17th Annual
WORLD PRECLINICAL CONGRESS
June 18-21, 2018 The Westin Copley Place, Boston, MA

2018 Event Features

• 300+ Speakers
• 18 Conferences, 5 Training Seminars and 16 Short Courses
• Exhibit Hall of 90+ Companies with Novel Technologies and Solutions
• Poster Sessions, Interactive Breakout Discussions and Active Networking
• 1,100+ International Delegates focusing on Drug Discovery and Development

PLENARY KEYNOTE PROGRAM:
Partnering for Sustainable Funding

Jens Eckstein, PhD, President, SR One
Barbara K. Sosnowski, PhD, Vice President and Global Head, External R&D Innovation, Pharmatherapeutics and WRD External Partnerships, Pfizer, Inc.
Kevin Bitterman, PhD, Partner, Atlas Venture
Vivian Berlin, PhD, Director of Business Development, Life Sciences, Office of Technology Development, Harvard University
Ben Thorner, Senior Vice President and Head, MRL Business Development & Licensing, Merck

Register Online!
WorldPreclinicalCongress.com
### Conference-at-a-Glance

#### Pre-Conference Short Courses*

<table>
<thead>
<tr>
<th>Monday, June 18</th>
<th>Morning, Afternoon &amp; Dinner Short Courses* (10:00AM – 9:00PM)</th>
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<tr>
<td><strong>TS1A:</strong> Introductory Immunology for Autoimmune and Cancer Drug Discovery</td>
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#### Conferences

##### SHORT COURSES

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<tr>
<td>C1A: Preclinical Strategies, Models &amp; Tools in Oncology</td>
<td>Tuesday, June 19</td>
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<td>C2A: Tumor Models for Cancer Immunotherapy</td>
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<td>C3A: 3D Cellular Models</td>
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<td>C4B: Next-Gen Genomics: Leveraging CRISPR &amp; Single-Cells</td>
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<td>C5B: Mastering Medicinal Chemistry Part 2</td>
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<td>C6B: Translational Strategies in CNS</td>
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<td>C7B: Predicting Drug Toxicity</td>
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<td><strong>C8A:</strong> Optimizing Drug Metabolism &amp; Pharmacokinetics</td>
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<td><strong>C9A:</strong> NanoDrugs: Design and Delivery</td>
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#### Training Seminars

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<td>TS5B: Practical Introduction to PK/PD Modeling in Drug Discovery and Development</td>
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Where Preclinical Minds Meet Discovery Technologies

The 17th Annual World Preclinical Congress focuses on the latest trends and technologies impacting drug discovery and translational research. The Congress offers a unique opportunity for chemists, biologists, pharmacologists, cancer researchers, neuroscience scientists, toxicologists, bioengineers, screening experts and translational scientists in industry and academia as well as technology providers to come together and exchange expertise and opinions. World Preclinical Congress is a key networking event yielding new partnerships that accelerate preclinical research and translation across all therapeutic areas.

What You Can Expect in 2018...

- **300+ Speakers** presenting across 18 Conferences and 5 Training Seminars
- Featuring:
  - Oncology & Immuno-Oncology
  - Medicinal Chemistry
  - Drug Metabolism & Toxicity
  - Disease Modeling
  - Screening Tools & Technologies
  - CNS
  - Vesicles & Nanoparticles
- **Interactive Short Courses** provide additional training and education to brush up on your knowledge or expand your horizons
- **Exhibit Hall** of 90+ companies with novel technologies and solutions
- **Plenary Keynote Presentations** featuring the importance of Partnering for Sustainable Funding
- **Poster Sessions** featuring cutting-edge, ongoing research
- **Interactive Breakout Discussions** for active networking
- **Student Fellowships** offer discounted registration for young researchers looking to make a difference
- **1,100+ International Delegates** focusing on drug discovery and development – 72% of delegates from Pharma & Biotech
- **Sponsored Talks** by leading technology and service providers showcasing new offering

Who to Expect in Boston this June...

![Company Type Distribution]

- Biotech & Pharma: 72%
- Academic & Financial: 16%
- Services & Societies: 6%
- Healthcare: 5%
- Other (Press, Financial): 1%

![Geographic Location Distribution]

- USA*: 82%
- Europe: 10%
- Asia: 6%
- Rest of World: 2%

*USA Breakdown:
- East Coast: 73%
- West Coast: 15%
- Midwest: 12%

![Delegate Title Distribution]

- Executive & Director: 33%
- Scientist/Technologist: 31%
- Sales & Marketing: 16%
- Professor: 9%
- Manager: 7%
- Assistant: 4%

Stay Connected

#CHIWPC18

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.
Sponsorship & Exhibit 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)

Exhibit
Exhibitors will enjoy facilitated networking opportunities with 1,100+ 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.

Additional branding & promotional opportunities include:

- Meter Boards
- Footprint Trails
- Water Bottles
- Conference Tote Bags
- Literature Distribution (Tote Bag Insert or Chair Drop)
- Badge Lanyards
- Notepads
- Program Guide Advertisement

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 more information, please contact:

Companies A-K
Rod Eymael
Manager, Business Development
781-247-6286
reymael@healthtech.com

Companies L-Z
Joseph Vacca, MS
Director, Business Development
781-972-5431
jvacca@healthtech.com
**SHORT COURSES* JUNE 18 & 20, 2018 | BOSTON, MA

*See Registration Page for pricing details.

**MONDAY, JUNE 18 10:00 AM – 1:00 PM**

**SC1: Introduction to GPCR-Based Drug Discovery**
Instructor:
Annette Gilchrist, PhD, Professor, Pharmacology, Midwestern University

**SC3: Drug Metabolism and Its Impact on Decisions in Lead Discovery and Drug Development**
Instructors:
Zhengyin Yan, PhD, Senior Scientist, Department of Drug Metabolism and Pharmacokinetics, Genentech, Inc.
Donglu Zhang, PhD, Senior Scientist, Department of Drug Metabolism and Pharmacokinetics, Genentech, Inc.
David Duignan, PhD, Principal Research Scientist, Drug Metabolism, Pharmacokinetics & Bioanalysis, AbbVie Bioresearch Center

**SC4: Practical Phenotypic Screening**
Instructor:
Fabien Vincent, PhD, Associate Research Fellow, Hit Discovery and Lead Profiling Group, Pfizer

**SC6: Collecting, Storing, and Utilizing Precious Patient-Derived Tumors for Drug Discovery and Development**
Instructors:
Mark A. Murakami, MD, Instructor in Medicine, Department of Medical Oncology, Dana-Farber Cancer Institute
Srivatsan Raghavan, MD, PhD, Instructor, Department of Medical Oncology, Gastrointestinal Cancer Center, Dana-Farber Cancer Institute

**SC7: Introduction to Nanoparticles and Extracellular Vesicles for Drug Delivery**
Instructor:
Hicham Fenniri, PhD, Professor, Chemical and Biomedical Engineering, Northeastern University
Additional Instructors to be Announced

**MONDAY, JUNE 18 6:00 – 9:00 PM (DINNER PROVIDED)**

**SC9: How to Best Utilize 3D Cells, Spheroids, PDX Models in Oncology**
Instructors:
Madhu Lal-Nag, PhD, Group Leader, Trans-NIH RNAi Facility, National Center for Advancing Translational Sciences, National Institutes of Health
Geoffrey Bartholomeusz, PhD, Associate Professor and Director, Target Identification and Validation Program, Department of Experimental Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

**SC10: Applications of Artificial Intelligence & Machine Learning in Drug Discovery & Development**
Instructors:
Arvind Rao, PhD, Associate Professor, Department of Computational Medicine and Bioinformatics, University of Michigan
Istvan Enyedy, PhD, Principal Scientist, Medicinal Chemistry, Biogen
Jin Yao, Ph.D., Scientific Investigator, Computational Biology and Statistics, Target Sciences, GlaxoSmithKline
Ronald Alfa, MD, PhD, Vice President, Discovery & Product, Recursion Pharmaceuticals

**SC11: Understanding and Dealing with Drug Disposition in CNS**
Instructor:
Qin Wang, PhD, Principal Scientist, Drug Metabolism and Pharmacokinetics, Biotherapeutics and Medicinal Sciences, Biogen, Inc.

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**See More on Next Page ...**
WEDNESDAY, JUNE 20 6:30 – 9:30 PM (DINNER PROVIDED)

SC12: Humanized Mouse Models for Preclinical Assessment of Cancer Immunotherapy
Instructors:
Barbara Joyce-Shaikh, Associate Principal Scientist, Merck Research Laboratories
Maria Pinzon-Ortiz, Scientific Technical Leader, Immuno Oncology (In vivo), Novartis

SC14: Advanced Bioprinting Strategies for Generation of 3D Tissue Models
Instructors:
Margaret Prendergast, Director, Bioengineering, Allevi, Inc.
Ricky Solorzano, CEO, Allevi, Inc.
Yu Shrike Zhang, PhD, Research Faculty & Associate Bioengineer, Division of Engineering in Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School & Harvard-MIT Division of Health Sciences and Technology

SC15: Evaluating and Characterizing in vitro Models of Drug Toxicity
Instructors:
Terry Van Vleet, PhD, DABT, Head of Molecular and Computational Toxicology, Department of Preclinical Safety, Abbvie
Will Proctor, PhD, Senior Scientist, Head of Investigative Toxicology, Department of Safety Assessment, Genentech

SC16: Applications of CRISPR and Single-Cells: Best Practices from Set-Up to Data Analysis
Instructors:
Stephanie Mohr, PhD, Lecturer, Genetics & Director, Drosophila RNAi Screening Center at Harvard Medical School
Jennifer Smith, PhD, Deputy Director, ICCB-Longwood Screening Facility, Harvard Medical School
Sarah Boswell, PhD, Director of Sequencing Technologies, Laboratory of Systems Pharmacology and Director, Single-Cell Sequencing Core, Harvard Medical School
Roderick Beijersbergen, PhD, Group Leader, Netherlands Cancer Institute and Head, NKI Robotics and Screening Center

*See Registration Page for pricing details.
Cambridge Healthtech Institute Training Seminars offer real-life case studies, problems encountered and solutions applied, and extensive coverage of the basic science underlying each topic. Experienced Training Seminar instructors offer a mix of formal lectures, interactive discussions and activities to help attendees maximize their learning experiences. These immersive trainings will be of value to scientists from industry and academic research groups who are entering new fields – and to those working in supporting roles that will benefit from an in-depth briefing on a specific aspect of the industry.

TUESDAY, JUNE 19 - WEDNESDAY, JUNE 20

Day 1: 9:00 am – 5:00 pm | Day 2: 9:00 am – 12:00 pm

**TS1A: Introductory Immunology for Autoimmune and Cancer Drug Discovery**

This 1.5-day training seminar will provide an introduction to human immunology for discovery pharmacologists, biologists and chemists working in the biopharmaceutical industry on inflammation, autoimmunity, or immuno-oncology programs. This training seminar will focus on how the immune system is organized and gives rise to both normal and pathogenic immune responses. This overview will also serve as a basis for discussions of how the immune system can be modulated through biopharmaceutical intervention to either suppress pathogenic inflammation or enhance anti-tumor immunity.

**Instructors:**

Tim Bauler, PhD, Assistant Professor, Department of Biomedical Sciences, Western Michigan University Homer Stryker M.D. School of Medicine

Tom Sundberg, PhD, Senior Research Scientist I, Center for the Development of Therapeutics, Broad Institute of MIT and Harvard

**TS2A: Applying Pharmacology to New Drug Discovery: The System-Independent Quantification of Molecular Drug Properties for Prediction of Therapeutic Utility**

Over the past 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 allosteric 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.

**Instructor:**

Terry Kenakin, PhD, Professor, Department of Pharmacology, University of North Carolina School of Medicine

**TS3A: Genome Editing with Targeted Nucleases: Theory and Practice of CRISPR/Cas9 Technology Applications from Basic Research to Precision Therapies**

This rigorous day and a half program is ideal for discovery and translational scientists who are looking for a balanced knowledge of gene editing applications in drug discovery and development. Taught by experts in the CRISPR/Cas9 field, this program was designed as a succinct introduction into the technology “nuts and bolts”. Beginning from describing the basic aspects, key molecular features, strengths and shortcomings of CRISPR/Cas9 technology, the workshop instructors will advance towards sharing in-depth knowledge touching upon all facets of state-of-art genome editing applications, e.g. constructing of experimental cell culture based systems, engineering disease in vivo models supporting preclinical drug development workflows, rational design and functional screening of sgRNA libraries, and many others. Instructors will furthermore strive to achieve a balance between presenting theory information and conducting hands-on exercises in exploring available digital frameworks for designing and resourcing CRISPR/Cas9 studies, as well as troubleshooting complex experimental scenarios and conducting Q&A sessions.

**Instructors:**

Serguei Kozlov, PhD, MBA, PMP, Principal Scientist/PM, Team Leader PTO, Center for Advanced Preclinical Research, Frederick National Laboratory for Cancer Research (NCI)

Danilo Maddalo, PhD, Lab Head, ONC Pharmacology, Novartis Institutes for BioMedical Research, Novartis Pharma AG
WEDNESDAY, JUNE 20 - THURSDAY, JUNE 21

Day 1: 2:30 – 5:30 pm | Day 2: 8:00 am – 4:00 pm

TS4B: Introduction to Small Molecule Drug Discovery and Development

This 1.5-day lecture-based interactive seminar focuses on strategies for identifying drug discovery targets, discovering and characterizing small molecule hits, and developing structure-activity relationships to advance hits through lead optimization, preclinical development, and clinical evaluation. Participants will learn the stages and processes required to advance programs from idea to clinic, through examples and case studies. This seminar is intended for scientists in either academia or industry who would like to become more familiar with small molecule drug discovery and development.

Instructor:
H. James Harwood Jr., PhD, Founder and CEO, Delphi BioMedical Consultants, LLC

TS5B: Practical Introduction to PKPD Modeling in Drug Discovery and Development: Better, Faster, Cheaper

Model-based drug development (MBDD) has evolved into a set of practical techniques that dramatically reduce pharma R&D costs without sacrificing quality. Pharmacokinetic/Pharmacodynamic (PKPD) modeling lies at the heart of MBDD. Part 1 of the seminar will teach the concepts of MBDD and its application in drug R&D. Part 2 will provide an in-depth introduction to key concepts in PKPD modeling, and teach hands-on implementation of PKPD modeling on real and simulated datasets.

Instructors:
Arijit Chakravarty, CEO, Fractal Therapeutics
Ryan Nolan, PhD, Research Fellow, Takeda Pharmaceuticals International Co.

Each CHI Training Seminar offers 1.5 Days of instruction with start and stop times for each day shown above and on the Event-at-a-Glance published in the onsite Program & Event Guide. Training Seminars will include morning and afternoon refreshment breaks, as applicable, and lunch will be provided to all registered attendees on the full day of the class. Each person registered specifically for the training seminar will be provided with a hard copy handbook for the seminar in which they are registered. A limited number of additional handbooks will be available for other delegates who wish to attend the seminar, but after these have been distributed no additional books will be available.

Though CHI encourages track hopping between conference programs, we ask that Training Seminars not be disturbed once they have begun. In the interest of maintaining the highest quality learning environment for Training Seminar attendees, and because Seminars are conducted differently than conference programming, we ask that attendees commit to attending the entire program, and NOT engaging in track hopping, as to not disturb the hands-on style instruction being offered to the other participants.
Interactive Breakout Discussions

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.

TUESDAY, JUNE 19

5:05 pm Interactive Breakout Discussion Groups

ONCOLOGY & IMMUNO-ONCOLOGY

Preclinical Strategies for Combination Therapies
Mithun Khattar, PhD, Immuno-Oncology Lead, Cancer Pharmacology, Takeda Pharmaceuticals
- Key factors to consider when selecting combination strategy
- Immunomodulatory effects of small molecules
- Translating preclinical models to the clinic - the expected and unexpected

VC Perspective on Immuno-Oncology
Leigh Zawel, PhD, Managing Director, Development, MPM Capital
- Are there translational tools that are truly predictive of what kind of patients are most likely to respond to a given non-PD1 drug to predict (or at least narrow) populations to focus on in Ph1? Or are we going to have to continue to rely on empirical exploration large All-comer Ph1 studies?
- Are there translational tools that are truly predictive of what kind of patients are most likely to respond to a given non-PD1 drug to predict (or at least narrow) populations to focus on in Ph1? Or are we going to have to continue to rely on empirical exploration large All-comer Ph1 studies?

Preclinical CAR T Cell Development Challenges in Solid Tumors
Matthew M. Hewitt, PhD, Principal Scientist, Tumor Biology & Director, Tumor Immunology/Microenvironment, Research & Development, Bellicum Pharmaceuticals, Inc.
- Discuss the current assays available and their relevance
- Translatability of in vitro and in vivo systems to predict efficacy/safety
- Thoughts on how preclinical data translates to the clinic

SCREENING TOOLS & TECHNOLOGIES

Modeling Neurodegenerative Disorders for Drug Discovery and Development
Bilada Bilican, PhD, Investigator II, Neuroscience, Novartis Institutes for BioMedical Research (NIBR)
- In vitro correlates of complex neurodegenerative diseases
- How to model apparently sporadic neurodegenerative disorders
- Advanced cellular models - how to address cell-autonomous vs. non-cell autonomous mechanisms of neurodegeneration
- Phenotype- vs. target-based drug screening

Infrastructure and Strategy for iPSC Cell-Based Drug Discovery
Gabriele Proetzel, PhD, Director, Regenerative Medicine, Takeda Pharmaceuticals, Inc.
- How many and how large such collections should be
- Fit-for-phenotype and pathway sets, general MoA-annotated screening decks, diversity decks and the use of fragments and possibly other modalities (aptamers, etc.)
- Screening modalities (fragments, small molecules, natural products, aptamers, peptides, proteins, RNAi and genome editing reagents)

Compound Collections for Phenotypic Screening and Chemical Biology
Francisco Garcia, PhD, Associate Scientist/Postdoctoral Research Fellow, Chemical Biology and Proteomics, Merck Research Laboratories
- How many and how large such collections should be
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Developments in Methodologies to Enable Target Identification
Ivan Cornella Taracido, PhD, Director, Chemical Biology, Merck Research Laboratories
- What is new in chemical building blocks, reagents and reactions to enable omics and target ID?
- Photo-affinity ligation and activity-based probe workflows
- Advances in chemical genomics in mammalian haploid systems

VC Perspective on Immuno-Oncology
Leigh Zawel, PhD, Managing Director, Development, MPM Capital
- Are more investments happening in the discovery of new IO targets or in strategies to enhance PD1/CTLA4 efficacy?
- What critical data is coming in the next 12 months in the cancer vaccine and/or cell therapy space?
- For your firm to consider an investment in an IO asset, what are the "must haves" in a data package?

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Screening Tools & Technologies

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- Phenotype- vs. target-based drug screening
Developing Anticancer Therapies with Dual Specific Kinases
Lijun Sun, PhD, Director, Center for Drug Discovery and Translational Research, Beth Israel Deaconess Medical Center, Harvard Medical School
• Dual specific kinases and their benefits in treating cancers
• Other therapeutic areas of interest?
• Potential uses of the Dyrk

Safety Considerations of Kinase Inhibitors
Samit, Bhattacharya, PhD, Senior Principal Scientist, World Wide Medicinal
• Chronic safety concerns for kinase inhibitor for you in non-oncology indications
• Advancing chemotypes
• Using orthogonal profiles to assess safety

The Suitability of Animal Models for Preclinical Studies
Caghan Kizil, PhD, Helmholtz Young Investigator Group Leader, German Center for Neurodegenerative Diseases (DZNE) within Helmholtz Association
• What type of animal/experimental models are used for neurodegenerative disease models?
• What limitations are there for experimental models?
• How well can we recapitulate the diseases in experimental animal models?
• How can humanized models be improved?
• What is the future of research for CNS disease models?

Identifying Cerebrovascular Links to Neurodevelopmental Disorders
Baptiste Lacoste, PhD, Assistant Professor, Cellular and Molecular Medicine/Neuroscience Program, The University of Ottawa/Ottawa Hospital Research Institute
• What are the biggest challenges in identifying cerebrovascular links to neurodevelopmental disorders?
• What are the most promising directions for this research?
• How can this information be used to further development of drugs that pass the BBB?

Reduce, Reuse, Recycle Pharma Proprietary Therapeutic Agents for New Life in CNS Diseases
Susan Rosenbaum, J.D., Founder, Chairman & CEO, Lauren Sciences LLC
• BBB delivery
• Targeting within CNS
• Administration options

Understanding Role of Drug Metabolism and Its Impact
Moderators:
Dongliu Zhang, PhD, Senior Scientist, Department of Drug Metabolism and Pharmacokinetics, Genentech, Inc.
Zhengyin Yan, PhD, Senior Scientist, Department of Drug Metabolism and Pharmacokinetics, Genentech, Inc.
• Understanding induction, inhibition, and polymorphisms of drug metabolism enzymes
• Differences in metabolism between ADCs and small molecule drugs

Use of Modeling Tools and Strategies for Predicting ADME-Tox Properties
Moderator: Maria A. Miteva, PhD, Research Director, Molécules Thérapeutiques in silico (Mti), Inserm Institute
• Machine-learning or structure-based approaches for ADME-Tox prediction and optimization?
• Should the modeling tools for toxicity predicting be specific for xenobiotics and drugs?
• Quantum-mechanics methods for drug metabolism prediction

Nanoparticle Fabrication
Ghazal Hariri, PhD, Senior Scientist, Pfizer Global Research and Development
• Challenges in nanoparticle fabrication and scale up for pharmaceutical production
• Opportunities and applications for nanoparticle technology in the pharmaceutical industry
• Impact of nanoparticle fabrication on drug development

ONCOLOGY & IMMUNO-ONCOLOGY
Emerging Targets in Immuno-Oncology
Quamrul Hassan, PhD, Group Leader, Molecular and Cellular Pharmacology, EMD Serono
• Advancement in technology to validate targets in immuno-oncology
• Chemo-genomic approach in target validation
• Mechanistic preference in target selection: stimulatory vs. inhibitory
• Modality of inhibition in selecting targets: small molecules vs Biologics
• Phenotypic Screen to target generation and validation
INTERACTIVE BREAKOUT DISCUSSIONS  JUNE 19 & 21, 2018  |  BOSTON, MA

Modeling Innate and Adaptive Immunity in Murine Models
Marcus Bosenberg, MD, PhD, Associate Professor of Dermatology and Pathology, Yale University, Co-Leader, Genomics, Genetics and Epigenetics Program, Yale Cancer Center

• Can animal models of cancer immunology predict human responses?
• How should preclinical models be used to guide drug development in immunology?
• How can existing models be improved?

Emergence of Microfluidic Models for Preclinical Assessment of Efficacy of Immune Checkpoint Inhibitors
Jeff Borenstein, PhD, Laboratory Technical Staff, Biomedical Microsystems, Draper

• Immune checkpoint inhibitors exhibit variable patient response rates for reasons that are not completely clear. What attributes of an in vitro model are seen as most critical for establishing it as a tool to study mechanisms of responder/non-responder behavior?
• Microfluidic model systems may find use as tools for drug development and ultimately for precision medicine applications, where patient response could be predicted before administering therapy. Where are the most significant opportunities for these systems, and would the attributes models for each respective application be different?
• May existing in vitro cancer models are cell culture systems, where cancer cells are cultured in a 3D microenvironment. Emerging systems are focusing on tumor spheroids and on unmodified tumor fragments obtained from patient (or animal) biopsy. What are the principal advantages and disadvantages of each type of model?

SCREENING TOOLS & TECHNOLOGIES

The Use of 3D Cellular Models, Organ-on-a-Chip Technologies, or Microphysiological Systems in Preclinical Evaluation of Pharmaceuticals
William Daly, PhD, Managing Director & Faculty Scientist, Orthopedics and Rehabilitation, University of Wisconsin - Madison

• What are the key barriers to adoption of 3D cellular models in preclinical workflows?
• What are pharmaceutical wish lists (biomarkers, function, histology, etc.) for validation of 3D cellular models (groups to split into organ of choice)?
• Where is the ideal fit for 3D cellular models in the drug development pipeline/pharmaceutical testing?
• What are the missing models/unmet needs for preclinical evaluation and efficacy testing?
• Are single organs enough or is there a strong need for multi-organ testing?

3D Models of Human Organs: Challenges and Prospects
Samira Musah, PhD, Dean’s Postdoctoral Fellow, Wyss Institute at Harvard University and Harvard Medical School

• Inducing stem cell differentiation, cell maturation, and functionality
• Organoids, organs-on-chips, 3D-bioprinted tissues
• Applications in disease modeling and therapeutic discovery

CRISPR/Cas9 for Drug Discovery Applications
Roderick Beijersbergen, Ph.D., Group Leader, Netherlands Cancer Institute and Head, NKI Robotics and Screening Center

• Impact of CRISPR/Cas9 for drug discovery in pharma and academia
• Applications for functional screens, creating cell lines and disease models
• Design and optimization of low- and high-throughput screens using CRISPR approaches
• Application of CRISPR-knockout, -activation and -inhibition
• Impact of new CRISPR technologies and reagents

Exploiting CRISPR, RNAi and Single-Cell Analysis: What You Need to Know Before and After
Sarah Boswell, PhD, Director of Sequencing Technologies, Laboratory of Systems Pharmacology and Director, Single-Cell Sequencing Core, Harvard Medical School

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

Stephanie Mohr, PhD, Lecturer, Genetics & Director, Drosophila RNAi Screening Center at Harvard Medical School

• Understanding inherent limitations and need for using complementary techniques
• Examples of how multiple techniques have been put to good use for addressing biological questions
• Evaluating and testing the reagents and tools
• Insights on inherent challenges and ways to overcome it
• Tackling data analysis

How to Design Machine Learning Models to Automatically Identify Biological Mechanisms
Greg Johnson, PhD, Scientist & Machine Learning Specialist, Allen Institute for Cell Science

• Data representation
• Model architecture
• Designing an objective function

Challenges in Phenotypic, Target Agnostic Drug Discovery
Jesus Medina, PhD, Manager, Medicinal Chemistry, GlaxoSmithKline

• Key challenges in cell-based phenotypic drug discovery efforts
• Early assessment of the validity and viability of hits obtained from screens
• What aspects of phenotypic drug discovery are the most advantages in drug discovery
INTERACTIVE BREAKOUT DISCUSSIONS  JUNE 19 & 21, 2018  |  BOSTON, MA

**MEDICINAL CHEMISTRY**

**Public-Private Partnerships in Drug Discovery**
*Dimtrios Tzalis, PhD, CEO, Taros Chemicals GmbH & Co. KG*
- How can collaborative public-private partnerships foster drug development?
- What steps are being taken to close the "innovation gap"?
- How can partnerships be beneficial for both parties?

