apoptosis is prevented by expressing the dominant negative SEK1 mutant. In contrast, the later phase of activation and apoptosis are equally prevented by expressing p21D112N, an uncleavable version of p21\textsuperscript{WAF1/CIP1}. Thus, the two-tiered activation of JNK1 is conducted by different mechanisms in a stage-specific manner during apoptosis. We also show that the stable expression of JNK1 suppresses apoptosis, while the dominant negative JNK1 mutant (DN-JNK1) promotes it. In contrast, the transient expression of DN-JNK1 or JBD, a JNK inhibitor suppresses apoptosis. Thus, the early phase of JNK1 activation prolongs cell survival during apoptosis, while the later phase of activation is required for the induction of apoptosis.

[PC3-6] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

**Activation Of p21-Activated Kinase1 Is Required For Autotaxin-Induced Focal Adhesion Kinase Phosphorylation and Cell Motility in A2058 cells**

**Jung In Duk**, Lee Jangsoon, Yun Seong Young, Park Jun Hong, Park Chang Gyo, Lee Hoi Young  
College of Medicine, Konyang University

Autotaxin (ATX) is a 125-kDa glycoprotein and a strong motogen that can increase invasiveness and angiogenesis, originally isolated from the conditioned medium of human melanoma A2058 cells. And it is a strong. Recently, we suggested that ATX promotes motility via G protein-coupled PI3K, and Cdc42/Rac1 are essential for ATX-induced tumor cell motility in A2058 melanoma cells. In the present study, we found that activation of p21-activated kinase 1 (PAK1) was required for ATX-induced cell motility. ATX activated PAK1 that was blocked by PTX, LY294002, and Genistein, but not by U73122, PD98059, and Y27632. ATX could not activate PAK1 in N17Rac1- or N17Cdc42-transfected cells (dominant negative mutants of Rac1and Cdc42, respectively), and PI3K K832R-transfected cell (catalytically inactive mutant of phosphoinositide 3-kinase (PI3K)). Transfection of PAK1 mutant (PAK1 K299R) inhibited the phosphorylation of focal adhesion kinase (FAK) and ATX-induced cell motility. These findings strongly indicate that PAK1 is located downstream of Gi, PI3K, Rac1, Cdc42, and plays a critical role in ATX-induced A2058 cell motility.

[PC3-7] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

**Allicin-induced apoptosis of gastric epithelial cells is associated with changes of caspase-independent effector and involvement of PKA**

**Baeg HyeKyoung**, Rhee Dong-Kwon, Pho Suhkneung  
Sungkunkwan University, College of Pharmacy

Garlic (Allium sativum) has been used as a general food and a remedy in Oriental for a long time. Since garlic compounds have been shown to inhibit growth of tumors and to modulate the activity of carcinogenesis, the effects of allicin on growth and survival in human gastric epithelial cells were evaluated by cell viability, cell cycle analysis and DNA fragmentation. Protein levels of cytochrome C, Bcl-xL, Bax and AIF were detected by Western blotting. Effects of recombinant VacA on caspase proteases activity were also determined. Allicin inhibited cell growth and induced apoptosis in gastric epithelial cells. Treatment resulted in DNA fragmentation and cell cycle analysis revealed subdiploid cells. Allicin also mediated a prolongation of the cell cycle progression in G2 phase. Allicin increased the expression of Bcl-xL, Bax and cytochrome C in gastric epithelial cells. However, cell death was observed with pancaspase inhibitor (Z-VA-D-FMK) and the absence of immunoreactivity for caspase-cleaved poly-ADP-ribose polymerase (PARP) was not shown. In addition, the level of AIF, caspase-independent effector, was increased. Apoptosis of gastric epithelial cells by allicin was partially suppressed by a specific protein kinase A (PKA) inhibitor. Taken together, the data suggest that allicin induces caspase-independent apoptosis and apoptotic effects of allicin is mediated through the activation of PKA.

[PC3-8] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

**Inducing effect of helenalin on the differentiation of HL-60 leukemia cells**