iPSC). We created iPSC from blood cells of AD patients and cognitive normal subjects, and we compared proteomics of iPSC-differentiated 3D neuronal culture. Efficacy of a beta-secretase inhibitor was tested in the same system.

4:20 Exploring the Epigenetic and Transcriptomic Signatures of Down Syndrome Using iPSC Derived Brain Cells
Hiruy Meharena, Ph.D., Postdoctoral Fellow, Tsai Lab, Massachusetts Institute of Technology (MIT)
Down Syndrome (DS) patients exhibit a spectrum of pathologies which include heart disease, cancer, craniofacial abnormalities and most predominantly ~99% of DS patients have deficits in memory and learning. However, the molecular mechanism of how triplication of Chromosome 21 elicits cognitive deficits remains unclear. Here we utilize patient derived iPSCs to generate specific cell types of the brain to capture the epigenetic and transcriptomic signatures unique to DS.

4:50 KEYNOTE PRESENTATION: Pitfalls and Promise of Using Human Stem Cells for Studying Disease
Kevin C. Eggan, Ph.D., Harvard Department of Stem Cell and Regenerative Biology, Howard Hughes Medical Institute
The discovery of human ES and iPS cells now makes it principally possible to produce a limitless quantity of diverse cell types for the study of disease. I will describe both success stories and challenges encountered during our efforts to implement these strategies in the context of studying developmental and degenerative disorders of the nervous system.

5:20 Close of Symposium

6:30 Dinner Short Course Registration
Click here for details on short courses offered.

Inaugural

New Tools for Disease Modeling

Exploring and Evaluating Innovative Ways to Better Understand Diseases

Recommended Event Package

Symposium June 12: New Tools for Disease Modeling

Short Course 6 June 12: How to Best Utilize 3D Spheroids and CRISPR Assays in Oncology

Conference June 13-14: Preclinical Models and Tools in Oncology - Part 1

Conference June 14-15: 3D Cellular Models

MONDAY, JUNE 12

7:00 am Registration Open and Morning Coffee

EXPLORING RELEVANT *IN VITRO* AND *IN VIVO* MODELS

8:30 Chairperson's Opening Remarks

James J. Hickman, Ph.D., Professor, Nanoscience Technology, Chemistry, Biomolecular Science, and Electrical Engineering, University of Central Florida

8:40 A Human Model of Neuromuscular Junction Activity for Investigating ALS and Other Neurological Diseases

James J. Hickman, Ph.D., Professor, Nanoscience Technology, Chemistry, Biomolecular Science, and Electrical Engineering, University of Central Florida

There is a lack of good models for neurodegenerative diseases, for efficacy and side effect determination during the drug discovery process. Our advances in culturing human stem cell derived neurons, astrocytes, muscle and Schwann cells in a defined serum-free medium, and integrating them with MEMS devices containing interactive functional multi-component systems is unique. The ability to differentiate the cells from iPSCs derived from patients offers potential for answering questions using functional human-on-a-chip systems.

9:10 An *ex vivo* Tumor Model Identifies Clinically Relevant Anticancer Therapies

Geoffrey Bartholomeusz, Ph.D., Associate Professor and Director, Target Identification and Validation Program, Department of Experimental Therapeutics, Division of Cancer Medicine, The University of Texas M.D. Anderson Cancer Center

We have developed an *ex vivo* tumor array for less expensive and faster drug development with PDX screening systems. The *ex vivo* tumors are similar in morphology and expression of biomarkers to the original PDX tumor and replicate the response profile of a panel of drugs tested in a PDX system. Our long-term goal is to incorporate our system into the clinical management of cancer to rapidly and cost-effectively identify patient-specific therapies.

9:40 Genetic and Non-Genetic Cardiomyopathies in Engineered Human Heart Muscle

Malte Tiburcy, M.D., Research Fellow, Institute of Pharmacology and Toxicology, University Medical Center Goettingen

Patient-specific and genetically modified pluripotent stem cells (iPSC) offer novel experimental approaches for studying human cells and disease-specific phenotypes *in vitro* with the prospect of making high fidelity predictions on therapeutic strategies *in vivo*. We provide evidence that organotypic tissue models like Engineered Heart Muscle (EHM) are instrumental in recapitulating pathophysiology of cardiac disease phenotypes. EHM may fill the gap between classical cell biology *in vitro* and physiological organ function *in vivo*.

10:10 Coffee Break

10:40 Modeling Cystic Fibrosis and Cachexia in Drosophila

Norbert Perrimon, Ph.D., Professor, Department of Genetics, Harvard Medical School

I will discuss two examples illustrating the power of Drosophila to model human diseases. First, through our studies on gut tumors, I will describe a model to dissect mechanisms involved in cachexia (Kwon et al., Dev Cell 2015). Second, I will present our data on ENaC showing that the intestine can be used as a model for Cystic Fibrosis (Kim et al., Dev Cell 2017).

11:10 TECHNOLOGY FORUM: Overcoming Challenges with Developing and Using New Tools for Disease Modeling

Moderator: James J. Hickman, Ph.D., Professor, Nanoscience Technology, Chemistry, Biomolecular Science, and Electrical Engineering, University of Central Florida

Participants: Speakers and Experts from Sponsoring Companies (Opportunity Available)

Investigators come together with service providers to discuss gaps in know-how

and technology. They discuss current challenges and ways to work together to bring forth new assays, models, and analysis tools for disease modeling.

11:40 pm Sponsored Presentation *(Opportunity Available)*

12:10 Enjoy Lunch on Your Own

LEVERAGING *IN SILICO* TOOLS FOR BETTER CLINICAL TRANSLATION

1:40 Chairperson's Remarks
Chengzu Long, Ph.D., Assistant Professor, Division of Cardiology, New York University School of Medicine

1:50 Network Medicine: Cellular Networks and Human Disease
Amitabh Sharma, Ph.D., Assistant Professor, Department of Medicine, Brigham & Women's Hospital and Harvard Medical School
The emerging field of network medicine offers a platform to discover not only the molecular complexity of a particular disease, leading to the identification of disease modules and associated molecular mechanisms but also the molecular relationships among distinct phenotypes. Recent studies have exploited the information contained within protein interaction networks (Interactome) to disclose some of the molecular mechanisms underlying complex pathobiological processes. This suggests that both interactions and networks could emerge as a new class of targetable entities.

