The Journal of Pharmacology and Experimental Therapeutics

A Publication of the American Society for Pharmacology and Experimental Therapeutics

July 2011 Vol. 338, No. 1

Contents

HIGHLIGHTED PAPERS

1

BEHAVIORAL PHARMACOLOGY

Preclinical Pharmacology of AZD2327: A Highly Selective Agonist of the δ-Opioid Receptor

Discriminative Stimulus Effects of Tramadol in Humans
Angela N. Duke, George E. Bigelow, Ryan K. Lanier, and Eric C. Strain

CARDIOVASCULAR

Celecoxib and 2,5-Dimethyl-Celecoxib Prevent Cardiac Remodeling Inhibiting Akt-Mediated Signal Transduction in an Inherited Dilated Cardiomyopathy Mouse Model
Xueli Fan, Fumi Takahashi-Yanaga, Sachio Morimoto, Dong-Yun Zhan, Kazunobu Igawa, Katsuhiko Tomooka, and Toshiyuki Sasaguri

Thienopyridines, but Not Elinogrel, Result in Off-Target Effects at the Vessel Wall That Contribute to Bleeding
Patrick André, Francis DeGuzman, Helena Haberstock-Debic, Scott Mills, Yvonne Pak, Mayuko Inagaki, Anjali Pandey, Stanley Hollenbach, David R. Phillips, and Pamela B. Conley

Catalase and Superoxide Dismutase Conjugated with Platelet-Endothelial Cell Adhesion Molecule Antibody Distinctly Alleviate Abnormal Endothelial Permeability Caused by Exogenous Reactive Oxygen Species and Vascular Endothelial Growth Factor
Jingyan Han, Vladimir V. Shuvaev, and Vladimir R. Mazykantov

The Bulky N(6) Substituent of Cabergoline Is Responsible for Agonism of This Drug at 5-Hydroxytryptamine (5-HT)2A and 5-HT2B Receptors and Thus Is a Determinant of Valvular Heart Disease
Alexandra Kekewska, Harald Hübner, Peter Gmeiner, and Heinz H. Pertz

CELLULAR AND MOLECULAR

Regulation of κ-Opioid Receptor Signaling in Peripheral Sensory Neurons In Vitro and In Vivo
Kelly A. Berg, Matthew P. Rowan, Teresa A. Sanchez, Michelle Silva, Amol M. Patwardhan, Stephen B. Milam, Kenneth M. Hargreaves, and William P. Clarke

Identification and Characterization of INCB9471, an Allosteric Noncompetitive Small-Molecule Antagonist of C-C Chemokine Receptor 5 with Potent Inhibitory Activity against Monocyte Migration and HIV-1 Infection
Niu Shin, Kim Solomon, Naining Zhou, Kathy He Wang, Vasudha Gariupati, Beth Thomas, Yanlong Li, Maryanne Covington, Frederic Baribaud, Susan Erickson-Vitanen, Phil Czerniak, Nancy Contel, Phillip Liu, Timothy Burn, Gregory Hollis, Swamy Yeleswaram, Kris Vaddi, Chu-Biao Xue, Brian Metcalf, Steve Friedman, Peggy Scherle, and Robert Newton
The Ligands of Estrogen Receptor α Regulate Cytochrome P4502C9 (CYP2C9) Expression
Jessica Mwinyi, Isa Cavaco, Begum Yurdakok, Souren Mkrtchian, and Magnus Ingelman-Sundberg

Identification of a High-Affinity Ligand That Exhibits Complete Aryl Hydrocarbon Receptor Antagonism
Kayla J. Smith, Iain A. Murray, Rachel Tanos, John Tello, Anthony E. Boitano, William H. Bisson, Siva K. Kolluri, Michael P. Cooke, and Gary H. Perdew

CHEMOTHERAPY, ANTIBIOTICS, AND GENE THERAPY

Rapamycin Inhibits Formation of Urethral Stricture in Rabbits
Tie Chong, De-lai Fu, He-cheng Li, Hui-bo Zhang, Peng Zhang, Wei-min Gan, and Zi-ming Wang

Synergistic Suppression of Prostatic Cancer Cells by Coexpression of Both Marine Double Minute 2 Small Interfering RNA and Wild-Type p53 Gene In Vitro and In Vivo
Kun Ji, Bo Wang, Yue-ting Shao, Ling Zhang, Ya-nan Liu, Chen Shao, Xiao-jie Li, Xin Li, Jia-di Hu, Xue-jian Zhao, De-qi Xu, Yang Li, and Lu Cai