**Challenges in Phenotypic, Target Agnostic Drug Discovery**
*Jesus Medina, PhD, Manager, Medicinal Chemistry, GlaxoSmithKline*
- Key challenges in cell-based phenotypic drug discovery efforts
- Early assessment of the validity and viability of hits obtained from screens
- What aspects of phenotypic drug discovery are the most advantages in drug discovery

**CNS**

**Lost in Translation? Asking the Right Questions in the Right Language**
*Dario Doller, PhD, Sage Therapeutics*
- CNS disease etiology understanding: who owns it?
- What are the major disconnects between lab experimentation and clinical research?
- Are differences in physiology between preclinical species and human affecting the translational gap?
- Patient segmentation: strategies and outcomes
- Correlation or causation? Importance of genetic links for different CNS diseases
- What are the attributes that have real impact minimizing risk during novel target selection?
- Human as a model for human – what is the future of experimental medicine in CNS drug discovery?

**Improving the Success Rate of CNS Therapies**
*Takaomi C. Saido, PhD, Laboratory Head, Laboratory for Proteolytic Neuroscience, RIKEN Brain Science Institute*
- Why have more than 400 medication candidates for Alzheimer’s Disease failed?
- Which therapies have the best chance to succeed, and why?
- Immunotherapy for neurodegenerative disease
- What is the future of immunotherapy?

**Using iPSC for Drug Safety Screening**
*Gary Gintant, PhD, Senior Research Fellow, Department of Integrative Pharmacology, Integrated Science and Technology, AbbVie*
- What are concerns for using human induced pluripotent stem cell (iPSC)-derived cells to assess drug safety screening?
- How to consider standardizing assays and comparing results? Assay reproducibility?
- Generation of patient derived hiPSC-derived cardiomyocytes: present and future roles.
- The role of newer co-cultures and 3D structures in present and future efficacy and safety studies.
- How to best adapt hiPSCs for high-throughput phenotypic screening.

**VESICLES & NANOPARTICLES**

**Best Source of Stem Cell Derived EVs**
*Paul Robbins, PhD, Professor and Director of the TSRI Center on Aging, Molecular Medicine, The Scripps Research Institute*
- Are EVs derived from embryonic stem cells as or more therapeutic than adult stem cells?
- How similar in phenotype and function are the EVs from different stem cell sources?
- Can allogeneic stem cell derived EVs be used clinically?

**Challenges in EV Characterization**
*Alain Brisson, PhD, Emeritus Professor, UMR-CBMN CNRS, University of Bordeaux*
- Why do we need to better characterize EVs?
- How reliable and efficient are the methods currently used for detecting, identifying, quantifying, isolating EVs?
- What do we need for improving EV detection, identification, quantification, isolation?

**DRUG METABOLISM & TOXICITY**

**Gaps in Translating Preclinical Findings to the Clinic**
*William Proctor, PhD, Senior Scientist, Head of Investigative Toxicology, Department of Safety Assessment, Genentech*
- Model assay sensitivity – what level (or magnitude) of change can we detect?
- Do we have appropriate study design, data analysis, statistical analysis, and statistical power?
- How predictive are our preclinical findings/models to the clinic?
- What is it we are missing? Are there other useful models? Are their gaps in our translation knowledge?
Partnering for Sustainable Funding

The panel is designed to discuss partnering between various stakeholders such as drug discovery startups, VC firms, large pharmaceutical companies and academic labs in order to advance new target discovery and preclinical research. VC companies, and pharma search & evaluation departments will be represented on the panel.

Jens Eckstein, PhD, President, SR One

Barbara K. Sosnowski, PhD, Vice President and Global Head, External R&D Innovation, Pharmatherapeutics and WRD External Partnerships, Pfizer, Inc.

Kevin Bitterman, PhD, Partner, Atlas Venture

Vivian Berlin, PhD, Director of Business Development, Life Sciences, Office of Technology Development, Harvard University

Ben Thorner, Senior Vice President and Head, MRL Business Development & Licensing, Merck

Plenary Technology Panel

Advancing Innovation in Drug Discovery and Translational Research

This year’s Plenary Technology 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.

Ashley Rae Kark, MBS, Director, Corporate Relations, Scientist.com

Additional Panelists will be Announced

Sponsorship Opportunities Available
With immunotherapy and combination therapy becoming the major focus of oncology research over the last several years, the 17th Annual World Preclinical Congress has strengthened and expanded its cancer coverage. Translational strategies for combination therapy development, funding and partnership opportunities in preclinical cancer research, novel preclinical models, human tissue-based organoids and tumoroids, new immuno-oncology targets, and tumor models for cancer immunotherapy are the key topics that will be discussed at the event. The cancer tracks will bring together top experts from industry and academia as well as technology-providing companies to discuss emerging trends and solutions to increase translational successes and decrease clinical failures for novel cancer therapies.

June 19-20

AGENDA Preclinical Strategies, Models & Tools in Oncology
AGENDA Tumoroids for Oncology Research

June 20-21

AGENDA Immuno-Oncology Targets
AGENDA Tumor Models for Cancer Immunotherapy
TUESDAY, JUNE 19

7:30 am Registration Open and Morning Coffee

IMMUNO-ONCOLOGY STRATEGIES

8:15 Chairperson's Opening Remarks
Ken Hance, Senior Director & Head, Immune Biology, Immuno-Oncology & Combinations Discovery Performance Unit, GlaxoSmithKline

8:20 In vitro and in vivo Model Development to Support Drug Discovery in Immuno-Oncology
Ken Hance, Senior Director & Head, Immune Biology, Immuno-Oncology & Combinations Discovery Performance Unit, 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.

8:50 Application of Human Germline Genetics and Novel Animal Disease Models for the Discovery and Development of Cancer Immunotherapy
Xingfeng Bao, PhD, Head, Immuno-Oncology, Integrated Biology Engine, Eisai AIM Institute, Eisai, Inc.
In the discovery and development of cancer immunotherapy, polymorphic nature of immune therapeutic targets and limited translatability of mouse models make prediction of human response to an immunotherapy challenging. In this presentation, we will discuss an application of human germline genetics and primary human tumor tissues for the characterization and translational biomarker discovery of a novel drug candidate.

9:20 Rational Immunotherapy Combination with Non-IO Agents through Preclinical Modeling
David Schaer, Principal Research Scientist, Cancer Immunobiology Experimental and Translational Immuno-Oncology Group, Eli Lilly and Company
The explosion of clinical trials testing IO checkpoint agents has placed the field at risk of becoming oversaturated with combination trials of IO agents with SOC, and new drugs entering clinical testing where IO agents are part of the therapeutic paradigm. Using mouse modeling and high content molecular profiling, we investigate novel combinations strategies involving immune checkpoint inhibitors and targeted therapeutics to help guide clinical translation/development of optimal combinations.

9:50 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

NEW TARGETS AND APPROACHES

10:35 Therapeutic Strategies for Targeting the EZH2 Methyltransferase in Cancer
Robert A. Rollins, PhD, Associate Director, Oncology Research & Development, Pfizer
Epigenetic alterations are a hallmark of cancer. This observation has prompted the development of targeted therapies that inhibit epigenetic modifiers and chromatin remodeling enzymes. As epigenetic regulators differ from classic oncogenic drivers, the challenge has been to identify optimal strategies for therapeutic intervention. We have discovered potent and selective inhibitors of the histone methyltransferase EZH2. Exploratory studies with these molecules have revealed genetic dependencies and novel combination strategies with both targeted and immunotherapies that may broaden the clinical landscape for this cancer target.

11:05 Discovery and Characterization of Functional Anti-Tumor Antibodies from Non-Progressing Cancer Patients Undergoing Immunotherapy
Norman Greenberg, PhD, CSO, Senior Vice President, Therapeutics, Atreca
We isolated plasmablasts from patients with metastatic non-progressing cancers that received checkpoint inhibitor immunotherapy. Using our proprietary Immune Repertoire Capture™ technology we determined paired heavy and light chain antibody sequences from these plasmablasts. From these hyper-accurate sequences we subsequently expressed recombinant antibodies that bound non-autologous human tumor tissues and cell lines. Importantly, some of these antibodies caused regression of, and durable immunity toward, heterologous syngeneic tumors in mice. Our research program demonstrates that functional anti-tumor antibody responses in cancer patients target public antigens following checkpoint inhibitor therapy and provides an approach to identify and develop important therapeutic antibodies.
11:35 Unique In Vivo Tests for Cancer Drug Discovery: Early Identification of High Value Leads
Jean Viellet, PhD, CEO, CSO, Invovtion
Since its introduction, the Chorioallantoic membrane of chick embryos has proven extremely valuable to efficiently support the growth of Human tumor Xenografts. Invovtion is harnessing the power of this model to provide a highly sensitive, fast, reproducible, standardized and affordable method for early in vivo assessment of new drug compounds on: tumor development, angiogenesis and malignant cell dissemination.

11:50 Sponsored Presentation (Opportunity Available)

12:05 pm Session Break

12:10 Luncheon Presentation: Mouse Syngeneic Models: Biological Variability in Response to Therapy and Underlying Cellular and Molecular Factors Involved
Edgar R. Wood, PhD, Senior Research Director, Discovery, Charles River
Syngeneic models have greater animal to animal variability as well as inter-study variability than standard xenograft models. We will discuss potential biological explanations for this, the relationship between gene expression changes and individual animal response and practical implications for study design and interpretation.

12:40 Session Break

AI FOR ONCOLOGY RESEARCH

1:15 Chairperson’s Remarks
David Schaefer, Principal Research Scientist, Cancer Immunobiology Experimental and Translational Immuno-Oncology Group, Eli Lilly and Company

1:20 Leveraging Artificial Intelligence for Drug Discovery to Help Identify and Rank Potential Promising Immuno-Oncology-Targets
John Gregory, Director, R&D Project & Portfolio Management Business Technology, Pfizer
Pfizer’s private cloud-based implementation of IBM Watson for drug discovery is intelligently helping our Oncology R&D researchers to analyze millions of scientific documents, and supporting Pfizer data, to help identify and rank potential promising immuno-oncology targets, and identify potential adverse events.

1:50 Machine Learning to Predict Combined Drug Response from Genomic Data
Kathleen Burke, PhD, Senior Scientist, Bioinformatics, Oncology, Innovative Medicines & Early Development, AstraZeneca
This presentation will discuss AI algorithms that can help predict drug response in oncology and other therapeutic areas using genomic data from clinical trials and patient care.

2:20 Triple Humanized Mouse Models
Benjamin Cuffia, PhD, Principal Scientist, Oncology, Biomodels, LLC

2:35 Hollow Fiber Model - In vivo Prescreen in Cancer Drug Discovery
Anja Baumgart, Business Development Manager, Sales, ProQinase
Anticancer lead compounds need to be prioritized for in vivo analysis. The Hollow Fiber Model (HFM) evaluates the anticancer efficacy of a drug in three cell lines simultaneously in a single mouse. The HFM prescreen was tested for Crizotinib and appeared better than in vitro proliferation for the outcome of xenograft studies. The HFM prescreen is highly predictive, cost- and time-effective, saving compound and mice.

2:50 Refreshment Break in the Exhibit Hall with Poster Viewing

VC AND SEARCH & EVALUATION PERSPECTIVE

3:30 Chairperson’s Remarks
Leigh Zawel, PhD, Managing Director, MPM

3:45 FEATURED PANEL DISCUSSION: Partnering Ecosystem in Immuno-Oncology
The rapid expansion of the field of immune-oncology provoked a spike of venture capital activity and increased the level of external collaboration among pharmaceutical and biotechnology companies. This panel discussion will focus on strategic consequences of the IO wave for pharma, biotech, and the venture ecosystem.
Panelists:
Leigh Zawel, PhD, Managing Director, MPM
Michael Gladstone, MD, Principal, Atlas Venture
Michael Woo, PharmD, MBA, Head, Search & Evaluation, Immuno-Oncology, External Innovation, EMD Serono Research & Development Institute
Maude Tessier, Executive Director, Business Development, Merck

Topics to be discussed include, but are not limited to:
• Can we expect to see new IO therapies with single agent activity akin to PD1, or is the future going to be all about combination partners?
• Are more investments happening in the discovery of new IO targets or in strategies to enhance PD1/CTLA4 efficacy?
• What critical data is coming in the next 12 months in the cancer vaccine and/or cell therapy space?
• For your firm to consider an investment in an IO asset, what are the “must haves” in a data package?

5:00 Find Your Table and Meet Your Moderator

5:05 Interactive Breakout Discussion Groups

Preclinical Strategies for Combination Therapies
Mithun Khattar, PhD, Immuno-Oncology Lead, Cancer Pharmacology, Takeda Pharmaceuticals
• Key factors to consider when selecting combination strategy
• Immunomodulatory effects of small molecules
• Translating preclinical models to the clinic - the expected and unexpected

VC Perspective on Immuno-Oncology
Leigh Zawel, PhD, Managing Director, MPM
Michael Gladstone, MD, Principal, Atlas Venture
• Are more investments happening in the discovery of new IO targets or in strategies to enhance PD1/CTLA4 efficacy?
• What critical data is coming in the next 12 months in the cancer vaccine and/or cell therapy space?
• For your firm to consider an investment in an IO asset, what are the “must-haves” in a data package?
• Are there translational tools that are truly predictive of what kind of patients are most likely to respond to a given non-PD1 drug to predict (or at least narrow) populations to focus on in Ph1? Or are we going to have to continue to rely on empirical exploration large All-comer Ph1 studies?

5:45 Reception in the Exhibit Hall with Poster Viewing
7:00 Close of Day

WEDNESDAY, JUNE 20

7:45 am Registration Open and Morning Coffee
8:25 Chairperson’s Remarks
Mithun Khattar, PhD, Immuno-Oncology Lead, Cancer Pharmacology, Takeda Pharmaceuticals

8:30 Tumor Microenvironment Biomarkers to Guide Translational Decisions in Immuno-Oncology
Mithun Khattar, PhD, Immuno-Oncology Lead, Cancer Pharmacology, Takeda Pharmaceuticals
Murine models for pre-clinical studies in immuno-oncology and cancer pharmacology have greatly evolved. However, not all pre-clinical breakthrough therapies translate into clinical successes. Fundamental differences in the immune composition, tumor microenvironments, progression of disease, etc. between mice and humans may contribute to translational failures. A deeper exploration of the relevant immunological MoAs and biomarker strategies can minimize such failures by facilitating patient selection as well as designing potential combination therapies.

9:00 KEYNOTE PRESENTATION: Immunotherapy for Cancer: The Need for More Effective Combination Therapies
Ronald Herbst, PhD, Vice President, R&D and Head, Oncology Research, MedImmune
Combination approaches are the keys to improving clinical response. From preclinical immune-oncology mouse models to patients enrolled on clinical trials, novel high throughput technologies enable us to understand the mechanisms underlying the complex interactions between the immune system and cancer, identify predictive biomarkers for the patients who will most likely benefit from current immunotherapies, avoid immune-related adverse events, and guide the future combination cancer immunotherapy.

9:30 Talk Title to be Announced
John Swart, PhD, President, Exemplar Genetics

10:00 Coffee Break in the Exhibit Hall with Poster Viewing
Inaugural  
Tumoroids for Oncology Research  
Capturing and Deciphering Cancer’s Heterogeneity

Recommended Event Package

Short Course 6: Collecting, Storing, and Utilizing Precious Patient-Derived Tumors for Drug Discovery and Development  
Short Course 9: How to Best Utilize 3D Cells, Spheroids, PDX Models in Oncology  
Short Course 14: Advanced Bioprinting Strategies for Generation of 3D Tissue Models  
Conference: Tumoroids for Oncology Research  
Conference: 3D Cellular Models

TUESDAY, JUNE 19

7:30 am Registration Open and Morning Coffee

ENGINEERING MODELS & APPLYING PLATFORMS

8:15 Chairperson’s Opening Remarks  
Geoffrey Bartholomeusz, PhD, Associate Professor and Director, Target Identification and Validation Program, Department of Experimental Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

8:20 Hyaluronan Hydrogels Enable 3D Culture of Cancer Cells and Drug Screening  
Alexander Baker, Research Scientist, Molly Shoichet Laboratory, Institute of Biomaterials and Biomedical Engineering, Chemical Engineering & Applied Chemistry, The Donnelly Centre, University of Toronto  
We synthesized a series of hyaluronan-based hydrogels with either matrix metalloproteinase (MMP)-degradable or poly(ethylene glycol) (PEG) crosslinks, resulting in 3D networks that cells can remodel and invade. By controlling the chemical functionality and modulus, we investigate their role on cell invasion and correlate that with drug response. We investigate a series of different cancer cell types, from breast and lung, and study their invasion into EGF-gradient and/or protein and peptide-modified hydrogels.

8:50 Building Empirical Culture Technology to Facilitate Rare Cancer ex vivo Models at Scale  
Moony (Yuen-Yi) Tseng, PhD, Group Leader, Research Scientist, Cancer Program, The Broad Institute of MIT and Harvard  
It is challenging to access fresh rare tumor samples across hospitals and we lack the ability to efficiently translate the limited biological knowledge for most rare tumors into disease-specific model generation SOPs. By partnering with foundations, social media to engage patients, and online consent, we have developed just-in-time biologistics to acquire fresh samples and empirically sample culture media space in a high-throughput, systematic manner to accelerate ex vivo model generation in rare cancers.

9:20 Air-Grown Lung Cancer Tumor Spheroids as a Novel in vitro Anti-Cancer Therapeutic Evaluation Platform  
Samantha A. Meenach, PhD, Assistant Professor, Department of Chemical Engineering, Department of Biomedical and Pharmaceutical Sciences, University of Rhode Island  
Our research focuses on the development of air-grown multicellular spheroid (MCS) that mimic in vivo avascular tumors for the evaluation of aerosol anti-cancer therapeutics. Thus far, we have produced MCS comprised of A549 lung adenocarcinoma cells that will be expanded to other cell lines in the future. This work involves the initial design of the technology and evaluation of MCS grown in this novel fashion. The growth kinetics, morphology, and response to the model drug paclitaxel have been completed.

9:50 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

10:35 Three-Dimensional Tumor Model Mimics Stromal–Breast Cancer Cells Signaling  
Hossein Tavana, PhD, PEng, Associate Professor, Department of Biomedical Engineering, The University of Akron  
Tumor microenvironment is a major contributor to tumor progression and is implicated in various stages of the disease. Using three-dimensional tumor spheroid models and molecular analysis, we demonstrate that CXCL12 (chemokine)–CXCR4 (receptor) signaling between carcinoma-associated fibroblasts and breast cancer cells drives proliferation and chemotherapy resistance of the cancer cells. Disrupting this signaling diminishes growth drug resistance of breast cancer cells.

11:05 Clinically Relevant Patient-Derived Xenograft–Derived (PDXEx) ex vivo Model for Evaluation of Tumor-Specific Therapies  
Geoffrey Bartholomeusz, PhD, Associate Professor and Director, Target Identification and Validation Program, Department of Experimental Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center  
Translation of successful therapies into the clinics requires in vitro preclinical models that accurately predict the response of the original tumor to therapy. Our preclinical PDXEx model closely replicates both the tissue architecture and genetic signature to the original tumor. We confirm the predictive value of our PDXEx model and demonstrate its importance as a platform for robotic-based high-throughput drug screens.
Acute lymphoblastic leukemia (ALL) is the commonest pediatric malignance. The current survival rate of ALL for pediatric patients with chemotherapy is approaching 90%. However, no promising results have been observed in refractory ALL due largely to chemoresistance. We herein explored in a 3D biomimetic ‘Leukemia-on-a-Chip’ how the leukemic bone marrow formed a supportive and protective vascularized niche to confer leukemia chemoresistance, highlighting the crucial role of the BM niche in leukemia progression and therapy resistance.

2:50 Refreshment Break in the Exhibit Hall with Poster Viewing

TRANSLATING IN VITRO ASSAYS TO IN VIVO SYSTEMS

3:30 Optical Imaging of Anti-Cancer Drug Response of Organoids
Alex Walsh, PhD, Assistant Scientist, Department of Medical Engineering, Morgridge Institute for Research, University of Wisconsin - Madison

Primary tumor organoids are a robust model of individual human cancers and present a unique platform for patient-specific drug testing. Optical metabolic imaging (OMI) is highly sensitive to drug response in organoids, and OMI in tumor organoids correlates with host survival. Therefore, functional optical imaging of organoids could enable accurate high-throughput screens of drug response for individualized cancer treatment.

4:00 Increasing CAR T Cell Efficacy in Solid Tumors via Understanding the Pro-Tumor Microenvironment
Matthew M. Hewitt, PhD, Principal Scientist, Tumor Biology & Director, Tumor Immunology/Microenvironment, Research & Development, Bellicum Pharmaceuticals, Inc.

The talk focuses on challenges in developing CAR T cell therapies for solid tumors. A focal point will be describing a novel in vitro assay, cocultured with pro-tumor cell populations, and its use to screen lead preclinical candidates. The talk touches on translatability of in vitro assays to in vivo rodent systems and whether the use of molecular activation switches can bypass pro-tumor immunosuppressive elements in the tumor microenvironment.

4:30 Late Breaking Presentation

5:00 Find Your Table and Meet Your Moderator

5:05 Interactive Breakout Discussion Groups
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. Details on the topics and moderators are available by clicking here.

Preclinical CAR T Cell Development Challenges in Solid Tumors
Matthew M. Hewitt, PhD, Principal Scientist, Tumor Biology & Director, Tumor Immunology/Microenvironment, Research & Development, Bellicum Pharmaceuticals, Inc.

- Discuss the current assays available and their relevance
- Translatability of in vitro and in vivo systems to predict efficacy/safety
- Thoughts on how preclinical data translates to the clinic

5:45 Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day
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. Details on the topics and moderators are available by clicking here.

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- Discuss the current assays available and their relevance
- Translatability of in vitro and in vivo systems to predict efficacy/safety
- Thoughts on how preclinical data translates to the clinic

**5:45 Reception in the Exhibit Hall with Poster Viewing**

**7:00 Close of Day**

**WEDNESDAY, JUNE 20**

**7:45 am Registration Open and Morning Coffee**

**8:25 Chairperson's Remarks**
Chao Zhou, PhD, Associate Professor, Founding Member, Department of Bioengineering, Department of Electrical and Computer Engineering, Lehigh University

**8:30 Multi-Dimensional Biomaterial Screening Reveals Microenvironmental Mechanisms of Drug Resistance**
Alyssa Schwartz, Graduate Research Assistant, Chemical Engineering, University of Massachusetts Amherst

We combined biomaterial platforms, drug screening, and systems biology to identify mechanisms of matrix-mediated resistance to RTK-targeted cancer therapies. Drug response varied with dimensionality and cell-cell contacts, and a systems analysis identified MEK phosphorylation as the key factor associated with this variation. This uncovered the combination of sorafenib with a MEK inhibitor, which decreased viability in vitro and reduced tumor burden, but was not captured by screening on plastic alone.

**9:00 High-Throughput Optical Coherence Tomography Imaging for Drug Screening with 3D Tumor Spheroids**
Chao Zhou, PhD, Associate Professor, Founding Member, Department of Bioengineering, Department of Electrical and Computer Engineering, Lehigh University

Three-dimensional (3D) tumor spheroid models have gained increased recognition as important tools in cancer research and anti-cancer drug development. However, currently available imaging approaches employed in high-throughput screening (HTS) drug discovery platforms are unable to resolve 3D structures deep inside (>50 μm) tumor spheroids. In this study, we established a label-free, non-invasive optical coherence tomography (OCT) imaging platform to characterize 3D morphological and physiological information of multicellular tumor spheroids.

**9:30 A Novel High-Throughput Multi-Parametric Drug Screening Method for 3D Tumor Spheroids Using Celigo Image Cytometer**
Leo Chan, Technology Research & Development Manager, Nexcelom Bioscience LLC

There is an increase in utilizing 3D spheroid for drug screening. We demonstrated a cancer drug scoring method using multi-parametric analysis to rank the anti-cancer effects of drugs on tumor spheroids. The assays conducted were growth inhibition, perimeter cell-death, and viability. The drug can be screened to identify potential drug candidates.

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

**10:45 CO-PRESENTATION: Creation of Patient Derived Cancer Models at Scale Leverages Patient Diversity for Improved Clinical Trials Predictions**
Kin-Hoe Chow, PhD, Associate Director, Center for Patient Derived Models, Dana-Farber Cancer Institute
Keith L. Ligon, MD, PhD, Director, Center for Patient Derived Models, Department of Oncologic Pathology, Dana-Farber Cancer Institute

The Center for Patient Derived Models is created to support large-scale generation of cancer models to sufficiently capture the diversity of patient biology encountered in clinical trials and makes them readily available to the cancer community. Currently supporting the studies of hundreds of CNS, hematologic, and solid cancer models, the Center aims to accelerate clinical trial results interpretation, foster collaborations with industry, and advance patient models into clinical functional diagnostic tools.

**11:15 Human Tumor Organoids as a Novel Model for Drug Discovery and Screening**
Janica Wong, PhD, Senior Scientist, Translational Pathology, Merck Research Labs

We generated in vitro recapitulating the cellular architecture and functions of the tumor, and which may be a more relevant model to study cancer biology. 3D tumoroids were established from human tumor tissues. Tumoroids generated in vitro recapitulating the cellular architecture and functions of the tumor, and which may be a more relevant model to study cancer biology. 3D in vitro tumoroids were established from human tumor tissues. Tumoroids transplanted into humanized mice produced tumors that resembled primary human tumors, suggesting organoids are a useful model for predicting drug responses with potential for use in precision medicine.

**11:45 Session Break**

**12:20 pm Dessert and Coffee Break in the Exhibit Hall with Poster Viewing**

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

**1:00 PLENARY KEYNOTE SESSION (click here for details)**

**2:30 Refreshment Break in the Exhibit Hall with Poster Viewing**

**3:10 Close of Conference**
WEDNESDAY, JUNE 20

11:00 am Registration Open

11:50 Bridging Luncheon Presentation: From Syngeneic to Humanized Mouse Models: Addressing the Needs for Novel Immunotherapies

Philippe Slos, PhD, Study Director, Oncodesign

Discovery of novel immunotherapy represents a main and intense focus of research in oncology. Proof-of-concept studies in animals represent a challenge and require well-characterized and appropriate animal models with most of the time customized approaches. Some recent development and data generated for immune checkpoint modulators, adoptive cell transfer therapy, vaccines and bispecific T cell engagers will be presented.

