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 NH2-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.

The protective mechanism of melatonin on carrageenan-induced paw edema generation in rats
Young Sil Min*, Kang Hee Yun, Song Hyun Ju, Jung Su Ryu, Uy Dong Sohn
Department of Pharmacology, College of Pharmacy, Chungang University

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 4 hour. The levels of nitric oxide (NO), malondialdehyde (MDA) or prostaglandin E2 (PGE2) 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-dependent manner. Melatonin treatment also decreased the levels of NO, MDA and PGE2. 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 PGE2.

Sphingosine-1-phosphate Inhibits Human Keratinocyte Proliferation via Akt/PKB Inactivation
Kim Dong-Seok*, Kim Sook-Young, Kim Kyu-Han, Park Kyoung-Chan
Research Division for Human Life Sciences, Seoul National University, Department of Dermatology, Seoul National University College of Medicine

Although sphingosine-1-phosphate (SIP) is a well-known mitogen, our results show that SIP 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 SIP. To further verify the anti-proliferative action of SIP, we examined changes in cell cycle related proteins. SIP inhibited cyclin D1 synthesis but stimulated p21WAF1/CIP1 (p21) and p27KIP1 (p27) synthesis; all are inhibitors of cyclin-dependent kinase. Furthermore, we found that the growth inhibition by SIP was in part abolished by pertussis toxin (PTX) treatment, but that ERK activation and Akt/PKB inhibition were not abrogated, suggesting that SIP 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, SIP was found to inhibit the keratinocyte proliferation and Akt/PKB activation induced by IGF-I. Our results suggest that SIP may play an important role in the negative regulation of keratinocyte proliferation by inhibiting the Akt/PKB pathway.