

# MOLECULAR PHARMACOLOGY

April 2006

Volume 69

Number 4

<http://molpharm.aspetjournals.org>

ISSN 0026-895X

## PERSPECTIVES

Adenosine Receptors Find a New Partner and Move Out 

*Myron L. Toews*


1075

 Bring Your Own G Protein 

*John D. Hildebrandt*

1079

## ORIGINAL ARTICLES

 The Ubiquitin-Specific Protease Usp4 Regulates the Cell Surface Level of the A<sub>2a</sub> Receptor  
*Tetyana Milojević, Veronika Reiterer, Eduard Stefan, Vladimir M. Korkhov, Mario M. Dorostkar, Eszter Ducza, Egon Ogris, Stefan Boehm, Michael Freissmuth, and Christian Nanoff*

1083

Serine 202 Regulates the Nuclear Translocation of Constitutive Active/Androstane Receptor  
*F. Hosseinpour, R. Moore, M. Negishi, and T. Sueyoshi*

1095

Oral Benzo[a]pyrene in *Cyp1* Knockout Mouse Lines: CYP1A1 Important in Detoxication, CYP1B1 Metabolism Required for Immune Damage Independent of Total-Body Burden and Clearance Rate  
*Shigeyuki Uno, Timothy P. Dalton, Nadine Dragin, Christine P. Curran, Sandrine Derkenne, Marian L. Miller, Howard G. Shertzer, Frank J. Gonzalez, and Daniel W. Nebert*

1103

Use of Penetrating Peptides Interacting with PP1/PP2A Proteins As a General Approach for a Drug Phosphatase Technology

*Julien Guergnon, Frédéric Dessauge, Victoria Dominguez, Jean Viallet, Serge Bonnefoy, Victor J. Yuste, Odile Mercereau-Puijalon, Xavier Cayla, Angelita Rebollo, Santos A. Susin, Pierre-Etienne Bost, and Alphonse Garcia*

1115

Bafilomycin A1 Inhibits Chloroquine-Induced Death of Cerebellar Granule Neurons

*John J. Shacka, Barbara J. Klocke, Masahiro Shibata, Yasuo Uchiyama, Geeta Datta, Robert E. Schmidt, and Kevin A. Roth*

1125

Emergence of Functional  $\delta$ -Opioid Receptors Induced by Long-Term Treatment with Morphine

*Junyi Ma, Yong Zhang, Alex E. Kalyuzhny, and Zhizhong Z. Pan*

1137

A Nonpeptide Antagonist Reveals a Highly Glycosylated State of the Rabbit Kinin B<sub>1</sub> Receptor

*Jean-Philippe Fortin, Edward K. Dziadulewicz, Lajos Gera, and François Marceau*

1146

The  and  symbols in the table of contents identify articles discussed in the *Perspectives*.

*Molecular Pharmacology* (ISSN 0026-895X) is published monthly (two volumes per year beginning in January and July) by the American Society for Pharmacology and Experimental Therapeutics, 9650 Rockville Pike, Bethesda, MD 20814-3995; e-mail: [info@aspet.org](mailto: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 *Molecular Pharmacology*, 9650 Rockville Pike, Bethesda, MD 20814-3995. Subscription Rates: U.S.: \$592.00 for institutions and \$241.00 for non-ASPET members. Outside the U.S.: \$673.00 for institutions and \$322.00 for non-ASPET members. Single copy:

\$57.00. GST Tax Number for Canadian subscribers: BN:13489 2330 RT. Indexed or abstracted by *Biochemistry & Biophysics Citation Index*®, *Biological Abstracts*, *BIOSIS Previews Database*, *Current Awareness in Biological Sciences*, *Current Contents*®/Life Sciences, *EMBASE/Excerpta Medica*, *Index Medicus*, *Medical Documentation Service*®, *Reference Update*®, *Research Alert*®, *Science Citation Index*®, *SciSearch*®, and *SIIC Data Bases*. Copyright © 2006 by the American Society for Pharmacology and Experimental Therapeutics. All rights reserved. Printed in the U.S.A.