12:20 pm Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

1:00 PLENARY KEYNOTE SESSION (click here for details)

2:30 Refreshment Break in the Exhibit Hall with Poster Viewing

NOVEL IMMUNE CHECKPOINTS AND IMMUNOMODULATORY STRATEGIES

3:10 Chairperson’s Opening Remarks

Li Peng, PhD, Vice President, Biotherapeutics Discovery, Palleon Pharmaceuticals

3:15 New Checkpoint Molecules

Laszlo Radvanyi, PhD, Senior Vice President & Senior Global Scientific Advisor, Immuno-Oncology, EMD Serono

3:45 New Immune Checkpoints for Human Cancer Immunotherapy

Xingxing Zang, PhD, Professor and Louis Goldstein Swan Endowed Chair, Microbiology and Immunology & Medicine, Albert Einstein College of Medicine

Dr. Zang will discuss function, structure, and immunotherapy of immune checkpoints B7x, B7-H3, HHLA2, TMIGD2, ICOS, Tim-3.

4:15 Sponsored Presentation (Opportunity Available)

4:45 A New Immunomodulatory Strategy of Releasing Immunosuppression in Tumor Microenvironment

Li Peng, PhD, Vice President, Biotherapeutics Discovery, Palleon Pharmaceuticals

Cancer therapy has been revolutionized by inhibiting immune-checkpoints to harness the power of the immune system in fighting cancer. Immune-checkpoint inhibitors, anti-CTLA-4 and PD-1/PD-L1 mAbs, have proved to achieve a durable response in a subset of cancer patients. However, the majority of patients are still resistant to the first generation of I/O drugs. Enormous effort is pursued to identify new immunomodulatory strategies. Here we describe a novel approach of blocking an immunosuppression pathway involved in the innate and adaptive response.

5:15 PANEL DISCUSSION: Novel Immunomodulatory Strategies

Moderator: Li Peng, PhD, Vice President, Biotherapeutics Discovery, Palleon Pharmaceuticals

Panelists: Sourav Ghosh, PhD, Associate Professor, Neurology and Pharmacology, Yale University School of Medicine
Joyson Karakunnel, MD, Vice President, Clinical Development, Arcus Biosciences
Xingxing Zang, PhD, Professor and Louis Goldstein Swan Endowed Chair, Microbiology and Immunology & Medicine, Albert Einstein College of Medicine
Chen Zhu, PhD, Lab Head, Sanofi Oncology

This discussion will cover the following topics:
• Compare immunomodulatory strategies of antagonizing inhibitory receptors vs. agonizing stimulatory receptors
• How innate immune system-based IO strategies complement and synergize the T-cell checkpoint-based therapies
• How to identify immunomodulatory strategies tailored for different tumor phenotypes
• Discuss emerging IO strategies such as microbiome and glycoimmune checkpoints

5:45 Close of Day and Dinner Short Course Registration*

THURSDAY, JUNE 21

7:30 am Registration Open and Morning Coffee
EMERGING TARGETS FOR COMBINATION IMMUNOTHERAPY

8:00 Chairperson’s Remarks
Maria Karasarides, PhD, Executive Director, Immuno-Oncology, Regeneron Pharmaceuticals

8:05 Next-Generation Immune Agent Combinations: Adenosine Pathway and TIGIT Combinations
Joyson Karakunnel, MD, Vice President, Clinical Development, Arcus Biosciences

Checkpoint inhibitors have made great progress in the past few years. Although responses have been impressive, new immune targets are needed to increase responses or provide potential therapies to those who have failed immunotherapies. Targeting alternative immune pathways such as adenosine and TIGIT could be a novel approach for immunotherapy. Combinatorial partners with adenosine and TIGIT with scientific rationale may be an approach to further advance immunotherapy treatments.

8:35 Emerging Concepts from Immunotherapy Combinations
Maria Karasarides, PhD, Executive Director, Immuno-Oncology, Regeneron Pharmaceuticals

This presentation will cover: 1) a summary of learning from Ph1 immunotherapy combinations and setting the context of published preliminary data, 2) interpretations and questions regarding early and unclear clinical response signals, 3) the role of correlative data and the long road from exploratory to validated correlates.

9:05 Immunophenotyping and Therapy Efficacy in Murine Tumor Models
Britnie James, PhD, Senior Vice President, Pre-Clinical Services, Immunology and Oncology, Pre-Clinical Laboratory Services, MD Biosciences, Inc.

The immune phenotype of a patient’s tumor pre/post treatment can have a large role in response to therapy. To address this role, we have been immunophenotyping the tumor microenvironment and peripheral organs in multiple pre-clinical tumor models. By understanding the changes in immune status with therapeutic intervention over time, we hope to correlate these immune phenotypes to tumor burden and/or survival.

9:35 Find Your Table and Meet Your Moderator

9:40 Interactive Breakout Discussion Groups

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. Details on the topics and moderators are available by clicking here.

Emerging Targets in Immuno-Oncology
Quamrul Hassan, PhD, Group Leader, Molecular and Cellular Pharmacology, EMD Serono

- Advancement in technology to validate targets in immuno-oncology
- Chemo-genomic approach in target validation
- Mechanistic preference in target selection: stimulatory vs. inhibitory
- Modality of inhibition in selecting targets: small molecules vs Biomarkers
- Phenotypic Screen to target generation and validation

Modeling Innate and Adaptive Immunity in Murine Models
Marcus Bosenberg, MD, PhD, Associate Professor of Dermatology and Pathology, Yale University, Co-Leader, Genomics, Genetics and Epigenetics Program, Yale Cancer Center

- Can animal models of cancer immunology predict human responses?
- How should preclinical models be used to guide drug development in immunology?
- How can existing models be improved?

10:20 Coffee Break in the Exhibit Hall with Poster Viewing

TARGETING INNATE IMMUNITY

11:05 CD8, an Emerging Immunotherapy Target
Chen Zhu, PhD, Lab Head, Sanofi Oncology
CD8 is a type II transmembrane enzyme-cum-receptor. Since multiple myeloma cells express high levels of CD8, targeting CD8-expressing myeloma cells by antibody dependent cellular cytotoxicity (ADCC), phagocytosis (ADCD) and complement dependent cytotoxicity (CDC) has demonstrated promising clinical activity in heavily pretreated relapsed/refractory multiple myeloma (RRMM) patients. In addition, as multiple lines of immune cells express CD8, the biological function of CD8 could be further explored for its potential application in tumor immunotherapy.

11:35 An Innate Immune Checkpoint in Cancer Immunotherapy
Sourav Ghosh, PhD, Associate Professor, Neurology and Pharmacology, Yale University School of Medicine

T cell checkpoint inhibitors (TCIs) have greatly enhanced the success rate of immunotherapy. Notwithstanding, overall response rate remains limited. We have identified an innate immune checkpoint that limits dendritic cell function, as well as induces tissue repair mechanism in macrophages. Since innate immunity is an obligate prerequisite for adaptive immunity, we hypothesize that the inhibition of this novel checkpoint could improve anti-tumor immune responses, including in TCI-resistant tumors.

12:05 pm TNFR2 Targeting in Cancer: Select Treg Elimination and Direct Tumor Killing
Denise L. Faustman, MD, PhD, Director, Immunobiology, Massachusetts General Hospital; Associate Professor, Medicine, Harvard Medical School
Although many surface targets are a focus of immuno-oncology therapies, a unique target is the TNFR2 receptor which is not only concentrated on the Treg cells of the tumor infiltrate but also now a newly identified and prevalent oncogene for diverse human tumors. In this presentation, we present human data on diverse fresh human cancers and their associated Tregs.

12:35 Session Break

12:40 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing
IMMUNOMODULATORY AGONIST TARGETS

1:55 Chairperson’s Remarks
Andrew Weinberg, PhD, Chief, Laboratory of Basic Immunology, Providence Health & Services

2:00 Understanding Costimulatory Agonists to OX40 for Cancer Immunotherapy
Andrew Weinberg, PhD, Chief, Laboratory of Basic Immunology, Providence Health & Service
Immune agonist Abs that target T cells have been shown to have potent therapeutic properties in cancer-bearing hosts. In particular, anti-OX40 agonist Abs target CD4 and CD8 T cells as well as Tregs and understanding the role of their stimulatory activity on each cell type will be discussed. Dosing and timing of delivery will also be discussed as they have quite different properties when compared to checkpoint blockade Abs.

2:30 Combination Approaches with Immune Agonist Antibodies
Patrick Mayes, PhD, Executive Director, Head, IO Antibody Research, Incyte
This presentation will cover the unique challenges of agonist mAb design and development as well as strategies for improving activity through combinations.

3:00 Preclinical Characterization of a Novel STING Agonist, MK-1454
Saso Cemerski, PhD, Principal Scientist, Merck Research Labs
MK-1454, a novel STING agonist, induces potent cytokine responses and activates several immune cell types in vitro including MDSCs and M2-macrophages, key suppressive myeloid cells in the TME. MK-1454 induces robust anti-tumor activity in mouse syngeneic tumor models and cytokine production and gene expression changes in ex vivo-stimulated human primary tumors. MK-1454 is currently being evaluated in cancer patients both as monotherapy and in combination with Keytruda.

3:30 ATOR-1017 - A Tumor-Directed Fcγ-Receptor Cross-Linking Dependent 4-1BB Agonistic Antibody
Karin Enell Smith, PhD, Senior Scientist, Preclinical Development, Alligator Bioscience AB
ATOR-1017 is an IgG4 antibody binding to the co-stimulatory receptor 4-1BB with a unique functional profile compared to the two 4-1BB antibodies currently in clinical development. The functional activity is dependent on cross-linking mediated by Fcγ receptors, which directs the immune activation to the tumor area where 4-1BB as well as certain Fcγ receptors are highly expressed. This reduces the risk of inducing systemic immune activation and liver toxicity. Therefore, ATOR-1017 has the potential to be a best-in-class 4-1BB antibody in terms of risk-benefit profile.

4:00 Close of Conference
Recommended Event Package

Short Course 6: Collecting, Storing, and Utilizing Precious Patient-Derived Tumors for Drug Discovery and Development
Short Course 9: How to Best Utilize 3D Cells, Spheroids, PDX Models in Oncology
Short Course 12: Humanized Mouse Models for Preclinical Assessment of Cancer Immunotherapy
Conference: Preclinical Strategies, Models & Tools in Oncology

WEDNESDAY, JUNE 20

11:00 am Registration Open
11:50 Enjoy Lunch on Your Own
12:20 pm Dessert and Coffee Break in the Exhibit Hall with Poster Viewing
1:00 PLENARY KEYNOTE SESSION (click here for details)

2:30 Refreshment Break in the Exhibit Hall with Poster Viewing

3D MODELS: NEXT GENERATION DRUG DISCOVERY AND PRECLINICAL ASSESSMENT

3:10 Chairperson's Opening Remarks
Zhao Chen, PhD, Investigator III, Exploratory Immuno-Oncology, Novartis Institutes for BioMedical Research

3:15 KEYNOTE PRESENTATION: Ex vivo Profiling of PD-1 Blockade Using Organotypic Tumor Spheroids
David Barbie, MD, Assistant Professor, Medical Oncology, Dana-Farber Cancer Institute

Just as precision cancer medicine has been essential to the successful development of oncogene-targeted therapies, it will be equally essential to deploy next generation immunotherapies in a targeted fashion and develop personalized combinations. To this end, our laboratory has developed and initially validated microfluidic 3-dimensional (3D) culture of patient-derived or murine-derived organotypic tumor spheroids (PDOTS/MDOTS) as a means of assessing the ex vivo response to PD1 immune checkpoint blockade.

3:45 Utilizing 3D Models for Cancer Stem Cell Target Validation and Drug Discovery
Anita Seshire, PhD, Lab Head, Cellular Pharmacology, Translational Innovation Platform Oncology, Merck KGaA

Tumor spheres are three-dimensional structures that spontaneously form under non-adherent and serum free conditions. Sphere formation is an exclusive function of tumor initiating cells (cancer stem cells). We show how to utilize 3D-spheres for in vitro and in vivo models for therapeutic antibody validation.

4:15 Translational Research: CANscript™ - A Better Predictive Model For Oncology
Mark Paris, PhD, Associate Director, Translational Applications, Mitra Biotech

Mitra Biotech has developed and clinically validated our human ex-vivo tumor platform technology (CANscript™). CANscript uses patient material (tumor, autologous ligands and PBMC) to explore the mechanism of action and predict efficacy for clinically-directed compounds in a modality-agnostic way using phenotypic effects. This talk will explore how CANscript was used to model the effect of checkpoint inhibition in HNSCC to identify predicted clinical responders and uncover mechanisms of resistance.

GENE EDITING TO ADVANCE DRUG DISCOVERY IN IO

4:45 CRISPR/Cas9 in Preclinical and Drug Discovery
Danilo Maddalo, PhD, Lab Head, ONC Pharmacology, Novartis Institutes for BioMedical Research, Novartis Pharma AG

The generation of preclinical models faithfully recapitulating genetic lesions found in patients represents one of the major limitations in drug discovery. In this talk, I will discuss the methods for generating preclinical animal models, what we can learn from such models in the process of drug discovery and target identification, and the future perspective of the CRISPR/Cas9 in pharma industry.

5:15 In vivo CRISPR Screen to Identify Immune Modulators in Tumor Cells
Zhao Chen, PhD, Investigator III, Exploratory Immuno-Oncology, Novartis Institutes for BioMedical Research

Target ID by in vivo genetic screens is particularly suitable for identification of immune modulatory targets due to the dynamic nature of the tumor microenvironment, on condition that the screen was designed and controlled carefully. We have obtained some insights on this topic over the past couple of years on a few key factors contributing to a successful in vivo screen.

5:45 Close of Day and Dinner Short Course Registration*
*Separate registration required. Please click here for more information.

Sponsored by
THURSDAY, JUNE 21

7:30 am Registration Open and Morning Coffee

DEVELOPING COMPREHENSIVE PRECLINICAL PROGRAMS IN IO

8:00 Chairperson's Remarks
Andrew Whale, PhD, Senior Scientist, Manager, Preclinical, Immunocore Ltd.

8:05 KEYNOTE PRESENTATION: Translational Approaches for CAR T Cell Therapy Development
Jennifer Brogdon, PhD, Director, Exploratory Immuno-Oncology, Novartis Institutes for BioMedical Research

T cells can be genetically modified to target tumors through the expression of a chimeric antigen receptor (CAR). Most notably, CAR T cells have demonstrated clinical efficacy in hematologic malignancies with more modest responses when targeting solid tumors. Understanding the complex tumor microenvironment and the initial T cell starting material may afford greater insights into parameters which potentially influence CAR T cell efficacy and safety.

8:35 An in vitro Preclinical Package to Assess the Safety and Efficacy of ImmTac™ Molecules Alone or in Combination
Andrew Whale, PhD, Senior Scientist, Manager, Preclinical, Immunocore Ltd.

ImmTAC molecules are soluble pico-molar affinity TCRs fused to an anti-CD3 scFv domain that recognise tumour antigen peptides presented by MHC-I and re-direct T cells, mediating tumour cell killing. As ImmTAC molecules are human specific, traditional in vivo models are unsuitable to evaluate safety and efficacy. We present how immunocore's in vitro preclinical package has approached the challenge to assess ImmTAC molecules as monotherapy and combination agents.

9:05 Late Breaking Presentation

9:35 Find Your Table and Meet Your Moderator

9:40 Interactive Breakout Discussion Groups
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. Details on the topics and moderators are available by clicking here.

Modeling Innate and Adaptive Immunity in Murine Models
Marcus Bosenberg, MD, PhD, Associate Professor of Dermatology and Pathology, Yale University, Co-Leader, Genomics, Genetics and Epigenetics Program, Yale Cancer Center

- Can animal models of cancer immunology predict human responses?
- How should pre-clinical models be used to guide drug development in immunology?
- How can existing models be improved?

Emergence of Microfluidic Models for Preclinical Assessment of Efficacy of Immune Checkpoint Inhibitors
Jeffrey Borenstein, PhD, Laboratory Technical Staff, Biomedical Microsystems, Draper

- Immune checkpoint inhibitors exhibit variable patient response rates for reasons that are not completely clear. What attributes of an in vitro model are seen as most critical for establishing it as a tool to study mechanisms of responder/non-responder behavior?
- Microfluidic model systems may find use as tools for drug development and ultimately for precision medicine applications, where patient response could be predicted before administering therapy. Where are the most significant opportunities for these systems, and would the attributes models for each respective application be different?

10:20 Coffee Break in the Exhibit Hall with Poster Viewing

NEXT-GENERATION MURINE MODELS

11:05 Optimized Syngeneic Models of Anti-Cancer Immune Responses
Marcus Bosenberg, MD, PhD, Associate Professor, 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 cell lines that form tumors following injection into immune competent C57Bl/6J mice. These models represent an ideal set of tools for the study of cancer immunology and response to immune therapies.

11:35 huPBMC Donor Selection for Humanized Mouse Model
Fangxian (Frank) Sun, Lead Research Investigator, Pharmacology, Sanofi NOD-scid IL2rgammanull, NSG mice engrafted with functional human cells and tissues, i.e., “humanized mice”, have become increasingly important as small pre-clinical animal models for the study of human diseases. Scientists have been able to engraft murine recipients with human hematopoietic stem cells or peripheral blood mononuclear cell (PBMC) that reconstitute functional human immune systems. These mice can also be engrafted with human tissues such as solid and hematologic cancers. Humanized mice are permitting significant progress in studies of human cancers. We characterized human PBMCs in vivo and in vitro from dozens of human donors. This information provided criteria for huPBMC donor selection for humanized mouse model.

12:05 pm Human Immune System Development in Humanized Mouse Models: Latest Advances
Barbara Joyce-Shaikh, Associate Principal Scientist, Merck Research Laboratories

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.
1:55 Chairperson's Remarks

Marco Ruella, MD, Clinical Instructor, Associate Director, Dr. June's Laboratory, Center for Cellular Immunotherapies (CCI), Perelman School of Medicine, University of Pennsylvania

2:00 Genome-Editing Technologies in Adoptive T Cell Immunotherapy for Cancer

Marco Ruella, MD, Clinical Instructor, Associate Director, Dr. June's Laboratory, Center for Cellular Immunotherapies (CCI), Perelman School of Medicine, University of Pennsylvania

Adoptive T cell therapies, and in particular chimeric antigen receptor T cells (CART), are leading to significant responses in cancer patients, in particular B-cell leukemias and lymphomas. New gene editing technologies, like CRISPR-Cas9, can offer an exciting tool for the manipulation of T cells to increase their feasibility and efficacy.

2:30 Preclinical Development of Dual-Switch CAR-T Cells for Cancer Therapy: Independent Control T Cell Efficacy and Safety with Small Molecules and Protein Switches

J. Henri Bayle, PhD, Director of Discovery, Bellicum Pharmaceuticals, Inc.

Chimeric Antigen Receptor (CAR)-based cell therapies show efficacy against disseminated cancers, but control over toxicity or activation can temper utility, particularly against solid tumors. We will describe preclinical studies of two distinct dual-control platforms that include ligand-inducible activation or apoptosis of T-cells, comprising inducible iMyD88/CD40 and iCaspase-9 components. These animal studies show exquisite dual-switch control of T cell expansion or contraction along with tumor control using non-crossreacting, clinical-grade ligands.

3:00 Developing Small Molecule Immune Checkpoint Inhibitors: Opportunities and Insights

Adam S. Lazorchak, PhD, Senior Scientist, Immunology & Translational Sciences, Curis, Inc.

Small molecules targeting immune inhibitory checkpoint pathways offer unique therapeutic opportunities relative to antibody based therapies, including the ability to target a broader range of extracellular or intracellular motifs and precisely control drug exposure to enhance safety. I will discuss Curis's pre-clinical development of oral small molecule checkpoint inhibitors, emphasizing novel questions relating to immune checkpoint biology that we are addressing with our specific small molecule checkpoint inhibitors.

3:30 CO-PRESENTATION: Dynamic Microfluidic Model for Predicting Tumor Response to Immune Checkpoint Inhibitors

Jeffrey Borenstein, PhD, Laboratory Technical Staff, Biomedical Microsystems, Draper

Hongmin Chen, PhD, Principle Scientist, Pharmacology, Merck

Current systems to assess tumor response to immune checkpoint inhibitors are limited to static culture systems and short duration studies. Here we report on progress toward a high throughput microfluidic system for assessing rodent and human tumor response to immune checkpoint therapy by recapitulating the dynamics of the immune microenvironment. This system permits real-time visualization of tumor-infiltrating lymphocyte (TIL) interactions with tumor biopsy samples and quantification of TIL infiltration and tumor killing.

4:00 Close of Conference
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, High-Content 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 19-20
AGENDA iPS Cells for Disease Modeling and Drug Discovery
AGENDA Phenotypic Screening and Chemical Biology

June 20-21
AGENDA 3D Cellular Models
AGENDA Next-Gen Genomics: Leveraging CRISPR & Single-Cells
AGENDA High-Content Analysis
iPS Cells for Disease Modeling and Drug Discovery
Pluripotent Stem Cells for Disease Research in Neuroscience and Other TAs

3rd Annual

Recommended Event Package
Short Course 10: Applications of Artificial Intelligence & Machine Learning in Drug Discovery & Development
Short Course 14: Advanced Bioprinting Strategies for Generation of 3D Tissue Models
Conference: iPS Cells for Disease Modeling and Drug Discovery
Conference: 3D Cellular Models

TUESDAY, JUNE 19

7:30 am Registration Open and Morning Coffee

MODELING COMPLEX DISEASES TO IDENTIFY NOVEL THERAPIES

8:15 Chairperson’s Opening Remarks
Peter Reinhardt, PhD, Head, Cell Programming and Transduction, Technology Core, Neuroscience Discovery, AbbVie

8:20 Application of Disease-Specific iPS Cells to Increase the Success Rate of Drug Discovery
Gabriele Proetzel, PhD, Director, Regenerative Medicine, Takeda Pharmaceuticals, Inc.

With the recent advances in human iPSC technologies their utility in drug development has become increasingly evident. Patient-derived iPSC assays have produced valuable data in phenotypic screens and target validation. We will discuss examples and how these impact the drug development process. I will describe how academic partnerships can accelerate such programs as exemplified by our collaboration with University of Kyoto, T-CiRA.

8:50 Strategies to Generate hiPSC-Derived Neural Cells for Robust in vitro Disease Modeling
Peter Reinhardt, PhD, Head, Cell Programming and Transduction, Technology Core, Neuroscience Discovery, AbbVie

The human induced pluripotent stem cell (hiPSC) technology promises to revolutionize the discovery of drugs and treatments against neurodegenerative diseases. However, differentiation protocols into affected neural cells are often not suited for the generation of large in vitro models. We will discuss several examples of how existing and novel protocols for the differentiation of hiPSCs into disease-affected neurons can be transformed into scalable and robust assays fit for purpose.

9:20 iPSC-Based Disease Modeling to Advance Diabetes Drug Discovery
Melissa Thomas, MD, PhD, Medical Fellow, Diabetes and Complications, Eli Lilly and Company

We can generate β-like pancreatic cells that are fully functional as proven by either in vitro or in vivo studies. This novel proof-of-concept stem cell technology brings new expectations on applying stem cell therapy for diabetes mellitus in clinical settings.

9:50 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

MODELING HEART, KIDNEY

10:35 Single Cell Models of Human Cardiac Development and Disease
Ibrahim Domian, MD, PhD, Assistant Physician, Massachusetts General Hospital, Assistant Professor of Medicine, Harvard Medical School

Human Pluripotent Stem Cell-Derived Cardiomyocytes (hPSC-CMs) have been proposed as a robust cell source for human disease modeling and drug discovery. However, hPSC-CMs cultured in vitro are highly heterogeneous in lineage commitment and metabolic maturation limiting their application. To address this, we have developed novel strategies to simultaneously assess gene expression and cell physiology in a multiplexed fashion at single living cell resolution for the study of metabolic cardiovascular disease.

11:05 KEYNOTE PRESENTATION: From Stem Cells to Kidney Organoids to Disease Modeling
Joseph Bonventre, MD, PhD, Chief of the Renal Unit, Director of the Bioengineering Division, Brigham and Women’s Hospital

This talk will describe current protocols for generation of kidney organoids from pluripotent embryonic stem cells and induced pluripotent stem cells (iPSCs), describe the use of these organoids for disease modeling, and describe initiatives to develop innovative approaches to replacement of renal function in humans.

11:35 Human iPSC-Derived Cardiac and Neural Systems and Novel Tools to Drive Preclinical Development
Stefan Braam, PhD, Technical Director, Ncardia

Drug development is witnessing a shift from conventional target-based drug discovery to a more phenotypic approach, which is enabled by the development of more physiological cellular tools. Here we provide several case studies that utilize human induced pluripotent stem cell-derived cardiomyocytes, neurons, and novel tools within this space. These systems offer a flexible, highly translational and typically more predictive cellular environment than immortalized cell lines or even primary rodent models.

12:05 pm Session Break
12:10 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own
12:40 Session Break

IPS CELLS FOR CNS DRUG DISCOVERY AND DEVELOPMENT

1:15 Chairperson’s Remarks
Ibrahim Domian, MD, PhD, Assistant Physician, Massachusetts General Hospital, Assistant Professor of Medicine, Harvard Medical School

1:20 Leveraging Stem Cell Technology to Fuel Drug Discovery for Neurodegenerative Diseases
Carlo Cusulin, PhD, Senior Scientist, Disease Relevant Cellular Assays, Chemical Biology, F. Hoffmann-La Roche

Drug discovery for neurodegenerative diseases presents several challenges because of the complexity of these disorders and the scarcity of reliable and translatable models. iPSC technology offers the possibility to produce the relevant cell types (i.e., neurons, microglia, astrocytes) and introduce disease stimuli to obtain an in vitro system amenable for screening. We focused on generating models of Alzheimer’s disease, starting from patient-derived iPSCs and assessing the effect of disease-modifying compounds.

