

# The Journal of PHARMACOLOGY

## And Experimental Therapeutics

A Publication of the American Society for Pharmacology and Experimental Therapeutics

December 2009

Vol. 331, No. 3

### Contents

<b>EDITOR'S NOTE</b>	765
<b>HIGHLIGHTED PAPERS</b>	766
<b>PERSPECTIVES IN PHARMACOLOGY</b>	
Quantitative Pharmacology or Pharmacokinetic Pharmacodynamic Integration Should Be a Vital Component in Integrative Pharmacology <i>J. Gabrielsson and A. R. Green</i>	767
<b>BEHAVIORAL PHARMACOLOGY</b>	
Nociceptin/Orphanin FQ Receptor Activation Attenuates Antinociception Induced by Mixed Nociceptin/Orphanin FQ/ $\mu$ -Opioid Receptor Agonists <i>Taline V. Khroyan, Willma E. Polgar, Faming Jiang, Nurulain T. Zaveri, and Lawrence Toll</i>	946
Comparison of the Antinociceptive and Antirewarding Profiles of Novel Bifunctional Nociceptin Receptor/ $\mu$ -Opioid Receptor Ligands: Implications for Therapeutic Applications <i>Lawrence Toll, Taline V. Khroyan, Willma E. Polgar, Faming Jiang, Cris Olsen, and Nurulain T. Zaveri</i>	954
<b>CARDIOVASCULAR</b>	
Involvement of Cyclooxygenase-2 in Carbachol-Induced Positive Inotropic Response in Mouse Isolated Left Atrium <i>Yukio Hara, Asako Ike, Riyo Tanida, Muneyoshi Okada, and Hideyuki Yamawaki</i>	808
Sensing of Blood Pressure Increase by Transient Receptor Potential Vanilloid 1 Receptors on Baroreceptors <i>Hao Sun, De-Pei Li, Shao-Rui Chen, Walter N. Hittelman, and Hui-Lin Pan</i>	851
Inhibition of Thromboxane A <sub>2</sub> -Induced Arrhythmias and Intracellular Calcium Changes in Cardiac Myocytes by Blockade of the Inositol Trisphosphate Pathway <i>M. J. Wacker, L. M. Kosloski, W. J. R. Gilbert, C. D. Touchberry, D. S. Moore, J. K. Kelly, M. Brotto, and J. A. Orr</i>	917
Inhibition of Endothelin ET <sub>B</sub> Receptor System Aggravates Neointimal Hyperplasia after Balloon Injury of Rat Carotid Artery <i>Kento Kitada, Nozomi Yui, Chika Matsumoto, Tatsuhiko Mori, Mamoru Ohkita, and Yasuo Matsumura</i>	998
20- <sup>125</sup> Iodo-14,15-Epoxyeicosa-5(Z)-enoic Acid: a High-Affinity Radioligand Used to Characterize the Epoxyeicosatrienoic Acid Antagonist Binding Site <i>Yuenmu Chen, John R. Falck, Venugopal R. Tuniki, and William B. Campbell</i>	1137

*The Journal of Pharmacology and Experimental Therapeutics* (ISSN 0022-3565) is published monthly by the American Society for Pharmacology and Experimental Therapeutics, 9650 Rockville Pike, Bethesda, MD 20814-3995; email: subscriptions@aspet.org; web site: aspet.org. Periodicals postage paid at Bethesda, MD, and at additional mailing offices. POSTMASTER: Send address changes to *The Journal of Pharmacology and Experimental Therapeutics*, 9650 Rockville Pike, Bethesda, MD 20814-3995. Subscription rates: U.S.: \$947; outside the U.S.: \$1,112. Single copy: \$82. 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 Services*, *Current Awareness in Biological Sciences*, *Current Contents*®/Life Sciences, *EMBASE/Excerpta Medica*, *Index Medicus*, *Medical Documentation Service*®, *PsycINFO*, *Reference Update*®, *Research Alerts*®, *Science Citation Index*®, *SciSearch*®, and *SIIC Data Bases*. Copyright © 2009 by the American Society for Pharmacology and Experimental Therapeutics. All rights reserved. Printed in the U.S.A.

