共同表現 μ 類鴉片與類鴉片孤兒受體之人類胚胎腎臟293細胞株中G蛋白質耦合內整流鉀離子通道之活化

Activation of G Protein-Coupled Inwardly Rectifying K+ Channels in Human Embryonic Kidney 293 Cells Coexpressing μ-Opioid and Opioid Receptor-Like 1 Receptors

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Objectives：Opioid analgesia and addiction are mediated by drug-induced activation of opioid receptors. In neuronal tissue, G protein-coupled inwardly rectifying potassium channels (GIRK) are responsible for mediating inhibitory postsynaptic potentials. The stimulation of opioid receptors coupled to inhibitory G proteins of the Gi/o family releases Gβγ dimers, which can subsequently trigger GIRK currents.

Methods：We used molecular biology and electrophysiological techniques to examine the ability of DAMGO, nociceptin, morphine, methadone and buprenorphine to activate GIRK channel subunits 1 and 2 in human embryonic kidney (HEK) 293 cells coexpressing μ-opioid (MOR) and opioid receptor-like 1 (ORL1) receptors.

Results：Both DAMGO and nociceptin induced GIRK1/2 activation when

MOR and ORL1 receptors are expressed either individually or simultaneously, indicating the functional coupling of the expressed opioid receptors and the introduced human GIRK1 and GIRK2 subunits. Furthermore, we found that morphine, methadone, and buprenorphine were less potent in activating the GIRK1/2 currents compared to DAMGO and nociceptin.

Conclusions : Opioid agonists induce different conformations of the overexpressed opioid receptors, and hence rendering neuronal cells susceptible to differential regulation of membrane excitability. This work was supported by National Health Research Institutes (MD-097-PP-13, PH-098-PP-35, PH-099-PP-36, PH-100-PP-36, and NHRI-101A1-PDCO -1312141) and China Medical University Hospital (DMR-101-123).