efficiency was achieved by treatment of a lysosomotropic agent, chloroquine. Compared with unmodified PLL, PLL-g-pluronic showed about 2-fold increase in transfection efficiency and lower cytotoxicity specifically at a 1:1 weigh ratio of polymer:DNA. In vivo gene expression experiment using this new polymer is under going.

[PE1-6] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Preparation and evaluation of polymeric nanoparticles composed of poly(L-Latic acid) and dextran

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In this study, we synthesized a new amphiphilic polymers composed of poly(L-Latic acid) (PLA) and dextran. PLA is one of the poly(a-hydroxy esters) with bioerodible characteristics, and it degrades into naturally occurring substances. We expected PLA to have more hydrophobic properties than polysaccharide dextran. Dextrans are colloidal, hydrophilic and water-soluble substances, inert in biological systems and do not affect cell viability. Dextrans can be degraded by the dextranase which was found to be present in the colon. Biodegradable core-shell structure nanoparticles were prepared from PLA and dextran by activation with carbonyldiimidazole. The physicochemical characteristics were evaluated by fluorescence spectroscopy, transmissiton electron microscope, x-ray diffractometry, and photon correlation spectroscopy. Indomethacin (IN) was loaded as a model drug, and IN release behaviors were observed in vitro.

[PE1-7] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Transferrin-Conjugated Cationic Liposome for In Vitro and In Vivo Gene Transfer

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Transferrin-conjugated cationic liposome (Tf-liposome) was developed as a targeted gene delivery system by using heterobifunctional cross-linking agent, SPDP, and gradient metrizamide ultracentrifugation method. Physico-chemical properties of Tf-liposome were determined by scanning/transmission electron microscopy (SEM/TEM) and dynamic laser-light scattering method (DLS) with the mean diameter being 584±15nm. Gel retardation assay was performed using various DDAB:DNA ratios and proved the 6:1 weight ratio formulation being the most compact with a slight positive zeta-potential. In vitro transfection was done in human cervical cancer cell line, HeLa, and the transfection efficiency of Tf-liposome was found to be 5-fold higher than that of un-conjugated (plain) DDAB liposome and 2-fold higher than that of Lipofectin™.
Interleukin 12 (IL-12) has a pivotal role in controlling cell-mediated immunity through a number of important biological activities, such as secretion of interferon-γ(INF-γ), and systemic administration of IL-12 can inhibit the growth of both established s.c. tumors and experimental metastasis. We inoculated C-26, murine colon carcinoma cells into Balb/c mice subcutaneously. When tumor volumn reached 100mm3 (~ 4 days after tumor inoculation), mice were injected intravenously with IL-12 plasmid/Tf-liposome complexes twice a week for 3 weeks. As a result, significant suppression of tumor growth was achieved by the Tf-liposome/DNA treatment. IL-12 plasmid 10μg/Tf-liposome complex had superior suppression effect among tested and this effect was similar to the same amount of Lipofectin™/DNA complex. Results from different therapy regimen will also be presented.
In conclusion, a target-oriented gene delivery system of transferrin-conjugated cationic liposome (Tf-liposome) was made successfully and proved to be very efficient in DNA delivery both in vitro and in vivo.