



Meeting Program

Short Courses | Sunday, October 19, 2014

Short Course I: Prediction of Drug-drug Interactions and Regulatory Recommendations for Assessment

9:00 a.m. - 12:00 p.m.

Co-Chairs: Shiew-Mei Huang, U.S. Food and Drug Administration and Takashi Izumi, Daiichi-Sankyo Co. Ltd.

Systematic Classification of Drugs Involved in Drug-Drug Interactions to Seamlessly Avoid Serious Events
Akihiro Hisaka, Chiba University

Utility and Impact of Physiologically-based Pharmacokinetic Modeling to Predict and Interpret Drug-drug Interactions: Cases of Astellas Pharma Inc.
Tsuyoshi Minematsu, Astellas Pharma Inc.

Clinical Impact of Drug-Drug Interactions: Consideration of Ethnic and Other Patient Factors
Shiew-Mei Huang, Food and Drug Administration (FDA)

Comparison of the EU, FDA and PMDA Drug Interaction Guidances
Eva Gil Berglund, European Medicines Agency

Short Course II: Metabolite Biosynthesis and Quantitation by NMR Spectroscopy

9:00 a.m. - 12:00 p.m.

Co-Chairs: R. Scott Obach, Pfizer Inc. Global Research and Development and Swapan Chowdhury, Takeda Pharmaceutical Co. Ltd.

Part 1: An Introduction to MIST Concepts and the Importance of Drug Metabolites
Swapan Chowdhury, Takeda Pharmaceutical Co., Ltd.

Part 2: Biosynthesis of Metabolites Using Mammalian *in Vitro* Systems and Technical Tricks in Isolation
R. Scott Obach, Pfizer Inc.

Part 3: Use of Microbial Systems to Biosynthesize Metabolites
Jonathan Steele, HyphaDiscovery Ltd.

Part 4: An Introduction to NMR Spectroscopy as Applied to Drug Metabolites
Gregory Walker, Pfizer Inc.

Part 5: Quantitative NMR Spectroscopy – Principles and Practice
Gregory Walker, Pfizer Inc.

Short Course III: Non-CYP Metabolism in Drug Discovery

1:00 p.m. - 4:00 p.m.

Co-Chairs: Jeffrey Jones, Washington State University and Teruko Imai, Kumamoto University

New Strategy to Identify Unknown Drug-metabolizing Enzymes by Proteomics
Kazuishi Kubota, Daiichi-Sankyo Rd Novare Co., Ltd.

Investigation of Drug Metabolism by Non-Cytochrome P450 Enzymes (11 β -hydroxysteroid dehydrogenase/UGT2B15) and Its Clinical Relevance
Mitsuhiro Nishihara, Takeda Pharmaceutical Co., Ltd.

Determining the Role of Molybdenum Oxidases in Drug Metabolism
Jeffrey Jones, Washington State University

The Impact of Chemistry on the ADME of Antibody Drug Conjugates
Dan Rock, Amgen

Short Course IV: How to Maximize the Use of DMPK and Drug-Drug Interaction Data Available in the Literature And Regulatory Reviews During Clinical Development of New Chemical Entities

1:00 p.m. - 4:00 p.m.

Co-Chairs: Nina Isoherranen, University of Washington and Yoshiyuki Shirasaka, Kanazawa University

Quantitative Predictions and Physiologically Based Pharmacokinetic Modeling of Drug-drug Interactions Based on Retrospective Literature Data
Ping Zhao, US Food and Drug Administration

Clinical Importance of Transporter-mediated Drug-Drug Interactions: Basics and Applications of Evidence-based Decision Making
Kazuya Maeda, The University of Tokyo

Co-medication Considerations to Rationalize Drug Interaction Strategies
Jackie Bloomer, GlaxoSmithKline

Strategies and Retrospective Data Analysis in Hepatic Impairment Studies
Rob Foti, Amgen

Plenary Session Lectures | Sunday, October 19, 2014

5:00 p.m. – 6:00 p.m.

Mechanistic Modeling of Bile Acid-Mediated Drug-Induced Liver Injury
Kim Brouwer, University of North Carolina

6:00 p.m. – 7:00 p.m.

