

DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

September 2007

Vol. 35, No. 9

CONTENTS

SHORT COMMUNICATIONS

- Hepatic Metabolism of MK-0457, a Potent Aurora Kinase Inhibitor: Interspecies Comparison and Role of Human Cytochrome P450 and Flavin-Containing Monooxygenase. *J. E. Ballard, T. Prueksaritanont, and C. Tang* **1447**
- Inhibition of Human Thiopurine S-Methyltransferase by Various Nonsteroidal Anti-inflammatory Drugs in Vitro: A Mechanism for Possible Drug Interactions. *Kersti Oselin and Kaili Anier* **1452**
- Cholesterol-Lowering Effect of Ezetimibe in Uridine Diphosphate Glucuronosyltransferase 1A-Deficient (Gunn) Rats. *Takehito Yamamoto, Kousei Ito, Masashi Honma, Tappei Takada, and Hiroshi Suzuki* **1455**
- Inhibition of P-glycoprotein Activity at the Primate Blood-Brain Barrier Increases the Distribution of Nelfinavir into the Brain but Not into the Cerebrospinal Fluid. *Amal Kaddoumi, Sung-Up Choi, Loren Kinman, Dale Whittington, Che-Chung Tsai, Rodney J.Y. Ho, Bradley D. Anderson, and Jashvant D. Unadkat* **1459**
- Detection of Haptenated Proteins in Organotypic Human Skin Explant Cultures Exposed to Dapsone. *Sanjoy Roychowdhury, Albert E. Cram, Al Aly, and Craig K. Svensson* **1463**

ARTICLES

- ☐ Computational Approaches That Predict Metabolic Intermediate Complex Formation with CYP3A4 (+b₅). *David R. Jones, Sean Ekins, Lang Li, and Stephen D. Hall* **1466**
- ☐ Data-Based Mathematical Modeling of Vectorial Transport across Double-Transfected Polarized

Cells. *Kilian Bartholomé, Maria Rius, Katrin Letschert, Daniela Keller, Jens Timmer, and Dietrich Keppler* **1476**

Kinetic Studies of 25-Hydroxy-19-nor-vitamin D₃ and 1 α ,25-Dihydroxy-19-nor-vitamin D₃ Hydroxylation by CYP27B1 and CYP24A1. *Naoko Urushino, Sachie Nakabayashi, Midori A. Arai, Atsushi Kittaka, Tai C. Chen, Keiko Yamamoto, Keiko Hayashi, Shigeaki Kato, Miho Ohta, Masaki Kamakura, Shinichi Ikushiro, and Toshiyuki Sakaki* **1482**

Subcellular Trafficking Signals of Constitutive Androstane Receptor: Evidence for a Nuclear Export Signal in the DNA-Binding Domain. *Jun Xia and Byron Kemper* **1489**

Dehydroepiandrosterone Induces Human CYP2B6 through the Constitutive Androstane Receptor. *Krisztina Kóhalmy, Viola Tamási, László Kóbori, Enikő Sárváry, Jean-Marc Pascussi, Pálma Porrogi, Damjana Rozman, Russell A. Prough, Urs A. Meyer, and Katalin Monostory* **1495**

Preparation and In Vivo Evaluation of a Water-Soluble Prodrug for 2R- γ -Tocotrienol and as a Two-Step Prodrug for 2,7,8-Trimethyl-2S-(β -carboxyethyl)-6-hydroxycroman (S- γ -CEHC) in Rat. *Nami Akaho, Jiro Takata, Takeshi Fukushima, Kazuhisa Matsunaga, Akihiro Hattori, Ryoji Hidaka, Kosuke Fukui, Miyako Yoshida, Toshihiro Fujioka, Yoshiharu Karube, and Kazuhiro Imai* **1502**

Involvement of Up-Regulation of Hepatic Breast Cancer Resistance Protein in Decreased Plasma Concentration of 7-Ethyl-10-hydroxycamptothecin (SN-38) by Coadministration of S-1 in Rats. *Koji*

