

DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

November 2018

Vol. 46, No. 11

CONTENTS

SPECIAL SECTION – NEW MODELS IN DRUG METABOLISM AND TRANSPORT

- Emerging Models of Drug Metabolism, Transporters, and Toxicity. *Aarti Sawant-Basak and R. Scott Obach* **1556**
- Cryopreserved Human Intestinal Mucosal Epithelium: A Novel In Vitro Experimental System for the Evaluation of Enteric Drug Metabolism, Cytochrome P450 Induction, and Enterotoxicity. *Albert P. Li, Novera Alam, Kirsten Amaral, Ming-Chih David Ho, Carol Loretz, Walter Mitchell, and Qian Yang* **1562**
- Generation of Intestinal Organoids Suitable for Pharmacokinetic Studies from Human Induced Pluripotent Stem Cells. *Daichi Onozato, Misaki Yamashita, Anna Nakanishi, Takumi Akagawa, Yuriko Kida, Isamu Ogawa, Tadahiro Hashita, Takahiro Iwao, and Tamihide Matsunaga* **1572**
- Physiologically Relevant, Humanized Intestinal Systems to Study Metabolism and Transport of Small Molecule Therapeutics. *Aarti Sawant-Basak, A. David Rodrigues, Matthew Lech, Regis Doyonnas, Marion Kasaian, Bhagwat Prasad, and Nikolaos Tsamandouras* **1581**
- How to Determine the Role of the Microbiome in Drug Disposition. *Jordan E. Bisanz, Peter Spanogiannopoulos, Lindsey M. Pieper, Annamarie E. Bustion, and Peter J. Turnbaugh* **1588**
- An Ex Vivo Fermentation Screening Platform to Study Drug Metabolism by Human Gut Microbiota. *E. van de Steeg, F. H. J. Schuren, R. Scott Obach, C. van Woudenberg, Gregory S. Walker, M. Heerikhuisen, I. H. G. Nooijen, and W. H. J. Vaes* **1596**
- A Novel In Vitro Experimental System for the Evaluation of Drug Metabolism: Cofactor-Supplemented Permeabilized Cryopreserved Human Hepatocytes (MetMax Cryopreserved Human Hepatocytes). *Albert P. Li, Ming-Chih David Ho, Kirsten Amaral, and Carol Loretz* **1608**
- Assessment of the Biotransformation of Low-Turnover Drugs in the H μ REL Human Hepatocyte Coculture Model. *Richard D. Burton, Todd Hieronymus, Taysir Chamem, David Heim, Shelby Anderson, Xiaochun Zhu, and J. Matthew Hutzler* **1617**
- Advances in Engineered Human Liver Platforms for Drug Metabolism Studies. *Gregory H. Underhill and Salman R. Khetani* **1626**
- Microfluidic Cell Culture Platforms to Capture Hepatic Physiology and Complex Cellular Interactions. *Shyam Sundhar Bale and Jeffrey T. Borenstein* **1638**
- Perspective on the Application of Microphysiological Systems to Drug Transporter Studies. *Pedro Caetano-Pinto and Simone H. Stahl* **1647**
- Do In Vitro Assays Predict Drug Candidate Idiosyncratic Drug-Induced Liver Injury Risk?. *J. Gerry Kenna and Jack Utrecht* **1658**
- Models and Approaches Describing the Metabolism, Transport, and Toxicity of Drugs Administered by the Ocular Route. *Jennifer L. Dumouchel, Nagendra Chemuturi, Mark N. Milton, Gian Camenisch, James Chastain, Markus Walles, Vito Sasseville, Mithat Gunduz, Ganesh R. Iyer, and Upendra A. Argikar* **1670**
- Fabrication of a Corneal Model Composed of Corneal Epithelial and Endothelial Cells via a Collagen Vitrigel Membrane Functioned as an Acellular Stroma and Its Application to the Corneal Permeability Test of Chemicals. *Hiroyuki Yamaguchi and Toshiaki Takezawa* **1684**
- Emerging Kidney Models to Investigate Metabolism, Transport, and Toxicity of Drugs and Xenobiotics. *Piyush Bajaj, Swapan K. Chowdhury, Robert Yucha, Edward J. Kelly, and Guangqing Xiao* **1692**
- Human Pluripotent Stem Cell-Derived Kidney Model for Nephrotoxicity Studies. *Piyush Bajaj, A. David Rodrigues, Claire M. Stepan, Sandra J. Engle, Sumathy Mathialagan, and Thomas Schroeter* **1703**