- 2-Cyano-3,12-dioxoleana-1,9(11)-diene-28-oic Acid Disrupts Microtubule Polymerization: A Possible Mechanism Contributing to Apoptosis  
*Robin D. Couch, Neil J. Ganem, Ming Zhou, Veljko M. Popov, Tadashi Honda, Timothy D. Veenstra, Michael B. Sporn, and Amy C. Anderson* 1158
- Kinetics of Penetration Influence the Apparent Potency of Vanilloids on TRPV1  
*Jozsef Lazar, Derek C. Braun, Attila Tóth, Yun Wang, Larry V. Pearce, Vladimir A. Pavlyukovets, Peter M. Blumberg, Susan H. Garfield, Stephen Wincovitch, Hyun-Kyung Choi, and Jeewoo Lee* 1166
- Inhibition of Cardiac Hypertrophy by Triflusal (4-Trifluoromethyl Derivative of Salicylate) and Its Active Metabolite  
*Anna Planavila, Ricardo Rodríguez-Calvo, Alberto Fernández de Arriba, Rosa M. Sánchez, Juan C. Laguna, Manuel Merlos, and Manuel Vázquez-Carrera* 1174
- A Novel Mechanism of Action of Methyl-2-cyano-3,12 Dioxolean-1,9 Diene-28-oate: Direct Permeabilization of the Inner Mitochondrial Membrane to Inhibit Electron Transport and Induce Apoptosis  
*Ismael Samudio, Marina Konopleva, Helene Pelicano, Peng Huang, Olga Frolova, William Bornmann, Yunming Ying, Randall Evans, Rooha Contractor, and Michael Andreeff* 1182
- Discovery of Naturally Occurring Splice Variants of the Rat Histamine H<sub>3</sub> Receptor That Act as Dominant-Negative Isoforms  
*Remko A. Bakker, Adrian Flores Lozada, André van Marle, Fiona C. Shenton, Guillaume Drutel, Kaj Karlstedt, Marcel Hoffmann, Minnamaija Lintunen, Yumiko Yamamoto, Richard M. van Rijn, Paul L. Chazot, Pertti Panula, and Rob Leurs* 1194
- The Microtubule Binding Drug Laulimalide Inhibits Vascular Endothelial Growth Factor-Induced Human Endothelial Cell Migration and Is Synergistic when Combined with Docetaxel (Taxotere)  
*Haiyan Lu, Janice Murtagh, and Edward L. Schwartz* 1207
- ☐ Antimony-Based Antileishmanial Compounds Prolong the Cardiac Action Potential by an Increase in Cardiac Calcium Currents  
*Yuri A. Kuryshhev, Lu Wang, Barbara A. Wible, Xiaoping Wan, and Eckhard Ficker* 1216
- Pseudolarix Acid B, a New Tubulin-Binding Agent, Inhibits Angiogenesis by Interacting with a Novel Binding Site on Tubulin  
*Yun-Guang Tong, Xiong-Wen Zhang, Mei-Yu Geng, Jian-Ming Yue, Xian-Liang Xin, Fang Tian, Xu Shen, Lin-Jiang Tong, Mei-Hong Li, Chao Zhang, Wei-Hong Li, Li-Ping Lin, and Jian Ding* 1226
- Insulin Secretion Is Controlled by mGlu5 Metabotropic Glutamate Receptors  
*Marianna Storto, Loredana Capobianco, Giuseppe Battaglia, Gemma Molinaro, Roberto Gradini, Barbara Riozzi, Alessandra Di Mambro, Kathryn J. Mitchell, Valeria Bruno, Maria P. Vairetti, Guy A. Rutter, and Ferdinando Nicoletti* 1234
- Dissection of an Allosteric Mechanism on the Serotonin Transporter: A Cross-Species Study  
*Henrik Amtoft Neubauer, Carsten Gram Hansen, and Ove Wiborg* 1242
- ☐ Subunit Dependencies of *N*-Methyl-D-aspartate (NMDA) Receptor-Induced  $\alpha$ -Amino-3-hydroxy-5-methyl-4-isoxazolepropionic Acid (AMPA) Receptor Internalization  
*C. M. Tigaret, A. Thalhammer, G. F. Rast, C. G. Specht, Y. P. Auberson, M. G. Stewart, and R. Schoepfer* 1251
- Biochemistry and Pharmacology of Novel Anthranilic Acid Derivatives Activating Heme-Oxidized Soluble Guanylyl Cyclase  
*Ursula Schindler, Hartmut Strobel, Karl Schönafinger, Wolfgang Linz, Matthias Löhn, Piero A. Martorana, Hartmut Rütten, Peter W. Schindler, Andreas E. Busch, Michael Sohn, Andrea Töpfer, Astrid Pistorius, Christoph Jannek, and Alexander Mülsch* 1260
- The 73-kDa Heat Shock Cognate Protein Is a CXCR4 Binding Protein that Regulates the Receptor Endocytosis and the Receptor-Mediated Chemotaxis  
*Yun Ding, Mika Li, Jinwu Zhang, Ningli Li, Zongqin Xia, Yaer Hu, Sunxin Wang, and Guo-Huang Fan* 1269