1:50 IPS Cell Derived Neurons and Microglia for in vitro Pharmacology
Johannes Grosse, PhD, Director, Neuroscience Drug Discovery/Alliances, Takeda

The discrepancy between the massive private and academic investments in drug discovery for neurological and psychiatric diseases and the small and still declining number in novel drug approvals is a clear indicator for the unique challenges of the field. Those have been identified at all phases of drug discovery from target validation and hypothesis via pre-clinical models for pharmacological tests to the design of clinical trials, use of biomarkers and regulatory affairs.

2:20 Advanced Physiologically Relevant hiPSC-Based Platforms for Drug Discovery
Sponsored by StemoniX
Fabian Zanella, Director, Research & Development, StemoniX

We present human induced pluripotent stem cell (hiPSC)-based platforms which were structurally engineered with greater physiological relevance aimed to elevate performance in drug discovery applications. microBrain® 3D comprises cortical neural spheroids that feature high functionality with robust spontaneous activity and expected responses to established neuromodulators. microHeart® allows cardiomyocytes to adopt cell geometries and intercellular organization that resemble native heart tissue, translating into differential pharmacological response to known cardiovascular compounds.

2:35 Sponsored Presentation (Opportunity Available)

2:50 Refreshment Break in the Exhibit Hall with Poster Viewing

3:30 Modeling ALS with Patient Specific iPSCs
Shila Mekhoubad, PhD, Scientist II, Stem Cell Research, Biogen

Advances in stem cell biology and neuronal differentiations have provided a new platform to study ALS in vitro. Here we will describe our use of induced pluripotent stem cells (iPSCs) from patients with familial ALS to establish new models and tools that can contribute to the development and validation of novel ALS therapeutics.

4:00 All-Optical Electrophysiology for Neuroscience Drug Discovery
Graham Dempsey, PhD, Vice President, Research and Development, Q-State Biosciences

Human induced pluripotent stem (iPS) cell-based models have become a powerful approach to disease phenotyping for drug discovery applications. We have created an optogenetic platform called Optopatch that rapidly and robustly characterizes the electrophysiological response of iPS cell-derived neurons. Our approach provides an information-rich readout of pharmacological changes in both intrinsic neuronal excitability and synaptic transmission with single-cell precision and dramatically improved throughput.

4:30 PANEL DISCUSSION: iPSC-Based Neurodegenerative Disease Modeling
Moderator: Johannes Grosse, PhD, Director, Neuroscience Drug Discovery/Alliances, Takeda
Panelists: Carlo Cusulin, PhD, Senior Scientist, Disease Relevant Cellular Assays, Chemical Biology, F. Hoffmann-La Roche
Chee Yeun Chung, PhD, Scientific Co-Founder and Associate Director, Discovery Biology, Yumanity Therapeutics

Human neurodegenerative disorders are among the most difficult to study. This panel will discuss existing and future models for major neurodegenerative diseases.
- How do we establish that phenotypes “in a dish” are relevant to the patient’s disease?
- Does the relative immaturity of neurons in the dish matter and, if so, what do we do about it?
- What are the major technical barriers to high-throughput screening of iPSC-derived neuronal models?
- Does the technology circumvent the need for rodent preclinical neurodegenerative disease models?

5:00 Find Your Table and Meet Your Moderator

5:05 Interactive Breakout Discussion Groups
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. Details on the topics and moderators are available by clicking here.

Modeling Neurodegenerative Disorders for Drug Discovery and Development
Bilada Bilican, PhD, Investigator II, Neuroscience, Novartis Institutes for BioMedical Research (NIBR)
- In vitro correlates of complex neurodegenerative diseases.
- How to model apparently sporadic neurodegenerative disorders.
- Advanced cellular models - how to address cell-autonomous vs. non-cell autonomous mechanisms of neurodegeneration.
- Phenotype vs. target-based drug screening.

Infrastructure and Strategy for iPS Cell Based Drug Discovery
Chee Yeun Chung, PhD, Scientific Co-Founder and Associate Director, Discovery Biology, Yumanity Therapeutics
7:45 am Registration Open and Morning Coffee

**BUILDING A STEM CELL BASED DISCOVERY PLATFORM**

8:25 Chairperson’s Remarks
Chee Yeun Chung, PhD, Scientific Co-Founder and Associate Director, Discovery Biology, Yumanity Therapeutics

8:30 Building a Robust Stem Cell-Based Discovery Platform for Neurodegenerative Diseases
Chee Yeun Chung, PhD, Scientific Co-Founder and Associate Director, Discovery Biology, Yumanity Therapeutics

Phenotypic screening in neurons and glia derived from patients is now conceivable through unprecedented developments in reprogramming, transdifferentiation, and genome editing. We outline progress in this nascent field, but also consider the formidable hurdles to identifying robust, disease-relevant and screenable cellular phenotypes in patient-derived cells. We illustrate how analysis in the simple baker’s yeast cell *Saccharomyces cerevisiae* is driving discovery in patient-derived neurons, and how approaches in this model organism can establish a paradigm to guide the development of stem cell-based phenotypic screens.

9:00 Functionalization of Schizophrenia GWAS Variants by High-Throughput Differentiation of Human Induced Pluripotent Stem Cells
Bilada Bilican, PhD, Investigator II, Neuroscience, Novartis Institutes for BioMedical Research (NIBR)

Schizophrenia is a complex multifactorial and polygenic disorder, with both rare and common genetic variants contributing to disease risk. Genome-wide association studies (GWAS) have highlighted a large number of genetic variants with potential disease association, but validation and prioritization of risk genes remains a challenge.

9:30 Developing Relevant In Vitro CNS Models for Drug Discovery
Daniel Haag, PhD, CSO, NeuCyte, Inc.

NeuCyte Inc. is a biotechnology company focusing on early phases of CNS drug discovery. Based on our SynFire™ technology, we have developed a proprietary human neural in vitro platform for complex electrophysiological and morphological readouts suited for target identification and validation, efficacy testing and neurotoxicity assessment. Using patient-derived and genetically engineered defined neural cell types, NeuCyte builds unique cell-based assays for modelling neurological and neurodegenerative disorders.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing
Final Weeks to Register!

5th Annual Phenotypic Screening and Chemical Biology
Cutting Edge Target and MOA Deconvolution

Recommended Event Package
- Short Course 4: Practical Phenotypic Screening
- Short Course 10: Applications of Artificial Intelligence & Machine Learning in Drug Discovery & Development
- Short Course 16: Applications of CRISPR and Single-Cells: Best Practices from Set-Up to Data Analysis
- Conference: Phenotypic Screening and Chemical Biology
- Conference: Mastering Medicinal Chemistry Part 2

TUESDAY, JUNE 19

7:30 am Registration Open and Morning Coffee

ADVANCES IN CHEMOPROTEOMICS

8:15 Chairperson’s Opening Remarks
Ivan Cornella Taracido, PhD, Director, Chemical Biology, Merck Research Laboratories

8:20 Application of Clickable Chemical Biology Probes in Drug Discovery
Doug Johnson, PhD, Director, Chemical Biology & Proteomics, Biogen
This talk will describe how we used clickable chemical biology probes for target identification and selectivity profiling for multiple projects in neuroscience drug discovery. For example, we generated clickable probes of covalent inhibitors to evaluate their proteome-wide selectivity. In another example, we used clickable γ-secretase modulator (GSM) and inhibitor (GSI) photoaffinity probes to determine the target and in one case the binding site within the γ-secretase complex. We also generated a clickable photoprobe of a BACE1 inhibitor.

8:50 Chemical Biology Strategies Applied to Drug Discovery: A Case Study on MCT4 Inhibition
Ronald Tomlinson, Associate Principal Scientist, Discovery Sciences – Chemical Biology, AstraZeneca
Monocarboxylate transporter 4 (MCT4) is a hypoxia regulated lactate transporter, which is upregulated across a range of solid tumors. Inhibition of MCT4 is predicted to result in glycolytic shut down and thus MCT4 inhibitors are potential therapeutic agents for the treatment of cancers. We would like to share our discovery of potent inhibitors of MCT4 and the use of chemical biology techniques to confirm target engagement of MCT4.

9:20 New Druggable Targets from Chemoproteomic Space Exploration
Lyn Jones, PhD, Vice President, Chemistry and Chemical Biology, Jnana Therapeutics

Advances being made in the development of the chemical biology toolkit to enable the study of previously unchartered areas of chemoproteomic space will be presented. Opportunities to improve chemogenomic coverage using chemical probes will be described.

9:50 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

10:35 Redefining Druggability Using Chemoproteomic Platforms
Daniel Nomura, PhD, Associate Professor, Chemistry, Molecular and Cell Biology, and Nutritional Sciences and Toxicology, University of California, Berkeley
One of the greatest challenges that we face in discovering new disease therapies is that most proteins are considered “undruggable” or difficult to target with small-molecules. Our research group addresses this challenge by developing chemoproteomic platforms to discover and pharmacologically target unique and novel therapeutic druggable hotspots for disease therapy. The talk will provide examples of how we have used these approaches to discover new therapeutic targets and agents for cancer.

11:05 Profiling Structurally Diverse Chemical Matter to Map Proteome-Wide Interactions
Francisco Garcia, PhD, Associate Scientist/Postdoctoral Research Fellow, Chemical Biology and Proteomics, Merck Research Laboratories
Affinity-based chemoproteomics utilizes small molecules as bait, high resolution mass spectrometry, and informatics to establish compound-protein target relationships. Chemoproteomics is routinely applied to characterize drug-target engagement and selectivity for discrete project specific biosamples, though a comprehensive and systematic evaluation of the whole proteome is typically overlooked. We therefore aim to analyze proteome-wide interactions for hundreds of compounds against physiologically relevant human cells and tissue.

11:50 Sponsored Presentation (Opportunity Available)

12:05 pm Session Break

12:10 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:40 Session Break

DECONVOLUTION OF NOVEL TARGETS

1:15 Chairperson’s Remarks
Ivan Cornella Taracido, PhD, Director, Chemical Biology, Merck Research Laboratories
1:20 A Case Study in the Deconvolution of Phenotypic Screening Hits: Discovery of a Novel Mechanism to Lower PCSK9

Philip Carpio, PhD, Formerly Associate Research Fellow, Medicine Design, Pfizer

Proprotein convertase subtilisin/kevin type 9 (PCSK9) is an example of a genetically validated target involved in the regulation of ‘bad’ forms of cholesterol (i.e., LDL cholesterol). The discovery of compounds that inhibit the secretion of PCSK9 via an unprecedented mechanism involving ribosomal stalling will be described. Some of the issues encountered during the triage of the screening hits will be presented.

1:50 Advances in Compound MOA Prediction

Jeremy Jenkins, PhD, Executive Director, Chemical Biology & Therapeutics, Novartis Institutes for BioMedical Research

Phenotypic screening can yield many bioactive compound molecules, although laborious characterization of the compound targets or cellular mechanisms may be necessary. While target identification is often carried out for individual lead molecules, technologies to characterizing chemical libraries at scale are emerging, including high content imaging, well-based transcriptomics, and new methods for in silico target prediction.

2:20 Target Deconvolution by In Silico Proteome Screening

Andrew Hope, PhD, Vice President, Business Development, Cyclica Inc

Cyclica’s new cloud-based and AI-augmented platform, Ligand Express allows a small molecule to be screened in silico against the structurally-characterized proteome to determine its polypharmacological profile. Moving beyond canonical binding sites it identifies known and novel binding sites, including allosteric sites. The talk will describe applications in deconvolution of phenotypic screens, such as guiding the repurposing of a retroviral drug to a rare autoimmune disease.

2:50 Refreshment Break in the Exhibit Hall with Poster Viewing

3:30 Chemical Biology Approaches for Target Identification and Validation

Kilian Huber, PhD, Principal Investigator, Structural Genomics Consortium (SGC), Target Discovery Institute, Nuffield Department of Medicine, University of Oxford

Drug target identification and validation represent paramount objectives for chemical biology. In this talk, I will focus on recent progress in the development of specific small molecule tool compounds, also referred to as chemical probes, for target validation and proteomic methods for target deconvolution and identification.

4:00 How Will Your Chemical Probes Data and Knowledge Outlive the Program?

Meir Glick, PhD, Director, Informatics, Chemistry, Merck Research Laboratories

We will describe our efforts in the following areas: improving information capture with respect to compound design hypotheses, strategy, and chemical reactivity. Second, we will discuss making better use of all of our captured data through improving data access, data visualization, and application of machine learning methods.

4:30 Profiling Host and Gut Microbiome Xenometabolism in Mammalian Development and upon Chemical Exposures

Aaron Wright, PhD, Principal Investigator and Group Leader, Chemical Biology & Exposure Sciences Group, Pacific Northwest National Laboratory

The expression and activity of drug metabolizing enzymes in the host are major determinants of the overall pharmacokinetic differences observed throughout human development. However, microbiome-mediated transformations of xenobiotics may also be a critical component of individual variability and susceptibility to toxicity, drug bioavailability, efficacy, and interactions. Using activity-based protein profiling, we are beginning to dissect the host-microbiome interplay involved in xenometabolism, and how external exposures and developmental stages alter metabolism.

5:00 Find Your Table and Meet Your Moderator

5:05 Interactive Breakout Discussion Groups

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. Details on the topics and moderators are available by clicking here.

Compound Collections for Phenotypic Screening and Chemical Biology

Francisco Garcia, PhD, Associate Scientist/Postdoctoral Research Fellow, Chemical Biology and Proteomics, Merck Research Laboratories

• How many and how large such collections should be
• Fit-for-phenotype and pathway sets, general MoA-annotated screening decks, diversity decks and the use of fragments and possibly other modalities (aptamers, etc.)
• Screening modalities (fragments, small molecules, natural products, aptamers, peptides, proteins, RNAi and genome editing reagents)

Developments in Methodologies to Enable Target Identification

Ivan Cornella Taracido, PhD, Director, Chemical Biology, Merck Research Laboratories

• What is new in chemical building blocks, reagents and reactions to enable omics and target ID?
• Photo-affinity ligation and activity-based probe workflows
• Advances in chemical genomics in mammalian haploid systems
• In silico (off)-target prediction and other computational tools
• Advances in analytical sciences (MS-based methods, imaging, bio-NMR...)

5:45 Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

WEDNESDAY, JUNE 20

7:45 am Registration Open and Morning Coffee

COMPLEMENTARY TECHNOLOGIES TO CHEMICAL BIOLOGY

8:20 Chairperson’s Remarks

Ivan Cornella Taracido, PhD, Director, Chemical Biology, Merck Research Laboratories

8:30 Reimagining Drug Discovery through AI

Ronald Alfa, MD, PhD, Vice President, Discovery & Product, Recursion Pharma
At Recursion, we are augmenting phenotypic screening with artificial intelligence to dramatically improve the power of screens, the pace of discovery, and the ability to prioritize hits in the discovery process. The foundation of our approach is an AI-enabled phenotypic screening platform through which we've generated over 700 TB of data to fuel predictive approaches to drug discovery. Here, I will describe applications of our platform across multiple therapeutic areas.

**9:00 Small Molecule and Pooled CRISPR Genomic Screens Targeting the IL-17 Pathway in Keratinocytes: Compare & Contrast Orthogonal Modes of Target Discovery**  
_Eric Goedken, PhD, Principal Scientist, Foundational Immunology, AbbVie Bioresearch Center_

My group has been working to study IL-17/TNF cytokine signaling in keratinocytes for applications in psoriasis and other dermatological diseases. We have performed screens using a CRISPR library as well as with small molecules. In this talk, I will outline this approach and compare/contrast the findings from these two orthogonal methods, and highlight a target with novel involvement in this pathway that we have identified in this manner.

**9:30 Shotgun Lipidomics Technology for High-Throughput Drug Discovery**  
_Christian Klose, PhD, Head, Research and Development, Lipotype GmbH_

We present a comprehensive, absolutely quantitative shotgun lipidomics technology for biological samples on high-throughput scale. Its applications include drug discovery, mode-of-action studies, target validation, biomarker identification and clinical screenings. We explain the mass spectrometry-based technology and its explanatory data analysis power with examples.

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

**10:45 Functional Annotation of Natural Products via Integration of Gene Expression and High Content Imaging Approaches**  
_John MacMillan, PhD, Professor, Chemistry and Biochemistry, University of California, San Diego_

Determination of the mechanism of action to botanicals, dietary supplements and natural products (mixtures and pure compounds) is a complex challenge that has limitations to their utility as supplements and therapeutics. To address this challenge, we have developed and integrated multiple phenotypic screening approaches to provide mechanistic hypotheses on a library scale. These platforms have been further integrated with metabolomics for a comprehensive chemical and biological evaluation of natural products.

**11:15 Small Molecule Inhibitors Identified by Morphological Profile-Based Virtual Screening**  
_Shantanu Singh, PhD, Senior Group Leader, Imaging Platform, Broad Institute_

Images contain rich information about the state of cells, tissues, and organs. We work with biomedical researchers around the world to extract quantitative information from images, particularly in high-content screening experiments involving physiologically relevant model systems. As the biological systems and phenotypes of interest become more complex, so are the computational approaches needed to properly extract the information of interest; we continue to bridge the gap between biologists' needs and the latest in computational science (e.g., deep learning).
WEDNESDAY, JUNE 20

11:00 am Registration Open

11:50 Bridging Luncheon Presentation: Nuclear Imaging of Neuroinflammation in Rodent Models of Neurodegenerative Diseases

Tuulia Huhtala, PhD, Head, Biomarkers and in vitro biology, Discovery Charles River

Activation of the mitochondrial translocator protein (TSPO) is linked to neuroinflammation and TSPO ligands can be used for in vivo PET or SPECT imaging. In the current studies, we utilized these ligands to assess the extent of neuroinflammation after lipopolysaccharide (LPS) infusion, following induction of multiple sclerosis (MS) and neuropathic pain.

12:20 pm Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

1:00 PLENARY KEYNOTE SESSION (click here for details)

2:30 Refreshment Break in the Exhibit Hall with Poster Viewing

TAKING SCREENING INTO THE THIRD DIMENSION

3:10 Chairperson's Opening Remarks

Jonathan Garlick, DDS, PhD, Professor, Oral Diagnosis, School of Dental Medicine, School of Medicine and Engineering, Tufts University

3:15 KEYNOTE PRESENTATION: Drug Discovery in the Third Dimension and Beyond

Marc Ferrer, PhD, Team Lead, NIH Chemical Genomics Center, NCATS, NIH

Three-dimensional (3D) cell cultures that mimic the spatial organization of cells in a live tissue are now being developed to test the activity of therapeutics in more predictive assay systems. Progress towards the development of an assay platform of 3D tissue models ranging from spheroids to 3D bioprinted tissues will be presented from the perspective of a laboratory focused on drug screening and discovery.

3:45 Talk Title to be Announced

Matt Wagoner, Associate Director, Mechanistic and Investigative Toxicology, Takeda Pharmaceuticals

4:15 Phenotypic Analysis of 3D Spheroids for Drug Screening Applications

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

Increasingly, the cancer research field is recognizing the need to transition to 3D screening approaches. However, with improved physiological relevance comes increased standard assay readouts and labor intensive or off-platform assays are often not desirable. We present data demonstrating the correlation of phenotypic metrics to traditional viability assays, and highlight methods for easily validating phenotypic metrics for use in establishing classifying treatment effects.

4:30 Novel 3D Assay for Immuno-Oncology and Evaluating ADCC

Andrea Alms, Consultant, Molding Component Business Department, Kuraray Co. Ltd

Tumor microenvironment of 3D-cultures includes cell-cell interactions and formations of metabolic gradients (which are vital to understanding drug efficacy and resistance). To understand ADCC, we developed novel method to evaluate cellular toxicity in spheroids; quantification of ADCC activity elicited by trastuzumab in 3D-culture vs 2D; and, fresh vs frozen cells.

ENGINEERING MODELS

4:45 What 3D Skin Models Teach Us: Lessons Learned from 20 Years of Building from the Ground Up

Jonathan Garlick, DDS, PhD, Professor, Oral Diagnosis, School of Dental Medicine, School of Medicine and Engineering, Tufts University

3D engineered tissue models of human skin have emerged as a platform technology for drug screening and modeling of human skin disease. These tissue models have evolved through integration of new understandings of stem cell biology, the cell
We have created 3D human tissue model systems (organoids) that can be studied in vitro for several weeks. The organoids replicate native tissue structure and function and are superior to traditional 2D cultures in order to study organ development, function and drug toxicity. Other applications focus on diseases such as tissue fibrosis and cancer, specifically, to study tumor growth and drug resistance for future use in personalized/precision medicine.

**8:35 Development and Application of Organotypic in vitro Liver Models to Screen Compounds for Drug-Induced Liver Injury and Transcriptomic Pathway Perturbations**

Stephen S. Ferguson, PhD, Chemist, Division of the National Toxicology Program (NTP), Biomolecular Screening Branch (BSB) & NTP Laboratories, National Institute of Environmental Health Sciences (NIEHS)

**9:05 Microfabricated Organ-on-Chip Models of Tissue with High-Throughput Compatibility for Drug Screening**

Joseph Charest, PhD, Program Manager, Commercial Programs, Draper

Draper’s PREDICT-96 system has 96 independent tissue replicates within a standard 96 well plate footprint, resulting in a high-throughput organ-on-chip technology. For each of the 96 independent replicates, the system has 2 microchannels with individual pumps, a transistential electrical resistance (TER) readout, and the ability to image with confocal and high-content screening systems. In addition, the system has been applied to several tissue and organ types which will be discussed.

**9:35 Find Your Table and Meet Your Moderator**

**9:40 Interactive Breakout Discussion Groups**

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. Details on the topics and moderators are available by clicking [here](#).

**The Use of 3D Cellular Models, Organ-on-a-Chip Technologies, or Microphysiological Systems in Preclinical Evaluation of Pharmaceuticals**

William Daly, PhD, Managing Director & Faculty Scientist, Orthopedics and Rehabilitation, University of Wisconsin - Madison

- What are the key barriers to adoption of 3D cellular models in preclinical workflows?
- What are pharmaceutical wish lists (biomarkers, function, histology, etc.) for validation of 3D cellular models (groups to split into organ of choice)?
- Where is the ideal fit for 3D cellular models in the drug development pipeline / pharmaceutical testing?
- What are the missing models / unmet needs for preclinical evaluation and efficacy testing?
- Are single organs enough or is there a strong need for multi-organ testing?

**3D Models of Human Organs: Challenges and Prospects**

Samira Musah, PhD, Dean's Postdoctoral Fellow, Wyss Institute at Harvard University and Harvard Medical School

- Inducing stem cell differentiation, cell maturation, and functionality
- Organoids, organs-on-chips, 3D-printed tissues
- Applications in disease modeling and therapeutic discovery

**10:20 Coffee Break in the Exhibit Hall with Poster Viewing**
**SCREENING FOR CNS**

11:05 **Vascularized 3D Models of the Developing Blood-Brain Barrier and Cerebral Cortex for Developmental Neurotoxicity Screening and Disease Modeling**

William Daly, PhD, Managing Director & Faculty Scientist, Orthopedics and Rehabilitation, University of Wisconsin - Madison

Here, we present a 3D vascularized stem cell derived organoid model (/microphysiological system) of the cerebral cortex in a microfluidics platform that has distinct neural, vascular and microglial components. The model captures the initial vascularization of the developing brain (i.e., blood-brain barrier formation) from the perineural vascular plexus in an enhanced throughput microfluidics model. The model has been used to screen for developmental neurotoxins and to model MeCP2 spectrum disorders.

11:35 **Blood-Brain Barrier Spheroids as an *in vitro* Screening Platform for Brain-Penetrating Agents**

Sean Lawler, PhD, Assistant Professor & Managing Director, Harvey Cushing Neurooncology Laboratories, Neurosurgery, Brigham and Women's Hospital

The BBB represents a major obstacle to the delivery of drugs to the brain. We have recently developed a 3D *in vitro* model of the BBB, composed of astrocytes, pericytes, and endothelial cells, which spontaneously form spheroids with BBB properties. We have identified novel peptide agents which can cross the BBB using this approach. This talk describes BBB spheroids and their capabilities as a predictive and screening tool.

11:45 Noon Break

12:05 pm **Neuroospheroid Arrays for *in vitro* Studies of Alzheimer's Disease**

Daniel Irimia, MD, PhD, Associate Professor, Division of Surgery, Science & Bioengineering, Massachusetts General Hospital, Harvard Medical School, and Shriners Hospitals for Children – Boston

Here, we present a 3D vascularized stem cell derived organoid model (**microphysiological system**) of the cerebral cortex in a microfluidics platform that has distinct neural, vascular and microglial components. The model captures the initial vascularization of the developing brain (i.e., blood-brain barrier formation) from the perineural vascular plexus in an enhanced throughput microfluidics model. The model has been used to screen for developmental neurotoxins and to model MeCP2 spectrum disorders.

12:35 **Session Break**

12:40 **Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own**

1:10 **Ice Cream Break in the Exhibit Hall with Poster Viewing**

**ADVANCING MODELS & APPLICATIONS**

1:55 **Chairperson's Remarks**

William Daly, PhD, Managing Director & Faculty Scientist, Orthopedics and Rehabilitation, University of Wisconsin - Madison

2:00 **Engineering Patient-Specific Organs-on-Chips from Human-Induced Pluripotent Stem Cells**

Samira Musah, PhD, Dean's Postdoctoral Fellow, Wyss Institute at Harvard University and Harvard Medical School

This talk describes our lab's use of interdisciplinary approaches to control stem cell fate decisions and engineer functional microfluidic conduits of the human kidney glomerulus. Our most recent work involves the establishment of a robust stem cell-based method to generate blood-filtering cells (podocytes), and integrating these cells with a microfluidic organ-on-a-chip system to recapitulate the structure, function, and specific drug toxicity of the human kidney's blood filtration unit.
Recommended Event Package

Short Course 4: Practical Phenotypic Screening
Short Course 9: How to Best Utilize 3D Cells, Spheroids, PDX Models in Oncology
Short Course 16: Applications of CRISPR and Single-Cells: Best Practices from Set-Up to Data Analysis
Conference: Phenotypic Screening and Chemical Biology
Conference: Next-Gen Genomics: Leveraging CRISPR & Single-Cells

WEDNESDAY, JUNE 20

11:00 am Registration Open

11:50 Bridging Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:20 pm Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

1:00 PLENARY KEYNOTE SESSION (click here for details)

2:30 Refreshment Break in the Exhibit Hall with Poster Viewing

KEYNOTE SESSION: NEW CRISPR EDITING TOOLS FOR TARGETED USE

3:10 Chairperson's Opening Remarks
Roderick L. Beijersbergen, PhD, Group Leader, Division of Molecular Carcinogenesis and Head, NKI Robotics and Screening Center, The Netherlands Cancer Institute

3:15 Strategies for Optimizing Homology Directed Repair for CRISPR Genome Engineering
John Feder, PhD, Associate Director of Genome Biology and Emerging Technologies, Department of Genetically Defined Diseases and Genomics, Bristol-Myers Squibb
New CRISPR systems, modalities and methods are being discovered and published at an unprecedented pace such that unbiased and agnostic comparisons and protocol optimizations are warranted if the promise of genome engineering is to be realized in the pharmaceutical setting. We will present our results to date for generating an optimized method for performing homology directed repair gene editing in induced pluripotent stem cells.

