

DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

December 2019

Vol. 47, No. 12

CONTENTS

MINIREVIEW

- Are Biotransformation Studies of Therapeutic Proteins Needed? Scientific Considerations and Technical Challenges. *Simone Schadt, Simon Hauri, Filipe Lopes, Martin R. Edelmann, Roland F. Staack, Roberto Villaseñor, Hubert Kettenberger, Adrian B. Roth, Franz Schuler, Wolfgang F. Richter, and Christoph Funk* **1443**

ARTICLES

- ☐ In Vitro–In Vivo Inaccuracy: The CYP3A4 Anomaly. *Christine M. Bowman, and Leslie Z. Benet* **1368**
- ☐ Ginsenoside Rc Is a New Selective UGT1A9 Inhibitor in Human Liver Microsomes and Recombinant Human UGT Isoforms. *Hyunyoung Lee, Jae-Kyung Heo, Ga-Hyun Lee, So-Young Park, Su-Nyeong Jang, Hyun-Ji Kim, Mi Jeong Kwon, Im-Sook Song, and Kwang-Hyeon Liu* **1372**
- ☐ An Accurate In Vitro Prediction of Human VD_{ss} Based on the Øie–Tozer Equation and Primary Physicochemical Descriptors. 3. Analysis and Assessment of Predictivity on a Large Dataset. *Giuliano Berellini and Franco Lombardo* **1380**
- ☐ Role of L- and D-Menthol in the Glucuronidation and Detoxification of the Major Lung Carcinogen, NNAL. *Shannon Kozlovich, Gang Chen, Christy J.W. Watson, William J. Blot, and Philip Lazarus* **1388**
- Protein Binding and Hepatic Clearance: Re-Examining the Discrimination between Models of Hepatic Clearance with Diazepam in the Isolated Perfused Rat Liver Preparation. *Hong-Jaan Wang and Leslie Z. Benet* **1397**
- Brain Distributional Kinetics of a Novel MDM2 Inhibitor SAR405838: Implications for Use in Brain Tumor Therapy. *Minjee Kim, Janice K. Laramy,*

- Gautham Gampa, Karen E. Parrish, Richard Brundage, Jann N. Sarkaria, and William F. Elmquist* **1403**

- Pregnancy and CYP3A5 Genotype Affect Day 7 Plasma Lumefantrine Concentrations. *Ritah F. Mutagonda, Omary M.S. Minzi, Sirel N. Massawe, Muhammad Asghar, Anna Färnert, Appolinary A.R. Kamuhabwa, and Eleni Aklillu* **1415**

- ☐ CYP2D1 Gene Knockout Reduces the Metabolism and Efficacy of Venlafaxine in Rats. *Hongqiu Zhou, Li Yang, Changsuo Wang, Zhiqiang Li, Zhen Ouyang, Mangting Shan, Jun Gu, and Yuan Wei* **1425**

- ☐ Organic Anion-Transporting Polypeptide Genes Are Not Induced by the Pregnane X Receptor Activator Rifampin: Studies in Hepatocytes In Vitro and in Monkeys In Vivo. *Congrong Niu, Yujin Wang, Xiaofeng Zhao, Sam Tep, Eisuke Murakami, Raju Subramanian, Bill Smith, and Yurong Lai* **1433**

- ☐ An Innovative Approach to Characterize Clinical ADME and Pharmacokinetics of the Inhaled Drug Nemiralisib Using an Intravenous Microtracer Combined with an Inhaled Dose and an Oral Radiolabel Dose in Healthy Male Subjects. *Andrew W. Harrell, Robert Wilson, Yau Lun Man, Kylie Riddell, Emily Jarvis, Graeme Young, Robert Chambers, Lee Crossman, Alex Georgiou, Adrian Pereira, David Kenworthy, Claire Beaumont, Miriam Marotti, Denisa Wilkes, Edith M. Hessel, and William A. Fahy* **1457**

- ☐ Toxicokinetic Interaction between Hepatic Disposition and Pulmonary Bioactivation of Inhaled Naphthalene Studied Using *Cyp2abfgs*-Null and CYP2A13/2F1-Humanized Mice with Deficient Hepatic Cytochrome P450 Activity. *Nataliia Kovalchuk, Qing-Yu Zhang, Jacklyn Kelty, Laura Van Winkle, and Xinxin Ding* **1469**

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

About the cover: Overview on cellular clearance and biotransformation processes in endothelial cells and hematopoietic cells (primarily macrophages). See the article by Schadt et al. ([dx.doi.org/10.1124/dmd.119.088997](https://doi.org/10.1124/dmd.119.088997)).