

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

May 2017

Vol. 45, No. 5

## CONTENTS

### ARTICLES

- Novel Mechanism of Decyanation of GDC-0425 by Cytochrome P450. *Ryan H. Takahashi, Jason S. Halladay, Michael Siu, Yuan Chen, Cornelis E. C. A. Hop, S. Cyrus Khojasteh, and Shuguang Ma* . . . . . **430**
- Nimesulide and 4'-Hydroxynimesulide as Bile Acid Transporters Inhibitors Are Contributory Factors for Drug-Induced Cholestasis. *Lei Zhou, Xiaoyan Pang, Jingfang Jiang, Dafang Zhong, and Xiaoyan Chen* . . . . . **441**
- Correlation between Membrane Protein Expression Levels and Transcellular Transport Activity for Breast Cancer Resistance Protein. *Houfu Liu, Liang Huang, Yi Li, Tingting Fu, Xueying Sun, Yan-Yan Zhang, Ruina Gao, Qingfang Chen, Wandong Zhang, Jasminder Sahi, Scott Summerfield, and Kelly Dong* . . . . . **449**
- Marmoset Cytochrome P450 3A4 Ortholog Expressed in Liver and Small-Intestine Tissues Efficiently Metabolizes Midazolam, Alprazolam, Nifedipine, and Testosterone. *Shotaro Uehara, Yasuhiro Uno, Kazuyuki Nakanishi, Sakura Ishii, Takashi Inoue, Erika Sasaki, and Hiroshi Yamazaki* . . . . . **457**
- Determination of Human Hepatic CYP2C8 and CYP1A2 Age-Dependent Expression to Support Human Health Risk Assessment for Early Ages. *Gina Song, Xueying Sun, Ronald N. Hines, D. Gail McCarver, Brian G. Lake, Thomas G. Osimitz, Moire R. Creek, Harvey J. Clewell, and Miyoung Yoon* . . . . . **468**
- Effect of Disease-Related Changes in Plasma Albumin on the Pharmacokinetics of Naproxen in Male and Female Arthritic Rats. *Xiaonan Li, Debra C. DuBois, Richard R. Almon, and William J. Jusko* . . . . . **476**
- Modeling Sex Differences in Pharmacokinetics, Pharmacodynamics, and Disease Progression Effects of Naproxen in Rats with Collagen-Induced Arthritis. *Xiaonan Li, Debra C. DuBois, Richard R. Almon, and William J. Jusko* . . . . . **484**
- Examination of the Human Cytochrome P4503A4 Induction Potential of PF-06282999, an Irreversible Myeloperoxidase Inactivator: Integration of Preclinical, In Silico, and Biomarker Methodologies in the Prediction of the Clinical Outcome. *Jennifer Q. Dong, James R. Gosset, Odette A. Fahmi, Zhiwu Lin, Jeffrey R. Chabot, Steven G. Terra, Vu Le, Kristin Chidsey, Parya Nouri, Albert Kim, Leonard Buckbinder, and Amit S. Kalgutkar* . . . . . **501**
- Effects of MicroRNA-34a on the Pharmacokinetics of Cytochrome P450 Probe Drugs in Mice. *Joseph L. Jilek, Ye Tian, and Ai-Ming Yu* . . . . . **512**
- Assessing the Risk of Drug-Induced Cholestasis Using Unbound Intrahepatic Concentrations. *Julia Riede, Birk Poller, Jörg Huwylar, and Gian Camenisch* . . . . . **523**
- Phenobarbital Meets Phosphorylation of Nuclear Receptors. *Masahiko Negishi* . . . . . **532**
- Midostaurin, a Novel Protein Kinase Inhibitor for the Treatment of Acute Myelogenous Leukemia: Insights from Human Absorption, Metabolism, and Excretion Studies of a BDDCS II Drug. *Handan He, Phi Tran, Helen Gu, Vivienne Tedesco, Jin Zhang, Wen Lin, Ewa Gatlik, Kai Klein, and Tycho Heimbach* . . . . . **540**
- Microsomal and Cytosolic Scaling Factors in Dog and Human Kidney Cortex and Application for In Vitro-In Vivo Extrapolation of Renal Metabolic Clearance. *Daniel Scotcher, Sarah Billington, Jay Brown, Christopher R. Jones, Colin D. A. Brown, Amin Rostami-Hodjegan, and Aleksandra Galetin* . . . . . **556**

Downloaded from dmd.aspetjournals.org at ASPET Journals on November 21, 2017

Continued on next page

Effect of Garlic, Gingko, and St. John's Wort Extracts on the Pharmacokinetics of Fexofenadine: A Mechanistic Study. *Jasmina Turkanovic, Michael B. Ward, Jacobus P. Gerber, and Robert W. Milne* . . . . . **569**

▣ Novel Method to Predict In Vivo Liver-to-Plasma  $K_{puu}$  for OATP Substrates Using Suspension Hepatocytes. *Keith Riccardi, Jian Lin, Zhenhong Li, Mark Niosi, Sangwoo Ryu, Wenyi Hua, Karen Atkinson, Rachel E. Kosa, John Litchfield, and Li Di* . . . . . **576**

### SHORT COMMUNICATIONS

▣ Implications for Metabolite Quantification by Mass Spectrometry in the Absence of Authentic Standards. *Panos Hatsis, Nigel J. Waters, and Upendra A. Argikar* . . . . . **492**

▣ Marmoset Flavin-Containing Monooxygenase 3 in the Liver Is a Major Benzydamine and Sulindac Sulfide Oxygenase. *Shotaro Uehara, Makiko Shimizu, Yasuhiro Uno, Takashi Inoue, Erika Sasaki, and Hiroshi Yamazaki* . . . . . **497**

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

*About the cover:* Two different dimer surfaces of nuclear receptors. Please see the article by Negishi\* ([doi.org/10.1124/dmd.116.074872](https://doi.org/10.1124/dmd.116.074872)).

\*2016 Bernard B. Brodie Lecture.