

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

October 2013

Vol. 41, No. 10

## CONTENTS

### SPECIAL SECTION ON EPIGENETIC REGULATION OF DRUG METABOLIZING ENZYMES AND TRANSPORTERS

- Epigenetic Regulation of ADME-Related Genes: Focus on Drug Metabolism and Transport. *Xiao-bo Zhong and J. Steven Leeder* . . . . . **1721**
- Potential Role of Epigenetic Mechanisms in the Regulation of Drug Metabolism and Transport. *Magnus Ingelman-Sundberg, Xiao-Bo Zhong, Oliver Hankinson, Sudheer Beedanagari, Ai-Ming Yu, Lai Peng, and Yoichi Osawa* . . . . . **1725**
- Role of Multiple MicroRNAs in the Sexually Dimorphic Expression of *Cyp2b9* in Mouse Liver. *Xiaofeng Xie, Lingling Miao, Jun Yao, Chenchen Feng, Chenggang Li, Man Gao, Mingxia Liu, Likun Gong, Yizheng Wang, Xinming Qi, and Jin Ren* . . . . . **1732**
- Epigenetic Regulation Is a Crucial Factor in the Repression of UGT1A1 Expression in the Human Kidney. *Shingo Oda, Tatsuki Fukami, Tsuyoshi Yokoi, and Miki Nakajima* . . . . . **1738**
- Small Nucleolar RNA-Derived MicroRNA hsa-miR-1291 Modulates Cellular Drug Disposition through Direct Targeting of ABC Transporter ABCC1. *Yu-Zhuo Pan, Amy Zhou, Zihua Hu, and Ai-Ming Yu* . . . . . **1744**
- Expression Variability of Absorption, Distribution, Metabolism, Excretion-Related MicroRNAs in Human Liver: Influence of Nongenetic Factors and Association with Gene Expression. *Jessica K. Rieger, Kathrin Klein, Stefan Winter, and Ulrich M. Zanger* . . . . . **1752**
- Regulation of MicroRNA Expression by Rifampin in Human Hepatocytes. *Anuradha Ramamoorthy, Yunlong Liu, Santosh Philips, Zeruesenay Desta, Hai Lin, Chirayu Goswami, Andrea Gaedigk, Lang Li, David A. Flockhart, and Todd C. Skaar* . . . . . **1763**

- Insights into Insulin-Mediated Regulation of CYP2E1: miR-132/-212 Targeting of CYP2E1 and Role of Phosphatidylinositol 3-Kinase, Akt (Protein Kinase B), Mammalian Target of Rapamycin Signaling in Regulating miR-132/-212 and miR-122/-181a Expression in Primary Cultured Rat Hepatocytes. *Upasana Shukla, Nithin Tamma, Theresa Gratsch, Alan Dombkowski, and Raymond F. Novak* . . . . . **1769**
- Incubation of Whole Blood at Room Temperature Does Not Alter the Plasma Concentrations of MicroRNA-16 and -223. *Eric A. Benson and Todd C. Skaar* . . . . . **1778**

### SHORT COMMUNICATION

- Downregulation of Mouse Hepatic CYP3A Protein by 3-Methylcholanthrene Does Not Require Cytochrome P450-Dependent Metabolism. *Chunja Lee, Xinxin Ding, and David S. Riddick* . . . . . **1782**

### ARTICLES

- In Vitro Investigation of Amyloid- $\beta$  Hepatobiliary Disposition in Sandwich-Cultured Primary Rat Hepatocytes. *Loqman A. Mohamed and Amal Kaddoumi* . . . . . **1787**
- Aldehyde Oxidase 1 (AOX1) in Human Liver Cytosols: Quantitative Characterization of AOX1 Expression Level and Activity Relationship. *Cexiong Fu, Li Di, Xiaogang Han, Cathy Soderstrom, Mark Snyder, Matthew D. Troutman, R. Scott Obach, and Hui Zhang* . . . . . **1797**
- Overlapping Substrate and Inhibitor Specificity of Human and Murine ABCG2. *Joshua Bakhsheshian, Matthew D. Hall, Robert W. Robey, Michelle A. Herrmann, Jin-Qiu Chen, Susan E. Bates, and Michael M. Gottesman* . . . . . **1805**
- The Effect of Ritonavir on Human CYP2B6 Catalytic Activity: Heme Modification Contributes to the Mechanism-Based Inactivation of CYP2B6 and CYP3A4 by Ritonavir. *Hsia-lien Lin, Jaime D'Agostino, Cesar Kenaan, Diane Calinski, and Paul F. Hollenberg* . . . . . **1813**

Continued on next page

- ☐ Multispecific Drug Transporter *Slc22a8* (*Oat3*) Regulates Multiple Metabolic and Signaling Pathways. *Wei Wu, Neema Jamshidi, Satish A. Eraly, Henry C. Liu, Kevin T. Bush, Bernhard O. Palsson, and Sanjay K. Nigam* . . . . . **1825**
- ☐ Transcriptomic Hepatotoxicity Signature of Chlorpromazine after Short- and Long-Term Exposure in Primary Human Sandwich Cultures. *Céline Parmentier, Germaine L. Truisi, Konrad Moenks, Sven Stanzel, Arno Lukas, Annette Kopp-Schneider, Eliane Alexandre, Philip G. Hewitt, Stefan O. Mueller, and Lysiane Richert* . . . . . **1835**
- Ritonavir and Efavirenz Significantly Alter the Metabolism of Erlotinib—an Observation in Primary Cultures of Human Hepatocytes That Is Relevant to HIV Patients with Cancer. *Venkateswaran C. Pillai, Raman Venkataramanan, Robert A. Parise, Susan M. Christner, Roberto Gramignoli, Stephen C. Strom, Michelle A. Rudek, and Jan H. Beumer* . . . . . **1843**
- ☐ Evaluation of Rhesus Monkey and Guinea Pig Hepatic Cytosol Fractions as Models for Human Aldehyde Oxidase. *Kanika V. Choughule, John T. Barr, and Jeffrey P. Jones* . . . . . **1852**
- ☐ Substrate-Dependent Inhibition of Organic Anion Transporting Polypeptide 1B1: Comparative Analysis with Prototypical Probe Substrates Estradiol-17 $\beta$ -Glucuronide, Estrone-3-Sulfate, and Sulfobromophthalein. *Saki Izumi, Yoshitane Nozaki, Takafumi Komori, Kazuya Maeda, Osamu Takenaka, Kazutomi Kusano, Tsutomu Yoshimura, Hiroyuki Kusuvara, and Yuichi Sugiyama*. . . . . **1859**
- Impact of Peptide Transporter 1 on the Intestinal Absorption and Pharmacokinetics of Valacyclovir after Oral Dose Escalation in Wild-Type and *PepT1* Knockout Mice. *Bei Yang, Yongjun Hu, and David E. Smith*. . . . . **1867**
- Pitavastatin as an In Vivo Probe for Studying Hepatic Organic Anion Transporting Polypeptide-Mediated Drug–Drug Interactions in Cynomolgus Monkeys. *Tsuyoshi Takahashi, Tatsuyuki Ohtsuka, Takahiro Yoshikawa, Ichiro Tatekawa, Yasuhiro Uno, Masahiro Utoh, Hiroshi Yamazaki, and Toshiyuki Kume* . . . . . **1875**

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

*About the cover:* MicroRNA hsa-miR-1291 modulates cellular drug disposition through targeting on 3'-UTR of ABCC1 efflux transporter mRNAs. See article by Pan et al. on page 1744 of this issue.