All-in-One nanoparticle for breast cancer treatment based on phototherapy and chemodynamic therapy

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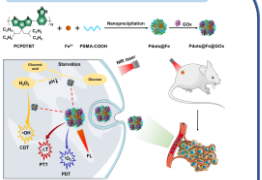
Abstract

Chemodynamic therapy (CDT) has emerged as an outstanding antitumor therapeutic method due to its selectivity and utilization of tumor microenvironment. However, there are still unmet requirements to achieve a high antitumor efficiency. Here, an iron-loaded semiconducting polymer dot modified with glucose oxidase (Pdots@Fe@GOx) is reported to deliver iron ions into tumor tissues and in situ generation of hydrogen peroxide in tumors. On one hand, Pdots@Fe@GOx converts glucose to gluconic acid and hydrogen peroxide (H_2O_2) in tumor, which not only consumes glucose of tumor cells, but also provides the H_2O_2 for the following Fenton reaction. On the other hand, the Pdots@Fe@GOx delivers active iron ions in tumor to perform CDT with the combination of the generated H_2O_2. In addition, the Pdots@Fe@GOx has both photothermal and photodynamic effects under the irradiation of near-infrared laser, which can improve and compensate the CDT effect to kill cancer cells. This Pdots@Fe@GOx-based multiple-mode therapeutic strategy has successfully achieved a synergistic anticancer effect with minimal side effects.

Experimental design



Scheme 1. Schematic illustration of the preparation of Pdot@Fe@GOx for enhanced multimodal cancer treatment.

Results

1. Characterization of Pdots@Fe@GOx

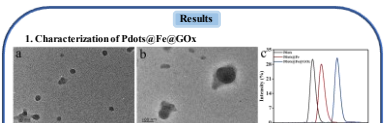


Fig 1. Characterization of temperature-sensitive Pdots@Fe@GOx. TEM images of a) Pdots and b) Pdots@Fe@GOx. c) Hydrodynamic diameter distribution of Pdots, Pdots@Fe and Pdots@Fe@GOx. d) Fluorescence intensity of SOSG under different conditions. e) IR thermal images of Pdots@Fe@GOx under different conditions. f) UV-vis absorbance intensities of TMB upon different concentrations of glucose (GO).

2. Effect of Pdots@Fe@GOx in vitro

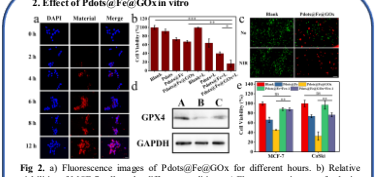


Fig 2. a) Fluorescence images of Pdots@Fe@GOx for different hours. b) Relative viabilities of MCF-7 cells under different conditions. c) Fluorescence images of calcein-AM/PI with different conditions. d) Western blot assay results of GPX4 and GAPDH expressions with PBS (A), Pdot@Fe@GOx (B), and Pdot@Fe@GOx with Fer-1 (C). e) Effects of Fer-1 on nanomaterial-induced cytotoxicity.

3. Multimodal therapy by Pdot@Fe@GOx in vivo

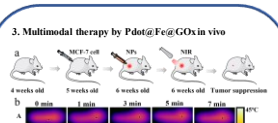


Fig 3. a) Schematic illustration of treatment schedule of multimodal combination therapy. b) IR thermal images of mice with Blank (A), Pdots (B), Pdots@Fe (C) and Pdots@Fe@GOx (D). c) Time-dependent tumor growth curves. d). Tumor weight with different samples.

Conclusions

In this study, we developed a Pdots@Fe@GOx to perform multimodal therapy for breast cancer treatment in vitro and in vivo. In vitro and in vivo experiments revealed that the multimode strategy was better than the single treatment mode, with completely tumor suppression by the treatment of Pdots@Fe@GOx and NIR irradiation.

Acknowledgements

This work was supported by the University of South Dakota, NIH U54GM128729.