2:20 Preclinical to Clinical Translation in Oncology Using Mathematical Modeling
Andy Zhu, Ph.D., Senior Manager, Department of Drug Metabolism and Pharmacokinetics, Takeda Pharmaceuticals International
Immune-deficient mice transplanted with subcutaneous tumors (xenografts) are routinely used to evaluate the efficacy of anti-tumor drug candidates pre-clinically. However, there are extensive debates about the clinical relevance of these models and whether they adequately predict clinical anti-tumor activity. This presentation will discuss the utility of pharmacokinetics and pharmacodynamics modeling for facilitating the preclinical to clinical translation of anti-tumor drug candidates.

2:50 Disease Tracking in Preclinical Studies of Cancer: More New Tools, the Same Old Issues
Chi-Ping Day, Ph.D., Staff Scientist, Cancer Modeling Section, Laboratory of Cancer Biology and Genetics, National Cancer Institute, National Institutes of Health
Incorporation of clinical relevant parameters into preclinical cancer studies requires disease tracking. Recent technological advances, including imaging methods and genetically engineered animals, have rendered real-time and/or long-term tracking more feasible in small animals. We will discuss the application of these new tools in preclinical modeling, as well as cancer growth kinetics required for guiding the evaluation of study outcomes and their clinical translation.

3:20 Refreshment Break

3:50 Genome Editing of Patient-Specific iPSCs to Model Cardiac Disease
Nazish Sayed, M.D., Ph.D., Instructor, Cardiovascular Institute, Stanford University School of Medicine
The mechanisms that underlie "cardiolaminopathy" remain elusive. Although LMNA mutations are known to induce endothelial-dysfunction, little is known about the EC-specific phenotype. Our data shows that iPSC-ECs derived from LMNA-mutated patients exhibit decreased EC functionality. Genome-editing of iPSCs enabled us to recapitulate the EC-disease phenotype to dissect the effects of LMNA mutations. This study is a first step towards understanding cardiolaminopathy by modeling endothelial-dysfunction.

4:20 Correction of Duchenne Muscular Dystrophy in Humanized Mouse Models by CRISPR-Mediated Genome Editing
Chengzu Long, Ph.D., Assistant Professor, Division of Cardiology, New York University School of Medicine
Previously, we used genome editing to correct the DMD mutation in mdx mice, a model for Duchenne muscular dystrophy (DMD). However, correction of the point mutation in mice does not fully address whether it is applicable across the heterogeneous spectrum of mutations in humans. To address this challenge, we are generating "humanized" mouse models of DMD by introducing the human mutations into the mouse DMD locus.

4:50 KEYNOTE PRESENTATION: Pitfalls and Promise of Using Human Stem Cells for Studying Disease
Kevin C. Eggan, Ph.D., Harvard Department of Stem Cell and Regenerative Biology, Director of Stem Cell Biology, Stanley Center for Psychiatric Research at the Broad Institute
The discovery of human ES and iPS cells now makes it principally possible to produce a limitless quantity of diverse cell types for the study of disease. I will describe both success stories and challenges encountered during our efforts to implement these strategies in the context of studying developmental and degenerative disorders of the nervous system.

5:20 Close of Symposium

6:30 Dinner Short Course Registration
Click here for details on short courses offered.

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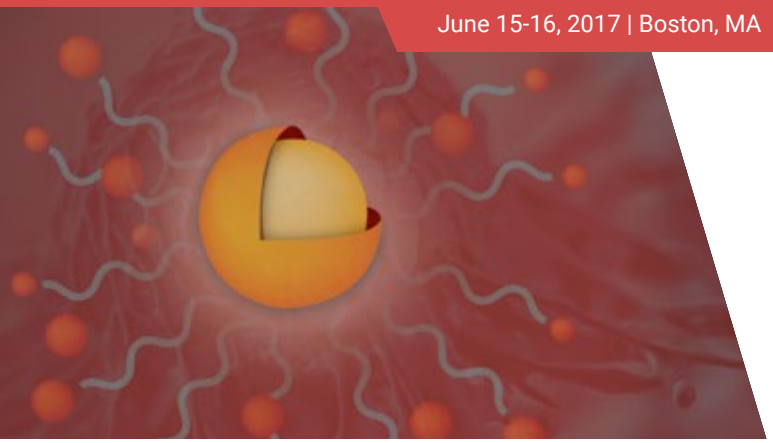
2nd Annual

Nano-Delivery:
Nucleic Acids, Cancer Immunotherapy and Beyond

Next-Generation Applications



Recommended Event Package

Conference June 13-14: Preclinical Models and Tools in Oncology

Conference June 14-15: Tumor Models for Cancer Immunotherapy

Symposium June 15-16: Nano-Delivery: Nucleic Acids, Cancer Immunotherapy and Beyond

THURSDAY, JUNE 15

12:00 pm Registration

RNA DELIVERY

5:30 Chairperson's Opening Remarks
Anil K. Sood, M.D., Professor, Department of Gynecologic Oncology and Department of Cancer Biology, MD Anderson Cancer Center

5:40 Nucleic Acid Delivery Systems for RNA Therapy and Gene Editing
Daniel G. Anderson, Ph.D., Associate Professor, Department of Chemical Engineering, Institute for Medical Engineering and Science, Harvard-MIT Division of Health Sciences & Technology, David H. Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

High throughput, combinatorial approaches have revolutionized small molecule drug discovery. Here we describe our work on high throughput methods for developing and characterizing RNA delivery and gene editing systems. Libraries of degradable polymers and lipid-like materials have been synthesized, formulated and screened for their ability to deliver RNA, both *in vitro* and *in vivo*. A number of delivery formulations have been developed with *in vivo* efficacy, and show potential therapeutic application for the treatment of genetic disease, viral infection, and cancer.

6:10 Systemic in vivo siRNA Delivery Using Biocompatible Nanoparticles
Anil K. Sood, M.D., Professor, Department of Gynecologic Oncology and Department of Cancer Biology, MD Anderson Cancer Center

Use of short interfering RNA (siRNA) as a method of gene silencing has rapidly become a powerful tool in protein function delineation, gene discovery, and drug development. To overcome existing limitations for therapeutic use of siRNA, we have developed a number of biocompatible nanoparticle strategies including DOPC, chitosan, and other nanoparticle platforms. In addition, we have also peptide and thioaptamer-based approaches for highly selective delivery. Collectively, these approaches offer new opportunities for therapeutic gene silencing.

