

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

October 2016

Vol. 44, No. 10

## CONTENTS

### MINIREVIEW

Drug Transport by the Blood–Aqueous Humor Barrier of the Eye. *Jonghwa Lee and Ryan M. Pelis* . . . **1675**

### PERSPECTIVE

□ Evaluation of CYP2B6 Induction and Prediction of Clinical Drug–Drug Interactions: Considerations from the IQ Consortium Induction Working Group—An Industry Perspective. *Odette A. Fahmi, Mohamad Shebley, Jairam Palamanda, Michael W. Sinz, Diane Ramsden, Heidi J. Einolf, Liangfu Chen, and Hongbing Wang* . . . **1720**

### ARTICLES

□ Lansoprazole Exacerbates Pemetrexed-Mediated Hematologic Toxicity by Competitive Inhibition of Renal Basolateral Human Organic Anion Transporter 3. *Kenji Ikemura, Yugo Hamada, Chinatsu Kaya, Tomoyuki Enokiya, Yuichi Muraki, Hiroki Nakahara, Hajime Fujimoto, Tetsu Kobayashi, Takuya Iwamoto, and Masahiro Okuda* . . . **1543**

□ Abundance of Hepatic Transporters in Caucasians: A Meta-Analysis. *Howard J. Burt, Arian Emami Riedmaier, Matthew D. Harwood, H. Kim Crewe, Katherine L. Gill, and Sibylle Neuhoff* . . . **1550**

□ Expression of Organic Anion Transporting Polypeptide 1A2 in Red Blood Cells and Its Potential Impact on Antimalarial Therapy. *Andrea Hubeny, Markus Keiser, Stefan Oswald, Gabriele Jedlitschky, Heyo K. Kroemer, Werner Siegmund, and Markus Grube* . . . **1562**

The Use of In Vitro Data and Physiologically-Based Pharmacokinetic Modeling to Predict Drug Metabolite Exposure: Desipramine Exposure in Cytochrome P4502D6 Extensive and Poor Metabolizers Following Administration of Imipramine. *Hoa Q. Nguyen, Ernesto Callegari, and R. Scott Obach* . . . **1569**

Cytochrome P450 3A4 and CYP3A5-Catalyzed Bioactivation of Lapatinib. *Joanna K. Towles, Rebecca N. Clark, Michelle D. Wahlin, Vinita Uttamsingh, Allan E. Rettie, and Klarissa D. Jackson* . . . **1584**

□ Analysis of Mechanism-Based Inhibition of CYP 3A4 by a Series of Fluoroquinolone Antibacterial Agents. *Akiko Watanabe, Hideo Takakusa, Takako Kimura, Shin-ichi Inoue, Hiroyuki Kusuhara, and Osamu Ando* . . . **1608**

Clarification of the Mechanism of Clopidogrel-Mediated Drug–Drug Interaction in a Clinical Cassette Small-dose Study and Its Prediction Based on In Vitro Information. *Soo-Jin Kim, Takashi Yoshikado, Ichiro Ieiri, Kazuya Maeda, Miyuki Kimura, Shin Irie, Hiroyuki Kusuhara, and Yuichi Sugiyama* . . . **1622**

□ Determination of Unbound Partition Coefficient and in Vitro–in Vivo Extrapolation for SLC13A Transporter-Mediated Uptake. *Keith Riccardi, Zhenhong Li, Janice A. Brown, Matthew F. Gorgoglione, Mark Niosi, James Gosset, Kim Huard, Derek M. Erion, and Li Di* . . . **1633**

□ Methylation of the Constitutive Androstane Receptor Is Involved in the Suppression of CYP2C19 in Hepatitis B Virus–Associated Hepatocellular Carcinoma. *Xiaojing Tang, Lele Ge, Zhongjian Chen, Sisi Kong, Wenhui Liu, Yingchun Xu, Su Zeng, and Shuqing Chen* . . . **1643**