## CELLULAR AND MOLECULAR

- Effect of the Calcimimetic R-568 [3-(2-Chlorophenyl)-N-((1R)-1-(3-methoxyphenyl)ethyl)-1-propanamine] on Correcting Inactivating Mutations in the Human Calcium-Sensing Receptor 775  
*Jenny Ying Lin Lu, Yuhua Yang, Gilles Gnacadja, Arthur Christopoulos, and Jeff D. Reagan*
- Omigapil Ameliorates the Pathology of Muscle Dystrophy Caused by Laminin- $\alpha$ 2 Deficiency 787  
*Michael Erb, Sarina Meinen, Patrizia Barzaghi, Lazar T. Sumanovski, Isabelle Courdier-Früh, Markus A. Rüegg, and Thomas Meier*
- Cellular Inhibition of Checkpoint Kinase 2 (Chk2) and Potentiation of Camptothecins and Radiation by the Novel Chk2 Inhibitor PV1019 [7-Nitro-1H-indole-2-carboxylic acid {4-[1-(guanidinohydrazone)-ethyl]-phenyl}-amide] 816  
*Andrew G. Jobson, George T. Lountos, Philip L. Lorenzi, Jenny Llamas, John Connelly, David Cerna, Joseph E. Tropea, Akikazu Onda, Gabriele Zoppoli, Sudhir Kondapaka, Guangtao Zhang, Natasha J. Caplen, John H. Cardellina II, Stephen S. Yoo, Anne Monks, Christopher Self, David S. Waugh, Robert H. Shoemaker, and Yves Pommier*
- Heme Oxygenase-2 Deletion Causes Endothelial Cell Activation Marked by Oxidative Stress, Inflammation, and Angiogenesis 925  
*Lars Bellner, Lucia Martinelli, Adna Halilovic, Kiran Patil, Nitin Puri, Michael W. Dunn, Raymond F. Regan, and Michal Laniado Schwartzman*
- Blockade of Ethanol-Induced Potentiation of Glycine Receptors by a Peptide That Interferes with G $\beta$  $\gamma$  Binding 933  
*Leonardo Guzman, Gustavo Moraga-Cid, Ariel Avila, Maximiliano Figueroa, Gonzalo E. Yevenes, Jorge Fuentealba, and Luis G. Aguayo*
- Contrasting Effects of Allosteric and Orthosteric Agonists on M $_1$  Muscarinic Acetylcholine Receptor Internalization and Down-regulation 1086  
*Rachel L. Thomas, Christopher J. Langmead, Martyn D. Wood, and R. A. John Challiss*

## ENDOCRINE AND DIABETES

- Long-Term Inhibition of the Glucagon Receptor with a Monoclonal Antibody in Mice Causes Sustained Improvement in Glycemic Control, with Reversible  $\alpha$ -Cell Hyperplasia and Hyperglucagonemia 871  
*Wei Gu, Hai Yan, Katherine A. Winters, Renée Komorowski, Steven Vonderfecht, Larissa Atangan, Glenn Sivits, David Hill, Jie Yang, Vivian Bi, Yuqing Shen, Sylvia Hu, Tom Boone, Richard A. Lindberg, and Murielle M. Véniant*
- Epoxyeicosatrienoic Acid Agonist Rescues the Metabolic Syndrome Phenotype of HO-2-Null Mice 906  
*Komal Sodhi, Kazuyoshi Inoue, Katherine H. Gotlinger, Martina Canestraro, Luca Vanella, Dong Hyun Kim, Vijay L. Manthati, Sreenivasulu Reddy Koduru, John R. Falck, Michal L. Schwartzman, and Nader G. Abraham*
- Selective Enhancement of Nutrient-Induced Insulin Secretion by ATP-Sensitive K $^+$  Channel-Blocking Imidazolines 1033  
*Kathrin Hatlapatka, Antje Wienbergen, Claudia Kühne, Anne Jörns, Michael Willenborg, and Ingo Rustenbeck*
- An Adipose Tissue-Independent Insulin-Sensitizing Action of Telmisartan: a Study in Lipodystrophic Mice 1096  
*X. Rong, Y. Li, K. Ebihara, M. Zhao, W. Aini, T. Kusakabe, M. Hirata, L. Miyamoto, M. Murray, and K. Nakao*

## GASTROINTESTINAL, HEPATIC, PULMONARY, AND RENAL

- c-Jun NH $_2$ -Terminal Kinase Is Crucially Involved in Renal Tubulo-Interstitial Inflammation 896  
*Martin H. de Borst, Jai Prakash, Maria Sandovici, Pieter A. Klok, Inge Hamming, Robbert Jan Kok, Gerjan Navis, and Harry van Goor*
- Comparative Effects of Aprotinin and Human Recombinant R24K KD1 on Temporal Renal Function in Long-Evans Rats 940  
*Prakasha Kempaiah, Leslie A. Danielson, Marc Barry, and Walter Kisiel*
- Mesalamine Restores Angiogenic Balance in Experimental Ulcerative Colitis by Reducing Expression of Endostatin and Angiostatin: Novel Molecular Mechanism for Therapeutic Action of Mesalamine 1071  
*Xiaoming Deng, Ganna Tolstanova, Tetyana Khomenko, Longchuan Chen, Andrzej Tarnawski, Sandor Szabo, and Zsuzsanna Sandor*
- Administration of Ampicillin Elevates Hepatic Primary Bile Acid Synthesis through Suppression of Ileal Fibroblast Growth Factor 15 Expression 1079  
*Masaaki Miyata, Yuki Takamatsu, Hideaki Kuribayashi, and Yasushi Yamazoe*

