College of Veterinary Medicine

The present study was performed to examine mitogen-activated protein kinase associated pathways in mediation of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-induced cell apoptosis in cultured Jurkat T cells. TCDD significantly decreased cell viability in a concentration-dependent manner ($p<0.05$ at 10-300 nM). TCDD (10 nM) also time-dependently decreased cell viability ($p<0.05$ at 12-48 h). c-Jun NH_2-terminal kinase was significantly phosphorylated with TCDD treatment in a time dependent manner. p38 MAPK was not significantly changed with TCDD treatment. Extracellular signal-regulated protein kinase was significantly phosphorylated with TCDD treatment for 8 h and gradually returned to baseline. TCDD induced up-regulation of ASK1 and C-Jun, which are up- and down-stream of JNK, respectively, and up-regulation of cytosolic cytochrome c and Caspase-3. These results demonstrate that MAPK signaling pathways including JNK and ERK 1/2, are activated with the treatment of TCDD in Jurkat T cells, which suggest that MAPK pathways may be involved in the TCDD-induced cell death.

[PA1-4] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

The protective mechanism of melatonin on carrageenan-induced paw edema generation in rats

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The influence of melatonin on carrageenan-induced paw edema in Sprague-Dawley rats has been studied. The injection of 1% carrageenan (given at 0.1ml/paw) into the intraplantar induced an inflammatory response, and the maximal increase of paw volume, edema, was observed at 4hour. The levels of nitric oxide (NO), malondialdehyde (MDA) or prostaglandin E_2 (PGE_2) were increased after edema generation. Also, the expression of the inducible NO synthase (iNOS) were increased in the western blot. Melatonin pretreatment (given at 0.1 to 10 mg/kg) reduced this edema at 1, 2, 3 and 4h in a dose-denpendent manner. Melatonin treatment also decreased the levels of NO, MDA and PGE_2. Our data suggest that these inflammatory effects of carrageenan may be derived from an increase of the expression iNOS, the production of NO or MDA. Melatonin may prevent this inflammatory responses; increases of the expression iNOS and the levels of NO, MDA or PGE_2.

[PA1-5] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Sphingosine-1-phosphate Inhibits Human Keratinocyte Proliferation via Akt/PKB Inactivation

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Although sphingosine-1-phosphate (S1P) is a well-known mitogen, our results show that S1P potently inhibits keratinocyte proliferation, and that this leads the inhibition of DNA synthesis. Interestingly, the prolonged activation of extracellular signal-regulated protein kinase (ERK) and the transient inactivation of Akt/protein kinase B (PKB) were also observed in concert with the inhibition of keratinocyte proliferation by S1P. To further verify the anti-proliferative action of S1P, we examined changes in cell cycle related proteins. S1P inhibited cyclin D_2 synthesis but stimulated $p21^{WAF1/CIP1}$ (p21) and $p27^{KIP1}$ (p27) synthesis; all are inhibitors of cyclin-dependent kinase. Furthermore, we found that the growth inhibition by S1P was in part abolished by pertussis toxin (PTX) treatment, but that ERK activation and Akt/PKB inhibition were not abrogated, suggesting that S1P functions both intracellularly, as a second messenger, and extracellularly, as a ligand for cell surface receptors. Insulin-like growth factor I (IGF-I) is a well established human keratinocyte mitogen and is known to stimulate Akt/PKB in various cell types. In the present study, S1P was found to inhibit the keratinocyte proliferation and Akt/PKB activation induced by IGF-I. Our results suggest that S1P may play an important role in the negative regulation of keratinocyte proliferation by inhibiting the Akt/PKB pathway.