Glutathione activatable photosensitizer-conjugated pseudopolyrotaxane nanocarriers for photodynamic theranostics

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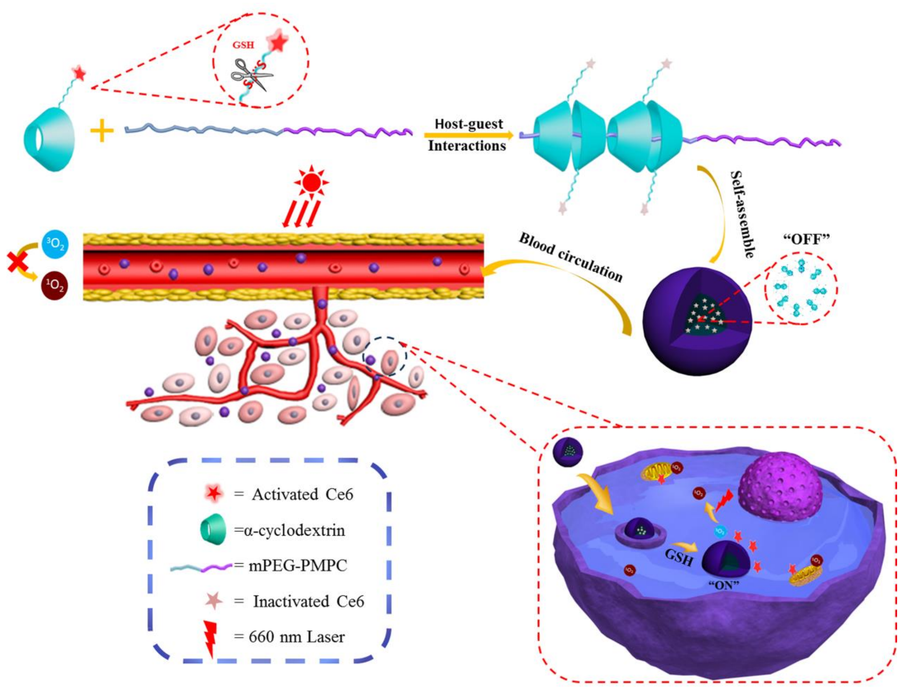
Abstract

Photodynamic theranostics has recently been extensively explored as a promising approach for precise localization and therapy. Herein, we reported glutathione activatable photosensitizer(PS) loaded pseudopolyrotaxane nanocarriers (α-CD-ss-Ce6 NPs) for enhanced photodynamic theranostics by taking advantage of the non-covalent interactions between α-cyclodextrin (α-CD) and poly(ethylene glycol) (PEG). The designed α-CD-ss-Ce6 NPs were non-activated and stable during circulation but exhibited strong photodynamic theranostics by glutathione (GSH) activating after arriving at tumor site. More importantly, compared to free Ce6, such kind of pseudopolyrotaxane nanocarriers could dramatically enhance Ce6 accumulation in tumor and prolong its tumor retention time, demonstrating excellent therapeutic effects after light irradiation. Overall, the designed GSH activatable PS-conjugated pseudopolyrotaxane nanocarriers possessing high-performance photodynamic therapeutic efficacy together with reduced side effects would provide a new way for photodynamic theranostics.



Scheme 1 Schematic illustration of GSH-activatable PS conjugated pseudopolyrotaxane nanocarriers for photodynamic theranostic