## INFLAMMATION, IMMUNOPHARMACOLOGY, AND ASTHMA

- PPAR- $\alpha$  Contributes to the Anti-Inflammatory Activity of 17 $\beta$ -Estradiol 796  
*Concetta Crisafulli, Stefano Bruscoli, Emanuela Esposito, Emanuela Mazzon, Rosanna Di Paola, Tiziana Genovese, Placido Bramanti, Graziella Migliorati, and Salvatore Cuzzocrea*
- A Study of the Specificity of Lymphocytes in Nevirapine-Induced Skin Rash 836  
*Xin Chen, Tharsika Tharmanathan, Baskar Mannargudi, Hong Gou, and Jack P. Uetrecht*

Contribution of the Prostaglandin E <sub>2</sub> /E-Prostanoid 2 Receptor Signaling Pathway in Abscess Formation in Rat Zymosan-Induced Pleurisy	860
<i>Toshihisa Inada, Keita Arai, Michiko Kawamura, Ko Hatanaka, Yuichi Sato, Makoto Noshiro, and Yoshiteru Harada</i>	
Anti-Inflammatory Properties of a Novel <i>N</i> -Phenyl Pyridinone Inhibitor of p38 Mitogen-Activated Protein Kinase: Preclinical-to-Clinical Translation	882
<i>Heidi R. Hope, Gary D. Anderson, Barry L. Burnette, Robert P. Compton, Rajesh V. Devraj, Jeffrey L. Hirsch, Robert H. Keith, Xiong Li, Gabriel Mbalaviele, Dean M. Messing, Matthew J. Saabye, John F. Schindler, Shaun R. Selness, Loreen I. Stillwell, Elizabeth G. Webb, Jian Zhang, and Joseph B. Monahan</i>	
Oral Administration of 1,4-Aryl-2-mercaptoimidazole Inhibits T-Cell Proliferation and Reduces Clinical Severity in the Murine Experimental Autoimmune Encephalomyelitis Model	1005
<i>Eun Joo Jung, Minkyu Hur, Young Lim Kim, Ge Hyeong Lee, Jeongmin Kim, Ikyon Kim, MinWoo Lee, Ho-Kyun Han, Mi-Soon Kim, Sejin Hwang, Sungjoo Kim, A. Mi Woo, Yeup Yoon, Heon Jin Park, and Jonghwa Won</i>	
Effect of Intra-articular 4-( <i>S</i> )-Amino-5-(4-{4-[2,4-dichloro-3-(2,4-dimethyl-8-quinolyloxymethyl)phenylsulfonamido]-tetrahydro-2 <i>H</i> -4-pyranylcarbonyl} piperazino)-5-oxopentyl](trimethyl)ammonium chloride hydrochloride (MEN16132), a Kinin B <sub>2</sub> Receptor Antagonist, on Nociceptive Response in Monosodium Iodoacetate-Induced Experimental Osteoarthritis in Rats	1025
<i>Cecilia Cialdai, Sandro Giuliani, Claudio Valenti, Manuela Tramontana, and Carlo Alberto Maggi</i>	
Pharmacological Characterization of 3-[3- <i>tert</i> -Butylsulfanyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-5-(pyridin-2-ylmethoxy)-1 <i>H</i> -indol-2-yl]-2,2-dimethyl-propionic Acid (AM103), a Novel Selective 5-Lipoxygenase-Activating Protein Inhibitor That Reduces Acute and Chronic Inflammation	1042
<i>Daniel S. Lorrain, Gretchen Bain, Lucia D. Correa, Charles Chapman, Alex R. Broadhead, Angelina M. Santini, Pat Prodanovich, Janice V. Darlington, John H. Hutchinson, Christopher King, Catherine Lee, Christopher Baccei, Yiwei Li, Jeannie M. Arruda, and Jilly F. Evans</i>	
Adenosine Suppresses Lipopolysaccharide-Induced Tumor Necrosis Factor- $\alpha$ Production by Murine Macrophages through a Protein Kinase A- and Exchange Protein Activated by cAMP-Independent Signaling Pathway	1051
<i>Laura M. Kreckler, Elizabeth Gizewski, Tina C. Wan, and John A. Auchampach</i>	
Differential Effects of Arachidonic and Eicosapentaenoic Acid-Derived Eicosanoids on Polymorphonuclear Transmigration Across Endothelial Cell Cultures	1111
<i>Juan J. Moreno</i>	
<b>METABOLISM, TRANSPORT, AND PHARMACOGENOMICS</b>	
Transplacental Pharmacokinetics of Glyburide, Rhodamine 123, and BODIPY FL Prazosin: Effect of Drug Efflux Transporters and Lipid Solubility	1118
<i>Lenka Hahnova Cyalova, Jakub Hofman, Martina Ceckova, and Frantisek Staud</i>	
<b>NEUROPHARMACOLOGY</b>	
Neuroprotective Profile of Novel Src Kinase Inhibitors in Rodent Models of Cerebral Ischemia	827
<i>Shi Liang, Kevin Pong, Cathleen Gonzales, Yi Chen, Huai-Ping Ling, Robert J. Mark, Frank Boschelli, Diane H. Boschelli, Fei Ye, Ana Carolina Barrios Sosa, Tarek S. Mansour, Philip Frost, Andrew Wood, Menelas N. Pangalos, and Margaret M. Zaleska</i>	
☐ Phosphodiesterase 5A Inhibitors Improve Functional Recovery after Stroke in Rats: Optimized Dosing Regimen with Implications for Mechanism	842
<i>Frank S. Menniti, JingMei Ren, Timothy M. Coskran, Jing Liu, Daniel Morton, Dana K. Sietsma, Angel Som, Diane T. Stephenson, Barbara A. Tate, and Seth P. Finklestein</i>	
☐ Modulation of Agonist Binding to AMPA Receptors by 1-(1,4-Benzodioxan-6-ylcarbonyl)piperidine (CX546): Differential Effects across Brain Regions and GluA1-4/Transmembrane AMPA Receptor Regulatory Protein Combinations	965
<i>Kyle E. Montgomery, Markus Kessler, and Amy C. Arai</i>	
Expression of Glycine-Activated Diheteromeric NR1/NR3 Receptors in Human Embryonic Kidney 293 Cells Is NR1 Splice Variant-Dependent	975
<i>C. Thetford Smothers and John J. Woodward</i>	
Low or High Cocaine Responding Rats Differ in Striatal Extracellular Dopamine Levels and Dopamine Transporter Number	985
<i>Anna M. Nelson, Gaynor A. Larson, and Nancy R. Zahniser</i>	
Signaling Pathways from Cannabinoid Receptor-1 Activation to Inhibition of <i>N</i> -Methyl-D-Aspartic Acid Mediated Calcium Influx and Neurotoxicity in Dorsal Root Ganglion Neurons	1062
<i>Qing Liu, Manjunatha Bhat, Wayne D. Bowen, and Jianguo Cheng</i>	
17 $\beta$ -Estradiol Mediates the Sex Difference in Capsaicin-Induced Nociception in Rats	1104
<i>Yu-Ching Lu, Chao-Wei Chen, Su-Yi Wang, and Fong-Sen Wu</i>	