Contributions of the Human Gut Microbiome to Drug Metabolism
Peter Turnbaugh, University of California

Parallel Sessions – Monday, October 20 – Thursday, October 23, 2014

Symposium 1: Humanized and Knockout Animal Models in PK Studies

Monday, October 20, 2014 | 9:00 a.m. - 11:30 a.m.

Co-Chairs: Hiroshi Yamazaki, Showa Pharmaceutical University and Robert Tukey, University of California

Reactive Metabolite Formation of Drugs by Human P450s in Chimeric Mice with Humanized Liver
Hiroshi Yamazaki, Showa Pharmaceutical University

Humanized Models in Mice/Rats that Express Drug Metabolizing Enzymes via Chromosome Engineering Technology
Yasuhiro Kazuki, Tottori University

Application of Mouse Models Targeting P450 Reductase and the Cyp2abfgs Gene Cluster
Xinxin Ding, State University of New York

Importance of Intestinal Glucuronidation in Bilirubin Metabolism. Use of Humanized and Targeted Gene Knockout Mouse Models
Robert Tukey, University of California

Symposium 2: Cancer Biomarker Discovery

Monday, October 20, 2014 | 9:00 a.m. - 11:30 a.m.

Co-Chairs: Sumio Ohtsuki, Kumamoto University and Frank J. Gonzalez, National Cancer Institute

Quantitative Proteomics for Accelerating Cancer Biomarker Research
Sumio Ohtsuki, Kumamoto University

Metabolomics Analysis for Medical Research
Masaru Yoshida, Kobe University

Colon and Lung Cancer Biomarkers
Frank Gonzalez, National Cancer Institute

Metabolomics in Biomarker Discovery
Oliver Fiehn, University of California

Symposium 3: Chronopharmacological Strategy for Drug Discovery and Evolution

Monday, October 20, 2014 | 2:00 p.m. - 4:30 p.m.

Co-Chairs: Shigehiro Ohdo, Kyushu University and Damjana Rozman, University of Ljubljana

Chrono-drug and Delivery System: Rhythm Monitoring, Disruption and Manipulation
Shigehiro Ohdo, Kyushu University

Molecular Clock Mechanisms Underlying Circadian Rhythm of Transporters and/or CYPs
Satoru Koyanagi, Kyushu University

Common Transcriptional Nodes of Cholesterol Homeostasis, Drug Metabolism and the Liver Clock
Damjana Rozman, University of Ljubljana

Regulation of Circadian Behavior and Metabolism by Synthetic REV-ERB Agonists
Garret FitzGerald, University of Pennsylvania

Symposium 4: Metabolomics in Drug Development and Drug Safety

Monday, October 20, 2014 | 2:00 p.m. - 4:30 p.m.

Co-Chairs: Yoshiro Saito, National Institute of Health Sciences and Xiaochao Ma, University of Pittsburgh

Metabolomics/Lipidomics for Drug Development in a Pharmaceutical Company
Yoshinori Satomi, Takeda Pharmaceutical Co., Ltd.

Metabolomics-based Analyses on Dilated Cardiomyopathy and Alzheimer's Disease
Yoshiro Saito, National Institute of Health Sciences

Metabolomics – Quality Assurance and Pathway Identification for the Human Toxome Project
Thomas Hartung, Johns Hopkins University

The Opportunities and Challenges of Metabolomics in Drug Safety Evaluation
Xiaochao Ma, University of Pittsburgh

Symposium 5: Is Systems Biology a Powerful Tool to Explore/Understand the Mechanism of Action, Especially for Toxicity?

Tuesday, October 21, 2014 | 9:00 a.m. - 11:30 a.m.

Co-Chairs: Hiroshi Suzuki, The University of Tokyo and Ivan Rusyn, University of North Carolina

Mechanism of Action-based Predictive Modeling of Potential Adverse Effects of Drugs Using a Large-scale Toxicogenomics Database
Takeki Uehara, Shionogi & Co., Ltd.

