

DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

January 2012

Vol. 40, No. 1

CONTENTS

SHORT COMMUNICATION

Human Hepatic Cytochrome P450-Specific Metabolism of the Organophosphorus Pesticides Methyl Parathion and Diazinon. *Corie A. Ellison, Yuan Tian, James B. Knaak, Paul J. Kostyniak, and James R. Olson*

1

ARTICLES

A Semiphysiologically Based Pharmacokinetic Modeling Approach to Predict the Dose-Exposure Relationship of an Antiparasitic Prodrug/Active Metabolite Pair. *Grace Zhixia Yan, Claudia N. Generaux, Miyoung Yoon, Rachel B. Goldsmith, Richard R. Tidwell, James E. Hall, Carol A. Olson, Harvey J. Clewell, Kim L. R. Brouwer, and Mary F. Paine*

6

CPY3A4-Mediated Lopinavir Bioactivation and Its Inhibition by Ritonavir. *Feng Li, Jie Lu, and Xiaochao Ma*

18

In Vitro Glucuronidation of the Antibacterial Triclocarban and Its Oxidative Metabolites. *N. H. Schebb, B. Franze, R. Maul, A. Ranganathan, and B. D. Hammock*

25

Bupropion Hydroxylation as a Selective Marker of Rat CYP2B1 Catalytic Activity. *Dumrongsak Pekthong, Coraline Desbans, Hélène Martin, and Lysiane Richert*

32

Effects of Chronic Renal Failure on Brain Drug Transporters in Rats. *Judith Naud, Louis-Philippe Laurin, Josée Michaud, Stéphanie Beauchemin, François A. Leblond, and Vincent Pichette*

39

Prediction of CYP2D6 Drug Interactions from In Vitro Data: Evidence for Substrate-Dependent Inhibition. *Brooke M. VandenBrink, Robert S. Foti, Dan A. Rock, Larry C. Wienkers, and Jan L. Wahlstrom*

47

Potential Contribution of Cytochrome P450 2B6 to Hepatic 4-Hydroxycyclophosphamide Formation In Vitro and In Vivo. *Brianne S. Raccor, Adam J.*

Claessens, Jean C. Dinh, Julie R. Park, Douglas S. Hawkins, Sushma S. Thomas, Karen W. Makar, Jeannine S. McCune, and Rheem A. Totah

54

γ -Hydroxybutyrate Blood/Plasma Partitioning: Effect of Physiologic pH on Transport by Monocarboxylate Transporters. *Bridget L. Morse, Melanie A. Felmlee, and Marilyn E. Morris*

64

Debrisoquine Metabolism and CYP2D Expression in Marmoset Liver Microsomes. *Brian R. Cooke, S. W. Annie Bligh, Z. Richard Cybulski, Costas Ioannides, and Michael Hall*

70

Prediction of Human Metabolism of FK3453 by Aldehyde Oxidase Using Chimeric Mice Transplanted with Human or Rat Hepatocytes. *Seigo Sanoh, Kazuyoshi Nozaki, Hidetsugu Murai, Shigeyuki Terashita, Toshio Teramura, and Shigeru Ohta*

76

Simultaneous Absolute Protein Quantification of Transporters, Cytochromes P450, and UDP-Glucuronosyltransferases as a Novel Approach for the Characterization of Individual Human Liver: Comparison with mRNA Levels and Activities. *Sumio Ohtsuki, Olaf Schaefer, Hirotaka Kawakami, Tae Inoue, Stephanie Liehner, Asami Saito, Naoki Ishiguro, Wataru Kishimoto, Eva Ludwig-Schwellinger, Thomas Ebner, and Tetsuya Terasaki*

83

Absolute Quantification and Differential Expression of Drug Transporters, Cytochrome P450 Enzymes, and UDP-Glucuronosyltransferases in Cultured Primary Human Hepatocytes. *Olaf Schaefer, Sumio Ohtsuki, Hirotaka Kawakami, Tae Inoue, Stephanie Liehner, Asami Saito, Atsushi Sakamoto, Naoki Ishiguro, Takehisa Matsumaru, Tetsuya Terasaki, and Thomas Ebner*

