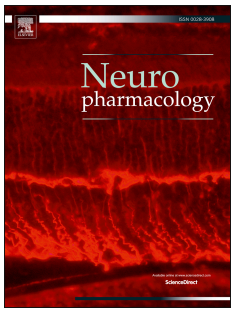
Accepted Manuscript



Investigation of the role of βarrestin2 in kappa opioid receptor modulation in a mouse model of pruritus

Jenny Morgenweck, Kevin J. Frankowski, Thomas E. Prisinzano, Jeffrey Aubé, Laura M. Bohn

PII: S0028-3908(15)30072-1

DOI: 10.1016/j.neuropharm.2015.08.027

Reference: NP 5973

To appear in: *Neuropharmacology*

Received Date: 15 June 2015

Revised Date: 29 July 2015

Accepted Date: 17 August 2015

Please cite this article as: Morgenweck, J., Frankowski, K.J., Prisinzano, T.E., Aubé, J., Bohn, L.M., Investigation of the role of βarrestin2 in kappa opioid receptor modulation in a mouse model of pruritus, *Neuropharmacology* (2015), doi: 10.1016/j.neuropharm.2015.08.027.

Investigation of the role of βarrestin2 in kappa opioid receptor modulation in a mouse model of pruritus

Jenny Morgenweck[1], Kevin J. Frankowski[2], Thomas E. Prisinzano[2], Jeffrey Aubé[2], Laura M. Bohn[1*]

[1]Departments of Molecular Therapeutics and Neuroscience, The Scripps Research Institute, 130 Scripps Way, Jupiter, FL 33458, USA

[2] Department of Medicinal Chemistry, University of Kansas, Lawrence, KS 66047, USA

*To whom correspondence should be addressed.

LMB: Departments of Molecular Therapeutics and Neuroscience, The Scripps Research Institute, 130 Scripps Way, #2A2, Jupiter, FL 33458, Telephone: (561) 228-2227; Fax: (561) 228-3081; Email: lbohn@scripps.edu

Keywords: pruritus, kappa opioid receptor, biased ligand, mouse models of itch, U50,488H, KOR antagonist

Abbreviations:

βarr2-KO, βarrestin2 knockout; CP, chloroquine phosphate; CPA, conditioned place aversion; DMSO, dimethyl sulfoxide; 5'-GNTI, 5'-guanidinonaltrindole; GPCR, G protein coupled receptor; GRK3, GPCR kinase 3; [^{35}S]GTPγS, guanosine 5'-O-(3-[^{35}S]thio)triphosphate; KOR, kappa opioid receptor; KOR-KO, kappa opioid receptor knockout; MOR, mu opioid receptor; NorBNI, nor-binaltorphimine; WT, wild type

Highlights:

KOR agonists are clinically used for pruritis yet most KOR agonists induce sedation.

G protein/βarrestin2 biased KOR agonists are antipruritic yet not sedating in mice.

Biased KOR agonists may have therapeutic utility in treating pruritis.