

DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

April 2007

Vol. 35, No. 4

CONTENTS

SHORT COMMUNICATIONS

- Zonal Gene Expression in Mouse Liver Resembles Expression Patterns of *Ha-ras* and β -Catenin Mutated Hepatomas. ALBERT BRAEUNING, CARINA ITTRICH, CHRISTOPH KOHLE, ALBRECHT BUCHMANN, AND MICHAEL SCHWARZ **503**
- Inhibitory Effects of Neurotransmitters and Steroids on Human CYP2A6. ERIKO HIGASHI, MIKI NAKAJIMA, MIKI KATOH, SHOGO TOKUDOME, AND TSUYOSHI YOKOI **508**
- A Novel Duplication Type of *CYP2A6* Gene in African-American Population. TATSUKI FUKAMI, MIKI NAKAJIMA, HIROYUKI YAMANAKA, YASUNARI FUKUSHIMA, HOWARD L. MCLEOD, AND TSUYOSHI YOKOI **515**
- Characterization of Two Cyclic Metabolites of Sitagliptin. DAVID Q. LIU, BYRON H. ARISON, RALPH A. STEARNS, DOOSEOP KIM, AND STELLA H. VINCENT **521**

ARTICLES

- Disposition of the Dipeptidyl Peptidase 4 Inhibitor Sitagliptin in Rats and Dogs. MARIA G. BECONI, JAMES R. REED, YOHANNES TEFFERA, YUAN-QING XIA, CHRISTOPHER J. KOCHANSKY, DAVID Q. LIU, SHIYAO XU, CHARLES S. ELMORE, SUZANNE CICCOTTO, DONALD F. HORA, RALPH A. STEARNS, AND STELLA H. VINCENT **525**
- Metabolism And Excretion of the Dipeptidyl Peptidase 4 Inhibitor [¹⁴C]Sitagliptin in Humans. STELLA H. VINCENT, JAMES R. REED, ARTHUR J. BERGMAN, CHARLES S. ELMORE, BING ZHU, SHIYAO XU, DAVID EBEL, PATRICK LARSON, WEI ZENG, LI CHEN, STACY DILZER, KENNETH LASSETER, KEITH

GOTTESDIENER, JOHN A. WAGNER, AND GARY A. HERMAN **533**

Role of P-glycoprotein in the Intestinal Absorption of Glabridin, an Active Flavonoid from the Root of *Glycyrrhiza glabra*. JIE CAO, XIAO CHEN, JUN LIANG, XUE-QING YU, AN-LONG XU, ELI CHAN, WEI DUAN, MIN HUANG, JING-YUAN WEN, XI-YONG YU, XIAO-TIAN LI, FWU-SHAN SHEU, AND SHU-FENG ZHOU **539**

The Absorption, Metabolism, and Excretion of the Novel Neuromodulator RWJ-333369 (1,2-Ethanediol, [1-(2-Chlorophenyl)-, 2-carbamate, (S)-] in Humans. G. S. J. MANNENS, J. HENDRICKX, C. G. M. JANSSEN, S. CHIEN, B. VAN HOOF, T. VERHAEGHE, M. KAO, M. F. KELLEY, I. GORIS, M. BOCKX, B. VERREET, M. BIALER, AND W. MEULDERMANS **554**

Metabolism and Excretion of RWJ-333369 [1,2-Ethanediol, 1-(2-Chlorophenyl)-, 2-carbamate, (S)-] in Mice, Rats, Rabbits, and Dogs. RAO N. V. S. MAMIDI, GEERT MANNENS, PIETER ANNAERT, JAN HENDRICKX, IVO GORIS, MARK BOCKX, COR G. M. JANSSEN, MARK KAO, MICHAEL F. KELLEY, AND WILLEM MEULDERMANS **566**

Interactions of Cyclosporin A with Breast Cancer Resistance Protein. CINDY Q. XIA, NING LIU, GERALD T. MIWA, AND LIANG-SHANG GAN **576**

Glucuronidation of Antiallergic Drug, Tranilast: Identification of Human UDP-Glucuronosyltransferase Isoforms and Effect of Its Phase I Metabolite. MIKI KATOH, TOMOHITO MATSUI, AND TSUYOSHI YOKOI **583**

□ Regional Distribution of Solute Carrier mRNA Expression Along the Human Intestinal Tract.