6:40 End of Day

FRIDAY, JUNE 16

KEYNOTE SESSION: CANCER TREATMENT WITH NANOPARTICLES

8:30 am Chairperson's Remarks
Frank Loganzo, Ph.D., Director, Oncology Research and Development, Pfizer

8:40 Role of Macrophages in Nanoparticle-Mediated Drug Targeting to Cancer Stem Cells
Esmaiel Jabbari, Ph.D., Professor, Chemical Engineering, University of South Carolina

A major contributing factor to mortality in cancer patients is relapse after surgery and targeted therapy, and developing resistance to therapy. Breast cancer recurrence affects 30% of the patients. Cancer recurrence and resistance is related to the existence of a very small population of initiating cells or stem cells (CSCs) in the tumor tissue with high expression of ATP-binding cassette (ABC) transporter proteins associated with drug resistance. After therapy, the bulk of tumor shrinks to <1% of its initial volume and the tumor tissue becomes enriched with CSCs that are highly resistant to conventional therapies. Further, as much as 40% of the volume of solid tumors is occupied by tumor-associated macrophages (TAMs), specifically immunosuppressive M2-macrophages, which play a central role in cancer progression. One approach to overcome carrier-mediated drug resistance in CSCs is to use nanoparticles (NPs) for drug encapsulation and intracellular delivery by endocytosis. Unlike drug molecules in which their uptake is affected by up-regulation of ABC transporter proteins, NPs utilize macropinocytosis, clathrin- and caveolin-mediated endocytosis for transcellular cell uptake. Although the uptake of NPs by the mononuclear phagocyte system (MPS) and NPs' enhanced permeation and retention in

the tumor tissue is extensively investigated, little is known about the role of TAMs on uptake and toxicity of drug-loaded NPs toward CSC sub-population of cancer cells. Results on the effect of macrophages on toxicity of Paclitaxel conjugated to polyhedral oligosilsesquioxane (POSS) NPs toward breast CSCs in a novel 3D culture system will be presented.

9:10 Targeting Approaches for Cancer: ADCs and Nanoparticles
Frank Loganzo, Ph.D., Director, Oncology Research and Development, Pfizer
Antibody-drug conjugates (ADCs) and nanoparticles are complementary approaches for the treatment of cancer. The development and application of linker-payloads for ADCs will be introduced, including opportunities for immune activation. Similarly, a polymeric nanoparticle platform with tunable features can be utilized for tumor targeting and immune modulation. There are multiple strategies to broaden the types of drugs encapsulated in nanoparticles, and various approaches to empower nanoparticles with targeting moieties to potentially enhance tumor distribution.

9:40 Delivery of Tumor Necrosis Factor (TNF) to Tumors
Lawrence Tamarkin, Ph.D., President & CEO, CytImmune
Nanomedicines, under 100 nm, target tumors by exiting the circulation through leaky tumor blood vessels. However, other similar-sized blood components also leak into the tumor interstitial space, creating a high interstitial fluid pressure (IFP) – a physical barrier preventing systemic cancer treatments from reaching their target, the cancer cells. By design, CYT-6091 and CYT-21000 are two nanomedicines that deliver tumor necrosis factor (TNF) to tumors, causing vascular disruption and reducing IFP. CYT-21000 also delivers paclitaxel.

10:10 Coffee Break

CANCER IMMUNOTHERAPY AND TARGETING THE TUMOR MICROENVIRONMENT

10:40 Improving Cancer Immunotherapy with Antigen-Capturing Nanoparticles
Andrew Wang, M.D., Associate Professor, Director of Clinical and Translational Research, Department of Radiation Oncology, Lineberger Comprehensive Cancer Center, University of North Carolina Chapel Hill
We report an improved cancer immunotherapy approach through the use of antigen-capturing nanoparticles (AC-NPs). We engineered several AC-NPs formulations, and we demonstrated that the set of protein antigens captured by each NP is dependent on NP surface properties. We showed that AC-NPs can deliver captured proteins to antigen-presenting cells and significantly improve the efficacy of αPD-1 treatment in the B10F10 melanoma model, generating up to 20% cure rate as compared to 0% without AC-NP.

11:10 Modulating Tumor Microenvironment via Nano-Carriers to Enhance Delivery and Function of Therapeutics and Anti-Tumor Lymphocytes
Zohreh Amoozgar, Pharm.D., Ph.D., Postdoctoral Research Fellow, Radiation Oncology, MGH, Harvard Medical School
Tumor microenvironment (TME) consists of tumor cells, lymphocytes, stromal cells, tumor associated vasculature and tumor supportive matrix. TME evades host's anti-tumor immunity and resists anti-cancer treatments. In order to find effective therapeutics, multiple elements of tumor microenvironment should be targeted to reduce resistance to therapy. Multi-compartment nano-carriers have the potential to deliver drugs to tumor cells, target stromal cells and tumor matrix with synergistic effect with host's immune system.

11:40 Selected Poster Presentation: A New Strategy to Deliver Anti-cancer Nanodrugs and Decrease their Toxic Side Effects by Temporarily Blunting the RES Uptake using Intralipid®
Li Liu, Ph.D., Research Biologist, Department of Biological Sciences, Carnegie Mellon University
We have developed a novel strategy to temporarily blunt the reticuloendothelial system (RES) uptake of nanoparticles, a major challenge for nanoparticle delivery, by using an FDA approved lipid emulsion, Intralipid®. We have tested our new strategy by using nano- and micron-sized imaging agents, an in-development platinum-containing nanodrug, and FDA approved anti-cancer nanodrugs, e.g., Abraxane®, Marqibo®, and Onivyde®, to decrease their RES uptake and reduce their toxic side effects in liver, spleen, and kidney.

12:10 pm Enjoy Lunch on Your Own

EMERGING APPLICATIONS OF NANOPARTICLES

1:40 Chairperson's Remarks
Esmaiel Jabbari, Ph.D., Professor, Chemical Engineering, University of South Carolina

1:50 Delivery of Self-Amplifying Replicon-Based RNA Vaccines
Jeffrey Ulmer, Head, Preclinical R&D US, GSK Vaccines
Recent advancements have demonstrated that vaccines based on self-amplifying mRNA have the potential to combine the positive attributes of other types of vaccines without their limitations. Although the mRNA vaccine field is in its infancy, the prospects are promising. The broad utility and rapid response potential of this novel vaccine technology may enable a new generation of vaccines able to address the health challenges of the 21st century. A key enabler of success will be efficient delivery of the synthetic RNA payload.

