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Acanthoic acid (AA) is a pimaradiene diterpene isolated from the Korean medicinal plant, Acanthopanax koreanum (Araliaceae), which has been traditionally used as a tonic and sedative as well as in the treatment of rheumatism and diabetes in korea. Proteinase-activated receptor-2 (PAR-2) agonist trypsin plays a role in inflammation, and human leukemic mast cells (HMC-1) express PAR-2. In the present study, the effect of acanthoic acid on production of tumor necrosis factor-α (TNF-α) and tryptase in trypsin-stimulated HMC-1 was examined. HMC-1 cells were stimulated with trypsin (100 nM) in the presence or absence of acanthoic acid (1, 10, and 100 μg/ml). TNF-α secretion was measured by enzyme-linked immunosorbent assay (ELISA). TNF-α and tryptase mRNA were measured by reverse transcription-PCR. Mitogen-activated protein kinase (MAPK) activation was assessed by Western blot analysis. Trypsin activity was measured using the substrate Bz-DL-Arg-p-nitroanilide (BAPNA). Acanthoic acid (10 and 100 μg/ml) significantly inhibited TNF- α secretion from trypsin-stimulated HMC-1. Acanthoic acid (10 and 100μg/ml) also inhibited TNF- α and tryptase mRNA expression in trypsin-stimulated HMC-1. Furthermore, acanthoic acid inhibited trypsin-induced extracellular signal-regulated kinase (ERK) phosphorylation, whereas acanthoic acid did not affect the trypsin activity even 100 μg/ml. Acanthoic acid inhibits PAR2-mediated human mast cell activation by not inhibition of trypsin activity but block of ERK pathway. (This work was supported by grant No. (R01-2002-000-00276-0) from the Basic Research Program of the Korea Science & Engineering Foundation.).

[PA1-36] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Direct and functional interaction between dopamine D2 receptor and ALY

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The signaling pathway of dopamine D_2 receptor was studied using yeast two-hybrid system. The 3rd cytoplasmic loop of rat D_2 receptor was fond to interact with ALY. The interaction in the yeast was observed only with the 3rd cytoplasmic loop of D_2 receptor but not with that of D_3 or D_4 dopamine receptor. The interaction between two proteins was also confirmed by GST pull-down assay. Co-expression of D_2 receptor and ALY enhanced the expression of Lef-1 promoter in C6 cells and the promoter of D_2 dopamine receptor itself.

[PA1-37] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Regulation of c-fos promoter through interaction between dopamine D3 receptor and RGL, ral GDP dissociation stimulator-like

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Ral GDP dissociation stimulator (Ral GDS) has been found to be an effector protein of Ras, and Ral, a member of small GTP-binding protein (G protein) superfamily, has been suggested to act downstream of Ras. Ral GDP dissociation stimulator-like (RGL) shares 50% amino acid identity with Ral GDP dissociation stimulator, and assumed to possess similar functional role. Using yeast two-hybrid screening, we found that dopamine D3 receptor interacts with RGL. Since RGL is known to regulate the expression of c-fos promoter, effects of D3R on gene expression of c-fos promoter was studied. Co-transfection of RGL and D3R greatly enhanced the expression.These results show that RGL and D3R regulate c-fos promoter activity, and ERK pathway was involved in this process.