γ antagonist, GW9662, rendered PC12 cells sensitized to SIN-1. The above findings suggest possible involvement of COX-2 induction and PG synthesis in regulating nitrosative PC12 cell death. PGE_2 may mediate apoptosis induced by peroxynitrite in PC12 cells. On the other hand, 15d-PGJ_2 may act as a negative feedback mediator of COX-2 signaling cascades.

[PC1-36] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Autotaxin-induced tumor cell motility requires the activation of Rac/Cdc42, PAK, and FAK

Jung In Duk°, Lee Jangsoon, Yun Seong Young, Park Chang Gyo, Lee Hoi Young

Department of Pharmacology, College of Medicine, Konyang University

Cell motility plays important physiological roles in embryogenesis, immune defense, wound healing, and metastasis of tumor cells. Cell motility of normal cells is tightly regulated, while tumor cell motility is aberrantly regulated or autoregulated. Autotaxin (ATX) is a 125-kDa glycoprotein, originally isolated from the conditioned medium of human melanoma A2058 cells. ATX stimulates random (chemokinetic) and directed (chemotactic) motility of human tumor cells at high picomolar to low nanomolar concentrations. Recently, ATX has been shown to augment invasive and metastatic potential of ras-transformed cells. In MatrigelTM invasive assays, NIH3T3 cells with full length ATX cDNA demonstrated greater spontaneous and ATX-stimulated invasion than control. In addition, in vivo study showed that combination of ATX expression with ras transformation amplified tumorigenesis and metastatic potential compared to ras-transformed control, suggesting that ATX augments cellular characteristics necessary for tumor aggressiveness. In the present study, we investigated the intracellular signaling pathway of ATX. Unlike N19Rho expressing cells, the cells expressing N17Cdc42 or N17Rac1 showed reduced motility against ATX. In addition, ATX increased PAK activity and phosphorylated focal adhesion kinase. Since FAK in cells expressing N17Rac1 or N17Cdc42 was not phosphorylated by ATX, FAK appears to be located downstream of Cdc42/Rac1. Collectively, these data indicate that Cdc42, Rac1, and FAK are involved in ATX-induced tumor cell motility in human melanoma cells.

[PC1-37] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Involvement of G1 arrest and caspase-3 activation in apoptosis induced by bovine lactoferricin

1 Yoo Yung-Choon°, 2 Lee Kyung-Bok

1 Department of Microbiology, 2 Department of Biochemistry, College of Medicine, Konyang University

We investigated the effect of bovine lactoferricin (Lfcin-B) on cell cycle regulation and caspase activation in tumor cells. Treatment with Lfcin-B resulted in the production of intracellular reactive oxygen species (ROS) during apoptosis of THP-1 cells. Biochemical analysis revealed that Lfcin-B-induced apoptosis, the cell cycle arrest and caspase activation were completely abrogated by addition of an antioxidant such as N-acetylcysteine (NAC). In cell cycle analysis using the bromodeoxyuridine (BrdU) labeling method, it was shown that Lfcin-B blocked the progression of the cell cycle to S phase (G1 arrest) in THP-1 cells undergoing apoptosis. In coincidence with G1 arrest, the results of western blot analysis showed that treatment with Lfcin-B prominently decreased the expression of Cyclin D2, CDK2, CDK4 and Cyclin E molecules responsible for progression to S phase. In addition, treatment with Lfcin-B enhanced the intracellular activity of caspase-3 and ?8 in the early period of apoptosis. When we investigated the correlation of ROS production, G1 arrest and caspase-3 activation in apoptosis induced by Lfcin-B, it was revealed that ROS regulated G1 arrest and caspase activation at a point of up-stream of the apoptosis cascade.

[PC1-38] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Retrovirus-mediated Delivery of TIMP-2 Inhibits Migration, Invasion and Angiogenesis

Ahn Seong-Min°, Sohn Yeowon[1], Kim Yun-Soo[2], Moon Aree

College of Pharmacy, Duksung Women's University, Seoul 132-714, Korea, [1]KFDA, [2]KRIBB