

[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 D₂ and D₃ receptors (D₂R and D₃R) 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 D₂R/D₃R-mediated activation of ERK1/2. For both D₂R/D₃R-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 addition, wortmannin, a specific inhibitor of phosphatidylinositol 3-kinase and Go6983, a PKC isotype-specific inhibitor also abolished both D₂R/D₃R mediated ERK1/2 activation. Interestingly, tryphostin AG1478, a selective inhibitor of tyrosine kinase of epidermal growth factor receptor and Δ N-Raf (dominant negative mutant of p74_{raf-1}) effectively blocked D₂R-mediated ERK1/2 activation, but not that mediated by D₃R. These results suggest that D₂R activates ERK1/2 through classical MAPK cascades involving transactivation with EGFR, however, D₃R 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 (GABA_A agonist), and baclofen (GABA_B agonist) had no effects on the relaxation, which is induced by VIP or EFS. Bicuculline (GABA_A antagonist) and phaclofen (GABA_B 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.

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

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