Supplementary Information

Intelligent Catalase-coated MnO_2 Nanoparticles with Programmed Oxygen Supply and Glutathione Depletion for Enhanced Photodynamic Therapy

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Experimental

Materials

$MnCl_2 \cdot 4H_2O$, Chlorin e6 (Ce6), 1,3-Diphenylisobenzofuran (DPBF), Tris (4,7-diphenyl-1,10-phenanthroline) ruthenium (II) dichloride complex ($[Ru(dpp)_3]Cl_2$, RDPP) and GSH detection kit were purchased from Shanghai Macklin Biochemical Co., Ltd (China). Human Serum Albumin and Catalase was purchased from Sigma-Aldrich (USA). Hoechst 33342, Thiazolyl blue tetrazolium bromide (MTT) and Live/Dead Cell Staining Kit were purchased from Beijing Solarbio Science & Technology Co., Ltd (China). Mito-Tracker Green and Lyso-Tracker Red were purchased from Beyotime Biotechnology (China). Dulbecco's modified Eagle's medium (DMEM) was obtained from Gibco Life Technologies (USA). Fetal bovine serum (FBS) was purchased from Biosharp Life Sciences (China).

Instrumental methods

The morphology of the nanoparticles was examined using a Talos-L120C transmission electron microscopy (Thermo Fischer, USA). Elemental mapping of MH@CAT was conducted with a Talos-F200X Lorenz transmission electron

microscopy (Thermo Fischer, USA). The particle size and zeta potentials of the nanoparticles were characterized by a Litesizer-500 instrument (Anton-Paar, USA). X-ray photoelectron spectroscopy analysis of MH@CAT was performed using an ESCALAB-250Xi spectrometer (Thermo Fischer, USA). UV–vis absorption spectra were recorded with a UV-L6 spectrometer (Youke, China). The production of O_2 was monitored using a DO-957 portable dissolved oxygen meter (INESA, China). Cell fluorescence images were captured using a FV3000 confocal laser scanning microscope (Olympus, Japan). Fluorescence imaging was acquired using the Smart-LF VISQUE in vivo imaging system (Vieworks, Korea).

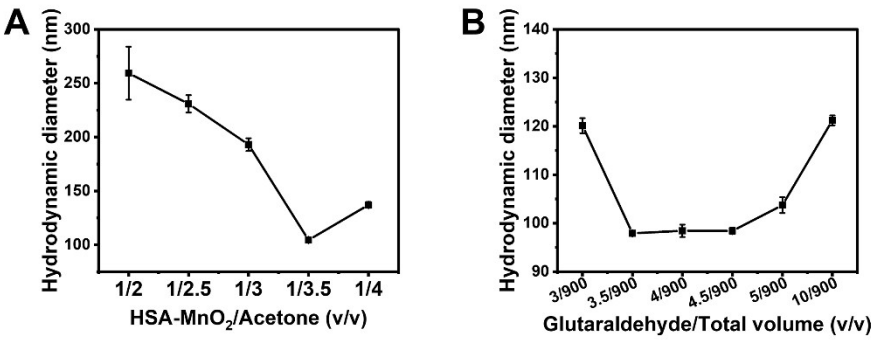

Fig. S1 Optimized the amount of (A) acetone and (B) cross-linking glutaraldehyde for MH preparation.

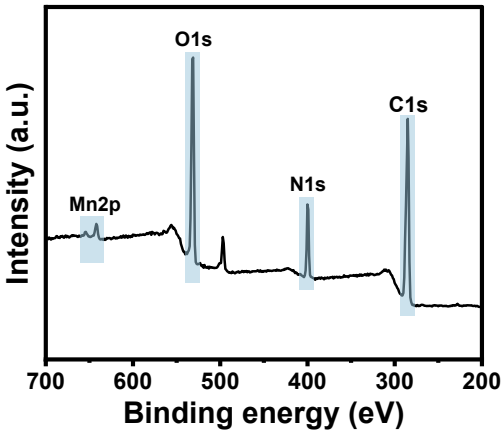

Fig. S2 HR-XPS spectrum of MH@CAT.