- Endogenous Regulator of G-Protein Signaling Proteins Regulate the Kinetics of  $G\alpha_{q/11}$ -Mediated Modulation of Ion Channels in Central Nervous System Neurons  
*Michael A. Clark and Nevin A. Lambert* 1280
- A Novel Cyclohexene Derivative, Ethyl (6R)-6-[N-(2-Chloro-4-fluorophenyl)sulfamoyl]cyclohex-1-ene-1-carboxylate (TAK-242), Selectively Inhibits Toll-Like Receptor 4-Mediated Cytokine Production through Suppression of Intracellular Signaling  
*Masayuki Ii, Naoko Matsunaga, Kaoru Hazeki, Kazuyo Nakamura, Katsunori Takashima, Tsukasa Seya, Osamu Hazeki, Tomoyuki Kitazaki, and Yuji Iizawa* 1288
- Probing N-Methyl-D-aspartate Receptor Desensitization with the Substituted-Cysteine Accessibility Method  
*Christopher G. Thomas, Johannes J. Krupp, Elena E. Bagley, Reginald Bauzon, Stephen F. Heinemann, Bryce Vissel, and Gary L. Westbrook* 1296
- Valproic Acid Increases Conservative Homologous Recombination Frequency and Reactive Oxygen Species Formation: A Potential Mechanism for Valproic Acid-Induced Neural Tube Defects  
*Ericka N. Defoort, Perry M. Kim, and Louise M. Winn* 1304
- Tumor Necrosis Factor- $\alpha$  Prevents Desensitization of  $G\alpha_s$ -Coupled Receptors by Regulating GRK2 Association with the Plasma Membrane  
*Nguyen D. Khoa, Michael Postow, Jennifer Danielsson, and Bruce N. Cronstein* 1311
- 3,3'-Diindolylmethane Is a Novel Topoisomerase II $\alpha$  Catalytic Inhibitor That Induces S-Phase Retardation and Mitotic Delay in Human Hepatoma HepG2 Cells  
*Yixuan Gong, Gary L. Firestone, and Leonard F. Bjeldanes* 1320
- Bradycardic and Proarrhythmic Properties of Sinus Node Inhibitors  
*Juliane Stieber, Karen Wieland, Georg Stöckl, Andreas Ludwig, and Franz Hofmann* 1328
- Transcriptional Regulation of the Human NRIP1/RIP140 Gene by Estrogen Is Modulated by Dioxin Signalling  
*Patrick Augereau, Eric Badia, Maryse Fuentes, Fanja Rabenoelina, Marine Corniou, Danièle Derocq, Patrick Balaguer, and Vincent Cavailles* 1338
- Reactive Oxygen Species Generation Is Involved in Epidermal Growth Factor Receptor Transactivation through the Transient Oxidization of Src Homology 2-Containing Tyrosine Phosphatase in Endothelin-1 Signaling Pathway in Rat Cardiac Fibroblasts  
*Cheng-Hsien Chen, Tzu-Hung Cheng, Heng Lin, Neng-Lang Shih, Yen-Ling Chen, Yee-Shiuan Chen, Ching-Feng Cheng, Wei-Shiung Lian, Tzu-Ching Meng, Wen-Ta Chiu, and Jin-Jer Chen* 1347
- Interaction of d-Tubocurarine with Potassium Channels: Molecular Modeling and Ligand Binding  
*Alexei Rossokhin, Georgeta Teodorescu, Stephan Grissmer, and Boris S. Zhorov* 1356
- Long-Term Exposure to the Atypical Antipsychotic Olanzapine Differently Up-Regulates Extracellular Signal-Regulated Kinases 1 and 2 Phosphorylation in Subcellular Compartments of Rat Prefrontal Cortex  
*Fabio Fumagalli, Angelisa Frasca, Maria Spartà, Filippo Drago, Giorgio Racagni, and Marco Andrea Riva* 1366
- Iodinated N-Acylvanillamines: Potential "Multiple-Target" Anti-Inflammatory Agents Acting via the Inhibition of T-Cell Activation and Antagonism at Vanilloid TRPV1 Channels  
*Nieves Márquez, Luciano De Petrocellis, Francisco J. Caballero, Antonio Macho, Aniello Schiano-Moriello, Alberto Minassi, Giovanni Appendino, Eduardo Muñoz, and Vincenzo Di Marzo* 1373
- Identification by Functional Cloning from a Retroviral cDNA Library of cDNAs for Ribosomal Protein L36 and the 10-kDa Heat Shock Protein that Confer Cisplatin Resistance  
*Ding-Wu Shen, Xing-Jie Liang, Toshihiro Suzuki, and Michael M. Gottesman* 1383
- Modulation of Uridine Phosphorylase Gene Expression by Tumor Necrosis Factor- $\alpha$  Enhances the Antiproliferative Activity of the Capecitabine Intermediate 5'-Deoxy-5-fluorouridine in Breast Cancer Cells  
*Laxiang Wan, Deliang Cao, Jianmin Zeng, Ruilan Yan, and Giuseppe Pizzorno* 1389

