Abstract 115

PHOTODYNAMIC TREATMENT OF RETINOBLASTOMA CELLS USING A FOLATE RECEPTOR-TARGETED NANOPHOTOSENSITIZERS

Poster

Park S.*[2], Yang S.[1]

[1]Chosun University ~ Gwangju-Metropolitan city ~ Korea, Republic of, [2]Kim Eye Hospital ~ Seoul ~ Korea, Republic of

Purpose:

We synthesized folic acid-conjugated poly(ethylene glycol)/Ce6 tetramer conjugates using 3-[3-(2-carboxyethoxy)-2,2-bis(2-carboxyethoxymethyl) propoxy]propanoic acid and fabricated nanophotosensitizers. Their targeting efficiency against a folate receptor and ROS-sensitivity against cancer cells were studied using Y79 retinoblastoma cells. We characterized the physicochemical and biological properties of FAPEGtaCe6 nanophotosensitizers in vitro and in vivo.

Methods:

Ce6 was conjugated with 3-[3-(2-carboxyethoxy)-2,2-bis(2-carboxyethoxymethyl) propoxy] propanoic acid to make Ce6 tetramer via selenocystamine linkages. Carboxylic acid end group of the TA-sese-Ce6 conjugates, FA-PEG was attached again using selenocystamine linkages to make FA-PEG/TA-sese-Ce6 conjugates. Nanophotosensitizers were fabricated by dialysis procedure. Morphological observations showed small diameters of less than 200 nm. Stability of the aqueous FAPEGtaCe6 nanophotosensitizer solution was maintained. When H2O2 was added to the nanophotosensitizer solution, the particle size distribution was changed from a monomodal pattern to a multimodal pattern. Fluorescence intensity and Ce6 release rate from the nanophotosensitizers were also increased by the addition of H2O2.

Results:

In cell culture study, an FAPEGtaCe6 nanophotosensitizer treatment against cancer cells increased the Ce6 uptake ratio, ROS generation and light-irradiated cytotoxicity (phototoxicity) compared with Ce6 alone against various cancer cells. When the folic acid was pretreated to block the folate receptors of the Y79 cells, the intracellular Ce6 uptake, ROS generation and thereby phototoxicity were decreased. These results indicated that they could be delivered by a folate receptor-mediated pathway. Furthermore, an in vivo pulmonary metastasis model using Y79 cells showed folate receptor-specific delivery of FAPEGtaCe6 nanophotosensitizers. The FAPEGtaCe6 nanophotosensitizers had folate receptor specificity in vitro and in vivo.

Conclusions:

The Y79 cells showed a folate receptor-specific delivery capacity for the nanophotosensitizers. When the folate receptor of the Y79 cells in the pulmonary metastatic model was blocked. We suggest that FAPEGtaCe6 nanophotosensitizers are promising candidates for a targeted photodynamic therapy (PDT) approach against Y79 cancer cells.