Continued on next page

YVONNE MEIER, JYRKI J. ELORANTA, JUTTA DARI-MONT, MANFRED G. ISMAIR, CHRISTIAN HILLER, MICHAEL FRIED, GERD A. KULLAK-ÜBLICK, AND STEPHAN R. VAVRICKA	590	Diverse Compounds in Rat Using Mechanism-Based Absorption, Distribution, and Metabolism Prediction Tools. STEFAN S. DE BUCK, VIKASH K. SINHA, LUCA A. FENU, RON A. GILISSEN, CLAIRE E. MACKIE, AND MARJOLEEN J. NIJSEN	649
Independent Regulation of Apical and Basolateral Drug Transporter Expression and Function in Placental Trophoblasts by Cytokines, Steroids, and Growth Factors. DENIS A. EVSEENKO, JAMES W. PAXTON, AND JEFFREY A. KEELAN	595	Use of Plasma and Brain Unbound Fractions to Assess the Extent of Brain Distribution of 34 Drugs: Comparison of Unbound Concentration Ratios to in Vivo P-Glycoprotein Efflux Ratios. J. CORY KALVASS, TRISTAN S. MAURER, AND GARY M. POLLACK	660
Comparison of Inhibition Potentials of Drugs against Zidovudine Glucuronidation in Rat Hepatocytes and Liver Microsomes. YUJI MANO, TAKASHI USUI, AND HIDETAKA KAMIMURA	602	Identification and Functional Characterization of Genetic Variants of Human Organic Cation Transporters in a Korean Population. HO-JIN KANG, IM-SOOK SONG, HO JUNG SHIN, WOO-YOUNG KIM, CHOONG-HEE LEE, JOO-CHEOL SHIM, HONG-HAO ZHOU, SANG SEOP LEE, AND JAE-GOOK SHIN	667
Deacetylclivorine: A Gender-Selective Metabolite of Clivorine Formed in Female Sprague-Dawley Rat Liver Microsomes. GE LIN, JUN TANG, XIAO QUAN LIU, YAN JIANG, AND JIANG ZHENG	607	Formation and Uptake of Arylhydroxylamine-Haptened Proteins in Human Dendritic Cells. SANJOY ROYCHOWDHURY, PIYUSH M. VYAS, AND CRAIG K. SVENSSON	676
Visible Spectra of Type II Cytochrome P450-Drug Complexes: Evidence that “Incomplete” Heme Coordination Is Common. CHARLES W. LOCUSON, J. MATTHEW HUTZLER, AND TIMOTHY S. TRACY	614	Detection of Human CYP2C8, CYP2C9, and CYP2J2 in Cardiovascular Tissues. TRACY C. DELOZIER, GRACE E. KISSLING, SHERRY J. COULTER, DIANA DAI, JULIE F. FOLEY, J. ALYCE BRADBURY, ELIZABETH MURPHY, CHARLES STEENBERGEN, DARRYL C. ZELDIN, AND JOYCE A. GOLDSTEIN	682
Identification and Functional Assessment of <i>BCRP</i> Polymorphisms in a Korean Population. SANG SEOP LEE, HYE-EUN JEONG, JOO-MI YI, HYUN-JU JUNG, JAE-EUN JANG, EUN-YOUNG KIM, SU-JUN LEE, AND JAE-GOOK SHIN	623	Possible Pathway(s) of Metyrapone Egress from the Active Site of Cytochrome P450 3A4: A Molecular Dynamics Simulation. WEIHUA LI, HONG LIU, XIAOMIN LUO, WEILIANG ZHU, YUN TANG, JAMES R. HALPERT, AND HUALIANG JIANG	689
Metabolism of a Heterocyclic Amine Colon Carcinogen in Young and Old Rats. HARVEY J. ARMBRECHT, VIJAYA M. LAKSHMI, JASON WICKSTRA, FONG FU HSU, AND TERRY V. ZENSER	633		
Development of Three Parallel Cytochrome P450 Enzyme Affinity Detection Systems Coupled Online to Gradient High-Performance Liquid Chromatography. JEROEN KOOL, SEBASTIAAN M. VAN LIEMPD, HUUB VAN ROSSUM, DANNY A. VAN ELSWIJK, HUBERTUS IRTH, JAN N. M. COMMANDEUR, AND NICO P. E. VERMEULEN	640	LETTER TO THE EDITOR	
The Prediction of Drug Metabolism, Tissue Distribution, and Bioavailability of 50 Structurally		The Time to Move Cytochrome P450 Induction into Mainstream Pharmacology Is Long Overdue. DENNIS A. SMITH, MAURICE DICKINS, ODETTE A. FAHMI, KAZUHIDE IWASAKI, CAROLINE LEE, R. SCOTT OBACH, GUY PADBURY, SONIA M. DE MORAIS, SHARON L. RIPP, JEFF STEVENS, RICHARD VOORMAN, AND KURESH YOUSIM	697

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

About the cover: Pairwise linkage disequilibrium (LD) among 16 SNPs of the *hOCT1*, *hOCT2*, and *hOCT3* genes in a Korean population. See the article by Kang et al. on page 667 of this issue.