Continued on next page

<i>Yokoo, Akinobu Hamada, Hiroshi Watanabe, Takanobu Matsuzaki, Tomoyuki Imai, Hiromi Fujimoto, Kengo Masa, Teruko Imai, and Hideyuki Saito</i>	1511	Effect of Silibinin on the Pharmacokinetics of Pyrazinamide and Pyrazinoic Acid in Rats. <i>Jhy-Wen Wu and Tung-Hu Tsai</i>	1603
Characterization of Benidipine and Its Enantiomers' Metabolism by Human Liver Cytochrome P450 Enzymes. <i>Yune-Jung Yoon, Kwon-Bok Kim, Hyunmi Kim, Kyung-Ah Seo, Ho-Sook Kim, In-June Cha, Eun-Young Kim, Kwang-Hyeon Liu, and Jae-Gook Shin</i>	1518	Decrease in Plasma Concentrations of Antiangiogenic Agent TSU-68 ((Z)-5-[(1,2-Dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-propanoic acid) during Oral Administration Twice a Day to Rats. <i>Ryuichi Kitamura, Yoshio Yamamoto, Sekio Nagayama, and Masaki Otagiri</i>	1611
A Minimal Physiological Model of Thiopental Distribution Kinetics Based on a Multiple Indicator Approach. <i>Michael Weiss, Tom C. Krejcie, and Michael J. Avram</i>	1525	Role of Small Intestinal Cytochromes P450 in the Bioavailability of Oral Nifedipine. <i>Qing-Yu Zhang, Laurence S. Kaminsky, Deborah Dunbar, Jin Zhang, and Xinxin Ding</i>	1617
ABCG2 (Breast Cancer Resistance Protein/Mitoxantrone Resistance-Associated Protein) ATPase Assay: A Useful Tool to Detect Drug-Transporter Interactions. <i>Hristos Glavinas, Emese Kis, Ákos Pál, Rita Kovács, Márton Jani, Erika Vági, Éva Molnár, Száva Bánsághi, Zoltán Kele, Tamás Janáky, György Báthori, Oliver von Richter, Gerit-Jan Koomen, and Péter Krajcsi</i>	1533	Absorption, Metabolism, and Excretion of [¹⁴ C]Imidafenacin, a New Compound for Treatment of Overactive Bladder, After Oral Administration to Healthy Male Subjects. <i>Satoshi Ohmori, Masahiro Miura, Chifuyu Toriumi, Yoshiaki Satoh, and Tsuyoshi Ooie</i>	1624
Metabolism, Excretion, and Pharmacokinetics of [¹⁴ C]Tigecycline, a First-In-Class Glycylcycline Antibiotic, after Intravenous Infusion to Healthy Male Subjects. <i>Matthew Hoffmann, William DeMaio, Ronald A. Jordan, Rasmy Talaat, Dawn Harper, John Speth, and JoAnn Scatina</i>	1543	Characterization of Diuron <i>N</i> -Demethylation by Mammalian Hepatic Microsomes and cDNA-Expressed Human Cytochrome P450 Enzymes. <i>Khaled Abass, Petri Reponen, Miia Turpeinen, Jorma Jalonen, and Olavi Pelkonen</i>	1634
In Vitro Metabolic Study of Temsirolimus: Preparation, Isolation, and Identification of the Metabolites. <i>Ping Cai, Rushung Tsao, and Mark E. Ruppen</i>	1554	Glucuronidation of Thyroxine in Human Liver, Jejunum, and Kidney Microsomes. <i>Hiroyuki Yamanaka, Miki Nakajima, Miki Katoh, and Tsuyoshi Yokoi</i>	1642
Isolation and Identification of Phase I Metabolites of Demethoxycurcumin in Rats. <i>Yongchi Zeng, Feng Qiu, Yuan Liu, Gexia Qu, and Xincheng Yao</i>	1564	Functional Analysis of the Human <i>N</i> -Acetyltransferase 1 Major Promoter: Quantitation of Tissue Expression and Identification of Critical Sequence Elements. <i>Anwar Husain, Xiaoyan Zhang, Mark A. Doll, J. Christopher States, David F. Barker, and David W. Hein</i>	1649
Decrease in Intracellular Concentration Causes the Shift in K_m Value of Efflux Pump Substrates. <i>Timo Korjamo, Heidi Kemiläinen, Aki T. Heikkinen, and Jukka Mönkkönen</i>	1574	Metabolism and Disposition in Humans of Raltegravir (MK-0518), an Anti-AIDS Drug Targeting the Human Immunodeficiency Virus 1 Integrase Enzyme. <i>Kelem Kassahun, Ian McIntosh, Donghui Cui, David Hreniuk, Shelia Merschman, Kenneth Lasseter, Neal Azrolan, Marian Iwamoto, John A. Wagner, and Larissa A. Wenning</i>	1657
Effect of Pregnane X Receptor Ligand on Pharmacokinetics of Substrates of Organic Cation Transporter Oct1 in Rats. <i>Tomoji Maeda, Masanobu Oyabu, Takafumi Yotsumoto, Ryunosuke Higashi, Kiyoshi Nagata, Yasushi Yamazoe, and Ikumi Tamai</i>	1580	Identification of Rat and Human Cytochrome P450 Isoforms and a Rat Serum Esterase That Metabolize the Pyrethroid Insecticides Deltamethrin and Esfenvalerate. <i>Stephen J. Godin, J. Allen Crow, Edward J. Scollon, Michael F. Hughes, Michael J. DeVito, and Matthew K. Ross</i>	1664
Pediatric Development of Glucuronidation: The Ontogeny of Hepatic UGT1A4. <i>Shogo J. Miyagi and Abby C. Collier</i>	1587	Interspecies Comparisons of Pharmacokinetics and Pharmacodynamics of Recombinant Human Erythropoietin. <i>Sukyung Woo and William J. Jusko</i>	1672
Evaluation of Capravirine as a CYP3A Probe Substrate: In Vitro and in Vivo Metabolism of Capravirine in Rats and Dogs. <i>Hai-Zhi Bu, Ping Zhao, Ping Kang, William F. Pool, Ellen Y. Wu, and Bhasker V. Shetty</i>	1593	Stereoselective Glucuronidation of 5-(4'-Hydroxyphenyl)-5-phenylhydantoin by Human UDP-Glu-	