Results and Discussion

1. Redox-responsive activation of α-CD-ss-Ce6 NPs

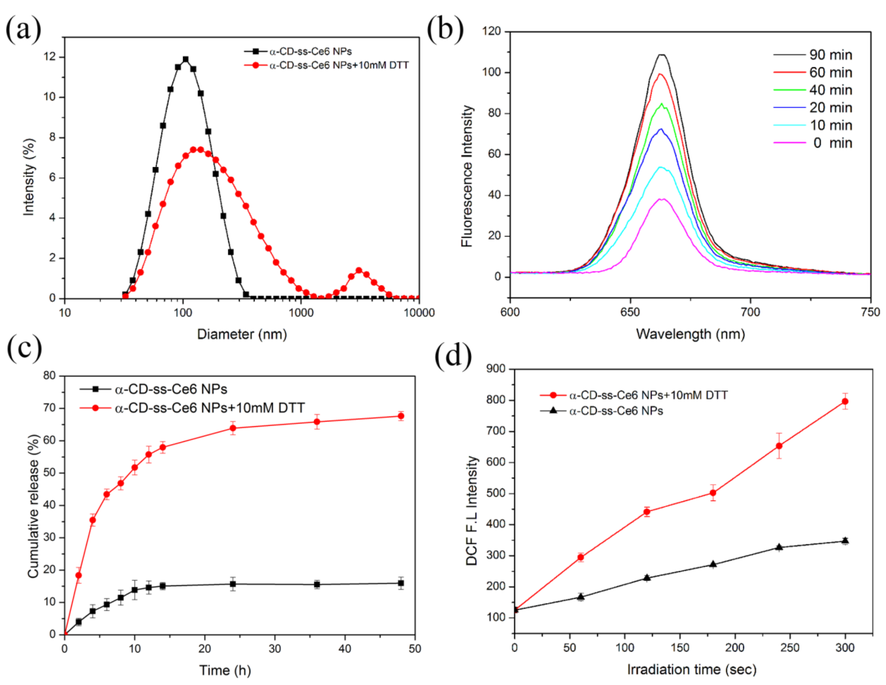


Fig. 1. The change of the size (a), time-dependent fluorescence spectra (b),in vitro Ce6 release (c) and time-dependent ROS generation (d)of the pseudopolyrotaxane nanocarriers after DTT treatment.

α-CD-ss-Ce6 NPs were successfully fabricated through a dialysis method. The NPs exhibited redox activatable fluorescence signal and phototoxicity for photodynamic theranotics.