2:20 *in vivo* Delivery of CRISPR/Cas9
Hao Yin, Ph.D., Research Scientist, The David H. Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology
CRISPR/Cas9 genome editing has been applied to correct disease-causing mutations in human cell lines, but delivery to adult mammalian organs to correct genetic disease genes has not been reported prior to our study. We indicate that, for the first time, CRISPR/Cas9-mediated genome editing is feasible in adult animals. In our second study, we combined lipid nanoparticle-mediated delivery of Cas9 mRNA with adeno-associated viruses encoding an sgRNA and a repair template to induce gene repair in disease animals.

2:50 Site-Specific Protein-Nanoparticle Conjugates for Cellular Targeting
R. James Christie, Scientist, Antibody Discovery and Protein Engineering, MedImmune
Targeted nanoparticles offer therapeutic potential to deliver drugs or manipulate biological targets at specific sites in the body. Here, strategies for site-specific attachment of cysteine-engineered antibody fragments (Fabs) to nanoparticles as well as characterization methods to determine the number of Fabs per nanoparticle

are presented. Evaluation of cell uptake comparing targeted nanoparticles, Fabs, and mAbs demonstrated that targeted nanoparticles achieved higher cell uptake when a dimerizing receptor was targeted.

3:20 CriPec® Oligonucleotides for a Superior Therapeutic Performance

Cristianne J.F. Rijcken, Pharm.D., Ph.D., Founder and CSO, Cristal Therapeutics

Cristal Therapeutics develops CriPec® nanomedicines with enhanced efficacy and less off-target toxicity. The lead product, CriPec® docetaxel, is in clinical development for the treatment of solid tumors. CriPec® oligonucleotides aim to overcome the traditional hurdles via prolonged circulation, less charge-related side effects, increased tumor accumulation, selective cellular uptake and potential for control of endosomal escape. CriPec® products are fully customizable and biocompatible, with a robust manufacturability at clinical scale.

3:50 Close of Symposium

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6th Annual

Property-Based Drug Design

Challenges and Opportunities for New and Difficult Molecules

Recommended Event Package

Conference 13-14: Mastering Medicinal Chemisty - Part 1
Conference June 14-15: Mastering Medicinal Chemistry - Part 2
Symposium June 15-16: Property-Based Drug Design

THURSDAY, JUNE 15

12:00 pm Registration

CONSIDERATIONS FOR PEPTIDES OTHER DIFFICULT MOLECULES

5:30 Chairperson's Opening Remarks
Mark Smythe, Ph.D., Founder & VP, Protagonist Therapeutics

5:40 KEYNOTE PRESENTATION: Optimizing Properties of Cyclic Peptides and Other Difficult Molecules
Scott Lokey, Ph.D., Professor, PBSci-Chemistry & Biochemistry Department, Physical & Biological Sciences, University of California Santa Cruz
Macrocyclic peptides whose properties place them well outside the Rule of 5 can nonetheless exhibit drug-like behavior, including passive cell permeability and oral bioavailability. These exceptional molecules have stimulated efforts to understand the structure-property relationships that underlie their outlier behavior. I will discuss our latest results from a series of studies using synthetic, biophysical, and analytical tools designed to probe the physicochemical constraints that govern ADME behavior in macrocycles in the MW~1000 range.

6:10 KEYNOTE PRESENTATION: Oral Delivery of Constrained Peptides to Treat Inflammatory Bowel Disease
Mark Smythe, Ph.D., Founder & VP, Protagonist Therapeutics
Protagonist Therapeutics is a clinical-stage company with a proprietary technology focused on discovering and developing peptide-based drug candidates to address unmet medical needs. Our focus is on developing first-in-class oral peptide drugs that target biological pathways of marketed injectable antibody drugs. This presentation will outline the strategies and molecular characteristics required to develop potent antagonists of undruggable targets that are stable to the gastrointestinal tract and suitable for oral delivery.

6:40 End of Day

FRIDAY, JUNE 16

MODELS AND MEASUREMENTS FOR TACKLING DMPK ISSUES

8:30 am Chairperson's Remarks
Martin Pettersson, Ph.D., Associate Research Fellow, Neuroscience & Pain Medicinal Chemistry, Pfizer Inc.

8:40 Quantitative Assessment of the Impact of Fluorine Substitution on P Glycoprotein Mediated Efflux, Permeability, Lipophilicity, and Metabolic Stability
Martin Pettersson, Ph.D., Associate Research Fellow, Neuroscience & Pain Medicinal Chemistry, Pfizer Inc.
Strategic use of fluorine is an important tactic in lead optimization. However, replacing a hydrogen atom with a fluorine atom leads to a significant increase in molecular weight that is disproportionate to the corresponding increase in molecular volume. This presentation will describe a pairwise analysis and statistical modeling of the impact of fluorine substitution on various ADME parameters such as P-gp mediated efflux, passive permeability, metabolic stability and lipophilicity.

9:10 Modeling *In Vivo* Drug Distribution and Efficiency using HPLC Based Membrane And Protein Binding Properties
Klara Valko, Ph.D., Director/Honorary professor, Bio-Mimetic Chromatography
Balancing between potency and chromatographically determined membrane and protein binding can help with the selection of drug discovery compounds that have a greater probability of having the desired *in vivo* ADME properties. The standardization of chromatographic procedures enables collection of data for inter-laboratory comparison and direct applications in published models. This technology can predict compounds' *in vivo* behavior for the fraction of the cost of *in vivo* profiling.

9:40 Combining Measurements and Predictions to Accelerate PK Optimization

Bernard Faller,Ph.D., Director Discovery ADME, Novartis Institutes for BioMedical Research, Basel, Switzerland

Discovery ADME assays have been implemented in the late nineties to reduce the attrition of development candidates caused by pharmacokinetic issues through identification of liabilities at a time the chemical structure could still be modified. Data accumulated using true discovery quality molecules help us understand better what is the assay variability in a real discovery setup. Factoring in variability allows filtering out assay noise more effectively and helps building more meaningful prediction models. This lecture will show what kind of assay resolution one can realistically achieve and what we are able to do/not do with current prediction models

10:10 Coffee Break

10:40 Predicting Clearance Active Rate Determining Step and DDI Using Extended Clearance Classification System: Industrial Perspective

Ayman El-Kattan, Ph.D., Associate Research Fellow, Pdm, Pfizer

Successful assessment of mechanism of action of a new chemical entity (NME) is in part determined by accurate prediction of clearance and potential DDI liabilities in human. Recently, the drug industry is realizing a major shift in the chemical space that is associated with change in drug disposition, where metabolism is no longer the main rate determining step of NME clearance. Early identification of this step in drug discovery will enable more proactive clearance profiling screening that is efficient and increase the likelihood of accurate clearance and DDI prediction and assessment of mechanism of action.

