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论文

基于单克隆抗体G250修饰的肿瘤细胞靶向基因载体研究

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摘要:

用宫颈癌细胞Hela表面高表达G250抗原的单克隆抗体G250修饰非病毒基因载体, 获得肿瘤靶向基因载体. 通过注射G250杂交瘤细胞于小鼠腹腔, 制备富含G250mAb的腹水, 用正辛酸-硫酸铵沉淀法和Protein A Agarose分离纯化, 获得高纯度的G250mAb. 通过二硫键将PEI与G250mAb偶联, 得到修饰的基因载体G250mAb-PEI, 研究其转基因靶向性. 结果表明, G250mAb-PEI对Hela细胞的基因转染具有显著的靶向性, 对Hela细胞的转基因效率是肝癌细胞HepG2(G250阴性)的2倍; 而对正常血管平滑肌细胞(SMC)的基因转染效率比Hela低近20倍, G250mAb修饰与否对SMC没有靶向性; 对3T3细胞的毒性显著低于未修饰的PEI, 表明G250mAb-PEI是一种高效、低毒和具有靶向性的基因载体.

关键词: 聚乙烯亚胺 G250mAb 肿瘤靶向 Hela细胞 基因治疗

Tumor Targeted Gene Vector Modified with G250 Monoclonal Antibody for Gene Therapy

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Abstract:

The present study developed a tumor targeted gene vector by modification of PEI with G250 monoclonal antibody. G250mAb can specially combine with the G250 which is a tumor associated with antigen expressed highly in Hela cells. G250mAb was prepared from the ascites of Balb/c mice, and conjugated to PEI *via* disulfide bonds and generated G250mAb-PEI conjugate.G250mAb-PEI can condense plasmid DNA and form G250mAb-PEI/DNA complex, which can protect DNA from DNaseI digestion. Targeting effect and transfection efficiency of G250mAb-PEI was evaluated *via* co-culture technology. The results demonstrate that G250mAb-PEI can specially target the Hela cells. The transfection efficiency to Hela is two folds of HepG2 which was G250 negative. The tumor targeting effect was also demonstrated in transfection of smooth muscle cells(SMC). The transfection efficiency of SMC is almost 20 folds lower

than that of Hela cells. In addition, the cytotoxicity of G250mAb-PEI which was determined by MTT assay on NIH 3T3 cells was much lower than PEI. In summary, G250mAb-PEI is a highly efficient gene vector with a low cytotoxicity and targeting effect. More work need to be done to evaluate the potential of the vector *in vivo* gene therapy.

Keywords: Polyethyleneimine(PEI) G250mAb Tumor targeted Hela cell Gene therapy

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