



8TH INTERNATIONAL ISSX MEETING

SENDAI, JAPAN | OCTOBER 9-12, 2007

Short Course and Symposium Overview

Tuesday, October 9, 2007

9:00 - 12:00

SHORT COURSE 1

P450-dependent Metabolism in Extrahepatic Tissues: Implications for Drug Disposition and Toxicology

*Co-Chairs: Kazuhide Iwasaki, Pfizer Global R&D, Aichi, Japan
Laurence Kaminsky, New York State Dept of Health, Albany, NY, USA*

P450-dependent Metabolism of Endogenous and Exogenous Compounds in the Brain

Rachel Tyndale, University of Toronto, Toronto, Canada

Role of P450 in Presystemic Disposition of Drugs in the Intestine

Kenneth Thummel, University of Washington, Seattle, WA, USA

P450-dependent Metabolism of Drugs in the Kidney

Jorge Capdevila, Vanderbilt University, Nashville, TN, USA

P450-dependent Disposition of Drugs from the Skin.

Hollie Swanson, University of Kentucky, Lexington, KY, USA

SHORT COURSE 2

Novel Technologies for Transport Study in Drug Discovery and Development

*Co-Chairs: Tetsuya Terasaki, Tohoku University, Sendai, Japan
David E. Smith, University of Michigan, Ann Arbor, MI, USA*

Overview: Significance and Challenges of Current Drug Transport Research

Tetsuya Terasaki, Tohoku University, Sendai, Japan

How Can LC-MS/MS Rationally Solve the Problems of Drug Transport?

Application to Quantitative Proteomics of Transporter and Cocktail Transport Studies

Tetsuya Terasaki, Tohoku University, Sendai, Japan

International Standardization of the Methods for In-vitro Functional Analysis of Drug Transporters

Toshihisa Ishikawa, Tokyo Institute of Technology, Tokyo, Japan

Utilization of Membrane Vesicle Preparations to Study Drug-ABC-Transporter Interactions

Hristos Glavinas, SOLVO, Budaors, Hungary

How Can Knockout Animals Be Used to Elucidate the Significance of Transport Proteins on Drug Kinetics and Dynamics?

David E. Smith, University of Michigan, Ann Arbor, MI, USA

Perspective: Conclusions, Insight and Future Directions

David E. Smith, University of Michigan, Ann Arbor, MI, USA

SHORT COURSE 3

Drug Toxicity and Safety Predicted by Toxicogenomics

*Co-Chairs: Shogo Ozawa, National Institute of Health Science, Tokyo, Japan
Fred P. Guengerich, Vanderbilt University, Nashville, TN, USA*

Percellome Toxicogenomics Project for Predictive Toxicology

Jun Kanno, National Institute of Health Sciences, Tokyo, Japan

New Approach for Toxicologically Responsible Biomarkers

Ikuo Horii, Pfizer Inc., Aichi, Japan or Hiroshi Yamada, Pfizer Inc., Aichi, Japan

Applying Mechanisms of Chemical Toxicity to Predict Drug Safety

Fred P. Guengerich, Vanderbilt University, Nashville, TN, USA

Application of Toxicogenomics in Drug Safety Assessment

James Stevens, Lilly Research Laboratories, Greenfield, MI, USA

12:00 - 14:00

LUNCH FOR SHORT COURSE ATTENDEES

14:00 - 17:00

SHORT COURSE 4

Prediction of Pharmacokinetics and Drug-drug Interactions in Humans: Quantitative In Vitro-In Vivo Extrapolation

*Co-Chairs: Ikumi Tamai, Tokyo University of Science, Tokyo, Japan
Geoff Tucker, University of Sheffield, Sheffield, UK*

In Vitro-In Vivo Extrapolation (IVIVE) of Clearance and Drug Interactions: From Known Knowns to Known Unknowns

Geoff Tucker, University of Sheffield, Sheffield, UK

IVIVE: An Industrial Viewpoint
Rob Riley, AstraZeneca, Leicestershire, UK

IVIVE Versus Allometric Scaling
Thierry Lave, Roche, Basel, Switzerland

Prediction of Oral Drug Absorption in Human - From Cultured Cell Lines and from Experimental Animals
Shinji Yamashita, Setsunan University, Osaka, Japan

SHORT COURSE 5

Metabolism-Based Neurotoxicity by Xenobiotics: Mechanisms & Biomarkers
*Co-Chairs: Shigero Ohta, Hiroshima University, Hiroshima, Japan
Ramesh C. Gupta, Murray State University, Hopkinsville, KY, USA*

Modulation of CYP1A1 and 1B1 Metabolizing Enzymes by Xenobiotics
Yhun Yhong Sheen, Ewha Womans University, Seoul, Korea