3:45 Genomic Approaches for Functionally Dissecting a STAT-dependent Super-enhancer
Warren J. Leonard, MD, NIH Distinguished Investigator, Chief, Laboratory of Molecular Immunology and Director, Immunology Center, National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health
Super-enhancers regulate genes critical for cell-type specification, but studies of their function and regulation in vivo remain limited. We have studied the actions of IL-2 and IL-21, cytokines that activate transcription factors STAT5 and STAT3, respectively, and their binding to super-enhancers in a cytokine-specific manner. We focused on the immunologically critical Il2ra gene. By combining genomic approaches, including ChIA-PET and CRISPR/Cas9, we have identified IL-2-induced chromatin looping at the Il2ra locus and discovered that multiple super-enhancer elements cooperate to control gene expression. Our findings provide a detailed functional analysis of the Il2ra super-enhancer, with broader lessons for cytokine-dependent super-enhancer function as well.

4:15 Synthetic sgRNA Enables Efficient, Consistent CRISPR Editing of Cells for Automation and Therapeutic Applications
Kevin Holden, PhD, Head, Synthetic Biology, Synthego
Achieving consistent and high editing efficiencies with CRISPR is critical for automation and therapeutic applications with primary cells, and remains a significant challenge. Through a collaborative effort, we demonstrate that use of synthetic sgRNA for CRISPR yields improved and consistent editing efficiencies that are required for such applications.

4:45 CRISPR-UMI: Single Cell Lineage Tracing of Pooled CRISPR/Cas9 Screens
Ulrich Elling, PhD, Principle Investigator, Institute of Molecular Biotechnology Austria (IMBA)
Pooled CRISPR screens are a powerful tool to assess gene function. We developed CRISPR-UMI (Unique Molecular Identifiers), a single cell lineage tracing methodology for pooled screening to account for cell heterogeneity. The added value of CRISPR-UMI both in positive and negative selection paradigms will be presented. CRISPR-UMI controls for inherent noise in genetic screens, increases reproducibility, and measures incident rates of phenotypes.

5:15 Large Scale Pooled CRISPR Screening: Reversing Resistance
Roderick L. Beijersbergen, PhD, Group Leader, Division of Molecular Carcinogenesis and Head, NKI Robotics and Screening Center, The Netherlands Cancer Institute
A major challenge is the recurrence of cancers resistant to treatment thereby limiting long-term success in the clinic. We have applied genome scale CRISPR/Cas9 screens to identify genes that upon inactivation, re-sensitize cancer cells to standard cancer treatments. Identification of such genes allows for the development of novel drug combinations. The results of this work and the clinical implications will be discussed.

5:45 Close of Day and Dinner Short Course Registration*
*Separate registration required. Please click here for more information.

THURSDAY, JUNE 21

7:30 am Registration Open and Morning Coffee

FUNCTIONAL GENOMICS STRATEGIES FOR DRUG DISCOVERY

8:00 Chairperson's Remarks
John Doench, PhD, Associate Director, Genetic Perturbation Platform, Broad Institute of Harvard and MIT

8:05 Decoding T Cell Circuity
Alexander Marson, MD, PhD, Assistant Professor, Department of Microbiology and Immunology and Divisions of Infectious Diseases and Rheumatology, Department of Medicine; and Diabetes Center, University of California, San Francisco

Our research goal is to identify genetic circuits that control human immune cell functions and understand how sequence variation in the genome can contribute to immune-mediated diseases. To study and treat the biological effects of genetic disease variants in human immune cells, my lab has developed new CRISPR technologies. We can now advance from correlative studies of genome mapping to mechanistic studies of genome perturbations in primary cells. We can readily re-write specific sequences in T cells and interrogate the causal biological effects to understand disease.

8:35 Cell Engineering by CRISPR and the Impact of Single Cell Analysis in Drug Discovery
Maryam Clausen, PhD, Senior Research Scientist, Translational Genomics, Discovery Sciences, Innovative Medicines and Early Development Biotech Unit (iMed), AstraZeneca

9:05 Targeted Single-Cell RNA Expression Profiling for Biomarker Discovery
Alex Chenkich, PhD, President, CSO, Cellecta, Inc.

We have developed the DriverMap™ Expression Profiling assay, a targeted RNA expression profiling assay using a genome-wide set of 19,000 validated primer pairs that leverages the sensitivity of multiplex RT-PCR with the throughput and digital readout depth of next-generation sequencing (NGS). We will present data describing the analysis of immune cell infiltration in tumor samples, and identify active pathways in tumor, xenograft samples, and small-molecule-treated cell lines.

9:35 Find Your Table and Meet Your Moderator

9:40 Interactive Breakout Discussion Groups
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. Details on the topics and moderators are available by clicking here.

CRISPR/Cas9 for Drug Discovery Applications
Roderick Beijersbergen, Ph.D., Group Leader, Netherlands Cancer Institute and Head, NKI Robotics and Screening Center

Stephanie Mohr, PhD, Lecturer, Genetics & Director, Drosophila RNAi Screening Center at Harvard Medical School

• Impact of CRISPR/Cas9 for drug discovery in pharma and academia
• Applications for functional screens, creating cell lines and disease models
• Design and optimization of low- and high-throughput screens using CRISPR approaches
• Application of CRISPR-knockout, -activation and -inhibition
• Impact of new CRISPR technologies and reagents

Exploiting CRISPR, RNAi and Single-Cell Analysis: What You Need to Know Before and After
Sarah Boswell, PhD, Director of Sequencing Technologies, Laboratory of Systems Pharmacology and Director, Single-Cell Sequencing Core, Harvard Medical School

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

• Understanding inherent limitations and need for using complementary techniques
• Examples of how multiple techniques have been put to good use for addressing biological questions
• Evaluating and testing the reagents and tools
• Insights on inherent challenges and ways to overcome it
• Tackling data analysis

10:20 Coffee Break in the Exhibit Hall with Poster Viewing

11:05 Combinatorial Genetic Screens with CRISPR-Cas9
John Doench, PhD, Associate Director, Genetic Perturbation Platform, Broad Institute of Harvard and MIT

CRISPR-Cas9 has enabled a new generation of genetic screens to interrogate gene function. Single gene knockout approaches, however, encounter limitations in exploring redundant genes and complex gene networks. Here I will discuss our 'Big Pap' approach, using orthogonal CRISPR-derived components to achieve efficient combinatorial screening, avoiding interference and maximizing gene targeting activity.

Scientists from pharma and academia come together with service providers to discuss current choices as well as gaps in know-how and technology for matching technology with the biological question that needs to be addressed. They will discuss current challenges, share best practices and their experiences using some of the new tools available for gene editing, expression profiling and sequencing such as, CRISPR and single cells.

Moderator: John Doench, PhD, Associate Director, Genetic Perturbation Platform, Broad Institute of Harvard and MIT
EXPLORING CRISPR, SINGLE-CELLS FOR ONCOLOGY RESEARCH

1:55 Chairperson's Remarks
Gus Frangou, PhD, Assistant Professor of Oncology, Department of Cancer Genetics, Roswell Park Cancer Institute; Senior Fellow, Harvard T.H. Chan School of Public Health

2:00 Genome-Wide CRISPR Screens and Single-Cell Analysis Identify New Genes and Pathways Driving Breast Cancer Development and Progression
Gus Frangou, PhD, Assistant Professor of Oncology, Department of Cancer Genetics, Roswell Park Cancer Institute; Senior Fellow, Harvard T.H. Chan School of Public Health

Identifying genetic drivers of metastatic breast cancer and the timing during which these lesions occur is critical to developing effective therapeutics. Using novel modifications of CRISPR/Cas9 we have developed high-efficiency in vivo phenotypic screens and inducible gene targeting, to interrogate the functions of cancer-driver mutations. These CRISPR/Cas9-based genetic screens provide a systematic phenotypic measurement of loss-of-function lesions in disease progression and provide novel insights into the molecular underpinnings of metastasis.

2:30 Single-Cell RNA Sequencing and CRISPR/Cas9-Mediated Gene Deletion Reveals an Altered Gene Expression Pattern in Human Lung Epithelial Cells
Dazhong Xu, PhD, Assistant Professor of Pathology, Vice Chair of Research, Department of Pathology, New York Medical College School of Medicine

We used single-cell RNA-Seq to compare gene expression profiles between BEAS-2B lung epithelial cells chronically treated with Cr(VI), with or without CRISPR/Cas9-mediated deletion of ERRFI1. We identified 83 significantly differentially expressed genes with cellular functions such as cell adhesion, oxidative stresses, and protein ubiquitination. Upregulation of some neuro-specific genes was also evident in ERRFI1-deleted cells, particularly UCHL-1, a deubiquitinase and potential marker for lung cancer.

3:00 Challenges Within the Shadows of CRISPR
Geoffrey Bartholomeusz, PhD, Associate Professor and Director, Target Identification and Validation Program, Department of Experimental Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

The benefits of CRISPR-based editing are far reaching. There are however, accompanying challenges that can slow down progress of CRISPR-based studies. It is therefore necessary to be aware of these underlying challenges both in study design and data interpretation. CRISPR-based challenges experienced by my group will be discussed.
16th Annual
High-Content Analysis
Incorporating Complex High-Content Screening into Preclinical Drug Discovery

Recommended Event Package

Short Course 4: Practical Phenotypic Screening
Short Course 10: Applications of Artificial Intelligence & Machine Learning in Drug Discovery & Development
Short Course 17: Use of Machine Learning to Help Reduce Gaps in Preclinical to Clinical Translation
Conference: Phenotypic Screening and Chemical Biology
Conference: High-Content Analysis

WEDNESDAY, JUNE 20

11:00 am Registration Open

11:50 Bridging Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:20 pm Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

1:00 PLENARY KEYNOTE SESSION (click here for details)

2:30 Refreshment Break in the Exhibit Hall with Poster Viewing

2:30 Phenotypic Drug Discovery Approaches

PHENOTYPIC DRUG DISCOVERY APPROACHES

3:10 Chairperson's Opening Remarks
Regis Doyonnas, PhD, Senior Principal Scientist, Primary Pharmacology Group, High Content Screening Lead, Worldwide R&D, Pfizer

3:15 The Phenomics Discovery Initiative (PDi): Recruiting and Translating Academic Disease-Predictive Biology into the Pharma Drug Discovery Pipeline
Denise Barrault, PhD, Executive Director, National Phenotypic Screening Centre
Academic and clinical communities carry out vast amounts of novel biological research, which is underexploited and lacks the rigour and purpose for effective translation. At the National Phenotypic Screening Centre (NPSC) we have formed a public-private consortium called the Phenomics Discovery Initiative (PDi) that allows the pre-competitive de-risking of phenotypic assays for development, screening and validation. PDi leverages NPSC's world class facilities, industry standard operation and extensive global networks to crowdsource and develop the best biology.

3:45 Image and Flow Cytometry-Based High-Content Phenotypic Screenings in Drug Discovery
Regis Doyonnas, PhD, Senior Principal Scientist, Primary Pharmacology Group, High Content Screening Lead, Worldwide R&D, Pfizer

High disease relevance in cell-based assays is one of the most important goals in phenotypic assay development. Opportunities and challenges to combine patient-derived, disease-specific cells with high-content screening technologies with the aim of finding new targets and new drugs will be discussed during this presentation.

4:15 Sponsored Presentation (Opportunity Available)

4:45 Phenotypic Screening of Small Molecule Enhancers of Basal Autophagy: HCS and New Informatics Tools
Rafael Fernandez, PhD, Principal Scientist, Pharmacology, Merck Research Laboratories

5:15 Agnostic Approaches for Drug Discovery
Thierry Dorval, PhD, HCS Group Leader, Institut de Recherches Servier
High-content screening provides an extremely powerful way to multiplex readouts from biological experiments in a high throughput way, generating statistically robust results. Screening and assay development could benefit from this approach to have better understanding of the biology and a more robust characterization of the selected hits during screening campaign. However, there is a need for adapted tools to visualize and automatically support decision. The presentation will cover what we have developed to address this aspect at Servier’s group.

5:45 Close of Day and Dinner Short Course Registration*
*Separate registration required. Please click here for more information.

THURSDAY, JUNE 21

7:30 am Registration Open and Morning Coffee

SCREENING OF iPSC-DERIVED NEURONS

8:00 Chairperson's Remarks
Christopher Untucht, PhD, Senior Scientist, Head of Cell Imaging Platform, Neuroscience Discovery Core Technologies, AbbVie Deutschland GmbH & Co. KG

8:05 HCS Neurite Outgrowth Assay Using iPSC-Derived Neurons
Christopher Untucht, PhD, Senior Scientist, Head of Cell Imaging Platform, Neuroscience Discovery Core Technologies, AbbVie Deutschland GmbH & Co. KG

Human induced pluripotent stem cell (hiPSC) derived neuronal cells are a promising source to fill the unmet need for human cells in preclinical drug discovery. Screening for compounds that affect growth and function of neurites is of particular importance for the discovery of treatment opportunities in the area of neurodegenerative diseases such as Alzheimer's Disease (AD) and Multiple Sclerosis (MS). Neurite outgrowth displays a scalable and quantifiable mechanism demonstrating the dynamic response of neurons to effectors from the environment.
8:35 Phenotypic Screening of hiPSC-Derived Neuronal Networks Using Multielectrode Arrays
Deborah Pre, PhD, Scientist, Conrad Prebys Center for Chemical Genomics, Sanford Burnham Prebys Medical Discovery Institute

Neurological disease modeling and drug discovery efforts would greatly benefit from human cell-based platforms to study neuronal networks and synaptic plasticity. Using human induced pluripotent stem cell (hiPSC)-derived neurons, we have developed a multielectrode array (MEA) assay in multi-well format that recapitulates physiologically relevant synchronized bursting properties sensitive to shifts in excitation/inhibition balance. We will discuss use of this assay for compound screening and modeling of synaptic plasticity.

9:05 Sponsored Presentation (Opportunity Available)

9:35 Find Your Table and Meet Your Moderator

9:40 Interactive Breakout Discussion Groups

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. Details on the topics and moderators are available by clicking here.

How to Design Machine Learning Models to Automatically Identify Biological Mechanisms
Greg Johnson, PhD, Scientist & Machine Learning Specialist, Allen Institute for Cell Science

• Data representation
• Model architecture
• Designing an objective function

Challenges in Phenotypic, Target Agnostic Drug Discovery
Jesus Medina, PhD, Manager, Medicinal Chemistry, GlaxoSmithKline

• Key challenges in cell-based phenotypic drug discovery efforts
• Early assessment of the validity and viability of hits obtained from screens
• What aspects of phenotypic drug discovery are the most advantages in drug discovery

10:20 Coffee Break in the Exhibit Hall with Poster Viewing

11:05 An Ultra HTS 3D Assay Platform for Enhancing T-Cell-Mediated Tumor Killing
Shane Horman, PhD, Research Investigator III, Genomic Institute of the Novartis Research Foundation

Overcoming tumor-mediated immunosuppression and enhancing cytotoxic T-cell activity within the tumor microenvironment are two central goals of immuno-oncology (IO) drug discovery initiatives. However, exploratory assays involving immune components are often plagued by low-throughput and poor clinical relevance. Here we present a novel ultra-high-content assay platform for interrogating T-cell-mediated killing of 3D tumor spheroids that yields multi-parametric, clinically-relevant data and can be employed kinetically for the discovery of novel IO therapeutic agents.

11:35 Image-Based Antibody Internalization Assays in Biologics Drug Development
Joern Hopke, PhD, Senior Research Investigator, Sanofi Biologics Research

In recent years, pharmaceutical drug discovery has increasingly focused on biologics and therapeutic antibodies in particular. Biologics research and development depend on the functional and mechanistic characterization of those antibodies. Their cellular internalization is a key feature that needs to be empirically determined, as it is either a desired or unwanted attribute, depending on the required mode of action. Utilizing high content imaging instrumentation and analysis, we have adopted a wide variety of strategies to interrogate antibody internalization.

12:05 pm High-Content Imaging to Enable Biologics Drug Discovery
Lorraine Irving, PhD, Research Scientist, Medimmune

Biologic drugs, which include monoclonal antibodies, recognise their target molecules with high specificity. To facilitate the identification of new biologic candidate drugs at Medimmune, functional high content imaging (HCI) assays are being applied throughout the biologics drug discovery process. Disease relevant HCI assays enable new target identification, functional lead selection, mechanistic studies and affinity/dose modelling predictions. PerkinElmer Opera and Molecular Devices Image Xpress Micro HCl systems are routinely used.

12:35 Session Break

12:40 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

ORGANOID-BASED HIGH-CONTENT SCREENING

1:55 Chairperson’s Remarks
Shay Soker, PhD, Professor, Institute for Regenerative Medicine, Wake Forest School of Medicine

2:00 Talk Title to be Announced
Daniel V. LaBarbera, PhD, Associate Professor, Drug Discovery and Medicinal Chemistry; Director, High-Throughput Screening and Chemical Biology Core Facility, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado

2:30 Multi-Tissue Interactions in an Integrated Three-Tissue Organ-on-a-Chip Platform
Shay Soker, PhD, Professor, Institute for Regenerative Medicine, Wake Forest School of Medicine

Organoid and organ-on-a-chip technologies are rapidly advancing towards deployment for drug and toxicology screening applications. Few engineered model systems, including the growing variety of organoid and organ-on-a-chip platforms, have so far reflected the interactive nature of the human body. To address this challenge, we have developed an assortment of bioengineered tissue organoids and tissue constructs that are integrated in a closed circulatory perfusion system, facilitating inter-organ responses. We describe a multi organ-on-a-chip system.
COMPLEX CELLULAR MODELING WITH HIGH-CONTENT ANALYSIS

3:00 Machine Learning of the Assembly Instructions of a Cell
Timothy Majarian, Associate Computational Biologist, Broad Institute

An important challenge enabled by the growth in microscope technologies is to be able to combine information from diverse images into comprehensive models of cell organization, rather than to just describe or compare images. Methods have been described for creating generative models of cells, and recent progress has been made on a critical remaining challenge: learning how the spatiotemporal distribution of each component depends upon those of other components.

3:30 The Allen Institute for Cell Science: Building an Integrated Cell
Greg Johnson, PhD, Scientist & Machine Learning Specialist, Allen Institute for Cell Science

Understanding the organization of the cell is an underlying goal of the Allen Institute for Cell Science. Here, we present two conditional models of subcellular localization that allow for the prediction of unobserved structures, learned directly from fluorescence images. We demonstrate our models generalize to a wide range of subcellular localization patterns and allow for a probabilistic interpretation of this organization. This project forms the foundation for further work the prediction of cell organization and behaviors.

4:00 Close of Conference
The 15th Annual Mastering Medicinal Chemistry event highlights the latest advancements in medicinal chemistry across therapeutic areas from top pharmaceutical, biotech, and academic institutions. We invite you to attend the conference to hear about successful case studies, see new cutting-edge poster presentations, network with peers during breakout discussions and learn about the new methods shaping the field of medicinal chemistry. This three-day event will discuss new targets and inhibitors within the hot therapeutic areas of immuno-oncology, inflammation, CNS disorders, as well as many others.

**June 19-20**

**AGENDA** Mastering Medicinal Chemistry Part 1

**June 20-21**

**AGENDA** Mastering Medicinal Chemistry Part 2
8:15 Chairperson's Opening Remarks  
Lijun Sun, PhD, Director, Center for Drug Discovery and Translational Research, Beth Israel Deaconess Medical Center, Harvard Medical School

8:20 Challenges in Phenotypic, Target Agnostic Drug Discovery: Lessons Learned from a Cell-Based Screen Designed to Identify Small Molecules that Decrease C-MYC in Cancer Cells  
Jesus Medina, PhD, Manager, Medicinal Chemistry, GlaxoSmithKline

One of the key challenges in cell-based phenotypic drug discovery efforts is the early assessment of the validity and viability of hits obtained from the screen. Using our c-MYC cellular screen as an example, we describe a strategy to determine whether the MOA of the hits has in vivo translatable. The details of our screening strategy/triage campaign, molecular target identification efforts, results from in vivo studies, and the lessons learned along the way will be discussed.

8:50 Rational Design of AKR1C3 Inhibitors as Chemotherapeutic Potentiators  
Paul Trippier, PhD, Professor, Department of Pharmaceutical Sciences, Texas Tech University Health Sciences Center

 Aldo-keto reductase 1C3 (AKR1C3) catalyzes the downstream conversion of androgen precursors to the potent androgen receptor ligands testosterone and 5α-dihydrotestosterone, and conversion of PGD2 to 11β-PGF2α and PGF2α prostanoids and hence acts as an important regulator of myeloid cell proliferation and differentiation. The enzyme is highly upregulated in prostate cancer and a number of leukemias. We have designed potent and highly selective inhibitors that act to potentiate clinical chemotherapeutics >200-fold. Such action results in reduced dosing, reduced toxic side effects and completely counters AKR1C3-mediated drug resistance. Our inhibitors provide a strategy for treating vulnerable patients diagnosed with these and other neoplasms in combination with existing chemotherapeutics
12:40 Session Break

KINASE INHIBITORS FOR CANCER

1:15 Chairperson's Remarks
Neil Grimster, Senior Scientist, Oncology Chemistry, AstraZeneca

1:20 Discovery and Optimization of a Novel Series of Highly Selective JAK1 Kinase Inhibitors
Neil Grimster, Senior Scientist, Oncology Chemistry, AstraZeneca

Janus kinases (JAKs) have been demonstrated to be critical in cytokine signaling, and have thus been implicated in both cancer and inflammatory diseases. The development of small molecule inhibitors that are selective for a specific family member would represent highly desirable tools for deconvoluting the intricacies of JAK family biology. Here we present the discovery of a potent and orally bioavailable JAK1 inhibitor, which possesses ~1000 fold selectivity over the other highly homologous JAK family members, and good selectivity over kinases in general.

1:50 Optimization of Kinact Delivers a First in Class Specific Covalent JAK3 inhibitor PF-06651600
Atli Thorarensen, PhD, Research Fellow, BioTc Medicinal Chemistry, Pfizer

2:20 Sponsored Presentation (Opportunity Available)

2:50 Refreshment Break in the Exhibit Hall with Poster Viewing

3:30 A Kinase Inhibitor for a Chronic Indication: A Case Study in Balancing Selectivity and Safety to Advance Potent, Selective and Orally Bioavailable MAP4K4 Leads to Preclinical Toxicity Studies
Samit Bhattacharya, PhD, Senior Principal Scientist, World Wide Medicinal Chemistry, Pfizer

This presentation will describe the identification of an aminopyridine lead series from virtual screening and evolution of multiple aminopyridine leads that led to discovery of advanced potent, selective and orally bioavailable MAP4K4 inhibitors. Given the concerns of chronic safety for a kinase inhibitor in a non-oncology indication, this presentation will discuss strategies that were employed to advance two chemotypes (PF-06279789 and PF-06745013) with excellent kinase selectivity but orthogonal profiles to assess safety of the mechanism.

IDENTIFICATION OF NOVEL INHIBITORS

4:00 Chemogenomic-driven Hit Identification to Deliver Novel dF508 CFTR Corrector Leads
John Mathias, PhD, Senior Director, Head of Inflammation & Immunology Design, Pfizer

4:30 Identification of Low Clearance Indole Acid AMPK Activators for the Treatment of Diabetic Nephropathy
David Ebner, PhD, Senior Scientist, Pfizer Research Labs

5:00 Find Your Table and Meet Your Moderator

5:05 Interactive Breakout Discussion Groups
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. Details on the topics and moderators are available by clicking here.

Developing Anticancer Therapies with Dual Specific Kinases
Lijun Sun, PhD, Director, Center for Drug Discovery and Translational Research, Beth Israel Deaconess Medical Center, Harvard Medical School
- Dual specific kinases and their benefits in treating cancers
- Other therapeutic areas of interest?
- Potential uses of the DYRK

Safety Considerations of Kinase Inhibitors
Samit Bhattacharya, PhD, Senior Principal Scientist, World Wide Medicinal Chemistry, Pfizer
- Chronic safety concerns for kinase inhibitors for you in non-oncology indications
- Advancing chemotypes
- Using orthogonal profiles to assess safety

5:45 Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

WEDNESDAY, JUNE 20

7:45 am Registration Open and Morning Coffee

IMPROVING KINETICS & PROFILING

8:25 Chairperson's Remarks
Jesus Medina, PhD, Manager, Medicinal Chemistry, GlaxoSmithKline

8:30 Kinetic and Thermodynamic Profiling in Drug Discovery: A Case Study with EED Hit-to-Lead Program
Ying Wang, PhD, Principal Scientist, Department of Chemistry & Technology, AbbVie

Our analysis revealed for the first time that ITC data should be interpreted in the context of chiral purity of the compounds. The thermodynamic signatures of the EED amino pyrrolidine compounds were found to be mainly enthalpy driven with improved enthalpic contributions as the program progressed. We will also present our perspectives on where we are at on harnessing the power of thermodynamic and kinetic profiling in drug discovery.

9:00 Small Molecule, Inverse Agonists of The Nuclear Hormone Receptor RORC2
Mark Schnute, PhD, Associate Research Fellow, Biotherapeutics Chemistry & Immunoscience, Pfizer Global R&D

9:30 Sponsored Presentation (Opportunity Available)
10:00 Coffee Break in the Exhibit Hall with Poster Viewing
10:45 PANEL DISCUSSION: Medicinal Chemistry in the Field on Oncology and Immuno-Oncology
Jesus Medina, PhD, Manager, Medicinal Chemistry, GlaxoSmithKline
Panelists:
Paul Trippier, PhD, Professor, Department of Pharmaceutical Sciences, Texas Tech University Health Sciences Center
Jesus Medina, PhD, Manager, Medicinal Chemistry, GlaxoSmithKline
Atli Thorarensen, PhD, Research Fellow, BioTc Medicinal Chemistry, Pfizer
Samit Bhattacharya, PhD, Senior Principal Scientist, World Wide Medicinal Chemistry, Pfizer
11:45 Session Break
11:50 Bridging Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own
12:20 pm Dessert and Coffee Break in the Exhibit Hall with Poster Viewing
1:00 PLENARY KEYNOTE SESSION (click here for details)
2:30 Refreshment Break in the Exhibit Hall with Poster Viewing
3:10 Close of Conference
Our analysis revealed for the first time that ITC data should be interpreted in the context of chiral purity of the compounds. The thermodynamic signatures of the EED amino pyrrolidine compounds were found to be mainly enthalpy driven with improved enthalpic contributions as the program progressed. We will also present our perspectives on where we are at on harnessing the power of thermodynamic and kinetic profiling in drug discovery.