DRUG DISCOVERY AND TRANSLATIONAL MEDICINE

A Method to Quantify Illicit Intake of Drugs from Urine: Methamphetamine
Linghui Li, Gantt P. Galloway, Davide Verotta, E. Thomas Everhart, Matthew J. Baggott, Jeremy R. Coyle, Juan C. Lopez, and John Mendelson

Mechanistic and Pharmacological Characterization of PF-04457845: A Highly Potent and Selective Fatty Acid Amide Hydrolase Inhibitor That Reduces Inflammatory and Noninflammatory Pain

ABT-869, a Multitargeted Receptor Tyrosine Kinase Inhibitor, Reduces Tumor Microvasculature and Improves Vascular Wall Integrity in Preclinical Tumor Models
Fang Jiang, Daniel H. Albert, Yanping Luo, Paul Tapang, Ke Zhang, Steven K. Davidsen, Gerard B. Fox, Richard Lesniewski, and Evelyn M. McKeegan

The Metabotropic Glutamate Receptor 7 Allosteric Modulator AMN082: A Monoaminergic Agent in Disguise?
Stacey J. Sukoff Rizzo, Sarah K. Leonard, Adam Gilbert, Paul Dollings, Deborah L. Smith, Mei-Yi Zhang, Li Di, Brian J. Platt, Sarah Neal, Jason M. Dwyer, Corey N. Bender, Jean Zhang, Tim Lock, Dianne Kowal, Angela Kramer, Andrew Randall, Christine Huselton, Karthick Vishwanathan, Susanna Y. Tse, John Butera, Robert H. Ring, Sharon Rosenzweig-Lipson, Zoë A. Hughes, and John Dunlop

ENDOCRINE AND DIABETES

Pharmacological Targeting of Glucagon and Glucagon-Like Peptide 1 Receptors Has Different Effects on Energy State and Glucose Homeostasis in Diet-Induced Obese Mice

Tamoxifen Regulation of Bone Growth and Endocrine Function in the Ovariectomized Rat: Discrimination of Responses Involving Estrogen Receptor α/Estrogen Receptor β, G Protein-Coupled Estrogen Receptor, or Estrogen-Related Receptor γ Using Fulvestrant (ICI 182780)
James M. Fitts, Robert M. Klein, and C. Andrew Powers

GASTROINTESTINAL, HEPATIC, PULMONARY, AND RENAL

Increased Activation of the Wnt/β-Catenin Pathway in Spontaneous Hepatocellular Carcinoma Observed in Farnesoid X Receptor Knockout Mice
Andy Wolfe, Ann Thomas, Genea Edwards, Shilpa Jaseja, Grace L. Guo, and Udayan Apte

Pharmacological Specificity of Nicotinic Receptor-Mediated Relaxation of Muscarinic Receptor Precontracted Human Gastric Clasp and Sling Muscle Fibers within the Gastroesophageal Junction
Alan S. Braverman, Anil K. Vegesna, Larry S. Miller, Mansoor Tiwana, Kashif Hussain, and Michael R. Ruggieri, Sr.

Retinol-Binding Protein 4 and Peroxisome Proliferator-Activated Receptor-γ in Steatotic Liver Transplantation
Arantx Casillas Ramírez, Isabel Alfany Ferrándiz, Marta Massip-Salcedo, M. Emilia Juan, Joana M. Planas, Anna Serafin, Mercè Pallás, Antoni Rimola, Juan Rodés, and Carmen Peralta

Comparative Analysis of the Effects of Antimuscarinic Agents on Bladder Functions in Both Nonhuman Primates and Rodents
Hiroshi Nagabukuro, Katherine L. Villa, L. Alexandra Wickham, Alison A. Kulick, Loise Gichuru, Marcie J. Donnelly, Gregory O. Voronin, Tony Pereira, Xinchun Tong, Andrew Nichols, Stephen E. Alves, Gary P. O’Neill, Christopher V. Johnson, and Emily J. Hickey
Distinct Actions of Endothelin A-Selective Versus Combined Endothelin A/B Receptor Antagonists in Early Diabetic Kidney Disease
Mohamed A. Saleh, Jennifer S. Pollock, and David M. Pollock

