A Targeted Non-viral Vector Based On Polyethylenimine Increases Transfection Efficiency of U87 Glioblastoma Cells

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Introduction

Glioblastoma multiforme (GBM) is the most common and highly malignant primary brain tumor. Recently, due to the combination of surgery, chemotherapy, radiotherapy and gene therapy, patients with GBM had a significantly improved survival, but some of them still had a poor prognosis. For gene therapy, one of key problems is lacking of safe, targeting and effective vector. VTW is a peptide with specially high binding ability to human glioblastoma cells such as U87 MG. Polyethylenimine (PEI, 25 kDa) is a typical cationic polymer used to make nanoparticles. Here, we prepared a novel nanoparticle made by PEI and VTW for targeting transfection into GBM cells.

Methods

PEI was activated by N-succinimidyl-3-(2-pyridyldithio)-propionate (SPDP) into PEI-PDP. Then VTW peptide solutions were added into PEI-PDP liquid before or after PEI-PDP being mixed with pDNA, to make pre- or post-modified nanoparticles respectively. Particle size, zeta-potential, transmission electron microscopic image and gel electrophoresis assay were performed to describe the characteristics of nanoparticles. Transfection efficiency was investigated via fluorescent microscope and flow cytometry. Lipofectamine2000, PEI nanoparticles and naked DNA were used as control.

Results

Compared with PEI nanoparticles, both the pre- and post-modified PEI nanoparticles improved the transfection efficiency of U87 MG cells, but the latter was better. VTW modified PEI nanoparticles did not improve the transfection efficiency of the control A549 (Human lung adenocarcinoma) cell line and the cortical neural cells isolated from rats. The post-modified nanoparticles at a certain VTW conjugation rate brought about the highest transfection efficiency near to that of Lipofectamine2000. Adding serum into medium led no significant difference for the transfection by VTW modified PEI nanoparticles.

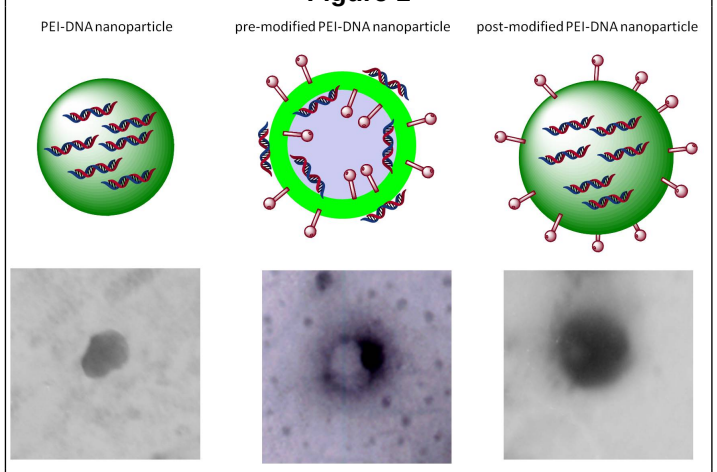
Conclusions

Nanoparticle based on VTW peptide and PEI can notably and specially improve gene transfection efficiency to U87 glioblastoma cells. The way of polymer conjugation and concentration of VTW peptide were two important factors influencing the transfection effect of nanoparticles.

Learning Objectives

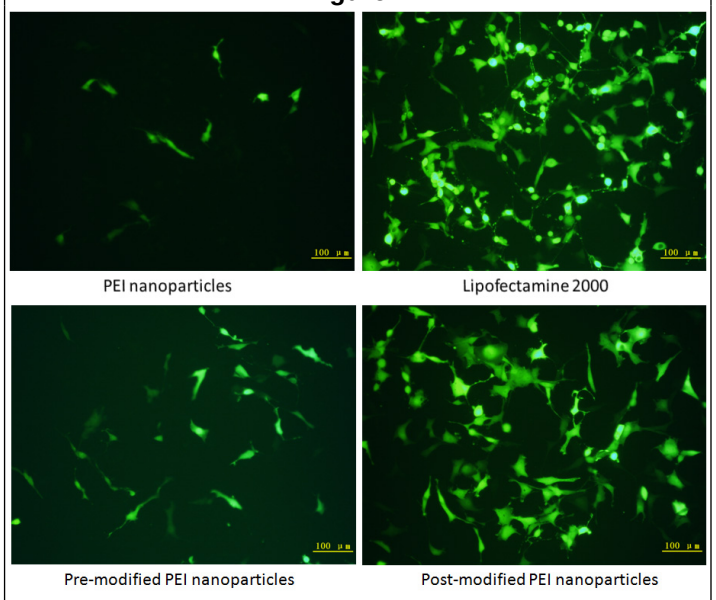
By the conclusion of this session, participants should be able to learn: 1) This is the first demonstration of the VTW peptide and PEI based carrier for intracellular gene delivery in a GBM cell-specific manner; 2) VTW peptide is an excellent targeting molecule for GBM cells and the nanoparticles made by VTW and PEI can lead to a special and effective transfection to GBM cells; 3) VTW-modified nanoparticles may become one kind of promising transfection vector for GBM.

Figure 1



The schemes and transmission electron microscopic images of three types of nanoparticles

Figure 2



Fluorescent microscope images of U87 cells transfected with pEGFP plasmid by modified nanoparticles and control.