Utilization of Systems-Biology in Analyzing and Predicting the Toxicity of Molecular Target Drugs
Hiroshi Suzuki, The University of Tokyo

Temporal and Dose-response Pathway Analysis for Predicting Chronic Chemical Toxicity
Russell Thomas, U.S. Environmental Protection Agency

Systems Biology Analysis of Genetic and Environmental Determinants of Toxicity
Ivan Rusyn, University of North Carolina

Symposium 6: From Understanding to Prediction: Opportunities and Challenges in Modeling Xenobiotic Metabolism and Disposition

Tuesday, October 21, 2014 | 9:00 a.m. - 11:30 a.m.

Co-Chairs: Yasushi Yamazoe, Food Safety Commission, Cabinet Office, Government of Japan and Paul Ortiz de Montellano, University of California

Template-based Prediction of Human CYP1A2-mediated Regio-/Stereo-selective Metabolism
Yasushi Yamazoe, Food Safety Commission, Cabinet Office, Government of Japan

Bridging ADME and PK Modeling for Xenobiotics: Towards a Multi-scale Model of the Blood-brain Barrier
Matthew Jacobson, University of California

Ligand Discovery for Membrane Transporters
Andrej Sali, University of California

Structure and Dynamics of Cytochromes P450 from Molecular Simulation
Chris Oostenbrink, University of Natural Resources and Life Sciences

Symposium 7: New Strategies in the Human CNS Barriers Research: The Development of New CNS Drugs and Therapies for the CNS Disorders

Tuesday, October 21, 2014 | 3:00 p.m. - 5:30 p.m.

Co-Chairs: Hiroyuki Kusuhara, The University of Tokyo and Xingrong Liu, Genentech, Inc.

Quantitative Targeted Absolute Proteomics for the Delivery of Drugs to the CNS
Tachikawa Masanori, Tohoku University

Drug Transporters at the CNS Barriers
Hiroyuki Kusuhara, The University of Tokyo

Drug Delivery Factors that Influence the Treatment of Primary and Secondary Brain Tumors
William Elmquist, University of Minnesota

Progress in Assessing BBB in Drug Discovery and Development
Xingrong Liu, Genentech, Inc.

Symposium 8: Solving ADME/Tox Challenges in Drug Discovery

Tuesday, October 21, 2014 | 3:00 p.m. - 5:30 p.m.

Co-Chairs: Toshiya Moriwaki, Takeda Pharmaceutical Co., Ltd. and Cyrus Khojasteh, Genentech, Inc.

Early Estimation of Human Effective and Maximum Tolerated Dose from Preclinical Results in Oncology Drug Development: Application to Compound Progression and Risk Assessments
Robert Griffin, Takeda Pharmaceutical Company Limited

Challenges for Overcoming ADMET Issues in a Drug Discovery Program; the Use of Sandwich-cultured Hepatocytes
Kazuhiro Tetsuka, Astellas Pharma Inc.

Overlap Between Drug and Endogenous Substrates of Cytochrome P450 Enzymes
F. Peter Guengerich, Vanderbilt University

Beyond Structural Alerts: Identification of an Unanticipated Bioactivation Pathway on Aryloxyperidine Motif in a Cardiovascular Drug Candidate
Amit Kalgutkar, Pfizer Inc.

Symposium 9: Drug-drug Interactions: Novel Mechanisms and Advances in Prediction

Wednesday, October 22, 2014 | 9:00 a.m. - 11:30 a.m.

Co-Chairs: Ikumi Tamai, Kanazawa University and Jane Kenny, Genentech, Inc.

Multiple Mechanisms of Juice Effect on Intestinal Uptake Transporters
Ikumi Tamai, Kanazawa University

Early Risk Assessment: Investigation of Endogenous Probe for Renal Transporter-related DDI
Yuichiro Imamura, Daiichi-Sankyo, Co. Ltd.

Challenges and Advances in Predicting Cytochrome P450 mediated Drug-Drug Interactions in Pharmaceutical Research and Development
R. Scott Obach, Pfizer Inc.

Translational Modeling of Metabolism-transporter Interplay and Drug-drug Interactions

Symposium 10: Translational PKPD Modeling & Simulation in Front Line of Drug Development

Wednesday, October 22, 2014 | 9:00 a.m. - 11:30 a.m.

Co-Chairs: Ryosei Kawai, Daiichi Sankyo Co., Ltd. and Shinji Yamazaki, Pfizer Inc.