Rho Kinase Inhibition by Fasudil Attenuates Cyclosporine-Induced Kidney Injury
Jeong Woo Park, Cheon Hoon Park, In Jin Kim, Eun Hui Bae, Seong Kwon Ma, Jong Un Lee, and Soo Wan Kim

JNJ-26070109 ([(R)-4-Bromo-N-[1-(2,4-difluoro-phenyl)-ethyl]-2-(quinoxaline-5-sulfonylamino)-benzamide]: A Novel, Potent, and Selective Cholecystokinin 2 Receptor Antagonist with Good Oral Bioavailability
Magda F. Morton, Terrance D. Barrett, Jamie Freedman, Lina Li, Michele C. Rizzolio, Clodagh E. Prendergast, Xiaodong Wu, Veronica Moreno, Jayashree Pyati, Katherine Figueroa, Laurence Cagnon, Guy Lagaud, Luc Ver Donck, Etienne Ghoo, Brett Allison, Michael H. Rabinowitz, and Nigel P. Shankley

Rapid, Nongenomic Stimulation of Multidrug Resistance Protein 2 (Mrp2) Activity by Glucocorticoids in Renal Proximal Tubule
Brigitte Prevo, David S. Miller, Femke M. van de Water, Kimberley E. Wever, Frans G. M. Russel, Gert Flik, and Rosalinde Masereeuw

Enhanced Sensitivity to Afferent Stimulation and Impact of Overactive Bladder Therapies in the Conscious, Spontaneously Hypertensive Rat
Phani B. Patra and Kevin S. Thorneloe

Type 1 Diabetes-Induced Hyper-Responsiveness to 5-Hydroxytryptamine in Rat Pulmonary Arteries via Oxidative Stress and Induction of Cyclooxygenase-2
Jose G. Lopez-Lopez, Javier Moral-Sanz, Giovanna Frazziano, Maria J. Gomez-Villalobos, Laura Moreno, Carmen Menendez, Jorge Flores-Hernandez, Jose A. Lorente, Angel Cogolludo, and Francisco Perez-Vizcaino

INFLAMMATION, IMMUNOPHARMACOLOGY, AND ASTHMA

Antiarthritics Effect of a Novel Bruton’s Tyrosine Kinase (BTK) Inhibitor in Rat Collagen-Induced Arthritis and Mechanism-Based Pharmacokinetic/Pharmacodynamic Modeling: Relationships between Inhibition of BTK Phosphorylation and Efficacy
Lichuan Liu, Julie Di Paolo, Jim Barbosa, Hong Rong, Karin Reif, and Harvey Wong

Cinnamyl-3,4-Dihydroxy-/H9251/-Cyanocinnamate Is a Potent Inhibitor of 5-Lipoxygenase
Carlo Pergola, Bianca Jazzar, Antonietta Rossi, Ulrike Buehring, Susann Luderer, Friederike Dehm, Hinnak Northoff, Lidia Sautebin, and Oliver Werz

Pharmacology of AM211, a Potent and Selective Prostaglandin D2 Receptor Type 2 Antagonist That Is Active in Animal Models of Allergic Inflammation
Gretchen Bain, Daniel S. Lorrain, Karin J. Stebbins, Alex R. Broadhead, Angelina M. Santini, Pat Prodanovich, Janice Darlington, Christopher D. King, Catherine Lee, Christopher Baccei, Brian Stearns, Yen Truong, John H. Hutchinson, Peppi Prasit, and Jilly F. Evans

METABOLISM, TRANSPORT, AND PHARMACOGENOMICS

Naturally Occurring Variations in the Human Cholinesterase Genes: Heritability and Association with Cardiovascular and Metabolic Traits

Metabolism and Disposition of 3,4-Methylenedioxyxymethamphetamine (“Ecstasy”) in Baboons after Oral Administration: Comparison with Humans Reveals Marked Differences
Melanie Mueller, Amy K. Goodwin, Nancy A. Ator, Una D. McCann, and George A. Ricaurte

In Vitro and In Vivo P-Glycoprotein Transport Characteristics of Rivaroxaban
Mark Jean Gnoth, Ulf Buethorn, Uwe Muenster, Thomas Schwarz, and Steffen Sandmann