11:10 Building New Bridges between *in vitro* and *in vivo* in Early Drug Discovery: Where Molecular Modeling Meets Systems Biology

Robert Pearlstein, Ph.D., Senior Research Investigator I, Novartis Institutes for BioMedical Research

We demonstrate the importance of drug design criteria based on target dynamics, drug PK, and binding kinetics versus the conventional use of static equilibrium drug-target occupancy criteria (e.g. IC50, Kd) that does not typically apply to the *in vivo* setting. We show that compounds can be designed on the basis of binding kinetics (as reflected in calculated target and drug solvation properties), which connects seamlessly with PK and target dynamics. Our work on herg blockade exemplifies the effect of extreme target dynamics on binding.

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11:40 Rational Bioavailability Design: Optimizing Bioavailability during Lead Optimization with Global Sensitivity Analysis of Physiologically-Based Pharmacokinetic Simulations

Pankaj R. Daga, Ph.D., Senior Scientist, Cheminformatics, Simulations-Plus, Inc.

Improving bioavailability of newly designed compounds during lead optimization is a challenging task; especially when over a dozen compound properties need to be adjusted. Since the difficulty of multi-parameter optimization grows exponentially with number of variables, efficient %F optimization requires identifying the few most influential properties for specific chemical series. This presentation will discuss how we collectively applied ADME (ADMET Predictor) and PBPK (GastroPlus) models for three different chemical series. The resulting analysis identified the important few properties to adjust for the series as a whole, as well as more specific advice for optimizing %F around particular compounds of interest.

12:10 pm Enjoy Lunch on Your Own

PREDICTION AND OPTIMIZATION OF BIOPHYSICAL AND PHYSICOCHEMICAL PROPERTIES

1:40 Chairperson's Remarks

Kap-Sun Yeung, Ph.D., Principal Scientist , Discovery Chemistry, Bristol-Myers Squibb

1:50 Improved Prediction Model of Lipophilicity and Its Integration with Other QSAR Models

Ignacio Aliagas, MSc, Scientist, Chemoinformatics, Discovery Chemistry, Genentech

An in-house QSAR model has been developed at Genentech to improve the LogD predictions from commercially available software. The model is trained using internally measured LogD. The LogD predictions are reduced significantly after applying the model correction. Other QSAR benefit from the improved lipophilicity predictions and have been integrated with desktop tools to facilitate their calculation.

2:20 Discovery of an HCV NS5B Replicase Allosteric Inhibitor Advanced to Phase 1 Clinical Studies

Kap-Sun Yeung, Ph.D., Principal Scientist , Discovery Chemistry, Bristol-Myers Squibb

HCV NS5B replicase is an important target for identifying direct acting anti-HCV drugs. Starting from a simple template and a screening hit, an NS5B allosteric inhibitor clinical candidate was identified via a structure-based approach. The optimization process to achieve a delicate balance of molecular properties for potency, ADMET profile, formulation, and the Phase I results that demonstrated the compound is safe and well-tolerated with human PK properties better than predicted, will be presented.

2:50 Using Physchem Measurements to Assess Tissue Distribution and Brain Free Fraction

Carol Moraff, Scientific Associate I, Novartis Institutes for BioMedical Research

Tissue distribution and brain free fraction measurements predict a compound's availability to its target in cell tissue or in the brain. Novartis explored three HPLC assays using stationary phases analogous to blood and tissue, providing a rapid screening technique for lipophilicity, tissue binding, and plasma binding. Linking these to brain free fraction and tissue distribution gives chemists a valuable tool to predict how their compounds will behave in biological assays.

3:20 Designing Bispecific Antibodies Targeting Angiogenesis for Improved Efficacy

Jijie Gu, Ph.D., Research Fellow, Immunology and Global Biologics, AbbVie Bioresearch Center

Angiogenesis is an important natural process of body used for wound healing and reproduction. Excessive angiogenesis occurs in more than 70 human disease conditions; growth of abnormal new blood vessels either feed diseased tissues as seen in cancer and rheumatoid arthritis, or are leaky that lead to destroy of normal tissues in diseases such as diabetic blindness and wet age-related macular degeneration. Antiangiogenic therapies have demonstrated clinical benefit to treat some of these conditions. In this talk, we will discuss examples (including clinical stage molecules) of designing novel anti-angiogenesis therapies against two angiogenic targets using DVD-Ig, a bispecific antibody technology, to further improve therapeutic effect

3:50 Close of Symposium

PLENARY KEYNOTE PROGRAM

June 14, 2017 | Boston, MA

Cambridge HEALTHTECH Institute
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1:30-2:45 pm PLENARY KEYNOTE PRESENTATIONS:

1:30 Welcome Remarks and Speaker Introductions

Marina Filshtinsky, M.D., Senior Director, Cambridge Healthtech Institute

1:45 Human Organs-On-Chips

Donald E. Ingber, M.D., Ph.D., Founding Director, Wyss Institute for Biologically Inspired Engineering, Harvard University; Judah Folkman Professor of Vascular Biology, Harvard Medical School & Boston Children's Hospital; and Professor of Bioengineering, John A. Paulson School of Engineering & Applied Sciences, Harvard University

This keynote presentation will highlight recent advances that my team has made in the engineering and microfabrication of "Organs-on-Chips"—microfluidic devices lined by living human cells created with computer microchip manufacturing techniques that recapitulate organ-level structure and functions as a way to replace animal testing for drug development, mechanistic discovery, and personalized medicine.

2:15 Preclinical and Translation Studies to Support the Anti-PD1 Antibody, Keytruda

Michael Rosenzweig, D.V.M., Ph.D., Executive Director, Oncology-Discovery, Merck Research Laboratories

The success of immune checkpoint therapies such as CTLA-4 and PD-1 has revolutionized the treatment of many types of cancer. However, not all patients or cancer types respond to these therapies. In this presentation, strategies to leverage preclinical studies to support combination strategies intended to enhance both the breadth and depth of response to checkpoint blockade will be discussed. Translational and biomarker efforts designed to support clinical studies will also be reviewed.