Translational Pharmacokinetic-pharmacodynamic Modeling of Rituximab and of Atumumab in Chronic Lymphocytic Leukemia

Xingrong Liu, Daiichi Sankyo Co., Ltd.

Modeling and Simulation for Cardiac Safety by Bottom-up Approach

Hidefumi Kasai, Certara

Projection of Efficacious Concentrations for Anticancer Drugs by Pharmacokinetic-Pharmacodynamic Modeling: A Case study of Multiple Tyrosine Kinase Inhibitor, Crizotinib

Shinji Yamazaki, Pfizer Inc.

Incorporating Systems Pharmacology and PKPD Modeling in Translational Drug Development

Ananth Kadambi, Rosa & Co. LLC

Symposium 11: Personalized Drug Therapy: Promise and Challenge of a Genomics Approach

Thursday, October 23, 2014 | 9:00 a.m. - 11:30 a.m.

Co-Chairs: Miki Nakajima, Kanazawa University and Wolfgang Sadee, The Ohio State University

Trend and Perspective of Personalized Medicine in Drug Development – Impact of Progressed Basic Research on R&D in Pharmaceutical Companies

Akira Nagumo, Merck Sharp and Dohme

MicroRNA-related Polymorphisms to Predict Drug Response

Miki Nakajima, Kanazawa University

Genetics of Gene Expression and RNA Biology in Drug Metabolism and Disposition

Wolfgang Sadee, The Ohio State University

cis-Regulatory Elements in the Human Genome Affecting Expression of Drug Metabolizing Enzymes and Transporters

Nadav Ahituv, University of California

Symposium 12: Frontier of Antibody Engineering for Next-generation Therapeutics, Including ADCs: Opportunities and Challenges

Thursday, October 23, 2014 | 9:00 a.m. - 11:30 a.m.

Co-Chairs: Masaki Ishigai, Chugai Pharmaceutical Co., Ltd. and Mauricio Leal, Pfizer Inc.

Discovery of Novel Antibody Drug Conjugate Technology

Yuki Abe, Daiichi Sankyo Co., Ltd.

Engineered Antibody to Sweep Antigen by pH-Dependent Antigen Binding and Increased FcR Binding

Tatsuhiko Tachibana, Chugai Pharmaceutical Co., Ltd.

Metabolism (including intracellular metabolism) of ADC's

Steve Alley, Seattle Genetics

Preclinical/Clinical mAb Imaging in Support of ADC Biology
Simon Williams, Genentech, Inc.

Symposium 13: Advances in PBPK Modeling and Simulation for Special Populations

Thursday, October 23, 2014 | 12:30 p.m. - 3:00 p.m.

Co-Chairs: Shinichi Inoue, Daiichi Sankyo Co., Ltd. and Steve Leeder, Children's Mercy Hospital and Clinics

Modeling & Simulation for Clinical Development of New Drugs
Takahiko Tanigawa, Bayer Pharma AG

Population Physiologically Based Pharmacokinetic Modeling and Simulation of Interethnic Differences in Pharmacokinetics
Shin-ichi Inoue, Daiichi Sankyo Co., Ltd.

Incorporating CYP2D6 Pharmacogenetics into Pediatric PBPK Models - *Joint Presentation: Steve Leeder, Children's Mercy Hospital and Clinics and Nina Isoherranen, University of Washington*

Development and Application of PBPK Models of Drug Disposition During Pregnancy
Jashvant Unadkat, University of Washington

Symposium 14: Post-Translational and Transcriptional Regulation of Transporters and Metabolism

Thursday, October 23, 2014 | 12:30 p.m. - 3:00 p.m.

Co-Chairs: Ichiro Ieiri, Kyushu University and Xiaobo Zhong, University of Connecticut

miRNA328 on BCRP Expression – Transcriptional Regulation and Clinical Application
Takeshi Hirota, Kyushu University

Utility of iPS Cells for Drug Metabolizing Enzyme Expression
Tamihide Matsunaga, Nagoya City University

Transcriptional Regulation of Drug Metabolizing Enzymes by Nuclear Receptors
Thomas Kocarek, Wayne State University

Regulation of Transporters in the CNS and Kidney
Joanne Wang, University of Washington