

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

April 2010

Vol. 38, No. 4

## CONTENTS

### SYMPOSIUM ARTICLE

- Targeting Drug-Metabolizing Enzymes for Effective Chemoprevention and Chemotherapy. *Hollie I. Swanson, Vincent C. O. Njar, Zhen Yu, David J. Castro, Frank J. Gonzalez, David E. Williams, Ying Huang, Ah-Ng T. Kong, Joshua C. Doloff, Jie Ma, David J. Waxman, and Emily E. Scott* . . . . . **539**

### ARTICLES

- Molecular Cloning of the Baboon UDP-Glucuronosyltransferase 2B Gene Family and Their Activity in Conjugating Morphine. *Kirsten Abildskov, Piper Weldy, and Marianne Garland* . . . . . **545**
- Disposition and Metabolism of Semagacestat, a  $\gamma$ -Secretase Inhibitor, in Humans. *Ping Yi, Chad Hadden, Palaniappan Kulanthaivel, Nathan Calvert, William Annes, Thomas Brown, Robert J. Barbuch, Archana Chaudhary, Mosun A. Ayan-Oshodi, and Barbara J. Ring* . . . . . **554**
- Monoclonal Antibody-Glial-Derived Neurotrophic Factor Fusion Protein Penetrates the Blood-Brain Barrier in the Mouse. *Qing-Hui Zhou, Ruben J. Boado, Jeff Zhiqiang Lu, Eric Ka-Wai Hui, and William M. Pardridge* . . . . . **566**
- Role of P-Glycoprotein in the Disposition of Macrocyclic Lactones: A Comparison between Ivermectin, Eprinomectin, and Moxidectin in Mice. *Solange Kiki-Mvouaka, Cécile Ménez, Christiane Borin, Faouri Lyazrhi, Magali Foucaud-Vignault, Jacques Dupuy, Xavier Collet, Michel Alvinerie, and Anne Lespine* . . . . . **573**
- Species Differences in the Formation of Vabicaserin Carbamoyl Glucuronide. *Zeen Tong, Appavu Chandrasekaran, William DeMaio, Ronald Jordan, Hongshan Li, Robin Moore, Nagaraju*

- Poola, Peter Burghart, Theresa Hultin, and JoAnn Scatina* . . . . . **581**

- Hepatocyte Nuclear Factor 4 $\alpha$  Regulates Rifampicin-Mediated Induction of *CYP2C* Genes in Primary Cultures of Human Hepatocytes. *Ritu Rana, Yuping Chen, Stephen S. Ferguson, Grace E. Kissling, Sailesh Surapureddi, and Joyce A. Goldstein* . . . . . **591**

- Pharmacokinetics of Humanized Monoclonal Anti-Tumor Necrosis Factor- $\alpha$  Antibody and Its Neonatal Fc Receptor Variants in Mice and Cynomolgus Monkeys. *Rong Deng, Kelly M. Loyet, Samantha Lien, Suhasini Iyer, Laura E. DeForge, Frank-Peter Theil, Henry B. Lowman, Paul J. Fielder, and Saileta Prabhu* . . . . . **600**

- Metabolism of Intravenous Methylnaltrexone in Mice, Rats, Dogs, and Humans. *Appavu Chandrasekaran, Zeen Tong, Hongshan Li, John C. L. Erve, William DeMaio, Igor Goljer, Oliver McConnell, Yakov Rotshteyn, Theresa Hultin, Rasmey Talaat, and JoAnn Scatina* . . . . . **606**

- Phase II Metabolism of Hesperetin by Individual UDP-Glucuronosyltransferases and Sulfotransferases and Rat and Human Tissue Samples. *Walter Brand, Marelle G. Boersma, Hanneke Bik, Elisabeth F. Hoek-van den Hil, Jacques Vervoort, Denis Barron, Walter Meinel, Hansruedi Glatt, Gary Williamson, Peter J. van Bladeren, and Ivonne M. C. M. Rietjens* . . . . . **617**

- Identification of the UDP-Glucuronosyltransferase Isozyme Involved in Senecionine Glucuronidation in Human Liver Microsomes. *Yu-Qi He, Yong Liu, Bin-Feng Zhang, Hui-Xin Liu, Yan-Liu Lu, Li Yang, Ai-zhen Xiong, Ling-Ling Xu,*

