

DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

February 2018

Vol. 46, No. 2

CONTENTS

EDITORIAL

Jeffrey C. Stevens 88

ARTICLES

Estimation of Circulating Drug Metabolite Exposure in Human Using In Vitro Data and Physiologically Based Pharmacokinetic Modeling: Example of a High Metabolite/Parent Drug Ratio. *R. Scott Obach, Jian Lin, Emi Kimoto, Sridhar Duvvuri, Timothy Nicholas, Eugene P. Kadar, Larry M. Tremaine, and Aarti Sawant-Basak* 89

Pregnancy Increases Norbuprenorphine Clearance in Mice by Induction of Hepatic Glucuronidation. *Michael Z. Liao, Chunying Gao, Brian R. Phillips, Naveen K. Neradugomma, Lyrialle W. Han, Deepak Kumar Bhatt, Bhagwat Prasad, Danny D. Shen, and Qingcheng Mao* 100

Simultaneous Physiologically Based Pharmacokinetic (PBPK) Modeling of Parent and Active Metabolites to Investigate Complex CYP3A4 Drug-Drug Interaction Potential: A Case Example of Midostaurin. *Helen Gu, Catherine Dutreix, Sam Rebello, Taoufik Ouatas, Lai Wang, Dung Yu Chun, Heidi J. Einolf, and Handan He* 109

Effect of Probiotics on Pharmacokinetics of Orally Administered Acetaminophen in Mice. *Jeon-Kyung Kim, Min Sun Choi, Jin-Ju Jeong, Su-Min Lim, In Sook Kim, Hye Hyun Yoo, and Dong-Hyun Kim* . . . 122

The JAK1/2 Inhibitor Ruxolitinib Reverses Interleukin-6-Mediated Suppression of Drug-Detoxifying Proteins in Cultured Human Hepatocytes. *Marie Febvre-James, Arnaud Bruyère, Marc Le Vée, and Olivier Fardel* . . 131

Clonidogrel Carboxylic Acid Glucuronidation is Mediated Mainly by UGT2B7, UGT2B4, and UGT2B17: Implications for Pharmacogenetics and Drug-Drug Interactions. *Helinä Kahma, Anne M. Filppula, Mikko Neuvonen, E. Katriina Tarkiainen, Aleksu Tornio, Mikko T. Holmberg, Matti K. Itkonen, Moshe Finel, Pertti J. Neuvonen, Mikko Niemi, and Janne T. Backman* 141

Toxicokinetics and Physiologically Based Pharmacokinetic Modeling of the Shellfish Toxin Domoic Acid in Nonhuman Primates. *Jing Jing, Rebekah Petroff, Sara Shum, Brenda Crouthamel, Ariel R. Topletz, Kimberly S. Grant, Thomas M. Burbacher, and Nina Isoherranen* 155

Quantitative Expression of Hepatobiliary Transporters and Functional Uptake of Substrates in Hepatic Two-Dimensional Sandwich Cultures: A Comparative Evaluation of Upcyte and Primary Human Hepatocytes. *Michelle Schaefer, Gaku Morinaga, Akiko Matsui, Gerhard Schänzle, Daniel Bischoff, and Roderich D. Süßmuth* 166

Discovery and Validation of Pyridoxic Acid and Homovanillic Acid as Novel Endogenous Plasma Biomarkers of Organic Anion Transporter (OAT) 1 and OAT3 in Cynomolgus Monkeys. *Hong Shen, David M. Nelson, Regina V. Oliveira, Yueping Zhang, Colleen A. Mcnaney, Xiaomei Gu, Weiqi Chen, Ching Su, Michael D. Reily, Petia A. Shipkova, Jinping Gan, Yurong Lai, Punit Marathe, and W. Griffith Humphreys* 178

Downloaded from dnd.aspetjournals.org at ASPET Journals on July 21, 2018

DRUG METABOLISM & DISPOSITION

Continued on next page

- ☐ Transporter Expression in Noncancerous and Cancerous Liver Tissue from Donors with Hepatocellular Carcinoma and Chronic Hepatitis C Infection Quantified by LC-MS/MS Proteomics. *Sarah Billington, Adrian S. Ray, Laurent Salphati, Guangqing Xiao, Xiaoyan Chu, W. Griffith Humphreys, Mingxiang Liao, Caroline A. Lee, Anita Mathias, Cornelis E. C. A. Hop, Christopher Rowbottom, Raymond Evers, Yurong Lai, Edward J. Kelly, Bhagwat Prasad, and Jashvant D. Unadkat . . . 189*

SHORT COMMUNICATION

- Mrp3 Transports Clopidogrel Acyl Glucuronide from the Hepatocytes into Blood. *Jin-Zi Ji, Ting Tai, Bei-Bei Huang, Tong-Tong Gu, Qiong-Yu Mi, and Hong-Guang Xie 151*

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

About the cover: Comparison of plasma concentrations vs time profiles for TBPT, M1 and M2 simulated by PBPK modeling vs actual clinical data. See the article by Obach et al. (dx.doi.org/10.1124/dmd.117.078279).