related genes in AML-2/DX100, a doxorubicin-resistant human acute myelocytic leukemia cell line. AML-2/DX100 cells showed 24-fold greater resistance to the doxorubicin-induced cytotoxic effect than AML-2/WT, the doxorubicin-sensitive parent cells. Total RNA was extracted from both AML-2/DX100 and AML-2/WT cells, and hybridized to the microarray gene chips containing 9217 human genes. Forty nine genes including thrombospondin 2 gene and immunoglobulin superfamily member 1 gene were identified, which were over- or down-expressed at least 3-fold change in AML-2/DX100 cells compared with in AML-2/WT cells. The expression level of representative genes was verified by Northern blot analysis. Most of differentially expressed genes in AML-2/DX100 cells were involved in escape out of immune responses or progression of cell cycle. Our studies demonstrate a signature profile of doxorubicin-resistance related gene expression in cancer cells using DNA microarray analysis. The identification of genes associated with anticancer drug resistance may give further insights into the drug resistance mechanisms and suggest alternative chemotherapy.

**[PC3-11] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]**

## Panaxadiol Arrests Cell Cycle by Elevating $p21^{WAF1/CIP1}$

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We show that panaxadiol (PD), a ginseng saponin with a dammarane skeleton, selectively interferes with the cell cycle in human cancer cell lines. PD inhibited DNA synthesis in a dose-dependent manner with $IC_{50}$ values ranging from 0.8 μM-1.2 μM in SK-HEP-1 cells and HeLa cells. PD-treated cells were arrested at G1/S phase, which coincided well with decreases in Cyclin A-Cdk2 activity, but not in Cyclin E-Cdk2 and Cdc2 activities. The intracellular levels of $p21^{WAF1/CIP1}$ were significantly and selectively elevated in a dose- and time-dependent manners in PD-treated HeLa cells. Similarly, levels of the $p21^{WAF1/CIP1}$ protein that is associated with the Cyclin A–Cdk2 complex increased, and these increases correlated well with the down-regulation of Cyclin A-Cdk2 activity. Thus, PD selectively elevates $p21^{WAF1/CIP1}$ levels and thereby arrests the cell cycle at G1/S phase by down-regulating Cyclin A-Cdk2 activity.

**[PC3-12] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]**

## Screening and Characterization of Novel Akt/PKB inhibitors, SWU5 and SWU9

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Akt/Ptotein Kinase B (PKB) is a serine/threonine kinase and activated by PI3K pathway. Akt/PKB regulates a variety of cellular responses including proliferations, differentiations and insulin signaling pathway. Recent evidence also indicates that the abnormal activities or expression of Akt/PKB is closely associated with cancer, diabetes and neuro-degenerative diseases. These findings mean that Akt/PKB is likely to be a new therapeutic target for the treatment of disease.We tested many compounds from various sources and screened a series of SWU compounds regulating Akt/PKB kinase activities. 2-[ 5-( 2–Oxo-1,2–diphenyl– ethylsulfanyl )–2–thioxo-[ 1,3 ] dithiol–4–ylsulfanyl ]-1,2–diphenyl–ethanone(SWU5) and 2-Thioxo-[ 1,3 ] dithiolo [ 4,5-β ][ 1,4 ] dithiine-5,6-dicarboxylic acid dimethyl ester(SWU9) of SWU compounds inhibited in vitro Akt/PKB kinase activities and cell growth at micromolar range of concentration. We further investigated whether these compounds inhibit cellular Akt /PKB activity and induce apoptotic cell death.

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

## Retroviral Delivery of TIMP-2 Inhibits H-ras-induced Migration and Invasion in

## MCF10A Human Breast Epithelial Cells

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The matrix metalloproteases (MMPs) play important roles in invasion, metastasis and angiogenesis in various cell types. Tissue inhibitor of metalloprotease (TIMP)-2, an endogenopus inhibitor of MMP-2, has been shown to inhibit invasion and metastasis. We have previously shown that MMP-2 is responsible for the H-ras-induced invasive and migrative phenotypes in MCF10A human breast epithelial cells. Here, we investigated the effect of TIMP-2 overexpression on invasion and migration in H-ras MCF10A cells. Human TIMP-2 gene was effectively introduced into H-ras MCF10A cells by retrovirus-mediated gene delivery. TIMP-2 overexpression mediated by retrovirus significantly inhibited invasiveness and migration of H-ras MCF10A cells in a dose-dependent manner. We also show the antiangiogenic effect of TIMP-2 gene delivery. Taken together, our study shows that retrovirus-mediated delivery of TIMP-2 efficiently inhibits metastatic progression of ras-trnasformed human breast epithelial cells, suggesting a potential use of the TIMP-2 gene therapy for the treatment of breast cancer.
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**[PC3-14] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]**

## Novel Cell-based Protease Assay System for Molecular Cell Biology and Drug Discovery

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Recently development of cell-based assay systems which are useful in molecular cell biology and drug discovery attracts significant attention. Here, we introduce a new technologies for monitoring enzyme activity and its inhibition inside living cells. Among various enzymes, proteases are important targets for studying various biological and disease-related processes such as viral infections, apoptosis and Alzheimer's disease. In this study, a sensitive cell-based protease detection system that enables direct fluorescence detection of a target protease and its inhibition inside living cells is introduced. The CellPA$^{TM}$ system provides a fluorescent molecular beacon protein comprising an intracellular translocation signal sequence(s), a protease-specific cleavage sequence(s) and a fluorescent marker sequence(s). The molecular beacon protein is designed to change its intracellular translocation upon cleavage by a target protease, e.g., from cytosol to a subcellular organelle, or from a subcellular organelle to cytosol or another subcellular organelle. Details of the mechanism and level of the protease action can be monitored at a single cell level, and accordingly the cell population in terms of the level of the protease activity can be accurately enumerated. The clear change in the fluorescence image of the cell makes the CellPA$^{TM}$ system as an ideal tool for various life science and drug discovery researches including the HTS&HCS applications. Various formats of the CellPA$^{TM}$ system for monitoring HCV NS3 protease, caspase-3, caspase-8, β-secretase etc. will be presented.

**[PC3-15] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]**

## Erythropoietin increases neuronal cell differentiation : association of transcriptional factors AP-1 and NF-κB activation

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Erythropietin (EPO), a hematopoietic factor is also required for normal brain development, and its receptor is localized in brain. Therefore, it is possible that EPO could act as a neurotropic factor inducing differentiation of neurons. The present study, we therefore investigated whether EPO can increase differentiation of undifferentiated cortical neuron isolated from postneonatal (Day 1) rat brains and PC12 cell, undifferentiated dopaminagic cell line. EPO dose (1-100 U/ml) dependently increased cell differentiation and expression of differentiation marker gene (neurofilament and tyrosine hydroxylase) in both cells. Since our previous study (Jung et al., 2003, Mol.