SPECIAL SECTION ON 50 YEARS OF OPIOID RESEARCH

Editorial: 50 Years of Opioid Research and the International Narcotics Research Conference
Manojkumar A. Puthenveedu

Opioid Research: Past and Future
Rita J. Valentino and Nora D. Volkow

A Concise Review of Concepts in Opioid Pharmacology up to the Discovery of Endogenous Opioids
Brian M. Cox

Recent Progress in Opioid Research from an Electrophysiological Perspective
William T. Birdsong, and John T. Williams

Intrinsic Efficacy of Opioid Ligands and Its Importance for Apparent Bias, Operational Analysis, and Therapeutic Window
Alexander Gillis, Varun Sreenivasan, and Macdonald J. Christie

Opioid Pharmacology under the Microscope
Damien Jullié, Arisbel B. Gondin, Mark von Zastrow, and Meritxell Canals

Pain, Motivation, Migraine, and the Microbiome: New Frontiers for Opioid Systems and Disease
Kyle E. Parker, Elizabeth Sugiarto, Anna M.W. Taylor, Amynah A. Pradhan, and Ream Al-Hasani

Bidirectional Relationship between Opioids and Disrupted Sleep: Putative Mechanisms
D. Eacret, S.C. Veasey, and J.A. Blendy

Neprilysin Controls the Synaptic Activity of Neuropeptides in the Intercalated Cells of the Amygdala
G.C. Gregoriou, S.D. Patel, B.L. Winters, and E.E. Bagley

Unique Pharmacological Properties of the Kappa Opioid Receptor Signaling Through Gα as Shown with Bioluminescence Resonance Energy Transfer
Miriam E. Barnett, Brian I. Knapp, and Jean M. Bidlack

Atomic-Level Characterization of the Methadone-Stabilized Active Conformation of μ-Opioid Receptor
Abhijeet Kapoor, Davide Provasi, and Marta Filizola

Spinal Opioid Tolerance Depends upon Platelet-Derived Growth Factor Receptor-β Signaling, Not μ-Opioid Receptor Internalization
S. Puig, K.E. Barker, S.R. Szott, P.T. Kann, J.S. Morris, and H.B. Gutstein

Chronic Treatment with Morphine Disrupts Acute Kinase-Dependent Desensitization of GPCRs
Emily R. Leff, Seksiri Arttamangkul, and John T. Williams
Fentanyl-Induced Block of hERG Channels Is Exacerbated by Hypoxia, Hypokalemia, Alkalosis, and the Presence of hERG1b
Jared N. Tschirhart and Shetuan Zhang

A Truncated Six Transmembrane Splice Variant MOR-1G Enhances Expression of the Full-Length Seven Transmembrane μ-Opioid Receptor through Heterodimerization
Tiffany Zhang, Jin Xu, and Ying-Xian Pan

EDITORIAL
“Emerging Concepts”: New Article Category in Molecular Pharmacology
David A. Gewirtz

EMERGING CONCEPTS
Weak Microbial Metabolites: a Treasure Trove for Using Biomimicry to Discover and Optimize Drugs

MINIREVIEW
Targeting Vesicular Glutamate Transporter Machinery: Implications on Metabotropic Glutamate Receptor 5 Signaling and Behavior
Karim S. Ibrahim, Khaled S. Abd-Elrahman, Salah El Mestikawy, and Stephen S.G. Ferguson

ARTICLES
Analysis of Modulation of the α1 GABA<sub>A</sub> Receptor by Combinations of Inhibitory and Potentiating Neurosteroids Reveals Shared and Distinct Binding Sites
Allison L. Germann, David E. Reichert, Ariel B. Burbridge, Spencer R. Pierce, Alex S. Evers, Joe Henry Steinbach, and Gustav Akk

Differing Activity Profiles of the Stereoisomers of 2,3,5,6TMP-TQS, a Putative Silent Allosteric Modulator of α7 nAChR
Roger L. Papke, Sumanta Garai, Clare Stokes, Nicole A. Horenstein, Arthur D. Zimmerman, Khalil A. Abboud, and Ganesh A. Thakur

Enhancement of Muscimol Binding and Gating by Allosteric Modulators of the GABA<sub>A</sub> Receptor: Relating Occupancy to State Functions
Gustav Akk, Allison L. Germann, Yusuke Sugasawa, Spencer R. Pierce, Alex S. Evers, and Joe Henry Steinbach

Nicotinic Acetylcholine Receptor Accessory Subunits Determine the Activity Profile of Epibatidine Derivatives
Lu Wenchi Corrie, Clare Stokes, Jenny L. Wilkerson, F. Ivy Carroll, Lance R. McMahon, and Roger L. Papke

Dietary Caffeine Synergizes Adverse Peripheral and Central Responses to Anesthesia in Malignant Hyperthermia Susceptible Mice
Monica Aleman, Rui Zhang, Wei Feng, Lihong Qi, Jose R. Lopez, Chelsea Crowe, Yao Dong, Genady Cherednichenko, and Isaac N. Pessah

Pharmacology and Molecular Mechanisms of Clinically Relevant Estrogen Estetrol and Estrogen Mimic BMI-135 for the Treatment of Endocrine-Resistant Breast Cancer
Balkees Abderrahman, Philipp Y. Maximov, Ramona F. Curpan, Jay S. Hanspal, Ping Fan, Rui Xiong, Debra A. Tonetti, Gregory R.J. Thatcher, and V. Craig Jordan

LETTER TO THE EDITOR
Commentary on: “Does COVID19 Infect the Brain? If So, Smokers Might Be at a Higher Risk”
Robert C. Speth