

morphological and physiological characteristics of strain PM 718 were investigated. The spore morphology, spore chain morphology and spore surface were observed by scanning electron microscope. The inhibitory activity of strain PM718 *in vivo* has been studied in mice made hyperglycemia by Streptozotocin treatment. The strain PM718 showed significant reduction of blood glucose level (more than 30%) in mice loaded with maltose.

[PC2-14] [ 10/17/2002 (Thr) 13:30 - 16:30 / Hall C ]

### Mn<sup>2+</sup> dependent ClpL ATPase in *Streptococcus pneumoniae*

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HSP100/Clp family functions as molecular chaperone and ATP dependent protease. The *Streptococcus pneumoniae* ClpL, a homologue of bacterial ClpB and yeast cytosolic HSP104, is one of major heat shock proteins but its biochemical properties are unknown. In this study, ClpL in *Streptococcus pneumoniae* was characterized using histidine tagged recombinant ClpL. When ATP hydrolysis activity was compared in the presence or absence of a variety of nucleotides or divalent ions, either ATP or Mn<sup>2+</sup> ion was found to increase significantly the rate of ATP hydrolysis. Furthermore, glutaraldehyde cross-linking and subsequent native-PAGE analysis showed that ClpL forms dimer, but in the presence of 4 mM concentration of Mn<sup>2+</sup> ion, ClpL was aggregated. Thus ClpL seems to require Mn<sup>2+</sup> ion as a cofactor for ATP hydrolysis and oligomerization *in vitro*.

## Poster Presentations – Field C3. Cell Biology

[PC3-1] [ 10/17/2002 (Thr) 13:30 - 16:30 / Hall C ]

### Vitamin K Antagonist, NQ12 Inhibits PDGF-BB-Induced MAP Kinases Activation in Rat Aortic Vascular Smooth Muscle Cells

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Several 1,4-naphthoquinone derivatives have been reported to possess many pharmacological effects such as anti-viral, anti-fungal, anti-cancer and anti-platelet activities. We have reported that 2-chloro-3-[4-(ethylcarboxy)-phenyl]-amino-1,4-naphthoquinone(NQ12) had a potent inhibitory effect on the platelet aggregation *in vitro* and thrombosis *in vivo*. However, little has been known about functional role of NQ12 on vascular smooth muscle cells (VSMCs). In this study, we examined a possible antiproliferative effect of NQ12 on rat aortic vascular smooth muscle cells (VSMCs). NQ12 (1-5  $\mu$ M) significantly inhibited the PDGF-BB-induced proliferation in a dose-dependent manner on rat aortic VSMCs. We also examined the intracellular signaling effect of NQ12 on the PDGF-BB-induced activation of mitogen-activated protein kinase (ERK1/2) by western blotting in cultured rat VSMCs. Pretreatment of rat VSMCs with NQ12 resulted in a significant inhibition of the PDGF-BB-induced ERK1/2. There was no evidence of cellular toxicity or apoptosis of NQ12 (5 $\mu$ M) as determined by trypan blue exclusion assay, flow cytometric analysis and DNA fragmentation assay. These results suggest that the antiproliferative effects of NQ12 may be exerted by the inhibition of the PDGF-BB-induced ERK1/2, which can contribute to prevent atherosclerosis by inhibiting VSMCs proliferation.

[PC3-2] [ 10/17/2002 (Thr) 13:30 - 16:30 / Hall C ]

### Involvement of Akt in naphthoquinone analog-induced apoptosis in HL-60 cells

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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 caspases, release of cytochrome c and upregulation of proapoptotic Bax protein. Furthermore, 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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