

# The 25th International Symposium on Microsomes and Drug Oxidations

„Microsomes and Drug Oxidations: From Structures to Regulations and Modeling“

Prague, Czech Republic, July 7 - 10, 2024

## Sunday (July 7, 2024)

15:00	Registration
17:30	<b>Opening Ceremony (Room A)</b> <b>Welcome Remarks</b> <i>Xinxin Ding</i> <i>Jiri Hudecek</i> <i>Petr Pavek</i>
17:45 – 18:10	<b>Opening keynote presentation</b> <b>Bettie Sue Masters Duke University, USA</b> <b>A Sojourn Down MDO Memory Lane</b>
18:10 – 18:35	<b>Opening Symposium</b> <b>In silico and PBPK(D) modeling of drug metabolism</b> <i>Amin Rostami-Hodjegan</i>

<b>18:35 – 19:25</b>	<b>Opening Symposium</b> <b>In vitro and in silico systems for prediction of drug metabolism and toxicity/ In vitro to in vivo extrapolation (IVIVE) in drug development</b>  <b>Matthew A. Cerny</b> - A Comparison of In Vitro and In Vivo Metabolite Profiles – How Predictive are our In Vitro Assays?  <b>Carl Petersson</b> - Addressing the challenge of low clearance drug candidates; solutions for the extrapolation from in vitro systems and reaction phenotyping.
<b>19:30</b>	<b>Welcome drink</b>

## **Monday (July 8, 2024)**

**Plenary lecture (Room A)**

**8:30 - 9:00**

**F. Peter Guengerich**

**Vanderbilt University, Nashville, Tennessee**

**Mechanisms of Complex Cytochrome P450 Reactions–New Insights**

**Concurrent Symposium 1 (Room A)**

**9:00 - 10:30**

**Novel structural insights and functions of cytochromes P450**

**Chairs:**

**Elizabeth M. J. Gillam**

**Emily E. Scott**

**Elizabeth M. J. Gillam** - Old folds can learn new tricks: what evolution can tell us about innovation in P450s

**John C. Hackett** - Cytochrome P450 19A1 dynamics and ligand recognition in membranes

**Stephen Bell** - Structural insights into cytochrome P450 enzymes from in *crystallo* reactions and variable-temperature X-ray crystallography

**Thomas Pochapsky**, Kurt Harris, Nathan Wong, Liam Flynn, Alaina M. Richard, and Emily E. Scott. - Selective binding and inhibition of CYPs by isonitriles

**Concurrent Symposium 2 (Room B)**

**9:00 - 10:30**

**Transcriptional and signaling-based regulation of drug metabolism**

**Chairs:**

**Oliver Burk**

**Taoseng Chen**

**Taoseng Chen** - Selective modulation of the promiscuous and dynamic PXR and CYP3A4/5

**William Bourguet** - Structural insights into ligand binding affinity, specificity and promiscuity in the aryl hydrocarbon receptor

**Thales Kronenberger** - Computational study of conformational changes in nuclear receptors upon ligand binding

**Jinjing Chen** - Hammerhead-type FXR agonists induce an enhancer RNA Fincor: Friend or Foe in metabolic liver disease? (shorter talk)

**10:30 - 11:00**

Coffee break (30 min)

**Concurrent Symposium 3 (Room A)**

**11:00 - 12:30**

**Mechanisms and dynamics of P450 and other xenobiotic-metabolizing enzymes**

**Chairs:**

**Jed N. Lampe**

**Emre M. Isin**

**J. N. Lampe** - Molecular dynamics simulations reveal a conserved role for the F/G loop domain in cytochrome P450 CYP3A family multiple ligand binding

**Emre M. Isin** - Unusual Biotransformation Reactions: Expecting the Unexpected

**James De Voss** - Mechanism of P450 catalysed dehydrogenation in the model bacterial P450 CYP199A4

**Rebecca C. Wade** - Multiscale molecular dynamics simulations to investigate how cytochrome P450 conformational plasticity affects its interactions and function

