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We previously reported that a synthetic naphthoquinone analog, 2,3-dichloro-5,8-dihydroxy-1,4-naphthoquinone (NA), effectively induces apoptosis in human leukemic HL-60 cells. However, the cellular mechanism by which NA induces cell death remain unclear. In this study, we show that NA induces activation of capases, release of cytochrome c and upregulation of proapoptotic Bax protein. Futhermore, NA suppressed phosphorylation of Akt and Bad, suggesting that Akt regulates NA-induced apoptosis. Expression of a dominant negative Akt enhanced NA-induced apoptosis, suggesting that naphthoquinone analog induces apoptosis through activating proapoptotic pathway and by the inactivation of antiapoptotic pathway.

[PC3-3] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Decursin derivative-004 protect renal cell damage via p38 MAPK inhibition

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Hypertrophy and the alteration of renal cell growth have been reported as early abnormality in diabetic nephropathy. However, the effects of high PKCglucose and its action mechanism in renal proximal tubular cell (PTC) have not been elucidated. High glucose condition increases diacyl glycerol (DAG) and activates protein kinase C (PKC) in renal tubular cells. The PKC activates mitogen-activated protein kinases (MAPK), such as extracellular regulated kinase (ERK) and p38 MAPK. It was reported that decursin, originally known as a PKC activator, protects kidney from high glucose condition. In this study, it was elucidated that decursin derivatives down-regulates PKC alpha and blocks activation p38 MAP kinase in renal proximal tubular cells, but they does not affect on ERK signaling. Our results demonstrate that the renal protective effect of decursin derivatives against high glucose-induced damage is mediated via the inhibition of PKC dependent p38 MAPK.

[PC3-4] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Anti-angiogenic activity of conjugated linoleic acid on the basic fibroblast growth factor-induced angiogenesis

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Conjugated linoleic acid (CLA) is a potent inhibitor of mammary carcinogenesis. Cancer cells produce various angiogenic factors which stimulate host vascular endothelial cell mitogenesis and chemotaxis for their growth and metastasis. Basic fibroblast growth factor (bFGF) is a potent angiogenic factor that is expressed in many tumors. In this study, we found that CLA decreased bFGF-induced endothelial cell proliferation and DNA synthesis in a dose-dependent manner. However, CLA did not inhibit endothelial cell migration. Furthermore, CLA showed a potent inhibitory effect on embryonic vasculogenesis and bFGF-induced angiogenesis in vivo. Collectively, these results suggest that CLA selectively inhibits the active proliferating endothelial cells induced by bFGF, which may explain its anti-carcinogenic properties in vivo.

[PC3-5] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Decusinol angelate inhibits UVB-induced MMP-1 induction via Mitogen-activated Protein Kinase Pathway in human skin fibroblasts

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