An Automated High-Throughput Metabolic Stability Assay Using an Integrated High-Resolution Accurate Mass Method and Automated Data Analysis Software. *Pranav Shah, Edward Kerns, Dac-Trung Nguyen, R. Scott Obach, Amy Q. Wang, Alexey Zakharov, John McKew, Anton Simeonov, Cornelis E. C. A. Hop, and Xin Xu* . . . **1653**

Characteristic Analysis of Intestinal Transport in Enterocyte-Like Cells Differentiated from Human Induced Pluripotent Stem Cells. *Nao Kodama, Takahiro Iwao, Takahiro Katano, Kinya Ohta, Hiroaki Yuasa, and Tamihide Matsunaga* . . . **1662**

Continued on next page

Roles of UGT, P450, and Gut Microbiota in the Metabolism of Epcadostat in Humans. *Jason Boer, Ruth Young-Sciame, Fiona Lee, Kevin J. Bowman, Xiaoqing Yang, Jack G. Shi, Frank M. Nedza, William Frietze, Laurine Galya, Andrew P. Combs, Swamy Yeleswaram, and Sharon Diamond* . . . . . **1668**

▣ In Vitro and In Vivo Drug-Drug Interaction Studies to Assess the Effect of Abiraterone Acetate, Abiraterone, and Metabolites of Abiraterone on CYP2C8 Activity. *Johan Monbaliu, Martha Gonzalez, Apexa Bernard, James Jiao, Carlo Sensenhauser, Jan Snoeys, Hans Stieltjes, Inneke Wynant, Johan W. Smit, and Caly Chien* . . . . . **1682**

▣ Utilization of Stable Isotope Labeling to Facilitate the Identification of Polar Metabolites of KAF156, an Antimalarial Agent. *Su-Er W. Huskey, Ry R. Forseth, Hongmei Li, Zhigang Jian, Alexandre Catoire, Jin Zhang, Tapan Ray, Handan He, Jimmy Flarakos, and James B. Mangold* . . . . . **1697**

Stereoselective Metabolism of Bupropion to OH-bupropion, Threohydrobupropion, Erythrohydrobupropion, and 4'-OH-bupropion in vitro. *Jennifer E. Sager, Lauren S. L. Price, and Nina Isoherranen* . . . . . **1709**

## SHORT COMMUNICATIONS

▣ Morbid Obesity Alters Both Pharmacokinetics and Pharmacodynamics of Propofol: Dosing Recommendation for Anesthesia Induction. *Dong Dong, Xuemei Peng, Jie Liu, Hao Qian, Jiayang Li, and Baojian Wu* . . . **1579**

Species Differences in Microsomal Oxidation and Glucuronidation of 4-Ipomeanol: Relationship to Target Organ Toxicity. *Oliver T. Parkinson, Aaron M. Teitelbaum, Dale Whittington, Edward J. Kelly, and Allan E. Rettie* . . . . . **1598**

Bioactivation of Trimethoprim to Protein-Reactive Metabolites in Human Liver Microsomes. *Jennifer L. Goldman, Yakov M. Koen, Steven A. Rogers, Kelin Li, James S. Leeder, and Robert P. Hanzlik* **1603**

Defining the Role of the NADH-Cytochrome-*b*<sub>5</sub> Reductase 3 in the Mitochondrial Amidoxime Reducing Component Enzyme System. *Birte Pletzko, Antje Havemeyer, Bettina Bork, Florian Bittner, Ralf Mendel, and Bernd Clement* . . . . . **1617**

▣ An Optimized Method for Protein Extraction from OCT-Embedded Human Kidney Tissue for Protein Quantification by LC-MS/MS Proteomics. *Marc Vrana, Anne Goodling, Maryam Afkarian, and Bhagwat Prasad* . . . . . **1692**

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

*About the cover:* Immunofluorescence staining analysis of villin and Na<sup>+</sup>-K<sup>+</sup> ATPase in the differentiated enterocyte-like cells. See the article by Iwao et al. ([dx.doi.org/10.1124/dmd.116.069336](http://dx.doi.org/10.1124/dmd.116.069336)).