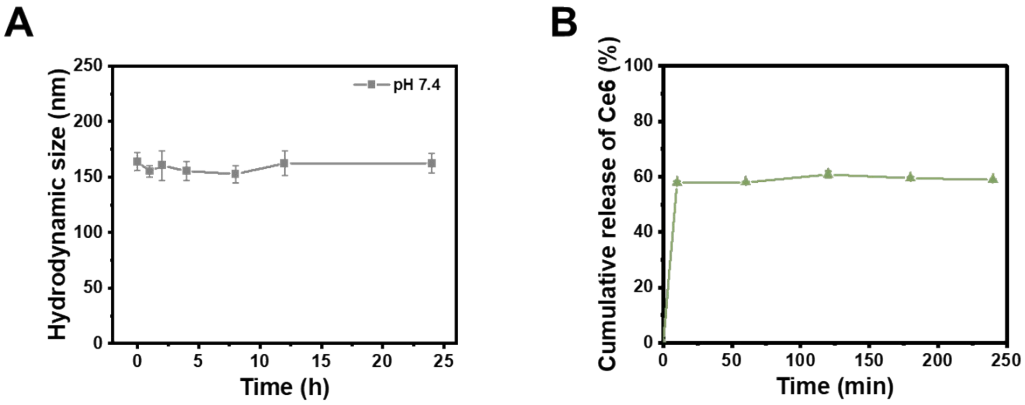

Fig. S3 (A) Stability and (B) release profile of MH@CAT under pH 7.4.

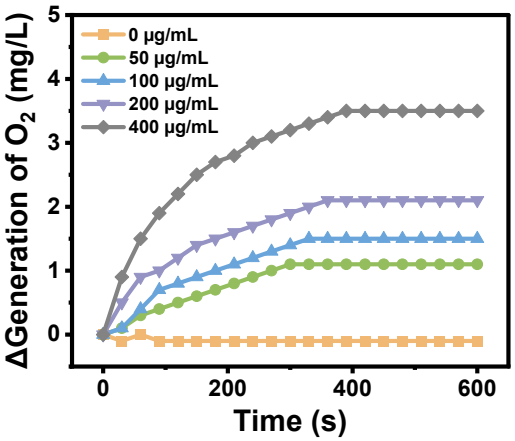

Fig. S4 O_2 generation curves after adding different concentrations of MH@CAT-Ce6 to 1 mM H_2O_2 solution.

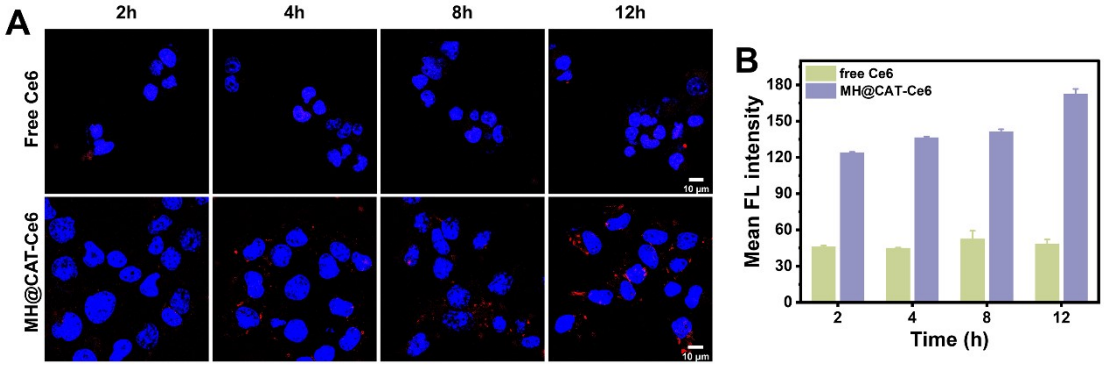

Fig. S5 (A) Fluorescent images of 4T1 cells after incubation with MH@CAT-Ce6 for 2, 4, 8 and 12h, and stained with Hoechst (Blue channel: Hoechst, Red channel: Ce6). (B) Ce6 fluorescence intensities of cells at different time points.