Toxicologic Implications of Carboxylesterases-Novel Biomarker of Organophosphate Exposure
Tetsuo Satoh, Chiba University, Chiba, Japan

Metabolomic Mechanisms and Biomarkers of Neuronal Damage
Ramesh C. Gupta, Murray State University, Hopkinsville, KY, USA

Disposition Process of Parkinsonism-causing Neurotoxins
Shigeru Ohta, Hiroshima University, Hiroshima, Japan

SHORT COURSE 6

Application of Genomic Data on Clinical Events
*Co-Chairs: Ken-ichi Inui, Kyoto University Hospital, Kyoto, Japan
Allan E. Rettie, University of Washington, Seattle, WA, USA*

Pharmacogenomics of Oral Anticoagulants
Allan E. Rettie, University of Washington, Seattle, WA, USA

Pharmacogenomics of Cancer Therapy
Howard L. McLeod, University of North Carolina, Chapel Hill, NC, USA

Drug Transporter Pharmacogenomics and Personalized Medicine
Richard B. Kim, University of Western Ontario, London, ON, Canada

Personalized Tacrolimus Therapy in Patients after Liver Transplantation
Ken-ichi Inui, Kyoto University Hospital, Kyoto, Japan

18:00 - 20:00

WELCOME RECEPTION



Wednesday, October 10, 2007

8:00 - 9:00

INFOMERCIAL SESSION

9:00 - 9:20

WELCOME ADDRESS - OPENING

9:20 - 10:30

PLENARY LECTURE 1

PPAR α : Biomarkers for Activation and Mechanism of Peroxisome Proliferator-induced Hepatocarcinogenesis
Frank J. Gonzalez, National Cancer Institute, Bethesda, MD, USA

10:30 - 11:30

ISSX AWARDS

11:30 - 13:00

LUNCHEON SEMINAR POSTER VIEWING

13:00 - 15:30

SYMPOSIUM 1

P450 Monooxygenases as Drug Targets

*Co-Chairs: Kan Chiba, Chiba University, Chiba, Japan
Russell Prough, University of Louisville, Louisville, KY, USA*

Aromatase Mechanism of Action in Cancer and Metabolic Disease
Evan Simpson, Prince Henry's Institute of Medical Research, Melbourne, Australia

Pharmacological Manipulation of P450s: Regulation of Smoking Addiction
Rachael Tyndale, University of Toronto, Toronto, Canada

Azole Resistance in Microorganisms

Yuzo Yoshida, Mukogawa Women's University, Hyogo, Japan

P450 System in Mycobacterium Tuberculosis: Structure, Function and Drug Targeting

Andrew Munro, University of Manchester, Manchester, UK

SYMPOSIUM 2

Rational Use of In Silico Technology in Drug Discovery and Development

*Co-Chairs: Shinji Yamashita, Setsunan University, Osaka, Japan
Alan Wilson, Lexicon Genetics, The Woodlands, TX, USA*

The Strategic Role of Predictive ADME and Toxicity Modeling in Drug Discovery and Development

Alan Wilson, Lexicon Genetics, The Woodlands, TX, USA

Knowledge Acquisition and Data Mining in the CYP-chemical Interaction Studies

Fumiyoshi Yamashita, Kyoto University, Kyoto, Japan

Prediction of Drug ADME Based on PBPK Modeling

Walt Woltoz, Simulations Plus, Inc., Lancaster, CA, USA

Applying Predictive Data Mining Strategies to Toxicity Assessment

Chihae Yang, Lead Scope, Inc., Columbus, OH, USA

SYMPOSIUM 3

In Vitro Toxicity Testing: How Effective Is This in Predicting In Vivo Toxicity?

*Co-chairs: Abdul Mutlib, Pfizer, Ann Arbor, MI, USA
Urs A. Boelsterli, National University of Singapore, Singapore and
University of Connecticut, Storrs, CT, USA*

Shifting Attrition in Drug Discovery Using Gene Expression Analysis

Jeff Waring, Abbott Laboratories Centers, Abbott Park, IL, USA

In Vitro Method for Predicting Clinical Hepatotoxicities

Seva Kostrubsky, Pfizer, Ann Arbor, MI, USA

In Vitro Human-based Experimental Systems for Drug Toxicity Evaluation

Albert Li, In Vitro Technologies, Inc, Rockville, MD, USA

Tailor-made In Vitro Toxicity Testing in Pharmaceutical Industry: Cases and Strategies

Armin Wolf, Novartis Pharma AG, Basel, Switzerland

15:30 - 16:00

COFFEE BREAK

16:00 - 18:30

SYMPOSIUM 4

New Aspects of Hydrolyses and Conjugation Reactions

*Co-Chairs: Hideyuki Yamada, Kyushu University, Fukuoka, Japan
John Miners, Flinders University, Adelaide, Australia*

