

(CAM) assay. The ethanolic extract of media-cultured *Paecilomyces japonica* also showed significant anti-angiogenic activity in CAM assay. The *Cordyceps militaris* extract was found to contain anti-inflammatory activity in the carrageenin-induced edema test, and cordycepin, a component of *C. militaris* also showed anti-inflammatory activity in the same test. The *C. militaris* extract was shown to contain antioxidant activity, which was able to scavenge the stable free radical DPPH.

[PA1-12] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

**(-) 3,5-Dicaffeoyl-muco-quinic acid isolated from *Aster scaber* contributes to the differentiation of PC12 cells: through tyrosine kinase cascade signaling**

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*Aster scaber* T. (Asteraceae) has been used in traditional Korean and Chinese medicine to treat bruises, snakebites, headaches and dizziness. (-) 3,5-Dicaffeoyl-muco-quinic acid (DQ) isolated from *Aster scaber* induced neurite outgrowth in PC12 cells. It has been reported that the activation of the extracellular signal regulated kinase1/2 (Erk 1/2) and phosphoinositide 3 (PI3) kinase plays a crucial role in the NGF-induced differentiation of PC12 cells. This study showed that the effect of DQ on neurite outgrowth is mediated via the Erk 1/2 and PI3 kinase-dependent pathways like NGF. Furthermore, DQ stimulated the phosphorylation of Trk A. Overall, DQ elicited the differentiation of PC12 cells through Trk A phosphorylation followed by Erk1/2 and PI3 kinase activation.

[PA1-13] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

**Minocycline Directly Blocks Activation of Caspases After Oxidative Stress in PC12 Cells**

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Minocycline is known to protect neurons from microglia-mediated cell death in many experimental models of brain diseases including ischemic stroke, Huntington's disease (HD), amyotrophic lateral sclerosis (ALS), traumatic brain injury, multiple sclerosis, and Parkinson's disease. Activation of caspase-2, 3, 8, and 9 was evident within 2–8 hr following oxidative insult with 0.5 mM hydrogen peroxide in PC12 cells. Minocycline significantly attenuated activation of these caspases up to 18 hr, resulting a significant increase in cell viability as assessed by MTT assay. However, caspase-3-independent cell death or necrosis still appeared to occur in the presence of minocycline since calpain activation was not affected by minocycline. Moreover, co-treatment with minocycline and calpain inhibitors synergistically inhibited hydrogen peroxide-induced cell death. These data suggest that minocycline directly inhibited apoptosis, but not necrosis, after oxidative insult in PC12 cells

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

**Effects of Anonaine on Dopamine Biosynthesis in PC12 Cells.**

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The effects of anonaine, an aporphine isoquinoline alkaloid, on dopamine biosynthesis and L-DOPA-induced neurotoxicity in PC12 cells were investigated. Treatment of PC12 cells with 0.05  $\mu$ M anonaine showed a significant inhibition of dopamine content. The IC<sub>50</sub> value of anonaine was 0.05  $\mu$ M. Under the same conditions,

0.05  $\mu\text{M}$  anonaine also inhibited tyrosine hydroxylase (TH) activity at 24 h (62.0% inhibition of the control level). TH mRNA levels were also decreased by the treatment with anonaine. Intracellular cyclic AMP level was decreased by anonaine. However, anonaine could not alter the  $\text{Ca}^{2+}$  concentration. Treatment with anonaine at concentrations higher than 3  $\mu\text{M}$  caused a cytotoxicity in PC12 cells as determined by MTT assay. Exposure of PC12 cells to non-cytotoxic concentration range of anonaine (0.05  $\mu\text{M}$ ) in association with L-DOPA (20  $\mu\text{M}$ , 50  $\mu\text{M}$  and 100  $\mu\text{M}$ ) after 24 h or 48 h had a trend to decrease cell death compared with L-DOPA alone. These results suggest that anonaine inhibit dopamine biosynthesis by the reduction of TH activity, and TH mRNA expression. In addition, anonaine inhibits the cytotoxicity caused by cell death in PC12 cells. The signal transduction pathways and the mechanisms of the protective effects in PC12 cells need to be investigated further.

[PA1-15] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **Suppression of IL-8 production by 18-beta-Glycyrrhetic acid is mediated by inhibition of MAPKs and NF-kappaB**

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Intestinal epithelial cells can produce cytokines and chemokines that play an important role in the mucosal immune response. Regulation of this production is important to prevent inflammatory tissue damage. Glycyrrhiza glabra has been shown to inhibit inflammation. The aim of this study was to examine the inhibitory effect of 18-beta-glycyrrhetic acid, a triterpenoid saponin of Glycyrrhiza glabra, on IL-8 production via mitogen-activated protein kinases (MAPKs) and nuclear factor-kappa B (NF-kB) in TNF-alpha-stimulated human colon epithelial cells. HT29 cells were stimulated with TNF-alpha in the presence or absence of 18beta-glycyrrhetic acid. IL-8 production was measured by enzyme-linked immunosorbent assay (ELISA), reverse transcription-PCR and Western blot analysis. MAPK activation and IkappaB/NF-kappaB expression were assessed by Western blot analysis. 18-beta-glycyrrhetic acid suppressed TNF-alpha-induced IL-8 production in dose-dependent manner. Moreover, 18-beta-glycyrrhetic acid inhibited activation of MAPKs (p38, JNK1/2, and ERK1/2), degradation of IkB, and nuclear translocation of NF-kappaB. 18-beta-glycyrrhetic acid inhibits TNF-alpha-mediated IL-8 production by blockade in the MAPKs and NF-kappaB pathway in HT29 cells. (This work was supported by grant No. (R04-2002-000-00166-0) from the Basic Research Program of the Korea Science & Engineering Foundation.)

[PA1-16] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **Antiviral Activities of L-FMAUS, a new L-FMAU derivative, Against Hepatitis B virus**

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The nucleoside analogue, L-FMAUS was synthesized from L-FMAU which has been shown to have significant antiviral activity against hepatitis B virus (HBV). The anti-HBV activity and toxicity of the L-FMAUS were examined by a cell culture system using a hepatitis B virus (HBV) producing cell line, HepG2 2.2.15. L-FMAUS was assayed for the inhibition of HBV multiplication by measurement of HBV DNA and surface antigen (HBsAg) levels in the extracellular medium of HepG2 2.2.15 cells after an 8-day treatment. L-FMAUS reduced the secretion of HBsAg, as determined using HBsAg ELISA test, and decreased the levels of extracellular HBV virion DNA, as determined by PCR analysis. Our findings suggest that L-FMAUS may have potential to develop as anti-HBV drugs in the future.

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

### **Catalase protects cardiomyocytes via its inhibition of nitric oxide synthesis**