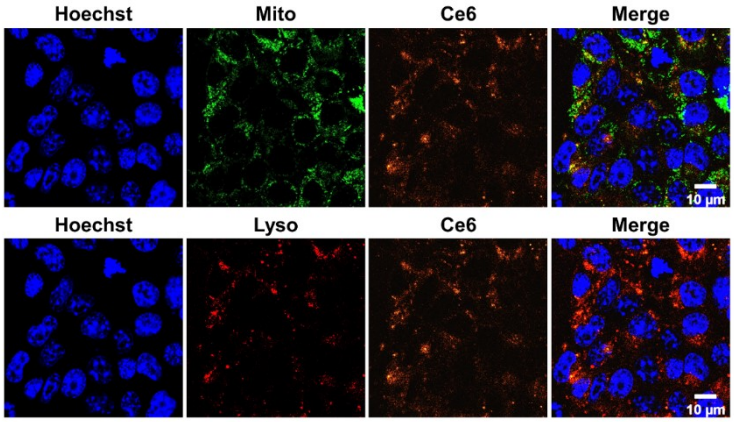

Fig. S6 Intracellular distribution of Ce6 in 4T1 cells after incubated with MH@CAT-Ce6.

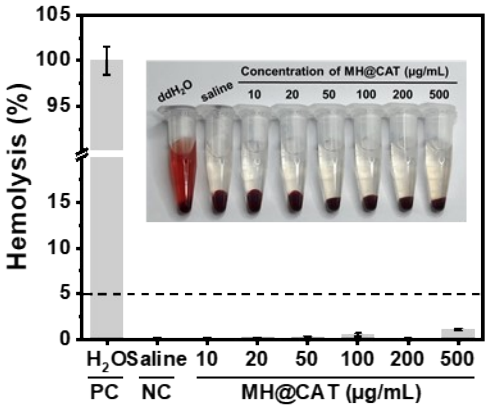

Fig. S7 Photographs of hemolysis experiments and hemolysis rate detection of MH@CAT-Ce6.

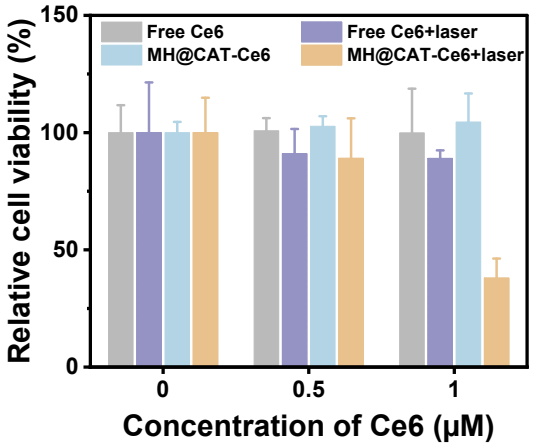

Fig. S8 Comparation the PDT activities between free Ce6 and MH@CAT-Ce6 on MDA-MB-231 cells in the absence of

H_2O_2 with or without laser.

