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**Pre-drug Self-assembled Nanoparticles: recovering activity and overcoming glutathione-associated cell antioxidant resistance against photodynamic therapy**

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**Abstract**

In photodynamic therapy (PDT), the elevated glutathione (GSH) of cancer cells have two sides for treatment efficacy, activation pre-drug by removing activity suppressor part (advantages) and consumption reactive oxygen species (ROS) to confer PDT resistance (disadvantages). Preparation all-in-one system by simple method to make best use of the advantages and bypass the disadvantages still were remains a technical challenge. Herein, we report a robust PDT nanoparticle with above function based on a self-assembled pyridine modified Zinc phthalocyanine (ZnPc-DTP). The activity suppressor and active part of ZnPc-DTP were linked by disulfide bond. After targeting cancer cells, GSH can react with ZnPc-DTP nanoparticles by cutting disulfide bond to release its active part (ZnPc-SH) and oxidize GSH. In vitro and in vivo results indicated that ZnPc-SH can effective suppress tumor growth under the low antioxidant tumor microenvironment (TME).

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