Continued on next page

<i>Chang-Hong Wang, Ling Yang, and Zheng-Tao Wang</i> . . . . .	<b>626</b>	<i>Corinne Barreau, Sophie Langouët, Chantal Benelli, Luc Penicaud, Philippe Beaune, and Isabelle de Waziers</i> . . . . .	<b>679</b>
Absorption, Distribution, and Biliary Excretion of Cafestol, a Potent Cholesterol-Elevating Compound in Unfiltered Coffees, in Mice. <i>S. T. J. van Cruchten, D. R. de Waart, C. Kunne, G. J. E. J. Hooiveld, M. V. Boekschoten, M. B. Katan, R. P. J. Oude Elferink, and R. F. Witkamp</i> . . . . .	<b>635</b>	□ How Many and Which Amino Acids Are Responsible for the Large Activity Differences between the Highly Homologous UDP-Glucuronosyltransferases (UGT) 1A9 and UGT1A10? <i>Katriina Itäaho, Liisa Laakkonen, and Moshe Finel</i> . . . . .	<b>687</b>
Cross-Species Comparison of the Metabolism and Excretion of Zoniporide: Contribution of Aldehyde Oxidase to Interspecies Differences. <i>Deepak Dalvie, Chenghong Zhang, Weichao Chen, Teresa Smolarek, R. Scott Obach, and Cho-Ming Loi</i> . . . . .	<b>641</b>	Polychlorinated Biphenyl-Mediated Decrease in Serum Thyroxine Level in Rodents. <i>Yoshihisa Kato, Koichi Haraguchi, Yuriko Ito, Aki Fujii, Tomoaki Yamazaki, Tetsuya Endo, Nobuyuki Koga, Shizuo Yamada, and Masakuni Degawa</i> . . . . .	<b>697</b>
Disposition of [1'- <sup>14</sup> C]Stavudine after Oral Administration to Humans. <i>Lian Zhou, Sanjeev Kaul, Peggy Liu-Kreyche, Scott B. Tran, Robert R. Espina, Bethanne M. Warrack, Vikram A. Roongta, and Ramaswamy A. Iyer</i> . . . . .	<b>655</b>	High-Activity P-Glycoprotein, Multidrug Resistance Protein 2, and Breast Cancer Resistance Protein Membrane Vesicles Prepared from Transiently Transfected Human Embryonic Kidney 293-Epstein-Barr Virus Nuclear Antigen Cells. <i>Johan E. Karlsson, Catherine Heddle, Aleksei Rozkov, Joke Rotticci-Mulder, Ola Tuveson, Constanze Hilgendorf, and Tommy B. Andersson</i> . . . . .	<b>705</b>
The Metabolism and Disposition of the Oral Dipeptidyl Peptidase-4 Inhibitor, Linagliptin, in Humans. <i>Stefan Blech, Eva Ludwig-Schwellinger, Eva Ulrike Gräfe-Mody, Barbara Withopf, and Klaus Wagner</i> . . . . .	<b>667</b>	Evaluation of 4',6-Diamidino-2-phenylindole as a Fluorescent Probe Substrate for Rapid Assays of the Functionality of Human Multidrug and Toxin Extrusion Proteins. <i>Tomoya Yasujima, Kin-ya Ohta, Katsuhisa Inoue, Munenori Ishimaru, and Hiroaki Yuasa</i> . . . . .	<b>715</b>
Xenobiotic-Metabolizing Cytochromes P450 in Human White Adipose Tissue: Expression and Induction. <i>Sandrine Ellero, Ghassan Chakhtoura,</i>			

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

*About the cover:* Uptake of DAPI in HEK293 cells transiently expressing hMATEs. The fluorescent microscopic images of DAPI were obtained after incubation of HEK293 cells transiently expressing hMATE1, those expressing hMATE2-K, and mock cells with DAPI (0.5 μM) at 37°C and pH 7.4 for 20 min. Also shown are the images of cotransfected GFP. See the article by Yasujima et al. on page 715 of this issue.