College of Pharmacy, Chungbuk National University, KFDA, and KRIBB

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 (Aβ) and cause of neuronal cell dath 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 (N1411) showed a significant increased vulnerability of cells determined by cell viability and induction of apoptosis after treatment of Aβ 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 vnlenrability, much greater enhanced intracellular calcium level were found in PC12 cells expressing mutant PS2 after treatment of Aβ 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 Aβ and L-glutamate. Moreover, pretreatment of dantrolene, an agent that block calcium release though 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 senstive 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

Yoon Seo Hyun°, Hong Mee Suk, Chung Joo Ho, Chung Sung Hyun
College of Pharmacy, Kyung Hee University and College of Medicine, Kyung Heel University

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 b-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 b-cell of pancreas, MTT assay, DAPI staining, TUNEL assay, RT-PCR and caspase-3 enzyme assay were performed in pancreatic b-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

Kim Dong-Seok°, Kim Sook-Young, Lee Jai-Eun, Kwon Sun-Bang, Sohn Uy-Dong, Park Kyoung-Chan
Research Division for Human Life Sciences, Seoul National University, Department of Dermatology, Seoul National University College of Medicine, Department of Pharmacology, College of Pharmacy, Chung-Ang University