NEUROPHARMACOLOGY

The Efficacy of Sodium Channel Blockers to Prevent Phencyclidine-Induced Cognitive Dysfunction in the Rat: Potential for Novel Treatments for Schizophrenia
Charles H. Large, Silvia Bison, Ilaria Sartori, Kevin D. Read, Alessandro Gozzi, Davide Quarta, Marinella Antolini, Emma Hollands, Catherine H. Gill, Martin J. Ganthorpe, Nagi Idris, Jo C. Neill, and Giuseppe S. Alvaro

Haloperidol Disrupts Opioid-Antinociceptive Tolerance and Physical Dependence
Cheng Yang, Yan Chen, Lei Tang, and Zaijie Jim Wang

Selective GABA Transporter Inhibitors Tiagabine and EF1502 Exhibit Mechanistic Differences in Their Ability to Modulate the Ataxia and Anticonvulsant Action of the Extrasynaptic GABA_A Receptor Agonist Gaboxodol
Karsten K. Madsen, Bjarke Ebert, Rasmus P. Clausen, Povl Krogsgaard-Larsen, Arne Schousboe, and H. Steve White
Amperometric Measurement of Glutamate Release Modulation by Gabapentin and Pregabalin in Rat Neocortical Slices: Role of Voltage-Sensitive Ca\(^{2+}\) \(\alpha_{\delta-1}\) Subunit  
*Jorge E. Quintero, David J. Dooley, François Pomerleau, Peter Huettl, and Greg A. Gerhardt*

Abuse Liability Profile of Three Substituted Tryptamines  
*Micahel B. Gatch, Michael J. Forster, Aaron Janowsky, and Amy J. Eschleman*

Fasudil and Ozagrel in Combination Show Neuroprotective Effects on Cerebral Infarction after Murine Middle Cerebral Artery Occlusion  
*Akihiro Koumura, Junya Hatanaka, Koh Kawasaki, Kazuhiro Tsuruma, Masamitsu Shimazawa, Isao Hozumi, Takashi Inuzuka, and Hideaki Hara*

**TOXICOLOGY**

Cerium Oxide Nanoparticles Inhibits Oxidative Stress and Nuclear Factor-κB Activation in H9c2 Cardiomyocytes Exposed to Cigarette Smoke Extract  
*Jianli Niu, Kangkai Wang, and Pappachan E. Kolattukudy*

Inhibition of Rab1 GTPase and Endoplasmic Reticulum-to-Golgi Trafficking Underlies Statin’s Toxicity in Rat Skeletal Myofibers  
*Kazuho Sakamoto, Ikuo Wada, and Junko Kimura*

Up-Regulation of Extracellular Signal-Regulated Kinase 1/2-Dependent Thymidylate Synthase and Thymidine Phosphorylase Contributes to Cisplatin Resistance in Human Non–Small-Cell Lung Cancer Cells  
*Jen-Chung Ko, Min-Shao Tsai, Shao-Hsing Weng, Ya-Hsun Kuo, and Yun-Wei Lin*

Metabolism of \([D_{10}]\)Phenanthrene to Tetroals in Smokers for Potential Lung Cancer Susceptibility Assessment: Comparison of Oral and Inhalation Routes of Administration  
*Yan Zhong, Jung Wang, Steven G. Carmella, J. Bradley Hochalter, Diane Rauch, Andrew Oliver, Joni Jensen, Dorothy K. Hatsukami, Pramod Upadhyaya, Cheryl Zimmerman, and Stephen S. Hecht*

**ERRATA**

Correction to “Systemic Activation of the Transient Receptor Potential Vanilloid Subtype 4 Channel Causes Endothelial Failure and Circulatory Collapse: Part 2”  

Correction to “N-(1S)-1-[[4-((2S)-2-[[2,4-Dichlorophenyl)sulfonyl]amino]-3-hydroxypropanoyl]-1-piperazinyl]carbonyl]-3-methylbutyl]-1-benzo thiophene-2-carboxamide (GSK1016790A), a Novel and Potent Transient Receptor Potential Vanilloid 4 Channel Agonist Induces Urinary Bladder Contraction and Hyperactivity: Part 1”

---

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

---

*About the cover:* Amide backbone ribbon and space filling diagram of a human acetylcholinesterase subunit showing nonsynonymous and synonymous SNPs as yellow and blue side chains studied in relation to catalytic activity and general cardiovascular parameters. The active center serine side chain is white and the turquoise space filling residues are sites of glycosylation. Individual SNPs are mapped in Fig. 1 and three-dimensional structure is shown in Fig. 7 of Valle et al., on page 125 of this issue.