- Identification and Characterization of Compounds That Potentiate NT-3-Mediated Trk Receptor Activity  
*Martin A. Lewis, Lisa Hunihan, Diana Franco, Barbara Robertson, Jane Palmer, Denis R. St. Laurent, Balu N. Balasubramanian, Yi Li, and Ryan S. Westphal* 1396
- A Molecular Mechanism for the Anti-Inflammatory Effect of Taurine-Conjugated 5-Aminosalicylic Acid in Inflamed Colon  
*Heejung Kim, Hyunchu Jeon, Hyesik Kong, Youngwook Yang, Boim Choi, Young Mi Kim, Len Neckers, and Yunjin Jung* 1405
- A Pyrazole Derivative Potently Inhibits Lymphocyte Ca<sup>2+</sup> Influx and Cytokine Production by Facilitating Transient Receptor Potential Melastatin 4 Channel Activity  
*Ryuichi Takezawa, Henrique Cheng, Andreas Beck, Jun Ishikawa, Pierre Launay, Hirokazu Kubota, Jean-Pierre Kinet, Andrea Fleig, Toshimitsu Yamada, and Reinhold Penner* 1413
- Adenylyl Cyclase Superactivation Induced by Long-Term Treatment with Opioid Agonist Is Dependent on Receptor Localized within Lipid Rafts and Is Independent of Receptor Internalization  
*Hui Zhao, Horace H. Loh, and P. Y. Law* 1421
- ◆ The G<sub>12</sub> Family of G Proteins as a Reporter of Thromboxane A<sub>2</sub> Receptor Activity  
*Li Zhang, Cherisse DiLizio, David Kim, Emer M. Smyth, and David R. Manning* 1433
- ▣ On the Mechanism of Interaction of Potent Surmountable and Insurmountable Antagonists with the Prostaglandin D<sub>2</sub> Receptor CRTH2  
*Jesper Mosolff Mathiesen, Arthur Christopoulos, Trond Ulven, Julia F. Royer, Mercedes Campillo, Akos Heinemann, Leonardo Pardo, and Evi Kostenis* 1441
- Preferential Inhibition of the Magnesium-Dependent Strand Transfer Reaction of HIV-1 Integrase by  $\alpha$ -Hydroxytropolones  
*Elena A. Semenova, Allison A. Johnson, Christophe Marchand, David A. Davis, Robert Yarchoan, and Yves Pommier* 1454
- The Anti-Yellow Fever Virus Activity of Ribavirin Is Independent of Error-Prone Replication  
*Pieter Leyssen, Erik De Clercq, and Johan Neyts* 1461
- The Contribution of TWIK-Related Acid-Sensitive K<sup>+</sup>-Containing Channels to the Function of Dorsal Lateral Geniculate Thalamocortical Relay Neurons  
*Sven G. Meuth, M. Isabel Aller, Thomas Munsch, Thekla Schuhmacher, Thomas Seidenbecher, Patrick Meuth, Christoph Kleinschnitz, Hans-Christian Pape, Heinz Wiendl, William Wisden, and Thomas Budde* 1468
- Merbarone Induces Activation of Caspase-Activated DNase and Excision of Chromosomal DNA Loops from the Nuclear Matrix  
*Yoko Otake, Alice Mims, and Daniel J. Fernandes* 1477
- Cannabinoid Receptor Type 2 Agonists Induce Transcription of the  $\mu$ -Opioid Receptor Gene in Jurkat T Cells  
*Christine Börner, Volker Höllt, and Jürgen Kraus* 1486
- Implication of the Phosphatidylinositol-3 Kinase/Protein Kinase B Signaling Pathway in the Neuroprotective Effect of Estradiol in the Striatum of 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine Mice  
*Myreille D'Astous, Pablo Mendez, Marc Morissette, Luis Miguel Garcia-Segura, and Thérèse Di Paolo* 1492
- Multidrug Resistance Protein 1 (MRP1, ABCC1) Mediates Resistance to Mitoxantrone via Glutathione-Dependent Drug Efflux  
*Charles S. Morrow, Christina Peklak-Scott, Bimjhana Bishwokarma, Timothy E. Kute, Pamela K. Smitherman, and Alan J. Townsend* 1499
- ▣ Supplemental material is available online at <http://molpharm.aspetjournals.org>.