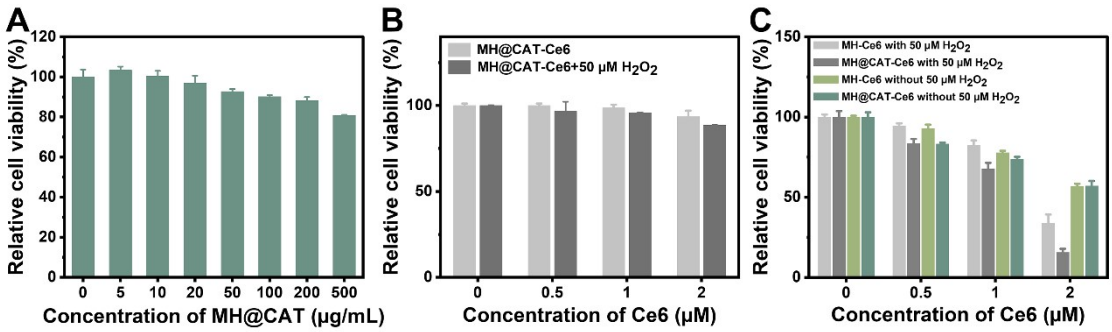

Fig. S9 (A) Cytotoxicity evaluation of various concentrations of MH@CAT on 4T1 cells. (B) Cytotoxicity test of MH@CAT-Ce6 on 4T1 cells with or without H_2O_2 in the absence of light irradiation. (C) PDT effect of MH-Ce6 or MH@CAT-Ce6 on 4T1 cells with or without H_2O_2, under 650 nm light irradiation (20 mW·cm^{-2} for 15 min) in a nitrogen atmosphere.

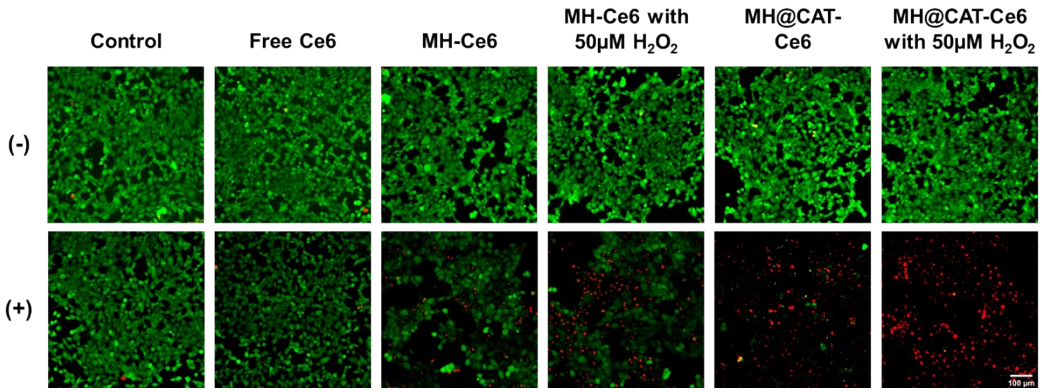

Fig. S10 Live/dead fluorescence staining images of 4T1 cells with (+) or without (-) irradiation. Green channel: live cells. Red channel: dead cells.

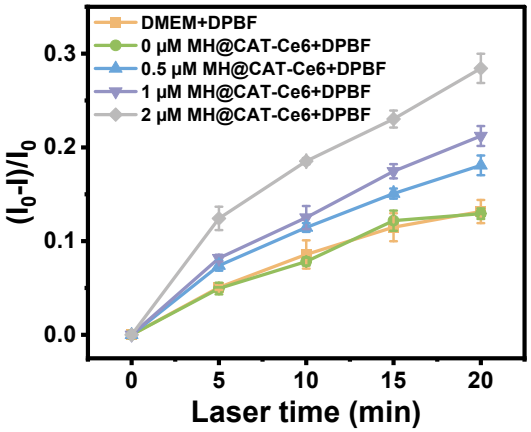

Fig. S11 Intracellular $^1O_2$ production of 4T1 cells examined using DPBF as the indicator under 650 nm light irradiation (20 mW·cm^{-2} for 20 min) in a nitrogen atmosphere.

