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Photosensitizer-Crosslinked In-Situ Polymerization on Catalase for Tumor Hypoxia Modulation & Enhanced Photodynamic Therapy

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Abstract

Tumor hypoxia is known to be one of critical factors that aggravate the tumor resistance to photodynamic therapy (PDT) in which oxygen is essential for tumor destruction. Herein, catalase, an enzyme to trigger hydrogen peroxide (H_2O_2) decomposition, is modified by in-situ free radical polymerization, using meso-tetra(*p*-hydroxyphenyl) porphine (THPP) as the cross-linker to enable condensed grafting of short polyethylene glycol (PEG) chains on the protein surface as a permeable brush-like safeguard. The formulated catalase-entrapped nanocapsules (CAT-THPP-PEG) with enhanced enzyme stability can be labeled with $^{99m}Tc^{4+}$, a radioisotope ion that is chelated by the porphyrin structure of THPP, to allow in vivo single-photon emission computed tomography (SPECT) imaging. It is found that such CAT-THPP-PEG nanoparticles exhibit efficient tumor passive retention after intravenous injection, and are able to greatly relieve tumor hypoxia by triggering the decomposition of tumor endogenous H_2O_2 into oxygen. With THPP functioning as a photosensitizer, in vivo PDT is further conducted, achieving a remarkable antitumor therapeutic effect. This work presents an enzyme modification strategy by in-situ polymerization with photosensitizer as the cross-linker to develop multifunctional nano-theranostics with strengthened enzymatic stability, efficient tumor passive homing, SPECT imaging capability, enhanced PDT efficacy as well as decreased immunogenicity, promising for clinical translation.

Keywords: In-Situ Polymerization, Catalase, Tumor Hypoxia Modulation, Photodynamic Therapy