

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

January 2013

Vol. 41, No. 1

## CONTENTS

### SYMPOSIUM REPORTS

Role of Nuclear Receptors in Lipid Dysfunction and Obesity-Related Diseases. *Hollie I. Swanson, Taira Wada, Wen Xie, Barbara Renga, Angela Zampella, Eleonora Distrutti, Stefano Fiorucci, Bo Kong, Ann M. Thomas, Grace L. Guo, Ramesh Narayanan, Muralimohan Yepuru, James T. Dalton, and John Y. L. Chiang . . . . .* **1**

NADPH-Cytochrome P450 Oxidoreductase: Roles in Physiology, Pharmacology, and Toxicology. *David S. Riddick, Xinxin Ding, C. Roland Wolf, Todd D. Porter, Amit V. Pandey, Qing-Yu Zhang, Jun Gu, Robert D. Finn, Sebastien Ronseaux, Lesley A. McLaughlin, Colin J. Henderson, Ling Zou, and Christa E. Flick . . . . .* **12**

### SHORT COMMUNICATIONS

□ Evidence for Substrate-Dependent Inhibition Profiles for Human Liver Aldehyde Oxidase. *John T. Barr and Jeffrey P. Jones . . . . .* **24**

□ Metabolism of Triethylenetetramine and 1,12-Diamino-3,6,9-Triazadodecane by the Spermidine/Spermine-*N*<sup>1</sup>-Acetyltransferase and Thialysine Acetyltransferase. *Mervi T. Hyvönen, Janne Weisell, Alex R. Khomutov, Leena Alhonen, Jouko Vepsäläinen, and Tuomo A. Keinänen . . . . .* **30**

### ARTICLES

Function of the Blood-Brain Barrier and Restriction of Drug Delivery to Invasive Glioma Cells: Findings in an Orthotopic Rat Xenograft Model of Glioma. *Sagar Agarwal, Pooja Manchanda, Michael A. Vogelbaum, John R. Ohlfest, and William F. Elmquist . . . . .* **33**

□ Carboxylesterases Are Uniquely Expressed among Tissues and Regulated by Nuclear Hormone Receptors in the Mouse. *Ryan D. Jones, Anna M. Taylor, Ernest Y. Tong, and Joyce J. Repa . . . . .* **40**

□ Autoinhibition of CYP3A4 Leads to Important Role of CYP2C8 in Imatinib Metabolism: Variability

in CYP2C8 Activity May Alter Plasma Concentrations and Response. *Anne M. Filppula, Mikko Neuvonen, Jouko Laitila, Pertti J. Neuvonen, and Janne T. Backman . . . . .* **50**

Discovery and Characterization of Novel, Potent, and Selective Cytochrome P450 2J2 Inhibitors. *Shuang Ren, Juan Zeng, Ye Mei, John Z. H. Zhang, S. Frank Yan, Jian Fei, and Li Chen . . . . .* **60**

□ DNA Methylation and Histone Modification Profiles of Mouse Organic Anion Transporting Polypeptides. *Satoki Imai, Ryota Kikuchi, Hiroyuki Kusuhara, and Yuichi Sugiyama . . . . .* **72**

□ Characterization of Differential Cocaine Metabolism in Mouse and Rat through Metabolomics-Guided Metabolite Profiling. *Dan Yao, Xiaolei Shi, Lei Wang, Blake A. Gosnell, and Chi Chen . . . . .* **79**

Metabolism and Disposition of Vilanterol, a Long-Acting  $\beta_2$ -Adrenoceptor Agonist for Inhalation Use in Humans. *Andrew W. Harrell, Sarah K. Siederer, Jo Bal, Nainesh H. Patel, Graeme C. Young, Clive C. Felgate, Sebastian J. Pearce, Andy D. Roberts, Claire Beaumont, Amanda J. Emmons, Adrian I. Pereira, and Rodger D. Kempsford . . . . .* **89**

Interactions between CYP2E1 and CYP2B4: Effects on Affinity for NADPH-Cytochrome P450 Reductase and Substrate Metabolism. *Cesar Kanaan, Erin V. Shea, Hsia-lien Lin, Haoming Zhang, Matthew J. Pratt-Hyatt, and Paul F. Hollenberg . . . . .* **101**

Interaction of  $\gamma$ -Glutamyltranspeptidase with Ibuprofen-S-Acyl-Glutathione In Vitro and In Vivo in Human. *Mark P. Grillo, Michelle Tadano Lohr, and Smriti Khera . . . . .* **111**

Metabolism and Quantification of [<sup>18</sup>F]DPA-714, a New TSPO Positron Emission Tomography Radioligand. *Marie-Anne Peyronneau, Wadad Saba, Sébastien Goutal, Annelaure Damont,*

