concentrations higher than 15 μM, THP showed a cytotoxicity through an apoptotic process. In addition, THP at 5-15 μM significantly enhanced L-DOPA-induced neurotoxicity (L-DOPA concentration, 50 μM). Treatment of PC12 cells with 15 μM THP and 50 μM L-DOPA, alone or in combination, also induced cell death via a mechanism which exhibited morphological and biochemical characteristics of apoptosis, including chromatin condensation and membrane blebbing. Exposure of PC12 cells to THP, L-DOPA and THP plus L-DOPA for 48 h resulted in a marked increase in the cell loss and percentage of apoptotic cells compared with exposure for 24 h. These findings indicate that the enhancing effects of THP on L-DOPA-induced neurotoxicity were time and concentration dependent. Furthermore, these results suggest that THP inhibits L-DOPA-induced increase in dopamine content and enhances L-DOPA-induced neurotoxic and apoptotic effects on PC12 cells.

[PB3-8] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Increase of intracellular Ca2+ and cytotoxicity induced by neuro-toxicants in PC12 cells carrying mutant presenilin-2

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Many cases of early onset autosomal dominant inherited forms of Alzheimer's disease (AD) are caused by mutation in the genes encoding presenilin-2 (PS-2) on chromosome 1. It is characterized by amyloid deposition and associated with loss of neuron. However, molecular mechanisms underlying the role of PS-2 mutation in the pathogenic AD are not known. Pathophysiological elevation of intracellular calcium concentration in the neuron has been demonstrated as an important responsible factor in the neuronal cell death. In this study, we compared real-time alteration of intra-cellular calcium concentration and cellular response (cytotoxicity) in the pheochromocytoma cells (PC12) and PC12 cells carrying mutant PS-2 stimulated either by beta-amyloid and glutamate. Prolonged elevation of intra-cellular calcium concentration by glutamate and beta-amyloid was significantly enhanced in cells carrying mutant PS-2. With reverse correlation with the level of intra-cellular calcium concentration, significant decrease of cell viability and increase of the induction of apoptosis was found in the cells carrying mutant PS-2. This results showing that PS-2 mutation elevates intra-cellular calcium concentration and thereby render neurons vulnerable to neuro-toxic stimuli, suggested that perturb of intra-cellular calcium homeostasis could play a important role in the pathogenesis of AD.

[PB3-9] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

15-DEOXY-△12,14-PROSTAGLANDIN J2, A LIGAND OF PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR-γ INDUCE APOPTOSIS THROUGH PHOSPHORYLATION OF ERK PATHWAY IN NEUROBLASTOMA CELLS

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15-Deoxy-Δ12,14-prostaglandin J2 (15-deoxy-PGJ2), a peroxisome proliferator-activated receptors (PPAR-γ) ligand, has been shown to stimulate the differentiation and induction of apoptosis in the several cancer cells including breast, prostate and lung cancer cells. In the previous our study, it was found that 15-deoxy-PGJ2 inhibit cell growth through induction of apoptosis in neuroblastoma cells (SK-N-MC and SK-N-SH cells). Here we demonstrated possible molecular mechanisms underlying the induction of apoptosis by 15-deoxy-PGJ2. 15-Deoxy-PGJ2 dose (2-16 μM) dependently induced apoptosis. Consistent with the induction of apoptosis,15-deoxy-PGJ2 reduced the expression of anti-apoptotic gene Bcl-2 but increased the expression of pro-apoptotic genes : caspase-3 and 9, and Bax. In parallel with the increasing of apoptosis, 15-deoxy-PGJ2 increased the expression of phosphorylated ERK. Moreover,

pretreatment of PD98059, a specific inhibitor of MEK (kinase immediately upstream of ERK) prevented 15-deoxy-PGJ2-induced increasing expression of phosphorylated ERK. This inhibitory effect correlated well with the inhibition of apoptosis-associated gene expression and apoptosis. These results suggest that PPAR-γ ligand, 15-deoxy-PGJ2 induce apoptosis of neuroblastoma cells through ERK pathway.

[PB3-10] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR GAMMA AGONIST 15-DEOXY-PROSTAGLANDIN J2 STIMULATES DIFFERENTIATION OF EMBRYONIC MIDBRAIN CELLS

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15-deoxy-Δ12,14-prostaglandin J2 (15-deoxy PGJ2), a cyclopentenone prostaglandin has various biological activities including anti-viral and anti-inflammatory activities. It has also been demonstrated that 15-deoxy PGJ2 induces differentiation of several cells such as adipocytes and macrophages. Moreover, PPAR-gamma antagonist inhibited cell differentiation of adipocyte. Recent study shows that PPAR-γ is expressed in certain central nervous system neuron. Our studies showed that 15-deoxy-PGJ2 stimulated differentiation of a dopaminergic differentiating pheochromocytoma 12 (PC-12) cells. The present study was therefore designated to determine whether 15-deoxy PGJ2 could stimulate the differentiation of *undifferentiated embryonic midbrain cell to dopaminergic midbrain neurons. Undifferentiated embryonic* midbrain cells were isolated from gestation 12-day embryos and were cultured with 15-deoxy PGJ2. 15-Deoxy PGJ2 stimulates neurite extension (a marker of cell differentiation) of embryonic midbrain cell with concomitant increase of the expression of neurofilament and PPAR-γ expression. The expression of neurofilament and PPAR-γ in the adult brain (post 13 day of brain) was much higher than in the midbrain of 12 or 17-day gestation embryos. This result shows that activation (expression) of PPAR-gamma could be involved in the neuronal cell differentiation.

Poster Presentations - Field B4. Immunology

[PB4-1] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Augmentation of cytokine production in murine macrophage cell line, RAW 264.7 by of Korean Propolis

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Monocytes and macrophages play a major role in defense mechanism of the host response to tumor, in part through the secretion of several potent products and macrophage cytokines. Monocytes and tissue macrophages produce at least two groups of protein mediators of inflammation, interleukin 1 (IL-1) and tumor necrosis factor (TNF). Recent studies emphasizes that TNF and IL-1 modulate the inflammatory function of endothelial cells, leukocytes, and fibroblasts. In this study, our work is directed toward studying the in vitro effects of Korean propolis on the ability to induce celluar and secretory responses in murine macrophage cell line, RAW 264.7. The production of the macrophage cytokines, IL-1 and TNF-α, by RAW 264.7 treated with Water Extract of proplis (WEP) was examined from 2.5 mg/ml up to 25 mg/ml with dose dependent manner. Nitric oxide (NO) production was also observed. Significantly, more NO was produced