**Concurrent Symposium 4 (Room B)**

**11:00 - 12:30**

**Nuclear Xenobiotic Receptors: PXR and CAR in metabolism and diseases**

**Chairs:**

**Jukka Hakkola**

**Petr Pavek**

**Jukka Hakkola** - PXR activation-induced effects on metabolic health

**Petr Pavek** - Novel PXR/CAR ligands as an intervention in metabolic diseases

**Oliver Burk** - PXR-dependent modulation of hepatic sphingolipid and phospholipid metabolism

**Itsuki Yokoseki** - BRD9, a chromatin remodeling factor, negatively regulates PPAR $\alpha$ -mediated transcription of CPT1A to attenuated lipid metabolism

**12:20 - 13:30**

**Lunch, Exhibit Hall Hours**

**13:30 - 14:30**

**Poster Viewing, Poster Presentation Session**

**Concurrent Symposium 5 (Room A)**

**14:30 - 15:50**

**CYPs in endogenous metabolism of lipids and steroids**

**Chairs:**

**Irina Pikuleva**

**Amit V. Pandey**

**Irina Pikuleva** - CYP46A1 in the Brain: It is Not Just Cholesterol Elimination

**Amit V. Pandey** - Regulation of Steroid Metabolism by Human Genetic Variations in the Redox Partners of Cytochrome P450 proteins

**Richard J. Auchus** - Why is P450 11B2 an aldosterone synthase and P450 11B1 is not?

**Concurrent Symposium 6 (Room B)**

**14:30 - 15:50**

**Drug metabolizing enzymes, transporters, and nuclear receptors as therapeutic targets**

**Chairs:**

**Hongbing Wang**

**Huichang Bi**

**Hongbing Wang** - Activation of CAR and Nrf2 in cyclophosphamide- and doxorubicin-based chemotherapy

**Huichang Bi** - The novel role of PXR in liver diseases and beyond

**Kouichi Yoshinari** - Cytochrome P450 inhibition, AHR activation, and liver injury

**15:50 - 16:20**

Coffee break (30 min)

**16:20 - 16:40**

**Commercial presentation**

Miroslav Kandar - Mattek Life Sciences – reproducible in vitro reconstructed human tissues as an alternative to testing on animals

**Concurrent Symposium 7 (Room A)**

**16:40 - 18:00**

**Structure and functions of non-cytochrome P450 enzymes and phase II conjugation enzymes in drug metabolism**

**Chairs:**

**Miki Nakajima**

**Wen Xie**

**Tatsuki Fukami** - Novel characteristics of non-P450 oxidases unraveled from functional analyses

**Wen Xie** - Sulfation in Drug-induced Liver Injury, the expected and unexpected

**Sheila J. Sadeghi** - Flavin-containing monooxygenases: polymorphic variants and their effect on drug metabolism

**Concurrent Symposium 8 (Room B)**

**16:40 - 18:00**

**Importance of ncRNAs and lncRNAs in metabolism regulation and liver diseases**

**Chairs:**

**Baitang Ning**

**David Waxman**

**Baitang Ning** - The importance of ncRNA and lncRNA in the regulation of metabolism and liver toxicity

**David Waxman** - Global analysis of hepatic lncRNA functions in liver disease: Cell type specificities, zonation patterns, hepatic intercellular communication, and gene regulatory networks deduced from single cell sequencing

**Shogo Takahashi** - The Hidden Regulators: Unveiling the Roles of Two CAR-Regulated lncRNAs in Liver Physiology Using Mouse Knockout Models

**20:00 - 22:00**

**Panoramic Vltava River Cruise with Conference Dinner (not included in the reg. fee)**

## **Tuesday (July 9, 2024)**

**Plenary lecture (Room A)**

**8:30 - 9:00**

**Magnus Ingelman-Sundberg**

**Department of Physiology and Pharmacology, Karolinska Institutet, Sweden**

**Enhancing Drug - Development Through Innovative 3D Liver Models**

**Concurrent Symposium 9 (Room A)**

**9:00 - 10:30**

**Pharmacogenomics of drug-metabolizing enzymes: clinical relevance and ethnic diversity**

**Chairs:**

**Magnus Ingelman-Sundberg**

**Rachel Tyndale**

**Todd C. Skaar** - Discovery of rare ancestry-enriched variants that impact drug metabolism.

**Rachel F. Tyndale** - Big data to investigate the role of polygenic, structurally variable CYP2A6 in disease

**Matthias Schwab** - Innovation in cancer pharmacotherapy through integrative consideration of pharmacogenomics profiles

