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ORIGINAL RESEARCH

Guiding Appropriate Timing of Laser Irradiation by Polymeric Micelles for Maximizing Chemo-Photodynamic Therapy

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Background: Photoactivity "on-off" switchable nano-agents could shield phototoxicity until reaching target region, which immensely promoted photodynamic therapy. However, the masking ratio of nano-agents in vivo was dynamic and positively correlated with the phototoxicity induced by laser irradiation, in which case the timing of laser irradiation was unpredictable to maximize antitumor efficacy.

Methods: Herein, low molecular weight chitosan and hydrophobic polymethylacrylamide derivatives were linked via GSH cleavable 3, 3′-dithiodipropionic acid to construct polymeric micelles (Ce6-CSPD). The doxorubicin loading nano-agent (Ce6-CSPD/DOX) could quench both photoactivity and fluorescence of photosensitizer chlorin e6 (Ce6) and doxorubicin (DOX) under physiological condition by homo-fluorescence resonance energy transfer (homoFRET).

Results: Once internalized by tumor cells, the photoactivity as well as fluorescence of Ce6 was recovered rapidly when motivated by intracellular high GSH. Specifically, the fluorescence intensity and photoactivity of Ce6 were proven to be positive linear correlated, upon which appropriate timing of laser irradiation could be determined by referring to the dynamic fluorescence intensity in vivo. In addition, the theranostic nano-agents also possessed the capacity of monitoring the DOX release process. Accordingly, under the guidance of fluorescence intensity, the experimental group subjected to laser irradiation at 18 h postadministration acquired the highest antitumor inhibition efficacy compared to that at four hours and 48 h, which held great potential for maximizing chemo-photodynamic therapy and avoiding nonspecific phototoxicity precisely to normal organs.

Conclusion: In summary, we prepared homoFRET-based theranostic nano-agent (Ce6-CSPD/DOX) for monitoring PDT precisely and decreasing phototoxicity to normal organs before reaching target region. Under the guidance of dynamic fluorescence intensity, the appropriate laser irradiation timing could be monitored to maximize antitumor therapy efficacy, which offered opportunities for monitoring efficiency of chemo-photodynamic therapy in a timely and accurate manner.

Keywords: theranostic, photodynamic therapy, tumor, micelle

Introduction

Cancers are still leadto millions of human deaths worldwide, although continuous efforts are afforded by scholars.[1,2] For the moment, chemotherapy and radiotherapy are still the standard strategies for the treatment of tumors. However, inefficiencies and severe side effects generally lead to compromised patient compliance.[3–5] Thus, novel advancements such as photodynamic therapy (PDT) have gradually become regarded as the clinical candidate for tumor treatment, with advantages of destroying localized tumor regions, minimizing damage of surrounding tissue with high spatiotemporal precision.[6,7]

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