2 In vitro cellular redox-responsive activatable behavior of α-CD-ss-Ce6 NPs

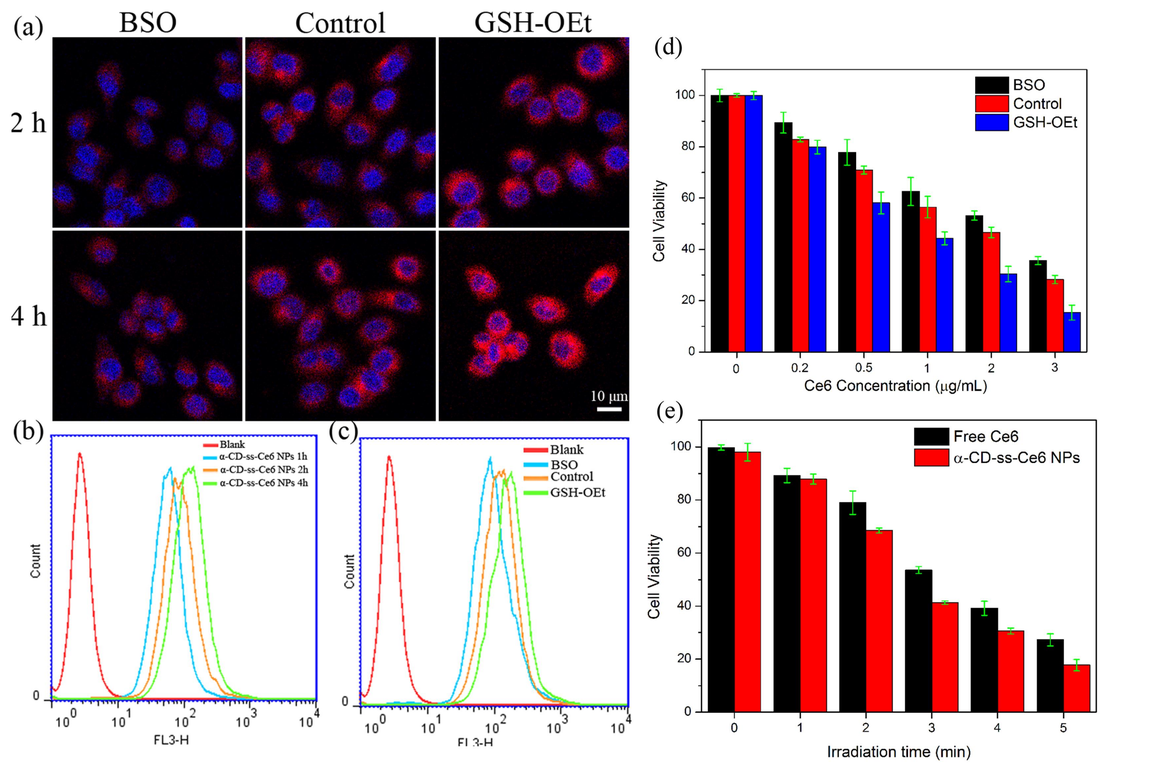


Fig. 2. CLSM images (a) and relative flow cytometric profiles (b)&(c) , concentration (d) and time (e) dependent proliferation inhibitions of KB cells incubated with pseudopolyrotaxane nanocarriers pre-treated with BSO or GSH-Oet.

α-CD-ss-Ce6 NPs demonstrated redox-responsive activatable fluorescence signal enhancement ability and efficient PDT potential upon irradiation due to activation of Ce6 at cellular level.

3. In vivo fluorescence imaging-guided PDT of α-CD-ss-Ce6 NPs in tumor-bearing mice.

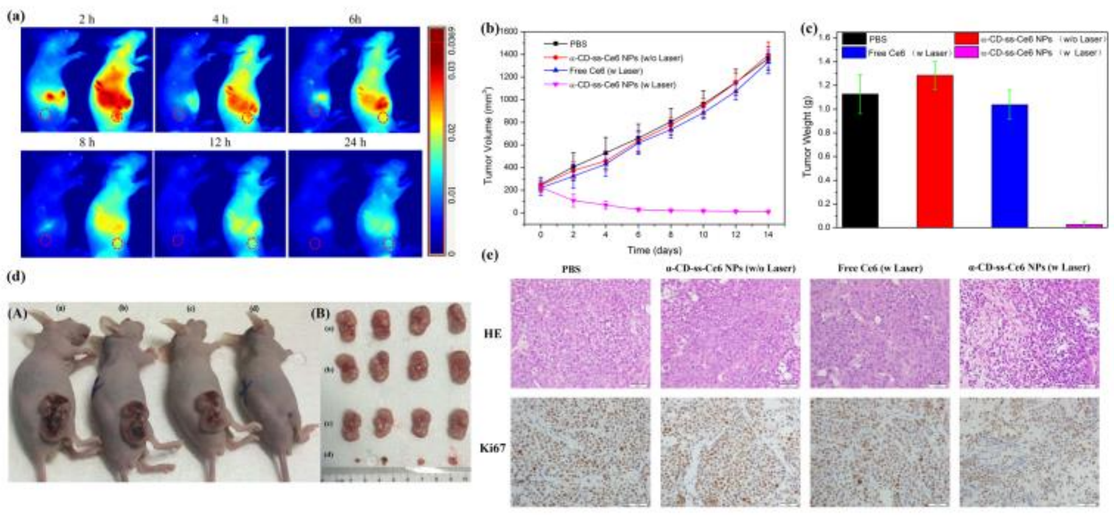


Fig. 3. In vivo time-dependent whole body fluorescence imaging (a) of KB tumor-bearing mice, tumor growth curves (b), tumor weight (c), tumor images (d) and H&E and Ki67 staining of tumor tissues (e) of different groups of tumor-bearing mice after treatment;

Compared with free Ce6, α-CD-ss-Ce6 NPs had excellent photodiagnostics capability without compromising the PDT efficacy, and were suitable for in vivo photodynamic theranotics.

Conclusions

Gutathione activatable photosensitizer loaded pseudopolyrotaxane nanocarriers (α-CD-ss-Ce6 NPs) were successfully constructed for photodynamic theranostics. α-CD-ss-Ce6 NPs were stable and non-phototoxic during circulation while exhibited strong photodynamic theranostics by GSH activating after arriving at tumor site through EPR effect. Meanwhile, such kind of pseudopolyrotaxane nanocarriers could significantly enhance Ce6 accumulation in tumors, prolong its tumor retention time and improve its therapeutic effect compared to free Ce6. α-CD-ss-Ce6 NPs could be considered as a facile yet effective platform for in vivo activatable photodynamic theranotics.

Acknowledgements

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