[PE3-3] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Topical delivery of smad3 antisense using cationic solid lipid nanoparticle(SLN): therapeutic potential use and prevention of keloids

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Keloids are characterized by abnormal proliferation of fibroblasts and overproduction of collagen. Recently, it is reported that transforming growth factor beta (TGFb) and its signaling molecule, SMAD3 are related to the mitogenic effect of fibroblasts and a stimulatory factor for collagen synthesis. Cationic SLN was developed to improve the complex formation of DNA/SLN and enhance the uptake efficiency to cells. SLN was formulated by DC-Chol, DOPE, trimyristin as a solid core and other surfactant. The physical properties of the SLN and the ATS/SLN complex were characterized. We have assessed the in vitro effects of smad3 antisense (ATS) on proliferation, collagen synthesis in keloid fibroblast and used cationic SLN for dermal carrier. After cells were transfected with ATS/SLN complex, uptake efficiency and pattern of the complex were evaluated using flow cytometry and confocal microscope. The inhibitory effects of ATS on keloid fibroblast proliferation were analyzed using growth inhibition assay and western blotting. The average size and zeta potential of SLN were 80.0 ± 6.53 nm and 42.1 ± 1.18 mV respectively. The SLN showed a stable distribution of size and zeta potential up to two months at least. The complex size of ATS/SLN increased to 200-300 nm. ATS inhibited keloid fibroblast proliferation and decreased collagen formation. Blocking SMAD3 activity with smad3 ATS led to growth inhibition of keloid fibroblast. From the results, it is suggested that SMAD-dependant TGFb signaling pathway involves in the regulation of keloid fibroblast proliferation. Smad3 ATS using stable cationic SLN may provide a novel approach in treatment and prevention of keloid.

[PE3-4] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Sialoglycoconjugate-specific lectin from Maackia fauriei

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A lectin has been purified from the bark of the legume Maackia fauriei. This lectin, MFA, was found to agglutinate human ABO erythrocytes at a titer of 256. The results from electrophoretic analyses, gel-filtration chromatography, and enzyme linked lectinsorbent assay indicate that MFA is an acidic glycoprotein, and exists as a tetramer of 30 kDa subunits that are linked by noncovalent bonds. The activity of MFA is critically dependent upon $CaCl_2$. MFA demonstrated high homogeneity with the lectins from M. amurensis, which is the only legume source of lectins that bind to sialoglycoconjugate, in its N-terminal amino acid sequence and amino acid composition, The hemagglutination activity of MFA was specifically inhibited by N-acetylneuraminic acid, Neu5Acα2-3Galβ1-4GlcNAc, and sialoglycoconjugates such as fetuin, bovine submaxillary mucin and thyroglobulin. MFA exerts cytotoxic effects on human breast cancer, human melanoma, and human liver cancer cell lines but had no effect on the human colorectal cancer cell line. It is especially noteworthy that the deleterious effect of MFA on the viability of human breast cancer cell was greater than that of other sialic acid-binding lectins.

[PE3-5] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Galactosylated PEI-PEG as nonviral gene transfer agent for hepatocyte targeting and imaging probe

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Objectives: Galatosylated PEI was synthesized and characterized for gene delivery to hepatocytes. It was modified by conjugating with hydrophilic PEG to improve in vivo circulation. And we studied the possibility as an imaging modality for monitoring of gene delivery using gal-PEI derivatives. Methods: The substitution values of galactose in PEI were calculated by resorcinol/sulfuric acid method and quantity of PEG was calculated by comparing NMR peak. Cytotoxicity was determined by MTT. Galactosylated PEI-PEG derivatives were labeled with ^{99m}Tc using stannous chloride and then determined there labeling efficiencies using ITLC. After injection via vein with ^{99m}Tc Gal-PEI derivatives, images were acquired with a gamma camera. Size and zeta potential of DNA complex was measured and transfection experiments were performed on HepG2 and Hela cells. Results: The substitution value of LA was estimated by 1.2 mol%. The compositions of PEGs in Gal-PEI were confirmed to be 4.1 and 7.6 mol% (10%, 50%). The MTT assay showed that cytotoxicity of Gal-PEI was decreased with increasing the degree of PEG substitution. The labeling efficiencies were shown all above >90% until 1 h. The rabbit images showed that with increasing degree of PEG grafting, non-specific interactions with plasma components and lung endothelium were reduced. Size of complex was found to increase with increasing PEGylation (65.05 nm for 0%, 194 nm for 4.1%, and 296.75 nm for 7.6%). Zeta potential decreased in inverse proportion to degree of PEG substitution (19.81, 15.27, and 5.75 mV). As transfection with ^{99m}Tc Gal-PEI-PEG 50%/DNA complexes (N/P=3.0), green fluorescent proteins were expressed just in galactose receptor positive-cell (HepG2). Conclusion: ^{99m}Tc labeled DNA complexes were efficiently entered into the cells through endocytosis in vitro and GFP gene was expressed regardless of ^{99m}Tc. These results suggest that Galactosylated PEI-PEG derivatives can be used hepatocyte targeting agent and imaging modality.

[PE3-6] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Chitosan-Iron casein succinylate nanoparticles as oral delivery systems : increasing the stability and enhancing the absorption of iron nanoparticles.

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The objective of the study was to develop an oral delivery system to increase the stability and efficacy of iron casein succinylate. Aqueous nanoparticles were prepared using complex coacervation of the oppositely charged chitosan and iron casein succinylate with polyethyleneglycol (PEG). The physicochemical properties of nanoparticles were investigated using dynamic light scattering, zeta potential and scanning electron microscopy. Chitosan-iron casein succinylate interactions were investigated in solid state by differential scanning calorimetry (DSC) and FT-IR spectrometry. The mucoadhesive properties of nanoparticles were evaluated by studying the interaction between mucin and nanoparticles in aqueous solution. Iron release kinetics were investigated in vitro in the simulated gastric fluid (pH 1.2, 2 hr) and intestinal fluid (pH 6.8, 4 hr). An in vitro digestion/Caco-2 cell culture model was used to compare iron transport from ferrous gluconate, two kinds of organic iron (sodium ferric gluconate complex, iron-hydroxide polymaltose complex), iron casein succinylate and chitosan-iron casein succinylate nanoparticles. The nanoparticles of chitosan and iron casein succinylate mixed in a weight rate of 3:2, 1:1, 2:1 and 4:3 were stable for 5 weeks. The nanoparticles carried a positive charge from 48 to 61 mV and showed the size in the range from 600 to 850 nm. DSC and FT-IR showed that the covalent bond of chitosan and iron casein succinylate did not change. A strong interaction between nanoparticles and mucin was detected from mucoadhesive study. The amount of iron released at 6 hr was more than 60%. The nanoparticles were stable physically and chemically at 4℃ for 5 weeks without preservatives. The permeability of iron was increased 25~50-fold (chitosan:iron casein succinylate=3:2, 1:1, 2:1 and 4:3) compared with iron casein succinylate solution. The chitosan-iron casein succinylate nanoparticles could increase the stability and enhance the absorption of iron.

[PF1-1] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Analysis of β-blockers Use in Chronic Heart Failure

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