

DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

June 2008

Vol. 36, No. 6

CONTENTS

CENTENNIAL PERSPECTIVE

- The Development of Drug Metabolism Research as Expressed in the Publications of ASPET: Part 2, 1959–1983. *Patrick J. Murphy* **981**

SHORT COMMUNICATIONS

- The Contributions of Cytochromes P450 3A4 and 3A5 to the Metabolism of the Phosphodiesterase Type 5 Inhibitors Sildenafil, Udenafil, and Vardenafil. *Hei-Young Ku, Hee-Jeong Ahn, Kyung-Ah Seo, Hyunmi Kim, Minkyung Oh, Soo Kyung Bae, Jae-Gook Shin, Ji-Hong Shon, and Kwang-Hyeon Liu* **986**

- Aldo-Keto Reductase 1C2 Fails to Metabolize Doxorubicin and Daunorubicin in Vitro. *Ryan H. Takahashi, Onkar S. Bains, Tom A. Pfeifer, Thomas A. Grigliatti, Ronald E. Reid, and K. Wayne Riggs* **991**

ARTICLES

- Quantitative Investigation of the Role of Breast Cancer Resistance Protein (*Bcrp/Abcg2*) in Limiting Brain and Testis Penetration of Xenobiotic Compounds. *Junichi Enokizono, Hiroyuki Kusuhara, Atsushi Ose, Alfred H. Schinkel, and Yuichi Sugiyama* **995**

- Identification of Human Liver Cytochrome P450 Isoforms Involved in Autoinduced Metabolism of the Antiangiogenic Agent (*Z*)-5-[(1,2-Dihydro-2-oxo-3*H*-indol-3-ylidene)methyl]-2,4-dimethyl-1*H*-pyrrole-3-propanoic Acid (TSU-68). *Ryuichi Kitamura, Hisae Asanoma, Sekio Nagayama, and Masaki Otagiri* **1003**

- Identification and Characterization of Potent CYP2B6 Inhibitors in Woohwangcheongsimwon Suspen-

- sion, an Herbal Preparation Used in the Treatment and Prevention of Apoplexy in Korea and China. *Hyunmi Kim, Kwon-Bok Kim, Hei-Young Ku, Soo Jin Park, Hoon Choi, Joon-Kwan Moon, Byeoung-Soo Park, Jeong-Han Kim, Sung Su Yea, Choong-Hwan Lee, Hye Suk Lee, Jae-Gook Shin, and Kwang-Hyeon Liu* **1010**

- Comparison of the Bioactivation Potential of the Antidepressant and Hepatotoxin Nefazodone with Aripiprazole, a Structural Analog and Marketed Drug. *Jonathan N. Bauman, Kosea S. Frederick, Aarti Sawant, Robert L. Walsky, Loretta M. Cox, Ronald S. Obach, and Amit S. Kalgutkar* **1016**

- Hepatic Uptake and Excretion of (–)-*N*-{2-[(*R*)-3-(6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinoline-2-carbonyl)piperidino]ethyl}-4-fluorobenzamide (YM758), a Novel If Channel Inhibitor, in Rats and Humans. *Ken-ichi Umehara, Megumi Iwai, Yasuhisa Adachi, Takafumi Iwatsubo, Takashi Usui, and Hidetaka Kamimura* **1030**

- Characterization of Cytochrome P450 Protein Expression along the Entire Length of the Intestine of Male and Female Rats. *Doreen Mitschke, Andreas Reichel, Gert Fricker, and Ursula Moening* **1039**

- Comparison of Immortalized Fa2N-4 Cells and Human Hepatocytes as in Vitro Models for Cytochrome P450 Induction. *Niresh Hariparsad, Brian A. Carr, Raymond Evers, and Xiaoyan Chu* **1046**

- The “Albumin Effect” and Drug Glucuronidation: Bovine Serum Albumin and Fatty Acid-Free Human Serum Albumin Enhance the Glucuronidation of UDP-Glucuronosyltransferase (UGT)

Continued on next page

Drug Metabolism and Disposition (ISSN 0090-9556) is published monthly (one volume per year) by the American Society for Pharmacology and Experimental Therapeutics, 9650 Rockville Pike, Bethesda, MD 20814-3995; e-mail: info@aspet.org; Web site: http://www.aspet.org. Periodicals postage paid at Bethesda, MD and at additional mailing offices. POSTMASTER: Send address changes to *Drug Metabolism and Disposition*, 9650 Rockville Pike, Bethesda, MD 20814-3995. Subscription rates: U.S.: \$374.00 for institutions and \$195.00 for non-ASPET members. Outside the U.S.: \$448.00 for institutions and \$269.00 for non-ASPET members. Single copy: \$36.00. GST Tax Number for Canadian subscribers: BN:13489 2330 RT. Indexed or abstracted by *Biochemistry & Biophysics Citation Index®*, *Biological Abstracts*, *BIOSIS Previews Database*, *BioSciences Information Service*, *Current Awareness in Biological Sciences*, *Current Contents®/Life Sciences*, *EMBASE/Excerpta Medica*, *Index Medicus*, *International Pharmaceutical Abstracts*, *Medical Documentation Service®*, *Reference Update®*, *Research Alert®*, *Science Citation Index®*, *SciSearch®*, and *SIIC Data Bases*. Copyright © 2008 by the American Society for Pharmacology and Experimental Therapeutics. All rights reserved. Printed in the U.S.A.

