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