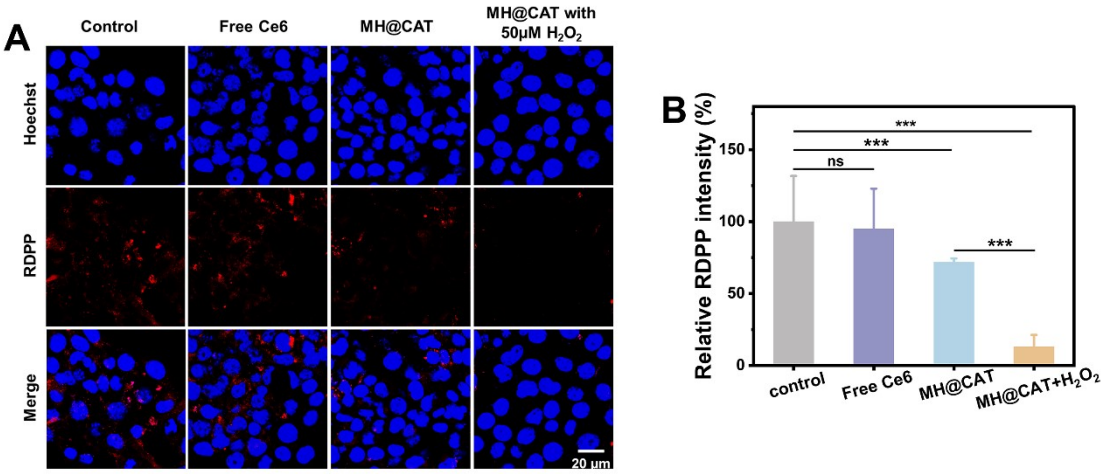

Fig. S12 (A) Intracellular O_2 generation of 4T1 cells determined by RDPP. (B) Relative RDPP intensity after various treatments.

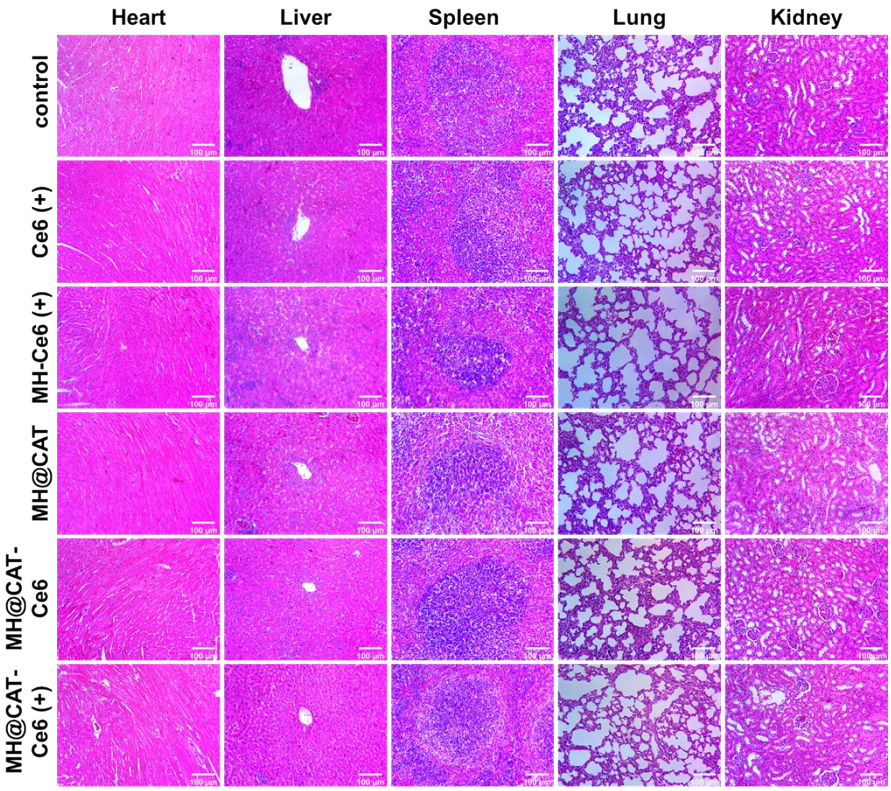

Fig. S13. H&E staining images of the major organs from 4T1 tumor-bearing mice collected at the end of the treatment period.