

The Journal of PHARMACOLOGY

And Experimental Therapeutics

A Publication of the American Society for Pharmacology and Experimental Therapeutics

March 2013

Vol. 344, No. 3

Contents

HIGHLIGHTED PAPERS

543

PERSPECTIVES IN PHARMACOLOGY

Autophagy Inhibition for Chemosensitization and Radiosensitization in Cancer: Do the Preclinical Data Support This Therapeutic Strategy?

544

Molly L. Bristol, Sean M. Emery, Paola Maycotte, Andrew Thorburn, Shweta Chakradeo, and David A. Gewirtz

BEHAVIORAL PHARMACOLOGY

Discriminative Stimulus Effects of the GABA_B Receptor-Positive Modulator rac-BHFF: Comparison with GABA_B Receptor Agonists and Drugs of Abuse

553

Wouter Koek, Kejun Cheng, and Kenner C. Rice

Cannabinoid Discrimination and Antagonism by CB₁ Neutral and Inverse Agonist Antagonists

561

Brian D. Kangas, Marcus S. Delatte, V. Kiran Vemuri, Ganesh A. Thakur, Spyridon P. Nikas, Kumara V. Subramanian, Vidyandand G. Shukla, Alexandros Makriyannis, and Jack Bergman

CELLULAR AND MOLECULAR

High-Throughput Identification and Characterization of Novel, Species-selective GPR35 Agonists

568

Zaynab Neetoo-Isseljee, Amanda E. MacKenzie, Craig Southern, Jeff Jerman, Edward G. McIver, Nicholas Harries, Debra L. Taylor, and Graeme Milligan

Identification of Stanniocalcin 2 as a Novel Aryl Hydrocarbon Receptor Target Gene

579

Tod A. Harper Jr., Aditya D. Joshi, and Cornelis J. Elferink

DRUG DISCOVERY AND TRANSLATIONAL MEDICINE

Structure-Based Optimization of Angiostatic Agent 6DBF7, an Allosteric Antagonist of Galectin-1

589

Ruud P. M. Dings, Nigam Kumar, Michelle C. Miller, Melissa Loren, Huzaiifa Rangwala, Thomas R. Hoyer, and Kevin H. Mayo

5-Benzylglyciny-Amiloride Kills Proliferating and Nonproliferating Malignant Glioma Cells through Caspase-Independent Necroptosis Mediated by Apoptosis-Inducing Factor

600

Nagarekha Pasupuleti, Leonardo Leon, Kermit L. Carraway III, and Fredric Gorin

An Engineered Human Follistatin Variant: Insights into the Pharmacokinetic and Pharmacodynamic Relationships of a Novel Molecule with Broad Therapeutic Potential

616

Amiata Datta-Mannan, Benjamin Yaden, Venkatesh Krishnan, Bryan E. Jones, and Johnny E. Croy

ADX71743, a Potent and Selective Negative Allosteric Modulator of Metabotropic Glutamate Receptor 7: In Vitro and In Vivo Characterization

624

Mikhail Kalinichev, Mélanie Rouillier, Françoise Girard, Isabelle Royer-Urios, Bruno Bournique, Terry Finn, Delphine Charvin, Brice Campo, Emmanuel Le Poul, Vincent Mutel, Sonia Poli, Stuart A. Neale, Thomas E. Salt, and Robert Lütjens

ENDOCRINE AND DIABETES

Pharmacological Inhibition of Mitochondrial Carbonic Anhydrases Protects Mouse Cerebral Pericytes from High Glucose-Induced Oxidative Stress and Apoptosis

637

Gul N. Shah, Tulin O. Price, William A. Banks, Yoichi Morofuji, Andrej Kovac, Nuran Ercal, Christine M. Sorenson, Eui S. Shin, and Nader Sheibani

GASTROINTESTINAL, HEPATIC, PULMONARY, AND RENAL

- ☐ Puerarin Ameliorates Experimental Alcoholic Liver Injury by Inhibition of Endotoxin Gut Leakage, Kupffer Cell Activation, and Endotoxin Receptors Expression 646
Jing-Hua Peng, Tuan Cui, Fu Huang, Liang Chen, Yu Zhao, Lin Xu, Li-Li Xu, Qin Feng, and Yi-Yang Hu

METABOLISM, TRANSPORT, AND PHARMACOGENOMICS

- ☐ Mechanisms Limiting Distribution of the Threonine-Protein Kinase B-RaF^{V600E} Inhibitor Dabrafenib to the Brain: Implications for the Treatment of Melanoma Brain Metastases 655
Rajendar K. Mittapalli, Shruthi Vaidhyanathan, Arkadiusz Z. Dudek, and William F. Elmquist
- ☐ Carboxylesterase 1 as a Determinant of Clopidogrel Metabolism and Activation 665
Hao-Jie Zhu, Xinwen Wang, Brian E. Gawronski, Bryan J. Brinda, Dominick J. Angiolillo, and John S. Markowitz
- ☐ Cynomolgus Monkey as a Potential Model to Assess Drug Interactions Involving Hepatic Organic Anion Transporting Polypeptides: In Vitro, In Vivo, and In Vitro-to-In Vivo Extrapolation 673
Hong Shen, Zheng Yang, Gabe Mintier, Yong-Hae Han, Cliff Chen, Praveen Balimane, Mohammed Jemal, Weiping Zhao, Renjie Zhang, Sanjith Kallipatti, Sabariya Selvam, Sunil Sukrutharaj, Prasad Krishnamurthy, Punit Marathe, and A. David Rodrigues

NEUROPHARMACOLOGY

- ☐ Pharmacodynamics of Selective Inhibition of γ -Secretase by Avagacestat 686
Charles F. Albright, Randy C. Dockens, Jere E. Meredith Jr., Richard E. Olson, Randy Slemmon, Kimberley A. Lentz, Jun-Sheng Wang, R. Rex Denton, Gary Pilcher, Paul W. Rhyne, Joseph J. Raybon, Donna M. Barten, Catherine Burton, Jeremy H. Toyn, Sethu Sankaranarayanan, Craig Polson, Valerie Guss, Randy White, Frank Simutis, Thomas Sanderson, Kevin W. Gillman, John E. Starrett, Jr., Joanne Bronson, Oleksandr Sverdlov, Shu-Pang Huang, Lorna Castaneda, Howard Feldman, Vlad Coric, Robert Zaczek, John E. Macor, John Houston, Robert M. Berman, and Gary Tong
- The Antinociceptive Effect of Milnacipran in the Monosodium Iodoacetate Model of Osteoarthritis Pain and Its Relation to Changes in Descending Inhibition 696
Liam J. Burnham and Anthony H. Dickenson
- ☐ A G Protein-Biased Ligand at the μ -Opioid Receptor Is Potently Analgesic with Reduced Gastrointestinal and Respiratory Dysfunction Compared with Morphine 708
Scott M. DeWire, Dennis S. Yamashita, David H. Rominger, Guodong Liu, Conrad L. Cowan, Thomas M. Graczyk, Xiao-Tao Chen, Philip M. Pitis, Dimitar Gotchev, Catherine Yuan, Michael Koblish, Michael W. Lark, and Jonathan D. Violin

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

About the cover: Intracellular trafficking of uPA to the mitochondria. See the article by Pasupuleti et al. on page 600 of this issue.