CONTENTS

SPECIAL SECTION ON PEDIATRIC DRUG DISPOSITION AND PHARMACOKINETICS

Challenges and Opportunities for Increasing the Knowledge Base Related to Drug Biotransformation and Pharmacokinetics during Growth and Development. J. Steven Leeder and Bernd Meibohm . 916

Role of Quantitative Clinical Pharmacology in Pediatric Approval and Labeling. Nitin Mehrotra, Atul Bhattaram, Justin C. Earp, Jeffry Florian, Kevin Kru dys, Jee Eun Lee, Joo Yeon Lee, Jiang Liu, Yeruk Mulugeta, Jingyu Yu, Ping Zhao, and Vikram Sinha . 924

Physiologically Based Pharmacokinetic Modeling in Pediatric Oncology Drug Development. Nathalie Rioux and Nigel J. Waters . 934

Effect of Age on The Hepatocellularity Number for Wistar rats. Sarinj Fattah, Patrick Augustijns, and Pieter Annaert . 944


Age-Dependent Human Hepatic Carboxylesterase 1 (CES1) and Carboxylesterase 2 (CES2) Postnatal Ontogeny. Ronald N. Hines, Pippa M. Simpson, and D. Gail McCarver . 959

The Ontogeny and Population Variability of Human Hepatic NADPH Dehydrogenase Quinone Oxido-Reductase 1 (NQO1). Luc R.A. Rougéé, Zoe Riches, Jacob M. Berman, and Abby C. Collier . 967

Quantification of Flavin-containing Monooxygenases 1, 3, and 5 in Human Liver Microsomes by UPLC-MRM-Based Targeted Quantitative Proteomics and Its Application to the Study of Ontogeny. Yao Chen, Nicole R. Zane, Dhiren R. Thakker, and Michael Zhuo Wang . 975


Ontogeny of Hepatic Drug Transporters and Relevance to Drugs Used in Pediatrics. Yasmine Elmorsi, Jill Barber, and Amin Rostami-Hodjegan . 992

Expression Patterns of Organic Anion Transporting Polypeptides 1B1 and 1B3 Protein in Human Pediatric Liver. Margaret M. S. Thomson, Ronald N. Hines, Erin C. Schuetz, and Bernd Meibohm . 999


Human Intestinal PEPT1 Transporter Expression and Localization in Preterm and Term Infants. Miriam G. Mooij, Barbara E. A. de Koning, Dicky J. Lindenbergh-Kortleve, Ytie Simons-Oosterhuis, Bianca D. van Groen, Dick Tibboel, Janneke N. Samsom, and Saskia N. de Wildt . 1014

Dynamics of Cytosine Methylation in the Proximal Promoters of CYP3A4 and CYP3A7 in Pediatric and Prenatal Livers. Carrie A. Vyhlidal, Chengpeng Bi, Shui Qing Ye, and J. Steven Leeder . 1020

Role of Chromatin Structural Changes in Regulating Human CYP3A Ontogeny. Nicholas L. Giebel, Jeffrey D. Shadley, D. Gail McCarver, Kenneth Dorko, Roberto Gramignoli, Stephen C. Strom, Ke Yan, Pippa M. Simpson, and Ronald N. Hines . 1027

Age-Specific Regulation of Drug-Processing Genes in Mouse Liver by Ligands of Xenobiotic-Sensing Transcription Factors. Cindy Yanfei Li, Helen J. Renaud, Curtis D. Klaassen, and Julia Yue Cui . 1038

Continued on next page

Correlation between Conjugated Bisphenol A Concentrations and Efflux Transporter Expression in Human Fetal Livers. Jamie E. Moscovitz, Muna S. Nahar, Stuart L. Shalat, Angela L. Slitt, Dana C. Dolinoy, and Lauren M. Aleksunes ............. 1061

Decreased Pregnane X Receptor Expression in Children with Active Crohn’s Disease. Valentina Shakhnovich, Carrie Vyhlidal, Craig Friesen, Amber Hildreth, Vivekanand Singh, James Daniel, Gregory L. Kears, and J. Steven Leeder ............ 1066

Characterization of Atomoxetine Biotransformation and Implications for Development of PBPK Models for Dose Individualization in Children. Jean C. Dinh, Robin E. Pearce, Leon Van Haandel, Andrea Gaedigk, and J. Steven Leeder ........ 1070

Examining Small Intestinal Transit Time as a Function of Age: Is There Evidence to Support Age-Dependent Differences among Children?. Anil R. Maharaj and Andrea N. Edginton ............. 1080

How Does In Vivo Biliary Elimination of Drugs Change with Age? Evidence from In Vitro and Clinical Data Using a Systems Pharmacology Approach. Trevor N. Johnson, Masoud Jamei, and Karen Rowland-Yeo ............ 1090

Considering Age Variation When Coining Drugs as High versus Low Hepatic Extraction Ratio. Farzaneh Salem, Khaled Abduljalil, Yoshiteru Kamiyama, and Amin Rostami-Hodjegan ........ 1099

Predicting Stereoselective Disposition of Carvedilol in Adult and Pediatric Chronic Heart Failure Patients by Incorporating Pathophysiological Changes in Organ Blood Flows—A Physiologically Based Pharmacokinetic Approach. Muhammad Fawad Rasool, Feras Khalil, and Stephanie Läer ............ 1103

Population Pharmacokinetics of Oral Topotecan in Infants and Very Young Children with Brain Tumors Demonstrates a Role of ABCG2 rs4148157 on the Absorption Rate Constant. Jessica K. Roberts, Anna V. Birg, Tong Lin, Vinay M. Daryani, John C. Panetta, Alberto Bronisner, Giles W. Robinson, Amar J. Gajjar, and Clinton F. Stewart .......... 1116

ARTICLES

Cardiotonic Pill Reduces Myocardial Ischemia-Reperfusion Injury via Increasing EET Concentrations in Rats. Meijuan Xu, Haiping Hao, Lijeng Jiang, Yidan Wei, Fang Zhou, Jianguo Sun, Jingwei Zhang, Hui Ji, Guangli Wang, Wenzheng Ju, and Ping Li .................. 878

Zomepirac Acyl Glucuronide Is Responsible for Zomepirac-Induced Acute Kidney Injury in Mice. Atsushi Iwamura, Katsuhito Watanabe, Sho Akai, Tsubasa Nishinosono, Koichi Tsuneyama, Shingo Oda, Toshiyuki Kume, and Tsuyoshi Yokoi .... 888


Individual Differences in Metabolic Clearance of S-Warfarin Efficiently Mediated by Polymorphic Marmoset Cytochrome P450 2C19 in Livers. Shotaro Uehara, Yasuhiro Uno, Takashi Inoue, Mirai Kawano, Makiko Shimizu, Akiko Toda, Masahiro Utoh, Erika Sasaki, and Hiroshi Yamazaki .................. 911

Metabolite Kinetics: The Segregated Flow Model for Intestinal and Whole Body Physiologically Based Pharmacokinetic Modeling to Describe Intestinal and Hepatic Glucuronidation of Morphine in Rats In Vivo. Qi J. Yang, Jianghong Fan, Shu Chen, Lutan Liu, Huadong Sun, and K. Sandy Pang .................. 1123

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

About the cover: Exposure response and dose-response of adalimumab in pediatric patients with CD during the maintenance phase. See the article by Mehrotra et al. (dx.doi.org/10.1124/dmd.116.069559).