metastasis

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The antimetastatic effect of BCG-CWS, which was emulsified in an oil-in-water form with either Drakeol 6VR mineral oil (BCG-CWS/DK) or squalane (BCG-CWS/SQA), on lung metastasis produced by highly metastatic murine tumor cells, Colon26-M3.1 carcinoma cells and B16-BL6 melanoma cells, was investigated in syngeneic mice. An intravenous administration of BCG-CWS (100 mg/mouse) 1 day after tumor inoculation significantly inhibited tumor metastasis of both Colon26-M3.1 carcinoma and B16-BL6 melanoma cells in experimental lung metastasis models. BCG-CWS/SQA administered through subcutaneous route was shown to be effective only when it was consecutively injected (3 times) after tumor inoculation. A single i.v. administration of BCG-CWS/SQA inhibited the number of tumor-induced blood vessels and suppressed tumor growth. Furthermore, the multiple administration of BCG-CWS/SQA given at on week intervals led to a significant reduction in spontaneous lung metastasis of B16-BL6 melanoma cells in a spontaneous metastasis model. These results suggest that BCG-CWS emulsified with squalane is a potent inhibitory agent of lung metastasis through the suppression of tumor growth and the inhibition of tumor-induced angiogenesis.

[PA2-4] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

non-viral gene delivery mediated by chitosan and PEI : developement of a gene carrier with serum stability and reduced cytotoxicity

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The purpose of this study was to develop PEI-based gene carriers with optimal serum stability and reduced cytotoxicity. PEI is an efficient gene transfer agent with the ability of DNA condensation and endosome escape; however, use of the polymer in vivo is hampered by signigicant reduction in transfection activity by the presence of serum. Chitosan is a non-toxic, biodegradable and biocompatible polymer with hydrophilic functional groups so it may provide a physical stability against challenge by serum proteins. To prepare a PEI-based polyplex formulation with increased serum stability we added chitosan to PEI/DNA complex. In this report, we show that the level of gene expression mediated by PEI/DNA complex can be significantly improved by the addition of chitosan in the presence of high serum concentration. In addition, cells transfected with DNA/PEI/chitosan complex remained 70~80% viable whereas the viability of PEI-treated cells ranged at 50~60%. The chitosan-modified DNA/PEI complex may provide an improved use for in-vivo gene delivery.

[PA2-5] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Examination of alginate/PEI/DNA polyplex as a gene delivery system: enhancing transfection efficiency in the presence of serum and reducing cytotoxicity

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Synthetic vectors have been considered as a safer and more versatile alternative to viral-based gene delivery systems. A variety of simple synthetic vector systems such as cationic lipid- and polymer-complexed plasmid DNA were shown to have a significant transfection activity in vitro but their use in

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