

DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

May 2012

Vol. 40, No. 5

CONTENTS

SHORT COMMUNICATIONS

- Ⓢ *N*-Isopropyl-*p*-iodoamphetamine Hydrochloride Is Predominantly Metabolized by CYP2C19. *Ken-ichi Fujita, Minako Sugiyama, Yuko Akiyama, Kazuhito Hioki, Munetaka Kunishima, Kodai Nishi, Masato Kobayashi, Keiichi Kawai, and Yasutsuna Sasaki* . . . **843**

- Ⓢ An Investigation of the Catalytic Activity of CYP2A13*4 with Coumarin and Polymorphisms of CYP2A13 in a Chinese Han Population. *Ting Liu, Yanjun Hong, Zhaohui Li, Junyan Hong, Su Zeng, Mingyue Zheng, and Shuqing Chen* **847**

- Interindividual Variability in Hepatic Expression of the Multidrug Resistance-Associated Protein 2 (MRP2/ABCC2): Quantification by Liquid Chromatography/Tandem Mass Spectrometry. *Anand K. Deo, Bhagwat Prasad, Larissa Balogh, Yurong Lai, and Jashvant D. Unadkat* **852**

ARTICLES

- Ⓢ The Impact of Single Nucleotide Polymorphisms on Human Aldehyde Oxidase. *Tobias Hartmann, Mineko Terao, Enrico Garattini, Christian Teutloff, Joshua F. Alfaro, Jeffrey P. Jones, and Silke Leimkühler* **856**

- Models to Predict Unbound Intracellular Drug Concentrations in the Presence of Transporters. *Ken R. Korzekwa, Swati Nagar, Jalia Tucker, Erica A. Weiskircher, Siddhartha Bhoopathy, and Ismael J. Hidalgo* **865**

- Exploratory Translational Modeling Approach in Drug Development to Predict Human Brain Pharmacokinetics and Pharmacologically Relevant Clinical Doses. *W. Kielbasa and R. E. Stratford, Jr.* **877**

- Ⓢ CYP2C9 Promoter Variable Number Tandem Repeat Polymorphism Regulates mRNA Expression in Human Livers. *Danxin Wang, Xiaochun Sun, Yan Gong, Brian E. Gawronski, Taimour Y. Langae, Mohamed Hossam A. Shahin, Sherief I. Khalifa, and Julie A. Johnson* **884**

- Using Expression Data for Quantification of Active Processes in Physiologically Based Pharmacoki-

- netic Modeling. *Michaela Meyer, Sebastian Schneckener, Bernd Ludewig, Lars Kuepfer, and Joerg Lippert* **892**

- Conclusive Identification of the Oxybutynin-Hydrolyzing Enzyme in Human Liver. *Yuichiro Sato, Aiji Miyashita, Takafumi Iwatsubo, and Takashi Usui* **902**

- Ⓢ Cytochrome P450 3A-Mediated Microsomal Bio-transformation of 1 α ,25-Dihydroxyvitamin D₃ in Mouse and Human Liver: Drug-Related Induction and Inhibition of Catabolism. *Subrata Deb, Mitali Pandey, Hans Adomat, and Emma S. Tomlinson Guns* **907**

- Preclinical Disposition of GDC-0973 and Prospective and Retrospective Analysis of Human Dose and Efficacy Predictions. *Edna F. Choo, Marcia Belvin, Jason Boggs, Yuzhong Deng, Klaus P. Hoeflich, Justin Ly, Mark Merchant, Christine Orr, Emile Plise, Kirk Robarge, Jean F. Martini, Robert Kassees, Ron G. Aoyama, Atulkumar Ramaiya, and Stuart H. Johnston* **919**

- Ⓢ Regiospecific and Stereospecific Triangulation of the Structures of Metabolites Formed by Sequential Metabolism at Multiple Prochiral Centers. *Robert J. Greene, John A. Davis, Raju Subramanian, Molly R. Deane, Maurice G. Emery, and J. Greg Slatter* **928**

- Ⓢ Identifying a Selective Substrate and Inhibitor Pair for the Evaluation of CYP2J2 Activity. *Caroline A. Lee, J. P. Jones III, Jonathan Katayama, Rüdiger Kaspera, Ying Jiang, Sascha Freiwald, Evan Smith, Gregory S. Walker, and Rheem A. Totah* **943**

