[PA1-46] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Comparative studies of molecular mechanisms of dopamine D2R and D3R receptors for the activation of mitogen activated protein kinase in HEK-293 cells

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Dopamine $D_2$and D_3 receptors (D_2R and D_3R) belong to G protein coupled receptor family. They are co-localized in some regions of brain, and share similar structural and functional characteristics, for example, activation of ERK1/2. In this study, we conducted series of experiments to understand the differential regulatory processes underlying D_2R/D_3R-mediated activation of ERK1/2. For both D_2R/D_3R-mediated ERK1/2 activation, pertussis toxin-sensitive G proteins were involved, and treatments that inhibit clathrin-mediated receptor endocytosis (sucrose, dominant negative mutants, dynamin-K44A or β-arrestin1-V53D) did not affect them. In additon, wortmannin, a specific inhibitor of phosphatidylinositol 3-kinase and Go6983, a PKC isotype-specifc inhibitor also abolished both D_2R/D_3R mediated ERK1/2 activation. Interestingly, tryphostin AG1478, a selective inhibitor of tyrosine kinase of epidermal growth factor receptor and ΔN-Raf (dominant negative mutant of $p74_{raf-1}$) effectively blocked D_2R-mediated ERK1/2 activetion, but not that mediated by D_3R. These results suggest that D_2R activates ERK1/2 through classical MAPK cascades involving transactivation with EGFR, however, D_3R uses distinct signaling pathways for the ERK1/2 activation.

[PA1-47] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

The involvement of benzodiazepine receptor on the relaxation of cat lower esophageal sphincter tone

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It has been previously suggested that NO and vasoactive intestinal polypeptide (VIP) are neurotransmitters which control Lower esophageal sphincter (LES) and esophageal peristalsis. However, it is also proposed that another transmitter(s) is involved in LES relaxation.
In the present study, we investigated the effect of GABA and benzodiazepine on the VIP- or electrical field stimulation (EFS)-induced relaxation in cat LES muscle.
GABA, muscimol (GABAa agonist), and baclofen (GABAb agonist) had no effects on the relaxation, which is induced by VIP or EFS. Bicuculline (GABAa antagonist) and phaclofen (GABAb antagonist) also had no effect on the relaxation, which is induced by VIP or EFS. However flumazenil (benzodiazepine antagonist) inhibited the VIP-induced LES relaxation, but had no effect on the EFS-induced LES relaxation.
Our results suggest that benzodiazepine receptor participates in the LES relaxation, which is mediated postsynaptically, but not presynaptically, via the interaction with VIP.

[PA1-48] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

The alteration of intracellular signaling on the smooth muscle cells relaxation in cat esophagitis

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