2:45-3:30 pm PLENARY KEYNOTE PANEL:

Insights on Innovative Technologies Enabling Preclinical Research

This year's Plenary Keynote Panel features a group of technical experts from life science technology and service companies, who share their perspectives on various trends and tools that will likely change the way in which we traditionally approach preclinical drug discovery and development. Attendees will have an opportunity to ask questions and understand the impact of recent technical advances.

Moderator:
Leigh Zawel, Vice President and Site Head, New York and Boston Centers for Therapeutic Innovation, Pfizer

Panelists:
Matt Gevaert, Ph.D., CEO and Co-Founder, KIYATEC
Pradip Majumder, Ph.D., CSO, Mitra Biotech
David Hutto, Ph.D., DVM, DACVP, CSO, Vium
Brian Bonnell, MBA, Marketplace Director, Scientist

For complete Plenary Keynote Program details visit:

WorldPreclinicalCongress.com/PlenaryKeynote

Biographies

Donald E. Ingber, M.D., Ph.D., is the Founding Director of the Wyss Institute for Biologically Inspired Engineering at Harvard University, the Judah Folkman Professor of Vascular Biology at Harvard Medical School and the Vascular Biology Program at Boston Children's Hospital, and Professor of Bioengineering at the Harvard John A. Paulson School of Engineering and Applied Sciences. He received his BA, MA, MPhil, M.D. and Ph.D. from Yale University.

Ingber is a pioneer in the field of biologically inspired engineering, and at the Wyss Institute, he currently leads a multifaceted effort to develop breakthrough bioinspired technologies to advance healthcare and to improve sustainability. His work has led to major advances in mechanobiology, tumor angiogenesis, tissue engineering, systems biology, nanobiotechnology and translational medicine. Through his work, Ingber also has helped to break down boundaries between science, art and design.

Some of Ingber's most recently developed technologies include an anticoagulant surface coating for medical devices that replaces the need for dangerous blood-thinning drugs; a dialysis-like sepsis therapeutic device that clears blood of pathogens and inflammatory toxins; a shear stress-activated nanotherapeutic that targets clot-busting drugs to sites of vascular occlusion; and Human Organs-on-Chips created with microchip manufacturing methods and lined by living human cells, which are being used to replace animal testing as a more accurate and affordable *in vitro* platform for drug development and personalized medicine. In 2015, Ingber's Organs-on-Chips technology was named Design of the Year by the London Design Museum and was also acquired by the Museum of Modern Art (MoMA) in New York City for its permanent design collection.

Michael Rosenzweig, D.V.M., Ph.D., is the Executive Director of Oncology, Immuno-Oncology and Immunology at Merck Research Laboratories in Boston, Merck and Co. (known as MSD outside of US and Canada). Michael leads the team developing new therapeutics targeting cancer and autoimmunity. A major focus of the team is to build a modality agnostic pipeline to follow on the success of Keytruda®.

Michael joined Merck in 2014 with more than 15 years of experience in biologics drug development, particularly in the fields of oncology, immunology and infectious diseases. He previously served as the VP of Research at Immunext and has held various positions in Biotechnology companies including Tolerx and Cordlife.

Michael received his D.V.M. from the University of Pretoria in South Africa and a Ph.D. in Immunology from the University of Pennsylvania. He then joined Harvard University where he was on the faculty at New England Primate Research Center.

Biographies (contd.)

Brian Bonnell, MBA , Marketplace Director, Scientist
Brian is an engineer/MBA with extensive experience in the pharmaceutical and biotech industry. Prior to joining Scientist.com he was an internal consultant driving strategic projects across R&D at AstraZeneca, including the AstraZeneca Innovation Marketplace. He developed the Strategic Sourcing function at Human Genome Sciences as the company launched its first commercial product. He led several successful capital projects as a process engineer at Merck & Co., and has taught as an Adjunct Professor at Mount St Mary's University. At Scientist.com he is focused on collaborating with industry partners to break down barriers to external innovation. Brian has a BS in Chemical Engineering and an MBA from Penn State and is currently completing a MS in Biotechnology at Johns Hopkins.

Matthew Gevaert, Ph.D., is the CEO of KIYATEC Inc., a life sciences company in Greenville, SC. KIYATEC specializes in *ex vivo* 3D cell culture and tissue systems that more accurately replicate *in vivo* human biology and function, with a focus on methods to accurately predict individual cancer patients' response to drugs by culturing and treating live patient derived primary cells. Dr. Gevaert co-founded the company and has served as CEO since 2007. Possessing a background which combines both business and technology, before his role at KIYATEC Dr. Gevaert led the commercialization of Clemson University's biomedical and biotechnology intellectual property portfolio for nearly 5 years, working with both entrepreneurial start-ups and large, industry leading corporations. He has previous experience with Merck, 3M and Dow Chemical, and has been published in Science magazine and the journal of the US National Academy of Engineering. Currently he serves as a board member of SCBIO, the state of South Carolina's life science industry organization, and a board member of NEXT, which provides entrepreneur services and infrastructure to high-growth ventures in Greenville and Upstate South Carolina. Dr. Gevaert grew up the fifth of six children on a farm in Ontario, Canada and graduated from the University of Waterloo with a bachelor's degree in Applied Chemistry. He also holds a master's degree and a doctorate in Bioengineering from Clemson University. He maintains current appointments as adjunct professor in the Clemson University Department of Bioengineering and as a lecturer in the Clemson MBA in Entrepreneurship & Innovation.

David Hutto, Ph.D., DVM, DACVP, CSO, Vium
Dr. Hutto has extensive experience as a nonclinical pharmaceutical scientist and executive and has led key aspects of drug discovery and drug development leading in several cases to drug marketing approvals. Most recently David was at Charles River Laboratories as the Chief Scientific Officer of Safety Assessment, Veterinary Services and Animal Welfare. David is a veterinarian with a PhD in immunology and specialty board certification in pathology and toxicology.

Pradip Majumder, Ph.D., is Co-Founder & Chief Scientific Officer of Mitra Biotech. Before joining Mitra, Pradip was member of the Faculty of Medicine at Harvard Medical School, a fellow at Merck Research Laboratories, and Principal Investigator of Ontario Institute for Cancer Research. Pradip holds a Ph.D. in Cancer Pharmacology from All India Institute of Medical Sciences. He has more than 50 research publications and has reviewed for leading scientific journals.