IA9 Substrates but Not UGT1A1 and UGT1A6 Activities. <i>Andrew Rowland, Kathleen M. Knights, Peter I. Mackenzie, and John O. Miners</i>	1056
ATF5 Is a Highly Abundant Liver-Enriched Transcription Factor that Cooperates with Constitutive Androstane Receptor in the Transactivation of <i>CYP2B6</i> : Implications in Hepatic Stress Responses. <i>Maya Pascual, M. José Gómez-Lechón, José V. Castell, and Ramiro Jover</i>	1063
□ P-Glycoprotein Contributes to the Blood-Brain, but Not Blood-Cerebrospinal Fluid, Barrier in a Spontaneous Canine P-Glycoprotein Knockout Model. <i>Katrina L. Mealey, Stephen Greene, Rodney Bagley, John Gay, Russ Tucker, Patrick Gavin, Kari Schmidt, and Frederick Nelson</i>	1073
Forkhead Box A2-Mediated Regulation of Female-Predominant Expression of the Mouse <i>Cyp2b9</i> Gene. <i>Tadahiro Hashita, Tsutomu Sakuma, Mami Akada, Asuka Nakajima, Hirofumi Yamahara, Sumiyo Ito, Hidekazu Takesako, and Nobuo Nemoto</i>	1080
Involvement of Multidrug Resistance-Associated Protein 2 (<i>Abcc2</i>) in Molecular Weight-Dependent Biliary Excretion of β -Lactam Antibiotics. <i>Yukio Kato, Seiko Takahara, Sayaka Kato, Yoshiyuki Kubo, Yoshimichi Sai, Ikumi Tamai, Hikaru Yabuuchi, and Akira Tsuji</i>	1088
Hydroxyitraconazole, Formed During Intestinal First-Pass Metabolism of Itraconazole, Controls the Time Course of Hepatic CYP3A Inhibition and the Bioavailability of Itraconazole in Rats. <i>Sara K. Quinney, Raymond E. Galinsky, Vanida A. Jiyamapa-Serna, Yong Chen, Mitchell A. Hamman, Stephen D. Hall, and Robert E. Kimura</i>	1097
Role of P-Glycoprotein and the Intestine in the Excretion of DPC 333 [(2 <i>R</i>)-2-[(3 <i>R</i>)-3-Amino-3-[4-(2-methylquinolin-4-ylmethoxy)phenyl]-2-oxopyrrolidin-1-yl]- <i>N</i> -hydroxy-4-methylpentanamide] in Rodents. <i>C. Edwin Garner, Eric Solon, Chii-Ming Lai, Jianrong Lin, Gang Luo, Kevin Jones, Jingwu Duan, Carl P. Decicco, Thomas Maduskuie, Stephen E. Mercer, Lian-Shen Gan, Mingxin Qian, Shimoga Prakash, Huey-Shin Shen, and Frank W. Lee</i>	1102
Long-Term Functional Stability of Human HepaRG Hepatocytes and Use for Chronic Toxicity and Genotoxicity Studies. <i>Rozenn Jossé, Caroline Aninat, Denise Glaise, Julie Dumont, Valérie Fessard, Fabrice Morel, Jean-Michel Poul, Christiane Guguen-Guillouzo, and André Guillouzo</i>	1111
Role of Flavin-Containing Monooxygenase in Oxidative Metabolism of Voriconazole by Human Liver Microsomes. <i>Souzan B. Yanni, Pieter P. Annaert, Patrick Augustijns, Arlene Bridges, Yan Gao, Daniel K. Benjamin, Jr., and Dhiren R. Thakker</i>	1119
Integrated in Vitro Analysis for the in Vivo Prediction of Cytochrome P450-Mediated Drug-Drug Interactions. <i>Dermot F. McGinnity, Nigel J. Waters, James Tucker, and Robert J. Riley</i>	1126
Metabolism of Boswellic Acids in Vitro and in Vivo. <i>Phillip Krüger, Rambod Daneshfar, Gunter P. Eckert, Jochen Klein, Dietrich A. Volmer, Ute Bahr, Walter E. Müller, Michael Karas, Manfred Schubert-Zsilavecz, and Mona Abdel-Tawab</i>	1135
<i>N</i> -Demethylation Is a Major Route of 2-Amino-3-Methylimidazo[4,5- <i>f</i>]quinoline Metabolism in Mouse. <i>Vijaya M. Lakshmi, Fong Fu Hsu, and Terry V. Zenser</i>	1143
Predictive Physiologically Based Pharmacokinetic Model for Antibody-Directed Enzyme Prodrug Therapy. <i>Lanyan Fang and Duxin Sun</i>	1153
Comparison of Two Immortalized Human Cell Lines to Study Nuclear Receptor-Mediated CYP3A4 Induction. <i>S. Harmsen, A. S. Koster, J. H. Beijnen, J. H. M. Schellens, and I. Meijerman</i>	1166
Intestinal Human Colon Adenocarcinoma Cell Line LS180 Is an Excellent Model to Study Pregnane X Receptor, but Not Constitutive Androstane Receptor, Mediated CYP3A4 and Multidrug Resistance Transporter 1 Induction: Studies with Anti-Human Immunodeficiency Virus Protease Inhibitors. <i>Anshul Gupta, Ganesh M. Mugundu, Pankaj B. Desai, Kenneth E. Thummel, and Jashvant D. Unadkat</i>	1172
PDZK1 Regulates Two Intestinal Solute Carriers (<i>Slc15a1</i> and <i>Slc22a5</i>) in Mice. <i>Tomoko Sugiura, Yukio Kato, Tomohiko Wakayama, David L. Silver, Yoshiyuki Kubo, Shoichi Iseki, and Akira Tsuji</i>	1181

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

About the cover: Immunohistochemical analysis of PEPT1 expression in the small intestine. See article by Sugiura et al. on page 1181 of this issue.