Enhancing antitumor efficacy by glutathione-depleted nanophotosensitizers with photo-triggered strong hyperthermia and ROS generation

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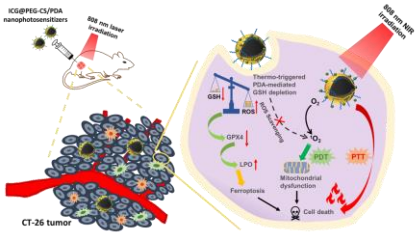
Dual-modal phototherapy based on the combination of photodynamic therapy (PDT) and photothermal therapy (PTT) has emerged as a promising strategy for cancer treatment. However, the poor photostability and photothermal conversion efficiency (PCE) of organic small-molecule photosensitizers, and the intracellular glutathione (GSH)-mediated reactive oxygen species scavenging result in unsatisfactory antitumor efficacy of dual-modal phototherapy. To address these issues, in this study, a versatile nanophotosensitizer system was successfully fabricated by ingenious incorporation of indocyanine green (ICG) into PEGylated chitosan (PEG-CS)-decorated polydopamine (PDA) via multiple π-π stacking, hydrophobic and electrostatic interactions. The attained ICG@PEG-CS/PDA nanophotosensitizers exhibited the outstanding photothermal stability, high PCE (ca 62.8 %), prominent singlet oxygen-generating and PDA-mediated GSH-consuming capability. After being internalized by CT26 cells, these nanophotosensitizers under 808 nm near-infrared (NIR) laser irradiation effectively produced singlet oxygen with the aid of thermo-enhanced intracellular GSH depletion to promote mitochondrial damage and lipid peroxide formation, thus eliciting ferroptosis and apoptosis. The in vivo antitumor efficacy studies further demonstrated that the ICG@PEG-CS/PDA nanophotosensitizers markedly inhibited CT26 tumor growth by NIR-activated intense hyperthermia and redox homeostasis disruption without systemic toxicity. Our study presents a new strategy to augment antitumor effect of dual-modal phototherapy by ICG@PEG-CS/PDA nanophotosensitizers.



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