

processes. The purpose of the present study is to elicit molecular mechanism of tetrandrine induced apoptosis in HepG2 cells. Treatment of the cells with tetrandrine resulted in the activation of caspase 3 and subsequent cleavage of PARP at a concentration of 30 μ M. It was blocked completely by the pretreatment of IETD-fmk, a specific inhibitor for caspase 8. Tetrandrine also induced caspase 8 activation. Active caspase 8 transduces apoptotic signal to mitochondria via Bid, which is located in the cytosol and translocates to the mitochondria in a truncated form (tBid) upon caspase 8 activation. By the treatment of the cells with tetrandrine expression of the full length Bid was decreased, which was also inhibited by IETD-fmk. Subsequently we observed the cytochrome c release and the decrease in the mitochondrial transmembrane potential. These results suggest that apoptosis of HepG2 cells by tetrandrine proceeds via caspase 8 induced activation of Bid which affects the mitochondrial transmembrane potential and the release of cytochrome c.

[PA3-3] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

An Anti-cancer Drug, Paclitaxel, Induces Apoptosis in MCF-7 Human Breast Cancer Cells by Generating Ceramide and Arachidonic Acid

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Accumulation of ceramide mass in MCF-7 cells by the anti-cancer agent, paclitaxel, was found to occur primarily due to activation of the de novo synthesis pathway. Moreover, the addition of paclitaxel resulted in the accumulation of ceramide, which was followed by a prolonged arachidonic acid release. Participation of ceramide de novo pathway in arachidonate signaling was detected since L-cycloserine, an inhibitor of de novo synthesis, was able to inhibit the paclitaxel-induced AA release and cytotoxicity. This suggests that the production of ceramide in response to paclitaxel appears to be related with in arachidonic acid release, probably cytotoxicity. Enzymatic assays revealed that serine palmitoyltransferase, the rate-limiting enzyme in ceramide de novo pathway, was activated 1.2-fold by paclitaxel treatment. An inhibitor of glucosylceramide synthesis, 1-phenyl-2-dacanylamino-3-morpholino-1-propanol, accumulated ceramide production and increased cytotoxicity when used in combination with paclitaxel. This data suggests that activation of serine palmitoyltransferase is responsible for increased ceramide production during de novo synthesis initiated by paclitaxel and de novo synthesis may serve a specific role in arachidonic acid release.

[PA3-4] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Effects of ascorbic acid according to administration doses on radiation induced DNA damage in mouse splenic and blood lymphocytes

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Ascorbic acid is very well known as one of various antioxidants and is used very popular in man. Melatonin, an endogenous compound secreted by the pineal gland in human brain has been reported to act as an antioxidant nowadays. The present study was performed to obtain the differences of the radioprotective function of ascorbic acid and combination with melatonin according to the administration dose a day on radiation induced DNA damage in mouse spleen and blood. Six-week-old ICR male mice were irradiated with 8.0 Gy of γ -ray five days after oral administration of ascorbic acid (low dose: 400mg/kg, high dose: 2000mg/kg) and plus melatonin (250mg/kg) and were sacrificed 3 days later. Spleens and blood were taken and then isolated lymphocytes. The tail moment of DNA single-strand breaks in mouse splenic and blood lymphocytes was evaluated by the Comet