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The signaling components of high affinity IgE receptor (FcεRI) were searched by yeast-hybrid screening of the cDNA library constructed from RBL-2H3 cells. The cytoplasmic part of the FcεRI-β chain was found to specifically interact with PLCγ2, and further comparative studies were conducted focusing on the differential regulation of two PLC- isoforms through FcεRI. The inhibitors of Src, Syk, and protein kinase C similarly affected the tyrosine phosphorylations of PLCγ1 and PLCγ2 but the inhibitors of PI3-kinase and p42/44 ERK effectively inhibited the activation of PLCγ1 but not PLCγ2. Our results provide for the first time the functional roles of the NH2-terminal of the chain in the signal transduction of FcRI, and the meaning for the existence of two closely related PLCγ isoforms in the mast cells.

[PA1-49] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Protective effect of metabolized Chungpesagan-tang on Hypoxia/ Reperfusion induced-PC12 cell damage

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This research was performed to investigate the protective effect of Chungpesagan-tang (CPS) against ischemic damage in PC12 cells. To elucidate the mechanism of the protective effect of CPS on ischemic insult, cell viability and changes in activities of Superoxide dismutase, Glutathione Peroxidase, Catalase, Caspase 3 and the production of Malondialdehyde were observed after treating PC12 cells with CPS which was metabolized by rat liver homogenate. Pretreatment of CPS with liver homogenate increased its protective effect against ischemic insult by reducing the harmful effect of CPS itself. The result showed that CPS had the highest protective effect against hypoxia/reperfusion at the dose of 1 mg/ml in PC12 cells, probably by recovering the redox enzyme activities and MDA to control level. (Supported by HMP 01-PJ9-PG1-01CO03-0003 and BK21 project, Korea)

[PA1-50] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

CJ-11668, A new selective and potent COX-2 inhibitor, reduces inflammation, fever and pain in animal models

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CJ-11668 is a new potent and selective COX-2 inhibitor. CJ-11668 showed COX-2 inhibition (IC50) of 65nM and selectivity ratio (COX-1/COX-2) of 770 in the cell based assay. In the human whole blood assay, CJ-11668 showed COX-2 inhibition (IC50) of 370nM and selectivity ratio (COX-1/COX-2), 135. The treatment of CJ-11668 (5 mg/kg, p.o.) produced a significant inhibition (35%) of inflamed rat paw volume in the carrageenan-induced acute inflammation. CJ-11668 also suppressed the PGE2 level (69% inhibition, 1 mg/kg, p.o.) in the zymosan-induced mouse air pouch model after 3 hrs. Furthermore, CJ-11668 showed a prolonged effect (36% inhibition, 1 mg/kg, p.o.) at 12 hrs post-dosing, whereas the same dose of Celebrex had no effect. The anti-fever and anti-hyperalgesia effects were also determined in rats. In conclusion, CJ-11668 is a selective COX-2 inhibitor with potent anti-inflammatory, anti-pyretic and analgesic activity.

[PA1-51] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Calcium signal dependent cell death by presenlin-2 mutation in PC12 cells and in cortical neuron from presenlin-2 mutation transgenic mice

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Familial form of Alzheimer's disease (FAD) is caused by mutations in presenilin-1 (PS-1) and presenilin-2 (PS-2). PS1 and PS2 mutation are known to similar effects on the production of amyloid β peptide ($A\beta$) and cause of neuronal cell death in the brain of patient of Alzheimer's disease. The importance of the alternation of cellular calcium homeostasis in the neuronal cell death by PS1 mutation in a variety of experimental systems has been demonstrated. However, no studies on the effect of PS2 or mutant PS2 on cellular calcium homeostasis, and relevance of its change to neuronal cell vulnerability against neurotoxins have been reported. In the present study, we investigated whether PS2 mutation increased vulnerability of PC12 cells and cortical neuronal cells against neurotoxic insults through perturbation of calcium homeostasis. Stable transfected PC12 cells with mutant (N141I) showed a significant increased vulnerability of cells determined by cell viability and induction of apoptosis after treatment of $A\beta$ and L-glutamate compared to those in PC12 cells, PC12 cells expressing vector alone or expressing wild type of PS2. Similar in PC12 cell, cortical neurons from PS2 transgenic mice resulted in a greater increase of vulnerability compared to those from wide type PS2 transgenic mice. Consistent with the increased cell vulnerability, much greater enhanced intracellular calcium level were found in PC12 cells expressing mutant PS2 after treatment of $A\beta$ and L-glutamate. Double-labeling confocal micrograph analysis shows that ryanodine receptor (RyR) and PS2 are colocalized in endoplasmic reticulum (ER) of PC12 cells and cortical neurons from transgenic mice. PS2 and RyR expression was increased by the treatment of $A\beta$ and L-glutamate. Moreover, pretreatment of dantrolene, an agent that block calcium release through RyR sensitive store protected against PS2 mutation-enhanced neuronal cell death. The present data suggest that PS2 mutation promotes neuronal degeneration in AD through perturbation of RyR sensitive calcium homeostasis in ER.

[PA1-52] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Anti-apoptotic effect of water extract of rheum undulatum in pancreatic β -Cell, HIT-T15

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Sopungsungi-won has been used as a traditional medicine for diabetes and it has been proved evidently as a potential remedy for type 2 diabetes mellitus. Both in vivo and in vitro experiments with water extract of Sopungsungi-won have been reported to exhibit anti-diabetic effects in our previous studies. In the present study, we have chosen Rheum undulatum (RU), which is the main component of Sopungsungi-won, to examine its anti-apoptotic effect on pancreatic β -cells, HIT-T15, against oxidative stress induced by hydrogen peroxide (H_2O_2). To investigate the anti-apoptotic effect of Rheum undulatum water extract (RUWE) against H_2O_2 -induced apoptosis in β -cell of pancreas, MTT assay, DAPI staining, TUNEL assay, RT-PCR and caspase-3 enzyme assay were performed in pancreatic β -cell line of hamster, HIT-T15. Through the morphological analysis, it was demonstrated that cells treated with H_2O_2 exhibit classical apoptotic features, while the occurrence of such changes was reduced in cells pre-treated with RUWE. In addition, it was shown that RUWE treated cells prior to H_2O_2 treatment induced the increase in levels of bcl-2 expression and decrease in caspase-3 enzyme activity compared to cells treated with H_2O_2 only. These results might suggest the possibility of usage of RU in patients with progressively deteriorated diabetes.

[PA1-53] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Sphingosine-1-Phosphate-Induced ERK Activation Protects Human Melanocytes from UVB-Induced Apoptosis

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