

UV-B irradiation increases the synthesis of matrix metalloproteinase-1 (MMP-1) that degrades skin collagen in human skin. In this work, we investigated the photoprotective effect of decursinol angelate (DEA) extracted from *Angelica gigas* on human skin fibroblasts. DEA inhibited UVB-induced MMP-1 induction, which was confirmed by western blot and ELISA. We examined upstream signal transduction pathway and the action mechanism of DEA on UVB induction of MMP in human skin fibroblasts. UV irradiation stimulated mitogen-activated protein kinase (MAPK), extracellular signal-regulated kinase (ERK), c-Jun amino-terminal kinase (JNK), and p38. Pretreatment of DEA on human skin fibroblasts inhibited ERK, p38 and JNK phosphorylation, while DEA had no effect on reducing ROS generation. DEA inhibited the UVB-induced MMP-1 induction by regulating MAPK phosphorylation in human skin fibroblast. These results demonstrate that DEA can be used as a potent anti-aging agent.

[PC3-6] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

A new strategy for high productivity of Erythropoietin in CHO cell by introducing urea cycle enzymes

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The efficient Erythropoietin(EPO)-expression system in mammalian cells is required for massive production for therapeutic use. Ammonium ion is a major problem in the production of useful proteins by cultured animal cells and therefore it is of importance to devise a system by which a high productivity of human therapeutic recombinant protein can be maintained or enhanced under low ammonium concentration. To reduce the ammonium ion accumulated in EPO producing CHO cell(I BE), we introduced the first two enzymes of urea cycle, carbamoyl phosphate synthetase (CPS) and ornithine transcarbamoylase (OTC) into IBE using a stable transfection method. Transfectants expressing CPS and OTC were selected and confirmed by RT-PCR. IBE expressing CPSI and OTC (CO5) showed 2-2.5 times higher productivity of EPO than the parental cell, IBE. Also, CO5 had 15-25% higher cell viability and 15-20% lower ammonia concentration per cell after 96 hr culture than IBE. These results indicate that improvement of higher ammonia removal activity in CHO cell by introducing urea cycle enzymes led to enhancement of recombinant human EPO productivity with higher cell viability. Comparisons of glycosylation and bioactivity of EPO purified from IBE and CO5 is currently in progress.

[PC3-7] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

p38 mitogen-activated protein kinase (MAPK) regulates ceramide-induced apoptosis in HL-60 cells.

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Ceramide is a lipid second messenger that is involved in apoptotic cell death. In this study, we show that p38 MAPK plays an important role in the regulation of ceramide-induced apoptosis. We found that SB203580, a p38 kinase inhibitor, blocked the effects of ceramide to induce Bax translocation to mitochondria, activation of caspase-3, and DNA fragmentation. Furthermore, expression of a dominant negative form of p38 MAPK suppressed ceramide-induced Bax translocation, suggesting that p38 kinase activity is essential for Bax translocation. In contrast, LY294002, a PI3K inhibitor had little effect on Bax translocation. Expression of a dominant negative form of Akt, a downstream effector of PI3K, moderately promoted cell death by ceramide. These data show that both the p38 and Akt pathways are involved in ceramide-mediated apoptotic pathway, but Bax translocation is only governed by p38-mediated pathway.

Poster Presentations - Field D1. Medicinal Chemistry