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 trypstatse 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 trypstatse 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 trypstatse 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 D2 receptor was studied using yeast two-hybrid system. The 3rd cytoplasmic loop of rat D2 receptor was fond to interact with ALY. The interaction in the yeast was observed only with the 3rd cytoplasmic loop of D2 receptor but not with that of D3 or D4 dopamine receptor. The interaction between two proteins was also confirmed by GST pull-down assay. Co-expression of D2 receptor and ALY enhanced the expression of Lef-1 promoter in C6 cells and the promoter of D2 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.