Tissue-specific Regulation of Human Microsomal Epoxide Hydrolase by Alternative Gene Promoters

Curtis J. Omiecinski, Pennsylvania State University, University Park, PA, USA

Cytosolic Sulfotransferases for Endogenous Substrates

Kouichi Yoshinari, Tohoku University, Sendai, Japan

Unraveling the Kinetic Anomalies of UDP-glucuronosyltransferases

John Miners, Flinders University, Adelaide, Australia

Arylamine N-acetyltransferases: From Structure to Function

Edith Sim, University of Oxford, Oxford, UK

SYMPOSIUM 5

Understanding the Plastic (flexible) Nature of the CYP Active Sites

*Co-Chairs: Eric F. Johnson, The Scripps Research Institute, La Jolla, CA, USA
Nicolas P.E. Vermeulen, Vrije Universiteit, Amsterdam, The Netherlands*

Plasticity of the CYP2C9 Active Site, Allelic Variation and Ligand Induced Changes

Eric F. Johnson, The Scripps Research Institute, La Jolla, CA, USA

Substrate/Protein Dynamics Simulations and Applications

Nicolas P.E. Vermeulen, Vrije Universiteit, Amsterdam, The Netherlands

Structure and Function of Cytochromes P450 2B: X-ray Crystallography and Solution Biophysical Studies

James Halpert, The University of Texas Medical Branch, Galveston, TX, USA

Quantum Mechanical Studies of P450 Catalyzed Reactions

Sason Shaik, The Hebrew University, Jerusalem, Israel

SYMPOSIUM 6

Lipid Homeostasis and Metabolic Regulation

*Co-Chairs: Jin Ding Huang, National Cheng University Medical College, Tainan, Taiwan
Jeff Staudinger, University of Kansas, Lawrence, KS, USA*

CAR Mediates Induction of Drug Metabolism in Poorly Managed Type 1 Diabetes

David Moore, Baylor College of Medicine, Houston, TX, USA

Orphan Nuclear Receptors in Xenobiotic and Endobiotic Homeostasis

Wen Xie, University of Pittsburgh, Pittsburgh, PA, USA

Nuclear Receptors, Cell Signaling, and Drug Metabolism

Jeff Staudinger, University of Kansas, Lawrence, KS, USA

Nuclear Receptor Regulation of Bile Acid and Drug Metabolism

John Chiang, Northeastern Ohio University College of Medicine, Rootstown, OH, USA



THURSDAY, October 11, 2007

9:00 - 11:30

SYMPOSIUM 7

Current Issues on Reactive or Unique Metabolites

*Co-Chairs: Tsuyoshi Yokoi, Kanazawa University, Kanazawa, Japan
Robert A. Roth, Michigan State University, East Lansing, MI, USA*

Inflammatory Stress as a Susceptibility Factor for Drug Hepatotoxicity

Robert A. Roth, Michigan State University, East Lansing, MI, USA

Covalent Adduction of Proteins Causing Alkylation Damage

Daniel Liebler, Vanderbilt University, Nashville, TN, USA

A Model System to Assess the GSH Conjugating Activity Using gclm(-/-) Gene-targeted Mice

Terrance J. Kavanagh, University of Washington, Seattle, WA, USA

Investigation of Drug Induced Hepatotoxicity by Knockdown of Glutathione Synthesis

Tsuyoshi Yokoi, Kanazawa University, Kanazawa, Japan

SYMPOSIUM 8

Interplay of Metabolism and Transport in Drug Disposition

*Co-chairs: Hiroshi Suzuki, Tokyo University, Tokyo, Japan
Dietrich Keppler, Deutsches Krebsforschungszentrum, Heidelberg, Germany*

The Role of MRPs in the Cellular Efflux of Glucuronides: Studies with KO Mice

Piet Borst, The Netherlands Cancer Institute, Amsterdam, The Netherlands

Interplay of Conjugating Enzymes with OATP and MRP Transporters in the Elimination of Drugs: Studies with Multiple-transfected Cells and Mathematical Modeling of Vectorial Transport

Dietrich Keppler, Deutsches Krebsforschungszentrum, Heidelberg, Germany

Unexpected Interactions Between Drug Transport and Phase I and Phase II Drug Metabolism

Thomas Friedberg, University of Dundee, Dundee, UK

Synergistic Role of Breast Cancer Resistance Protein (BCRP/ABCG2) and Sulfotransferases in Regulating the Drug Disposition

Jun-ichi Enokizono, Kyowa Hakko Kogyo Co., Shizuoka, Japan

Interplay of P-450 Enzymes with Uptake and Efflux Transporters in Drug Disposition: Studies in Cellular Systems, Perfused Organs, Whole Animals and Humans