4:15 **Sponsored Presentation** (Opportunity Available)

4:45 **Drug Leads Originating from the Public/Private Consortium: European Lead Factory**
Dimitrios Tzalis, PhD, CEO Taros Chemicals GmbH & Co. KG

The European Lead Factory is a public-private partnership that provides researchers in Europe a unique platform for translating innovative biology and chemistry into high-quality starting points for drug discovery. 200,000 *de novo* synthesized compounds are complimenting 300,000 compounds provided by participating pharmaceutical partners. So far resulted in >5,000 hit compounds with a defined biological activity from >90 successfully completed HTS and hit evaluation campaigns out of which a significant number of targets are PPIs.

5:15 **Positive Allosteric Modulators for Melanocortin Receptors**
Craig W. Lindsley, PhD, Vanderbilt Center for Neuroscience Drug Discovery

Positive allosteric modulators of melanocortin receptors, especially allosteric potentiators of the receptors MC3R and MC4R are described herein. Also provided are pharmaceutical compositions containing the positive allosteric modulators and methods of treating obesity or an obesity-related disorder such as type 2 diabetes, comprising administering an effective amount of the positive allosteric modulator.

5:45 **Close of Day and Dinner Short Course Registration***

*Separate registration required. Please click [here](#) for more information.

**THURSDAY, JUNE 21**

7:30 am **Registration Open and Morning Coffee**

**APPROACHES TO OPTIMIZATION AND CHARACTERIZATION (CONT)**

8:00 **Chairperson’s Remarks**
Catherine Lebrun, PhD, Medicinal Chemist, Medicinal Chemistry, EMD-SERONO
8:05 3D-Fragments: A Short Path for the Design of Low Mw Cyclophilin D Inhibitors
Catherine Lebrun, PhD, Medicinal Chemist, Medicinal Chemistry, EMD-SERONO
Cyclophilins, or peptidyl-prolyl isomerase (PPIases), play a critical role in multiple cellular pathways. Cyclophilins have been proposed as potential targets for the treatment of a number of diseases such as viral infections, inflammation, neurologic disorders, cardiac failure, and cancer. Until recently, only high molecular weight macrocyclic peptides were described as modulators of this target class. Here we describe a design of potent small molecular weight Cyclophilin D inhibitors starting from weak fragments that bind Cyclophilin D.

8:35 Project Tractability: When Enough is Enough
Jeremy Edmunds, PhD, Director, Immunology Medicinal Chemistry, AbbVie

9:05 Sponsored Presentation (Opportunity Available)

9:35 Find Your Table and Meet Your Moderator

9:40 Interactive Breakout Discussion Groups
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. Details on the topics and moderators are available by clicking here.

Public-Private Partnerships in Drug Discovery
Dimitrios Tzalis, PhD, CEO Taros Chemicals GmbH & Co. KG
– How can collaborative public-private partnerships foster drug development?
– What steps are being taken to close the "innovation gap"?
– How can partnerships be beneficially for both parties?

Challenges in Phenotypic, Target Agnostic Drug Discovery
Jesus Medina, PhD, Manager, Medicinal Chemistry, GlaxoSmithKline
– Key challenges in cell-based phenotypic drug discovery efforts
– Early assessment of the validity and viability of hits obtained from screens
– What aspects of phenotypic drug discovery are the most advantages in drug discovery

10:20 Coffee Break in the Exhibit Hall with Poster Viewing

11:05 Drug Target Kinetics and Drug Discovery
Peter Tonge, PhD, Professor, Chemistry, Stony Brook University
Data on three systems will be discussed including reversible inhibitors of two antibacterial targets, and a covalent inhibitor of Bruton’s tyrosine kinase (BTK), a target for treating diseases stemming from B cell dysregulation. The ability to accurately quantify target engagement as a function of time and drug concentration is expected to dramatically improve the prediction of in vivo drug activity across all therapeutic areas.

11:35 A Novel Class of Autophagy Activators to Combat a Rare Pediatric Neurodegenerative Disease
Paul Trippier, PhD, Professor, Department of Pharmaceutical Sciences, Texas Tech University Health Sciences Center

12:05 pm Discovery of Small Molecule Macrocycles as Powerful Modulators of Cystic Fibrosis and Potent Flaviviral Protease Inhibitors for the Treatment of Zika and Dengue Virus Infections
Helmut Thomas, PhD, DABT, President and CEO, Cyclenium Pharma, Inc.
Cyclenium Pharma has designed a unique small-molecule (CMRT™) macrocycle technology with conventional small-molecule like properties for drug discovery on difficult targets. CMRT compounds are stable chemically and metabolically, demonstrate exceptional safety due to their target specificity as a consequence of their constrained and stereochemically defined nature, and display good cell penetration and oral bioavailability. Initial screens have spawned more than a dozen early programs with protein-protein interactions, enzymes, receptor kinases and brain-bound GPCRs as targets. The discovery of a triple active modulator of cystic fibrosis as a unique example for a protein-protein interaction stabilizing compound as well as a potent pan-inhibitor of flaviviral proteases will be presented as examples of the versatility of this technology.
Following increasing interest in neuroscience and CNS drug development, World Preclinical Congress will be launching an exciting new conference track in 2018 focusing specifically on CNS and the latest developments in drug discovery, development and delivery. Key themes include CNS disease models, both animal and cell-based, biomarkers, imaging, translational strategies in CNS and how therapies can cross the blood-brain barrier. Join leading pharmaceutical, biotech, and academic stakeholders working in CNS for interactive sessions, panel discussions, and short courses, all of which are geared toward providing opportunities for active networking and collaboration.

**June 19-20**

**AGENDA** CNS Disease Models  
**AGENDA** Blood-Brain Barrier

**June 20-21**

**AGENDA** Translational Strategies in CNS
The conventional models of Alzheimer's disease (AD) suffer from a number of artifacts such as endogenous gene locus destruction, presynaptic molecular crowding, sudden death, overproduction of non-A APP fragments, non-specific ER stress, non-specific calcium dysmetabolism, etc. The failure of more than 400 medication candidates in clinical trials is likely due to the use of inappropriate pre-clinical investigations. The talk will focus on these comparative models and their use in biological and cognitive performance in patients. This advocates more refined assessment of behavioral effects of drugs in Alzheimer's models. The talk will describe how prevention/reduction of pathology in AD models hasn't translated to improved outcomes in clinical trials.

**ANIMAL MODELS FOR ALZHEIMER’S**

**8:15 Chairperson’s Opening Remarks**
Takaomi C. Saito, PhD, Laboratory Head, Laboratory for Proteolytic Neuroscience, RIKEN Brain Science Institute

**8:20 Single App Knock-In Mouse Models of Alzheimer’s Disease without Overexpression Artifacts for the Best R&D**
Takaomi C. Saito, PhD, Laboratory Head, Laboratory for Proteolytic Neuroscience, RIKEN Brain Science Institute

The conventional models of Alzheimer’s disease (AD) suffer from a number of artifacts such as endogenous gene locus destruction, presynaptic molecular crowing, sudden death, overproduction of non-A APP fragments, non-specific ER stress, non-specific calcium dysmetabolism, etc. The failure of more than 400 medication candidates in clinical trials is likely due to the use of inappropriate models for preclinical studies. Pros and cons of the conventional and new models will be described in detail.

**8:50 MODEL-AD: Model Organism Development and Evaluation for Late Onset Alzheimer’s Disease**
Michael Sasner, PhD, Co-Director, Disease Modeling Program, MODEL-AD Center

The MODEL-AD Center was established to generate translational models for late-onset AD. The goals of the Center are: to identify novel genetic variants, genes and biomarkers from AD patient data; to generate and validate new animal models based on these LOAD variants; and to utilize these novel models in a preclinical testing paradigm.
high content, behavioral platforms, together with proprietary machine learning, can detect the phenotype of AD mouse models earlier and more robustly than standard testing. This approach offers opportunities to reinvigorate the drug discovery process by identifying compounds that reverse the AD phenotype.

12:05 pm Session Break

12:10 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:40 Session Break

**IPS CELLS FOR CNS DRUG DISCOVERY AND DEVELOPMENT**

1:15 Chairperson's Remarks

**Ibrahim Domian, MD, PhD, Assistant Physician, Massachusetts General Hospital, Assistant Professor of Medicine, Harvard Medical School**

1:20 Leveraging Stem Cell Technology to Fuel Drug Discovery for Neurodegenerative Diseases

**Carlo Cusulin, PhD, Senior Scientist, Disease Relevant Cellular Assays, Chemical Biology, F. Hoffmann-La Roche**

Drug discovery for neurodegenerative diseases presents several challenges, because of the complexity of these disorders and the scarcity of reliable and translatable models. iPS technology offers the possibility to produce the relevant cell types (i.e., neurons, microglia, astrocytes) and introduce disease stimuli to obtain an in vitro system amenable for screening. We focused on generating models of Alzheimer's disease, starting from patient-derived iPSCs and assessing the effect of disease-modifying compounds.

1:50 IPS Derived Neurons and Microglia for in vitro Pharmacology

**Johannes Grosse, PhD, Director, Neuroscience Drug Discovery/Alliances, Takeda**

The discrepancy between the massive private and academic investments in drug discovery for neurological and psychiatric diseases and the small and still declining number in novel drug approvals is a clear indicator for the unique challenges of the field. Those have been identified at all phases of drug discovery from target validation and hypothesis via pre-clinical models for pharmacological tests to the design of clinical trials, use of biomarkers and regulatory affairs.

2:20 Advanced Physiologically Relevant hiPSC-Based Platforms for Drug Discovery

**Fabian Zanella, Director, Research & Development, StemonIX**

We present human induced pluripotent stem cell (hiPSC)-based platforms which were structurally engineered with greater physiological relevance aimed to elevate performance in drug discovery applications. microBrain® 3D comprises cortical neural spheroids that feature high functionality with robust spontaneous activity and expected responses to established neuromodulators. microHeart® allows cardiomyocytes to adopt cell geometries and intercellular organization that resemble native heart tissue, translating into differential pharmacological response to known cardioactive compounds.

2:35 Sponsored Presentation (Opportunity Available)

2:50 Refreshment Presentation in the Exhibit Hall with Poster Viewing

3:30 Modeling ALS with Patient Specific iPSCs

**Shila Mekhoubad, PhD, Scientist II, Stem Cell Research, Biogen**

Advances in stem cell biology and neuronal differentiations have provided a new platform to study ALS in vitro. Here we will describe our use of induced pluripotent stem cells (iPSCs) from patients with familial ALS to establish new models and tools that can contribute to the development and validation of novel ALS therapeutics.

4:00 All-Optical Electrophysiology for Neuroscience Drug Discovery

**Graham Dempsey, PhD, Vice President, Research and Development, Q-State Biosciences**

Human induced pluripotent stem (iPS) cell-based models have become a powerful approach to disease phenotyping for drug discovery applications. We have created an optogenetic platform called Optopatch that rapidly and robustly characterizes the electrophysiological response of iPS cell-derived neurons. Our approach provides an information-rich readout of pharmacological changes in both intrinsic neuronal excitability and synaptic transmission with single cell precision and dramatically improved throughput.

4:30 PANEL DISCUSSION: iPSC-Based Neurodegenerative Disease Modeling

**Moderator: Johannes Grosse, PhD, Director, Neuroscience Drug Discovery/Alliances, Takeda**

Human neurodegenerative disorders are among the most difficult to study. This panel will discuss existing and future models for major neurodegenerative diseases.

- How do we establish that phenotypes “in a dish” are relevant to the patient’s disease?
- Does the relative immaturity of neurons in the dish matter and, if so, what do we do about it?
- What are the major technical barriers to high-throughput screening of iPSc-derived neuronal models?
- Does the technology circumvent the need for rodent preclinical neurodegenerative disease models?

5:00 Find Your Table and Meet Your Moderator

5:05 Interactive Breakout Discussion Groups

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. Details on the topics and moderators are available by clicking here.

The Suitability of Animal Models for Preclinical Studies

**Caghan Kizil, PhD, Helmholtz Young Investigator Group Leader, German Center for Neurodegenerative Diseases (DZNE) within Helmholtz Association**

- What type of animal/experimental models are used for neurodegenerative disease models?
- What limitations are there for experimental models?
- How well can we recapitulate the diseases in experimental animal models?
- How can humanized models be improved?
- What is the future of research for CNS disease models?
**Modeling Neurodegenerative Disorders for Drug Discovery and Development**

**Bilada Bilican, Ph.D., Investigator II, Neuroscience, Novartis Institutes for BioMedical Research (NIBR)**

- *In vitro* correlates of complex neurodegenerative diseases.
- How to model apparently sporadic neurodegenerative disorders?
- Advanced cellular models - how to address cell-autonomous vs non-cell autonomous mechanisms of neurodegeneration?
- Phenotype-vs-target-based drug screening

**5:45 Reception in the Exhibit Hall with Poster Viewing**

**7:00 Close of Day**

**WEDNESDAY, JUNE 20**

**7:45 am Registration Open and Morning Coffee**

**BUILDING A STEM CELL BASED DISCOVERY PLATFORM**

**8:25 Chairperson's Remarks**

**Chee Yeun Chung, PhD, Scientific Co-Founder and Associate Director, Discovery Biology, Yumanity Therapeutics**

**8:30 Building a Robust Stem Cell-Based Discovery Platform for Neurodegenerative Diseases**

**Chee Yeun Chung, PhD, Scientific Co-Founder and Associate Director, Discovery Biology, Yumanity Therapeutics**

Phenotypic screening in neurons and glia derived from patients is now conceivable through unprecedented developments in reprogramming, transdifferentiation, and genome editing. We outline progress in this nascent field, but also consider the formidable hurdles to identifying robust, disease-relevant and screenable cellular phenotypes in patient-derived cells. We illustrate how analysis in the simple baker's yeast cell Saccharomyces cerevisiae is driving discovery in patient-derived neurons, and how approaches in this model organism can establish a paradigm to guide the development of stem cell-based phenotypic screens.

**9:00 Functionalization of Schizophrenia GWAS Variants by High-Throughput Differentiation of Human Induced Pluripotent Stem Cells**

**Bilada Bilican, Ph.D., Investigator II, Neuroscience, Novartis Institutes for BioMedical Research (NIBR)**

Schizophrenia is a complex multifactorial and polygenic disorder, with both rare and common genetic variants contributing to disease risk. Genome-wide association studies (GWAS) have highlighted a large number of genetic variants with potential disease association, but validation and prioritization of risk genes remains a challenge.

**9:30 Developing Relevant *In Vitro* CNS Models for Drug Discovery**

**Daniel Haag, PhD, CSO, NeuCyte, Inc.**

NeuCyte Inc. is a biotechnology company focusing on early phases of CNS drug discovery. Based on our SynFire™ technology, we have developed a proprietary human neural *in vitro* platform for complex electrophysiological and morphological readouts suited for target identification and validation, efficacy testing and neurotoxicity assessment. Using patient-derived and genetically engineered defined neural cell types, NeuCyte builds unique cell-based assays for modelling neurological and neurodegenerative disorders.

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

**TOWARDS CURE IN A DISH**

**10:45 A 3D Culture Model of Alzheimer’s Disease: Towards a Cure-in-a-Dish?**

**Doo Yeon Kim, PhD, Assistant Professor of Neurology, Genetics and Aging Research Unit, Massachusetts General Hospital / Harvard Medical School**

Recently, we developed a novel 3D human neural culture model of Alzheimer’s disease (AD) that recapitulates key pathological markers of AD. In this presentation, I will show our recent progress including 1) improved 3D culture models based on single-clonal hNPCs and microfluidic devices, 2) mechanistic studies to dissect pathogenic cascades that lead to NFT and neuronal death, and 3) our efforts to optimize 3D culture models for mid-throughput AD drug screening against FDA-approved drugs.

**11:15 Identification of Axon Growth Promoting Small Molecules Using a High Throughput Phenotypic Assay Exploiting HiPSC Derived Human Motor and Cortical Neurons**

**Bhagat Singh, PhD, Research Fellow, Neurobiology, Clifford Wolf's Lab, Boston Children's Hospital, Harvard Medical School**

We have generated standardized protocols to differentiate motor and cortical neurons from hiPSCs and also have developed a robust, sensitive and reproducible phenotypic neurite outgrowth assay (Z’ > 0.5) that recapitulates CNS specific growth phenotypes *in vitro*. This provides us with a means to screen for regeneration-promoting compounds in a high throughput mode.

**11:45 Session Break**

**11:50 Bridging Luncheon Presentation: Nuclear Imaging of Neuroinflammation in Rodent Models of Neurodegenerative Diseases**

**Tuulia Huhtala, PhD, Head, Biomarkers and in vitro Biology, Discovery, Charles River**

Activation of the mitochondrial translocator protein (TSPO) is linked to neuroinflammation, and TSPO ligands can be used for *in vivo* PET or SPECT imaging. In the current studies, we utilized these ligands to assess the extent of neuroinflammation after lipopolysaccharide (LPS) infusion, following induction of multiple sclerosis (MS) and neuropathic pain.

**12:20 pm Dessert and Coffee Break in the Exhibit Hall with Poster Viewing**

**1:00 PLENARY KEYNOTE SESSION (click here for details)**

**Sponsored by**

**June 19-20, 2018 | Boston, MA**
A brief overview will provide a working definition of the BBB and set up for these overlooked strategies. Three examples will be given: The Undiscovered Transporter with application to antisense transport into brain; Regulation of Endogenous Transporters with Small Molecules will show how to treat brain with the patient’s own hormones; Exosomes will explore the surprising finding that they cross the BBB quite readily.

8:20 Drug Delivery to the Brain: Overlooked and Underexplored Strategies to Cross the Blood-Brain Barrier

William A. Banks, MD, Associate Chief of Staff – R&D, Geriatric Research Education & Clinical Center, Veterans Affairs Medical Center & University of Washington

A brief overview will provide a working definition of the BBB and set up for these overlooked strategies. Three examples will be given: The Undiscovered Transporter with application to antisense transport into brain; Regulation of Endogenous Transporters with Small Molecules will show how to treat brain with the patient’s own hormones; Exosomes will explore the surprising finding that they cross the BBB quite readily.

8:50 Drug Delivery through the Ultrasound-Mediated Blood-Brain Barrier

Shih-Ying Wu, PhD, Translational Fellow / Postdoctoral Research Scientist, Department of Biomedical Engineering, Columbia University

Current treatments of neurological and neurodegenerative diseases are limited due to the lack of a truly non-invasive, transient, and regionally selective brain drug delivery method because of the blood-brain barrier (BBB). Focused Ultrasound (FUS) has been shown to offer the unique capability of noninvasively, locally and transiently opening the BBB. The FUS premise in brain drug delivery including clinical applications will be presented.

9:20 ApoE-Based Peptide Mediator to Deliver Proteins across the Blood-Brain Barrier: Long-Term Efficacy, Toxicity, and Mechanism

Peter Lobel, PhD, Professor, Center for Advanced Biotechnology and Medicine, Rutgers University

Sarkar and colleagues pioneered use of a peptide mediator, K16ApoE, to promote transport of intravenously-administered proteins and small molecules across the blood-brain barrier. We have explored use of K16ApoE and derivatives for acute and chronic delivery of the lysosomal enzyme TPP1 to the mouse brain. The peptide mediators are extremely useful for evaluating brain therapeutics in animal models but appear to possess intrinsic toxicity that precludes clinical applications.

9:50 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

10:35 Safety and Clinical Efficacy of a Brain-Penetrating Human IgG-Iduronidase Fusion Protein in a Phase II Study in Pediatric Patients with Severe Mucopolysaccharidosis Type I

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

A brain penetrating IgG-enzyme fusion protein comprised of iduronidase (IDUA) and a monoclonal antibody against the human insulin receptor was engineered to cross the blood-brain barrier (BBB) and to address both the neurocognitive and peripheral burden in Mucopolysaccharidosis Type I (MPS I). Neurocognitive function, somatic effects and safety of a Phase II proof-of-concept clinical trial in Hurler MPSI pediatric patients will be discussed. This represents the first-in-human clinical trial of a fusion protein engineered to cross the BBB.

10:55 Boosting Brain Uptake of a Therapeutic Antibody Through Conjugation to an Aptamer Against Transferrin Receptor

Yanmei Lu, Ph.D., Scientist, Biochemical and Cellular Pharmacology, Genentech, Inc.

The Transferrin receptor (TfR) has been shown to transport monoclonal antibodies across the blood-brain barrier in a bispecific antibody format with one arm binding to a therapeutic target and another arm binding TfR. The bispecific antibody format has its limitation in losing bivalency and apparent binding affinity, which results in weaker target engagement. Another issue is that the wt Fc domain can induce toxicity, which may limit use to only effectorless antibodies as a therapeutic. To overcome these challenges, a nuclease stabilized RNA aptamer against human TfR was conjugated to a bivalent therapeutic antibody. Taking advantage of the small size of aptamers, this proof of concept study opens up possibilities of increasing brain uptake capacities using novel multi-specific therapeutic modalities.
11:15 Size-Selective Loosening of Blood-Brain Barrier by Genetic and Pharmacological Targeting of Endothelial S1P1
Keisuke Yanagida, PhD, Research Fellow, Vascular Biology Program, Boston Children’s Hospital/Harvard Medical School
The intact blood-brain barrier (BBB) restricts efficient penetration of central nervous system (CNS)-targeted drugs. Here we report the BBB-regulatory role of endothelial sphingosine 1-phosphate receptor-1 (S1P1). Endothelial-specific S1P1 knockout mice showed BBB breach for small molecular weight fluorescence tracers. Consistently, pharmacological inhibition of S1P1 lead to transient BBB breach. The inhibition of brain endothelial S1P1 may be a promising strategy for efficient delivery of small molecules into the CNS.

11:35 Sponsored Presentation (Opportunity Available)

12:05 pm Session Break

12:10 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:40 Session Break

UNDERSTANDING THE BLOOD-BRAIN BARRIER IN STATES OF DISEASE

1:15 Chairperson’s Remarks
William A. Banks, MD, Associate Chief of Staff – R&D, Geriatric Research Education & Clinical Center, Veterans Affairs Medical Center & University of Washington

1:20 Targeting Vascular Dysfunction in Alzheimer’s Disease
Georgette L. Suidan, PhD, Principal Scientist, Lab Head, Internal Medicine Research Unit, Pfizer, Inc.
*Currently at Biogen, Inc
Apart from the classical pathological characteristics of AD, studies have shown that the majority of AD patients present with cerebrovascular abnormalities. These abnormalities include reduced cerebral blood flow (CBF) leading to impaired tissue perfusion and BBB damage resulting in increased permeability to neurotoxins. I will give an overview of the reported vascular dysfunction in AD and discuss a current project targeting a plasma protein to improve CBF and BBB integrity.

1:50 Cerebrovascular Remodeling in Neurological Disorders
Baptiste Lacoste, PhD, Assistant Professor, Cellular and Molecular Medicine/Neuroscience Program, The University of Ottawa/Ottawa Hospital Research Institute
Neurological disorders can originate from, or be perpetuated by, the brain vasculature. Acute and/or chronic abnormalities of cerebrovascular networks have been linked to the onset/progression of stroke, migraine, as well as mental illness. Treatment for many of these conditions is lacking, hence the need to identify new therapeutic targets is pressing. To illustrate these concepts, Dr. Lacoste will provide examples of cerebrovascular alterations that occur in pathological conditions.

2:00 Sponsored Presentation (Opportunity Available)

2:50 Refreshment Break in the Exhibit Hall with Poster Viewing

NOVEL APPROACHES FOR BBB MODELS

3:30 CNS and BBB Experimental Models with Enhanced Cellular Complexity and Architecture
Monica Moya, PhD, Research Engineer, Materials Engineering Division, Lawrence Livermore National Laboratory
In this work, we have developed a dynamic 3D human BBB culture platform to more accurately investigate compound permeability from the bloodstream to the CNS. Our BBB model is a 3D system based around a synthetic scaffold with physiologically relevant shear stress across a co-culture of astrocytes and neurons. Current work is focused on reproducing this BBB model without a synthetic fiber using a direct ink write system to 3D bioprint the BBB. To date, we have successfully cultured 3D bio-printed brain vasculature under flow conditions for three weeks.

3:55 Tissue Engineering Models of the Blood-Brain Barrier
Peter Searson, PhD, Professor, Institute for Nanobiotechnology, Johns Hopkins University
In vitro tissue-engineered models of the neurovasculature enable dynamic studies of barrier function in health and disease under controlled conditions. The incorporation of patient-derived cells has enabled the development of disease models and the study of specific mutations. Here we describe recent advances in tissue-engineered models and provide examples illustrating how they can be used to study drug delivery and disease.

4:20 Stem Cell Derived Blood-Brain Barrier Models: Applicability to Study Antibody-Triggered Receptor-Mediated Transcytosis
Anna Jezierski, PhD, Research Associate, Human Health Therapeutics, National Research Council of Canada
We have developed a human induced pluripotent stem cell-derived BBB model, composed of brain endothelial cells (iBECs), employing a novel direct monolayer differentiation protocol. This model discriminates species-selective antibody-mediated transcytosis mechanisms, is predictive of in vivo CNS exposure of rodent cross-reactive antibodies and is actively implemented into pre-clinical CNS drug discovery and development processes.

4:40 BBB Organoids: A Next-Generation in vitro Screening Platform
Choi-Fong Cho, PhD, Instructor, Department of Neurosurgery, Brigham and Women's Hospital, Harvard Medical School
The presentation will focus on the utility of 3D multicellular BBB organoids made of human brain endothelial cells (ECs), brain pericytes and astrocytes as a next-generation screening model for brain-penetrating molecules. The outer surface of the organoid, composed primarily of ECs and pericytes, forms a barrier that is characterized by tight junctions and efflux-pump activity. This high-throughput model can facilitate drug development and help predict drug delivery into the brain, paving the way for breakthrough discoveries in neuroscience.

