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**


Disposition and Metabolism of Semagacestat, a γ-Secretase Inhibitor, in Humans. Ping Yi, Chad Hadden, Pulumippapan Kulanthaivel, Nathan Calvert, William Annes, Thomas Brown, Robert J. Barbuch, Archana Chaudhary, Mosan A. Ayanoshide, and Barbara J. Ring ............... 554

Monoclonal Antibody-Glia-Based Neurotrophic Factor Fusion Protein Penetrates the Blood-Brain Barrier in the Mouse. Qing-Hui Zhou, Ruben J. Boado, Jeff Zhiquian Lu, Eric Ka-Wai Hui, and William M. Partridge .................. 566

Role of P-Glycoprotein in the Disposition of Macro cyclic Lactones: A Comparison between Ivermectin, Eprominectin, and Moxidectin in Mice. Solange Kiki-Mvoouaka, Cécile Ménez, Christiane Borin, Faouri Lyazrhi, Magali Foucaud-Vignault, Jacques Dupuy, Xavier Collet, Michel Alvinerie, and Anne Lepagnol .................. 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 4α Regulates Rifampicin-Mediated Induction of CYP2C Genes in Primary Cultures of Human Hepatocytes. Rita Rana, Yap Ying Chen, Stephen S. Ferguson, Grace E. Kissling, Sailesh Surapureddy, and Joyce A. Goldstein .................. 591

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

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

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

Identification of the UDP-Glucuronosyltransferase Isozyme Involved in Seneclonice Glucuronida tion 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, and Craig A. Balsdon .................. 626

Continued on next page

*Drug Metabolism and Disposition* (ISSN 0090-9556) is published monthly (one volume per year) by the American Society for Pharmacology and Experimental Therapeutics, 9650 Rockville Pike, Bethesda, MD 20814-3995; e-mail: subscriptions@aspet.org; Web site: aspet.org. Periodicals postage paid at Bethesda, MD, and at additional mailing offices. POSTMASTER: Send address changes to *Drug Metabolism and Disposition*, 9650 Rockville Pike, Bethesda, MD 20814-3995. Subscription rates: U.S.: $436.00; outside the U.S.: $515. Single copy: $40. GST Tax Number for Canadian subscribers: BN:13489 2330 RT. Indexed or abstracted by Biochemistry & Biophysics Citation Index®, Biological Abstracts, BIOSIS Reviews Database, BiSciences Information Services, Current Awareness in Biological Sciences, Current Contents/Life Sciences, EMBASE/Excerpta Medica, Index Medicus, International Pharmaceutical Abstracts, Medical Documentation Service®, Reference Update®, Research Alert®, Science Citation Index®, SciSearch®, and SIIC Data Bases Copyright © 2010 by the American Society for Pharmacology and Experimental Therapeutics. All rights reserved. Printed in the U.S.A.
Contents (cont’d.)

Chang-Hong Wang, Ling Yang, and Zheng-Tao Wang ........................................ 626


Cross-Species Comparison of the Metabolism and Excretion of Zoniporide: Contribution of Aldehyde Oxidase to Interspecies Differences. Deepak Dalvie, Chenghong Zhang, Weichao Chen, Teresa Smolarek, R. Scott Obach, and Cho-Ming Loi .................. 641


Xenobiotic-Metabolizing Cytochromes P450 in Human White Adipose Tissue: Expression and Induction. Sandrine Ellero, Ghassan Chakhtoura, Corinne Barreau, Sophie Langouët, Chantal Benelli, Luc Penicaud, Philippe Beaume, and Isabelle de Waziers ..................... 679

How Many and Which Amino Acids Are Responsible for the Large Activity Differences between the Highly Homologous UDP-Glucuronosyltransferases (UGT) 1A9 and UGT1A10? Katriina Itäaho, Liisa Laakkonen, and Moshe Finel ..... 687

Polychlorinated Biphenyl-Mediated Decrease in Serum Thyroxine Level in Rodents. Yoshihisa Kato, Koichi Haraguchi, Yuriko Ito, Aki Fujii, Tomoaki Yamazaki, Tetsuya Endo, Nobuyuki Koga, Shizuo Yamada, and Masakuni Degawa ........ 697


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.