Continued on next page

Porcine Prediction of Pharmacokinetic Parameters in People: A Pig in a Poke?. <i>Huadong Tang and Michael Mayersohn</i>	1712	<i>John D. Clarke, Anna Vildhede, Michael Goedken, and Nathan J. Cherrington</i>	1478
☐ Pheophorbide A: Fluorescent Bcrp Substrate to Measure Oral Drug-Drug Interactions in Real-Time In Vivo. <i>Kazuto Yasuda, Samit Ganguly, and Erin G. Schuetz</i>	1725	☐ When Does the Rate-Determining Step in the Hepatic Clearance of a Drug Switch from Sinusoidal Uptake to All Hepatobiliary Clearances? Implications for Predicting Drug-Drug Interactions. <i>Gabriela I. Patilea-Vrana, and Jashvant D. Unadkat</i>	1487
P450-Humanized and Human Liver Chimeric Mouse Models for Studying Xenobiotic Metabolism and Toxicity. <i>Karl-Dimiter Bissig, Weiguo Han, Mercedes Barzi, Nataliia Kovalchuk, Liang Ding, Xiaoyu Fan, Francis P. Pankowicz, Qing-Yu Zhang, and Xinxin Ding</i>	1734	☐ Application of Intestinal Epithelial Cells Differentiated from Human Induced Pluripotent Stem Cells for Studies of Prodrug Hydrolysis and Drug Absorption in the Small Intestine. <i>Takanori Akazawa, Shinpei Yoshida, Shuichi Ohnishi, Takushi Kanazu, Makoto Kawai, and Koji Takahashi</i>	1497
Humanized <i>UGT1</i> Mice, Regulation of <i>UGT1A1</i> , and the Role of the Intestinal Tract in Neonatal Hyperbilirubinemia and Breast Milk-Induced Jaundice. <i>Shujuan Chen and Robert H. Tukey</i>	1745	☐ Relationship between In Vivo CYP3A4 Activity, CYP3A5 Genotype, and Systemic Tacrolimus Metabolite/Parent Drug Ratio in Renal Transplant Recipients and Healthy Volunteers. <i>Thomas Vanhove, Hylke de Jonge, Henriëtte de Loor, Marlies Oorts, Jan de Hoon, Anton Pohanka, Pieter Annaert, and Dirk R. J. Kuypers</i>	1507
☐ Characterization of P-Glycoprotein Humanized Mice Generated by Chromosome Engineering Technology: Its Utility for Prediction of Drug Distribution to the Brain in Humans. <i>Yuki Yamasaki, Kaoru Kobayashi, Fuka Okuya, Naoyo Kajitani, Kanako Kazuki, Satoshi Abe, Shoko Takehara, Shingo Ito, Seiryu Ogata, Tatsuki Uemura, Sumio Ohtsuki, Genki Minegishi, Hidetaka Akita, Kan Chiba, Mitsuo Oshimura, and Yasuhiro Kazuki</i>	1756	Effect of Celecoxib on Differentiation of Human Induced Pluripotent Stem Cells into Hepatocytes Involves STAT5 Activation. <i>Hiroki Okumura, Anna Nakanishi, Tadahiro Hashita, Takahiro Iwao, and Tamihide Matsunaga</i>	1519
☐ Evaluation of Organic Anion Transporter 1A2-knock-in Mice as a Model of Human Blood-brain Barrier. <i>Yamato Sano, Tadahaya Mizuno, Tatsuki Mochizuki, Yasuo Uchida, Mina Umetsu, Tetsuya Terasaki, and Hiroyuki Kusuvara</i>	1767	Retinal Cholesterol Content Is Reduced in Simvastatin-Treated Mice Due to Inhibited Local Biosynthesis Albeit Increased Uptake of Serum Cholesterol. <i>Natalia Mast, Ilya R. Bederman, and Irina A. Pikuleva</i>	1528
CRISPR-Cas9: A New Addition to the Drug Metabolism and Disposition Tool Box. <i>M. Karlgren, I. Simoff, M. Keiser, S. Oswald, and P. Artursson</i>	1776	☐ Circadian Regulation of Hepatic Cytochrome P450 2a5 by Peroxisome Proliferator-Activated Receptor γ . <i>Jiangming Deng, Lianxia Guo, and Baojian Wu</i>	1538
Mouse Population-Based Approaches to Investigate Adverse Drug Reactions. <i>Merrie Mosedale</i>	1787	☐ Biotransformation of Finerenone, a Novel Nonsteroidal Mineralocorticoid Receptor Antagonist, in Dogs, Rats, and Humans, In Vivo and In Vitro. <i>Michael Gerisch, Roland Heinig, Anna Engelen, Dieter Lang, Peter Kolkhof, Martin Radtke, Johannes Platzek, Kai Lovis, Gabriele Rohde, and Thomas Schwarz</i>	1546
COMMENTARY		☐ Accurate Estimation of In Vivo Inhibition Constants of Inhibitors and Fraction Metabolized of Substrates with Physiologically Based Pharmacokinetic Drug-Drug Interaction Models Incorporating Parent Drugs and Metabolites of Substrates with Cluster Newton Method. <i>Kenta Yoshida, Kazuya Maeda, Akihiko Konagaya, and Hiroyuki Kusuvara</i>	1805
Finding T_{max} and C_{max} in Multicompartmental Models. <i>Yi Rang Han, Ping I. Lee, and K. Sandy Pang</i>	1796		
ARTICLES			
☐ Trend Analysis of a Database of Intravenous Pharmacokinetic Parameters in Humans for 1352 Drug Compounds. <i>Franco Lombardo, Giuliano Berellini, and R. Scott Obach</i>	1466		
Gene-by-Environment Interaction of Bcrp ^{-/-} and Methionine- and Choline-Deficient Diet-Induced Nonalcoholic Steatohepatitis Alters SN-38 Disposition. <i>Erica L. Toth, Hui Li, Anika L. Dzierlenga,</i>			