5:00 Find Your Table and Meet Your Moderator

5:05 Interactive Breakout Discussion Groups
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. Details on the topics and moderators are available by clicking here.
Challenge. In this talk, I will first introduce a serial of techniques established in our laboratory for locoregional drug delivery to the brain, systemic drug delivery to the brain, and more recently, oral drug delivery to the brain. Next, I will give a few examples to show how these techniques can be utilized for treatment of neurological disorders.

9:30 V-Smart® Nanomedicines: Non-Invasive Targeted Therapeutics for Brain Diseases
Susan Rosenbaum, J.D., Founder, Chairman & CEO, Lauren Sciences LLC
V-Smart® breakthrough innovation solves greatest medical challenge in brain disease treatment – non-invasive targeted delivery of therapeutics to brain. V-Smart® novel nanotechnology platform enables non-brain penetrant therapeutic agents to both cross BBB into brain by non-invasive administration, and target to, and selectively release at, CNS disease-specific brain sites. V-Smart® Nanomedicines pipeline of transformative therapeutics to meet medical needs of patients with brain diseases, such as Parkinson's, ALS, GBM and Alzheimer's.

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

10:45 MR Image-Guided Nanoparticle Delivery across the Blood-Brain Barrier with Focused Ultrasound
Richard J. Price, PhD, Professor, Biomedical Engineering, University of Virginia
MR image-guided focused ultrasound can safely open the blood-brain barrier, facilitating highly localized delivery of systemically-administered brain-penetrating nanoparticles to the CNS. Our group is developing this approach as a means to treat (i) Parkinson's disease via neurotrophic gene therapy and (ii) brain tumors via controlled-release chemotherapy, tumor suppressive miRNAs, and immunotherapies.

11:15 Delivery of Transferrin Receptor-Targeted Nanoparticles and Biologics to the Brain Via Transport Through the Blood-Brain Barrier
Torben Moos, PhD, Professor, Section for Neurobiology, Aalborg University
Directed delivery to the brain using targeted therapeutics represents a feasible method for drug delivery to the CNS. Our research group is developing targeting constructs to enable delivery of nanoparticles and biologics to the CNS in conditions without perturbation of the blood-brain barrier. In my presentation I will give an update on our attempts to transport transferrin receptor targeted nanoparticles and biologics through this blood-brain barrier.

11:45 Session Break

11:50 Bridging Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:20 pm Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

1:00 PLENARY KEYNOTE SESSION (click here for details)

2:30 Refreshment Break in the Exhibit Hall with Poster Viewing

3:10 Close of Conference

**Identifying Cerebrovascular Links to Neurodevelopmental Disorders**
Baptiste Lacoste, PhD, Assistant Professor, Cellular and Molecular Medicine/Neuroscience Program, The University of Ottawa/Ottawa Hospital Research Institute
- What are the biggest challenges in identifying cerebrovascular links to neurodevelopmental disorders?
- What are the most promising directions for this research?
- How can this information be used to further development of drugs that pass the BBB?

**Reduce, Reuse, Recycle Pharma Proprietary Therapeutic Agents for New Life in CNS Diseases**
Susan Rosenbaum, J.D., Founder, Chairman & CEO, Lauren Sciences LLC
- BBB delivery
- Targeting within CNS
- Administration options

5:45 Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

**WEDNESDAY, JUNE 20**

7:45 am Registration Open and Morning Coffee

8:25 Chairperson's Remarks
Jiangbing Zhou, Assistant Professor of Neurosurgery and of Biomedical Engineering, Department of Neurosurgery, Yale University

8:30 **FEATURED PRESENTATION**: Nanoparticle-Loaded Cells and Exosomes for Treatment of Brain Diseases
Alexander (Sasha) Kabanov, PhD, DrSci, MAE, Director, Center for Nanotechnology in Drug Delivery, Co-Director, Carolina Institute for Nanomedicine, Mescal S. Ferguson, Distinguished Professor, Eshelman School of Pharmacy, University of North Carolina and Chapel Hill

Macrophages traverse the BBB and deliver therapeutic “nanozymes” and genes (such as GDNF) to inflammatory sites in the brains of Parkinson's disease (PD) mouse models. This produces anti-inflammatory and neuroprotective effects and improves behavior in PD models. The enzymes and neurotrophins are also packaged into exosomes secreted by macrophages to improve delivery of these proteins to the brain. The uptake of exosomes is increased in the presence of inflammation.

9:00 Nanotechnology Approaches for Drug Delivery to the Brain
Jiangbing Zhou, Assistant Professor of Neurosurgery and of Biomedical Engineering, Department of Neurosurgery, Yale University

Due to the existence of the BBB, drug delivery to the brain has been a major challenge. In this talk, I will first introduce a serial of techniques established in...
The amyloid cascade hypothesis (AH) has been the predominant view of Alzheimer's disease pathogenesis. The AH in particular has informed many of the pharmacological approaches that have been tested in Phase III clinical trials, none of which has demonstrated efficacy. Given this disappointing outcome, the validity of the AH has been questioned, and this presentation will review the status of both clinical research and the AH.


drugs metabolism, technologies, screening tools & disease modeling, nanoparticles

3:15 What Does Recent Clinical Data Tell Us about the Amyloid Cascade Hypothesis?
Eric Karran, PhD, Vice President, Foundational Neuroscience Center, AbbVie

The amyloid cascade hypothesis (AH) has been the predominant view of Alzheimer's disease pathogenesis. The AH in particular has informed many of the pharmacological approaches that have been tested in Phase III clinical trials, none of which has demonstrated efficacy. Given this disappointing outcome, the validity of the AH has been questioned, and this presentation will review the status of both clinical research and the AH.
THURSDAY, JUNE 21

8:00 Chairperson's Remarks
Dario Doller, PhD, Senior Director, Exploratory Science, SAGE Therapeutics

8:05 FEATURED PRESENTATION: Translatability of Early Development Proof of Principle Trials in Neurology
Johan Luthman, PhD, Vice President, Neuroscience Clinical Development, Neurology Business Group, Eisai, Inc.

8:35 Thinking beyond the Well-Known Biomarkers for Patient Selection and Monitoring in Alzheimer's Disease Clinical Trials
Viswanath Devanarayan, PhD, Adjunt Professor, University of Illinois, Chicago

8:50 Late Breaking Presentation

9:20 Optimising Intraparenchymal Convection Enhanced Delivery
Max Woolley, PhD, BEng (Hons), BEng, Neuro Applications, Renishaw plc

9:35 Find Your Table and Meet Your Moderator

9:40 Interactive Breakout Discussion Groups

Lost in translation? Asking the Right Questions in the Right Language
Dario Doller, PhD., SAGE Therapeutics
- CNS disease etiology understanding: Who owns it?
- What are the major disconnects between lab experimentation and clinical research?
- Are differences in physiology between preclinical species and human affecting the translational gap?
- Patient segmentation: Strategies and outcomes
- Correlation or causation? Importance of genetic links for different CNS diseases
- What are the attributes that have real impact minimizing risk during novel target selection?
- Human as a model for human – What is the future of experimental medicine in CNS drug discovery?

Improving the Success Rate of CNS Therapies
Takaomi C. Saido, PhD, Laboratory Head, Laboratory for Proteolytic Neuroscience, RIKEN Brain Science Institute
- Why have more than 400 medication candidates for Alzheimer’s Disease failed?
- Which therapies have the best chance to succeed, and why?
- Immunotherapy for neurodegenerative disease
- What is the future of immunotherapy?

10:20 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 A New Paradigm for Therapeutic Discovery in Psychiatry
Gopi Shanker, PhD, Head of Psychiatry, Neuroscience Department, Novartis Institutes for Biomedical Research (NIBR)
Recent advances in the genetics of psychiatric disorders have led to a renewed focus on development of effective therapies in this area. However, the lack of predictive animal models continues to be a challenge for drug discovery. New advances in biomarker discovery have been employed in the development of Sage-217, a novel investigational drug for treatment-resistant depression and Parkinson’s disease. This presentation will discuss the clinical characterization of Sage-217 from a PK/PD modeling perspective, comparing endpoints in preclinical species and human subjects. The presentation will also highlight the importance of patient selection, monitoring and potentially as surrogate endpoints are needed for developing viable disease modifying treatments for AD.

11:30 A Quantitative Pharmacology Model of Neuroactive Steroid Efficacy in Movement Disorder
David Nguyen, PhD, Principal Scientist, SAGE Therapeutics
SAGE-217 is a novel GABA-potentiator which is currently in clinical development for mood and motor related disorders. This presentation will discuss the clinical characterization of SAGE-217 from a PK/PD modeling perspective, comparing endpoints measured in Phase I related to efficacy, target engagement, and adverse events.

12:05 pm Digital Technologies for CNS Translational Studies
Brandon Farley, PhD, Senior Scientist, SAGE Therapeutics
Wearable devices can complement clinical assessments by providing continuous monitoring of movement parameters and other physiological signals, both inside and outside of the clinic. We present data from Parkinson’s disease and essential tremor clinical trials which validate device-measured tremor against clinical tremor scales, and which demonstrate that devices are sensitive to pharmacological modulation of tremor. The rich pharmacodynamic datasets enabled by wearables are being employed in the development of SAGE-217 and other GABAA receptor modulators for movement disorders.
12:00 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

NEUROINFLAMMATION AND EMERGING TARGETS

1:55 Chairperson’s Remarks
Kent Werner, MD, PhD, Co-Founder and CEO, Cogentis Therapeutics; Johns Hopkins Neurology Adjunct Faculty

2:00 Targeting the Immune System to Treat Diseases of the Central Nervous System
Stevin Zorn, PhD, President and CEO, MindImmune Therapeutics, Inc.

It is increasingly clear that the central nervous system and the immune system are intimately integrated. Consequently, immune system dysfunction is a critical, often causative, factor in brain dysfunction. MindImmune are at the forefront in recognizing the therapeutic opportunities in targeting the immune system to treat brain disease.

2:30 The TREM2-APOE Pathway Drives the Transcriptional Phenotype of Dysfunctional Microglia in Neurodegenerative Diseases
Oleg Butovsky, PhD, Assistant Professor of Neurology, Harvard Medical School, Associate Scientist, Ann Romney Center for Neurologic Diseases, Department of Neurology, Brigham and Women’s Hospital

Microglia play a pivotal role in the maintenance of brain homeostasis but lose homeostatic function during neurodegenerative disorders. In recent studies, TREM2 (triggering receptor expressed on myeloid cells 2) induced APOE signaling, and targeting the TREM2-APOE pathway restored the homeostatic signature of microglia in ALS and AD mouse models and prevented neuronal loss in an acute model of neurodegeneration. This presentation will discuss the latest work in this area.

3:00 CT-526: A Peptide Targeting CDK5 in Neurodegenerative Disease
Kent Werner, MD, PhD, 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.

3:30 Late Breaking Presentation
4:00 Close of Conference
WPC continues to expand its coverage of drug safety by offering two back-to-back conferences and short courses addressing this topic. The Optimizing Drug Metabolism & Pharmacokinetics conference will bring together experts to discuss ways to optimize lead candidates to prevent adverse events related to drug metabolism, transport, drug-drug interactions and drug clearance, which sometimes do not surface until later in development. This will be followed by the Predicting Drug Toxicity conference, which will highlight the scientific and technological progress being made to predict drug-induced toxicities. Both conferences will discuss developments in new screening technologies, \textit{in vitro} assays, \textit{in vivo} models and computational tools, along with insights from experts on which models to use, how reliable is the data, and how predictive is the translation from \textit{in vitro} to \textit{in vivo}.


\begin{tabular}{ll}
\textbf{June 19-20} & \textbf{AGENDA} Optimizing Drug Metabolism & Pharmacokinetics \\
\textbf{June 20-21} & \textbf{AGENDA} Predicting Drug Toxicity \\
\end{tabular}
8:15 Chairperson’s Opening Remarks  
John Reilly, PhD, Senior Research Investigator, Global Chemistry, Novartis

8:20 Determination of Free Fraction of Highly Bound Drugs in Plasma  
Zhengyin Yan, PhD, Senior Scientist, Department of Drug Metabolism and Pharmacokinetics, Genentech, Inc.

Equilibrium dialysis has been widely used in plasma protein binding studies to measure the fraction of drug unbound (fu), an important pharmacokinetic parameter for both dose projection and drug-drug interaction (DDI) prediction. However, there has been a shared concern over the accuracy of fu values for highly bound compounds and current guidelines arbitrarily cap the lower limit of fu values at 0.01 to avoid potential false negatives in DDI prediction. A simple strategy is proposed to reliably measure fu values and ensure true equilibrium attained for high binders.

8:50 Intracellular Unbound Drug Concentrations in Presence of Metabolism and Transport  
Priyanka Kulkarni, PhD, Scientist, Pharmacokinetics and Drug Metabolism, Amgen, Inc.

Accurate prediction of target activity of a drug and rational design of dosing regimen requires knowledge of drug concentration at the target. Liver perfusion experiments in rats along with modeling and simulation techniques were used to model the unbound intracellular drug concentrations and characterize the differential effect of metabolism and transport on the same. Together, these results support the use of compartmental modeling to predict intracellular concentrations in dynamic organ-based systems.
12:10 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:40 Session Break

OPTIMIZING EARLY DRUG DOSING

1:15 Chairperson's Remarks
Ganesh Rajaraman, PhD MBA, Associate Director, DMPK, Celgene Corporation

1:20 An Integrated Discovery Rank Dose Approach for an Optimal Balance of Properties to Progress Compounds
Ganesh Rajaraman, PhD MBA, Associate Director, DMPK, Celgene Corporation
For oral drugs, delivering a candidate with low efficacious dose is the primary objective. Based on designated cut-off values from in vitro screens, compounds are funneled down but without guidelines as to how each property impacts dose estimation at the early stage. The talk aims at integrating properties to calculate efficacious doses to rank order compounds for an optimal balance rather than individual cut-offs.

1:50 Strategy for CYP3A Induction Risk Assessment from Preclinical Signal to Human: Case Study of a Late-Stage Discovery Compound
Jialin Mao, PhD, Senior Scientist, DMPK, Genentech
The exposure of Comp X decreased by four-fold at oral doses of 100 mg/kg twice daily for seven days in cynomolgus monkeys. Additional in vitro and PBPK work was conducted to understand: (1) the causes for the significant reduction in monkeys, (2) the extrapolation of in vitro induction data to in vivo findings in monkeys, and (3) the relevance of this pre-clinical finding to humans at the projected human efficacious dose.

2:20 A Pharmacokinetic/Pharmacodynamic(PK/PD)-Based Approach to Lead Optimisation in Drug Discovery Programs
Ramesh Jayaraman, CSO, TheralIndx Lifesciences Pvt Ltd
In preclinical drug discovery, emphasis is based on potency and pharmacokinetics (PK) to optimize candidates while less attention is given to linking of PK to pharmacodynamics (PD) effects - onset, intensity and duration of pharmacological effect. Early characterization of PK/PD helps in selecting compounds with optimum properties for progression to advanced stages. This talk will discuss the applications of PK/PD combined approach to optimize candidates.

2:35 Sponsored Presentation (Opportunity Available)

2:50 Refreshment Break in the Exhibit Hall with Poster Viewing

USING MODEL-BASED STRATEGIES FOR BETTER IN VITRO TO IN VIVO TRANSLATION

3:30 Drug Development Using QSP Modeling and Its Application to Oncology and Immunology
Rangaraj Narayanan, PhD, Director, Drug Metabolism and Pharmacokinetics, Shire Pharmaceuticals

4:00 Assessment of Transporter Mediated DDI for Compound X Using PBPK Modeling
Yuan Chen, PhD, Principal Scientist, DMPK, Genentech
PBPK modeling-based prediction of transporter-mediated DDI is a growing area that can benefit clinical candidate selection and early development in humans. Compound X is a potent inhibitor of OATP1B1/1B3 in vitro. To inform clinical DDI risk, a PBPK model was developed to predict DDI between compound X and OATP substrate pravastatin in humans.

4:30 Machine-Learning Approaches for ADME Optimization
Istvan Enyedy, PhD, Principal Scientist, Medicinal Chemistry, Biogen
Machine learning approaches help us build prediction models based on data we have accumulated. We started using Kriging for efficiently building and maintaining ADMET prediction models that help us do multiparameter optimization. The predicted probability of a compound to satisfy the required ADMET properties may be useful for prioritizing compounds. Kriging can also estimate the error of the prediction and of the experiment.

5:00 Find Your Table and Meet Your Moderator

5:05 Interactive Breakout Discussion Groups
This session features various discussion groups that are led by a moderator/s who ensue 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. Details on the topics and moderators are available by clicking here.

Key Issues Related to Drug Transporters in a Pharma R&D Setting
Moderator:
Li Di, PhD, Research Fellow, Pharmacokinetics, Dynamics and Metabolism, Pfizer
- How can we best generate reliable in vitro transport kinetics and inhibition data?
- Many transporters do have overlapping substrate-specificity, how can we assess and quantify an individual transporters' contribution?
- Regulation of transporters (induction, disease, epigenetics) can significantly modulate overall transport capacity. How can this be integrated into current in vitro - in vivo extrapolations?

Understanding Role of Drug Metabolism and Its Impact
Moderators:
Donglu Zhang, PhD, Senior Scientist, Department of Drug Metabolism and Pharmacokinetics, Genentech, Inc.
Zhengyin Yan, PhD, Senior Scientist, Department of Drug Metabolism and Pharmacokinetics, Genentech, Inc.
- Understanding induction, inhibition, and polymorphisms of drug metabolism enzymes
- Differences in metabolism between ADCs and small molecule drugs

Use of Modeling Tools and Strategies for Predicting ADME-Tox Properties
Moderator: Maria A. Miteva, PhD, Research Director, Molécules Thérapeutiques in silico (MTi), Inserm Institute
- Machine-learning or structure-based approaches for ADME-Tox prediction and optimization.
UNDERSTANDING AND PREDICTING DRUG METABOLISM AND TRANSPORT

8:25 Chairperson's Remarks
Li Di, PhD, Research Fellow, Pharmacokinetics, Dynamics and Metabolism, Pfizer

8:30 New Advances in Clearance Prediction with Hepatocytes
Li Di, PhD, Research Fellow, Pharmacokinetics, Dynamics and Metabolism, Pfizer

Significant advances have been made recently to predict clearance of low turnover compounds and clearance involved both enzyme- and transporter-mediated processes. This presentation will discuss novel methods to measure low clearance and a unified approach to predict clearance involved both metabolic and transport mechanisms with cryopreserved hepatocytes.

9:00 Integrated in silico Approach to Predict CYP Inhibitors and Pharmacogenetics Considerations
Maria A. Miteva, PhD, Research Director, Molécules Thérapeutiques in silico (MTI), Inserm Institute

Cytochrome P450 (CYP) and its central role in drug metabolism, drug-drug interactions and pharmacogenetics will be discussed. The malfunction of CYP, e.g. due to single nucleotide polymorphism, could lead to decreased drug metabolism causing toxicity, or affected prodrug activation. An integrated structure- and ligand-based in silico approach to predict inhibitors of CYP and to analyse the impact of missense mutations on CYP drug metabolism will be presented.

9:30 Accessing Marketed Drug Information to Inform PreClinical Safety
Duncan Armstrong, PhD, PreClinical Safety, Novartis Institutes for BioMedical Research
Pooja Jain, MSc, MBA, Product Manager, R&D Solutions, Elsevier

Marketed and withdrawn drugs provide a rich source of information on the clinical effects of pharmaceutical intervention which can be brought back in to the Pre-Clinical space to improve the translational and predictive power of non-clinical assays and models. Accessing adverse event report data (FAERS) and clinical PK in a structured manner, through PharmaPendium, enables improved understanding of the performance non-clinical assays and facilitates more detailed risk assessment for candidate drugs.

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

DMPK FOR NEW DRUG MODALITIES AND COMBINATION THERAPIES

10:45 Dynamic Drug Combination Analysis Platform for Preclinical to Clinical Translation of Novel Oncology Drug Combinations
Tomoki Yoneyama, PhD, Senior Scientist 1, DMPK, Takeda

The dynamic PK-efficacy model for combinational therapies in oncology was established in mice and translated in humans. The established model provides the means of quantitatively comparing the dynamic combinational antitumor effects of two potential combinational therapies in humans based on mouse experimental data. The model is also powerful for dose regimen optimization.

11:15 DMPK Support for Screening Antibody Drug Conjugates (ADCs)
Ekta Kadakia, MS, Scientist 1, DMPK, Takeda

DMPK support for ADCs focuses not only on characterizing attributes associated with suboptimal pharmacokinetic (PK) behavior, but also on integrating PK, PD (pharmacodynamic) and efficacy data to identify potential ADC drug candidates with the most favorable properties to interact with target-expressing cancer cells. This presentation will discuss the application of different PK and PK/PD-related analysis to inform the selection of ADCs.

11:45 Session Break

11:50 Bridging Luncheon Presentation: Use of a Collaborative Tool to Simplify the Outsourcing of Preclinical Safety Studies
Amanda Benjamin, Head, Alliance and Project Management, Drug Safety and Metabolism, AstraZeneca
Ruth Maclean, Senior Client Manager, Charles River

In 2012, AstraZeneca entered into a strategic relationship with Charles River whereby preclinical safety packages comprising safety pharmacology, toxicology, formulation analysis, in vivo ADME, and pharmacokinetics studies were outsourced. Processes were created to ensure seamless workflows in order to accelerate the delivery of new medicines to patients. This talk explores the preclinical safety outsourcing model and how a collaborative tool helped translate processes into simpler integrated workflows across two companies.

12:20 pm Dessert and Coffee Break in the Exhibit Hall with Poster Viewing
The promise (and limitations) of human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) as models of toxicity continue to be refined as experience with these preparations grow (along with variations in the preparations themselves). This presentation will discuss the evolving roles of hiPSC-CMs in assessing electrophysiologic as well as structural cardiotoxicity of novel pharmaceutical candidates, along with paths forward for their implementation in drug development and regulatory arenas.

3:45 Bridging the Gap between Determining Hepatotoxicity Potential Using in vitro Assays and Clinical Outcomes

Renato (Ron) Scialis, PhD, Senior Research Investigator, Preclinical Candidate Optimization, Bristol-Myers Squibb

In terms of hepatotoxicity, certain assays focus on discrete endpoints, however what is more relevant are toxicity models that can holistically cover a spectrum of developmental, cardiovascular, neurological and hepatic safety evaluation, consequently minimizing risks and cost.

4:15 Zebrafish: An Alternative Model for Toxicity Screening in Early Discovery and Development

Arantza Muriana, MBA, CEO, Biobide USA

The many advantages that zebrafish presents make it a suitable alternative model for toxicity screening in Drug Discovery. As a powerful High Content Analysis tool, during this presentation we will provide a better understanding of how zebrafish relates to mammalian systems, and the strengths and challenges of using this model in the early preclinical phase, specifically in assessing electrophysiologic as well as structural cardiotoxicity of novel pharmaceutical candidates, along with paths forward for their implementation in drug development and regulatory arenas.


Terry Van Vleet, PhD, DABT, Head of Molecular and Computational Toxicology, Department of Preclinical Safety, Abbvie

Unintended interactions are common with small molecule drugs, especially at higher exposures and concentrations. With the development of ADCs, non-targeting interactions of antibody based biologics (leading to uptake in unintended tissues) have become more apparent and consequential as well. This presentation outlines the careful characterization and use of in vitro platforms and technologies to identify these routes of uptake.
5:15 Challenges in Assessing Mitochondrial Toxicities and Liabilities in Drug Discovery
William Proctor, PhD, Senior Scientist, Head of Investigative Toxicology, Department of Safety Assessment, Genentech

Early identification of compounds that induce mitochondrial toxicities is an important part of lead-optimization. This talk will focus on mitochondrial toxicity assessment and included in here will be a cross-comparison of popular assays using a test set of commercial drugs with known clinical toxicities, as well as, data from a novel live-cell imaging approach to detect mitochondrial toxicities. Case studies of how these assays informed hepatotoxicity risk assessment as well as mechanistic understanding or preclinical toxicities will be presented.

5:45 Close of Day and Dinner Short Course Registration*
*Separate registration required. Please click here for more information.

THURSDAY, JUNE 21

7:30 am Registration Open and Morning Coffee

NARROWING THE IN VITRO TO IN VIVO TRANSLATION GAP

8:00 Chairperson's Remarks
William Proctor, PhD, Senior Scientist, Head of Investigative Toxicology, Department of Safety Assessment, Genentech

8:05 Accurate Prediction of Clinical Parameters Utilizing Multi-Organ Human Systems
James J. Hickman, PhD, Founding Director, NanoScience Technology Center; Professor, Nanoscience Technology, Chemistry, Biomolecular Science, Material Science and Electrical Engineering, University of Central Florida

Our human-on-a-chip systems utilize functional models to capture multi-organ complexity to produce relevant modeling information related to drug responses in clinical settings. We have evaluated multi-organ toxicity and efficacy under continuous flow in a serum-free defined medium utilizing a pumpless platform for 28 days. The pharmacological relevance was evaluated with drugs and compared to human and animal data and these results will be presented.

8:35 The NIH Tissue Chips Program for Toxicity and Efficacy Testing
Danilo A. Tagle, PhD, Associate Director for Special Initiatives, National Center for Advancing Translational Sciences, National Institutes of Health

The current drug development process has a failure rate of 90% in being able to predict safety and efficacy of candidate drugs. To address this challenge in drug development, the NCATS Tissue Chip for Drug Screening program supports the development of alternative approaches for more reliable readouts of toxicity and efficacy. By emulating human physiology, tissue chips can increase the predictive power of preclinical modeling, for modeling human diseases, and for studies in precision medicine and environment exposures.

9:05 ZeCardio, An Innovative Zebrafish High Throughput Screening Platform for Cardiovascular Assessments
Simone Calzolari, MSc, PhD, Co-Founder, Chief Commercial Officer, ZeClinics S.L.

We present ZeCardio, a zebrafish larvae platform for the in vivo study of cardiotoxicity and cardiomyopathy therapy discovery. ZeCardio allows for the high throughput, fully automatized image acquisition of multiple cardiovascular parameters in living individuals, including readouts which are costly, time-consuming or simply unattainable with conventional methods.