Leigh Zawel, Ph.D. Dr. Leigh Zawel joined Pfizer in 2013 to lead CTIs work in the Boston office. In 2014 Dr. Zawel took on site leadership responsibilities for CTI-Boston and CTI-New York. Before CTI, Dr. Zawel was the oncology site lead at Merck Research Laboratories (MRL) Boston. In this role, he was responsible for drug discovery efforts focused on the identification of development candidates for programs in the oncology franchise. Dr. Zawel worked previously at Sanofi-Aventis, where he was Director of Cancer Biology, and Novartis Institutes for BiomedicalResearch/Oncology, where he was an Oncology Group Leader. Dr. Zawel has a deep background in identifying and validating oncology drug targets and in transitioning drug discovery programs through lead optimization to Phase 1 clinical Trials. Dr. Zawel earned his Ph.D. in the laboratory of Danny Reinberg where he identified and characterized components of the RNA Polymerase II basal transcription machinery. Dr. Zawels postdoctoral training was in the laboratory of Bert Vogelstein and Ken Kinzler and focused on dysregulation of TGFB signaling in cancer. Dr. Zawel also holds a MS in Bacteriology from the University of Wisconsin, as well as a BS in Biology from Rutgers University. He has published more than 30 scientific publications. He is also an author on 45 patents covering chemical matter, drug combinations, biomarker utility and gene function in areas of apoptosis, inflammation and TGFB signaling.

Applying Pharmacology to New Drug Discovery:

The System-independent quantification of molecular drug properties for prediction of therapeutic utility

Wednesday, June 14 | 1:30 - 6:30 pm / **Thursday, June 15** | 8:30 am - 5:00 pm

Over the past 6 six years, the primary cause of new drug candidate failures (50%) has been failure of therapeutic efficacy. Put another way, drug discovery programs do everything right, get the defined candidate molecule, only to have it fail in therapeutic trials. Among the most prevalent reasons proposed for this shortcoming is the lack of translation of *in vitro* and recombinant drug activity to therapeutic *in vivo* whole systems. Drug activity in complete systems can be characterized with the application of pharmacological principles which translate drug behaviors in various organs with molecular scales of affinity and efficacy.

Pharmacological techniques are unique in that they can convert descriptive data (what we see, potency, activity in a given system) to predictive data (molecular scales of activity that can be used to predict activity in all systems including the therapeutic one, i.e. affinity, efficacy). The predicted outcome of this process is a far lower failure rate as molecules are progressed toward clinical testing. This course will describe pharmacological principles and procedures to quantify affinity, efficacy, biased signaling and allostery to better screen for new drugs and characterize drug candidates in lead optimization assays. In particular, new concepts that have entered the fabric of discovery over the past few years, namely biased signaling and allosteric drug function, will be emphasized as new ways forward to reduce new candidate attrition in the drug discovery process.

Day 1: PM: (1) New Drug Discovery Infrastructure: Strategies- vs Target- vs Systems-Based, Discovery Teams, Target Selection; (2) Cellular Activation (agonism): Affinity and Efficacy, Potency, Biased Signaling, Selectivity, Screening for Agonists

Day 2: AM: (3) Antagonism: Orthosteric (competitive, non-competitive, hemi-equilibria), Partial Agonism, Screening for Antagonists; (4) Inverse Agonism; (5) Allosteric Modulation, PAMs, NAMs, Screening for Allosterics; (6) Candidate Selection: Real Time Kinetics and *in vivo* Target Coverage

Day 2: PM: Drug Development: (7) Pharmacokinetics: Druglike Character, *in vivo* Absorption, Distribution, Metabolism; (8) Excretion, *in vivo* PK, Non-Linear PK (9) Safety Pharmacology: Safety vs Toxicity Risk Benefit Analyses

Instructor: Terry Kenakin, Ph.D., Professor, Department of Pharmacology, University of North Carolina School of Medicine

Dr. Kenakin has 32 years of experience in drug industry (7 at Burroughs-Wellcome and 25 at GlaxoSmithKline) as a project leader and lead optimization pharmacologist. The course is based on the book: A Pharmacology Primer: Techniques for more Effective and Strategic Drug Discovery' written by the instructor (Elsevier/Academic Press, 4th edition, 2014, pp 1-450). Summary sheets, exercises with answers, relevant papers will be provided to students, as well as a pdf of all presentation slides.

Register Online!
WorldPreclinicalCongress.com

Cambridge HEALTHTECH Institute
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Sponsorship, Exhibit & Lead Generation Opportunities

Comprehensive sponsorship packages allow you to achieve your objectives before, during, and long after the event. Signing on earlier will allow you to maximize exposure to hard-to-reach decision-makers.

PODIUM PRESENTATIONS — AVAILABLE WITHIN MAIN AGENDA!

Showcase your solutions to a guaranteed, targeted audience through a 15- or 30-minute presentation during a specific conference program, breakfast, lunch, or separate from the main agenda within a pre-conference workshop. Package includes exhibit space, on-site branding, and access to cooperative marketing efforts by CHI. For the luncheon option, lunches are delivered to attendees who are already seated in the main session room. Presentations will sell out quickly, so sign on early to secure your talk!

ONE-ON-ONE MEETINGS

Select your top prospects from the pre-conference registration list. CHI will reach out to your prospects and arrange the meeting for you. A minimum number of meetings will be guaranteed, depending on your marketing objectives and needs. A very limited number of these packages will be sold.

INVITATION-ONLY VIP DINNER/HOSPITALITY SUITE

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

Additional branding & promotional opportunities include:

- Hotel Room Keys
- Footprint Trails
- Staircase Ads
- Conference Tote Bags
- Literature Distribution (Tote Bag Insert or Chair Drop)
- Badge Lanyards
- Padfolios
- Program Guide Advertisement

EXHIBIT

Exhibitors will enjoy facilitated networking opportunities with 1,000+ qualified delegates, making it the perfect platform to launch a new product, collect feedback, and generate new leads. Exhibit space sells out quickly, so reserve yours today.

View Current Exhibitor List & Floor Plan

Looking for additional ways to drive leads to your sales team?

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

- Live Webinars
- White Papers
- Market Surveys
- Podcasts and More!

