

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

September 2015

Vol. 43, No. 9

## CONTENTS

### SHORT COMMUNICATIONS

- Opioid Analgesia in P450 Gene Cluster Knockout Mice: A Search for Analgesia-Relevant Isoforms. *Lindsay B. Hough, Julia W. Nalwalk, Xinxin Ding, and Nico Scheer* . . . . . **1326**
- Multiplexed Targeted Quantitative Proteomics Predicts Hepatic Glucuronidation Potential. *Guillaume Margaillan, Michèle Rouleau, Kathrin Klein, John K. Fallon, Patrick Caron, Lyne Villeneuve, Philip C. Smith, Ulrich M. Zanger, and Chantal Guillemette* . . . . . **1331**
- Expression of Bama Minipig and Human CYP3A Enzymes: Comparison of the Catalytic Characteristics with Each Other and Their Liver Microsomes. *Yicong Bian, Qingqing Yao, Haitao Shang, Jinxiu Lei, Haihong Hu, Kenan Guo, Huidi Jiang, Lushan Yu, Hong Wei, and Su Zeng* . . . . . **1336**
- Intracellular Catabolism of an Antibody Drug Conjugate with a Noncleavable Linker. *Brooke M. Rock, Mark E. Tometsko, Sonal K. Patel, Kevin J. Hamblett, William C. Fanslow, and Dan A. Rock* . . . . . **1341**

### ARTICLES

- Further Characterization of the Metabolism of Desloratadine and Its Cytochrome P450 and UDP-glucuronosyltransferase Inhibition Potential: Identification of Desloratadine as a Relatively Selective UGT2B10 Inhibitor. *Faraz Kazmi, Phyllis Yerino, Joanna E. Barbara, and Andrew Parkinson* . . . . . **1294**
- Novel Bioactivation Pathway of Benzbromarone Mediated by Cytochrome P450. *Yumina Kitagawara, Tomoyuki Ohe, Kumiko Tachibana, Kyoko*

*Takahashi, Shigeo Nakamura, and Tadahiko Mashino* . . . . . **1303**

Determination of a Degradation Constant for CYP3A4 by Direct Suppression of mRNA in a Novel Human Hepatocyte Model, HepatoPac. *Diane Ramsden, Jin Zhou, and Donald J. Tweedie* . . . . . **1307**

SUMOylation and Ubiquitylation Circuitry Controls Pregnane X Receptor Biology in Hepatocytes. *Wenqi Cui, Mengxi Sun, Nadezhda Galeva, Todd D. Williams, Yoshiaki Azuma, and Jeff L. Staudinger* . . . . . **1316**

Damage to the Brain Serotonergic System Increases the Expression of Liver Cytochrome P450. *Marta Rysz, Ewa Bromek, Anna Haduch, Anna Sadakierska-Chudy, and Władysława A. Daniel* . . . **1345**

Milk Thistle Constituents Inhibit Raloxifene Intestinal Glucuronidation: A Potential Clinically Relevant Natural Product–Drug Interaction. *Brandon T. Gufford, Gang Chen, Ana G. Vergara, Philip Lazarus, Nicholas H. Oberlies, and Mary F. Paine* . . . . . **1353**

□ Brain Exposure of Two Selective Dual CDK4 and CDK6 Inhibitors and the Antitumor Activity of CDK4 and CDK6 Inhibition in Combination with Temozolomide in an Intracranial Glioblastoma Xenograft. *Thomas J. Raub, Graham N. Wishart, Palaniappan Kulanthaivel, Brian A. Staton, Rose T. Ajamie, Geri A. Sawada, Lawrence M. Gelbert, Harlan E. Shannon, Concepcion Sanchez-Martinez, and Alfonso De Dios* . . . . . **1360**

In Vitro Hepatic Oxidative Biotransformation of Trimethoprim. *Jennifer L. Goldman, J. Steven Leeder, Leon Van Haandel, and Robin E. Pearce* . . . . . **1372**

Downloaded from dmd.aspetjournals.org at ASPET Journals on April 19, 2019

Continued on next page

Cross-Species Differences in the Preclinical Pharmacokinetics of CT7758, an  $\alpha 4\beta 1/\alpha 4\beta 7$  Integrin Antagonist. *Hugues Chanteux, Ludovic Staelens, Valérie Mancel, Brigitte Gerin, David Boucaut, Chandra Prakash, and Jean-Marie Nicolas* . . . . . **1381**

Influence of ABCB1 Genotype in Collies on the Pharmacokinetics and Pharmacodynamics of Loperamide in a Dose-Escalation Study. *Michael J. Myers, Marilyn Martinez, Hui Li, Junshan Qiu, Lisa Troutman, Michele Sharkey, and Haile F. Yancy* . . . . . **1392**

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

*About the cover:* Figure 1. (A) General structure of non-cleavable antibody maytansinoid conjugate (B) Mechanism of ADC activity where, (A) localization of ADC to the tumor cell, (B) binding of ADC to specific antigen, (C) internalization into the endosome release the antigen from ADC, (D) catabolism of ADC in the lysosome, (E) release of Lys-MCC-DM1 into the cytoplasm, and (F) binding of Lys-MCC-DM1 to tubulin resulting in cell cycle arrest and apoptosis. Please see the article by Rock et al. ([dx.doi.org/10.1124/dmd.115.064253](http://dx.doi.org/10.1124/dmd.115.064253)).