

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

January 2007

Vol. 35, No. 1

## CONTENTS

<b>THE 2006 BERNARD B. BRODIE AWARD LECTURE</b>	
CYP2E1. FRANK J. GONZALEZ . . . . .	1
<b>MINIREVIEW</b>	
PEGylated Proteins: Evaluation of Their Safety in the Absence of Definitive Metabolism Studies. ROB WEBSTER, ERIC DIDIER, PHILIP HARRIS, NED SIEGEL, JEANNE STADLER, LORRAINE TILBURY, AND DENNIS SMITH . . . . .	9
<b>SHORT COMMUNICATION</b>	
Cellular Localization Studies on Human Estrogen Sulfotransferase SULT1E1 in Human Embryonic Kidney 293 Cells. RUCHITA KAPOOR, DEEPTHI NIMMAGADDA, AND JONATHAN J. SHENG . . . . .	17
<b>ARTICLES</b>	
Biotransformation of Geldanamycin and 17-Allyl-amino-17-Demethoxygeldanamycin by Human Liver Microsomes: Reductive versus Oxidative Metabolism and Implications. WENSHENG LANG, GARY W. CALDWELL, JIAN LI, GREGORY C. LEO, WILLIAM J. JONES, AND JOHN A. MASUCCI . . . . .	21
Organic Anion Transporting Polypeptide 2B1 and Breast Cancer Resistance Protein Interact in the Transepithelial Transport of Steroid Sulfates in Human Placenta. MARKUS GRUBE, SEBASTIAN REUTHER, HENRIETTE MEYER ZU SCHWABEDISSEN, KATHLEEN KÖCK, KATRIN DRABER, CHRISTOPH A. RITTER, CHRISTOPH FUSCH, GABRIELE JEDLITSCHKY, AND HEYO K. KROEMER . . . . .	30
Gender Dictates the Nuclear Receptor-Mediated Regulation of CYP3A44. SAYEEPRIYADARSHINI ANAKK, WENDONG HUANG, JEFFREY L. STAUDINGER, KHENG TAN, TIMOTHY J. COLE, DAVID D. MOORE, AND HENRY W. STROBEL . . . . .	36
Specificity of Aminoacylase III-Mediated Deacetylation of Mercapturic Acids. DEBRA NEWMAN, NATALIA ABULADZE, KAROLINE SCHOLZ, WOLFGANG DEKANT, VLADIMIR TSUPRUN, SERGEY RYAZANTSEV, GALYNA BONDAR, PAKAN SASSANI, IRA KURTZ, AND ALEXANDER PUSHKIN . . . . .	43
The Disposition and Metabolism of Naveglitazar, a Peroxisome Proliferator-Activated Receptor $\alpha$ - $\gamma$ Dual, $\gamma$ -Dominant Agonist in Mice, Rats, and Monkeys. PING YI, CHAD E. HADDEN, WILLIAM F. ANNES, DAVID A. JACKSON, BARRY C. PETERSON, TODD A. GILLESPIE, AND JASON T. JOHNSON . . . . .	51
Elevated Warfarin Metabolism in Warfarin-Resistant Roof Rats ( <i>Rattus rattus</i> ) in Tokyo. MAYUMI ISHIZUKA, FUMIE OKAJIMA, TSUTOMU TANIKAWA, HEEWON MIN, KAZUYUKI D. TANAKA, KENTARO Q. SAKAMOTO, AND SHOICHI FUJITA . . . . .	62
A New CYP3A5 Variant, CYP3A5*11, Is Shown to Be Defective in Nifedipine Metabolism in a Recombinant cDNA Expression System. SUJUN LEE, ILSE P. VAN DER HEIDEN, JOYCE A. GOLDSTEIN, AND RON H. N. VAN SCHAİK . . . . .	67
Identification of Human Cytochrome P450 Isozymes Involved in Diphenhydramine <i>N</i> -Demethylation. TOMOKO AKUTSU, KAORU KOBAYASHI, KOICHI SAKURADA, HIROSHI IKEGAYA, TOMOMI FURIHATA, AND KAN CHIBA . . . . .	72
A Novel Model for the Prediction of Drug-Drug Interactions in Humans Based on in Vitro Cytochrome P450 Phenotypic Data. CHUANG LU, GERALD T. MIWA, SHIMOGA R. PRAKASH, LIANGSHANG GAN, AND SURESH K. BALANI . . . . .	79
Humanized IgG <sub>1</sub> Variants with Differential Binding Properties to the Neonatal Fc Receptor: Relation-	

