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


Key Amino Acid Residues Responsible for the Differences in Substrate Specificity of Human UDP-Glucuronosyltransferase (UGT)1A9 and UGT1A8. Ryoichi Fujiiwara, Miki Nakajima, Hiroyuki Yamana, Go, and Tsuyoshi Yokoj .........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 Lennermå, Tommy B. Andersson, Johan Gräsjo, and Ulf Bredberg ..........47

Mechanism-Based Inactivation of Cytochrome P450 2C9 by Tienilic Acid and (±)-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 Multi-drug Resistance-Associated Protein (MRP2/Mrp2) in Liver Tissues and Isolated Hepatocytes from Rat, Dog, Mouse, and Human. Na Li, Yiqun Zhang, Fengmei Hua, and Yurong Lai ..........66

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

Continued on next page
Prediction of Drug Clearance by Glucuronidation from In Vitro Data: Use of Combined Cytochrome P450 and UDP-Glucuronosyltransferase Cofactors in Alumemticin-Activated Human Liver Microsomes. Peter J. Kilford, Rowan Stringer, Bindi Sohal, J. Brian Houston, and Aleksandra Galetin .......................... 82


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


Transport of Diclofenac by Breast Cancer Resistance Protein (ABCG2) and Stimulation of Multidrug Resistance Protein 2 (ABCC2)-Mediated Drug Transport by Diclofenac and Benz bromarone. Jurjen S. Lagus, Cornelia M. M. van der Kuijzen, Koen van de Watering, Jos H. Beijnen, and Alfred H. Schinkel .................. 129

Microdialysis Evaluation of Amotoxetine Brain Penetration and Central Nervous System Pharmacokinetics in Rats. William Kielbasai, J. Cory Kalvass, and Robert Stratford ............................. 137

High-Affinity Interaction of Sartans with H+/Peptide Transporters. Ilka Knüter, 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. Feldman, 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. Upendra A. Argikar and Rory P. Remmel ..................... 229

Discovering Plausible Mechanistic Details of Hepatic Drug Interactions. Tai Ning Lai 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 3AA4 (A) and a homology model of P450 3A5 (B). See article by Okada et al. on page 18 of this issue.