93

Comparison of Cryopreserved HepaRG Cells with Cryopreserved Human Hepatocytes for Prediction of Clearance for 26 Drugs. *Ugo Zanelli, Nicola Pasquale Caradonna, David Hallifax, Elisa Turlizzi, and J. Brian Houston*

104

Continued on next page

Frequency of Undetected <i>CYP2D6</i> Hybrid Genes in Clinical Samples: Impact on Phenotype Prediction. <i>John Logan Black III, Denise L. Walker, Dennis J. O'Kane, and Maria Harmandayan</i>	111	Species-Dependent and Receptor-Selective Action of Bilobalide on the Function of Constitutive Androstane Receptor and Pregnane X Receptor. <i>Aik Jiang Lau, Guixiang Yang, Ganesh Rajaraman, Christie C. Baucom, and Thomas K. H. Chang</i>	178
☐ Cytoprotective Effect of 20(S)-Rg3 on Benzo[<i>a</i>]pyrene-Induced DNA Damage. <i>Po Ying Poon, Hoi Hin Kwok, Patrick Y. K. Yue, Mildred S. M. Yang, Nai Ki Mak, Chris K. C. Wong, and Ricky N. S. Wong</i>	120	☐ Effects of Omeprazole and Genetic Polymorphism of <i>CYP2C19</i> on the Clopidogrel Active Metabolite. <i>Xavier Boulenc, Nassim Djebli, Juan Shi, Laurent Perrin, William Brian, Robert Van Horn, and Fabrice Hurbin</i>	187
☐ In Vitro Inhibition of the Bile Salt Export Pump Correlates with Risk of Cholestatic Drug-Induced Liver Injury in Humans. <i>Sarah Dawson, Simone Stahl, Nikki Paul, Jane Barber, and J. Gerald Kenna</i>	130	Phenotype of the Most Common “Slow Acetylator” Arylamine <i>N</i> -Acetyltransferase 1 Genetic Variant (<i>NAT1*14B</i>) Is Substrate-Dependent. <i>Lori M. Millner, Mark A. Doll, Jian Cai, J. Christopher States, and David W. Hein</i>	198
Human Metabolism of Lapatinib, a Dual Kinase Inhibitor: Implications for Hepatotoxicity. <i>Stephen Castellino, Michael O'Mara, Kevin Koch, David J. Borts, Gary D. Bowers, and Christopher MacLauchlin</i>	139	Regulation of Cytochrome P450 4F11 by Nuclear Transcription Factor- κ B. <i>Jordan C. Bell and Henry W. Strobel</i>	205
☐ Interindividual Variability in Gene Expression Profiles in Human Hepatocytes and Comparison with HepaRG Cells. <i>Alexandra Rogue, Carine Lambert, Catherine Spire, Nancy Claude, and André Guillouzo</i>	151	Brain Uptake of the Drug of Abuse γ -Hydroxybutyric Acid in Rats. <i>Samuel A. Roiko, Melanie A. Felmlee, and Marilyn E. Morris</i>	212
Prediction of Relative In Vivo Metabolite Exposure from In Vitro Data Using Two Model Drugs: Dextromethorphan and Omeprazole. <i>Justin D. Lutz and Nina Isoherranen</i>	159	☐ Identification of the Oxidative and Conjugative Enzymes Involved in the Biotransformation of Brivanib. <i>Jiachang Gong, Jinping Gan, and Ramaswamy A. Iyer</i>	219
Acetaminophen-Induced Hepatotoxicity in a Liver Tissue Model Consisting of Primary Hepatocytes Assembling around an Endothelial Cell Network. <i>Yu Toyoda, Miho Tamai, Kasumi Kashikura, Shunsuke Kobayashi, Yoichi Fujiyama, Tomoyoshi Soga, and Yoh-ichi Tagawa</i>	169		
		ERRATUM	
		Correction to “Cytochrome P450 Pig Liver Pie: Determination of Individual Cytochrome P450 Isoform Contents in Microsomes from Two Pig Livers Using Liquid Chromatography in Conjunction with Mass Spectroscopy”	227

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

About the cover: Comparison between $C_{\max, u}$, DILI class, and potency of hBSEP inhibition for 85 pharmaceuticals. See the article by Dawson et al. on page 130 of this issue.