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It is desirable to improve the tumor targeting and blood clearance pharmacokinetics of radiolabeled monoclonal antibodies. To achieve this goal, several avidin-biotin (Bt) binding systems have been developed to decouple large molecular weight antibodies from small radiolabels, thereby achieving high tumor-to-background radioactivity ratios. We inserted a readily catabolizable linker, triglycine (TG), between 3-[^{125}I]iodobenzoate and dendrimer (G3). We also neutralized the positive charges of G3 by acylation with tetrafluorophenyl glycolate, thereby blocking proximal tubular reabsorption of G3 mediated by charge attraction. [^{125}I]MIB-TG-G3-norBt rapidly cleared from the blood (0.95% ID/g) and highly accumulated in the liver (13.2% ID/g), kidney (132.4% ID/g), and spleen (6.4% ID/g) at 0.33 hr. Thereafter this product was gradually decreased in the kidney (66.7% ID/g) and spleen (5.3% ID/g) at 3 hr. Similar to organ uptake, the whole body retention of [^{125}I]MIB-TG-G3-norBt gradually decreased from 69.1% ID (0.33 hr) to 42.9% ID (3 hr). In contrast, the [^{125}I]MIB-TG-(G3-Glycol)-norBt produced a significant decrease in liver (4.5% ID/g) and kidney (19.9% ID/g) uptake compared with [^{125}I]MIB-TG-G3-norBt at 0.33 hr. In addition, the whole body retention (27.1%, 14.1% and 7.1% ID at 0.33, 1 and 3 hr, respectively) was significantly lower than that of [^{125}I]MIB-TG-G3-norBt. The chemical modification by inserting a triglycine linker between G3 and MIB and neutralizing the positive charges by glycolation was effective in reducing the organ uptake and enhancing the WB clearance. This approach is worth considering for the use of At-211 labeled dendrimer-based biotin in a 3-step tumor targeting with pretargeted MoAb-strepavidin.

[PA2-3] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

A study on the evaluation of artificial cartilage using synthetic biodegradable polymers

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Tissue engineering has arisen to address the extreme shortage of tissues and organs for transplantation and repair. One of the most successful techniques has been the seeding and culturing cells on three-dimensional biodegradable scaffolds in vitro followed by implantaion in vivo. We used PLA and PLGA as biodegradable polymers and rabbit chondrocytes were isolated and applied to PLA and PLGA to make artificial cartilage. To evaluate the biocompatibility and biological safety of polymers, in vitro cytotoxicity and in vivo animal tests were investigated. PLA and PLGA showed excellent biocompatibility and no biological effects in animal. Rabbit articular chondrocytes were isolated and characterized using MTT assay, alcian blue staining, immunohistochemical staining, and RT-PCR for type-II collagen. Chondrocytes were easily dedifferentiated and lost their phenotype in monolayer culture, so we recommend to use 0 and/or 1st passage cells for seeding. For biological safety evaluation, we checked adventitous agents such as bacteria, fungi, mycoplasma and they were shown no effects. To evaluate the ability of these polymers for delivering chondrocytes, after seeding the cells, we characterized chondrocytes using immunohistochemistry. Based on these observations it is suggested that PLA and PLGA offer a promising approach to deliver chondrocytes to the cartilage defects.

[PA2-4] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

In vitro culture of skin cells on a crosslinked gelatin based scaffold for artificial skin

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