- Lymphatic Transport and Catabolism of Therapeutic Proteins after Subcutaneous Administration to Rats and Dogs. *Weirong Wang, Nancy Chen, Xiaolan Shen, Paul Cunningham, Scott Fauty, Kimberly Michel, Bo Wang, Xuening Hong, Christine Adreani, Christian N. Nunes, Chris V. Johnson, Kuo-chang Yin, Michelle Groff, Yan Zou, Liming Liu, Lora Hamuro, and Thomayant Prueksaritanont* **952**

- Use of the Cassette-Dosing Approach to Assess Brain Penetration in Drug Discovery. *Xingrong Liu,*

Downloaded from dmd.aspetjournals.org at ASPET Journals on April 25, 2019

Continued on next page

	<i>Xiao Ding, Gauri Deshmukh, Bianca M. Liederer, and Cornelis E. C. A. Hop</i>	963		<i>Kimoto, Sarah Kempshall, Sonya C. Tate, Ayman El-Kattan, J. Brian Houston, Aleksandra Galetin, and Katherine S. Fenner</i>	1007
☐	Metabolism, Pharmacokinetics, Tissue Distribution, and Stability Studies of the Prodrug Analog of an Anti-Hepatitis B Virus Dinucleoside Phosphorothioate. <i>John E. Coughlin, Rajendra K. Pandey, Seetharamaiyer Padmanabhan, Kathleen G. O'Loughlin, Judith Marquis, Carol E. Green, Jon C. Mirsalis, and Radhakrishnan P. Iyer</i>	970		Stereoselective Interaction of Pantoprazole with ABCG2. I. Drug Accumulation in Rat Milk. <i>Lipeng Wang and Patrick J. McNamara</i>	1018
	Effect of Albumin on Human Liver Microsomal and Recombinant CYP1A2 Activities: Impact on In Vitro-In Vivo Extrapolation of Drug Clearance. <i>Nitsupa Wattanachai, Wichitra Tassaneeyakul, Andrew Rowland, David J. Elliot, Kushari Bowalgaha, Kathleen M. Knights, and John O. Miners</i>	982		Stereoselective Interaction of Pantoprazole with ABCG2. II. In Vitro Flux Analysis. <i>Lipeng Wang, Markos Leggas, Philip E. Empey, and Patrick J. McNamara</i>	1024
	Target-Mediated Pharmacokinetic and Pharmacodynamic Model of Exendin-4 in Rats, Monkeys, and Humans. <i>Wei Gao and William J. Jusko</i>	990	☐	<i>p</i> -Anilinoaniline Enhancement of Dioxin-Induced CYP1A1 Transcription and Aryl Hydrocarbon Receptor Occupancy of CYP1A1 Promoter: Role of the Cell Cycle. <i>Althea Elliott, Aby Joiakim, Patricia A. Mathieu, Zofia Duniec-Dmuchowski, Thomas A. Kocarek, and John J. Reiners, Jr.</i>	1032
	Identification of the Residue in Human CYP3A4 That Is Covalently Modified by Bergamottin and the Reactive Intermediate That Contributes to the Grapefruit Juice Effect. <i>Hsia-lien Lin, Cesar Keenan, and Paul F. Hollenberg</i>	998		Biocatalytic Synthesis and Structure Elucidation of Cyclized Metabolites of the Deacetylase Inhibitor Panobinostat (LBH589). <i>Andreas Fredenhagen, Matthias Kittelmann, Lukas Oberer, Anton Kuhn, Jürgen Kühnöl, Thierry Délémonté, Reiner Aichholz, Ping Wang, Peter Atadja, and Michael D. Shultz</i>	1041
☐	Mechanistic Pharmacokinetic Modeling for the Prediction of Transporter-Mediated Disposition in Humans from Sandwich Culture Human Hepatocyte Data. <i>Hannah M. Jones, Hugh A. Barton, Yurong Lai, Yi-an Bi, Emi</i>		☐	Optimized Assays for Human UDP-Glucuronosyltransferase (UGT) Activities: Altered Alamethicin Concentration and Utility to Screen for UGT Inhibitors. <i>Robert L. Walsky, Jonathan N. Bauman, Karine Bourcier, Georgina Giddens, Kimberly Lapham, Andre Negahban, Tim F. Ryder, R. Scott Obach, Ruth Hyland, and Theunis C. Goosen</i>	1051

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

About the cover: Model of the locations of the amino acid exchanges as a result of SNPs identified in the *hAOX1* gene. See the article by Hartmann et al. on page 856 of this issue.