CONTENTS

SHORT COMMUNICATIONS

Expression and Functional Analysis of CYP2D6.24, CYP2D6.26, CYP2D6.27, and CYP2D7 Isozymes. Wei-Yan Zhang, You-Bin Tu, Robert L. Haining, and Ai-Ming Yu .......................... 1


Is 1-Aminobenzotriazole an Appropriate in Vitro Tool as a Nonspecific Cytochrome P450 Inactivator? Collette D. Linder, Nicole A. Renaud, and J. Matthew Hutzler ........................................... 10


ARTICLES

Drug Interactions of Thalidomide with Midazolam and Cyclosporine A: Heterotropic Cooperativity of Human Cytochrome P450 3A5. Yusuke Okada, Norie Murayama, Chihiro Yanagida, Makiko Shimizu, F. Peter Guengerich, and Hiroshi Yamazaki ..................... 18

Cytoskeleton Interruption in Human Hepatoma HepG2 Cells Induced by Ketamine Occurs Possibly through Suppression of Calcium Mobilization and Mitochondrial Function. Hua-Chia Chang, Ta-Liang Chen, and Rui-Ming Chen ...................... 24

Determination of mRNA Expression of Human UDP-Glucuronosyltransferases and Application for Localization in Various Human Tissues by Real-Time Reverse Transcriptase-Polymerase Chain Reaction. Shuji Ohno and Shizuo Nakajin .... 32

Key Amino Acid Residues Responsible for the Differences in Substrate Specificity of Human UDP-Glucuronosyltransferase (UGT)1A9 and UGT1A8. Ryoichi Fujiwara, Miki Nakajima, Hiroyuki Yamakawa, and Tsuyoshi Yokoi ......................... 41

The Multiple Depletion Curves Method Provides Accurate Estimates of Intrinsic Clearance (CLint), Maximum Velocity of the Metabolic Reaction (Vmax), and Michaelis Constant (Km): Accuracy and Robustness Evaluated through Experimental Data and Monte Carlo Simulations. Erik Sjögren, Hans Lennermä, Tommy B. Andersson, Johan Gräsö, and Ulf Bredberg ................... 47

Mechanism-Based Inactivation of Cytochrome P450 2C9 by Tienilic Acid and ([3H]11006)-Suprofen: A Comparison of Kinetics and Probe Substrate Selection. J. Matthew Hutzler, Larissa M. Balogh, Michael Zientek, Vikas Kumar, and Timothy S. Tracy .... 59

Absolute Difference of Hepatobiliary Transporter Multidrug Resistance-Associated Protein (MRP2/Mrp2) in Liver Tissues and Isolated Hepatocytes from Rat, Dog, Monkey, and Human. Na Li, Yiqun Zhang, Fingnet Hua, and Yurong Lai .......................... 66

Apixaban Metabolism and Pharmacokinetics after Oral Administration to Humans. Nirmala Ragavan, Charles E. Frost, Zhigang Yu, Kan He, Haiying Zhang, W. Griffith Humphreys, Donald Pinto, Shiyuan Chen, Samuel Bonacorsi, Pancras C. Wong, and Donglu Zhang .... 74

Continued on next page


Role of Enzymatic N-Hydroxylation and Reduction in Flutamide Metabolite-Induced Liver Toxicity. Masato Ohbuchi, Masaaki Miyata, Daichi Nagai, Miki Shimada, Kouichi Yoshinari, and Yasushi Yamazoe .................... 97

Circadian Expression Profiles of Drug-Processing Genes and Transcription Factors in Mouse Liver. Yu-Kun Jennifer Zhang, Ronnie L. Yeager, and Curtis D. Klaassen .................... 106

Three Patterns of Cytochrome P450 Gene Expression during Liver Maturation in Mice. Steven N. Hart, Yue Cui, Curtis D. Klaassen, and Xiao-bo Zhong .................... 116

Effect of Oral Ketoconazole on Oral and Intravenous Pharmacokinetics of Simvastatin and Its Acid in Cynomolgus Monkeys. Akihito Ogasawara, Masahiro Utoh, Kazuo Nii, Ayumi Ueda, Takahiro Yoshikawa, Toshiyuki Kume, and Koichiro Fukuzaki .................... 122

Transport of Diclofenac by Breast Cancer Resistance Protein (ABCG2) and Stimulation of Multidrug Resistance Protein 2 (ABCC2)-Mediated Drug Transport by Diclofenac and Benzbramoreone. Jurjen S. Lagas, Cornelia M. M. van der Kruiszen, Koen van de Wetering, Jos H. Beijnen, and Alfred H. Schinkel .................... 129


High-Affinity Interaction of Sartans with H+/Peptide Transporters. Ilka Knüttner, Gabor Kottra, Wiebke Fischer, Hannelore Daniel, and Matthias Brandsch .................... 143

Prediction of the Effect of Erythromycin, Diltiazem, and Their Metabolites, Alone and in Combina-
tion, on CYP3A4 Inhibition. Xin Zhang, David R. Jones, and Stephen D. Hall .................... 150


Quantitation of Human Cytochrome P450 2D6 Protein with Immunoblot and Mass Spectrometry Analysis. Ai-Ming Yu, Jun Qu, Melanie A. Felmlee, Jin Cao, and Xi-Ling Jiang .................... 170


Disparity in Intestine Disposition between Formed and Preformed Metabolites and Implications: A Theoretical Study. Huadong Sun and K. Sandy Pang .................... 187

Tissue Distribution, Gender-Divergent Expression, Ontogeny, and Chemical Induction of Multidrug Resistance Transporter Genes (Mdr1a, Mdr1b, Mdr2) in Mice. Yue Julia Cui, Xingguo Cheng, Yi Miao Weaver, and Curtis D. Klaassen .................... 203


 In Vitro Metabolism of Pyrethroid Pesticides by Rat and Human Hepatic Microsomes and Cytochrome P450 Isoforms. Edward J. Scollon, James M. Starr, Stephen J. Godin, Michael J. DeVito, and Michael F. Hughes .................... 221

 Effect of Aging on Glucuronidation of Valproic Acid in Human Liver Microsomes and the Role of UDP Glucuronosyltransferase UGT1A4, UGT1A8, and UGT1A10. Upeneda A. Argikar and Rory P. Remmel .................... 229

 Discovering Plausible Mechanistic Details of Hepatic Drug Interactions. Tai Ning Lam and C. Anthony Hunt .................... 237

[Supplemental material is available online at http://dmd.aspetjournals.org.]

About the cover: Docking simulation of thalidomide into a reported structure of P450 3A4 (A) and a homology model of P450 3A5 (B). See article by Okada et al. on page 18 of this issue.