**Christopher A. Reilly**, Marysol Almestica-Roberts, and Flory L. Nkoy. Differential metabolism of linoleic acid and cortisol by cytochrome P450 2C8\*3 and 3A5\*3 enzyme variants influences asthma symptom control in children (a shorter talk)

**Concurrent Symposium 10 (Room B)**

**9:00 - 10:30**

**Novel animal models to predict drug metabolism and toxicity**

**Chairs:**

**Hiroshi Yamazaki**

**José E. Manautou**

**Hiroshi Yamazaki** - Pharmacokinetic modeling for drugs using inactivated-P450 human hepatocytes after transplantation into immunodeficient mice

**José E. Manautou** - Deciphering the impact of hepatic Multidrug resistance protein 4 (Mrp4) in liver steatosis and metabolic syndrome pathogenesis

**Mario Mezler** - Analysis of the bile acid composition in a fibroblast growth factor 19-expressing liver-humanized mouse model and its use for CYP3A4-mediated drug-drug interaction studies

**Grace Guo** - Generation of Low-bile Acid Mouse Model to Decipher Roles of Individual Bile Acids in MASH Development (a shorter talk)

**10:30 - 11:00**

Coffee break (30 min)

**Concurrent Symposium 11 (Room A)**

**11:00 - 12:20**

**Biomarkers for prediction of drug metabolism and toxicity**

**Chairs:**

**Ann Daly**

**Christopher Goldring**

**Ann Daly** - Pharmacogenomics of drug-induced liver injury-metabolic and immunogenetic biomarkers

**Christopher Goldring** - Biomarkers for drug-induced liver injury and the TransBioLine study

**Mikko Niemi** - Circulating biomarkers for drug transporters

**Concurrent Symposium 12 (Room B)**

**11:00 - 12:30**

**3D experimental models and organ-on-chips in drug metabolism**

**Chairs:**

**Volker M. Lauschke**

**Tore B. Stage**

**Volker M. Lauschke** - Organotypic and microphysiological primary human tissue models for translational pharmacology

**Jonathan Sexton** - Personalized Liver Injury Risk Prediction: Patient-Derived Organoids on Chip

**Masaru Koido** - How can we translate findings from human genetic association studies?

**Jasleen K. Sodhi** - Hepatic 3D Liver Models and IVIVE

**12:30 - 13:30**

**Lunch, Exhibit Hall Hours**

**13:30 - 14:30**

**Poster Viewing, Poster Presentation Session**



**Concurrent Symposium 13 (Room A)**

**14:30 - 15:50**

**Inflammatory regulation of cytochrome P450 enzymes and COVID-19**

**Chairs:**

**Kerry B. Goralski**

**Tore B. Stage**

**Kerry B. Goralski** - COVID-19 and CYP3A4 drug metabolism interactions: A review of the evidence

**Tore B. Stage** - Translational aspects of drug metabolism during inflammation from clinical studies and 3D primary human hepatocytes

**Gülsah Gabriel** - Respiratory virus infection mediated dysregulation of sex hormone metabolism

**Concurrent Symposium 14 (Room B)**

**14:30 - 15:50**

**Omics and single-cell-based technologies in the study of drug metabolism**

**Chairs:**

**Albert Braeuning**

**Damjana Rozman**

**Albert Braeuning** - The use of proteomic approaches to analyze in vivo effects of phenobarbital in mice with humanized livers