Contents (cont'd.)

uronosyltransferase (UGT) 1A1, UGT1A9, and UGT2B15: Effects of UGT-UGT Interactions. <i>Miki Nakajima, Hiroyuki Yamanaka, Ryoichi Fujiwara, Miki Katoh, and Tsuyoshi Yokoi</i>	1679	<i>S. Gujral, Kurt Zatloukal, Helmut Denk, Hartmut Jaeschke, and Michael Trauner</i>	1694
Gene-Specific Effects of Inflammatory Cytokines on Cytochrome P450 2C, 2B6 and 3A4 mRNA Levels in Human Hepatocytes. <i>Alison E. Aitken and Edward T. Morgan</i>	1687	Expression of Constitutive Androstane Receptor, Hepatic Nuclear Factor 4 α , and P450 Oxidoreductase Genes Determines Interindividual Variability in Basal Expression and Activity of a Broad Scope of Xenobiotic Metabolism Genes in the Human Liver. <i>Matthew Wortham, Maciej Czerwinski, Lin He, Andrew Parkinson, and Yu-Jui Yvonne Wan</i>	1700
Hepatobiliary Transporter Expression in Intercellular Adhesion Molecule 1 Knockout and Fas Receptor-Deficient Mice after Common Bile Duct Ligation Is Independent of the Degree of Inflammation and Oxidative Stress. <i>Martin Wagner, Gernot Zollner, Peter Fickert, Judith Gumhold, Dagmar Silbert, Andrea Fuchsbichler, Jaspreet</i>		[S] In Vitro Methods for Estimating Unbound Drug Concentrations in the Brain Interstitial and Intracellular Fluids. <i>Markus Fridén, Anubha Gupta, Madeleine Antonsson, Ulf Bredberg, and Margareta Hammarlund-Udenaes</i>	1711

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

About the cover: Cellular basis for the mathematical model of vectorial transport in polarized MDCKII cells. See the article by Bartholomé et al. on page 1476 of this issue.