- ☐ In Vitro and in Vivo Evidence for a Lack of Interaction with Dopamine D<sub>2</sub> Receptors by the Metabotropic Glutamate 2/3 Receptor Agonists 1S,2S,5R,6S-2-Aminobicyclo[3.1.0]hexane-2,6-bicaroxylate Monohydrate (LY354740) and (-)-2-Oxa-4-aminobicyclo[3.1.0] Hexane-4,6-dicarboxylic Acid (LY379268) 1126  
*Matthew J. Fell, Kenneth W. Perry, Julie F. Falcone, Bryan G. Johnson, Vanessa N. Barth, Karen S. Rash, Virginia L. Lucaites, Penny G. Threlkeld, James A. Monn, David L. McKinzie, Gerard J. Marek, Kjell A. Svensson, and David L. Nelson*

## TOXICOLOGY

- Effectiveness of Donepezil, Rivastigmine, and (±)Huperzine A in Counteracting the Acute Toxicity of Organophosphorus Nerve Agents: Comparison with Galantamine 1014  
*Yasco Aracava, Edna F. R. Pereira, Miriam Akkerman, Michael Adler, and Edson X. Albuquerque*

## ERRATUM

- Correction to “An Allosteric Modulator of the  $\alpha$ 7 Nicotinic Acetylcholine Receptor Possessing Cognition-Enhancing Properties in Vivo” 1146

## NOTICE OF RETRACTION

1147

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

*About the cover:* Confocal images depict the presence of TRPV1 and IB4 positive neurons in the NG and DRG. See the article by Sun et al. on page 853 of this issue.