**Damjana Rozman** - Targeted omics for innovative decision support systems: examples of COVID-19 and liver cancer

**Celia P. Martinez-Jimenez** - Unraveling Hepatocyte Heterogeneity: Implications for Drug Metabolism and Toxicity Under Metabolic Stress

**15:50 - 16:20**

Coffee break (30 min)

**16:20 - 16:40 Commercial presentations**

K. Yildirim - Empowering Microbiome-Drug Interaction Research: Innovative Tools from Promega

R. Xinxin Ding - Publishing your work in ASPET journals.

**Concurrent Symposium 15 (Room A)**

**16:40 - 18:00**

**Interactions of microbiome on drug metabolism**

**Chairs:**

**Pavel Anzenbacher**

**Hyunyoung (Young) Jeong**

***Pavel Anzenbacher*** - Drug Metabolism and Gut Microbiome

***Hyunyoung (Young) Jeong*** - Modulation of Drug-induced Hepatotoxicity by Gut Microbial Metabolite

***Sridhar Mani*** - Intestinal Microbial metabolites, Nuclear Receptors, and Microbial Metabolite Mimicry: An Update

**Concurrent Symposium 16 (Room B)**

**16:40 - 18:00**

**Oligonucleotide and peptide ADME**

**Chairs:**

**Xiaobo Zhong**

**Hongbin Yu**

***Hongbin Yu*** - Perspectives on ADME of therapeutic proteins

***Aiming Yu*** - ADME of therapeutic RNAs

***Sherouk Tawfik*** - Triple E challenges for better efficacy of siRNA therapeutics: targeted endocytosis, endosomal escape, and exocytosis

**19:00**

**Organ Concert in Carolinum, medieval Hall of the Charles University**

## **Wednesday (July 10, 2024)**

**Plenary lecture (Room A)**

**8:30 - 9:00**

**Emily E. Scott, Ph.D.**

**University of Michigan**

**Human microsomal and mitochondrial P450 interactions with substrates and redox partners**

**Concurrent Symposium 17 (Room A)**

**9:00 - 10:30**

**Intestinal and extrahepatic metabolizing enzymes in bioavailability and disposition**

**Chairs:**

**Xinxin Ding**

**Stefan Oswald**

**Xinxin Ding** - Dissecting hepatic and extrahepatic contributions to xenobiotic metabolism using transgenic mouse models

**Stefan Oswald** - Intra-subject analysis of gene expression and protein abundance of major and minor drug metabolizing enzymes along the healthy human intestine

**Joan Z. Zuo** - Intestinal carboxylesterase mediated activation of irinotecan and its impact on herb-drug interactions

**Bhagavatula Moorthy** - Attenuation of polycyclic aromatic hydrocarbon (PAH)-induced carcinogenesis by omega 3-fatty acids in vivo (shorter talk)

**Concurrent Symposium 18 (Room B)**

**9:00 - 10:30**

**Drug transporters and their impact on drug metabolism and disposition**

**Chairs:**

**Sibylle Neuhoff**

**Jean Terrier**

**Matus Sotak** - Circadian regulation of transporter expression: Implications for drug disposition and translational challenges

**Dirk Theile** - The unequal perpetrator effects of rifampicin vs. rifabutin on P-glycoprotein and substrate drugs pharmacokinetics

**Jean Terrier** - Drug transporters and their impact on the pharmacokinetics of direct oral anticoagulants using PK modelling.

**Sibylle Neuhoff/Matthew D. Harwood** - PBPK modeling of endogenous biomarker to assess hepatic and renal transporter-mediated DDIs in healthy and disease

**10:30 - 11:00**

Coffee break (30 min)

**11:00 - 12:00**

**Best Posters Awards and Best Poster Winner Presentations**

**12:00**

**Closing Ceremony**

Closing Remarks

The upcoming 26<sup>th</sup> MDO meeting in Hong Kong

**12:30 - 13:30**

MATTEK Workshop (Room B) (<https://mdoprague2024.cz/mattek-workshop/>)

**Optional Visit to Prague Castle (not incl. in the registration fee)**



## **Symposium Secretariat: Congress Business Travel**

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