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Site-Specific Delivery of Hybrid Upconversion Nanoparticles for Photo-Activated Multimodal Therapies of Glioblastoma

Authors : Yuan-Chung Tsai, Masao Kamimura, Kohei Soga, Hsin-Cheng Chiu

Abstract : In order to enhance the photodynamic/photothermal therapeutic efficacy on glioblastoma, the functionized upconversion nanoparticles with the capability of converting the deep tissue penetrating near-infrared light into visible wavelength for activating photochemical reaction were developed. The drug-loaded nanoparticles (NPs) were obtained from the self-assembly of oleic acid-coated upconversion nanoparticles along with maleimide-conjugated poly(ethylene glycol)-cholesterol (Mal-PEG-Chol), as the NP stabilizer, and hydrophobic photosensitizers, IR-780 (for photothermal therapy, PTT) and mTHPC (for photodynamic therapy, PDT), in aqueous phase. Both the IR-780 and mTHPC were loaded into the hydrophobic domains within NPs via hydrophobic association. The peptide targeting ligand, angiopep-2, was further conjugated with the maleimide groups at the end of PEG adducts on the NP surfaces, enabling the affinity coupling with the low-density lipoprotein receptor-related protein-1 of tumor endothelial cells and malignant astrocytes. The drug-loaded NPs with the size of ca 80 nm in diameter exhibit a good colloidal stability in physiological conditions. The in vitro data demonstrate the successful targeting delivery of drug-loaded NPs toward the ALTS1C1 cells (murine astrocytoma cells) and the pronounced cytotoxicity elicited by combinational effect of PDT and PTT. The in vivo results show the promising brain orthotopic tumor targeting of drug-loaded NPs and sound efficacy for brain tumor dual-modality treatment. This work shows great potential for improving photodynamic/photothermal therapeutic efficacy of brain cancer.

Keywords : drug delivery, orthotopic brain tumor, photodynamic/photothermal therapies, upconversion nanoparticles
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