For additional information regarding sponsorship and exhibit opportunities, please contact:

Companies A-K
Ilana Quigley
Sr Business Development Manager
781-972-5457
iquigley@healthtech.com

Companies L-Z
Joseph Vacca, M.S.
Director, Business Development
781-972-5431
jvacca@healthtech.com

REGISTER AS AN EXHIBITOR!

FINAL WEEKS
TO REGISTER

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Hotel & Travel Information

CONFERENCE VENUE AND HOST HOTEL:

The Westin Copley Place
10 Huntington Ave
Boston, MA 02116
Phone: 1-617-262-9600

RESERVATIONS: Go to WorldPreclinicalCongress.com/Travel
Discounted Room Rate: $319 s/d

Discounted Room Rate Cut-off Date: May 15, 2017

Please call the hotel directly to reserve your room. 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.

TOP REASONS TO STAY AT THE WESTIN COPLEY -

Take advantage of the discounted group rate!

- Complimentary wireless internet access in guest rooms
- A short walk, bus, taxi or train ride to Boston's historic sites and family attractions
- Minutes from some of Boston's finest restaurants and shops
- Pet friendly

For more information, visit
WorldPreclinicalCongress.com/Travel

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Student Fellowship

Full time graduate students and Ph.D. Candidates are encouraged to apply for the World Preclinical Congress Student Fellowship. Applications are due by **April 14, 2017**.

- Interested students must complete the below application for the 2017 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 31, 2017 if they were accepted for the 2017 Student Fellowship.
- Accepted 2017 Student Fellows will receive a discounted conference rate of $195*, which must be paid in full by April 21, 2017. Credit card information is requested at the time of the application and will be charged upon application approval.
- This fellowship is limited to 20 students and is for the Main Conference Only*, June 13-15, 2017.
- All accepted 2017 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 2017 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 registration does not grant access to any of the short courses or pre-conference events. It also does not include hotel, travel or meals.*

Present a Poster and SAVE $50

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by **April 28, 2017.**

Reasons you should present your research poster at this conference:

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

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How to Register: WorldPreclinicalCongress.com

reg@healthtech.com • P: 781.972.5400 or Toll-free in the U.S. 888.999.6288

Please use keycode WPC F when registering

16th Annual

WPC WORLD PRECLINICAL CONGRESS

June 12-16, 2017

The Westin Copley Place, Boston, MA

CONFERENCE PRICING

	Commercial	Academic, Government, Hospital-affiliated
ALL ACCESS (Includes access to 2 Short Courses or 1 Symposium and 2 Conferences/Training Seminar)		
Registrations after May 26, 2017 and on-site	$3,149	$1,849
STANDARD PACKAGE (Includes access to 2 Conferences/Training Seminar, excludes Short Courses and Symposia)		
Registrations after May 26, 2017 and on-site	$2,849	$1,299
SINGLE CONFERENCE PRICING (Includes access to 1 Conference/Training Seminar, excludes Short Courses and Symposia)		
Registrations after May 26, 2017 and on-site	$1,849	$879

SHORT COURSE PRICING

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

SYMPOSIA PRICING

One Symposium	$999	$699
Two Symposia	$1299	$999

ADDITIONAL REGISTRATION DETAILS

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.

To view our Substitutions/ Cancellations Policy, go to healthtech.com/regdetails

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

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Please use keycode WPC F when registering

CONFERENCE PROGRAMS

MEDICINAL CHEMISTRY

June 13-15, 2017
Mastering Medicinal Chemistry - Part 1
Mastering Medicinal Chemistry - Part 2

ONCOLOGY

June 13-15, 2017
Preclinical Models and Tools in Oncology - Part 1
Tumor Models for Cancer Immunotherapy - Part 2
Cancer Immunotherapy and Combinations
Immuno-Oncology Targets

SCREENING

June 13-15, 2017
Phenotypic Screening and Chemical Biology
CRISPR for Target Discovery
3D Cellular Models

DISCOVERY & DEVELOPMENT

June 13-15, 2017
Predicting Drug Toxicity
Blood-Brain Barrier
Translational Strategies in CNS
~~CRISPR-Based Genome Editing - Part 2~~

SYMPOSIA

June 12, 2017
iPS Cells for Disease Modeling and Drug Discovery
New Tools for Disease Modeling
~~Phenotypic and Genotypic Cell Analysis in Immuno-Oncology~~

June 15-16, 2017
Nano-Delivery: Nucleic Acids, Cancer Immunotherapy and Beyond
Property-Based Drug Design

TRAINING SEMINAR

June 14-15, 2017
Applying Pharmacology to New Drug Discovery

SHORT COURSES

June 12, 2017 (12:00pm-3:00pm)
~~SC1: Introduction to Allosteric Modulators and Biased Ligands of GPCRs~~
SC2: Drug Metabolism and Its Impact on Decisions in Lead Discovery - Part 1

June 12, 2017 (3:30pm-6:30pm)
SC3: Drug Metabolism and Its Impact on Decisions in Drug Development - Part 2
SC4: Understanding and Dealing with Drug Disposition in CNS
SC5: Convergence of Immunotherapy and Epigenetics for Cancer Treatment

June 12, 2017 (7:00pm-9:30pm) Dinner provided
SC6: How to Best Utilize 3D Spheroids and CRISPR Assays in Oncology
SC7: Evaluating and Characterizing *in vitro* Models of Drug Toxicity

June 14, 2017 (7:00pm-9:30pm) Dinner provided
SC8: Applications of Functional Screening Using CRISPR and RNAi
~~SC9: Importance of Solubility in Drug Discovery and Development Applications~~
SC10: Humanized Mouse Models for Preclinical Assessment of Cancer Immunotherapy
~~SC11: 3D Lung Models~~

CONFERENCE DISCOUNTS

Poster Submission - **Discount ($50 Off)**: Poster abstracts are due by April 28, 2017. 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.

REGISTER 3 - 4th IS FREE: Individuals must register for the same conference or conference combination and submit completed registration form together for discount to apply.

Alumni Discount: Cambridge Healthtech Institute (CHI) appreciates your past participation at World Preclinical Congress. As a result of the great loyalty you have shown us, we are pleased to extend to you the exclusive opportunity to save an additional 20% off the registration rate.

Group Discounts: Discounts are available for multiple attendees from the same organization. For more information on group rates contact Cheryle Rosenberg at 781-972-5489, crosenberg@healthtech.com.

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

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