Downloaded from dnd.aspetjournals.org at ASPET Journals on November 19, 2017

Continued on next page

<i>Frédéric Dollé, Michael Kassiou, Michel Bottlaender, and Héric Valette . . . . .</i>	<b>122</b>	Differential Influences of Ethanol on Early Exposure to Racemic Methylphenidate Compared with Dexmethylphenidate in Humans. <i>Kennerly S. Patrick, Arthur B. Straughn, Owen T. Reeves, III, Hilary Bernstein, Guinevere H. Bell, Erica R. Anderson, and Robert J. Malcolm. . . . .</i>	<b>197</b>
Generation and Characterization of a Novel <i>Cyp2a</i> (4/5) <i>bgs</i> -Null Mouse Model. <i>Yuan Wei, Lei Li, Xin Zhou, Qing-Yu Zhang, Anwar Dunbar, Fang Liu, Kerri Kluetzman, Weizhu Yang, and Xinxin Ding</i>	<b>132</b>	Effect of Coadministration of Single and Multiple Doses of Rifampicin on the Pharmacokinetics of Fexofenadine Enantiomers in Healthy Subjects. <i>Hiroyuki Kusuhara, Masatomo Miura, Norio Yasui-Furukori, Kenta Yoshida, Yumiko Akamine, Miyu Yokochi, Shinya Fukizawa, Kazuaki Ikejiri, Kayoko Kanamitsu, Tsukasa Uno, and Yuichi Sugiyama. . . . .</i>	<b>206</b>
Carbon Monoxide-Bound Red Blood Cells Protect Red Blood Cell Transfusion-Induced Hepatic Cytochrome P450 Impairment in Hemorrhagic-Shock Rats. <i>Shigeru Ogaki, Kazuaki Taguchi, Hiroshi Watanabe, Masaki Otagiri, and Toru Maruyama . . . . .</i>	<b>141</b>	Effects of Hypothermia on the Disposition of Morphine, Midazolam, Fentanyl, and Propofol in Intensive Care Unit Patients. <i>Thor Wilhelm Bjelland, Pål Klepstad, Bjørn Olav Haugen, Turid Nilsen, and Ola Dale . . . . .</i>	<b>214</b>
Evaluation and Prediction of Potential Drug-Drug Interactions of Linagliptin Using In Vitro Cell Culture Methods. <i>Naoki Ishiguro, Hidetada Shimizu, Wataru Kishimoto, Thomas Ebner, and Olaf Schaefer . . . . .</i>	<b>149</b>	☐ Evaluation of the Relationship between Sex, Polymorphisms in <i>CYP2C8</i> and <i>CYP2C9</i> , and Pharmacokinetics of Angiotensin Receptor Blockers. <i>Teresa Cabaleiro, Manuel Román, Dolores Ochoa, María Talegón, Rocío Prieto-Pérez, Aneta Wojnicz, Rosario López-Rodríguez, Jesús Novalbos, and Francisco Abad-Santos . . . . .</i>	<b>224</b>
Effect of Solvents on the Time-Dependent Inhibition of CYP3A4 and the Biotransformation of AZD3839 in Human Liver Microsomes and Hepatocytes. <i>Jenny Aasa, Yin Hu, Göran Eklund, Anders Lindgren, Pawel Baranczewski, Jonas Malmquist, Dominika Turek, and Tjerk Bueters. . . . .</i>	<b>159</b>	☐ Clinical Pharmacokinetics, Metabolism, and Drug-Drug Interaction of Carfilzomib. <i>Zhengping Wang, Jinfu Yang, Christopher Kirk, Ying Fang, Melissa Alsina, Ashraf Badros, Kyriakos Papadopoulos, Alvin Wong, Tina Woo, Darrin Bomba, Jin Li, and Jeffrey R. Infante . . . . .</i>	<b>230</b>
Importance of UDP-Glucuronosyltransferases 2A2 and 2A3 in Tobacco Carcinogen Metabolism. <i>Ryan T. Bushey, Douglas F. Dluzen, and Philip Lazarus . . . . .</i>	<b>170</b>	Impact of Hydrolysis-Mediated Clearance on the Pharmacokinetics of Novel Anaplastic Lymphoma Kinase Inhibitors. <i>Yohannes Teffera, Loren M. Berry, Rachael L. Brake, Richard T. Lewis, Douglas C. Saffran, Earl Moore, Jingzhou Liu, and Zhiyang Zhao . . . . .</i>	<b>238</b>
Pharmacokinetic Mechanism Involved in the Prolonged High Retention of Laninamivir in Mouse Respiratory Tissues after Intranasal Administration of its Prodrug Laninamivir Octanoate. <i>Kumiko Koyama, Daisuke Nakai, Makoto Takahashi, Naoko Nakai, Nobuhiro Kobayashi, Teruko Imai, and Takashi Izumi . . . . .</i>	<b>180</b>	☐ Mechanisms of Subcutaneous Absorption of Rituximab in Rats. <i>Leonid Kagan and Donald E. Mager. . . . .</i>	<b>248</b>
Combination Lopinavir and Ritonavir Alter Exogenous and Endogenous Bile Acid Disposition in Sandwich-Cultured Rat Hepatocytes. <i>LaToya M. Griffin, Paul B. Watkins, Cassandra H. Perry, Robert L. St. Claire, III, and Kim L. R. Brouwer. . . . .</i>	<b>188</b>		

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

*About the cover:* The role of hepatic and intestinal FXR in bile acid homeostasis. See the symposium report by Swanson et al. on page 1 of this issue.