

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

July 2024

Vol. 52, No. 7

## Contents

### ARTICLES

- ☐ Survey of Pharmaceutical Industry's Best Practices around In Vitro Transporter Assessment and Implications for Drug Development: Considerations from the International Consortium for Innovation and Quality for Pharmaceutical Development Transporter Working Group 582  
*Helen E. Rollison, Pallabi Mitra, Hugues Chanteux, Zhizhou Fang, Xiaomin Liang, Seong Hee Park, Chester Costales, Imad Hanna, Nilay Thakkar, James M. Vergis, Daniel A.J. Bow, Kathleen M. Hillgren, Jochen Brumm, Xiaoyan Chu, Cornelis E.C.A. Hop, Yurong Lai, Cindy Yanfei Li, Kelly M. Mahar, Laurent Salphati, Rucha Sane, Hong Shen, Kunal Taskar, Mitchell Taub, Kimio Tohyama, Christine Xu, and Katherine S. Fenner*
- ☐ Gut Microbiota Affects Mouse Pregnane X Receptor Agonist Pregnenolone 16 $\alpha$ -Carbonitrile-Induced Hepatomegaly by Regulating Pregnane X Receptor and Yes-Associated Protein Activation 597  
*Ting Wu, Lu Li, Wenhong Zhou, Guofang Bi, Xiaowen Jiang, Manlan Guo, Xiao Yang, Jianhong Fang, Jianxin Pang, Shicheng Fan, and Huichang Bi*
- ☐ KLF15-Cyp3a11 Axis Regulates Rifampicin-Induced Liver Injury 606  
*Wanqing Hou, Ku-Geng Huo, Xiaohua Guo, Mengtong Xu, Yongting Yang, Zhuangqi Shi, Weixiong Xu, Jinqi Tu, Tangxin Gao, Zhenghai Ma, and Shuxin Han*
- ☐ Physiologically Based Pharmacokinetic Modeling to Predict the Impact of Liver Cirrhosis on Glucuronidation via UGT1A4 and UGT2B7/2B4—A Case Study with Midazolam 614  
*Agustos C. Ozbey, Janneke Keemink, Bjoern Wagner, Alessandra Pugliano, Stephan Krähenbühl, Pieter Annaert, Stephen Fowler, Neil Parrott, and Kenichi Umehara*
- ☐ The Role of Intramolecular Reactions and Chemical Degradation in the Apparent Biotransformation Pathways of a Series of SYK Inhibitors 626  
*Beatriz Calle, Bernard Barlaam, Coura Diène, Eva Lenz, Scott Martin, Ujjal Sarkar, Stephen Wilkinson, and Andy Pike*
- ☐ Application of Electro-Activated Dissociation Fragmentation Technique to Identifying Glucuronidation and Oxidative Metabolism Sites of Vepdegestrant by Liquid Chromatography-High Resolution Mass Spectrometry 634  
*Yifei He, Pengyi Hou, Zhimin Long, Yuandong Zheng, Chongzhuang Tang, Elliott Jones, Xingxing Diao, and Mingshe Zhu*
- ☐ Xenografted Tumors Share Comparable Fraction Unbound and Can Be Surrogated by Mouse Lung Tissue 644  
*Min Wang, Sandip Kuldharan, Aravind Shenoy, Satyanarayana Reddy, Karen Rex, Tao Osgood, Jan Wahlstrom, and Upendra P. Dahal*
- ☐ Pharmacokinetic/Pharmacodynamic Assessment of the Structural Refinement of Clopidogrel Focusing on the Balance between Bioactivation and Deactivation 654  
*Dong Sun, Yingze Liu, Lin Zhu, Zhiping Xu, Yuyao Zhang, Haipeng Li, Huan Yang, Xia Cao, and Jingkai Gu*

☐ Supplemental material is available at [dmd.aspetjournals.org](http://dmd.aspetjournals.org).

About the cover: "Gut microbiota affects mPXR agonist PCN-induced hepatomegaly." See the article by Wu et al. ([dx.doi.org/10.1124/dmd.123.001604](https://doi.org/10.1124/dmd.123.001604)).

- ☐ Physiologically Based Pharmacokinetic Modeling: The Reversible Metabolism and Tissue-Specific Partitioning of Methylprednisolone and Methylprednisone in Rats 662  
*Ruihong Yu and William J. Jusko*
- ☐ MALDI Imaging Mass Spectrometry Visualizes the Distribution of Antidepressant Duloxetine and Its Major Metabolites in Mouse Brain, Liver, Kidney, and Spleen Tissues 673  
*Saleh M. Khalil, Xuan Qin, John M. Hakenjos, Jian Wang, Zhaoyong Hu, Xinli Liu, Jin Wang, Mirjana Maletic-Savatic, Kevin R. MacKenzie, Martin M. Matzuk, and Feng Li*
- ☐ Tissue-, Region-, and Gene-Specific Induction of Microsomal Epoxide Hydrolase Expression and Activity in the Mouse Intestine by Arsenic in Drinking Water 681  
*Hui Li, Xiaoyu Fan, Xinxin Ding, and Qing-Yu Zhang*
- ☐ The Metabolism and Disposition of Brepocitinib in Humans and Characterization of the Formation Mechanism of an Aminopyridine Metabolite 690  
*Martin E. Dowty, Ruolun Qiu, Alyssa Dantonio, Mark Niosi, Angela Doran, Amanda Balesano, Stephen W. Wright, Gregory S. Walker, and Raman Sharma*

## ERRATUM

- Correction to “Quantitative Analysis of mRNA and Protein Expression Levels of Aldo-Keto Reductase and Short-Chain Dehydrogenase/Reductase Isoforms in the Human Intestine” 703