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: info@aspet.org; Web site: <http://www.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.: \$353.00 for institutions and \$184.00 for non-ASPET members. Outside the U.S.: \$423.00 for institutions and \$254.00 for non-ASPET members. Single copy: \$35.00. GST Tax Number for Canadian subscribers: BN:13489 2330 RT. Indexed or abstracted by *Biochemistry & Biophysics Citation Index*®, *Biological Abstracts*, *BIOSIS Previews Database*, *BioSciences Information Service*, *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 © 2007 by the American Society for Pharmacology and Experimental Therapeutics. All rights reserved. Printed in the U.S.A.

ship to Pharmacokinetics in Mice and Primates. AMITA DATTA-MANNAN, DERRICK R. WITCHER, YING TANG, JEFFRY WATKINS, WEIDONG JIANG, AND VICTOR J. WROBLEWSKI . . . . .	<b>86</b>	SOMOGYI, ROBERT W. MILNE, , AND BENEDETTA C. SALLUSTIO . . . . .	<b>128</b>
Pregnane X Receptor-Dependent Induction of the <i>CYP3A4</i> Gene by <i>o,p'</i> -1,1,1-Trichloro-2,2-Bis ( <i>p</i> -Chlorophenyl)ethane. IRMA M. MEDINA-DÍAZ, GEORGINA ARTEAGA-ILLAN, MARIO BERMUDEZ DE LEON, BULMARO CISNEROS, ADOLFO SIERRA-SANTOYO, LIBIA VEGA, FRANK J. GONZALEZ, AND GUILLERMO ELIZONDO . . . . .	<b>95</b>	Involvement of Multiple Cytochrome P450 and UDP-Glucuronosyltransferase Enzymes in the in Vitro Metabolism of Muraglitazar. DONGLU ZHANG, LIFEI WANG, GAMINI CHANDRASENA, LI MA, MING-SHE ZHU, HONGJIAN ZHANG, CARL D. DAVIS, AND W. GRIFFITH HUMPHREYS . . . . .	<b>139</b>
A Real-Time Fluorescence Assay for Measuring <i>N</i> -Dealkylation. RICHARD T. MAYER, E. KURT DOLENCE, AND GABRIELE E. MAYER . . . . .	<b>103</b>	Comparative Metabolism of Radiolabeled Muraglitazar in Animals and Humans by Quantitative and Qualitative Metabolite Profiling. DONGLU ZHANG, LIFEI WANG, NIRMALA RAGHAVAN, HAIYING ZHANG, WENYING LI, PETER T. CHENG, MING YAO, LITAO ZHANG, MINGSHE ZHU, SAMUEL BONACORSI, SURESH YEOLA, JAMES MITROKA, NARAYANAN HARIHARAN, VINAYAK HOSAGRAHARA, GAMINI CHANDRASENA, WEN CHYI SHYU, AND W. GRIFFITH HUMPHREYS . . . . .	<b>150</b>
Impact of Curcumin-Induced Changes in P-Glycoprotein and CYP3A Expression on the Pharmacokinetics of Peroral Celiprolol and Midazolam in Rats. WENXIA ZHANG, THERESA MAY CHIN TAN, AND LEE-YONG LIM . . . . .	<b>110</b>	Cytochrome P450 and Glutathione <i>S</i> -Transferase mRNA Expression in Human Fetal Liver Hematopoietic Stem Cells. JING SHAO, PATRICIA L. STAPLETON, YVONNE S. LIN, AND EVAN P. GALLAGHER . . . . .	<b>168</b>
Isolation of the UDP-Glucuronosyltransferase 1A3 and 1A4 Proximal Promoters and Characterization of Their Dependence on the Transcription Factor Hepatocyte Nuclear Factor 1 $\alpha$ . DIONE A. GARDNER-STEPHEN AND PETER I. MACKENZIE . . . . .	<b>116</b>	Genetic Variation of Human Cytochrome P450 Reductase as a Potential Biomarker for Mitomycin C-Induced Cytotoxicity. SHOU-LIN WANG, JING-FEN HAN, XIAO-YANG HE, XIN-RU WANG, AND JUN-YAN HONG . . . . .	<b>176</b>
□ Tissue- and Gender-Specific mRNA Expression of UDP-Glucuronosyltransferases (UGTs) in Mice. DAVID B. BUCKLEY AND CURTIS D. KLAASSEN . . . . .	<b>121</b>	An Evaluation of the Cytochrome P450 Inhibition Potential of Lisdexamfetamine in Human Liver Microsomes. SUMA KRISHNAN AND SCOTT MONCRIEF . . . . .	<b>180</b>
CYP2B6, CYP2D6, and CYP3A4 Catalyze the Primary Oxidative Metabolism of Perhexiline Enantiomers by Human Liver Microsomes. BENJAMIN J. DAVIES, JANET K. COLLER, ANDREW A.			

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

About the cover: Immunolocalization of BCRP and OATP2B1 in the human placenta, as well as in BCRP-, OATP2B1-, and double-transfected MDCKII cells. See the article by Grube et al. on page 30 of this issue.