

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

January 2008

Vol. 36, No. 1

## CONTENTS

### CENTENNIAL PERSPECTIVE

- The Development of Drug Metabolism Research as Expressed in the Publications of ASPET: Part 1, 1909–1958. *Patrick J. Murphy* . . . . . 1

### SHORT COMMUNICATIONS

- Osetamivir (Tamiflu) Efflux Transport at the Blood-Brain Barrier via P-Glycoprotein. *Kaori Morimoto, Masanori Nakakariya, Yoshiyuki Shirasaka, Chihaya Kakinuma, Takuya Fujita, Ikumi Tamai, and Takuo Ogihara* . . . . . 6

- The Effects of *ABCB1* 3'-Untranslated Region Variants on mRNA Stability. *Jason M. Gow, Leslie W. Chinn, and Deanna L. Kroetz* . . . . . 10

### ARTICLES

- Gender Differences in mRNA Expression of ATP-Binding Cassette Efflux and Bile Acid Transporters in Kidney, Liver, and Intestine of 5/6 Nephrectomized Rats. *Hong Lu and Curtis Klaassen* . . . . . 16

- Disposition and Metabolism of [<sup>14</sup>C]Brasofensine in Rats, Monkeys, and Humans. *Mingshe Zhu, Daisy B. Whigan, Shu Y. Chang, and Randy C. Dockens* . . . . . 24

- Pharmacokinetics and Metabolism of <sup>14</sup>C-Brivaracetam, a Novel SV2A Ligand, in Healthy Subjects. *Maria Laura Sargentini-Maier, Pascal Espié, Alain Coquette, and Armel Stockis* . . . . . 36

- Glucuronidation of Mycophenolic Acid by Wistar and Mrp2-Deficient TR<sup>-</sup> Rat Liver Microsomes. *Ian S. Westley, Raymond G. Morris, Allan M. Evans, and Benedetta C. Sallustio* . . . . . 46

- Hepatic UDP-Glucuronosyltransferases Responsible for Glucuronidation of Thyroxine in Humans.

- Yoshihisa Kato, Shin-ichi Ikushiro, Yoshikazu Emi, Sekihiro Tamaki, Hiroshi Suzuki, Toshiyuki Sakaki, Shizuo Yamada, and Masakuni Degawa* . . . . . 51

- Regulation of CYP2A6 Protein Expression by Skatole, Indole, and Testicular Steroids in Primary Cultured Pig Hepatocytes. *Gang Chen, Rebecca-Ayme Cue, Kerstin Lundstrom, Jeffrey D. Wood, and Olena Doran* . . . . . 56

- Multidrug Resistance-Associated Protein 2 Is Primarily Responsible for the Biliary Excretion of Fexofenadine in Mice. *Xianbin Tian, Maciej J. Zamek-Gliszczynski, Jun Li, Arlene S. Bridges, Ken-ichi Nezasa, Nita J. Patel, Thomas J. Raub, and Kim L. R. Brouwer* . . . . . 61

- Pharmacokinetics and Metabolic Profile of Free, Conjugated, and Total Silymarin Flavonolignans in Human Plasma after Oral Administration of Milk Thistle Extract. *Zhiming Wen, Todd E. Dumas, Sarah J. Schrieber, Roy L. Hawke, Michael W. Fried, and Philip C. Smith* . . . . . 65

- Trimethoprim and the *CYP2C8\*3* Allele Have Opposite Effects on the Pharmacokinetics of Pioglitazone. *Aleksi Tornio, Mikko Niemi, Pertti J. Neuvonen, and Janne T. Backman* . . . . . 73

- Subdomain IIIA of Dog Albumin Contains a Binding Site Similar to Site II of Human Albumin. *Ken-ichi Kaneko, Hikaru Fukuda, Victor Tuan Giam Chuang, Keishi Yamasaki, Kohichi Kawahara, Hitoshi Nakayama, Ayaka Suenaga, Toru Maruyama, and Masaki Otagiri* . . . . . 81

- Investigation of Regional Mechanisms Responsible for Poor Oral Absorption in Humans of a Modified Release Preparation of the  $\alpha$ -Adrenoreceptor