Leslie Z. Benet, University of California San Francisco, San Francisco, CA, USA

11:30 - 13:00

LUNCHEON SEMINAR

POSTER VIEWING

13:00 - 14:00

PLENARY LECTURE 2

Mitochondrial Toxicity – From Basic Mechanisms to Idiosyncratic Drug-induced Liver Injury

Urs A. Boelsterli, National University of Singapore, Singapore and University of Connecticut, Storrs, CT, USA

14:30 - 17:30

EXCURSION/MATSUSHIMA

18:00 - 21:00

BANQUET



FRIDAY, October 12, 2007

9:00 - 11:30

SYMPOSIUM 9

Nuclear Transfactor Interplay

*Co-Chairs: Kiyoshi Nagata, Tohoku Pharmaceutical University, Sendai, Japan
Frank J. Gonzalez, NIH/NCI, Bethesda, MD, USA*

Introduction

Frank J. Gonzalez, NIH/NCI, Bethesda, MD, USA

Analysis of the Intrinsic Physiological Function of AhR

Yoshiaki Fujii-Kuriyama, University of Tsukuba, Tsukuba, Japan

Nuclear Receptor: Cross-talk and Consequences

Patrick Maurel, INSERM, Montpellier, France

Nuclear Receptors CAR and PXR Mediate Xeno-Endo Cross-talk in Hepatic Energy Metabolism

Masahiko Negishi, NIEHS, Research Triangle Park, NC, USA

Analysis of Transcription Factor Interplay Assessed by Adenovirus siRNA

Kiyoshi Nagata, Tohoku Pharmaceutical University, Sendai, Japan

SYMPOSIUM 10

New Technology and Bioinformatics in Evaluating and Preventing Drug Toxicity

*Co-chairs: Toshihiko Ikeda, Sankyo Co. Ltd., Tokyo, Japan
Garold S. Yost, University of Utah, Salt Lake City, UT, USA*

Glutathione Adducts: Finding and Identifying Electrophiles

Garold S. Yost, University of Utah, Salt Lake City, UT, USA

Biomarker Discovery by Metabolome Analysis

Tomoyoshi Soga, Keio University, Yamagata, Japan

2D Electrophoresis Coupled to MS/MS - Identification of Protein Targets of Toxic Lipid Aldehydes

Dennis Petersen, University of Colorado, Denver, CO, USA

Sophisticated MS Techniques Used to Identify Alkylation of Proteins from Prototypical Electrophiles

Daniel Liebler, Vanderbilt University, Nashville, TN, USA

11:30 - 13:00

LUNCHEON SEMINAR

POSTER VIEWING

13:00 - 15:30

SYMPOSIUM 11

What Determines a Significant Metabolite?

(Organized by the Committee on Regulatory Affairs)

*Co-chairs: Takahiko Baba, Shionogi & Co Ltd, Osaka, Japan
Steven Wrighton, Eli Lilly & Co., Indianapolis, IN, USA*

Safety Assessments of Drug Metabolites

Masahiro Tohkin, NIHS, Tokyo, Japan

Case Studies in Pharmaceutical Industries and Perspective

Takafumi Iwatsubo, Astellas, Tokyo, Japan

Leveraging Drug Metabolism and Excretion Data in MIST (Metabolites In Safety Testing) Strategies

Scott Obach, Pfizer, Groton, CT, USA

Unique/major Human Metabolites: Why, How and When to Test for Safety in Animals

Debra Luffer-Atlas, Eli Lilly & Co., Indianapolis, IN, USA

SYMPOSIUM 12

Role of Pharmacokinetic Modeling and Simulation in Drug Development

*Co-Chairs: Yuichi Sugiyama, University of Tokyo, Tokyo, Japan
Stephen D. Hall, Indiana University Dept. of Medicine, Indianapolis, IN, USA*

PBPK Modeling for Transporter-mediated Drug Disposition in the Body:
Prediction from In Vitro to In Vivo and from Animal to Human

Yuichi Sugiyama, University of Tokyo, Tokyo, Japan

Mechanism Based PK/PD Modeling

Meindert Danhof, Leiden/Amsterdam Center for Drug Research, Amsterdam, The Netherlands

Clinical PK/PD Studies for the Validation of Biomarkers as Surrogate Endpoints

Akihiro Hisaka, University of Tokyo, Tokyo, Japan

Propagation of Genetic & Ethnic Variability in Drug Metabolism to Pharmacological Response: Expectations vs. Realities

Amin Rostami-Hodjegan, University of Sheffield, Sheffield, UK

15:30 - 16:00

COFFEE BREAK

16:00 - 17:00

POSTER AWARDS

17:00

CLOSING

Announcing the 9th International ISSX Meeting

Announcing other ISSX Meetings