Equilibrative Nucleoside Transporter 1 (ENT1, *SLC29A1*) Facilitates Transfer of the Antiretroviral Drug Abacavir across the Placenta. *Lukas Cervený, Zuzana Ptacková, Martina Cecková, Rona Karahoda, Sara Karbanová, Lucie Jirasková, Susan L. Greenwood, Jocelyn D. Glazier, and Frantisek Staud 1817*

☐ Health-Relevant Phenotypes in the Offspring of Mice Given CAR Activators Prior to Pregnancy. *Karin Dietrich, Jan Baumgart, Leonid Eshkind, Lea Reuter, Ute Gödtel-Armbrust, Elke Butt, Michael Musheev, Federico Marini, Piyush More, Tanja Grosser, Christof Niehrs, Leszek Wojnowski, and Marianne Mathäs 1827*

SHORT COMMUNICATIONS

☐ Mouse Hepatomas with *Ha-ras* and *B-raf* Mutations Differ in Mitogen-Activated Protein Kinase Signaling and Response to Constitutive Androstane Receptor Activation. *Albert Braeuning, Ferdinand Kollotzek, Eva Zeller, Thomas Knorpp, Markus F. Templin, and Michael Schwarz 1462*

☐ Brain Uptake of [¹³C] and [¹⁴C]Sucrose Quantified by Microdialysis and Whole Tissue Analysis in Mice. *Faleh Alqahtani, Ekram Ahmed Chowdhury, Raktima Bhattacharya, Behnam Noorani, Reza Mehvar, and Ulrich Bickel 1514*

☐ Supplemental material is available online at <http://dmd.aspetjournals.org>.

About the cover: Absence of Bcrp leads to higher absorption of PhA in enterocytes. See the article by Yasuda et al. (<https://doi.org/10.1124/dmd.118.083584>).