药学学报 2006, 41(2) 142-148 DOI: ISSN: CN:

论文

细胞膜穿透肽促进脂质体包载的siRNA细胞内转运、定位及其功能

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摘要：

目的研究细胞膜穿透性寡肽——八聚精氨酸(R8)输送包载siRNA的脂质体进入细胞能力的促进作用。方法将合成的R8与PEG-PE形成偶联物并定向定量地插入包载siRNA脂质体的外层膜上制成R8-liposomal siRNA。荧光分光光度计测定脂质体中R8的含量，荧光倒置显微镜观察R8修饰的脂质体与常用转染试剂lipofectamine 2000携带siRNA对小细胞肺癌NCI-H446的转染效果，MTT法检测R8-liposomal siRNA对NCI-H446细胞的生长抑制作用。结果R8未修饰的脂质体不能穿过细胞膜，而R8修饰的脂质体则能迅速进入细胞内，随着作用时间的延长逐渐定位在细胞浆和细胞核。R8修饰的脂质体介导hdm2-siRNA转染肿瘤细胞的效率和对肿瘤细胞的生长抑制作用明显强于lipofectamine 2000。结论R8修饰的脂质体可以有效输送siRNA进入细胞并增强其生物学功能。

关键词： 细胞膜穿透性寡肽 八聚精氨酸 脂质体 小分子干扰RNA 细胞内摄取

Cell penetrating peptides enhance intracellular translocation and function of siRNA encapsulated in PEGylated liposomes

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Abstract:

AimTo prepare the PEGylated liposomes modified with cell penetrating peptides, which protect siRNA from nuclease degradation and deliver efficiently siRNA into cells to facilitate silencing of target gene. MethodsThe purity of R8-PEG-PE and *p*NP-PEG-PE was detected by HPLC; the quantity of R8, PEG-DPPE modified R8, and R8 attached to the out membrane surface of the liposomal siRNA by transfer from R8-PEG-DPPE micelles to the liposomes was tested by fluorescence; Size and size distribution of siRNA loaded liposomes with and without attached R8 were determined by Zetasizer 5000; A comparison of mediated siRNA transfection efficiency between R8-liposomes and lipofectamine 2000 was examined by individual inside cell fluorescence intensity; The growth inhibition of small cell lung carcinoma NCI-H446 cells treated with R8-liposomal hdm2-siRNA or lipofectamine 2000-hdm2-siRNA complex was tested by MTT assay. ResultsThe retention times of PEG-DPPE and R8-PEG-DPPE were 9.0 min and 7.8 min, respectively. Fluorescence scanning indicated that lipids composed of liposomes and siRNAs didn't interfere to the determination of R8 when it was attached to the liposomal siRNA. The cells treated with R8-liposomal hdm2-siRNA significantly enhanced the cellular uptake of hdm2-siRNA and facilitated the functions of hdm2-siRNA through silencing of target gene which, in turn, inhibited tumor cell growth, compared with lipofectamine 2000. ConclusionThe R8 attached liposomes are shown to be powerful carriers for delivery siRNAs into cell to silence targeted gene.

Keywords: R8 liposomes siRNA cellular uptake cell penetrating peptide

收稿日期 2005-03-11 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者: 梁伟

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