vivo has been hampered by the decrease in transfection efficiency mediated by non-specific electrostatic interactions with serum components. In order to avoid these problems, we designed a polyplex with decreased positive charge on the complex surface. To this end we prepared PEI/DNA complex coated with anionic biodegradable polymer, alginate, and compared their gene delivery behavior with PEI/DNA. The 0.01% alginate-coated PEI/DNA polyplex showed about 50-100 fold increased transfection efficiency compared to non-coated complexes in the presence of 50% serum. The surface charge of the alginate-coated complex was approximately half that of the alginate-lacking complex. The size of alginate-coated complex was slightly smaller than that of the complex without alginate. The former complex also showed reduced erythrocyte aggregation and decreased cytotoxicities to target cells in comparison with PEI/DNA complex. In conclusion, the alginate-coated PEI/DNA polyplexes could enhance the transfection efficiency by reducing non-specific binding with serum component and by decreasing the cytotoxicity.

Poster Presentations - Field A3. Hygienics

[PA3-1] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Antiplatelet Activity of NQ12 May Be Mediated by Inhibition of Cyclooxygenase and Generation of 12-HETE

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In the previous study, we reported that NQ12, a vitamin K antagonist, showed a potent antithrombotic and antiplatelet activities.
In order to elucidate the antiplatelet activity of NQ12, we investigated the effect of NQ12 on arachidonic acid cascade parameters such as cPLA2, cyclooxygenase (COX), and the downstream production such as TxA2, PGD2 and 12-HETE. NQ12 inhibited COX activity in a concentration-dependent manner in U937 cells. NQ12 showed a concentration-dependent inhibitory effects on washed rabbit platelets aggregation induced by collagen and arachidonic acid. NQ12 slightly inhibited arachidonic acid-induced thromboxane B2 generation and also suppressed 12-HETE generation concentration-dependently in rabbit platelets. NQ12, however, did not affect cPLA2 activity at the concentration which inhibited TxB2 formation in stimulated platelets. In conclusion, these results suggest that the antiplatelet mechanism of NQ12 may be resulted from inhibition of cyclooxygenase activity and the generation of 12-HETE.

[PA3-2] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Tetrandrine induces mitochondria-dependent apoptosis in HepG2 cells

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Tetrandrine is a bis-benzyl isoquinoline alkaloid derived from the root of Stephania tetrandra S. Moore, which was reported to elicit in vitro cytotoxic effect on HeLa cells and in vivo supprresive effects on mouse ascite tumor. Tetrandrine also induced apoptosis in a various cell lines. Recent studies have revealed that mitochondria has been shown to play an important role in the regulation of apoptotic

processes. The purpose of the present study is to elicit molecular mechanism of tetrandrien 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 uM. 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 tranduces 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 activaiton. By the treatment of the cells with tetrandrine expression of the full length Bid was decreased, which was also inhibited by IETD-fmk. Subsequntly 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. Morever, 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 suggest 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-dacanoylamino-3-morpholino-1-propanol, accumulated ceramide production and increased cytotoxicity when used in combination with paclitaxel. This data suggest 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 ntioxidants 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