Continued on next page

Antagonist, 4-Amino-6,7-dimethoxy-2- (5-methanesulfonamido-1,2,3,4 tetrahydroisoquinol-2-yl)-5- (2-pyridyl)quinazoline (UK-338,003): The Rational Use of ex Vivo Intestine to Predict in Vivo Absorption. <i>A. Collett, R. H. Stephens, M. D. Harwood, M. Humphrey, L. Dallman, J. Bennett, J. Davis, G. L. Carlson, and G. Warhurst</i> . . . . .	<b>87</b>	<i>Iwanaga, Roy L. Hawke, Erin G. Schuetz, Paul B. Watkins, Kenneth E. Thummel, and Mary F. Paine</i> . . . . .	<b>146</b>
Regulation of Hepatic Drug-Metabolizing Enzyme Genes by Toll-Like Receptor 4 Signaling Is Independent of Toll-Interleukin 1 Receptor Domain-Containing Adaptor Protein. <i>Romi Ghose, Damara White, Tao Guo, Jesus Vallejo, and Saul J. Karpen</i> . . . . .	<b>95</b>	Mechanism-Based Inactivation of Lung-Selective Cytochrome P450 CYP2F Enzymes. <i>Jaya S. Kartha and Garold S. Yost</i> . . . . .	<b>155</b>
Permeability, Transport, and Metabolism of Solutes in Caco-2 Cell Monolayers: A Theoretical Study. <i>Huadong Sun and K. Sandy Pang</i> . . . . .	<b>102</b>	Identification of Cytochrome P450 Enzymes Involved in the Metabolism of the New Designer Drug 4'-Methyl- $\alpha$ -pyrrolidinobutyrophenone. <i>Frank T. Peters, Markus R. Meyer, Denis S. Theobald, and Hans H. Maurer</i> . . . . .	<b>163</b>
Effects of Chronic Renal Failure on Liver Drug Transporters. <i>Judith Naud, Josée Michaud, Francois A. Leblond, Stéphane Lefrancois, Alain Bonnardeaux, and Vincent Pichette</i> . . . . .	<b>124</b>	Novel Single Nucleotide Polymorphisms in the Promoter and Intron 1 of Human Pregnane X Receptor/NR1I2 and Their Association with CYP3A4 Expression. <i>Jatinder Lamba, Vishal Lamba, Stephen Strom, Raman Venkataramanan, and Erin Schuetz</i> . . . . .	<b>169</b>
Effect of Resveratrol on 17 $\beta$ -Estradiol Sulfation by Human Hepatic and Jejunal S9 and Recombinant Sulfotransferase 1E1. <i>Anna M. Furimsky, Carol E. Green, Lewanne E. Hunt Sharp, Paul Catz, Araba A. Adjei, Toufan Parman, Izet M. Kapetanovic, Richard M. Weinshilboum, and Lalitha V. Iyer</i> . . . . .	<b>129</b>	Transcription Factor and Drug-Metabolizing Enzyme Gene Expression in Lymphocytes from Healthy Human Subjects. <i>Gérard Siest, Elise Jeannesson, Jean-Brice Marteau, Anastasia Samara, Bé-rangère Marie, Michèle Pfister, and Sophie Visvikis-Siest</i> . . . . .	<b>182</b>
HepaRG Cells as an in Vitro Model for Evaluation of Cytochrome P450 Induction in Humans. <i>Kajsa P. Kanebratt and Tommy B. Andersson</i> . . . . .	<b>137</b>	Transport and Metabolism of Ferulic Acid through the Colonic Epithelium. <i>Laure Poquet, Michael N. Clifford, and Gary Williamson</i> . . . . .	<b>190</b>
The Influence of CYP3A5 Expression on the Extent of Hepatic CYP3A Inhibition Is Substrate-Dependent: An in Vitro-in Vivo Evaluation. <i>Nina Isoherranen, Shana R. Ludington, Raymond C. Givens, Jatinder K. Lamba, Susan N. Pusek, E. Claire Dees, David K. Blough, Kazunori</i>		Localization of P-gp (Abcb1) and Mrp2 (Abcc2) in Freshly Isolated Rat Hepatocytes. <i>Daniel A. J. Bow, Jennifer L. Perry, David S. Miller, John B. Pritchard, and Kim L. R. Brouwer</i> . . . . .	<b>198</b>
		<b>ERRATUM</b>	
		Correction to "Use of Isolated Hepatocyte Preparations for Cytochrome P450 Inhibition Studies: Comparison with Microsomes for K <sub>i</sub> Determination". . . . .	<b>203</b>

About the cover: Cister analysis of PXR (Fig. 1D). Regions with clusters of binding sites for liver-enriched transcription factors and hormone receptors are indicated. See article by Lamba et al. on page 169 of this issue.