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Among the promising cancer therapy is targeting of the drug to tumor cells via receptor specific ligands. CR2945, β-[2-([2-(8-azaspiro[4.5] dec-8-ylcarbonyl)-4,6-dimethylphenyl]amino-2-oxoethyl]-(R)-1-naphthalenepropanoic acid, is known to have an inhibitory effect on a gastrin receptor of colorectal cancer cells. As the human pancreatic cancer cells (BxPC-3) express gastrin receptors, interruption of binding of gastrin with gastrin receptor of human pancreatic cancer cells by CR2945 inhibits the growth of human pancreatic cancer cells. The purpose of this study is to synergistically inhibit the growth of pancreatic cancer cells by CR2945-conjugated liposome encapsulating anticancer DNA. Conjugation of CR2945 with phospholipid(DSPE) was performed by the reaction of a carboxyl group in CR2945 with an amine group introduced into DSPE. The structural analysis of DSPE-CR2945 was carried out using FT-IR, 1H-NMR, and UV spectroscopy. The IR spectra of DSPE-CR2945 with peptide bond exhibit the characteristic bond of primary amine group at 3223cm^{-1}. The 1H-NMR spectrum of the same modified polymers shows peak at δ=8.830 which can be assigned to protons of the peptide bond. Naphthalene group of DSPE-CR2945 appears at δ=7.437~δ=7.297. The results of IR spectra and 1H-NMR spectrum show that a carboxyl group in CR2945 conjugated to an amine group in DSPE. CR2945 seems to target human pancreatic cancer cells and results from in vitro growth inhibitory study will also be presented.

[PE1-24] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Characterization of the rhGH released from rhGH-loaded PLGA microspheres

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The in vitro release of rhGH from PLGA microspheres was characterized. rhGH-loaded PLGA microspheres were prepared with 50:50 poly(D,L-lactide-co-glycolide) (PLGA) polymers using a double emulsion process. To simulate rhGH release under physiological conditions, the microspheres were suspended in a physiological buffer at 37℃. Quantification of the rhGH released and its molecular form analysis were carried out using SE-HPLC. Approximately 15% of the encapsulated rhGH was released within the first day, with a continuous release occurring during the following days. 95.1% of rhGH released during the first day was in the monomeric form. The monomer ratios at day 5 and day 8 were 99.4% and 98.6% respectively. At day 11 and day 14, rhGH was observed exclusively in the monomeric form. And rhGH released from microspheres was verified to be essentially in the biologically active form.
The results suggest that dimers and aggregates formed during the manufacturing process were located mostly at the surface of the microspheres and released during the early stage of release. In contrast, the rhGH in the interior of the microspheres is hypothesized to be mainly in the monomeric form, resulting in an increased monomer ratio during the mid- and late phase release.

[PE1-25] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Effects of Sustained-Release Formulation of Recombinant Human Growth Hormone on Body weight, Bone growth and Organs in Hypophysectomized Rats

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The rhGH-loaded PLGA microsphere formulation was prepared using a double emulsion process from hydrophilic 50:50 poly(D,L-lactide-co-glycolide) (PLGA) polymers. To investigate the sustained efficacy of this formulation, its pharmacodynamic characteristics were analyzed. It showed particle size of ca 53.1μm with high drug incorporation efficiency and it was subcutaneously administrated to hypophysectomized rats and whole body growth responses of this formulation were compared to those of the different dosing patterns of rhGH. Statistically significant increases were noted in body weight, growth plate(bone growth) and thymus size without affecting the size of other organs after 7 days at which formation of antibodies to rhGH was observed. These studies suggested that rhGH delivered continuously via these formulations showed the same efficacy on increasing body weight and bone growth as rhGH delivered via twice daily injection or osmotic minipump in