Hepatitis B virus-like particle: targeted delivery of plasmid expressing short hairpin RNA for silencing the Bcl-2 gene in cervical cancer cells

ABSTRACT

Gene therapy research has advanced to clinical trials, but it is hampered by unstable nucleic acids packaged inside carriers and there is a lack of specificity towards targeted sites in the body. This study aims to address gene therapy limitations by encapsidating a plasmid synthesizing a short hairpin RNA (shRNA) that targets the anti-apoptotic Bcl-2 gene using truncated hepatitis B core antigen (tHBcAg) virus-like particle (VLP). A shRNA sequence targeting anti-apoptotic Bcl-2 was synthesized and cloned into the pSilencer 2.0-U6 vector. The recombinant plasmid, namely PshRNA, was encapsidated inside tHBcAg VLP and conjugated with folic acid (FA) to produce FA-tHBcAg-PshRNA VLP. Electron microscopy revealed that the FA-tHBcAg-PshRNA VLP has an icosahedral structure that is similar to the unmodified tHBcAg VLP. Delivery of FA-tHBcAg-PshRNA VLP into HeLa cells overexpressing the folate receptor significantly downregulated the expression of anti-apoptotic Bcl-2 at 48 and 72 h post-transfection. The 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay demonstrated that the cells' viability was significantly reduced from 89.46% at 24 h to 64.52% and 60.63%, respectively, at 48 and 72 h post-transfection. As a conclusion, tHBcAg VLP can be used as a carrier for a receptor-mediated targeted delivery of a therapeutic plasmid encoding shRNA for gene silencing in cancer cells.

Keyword: Short interference RNA; Virus-like particle; Anti-apoptotic Bcl-2; Plasmid delivery; Folic acid