9:20 Development of a Semi-Automated Segmentation Tool for High Frequency Ultrasound Image Analysis of Mouse Echocardiograms
Raymond Chung, PhD, Biomedical Research Scientist, Cardiovascular Research, Regeneron Pharmaceuticals

Echocardiography is a widely used and clinically translatable imaging modality for the evaluation of myocardial structure and function in preclinical drug discovery and development. The objectives of this study were to develop a robust analysis algorithm for semi-automated segmentation of left ventricle (LV) ultrasound images acquired from control and cardiovascular disease model mice.

9:35 Find Your Table and Meet Your Moderator

9:40 Interactive Breakout Discussion Groups

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. Details on the topics and moderators are available by clicking here.

Gaps in Translating Preclinical Findings to the Clinic
William Proctor, PhD, Senior Scientist, Head of Investigative Toxicology, Department of Safety Assessment, Genentech

• Model/assay sensitivity – What level (or magnitude) of change can we detect?
• Do we have appropriate study design, data analysis, statistical analysis, and statistical power?
• How predictive are our preclinical findings/models to the clinic?
• What is it we are missing? Are there other useful models? Are there gaps in our training knowledge?

Using iPSC for Drug Safety Screening
Gary Gintant, PhD, Senior Research Fellow, Department of Integrative Pharmacology, Integrated Science and Technology, AbbVie

• What are concerns for using human induced pluripotent stem cell (iPSC)-derived cells to assess drug safety screening?
• How to consider standardizing assays and comparing results? Assay reproducibility?
• Generation of patient derived hiPSC-derived cardiomyocytes: present and future roles.
• The role of newer co-cultures and 3D structures in present and future efficacy and safety studies.
• How to best adapt hiPSCs for high-throughput phenotypic screening.

10:20 Coffee Break in the Exhibit Hall with Poster Viewing

11:05 High-Throughput Toxicokinetics for Rapid Risk Prioritization
John Wambaugh, PhD, Physical Scientist, National Center for Computational Toxicology, U.S. Environmental Protection Agency
Chemical prioritization based on potential human health hazard requires exposure, toxicity, and toxicokinetic (TK) data which are unavailable for thousands of chemicals. To provide TK estimates, high-throughput, in vitro TK (HTTK) pharmaceutical methods have been adapted for environmental chemicals. Systematically comparing HTTK predictions to in vivo data allows quantification of model uncertainty enabling chemical prioritization. This abstract does not necessarily reflect U.S. EPA policy.

11:35 The IQ DruSafe Nonclinical to Clinical Translational Database: Value of Animal Data in Drug Safety Testing
Vivek (Vic) Kadambi, PhD, Vice President, Nonclinical Development, Blueprint Medicines

The safety assessment of new drugs requires the conduct of animal toxicity studies, based on the assumption that the results provide translational value in identifying potential human hazards. Results of the IQ Consortium nonclinical to clinical translational database for Phase I trials will be presented, highlighting both the positive and negative predictive value of animal studies that support the safe entry of new drugs into the clinic.

12:05 pm Possible Regulatory Considerations for Secondary Pharmacology Related Adverse Drug Events (ADRs)
Laszlo Urban, MD, PhD, Global Head, Preclinical Secondary Pharmacology, Novartis Institutes for Biomedical Research

In this presentation, I will describe how off-target pharmacology became a mainstream tool to mitigate and manage unwanted ADRs and to be considered for guidance in regulatory affairs. Ongoing discussions with FDA focus on the determination of safety margins for off-target activities of drug candidates and their anticipated side effects in the clinical setting. Thus off-target pharmacology can help shaping the design of clinical trials.

12:35 Session Break

12:40 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

COMPUTATIONAL TOOLS, DATABASES AND MACHINE LEARNING FOR SAFETY PREDICTIONS

1:55 Chairperson's Remarks
S. Joshua Swamidass, MD, PhD, Assistant Professor, Department of Immunology and Pathology, Division of Laboratory and Genomic Medicine; Faculty Lead, Translational Informatics, Institute for Informatics, Washington University

2:00 Managing Drug Toxicity Risks with Deep Learning Models of Bioactivation
S. Joshua Swamidass, MD, PhD, Assistant Professor, Department of Immunology and Pathology, Division of Laboratory and Genomic Medicine, Washington University

Many medicines become toxic only after bioactivation by metabolizing enzymes, sometimes into chemically reactive species. Idiosyncratic reactions are the most difficult to predict and often depend on bioactivation. Recent advances in deep learning can model bioactivation pathways with increasing accuracy, and these approaches are giving us deeper understanding of why some drugs become toxic, and others do not. At the same time, deep learning can be used to understand drug toxicity as it arises in clinical data, and why some patients are affected, but not others.

2:30 Predicting Likelihood of in vivo Interaction Using High-Throughput Screening Data and High-Throughput Toxicokinetics
Nisha S. Sipes, PhD, Health Science Evaluator, Biomolecular Screening Branch/Toxicoinformatics Group, National Toxicology Program Division, National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health

In vitro-in vivo extrapolation (IVIVE) facilitates translation of data on hundreds of high-throughput screening (HTS) assays on thousands of diverse chemicals (e.g., pharmaceuticals and environmental chemicals) toward human relevance. An intuitive framework has been proposed using a generalized freely available high-throughput toxicokinetics model with parameters obtained from in silico and in vitro methods to estimate the plausibility of the biological interactions seen using HTS.

3:00 INTERVALS, A Data & Results Sharing Platform, Can Improve Transparency in Industry-Funded Research
Stéphanie Boué, Manager Scientific Transparency & Verification, PMI R&D, Philip Morris Products S.A., Part of Philip Morris International Group

INTERVALS was developed to allow a proactive sharing of the data from assessment studies examining the potential of harm reduction of modified risk tobacco products. INTERVALS enables data analysis by independent third parties and browsing the data by product, study, mechanism or endpoint. It also gives relevant information related to study design, methods, and the most important results from preclinical as well as clinical studies.

3:30 Lead Optimization of Kinase Inhibitors via Their CYP3A4 Metabolic Profiling
Siva Kumar Belliraj, PhD, Associate Professor, Department of Chemistry, Sri Sathya Sai Institute of Higher Learning

Soft spot analysis plays a key role in the analysis of metabolic liability that directly impacts the bioavailability of the drug. However, given the tedious and expensive experimentation in the soft spot metabolic analysis of drugs, we propose a cost effective and reliable in silico strategy. In this context, we firstly compared the structures of the metabolizing class of enzymes and classified the corresponding drugs metabolized. Further, the thermodynamics of this spontaneity of metabolism in 95 approved drug molecules obtained from the drug bank was evaluated.

4:00 Close of Conference
Overcoming the challenge of safely delivering the correct drug to the correct location, all while evading any immunological reaction, is a difficult task. Nanoparticles represent an important pathway towards targeted, immuno-neutral drug delivery. As well as having a lot of promise in drug delivery, extracellular vesicles also represent an incredibly exciting opportunity for therapeutics developers, both as treatments themselves and as potential biomarkers. The World Preclinical Congress will host two back to back conferences, NanoDrug: Design and Delivery, and Extracellular Vesicles, to discuss strategies for isolation, formulation, characterization, mechanism of action deconvolution and scalability.
interactions with off-target biological systems. In this presentation, a quantitative analysis of nanoparticle delivery to tumors from a preclinical perspective will be provided, followed by a discussion of the impact of results on clinical translation of cancer nanomedicine.

9:20 High-Throughput in vivo Nanoparticle Analysis Using DNA Barcodes
James Dahlman, PhD, Assistant Professor, Department of Biomedical Engineering, Georgia Institute of Technology/Emory Medical School
Genetic drugs are limited by inefficient delivery to target cells, and unwanted delivery to off-target cells. Thousands of chemically distinct nanoparticles can be synthesized to deliver genetic drugs. However, it is difficult to study many nanoparticles in vivo. Here we report JORDAN, a DNA barcoding system to study over 150 nanoparticles at once in vivo. JORDAN can be used to ask fundamental questions about in vivo drug delivery.

9:50 Grand Opening Coffee Break in the Exhibit Hall with Poster Viewing

CANCER AND NANO TECHNOLOGY

10:35 FEATURED PRESENTATION: Stimuli-Sensitive Combination Nanopreparations for Multidrug Resistant Cancer
Vladimir Torchilin, PhD, Distinguished Professor and Director, Center for Pharmaceutical Biotechnology and Nanomedicine, Bouvé College of Health Sciences, Northeastern University
Therapy of MDR cancers could be enhanced by using siRNA down-regulating proteins involved in cancer resistance together with chemotherapeutics. We have developed several types of nanopreparations, which are biologically inert, lowered pH, hypoxia, or overexpressed certain enzymes. In contrast to conventional "local" tumor targeting by nanoparticles, we propose a new mechanism whereby nanoparticles trigger priming of the T cells towards tumor destruction. The heterogenous biodistribution of nanoparticles lends itself to stimulating immune cells systemically in a "global" manner and with the right therapeutic combinations will be able to destroy tumor cells.
11:35 Sponsored Presentation (Opportunity Available)

12:05 pm Session Break

12:10 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:40 Session Break

CLINICAL TRANSLATION OF NANOTECHNOLOGY

1:15 Chairperson's Remarks
Christopher Hartshorn, PhD, Program Director, Division of Cancer Treatment and Diagnosis, National Cancer Institute

1:20 NCI Funding of Nanotechnology Strategies to Advance Outcomes for Clinical Cancer Care
Christopher Hartshorn, PhD, Program Director, Division of Cancer Treatment and Diagnosis, National Cancer Institute

The National Cancer Institute launched the Alliance for Nanotechnology in Cancer (Alliance) in 2004 to advance a number of promising nanotechnologies for the diagnosis, treatment and prevention of cancer. The progress since this time has been substantial and has led NCI to begin several more initiatives in this space with continued program support. This talk will focus on many of the platforms, outcomes, and future relative to the vision of the NCI.

1:50 Nanobiointerfaces: Implications of Biomolecular Corona
Morteza Mahmoudi, PhD, Instructor, Center for Nanomedicine and Department of Anesthesiology, BWH, Harvard Medical School

Nanoparticles (NPs) are becoming increasingly promising tools for medical diagnostics and therapeutics. Despite the advances in their biomedical applications and numerous publications, fewer than expected NPs have made it to clinical trials and even fewer have reached clinical practice. This wide gap between bench discoveries and clinical applications is mainly because of our limited understanding of the nanobiointerfaces. Although extensive studies have been conducted to enhance our understanding of the nanobiointerfaces, the literature remains unclear and contains conflicting information, even for seemingly identical NPs. The main goal of this talk is to introduce some of the existing "hidden" factors at the nanobiointerfaces to determine – unambiguously and reproducibly – the biological fate of NPs both in vitro and in vivo. Deeper understanding of the nanobiointerfaces, using the hidden factors, may accelerate clinical translation of nanobiotechnologies.

2:20 Sponsored Presentation (Opportunity Available)

2:50 Refreshment Break in the Exhibit Hall with Poster Viewing

3:30 Hafnium Oxide Nanoparticles Activated by Radiotherapy for Treatment of Solid Tumors
Stéphanie Decollogne, PhD, Senior Manager, Preclinical & Toxicology, Clinical Development, Nanobiotix

A new class of material with high electron density, hafnium oxide, was designed and contains conflicting information, even for seemingly identical NPs. The main goal of this talk is to introduce some of the existing "hidden" factors at the nanobiointerfaces to determine – unambiguously and reproducibly – the biological fate of NPs both in vitro and in vivo. Deeper understanding of the nanobiointerfaces, using the hidden factors, may accelerate clinical translation of nanobiotechnologies.

3:50 Ex vivo Perfusion of Isolated Human Organs: A New Setting for Clinical Translation of Vascular-Targeted Nanomedicines
Gregory Tietjen, PhD, Assistant Professor, Department of Surgery, Section of Transplantation and Immunology, Yale School of Medicine

Ex vivo normothermic machine perfusion, a new tool in clinical transplant used to revive marginal organs, provides a unique opportunity to deliver therapeutics directly to an isolated organ. Working in collaboration with leading transplant clinicians at the University of Cambridge, we have taken advantage of this setting to perform preclinical quantitative studies to assess retention of vascular-targeted nanomedicines in a series of isolated human kidneys.

4:10 Biosynthesized Antioxidative Nanomaterials for Ischemic Stroke
Jinjun Shi, PhD, Assistant Professor, Harvard Medical School; Director, Laboratory for Nanotechnology & Drug Delivery, Brigham and Women's Hospital

Antioxidative nanomaterials are emerging as a novel strategy for treating a myriad of important diseases through scavenging excessive reactive oxygen and nitrogen species (RONS). Herein, we develop biosynthesized melanin nanoparticles (MeNPs) for more potent and safer antioxidative therapy. We provide exhaustive characterization of the activities of MeNPs against multiple RONS and RONS-mediated inflammatory responses. In vivo results demonstrate that the MeNPs can effectively protect ischemic brains with negligible side effects.

4:40 Application of Wet Media Milling in Preclinical and Early Phase Studies
Sonali Bose, PhD, Associate Technical Project Leader, TRD (Technical Research and Development), Novartis

5:00 Find Your Table and Meet Your Moderator

5:05 Interactive Breakout Discussion Groups

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. Details on the topics and moderators are available by clicking here.

Using Big Data to Help Nanotechnology
Cory Sago, PhD Student, James Dahlman Lab, Georgia Institute of Technology / Emory Medical School

- DNA barcodes can be used to track more than 100 nanoparticles in a single mouse.
- Big data analytics can be applied to understand how nanoparticle traits affect delivery in vivo.
- The biology of drug delivery can be studied using DNA barcodes.

Nanoparticle Fabrication
Ghazal Hariri, PhD, Senior Scientist, Pfizer Global Research and Development

- Challenges in nanoparticle fabrication and scale up for pharmaceutical production
- Opportunities and applications for nanoparticle technology in the pharmaceutical industry
- Impact of nanoparticle fabrication on drug development

5:45 Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day
WEDNESDAY, JUNE 20

7:45 am Registration Open and Morning Coffee

NANOPARTICLE DELIVERY ACROSS THE BBB

8:25 Chairperson's Remarks
Jiangbing Zhou, Assistant Professor of Neurosurgery and of Biomedical Engineering, Department of Neurosurgery, Yale University

8:30 FEATURED PRESENTATION: Nanoparticle-Loaded Cells and Exosomes for Treatment of Brain Diseases
Alexander (Sasha) Kabarov, PhD, DrSci, MAE, Director, Center for Nanotechnology in Drug Delivery; Co-Director, Carolina Institute for Nanomedicine; Mescal S. Ferguson Distinguished Professor, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill

Macrophages traverse the BBB and deliver therapeutic "nanozymes" and genes (such as GDNF) to inflammatory sites in the brains of Parkinson's disease (PD) mouse models. This produces anti-inflammatory and neuroprotective effects and improves behavior in PD models. The enzymes and neurotrophins are also packaged into exosomes secreted by macrophages to improve delivery of these proteins to the brain. The uptake of exosomes is increased in the presence of inflammation.

9:00 Nanotechnology Approaches for Drug Delivery to the Brain
Jiangbing Zhou, Assistant Professor of Neurosurgery and of Biomedical Engineering, Department of Neurosurgery, Yale University

Due to the existence of the BBB, drug delivery to the brain has been a major challenge. In this talk, I will first introduce a serial of techniques established in our laboratory for locoregional drug delivery to the brain, systemic drug delivery to the brain, and more recently, oral drug delivery to the brain. Next, I will give a few examples to show how these techniques can be utilized for treatment of neurological disorders.

9:30 V-Smart® Nanomedicines: Non-Invasive Targeted Therapeutics for Brain Diseases
Susan Rosenbaum, J.D., Founder, Chairman & CEO, Lauren Sciences LLC

V-Smart® breakthrough innovation solves greatest medical challenge in brain disease treatment – non-invasive targeted delivery of therapeutics to brain. V-Smart® novel nanotechnology platform enables non-brain penetrant therapeutic agents to both cross BBB into brain by non-invasive administration, and target to, and selectively release at, CNS disease-specific brain sites. V-Smart® Nanomedicines pipeline of transformative therapeutics to meet medical needs of patients with brain diseases, such as Parkinson's, ALS, GBM and Alzheimer's.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing
The fast developing field of extracellular vesicle (EV) research is hampered by the notorious lack of reliable methods allowing EVs' characterization. This is mainly due to their small size and the heterogeneity of EV suspensions. This presentation will illustrate the power and contribution of novel methods allowing to image, phenotype, quantify and isolate EVs in complex fluids.

4:15 Meet the Nanoimager
Jonathan Shewring, PhD, Field Application Specialist, ONI
The Nanoimager from ONI is a desktop-compatible, super-resolution, single-molecule fluorescence microscope with localization precision reaching 20 nm. This talk will discuss its key features relevant for life scientists, such as single-molecule localization-based super-resolution, single particle tracking, single-molecule FRET, and SIM, as well as the most recent results.

4:45 Engineered Extracellular Vesicles for CRISPR/Cas9 Gene Editing
Niek Dekker, PhD, Principal Scientist, Discovery Sciences, AstraZeneca
Extracellular vesicles (EVs) represent an exciting opportunity as biological delivery vehicles for therapeutic cargo with excellent safety, low intrinsic immunogenicity, cell-specific tropism and biological delivery efficiency. There are multiple approaches for the introduction of protein and RNA cargo into EVs, including physical, chemical and cell engineering. I will overview a wide range of loading technologies with examples of cell line engineering for both protein and RNA cargo loading.

5:15 The NIH Extracellular RNA Communication Program Towards Biomarker and Therapy Development
Kayla Valdes, PhD, Scientific Program Manager, Office of the Director, Division of Special Initiatives, National Center for Advancing Translational Sciences, National Institutes of Health
Extracellular RNA (exRNA) can act as a signaling molecule, communicating with other cells and carrying information from cell to cell throughout the body. The NIH supports the cross-cutting research towards a better understanding of basic exRNA biology with the goal of improving the diagnosis, prognosis and treatment of various diseases and conditions such as cancer, bone marrow disorders, heart disease, Alzheimer's disease and multiple sclerosis.

5:45 Close of Day and Dinner Short Course Registration*
*Separate registration required. Please click here for more information.
8:00 Chairperson's Remarks  
John Pezacki, PhD, Professor, Chemistry and Biomolecular Sciences, University of Ottawa

8:05 Harnessing the Diversity of Highly Scalable Cell Lines Derived from Human Pluripotent Stem Cells for EV Discovery and Production  
Dana Larocca, PhD, Vice President, Discovery Research, AgeX Therapeutics, Inc.
Our diverse cell bank of hundreds of highly scalable and clonally pure pluripotent stem cell-derived progenitor cell lines is an excellent source of cells for EV discovery and therapeutics. We are mining the cell bank using EV content and cell-based assays to screen for desirable EV bioactivities and stably high yields. We successfully identified several candidate production cell lines for manufacturing angiogenic EVs for preclinical studies in cardiovascular disease models.

8:35 Manufacturing of Immunomodulatory Human Umbilical Cord Stem Cell EVs for Clinical Application  
Mario Gimona, PhD, Head of Production GMP & Head of Research Program “Nanovesicular Therapeutics”, GMP Unit, Paracelsus Medical University Salzburg  
MSC-derived extracellular vesicles (EVs) may have therapeutic effects comparable to their parental cells. Strategies must now be designed to successfully translate EV research and to develop powerful therapies, whilst taking into account the applicable regulations regarding safety and efficacy testing. The identification of the mode of action underlying a suggested potency in each therapeutic approach remains a major challenge to the translational path.

9:05 Sponsored Presentation (Opportunity Available)

9:35 Find Your Table and Meet Your Moderator

9:40 Interactive Breakout Discussion Groups
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. Details on the topics and moderators are available by clicking here.

Best Source of Stem Cell Derived EVs  
Paul Robbins, PhD, Professor and Director of the TSRI Center on Aging, Molecular Medicine, The Scripps Research Institute
- Are EVs derived from embryonic stem cells as or more therapeutic than adult stem cells?
- How similar in phenotype and function are the EVs from different stem cell sources?
- Can allogeneic stem cell derived EVs be used clinically?

Challenges in EV Characterization  
Alain Brisson, PhD, Emeritus Professor, UMR-CBMN CNRS, University of Bordeaux
- Why do we need to better characterize EVs?
- How reliable and efficient are the methods currently used for detecting, identifying, quantifying, isolating EVs?
- What do we need for improving EV detection, identification, quantification, isolation?

10:20 Coffee Break in the Exhibit Hall with Poster Viewing

11:05 Production of Functionally Bioactive EVs from an Immortalized Human Neural Stem Cell Line and Their Therapeutic Application  
Randolph Corteling, PhD, Head of Research, R&D, ReNeuron, Ltd.
To ensure the scale required for clinical research and development, producer cell immortalization and clonal isolation is a practical strategy to produce consistent, functionally bioactive exosomes for use as therapeutic agents. Using the conditioned media produced during GMP manufacture, we have shown that the cell line is an abundant producer of exosomes which can be readily isolated, purified at scale and has demonstrated efficacy in a number of preclinical models.

11:35 Exosome Engineering for Delivery of Therapeutic Proteins: Principles and Applications  
Chulhee Choi, MD, PhD, Professor, Department of Bio and Brain Engineering, KAIST, Korea
Our group has recently developed an opto-genetically engineered exosome system, named “exosomes for protein loading via optically reversible protein-protein interaction” (EXPLOR) that can deliver soluble proteins into the cytosol via controlled, reversible protein-protein interactions (PPI). Protein-loaded EXPLORs were shown to significantly increase intracellular levels of cargo proteins and their function in recipient cells in both a time- and dose-dependent manner. In this presentation, I will introduce the basic principles of EXPLOR technology and follow-up studies.

12:05 pm Engineered Bacterial Outer Membrane Vesicles in Cancer Immunotherapy  
Guido Grandi, PhD, Professor, Synthetic and Structural Vaccinology - CIBIO, University of Trento, Formerly Senior Project Leader, Novartis Vaccines and Diagnostics
Bacterial Outer Membrane Vesicles (OMVs) are naturally released by all Gram negative bacteria and are emerging as an attractive vaccine platform in that they (i) carry immunostimulatory molecules, (ii) can be genetically manipulated with heterologous antigens, and (iii) can be easily purified from the culture supernatant. Our most recent results in different mouse models will be presented to demonstrate the potential of OMVs in personalized cancer vaccines.

12:35 Session Break

12:40 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

1:10 Ice Cream Break in the Exhibit Hall with Poster Viewing

1:55 Chairperson's Remarks  
John Pezacki, PhD, Professor, Chemistry and Biomolecular Sciences, University of Ottawa

2:00 Cell Entry Routes and Subcellular Fate of Exosomes — Towards Next-Generation Drug Delivery Vehicles  
Nicole Meisner-Kober, PhD, Scientific Director, Research Studios Austria, University of Salzburg, Formerly Senior Investigator, Novartis Institutes for Biomedical Research
Current state of the art liposomal delivery vehicles are quantitatively inefficient in delivering siRNA, due to both, limitations in cell entry as well as inefficient
subcellular trafficking to the RNA silencing machinery which is nucleated at the rough endoplasmatic reticulum. Since the liposomal vehicles are typically responsible for dose limiting toxicity rather than the active oligonucleotide cargo, an improvement in cellular and subcellular trafficking activity presents a major opportunity for increasing the therapeutic index. In this seminar I will discuss how exosomes have evolved a specific route for cell entry with efficiency and pathways converging with highly infective pathogens, which licenses them for directed subcellular transport to the sites of translation and RNA silencing, and provide a perspective for translation of this biology into next generation RNA and drug delivery strategies.

2:30 Immune Modulation Mechanisms Exerted by Extracellular Vesicles from Umbilical Tissue Mesenchymal Stem Cells
Andrew Hoffman, DVM, DVSc, Diplomate ACVIM, Director of the Regenerative Medicine Laboratory, Professor, Large Animal Medicine, Department of Clinical Sciences, Tufts University Cummings School of Veterinary Medicine
Numerous clinical trials addressing a myriad of disease processes are in progress employing mesenchymal stem cells (MSC), yet the role of extracellular vesicles (EV) in MSC therapeutics is uncertain. Our laboratory examines signaling pathways exerted through EV derived from Wharton's Jelly MSC. We have found that several classical signaling pathways are largely transduced through the EV fraction of the secretome. These observations have significant implications for development of EV therapeutics.

3:00 Therapeutic Approaches Using Extracellular Vesicles for Treating Age-Related Degenerative Diseases
Paul Robbins, PhD, Professor and Director of the TSRI Center on Aging, Molecular Medicine, The Scripps Research Institute
We have demonstrated that intraperitoneal (IP) administration muscle-derived stem/progenitor cells (MDSPCs) and mesenchymal stem cells isolated from young wild-type mice into mouse models of aging conferred significant lifespan and healthspan extension through a paracrine/endocrine mechanism involving extracellular vesicles (EVs). An update on the use of stem cell EVs as therapeutics for aging and as diagnostics for unhealthy aging will be presented.

3:30 Utilizing Extracellular Vesicles from Patient Plasma to Identify Biomarkers of Autoimmune Disease
Swetha Srinivasan, PhD, Postdoctoral Fellow, Translational Immunology, AbbVie, Inc.
Identifying clinically significant differences in EV-derived RNA is not trivial due to the large inter-individual variability even in healthy individuals as well as the bias and confounding factors introduced by measurement methods. Thus, the initial objective was to assess both the biological and technical variability of EV RNA frequency in healthy individuals. Subsequently, this analysis will enable the identification of exosomal RNA based disease biomarker in autoimmune disorders.

4:00 Close of Conference
Disease modeling remains the backbone, and at the same time a bottleneck, of translational research. Reproducible and predictive preclinical studies, smart screens for new targets and hits, opportunities to model drug resistance, and rational design of first-in-human studies are invaluable steps in drug discovery and translational research. All of these goals require reliable and affordable disease models. The 17th Annual World Preclinical Congress is expanding the coverage of disease models and modeling technologies and invites you to attend the following conferences: Tumoroids for Oncology Research, Tumor Models for Cancer Immunotherapy, 3D Cellular Models, iPS Cells for Disease Modeling and Drug Discovery, and CNS Disease Models.

June 19-20

AGENDA Preclinical Strategies, Models & Tools in Oncology
AGENDA Tumoroids for Oncology Research
AGENDA iPS Cells for Disease Modeling and Drug Discovery
AGENDA CNS Disease Models

June 20-21

AGENDA Tumor Models for Cancer Immunotherapy
AGENDA 3D Cellular Models
Hotel & Travel Information

CONFERENCE VENUE AND HOST HOTEL:
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Discounted Room Rate Cut-off Date: May 22, 2018

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