Supporting Information

Integrating *in situ* formation of nanozyme with three-dimensional dendritic mesoporous silica nanospheres for hypoxia-overcoming photodynamic therapy

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Materials and Chemicals. Cetyltrimethylammonium chloride (CTAC) solution (25 wt % in H_2O), triethanolamine (TEA)，tetraethyl orthosilicate (TEOS)， 3-aminopropyltrimethoxysilane (APTES), cyclohexane, sodium borohydride ($NaBH_4$), potassium hexachloroplatinate(IV) (K_2PtCl_6), N-hydroxysuccinimide (NHS) and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC), 9,10-anthracenediyl-bis(methylene) dimalonic acid (ABDA), 2,7-dichlorodihydrofluoresceindiacetate (DCFH-DA), Rhodamine 123 (Rho123), 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), dimethyl sulfoxide (DMSO), 6-diamidino-2-phenylindole (DAPI), poly (ethylene glycol) (NH_2-PEG-NH_2, Mw 3000) and 4% formaldehyde were all purchased from Sigma-Aldrich (MA, USA). 4-(Carboxybutyl)triphenyl-phosphonium Bromide (TPP) and chlorin e6 (Ce6) were purchased from TCI company and Frontier Scientific, respectively. Live/dead viability kit, Mito-Tracker Green and phosphate buffer saline (PBS) were obtained from Thermo Fisher Scientific (USA). Fetal bovine serum (FBS), penicillin, streptomycin and Ham's F-12K (Kaighn's) Medium (F-12K medium) for cell cultures were purchased from ATCC. The A549 cell lines were ordered from ATCC. Other reagents, if not specified, were purchased from local suppliers. The water in all experiments was prepared in a three-stage Millipore Milli-Q plus 185 purification system and had a resistivity higher than 18.2 MΩ cm.

Apparatus. Transmission electron microscopy (TEM) images were obtained using a Philips CM200 UT (Field Emission Instruments, USA). UV-vis spectra and fluorescence spectrum were obtained with a Tecan Safire2 microplate reader. Fourier transform infrared (FTIR) spectra were carried out with a Tensor 27 FTIR

spectrophotometer. Confocal laser scanning microscope (CLSM) studies were observed using a Leica TCS SP8 microscope.

Synthesis of Amino-DMSNs. Firstly, a biphase stratification method was used to synthesize the 3D-dendritic MSNs as reported. 25 wt% CTAC (48 mL) solution and TEA (0.36 g) were added to 72 mL of water, and heated to 60℃. After stirring for 1 h, a volume of 40 mL cyclohexane containing 20 v/v % TEOS was added to the above solution drop by drop. The mixture was kept stirring at 60℃ in an oil bath for 12 h. Then, the upper oil was discarded and the white products were collected by centrifugation, followed by washing with ethanol several times. The collected products then undergone a reflux process in 50 mL of ammonium nitrate ethanol solution (0.6 wt %) at 60℃ for 6 h to remove the template. To obtain amino-DMSNs, lyophilized 3D-dendritic MSNs dry powder was dissolved in 15 mL of anhydrous toluene and mixed with 1.0 mL of APTES. After refluxing at 110℃ for 20 h, amino-MSNs were obtained by lyophilization.

Synthesis of DMSNs/Ce6. 2.5 mg of amino-DMSNs lyophilization powder were suspended in ethanol (1 mL) and mixed with 1.0 mg of Ce6 in DMSO. The mixture was stirred overnight in the dark. Then, the DMSNs/Ce6 product was obtained by centrifugation to remove unbound Ce6. Finally, DMSNs/Ce6 was dispersed in water to determine the drug loading content by recording the UV-vis absorbance at 403 nm. The amount of Ce6 loaded into the system was determined from a calibration curve obtained from a series of Ce6 solution at different concentrations (see Figure S1 below). The drug loading content was determined by the following equations:

$$\text{Ce6 loading content (\%)} = \frac{\text{weight of Ce6 in nanoparticles}}{\text{weight of nanoparticles taken}} \times 100$$

By UV−vis absorbance of DMSNs/Ce6 solution, the drug loading content was measured as ~13 %.

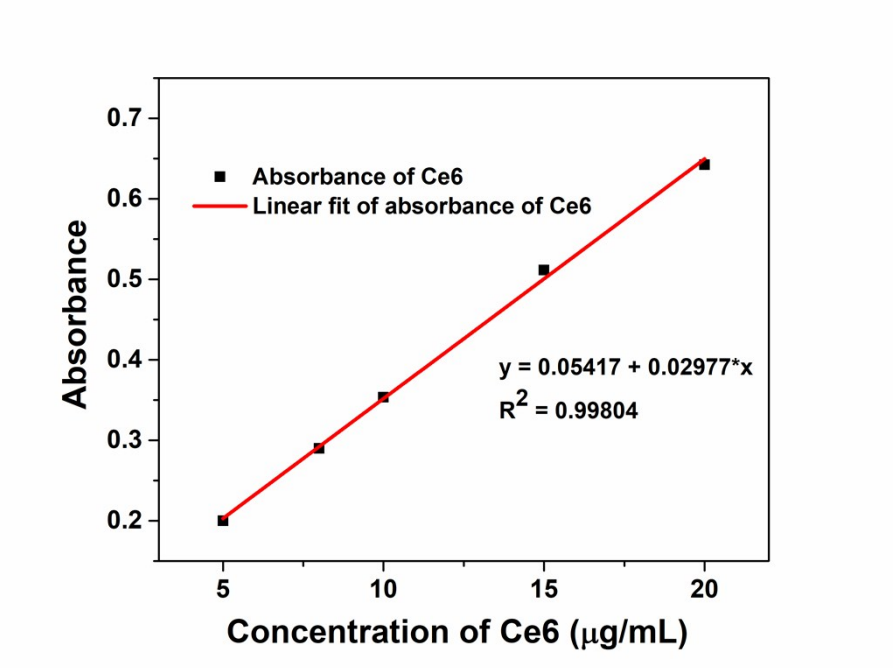

Figure S1. The calibration curve of Ce6 solution. The absorption peaks at 403 nm were used to determine Ce6 concentration.

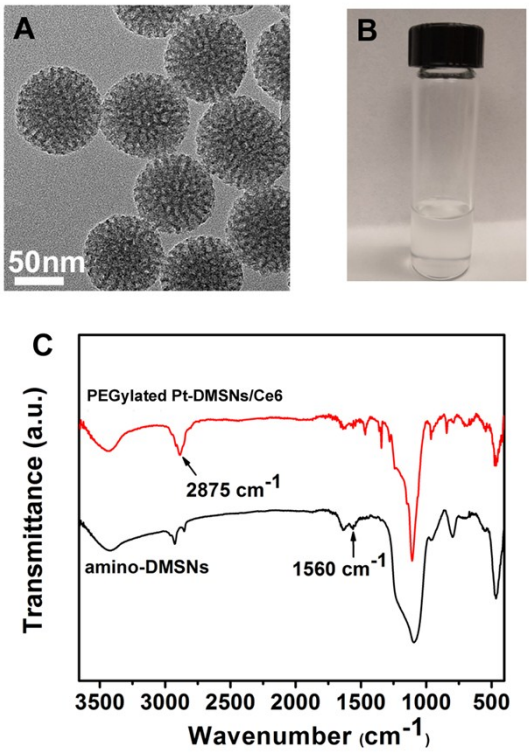

Figure S2. TEM image of amino-DMSNs (A) and their photograph in aqueous solution (B). (C) FTIR spectra of amino-DMSNs and PEGylated Pt-DMSNs/Ce6.

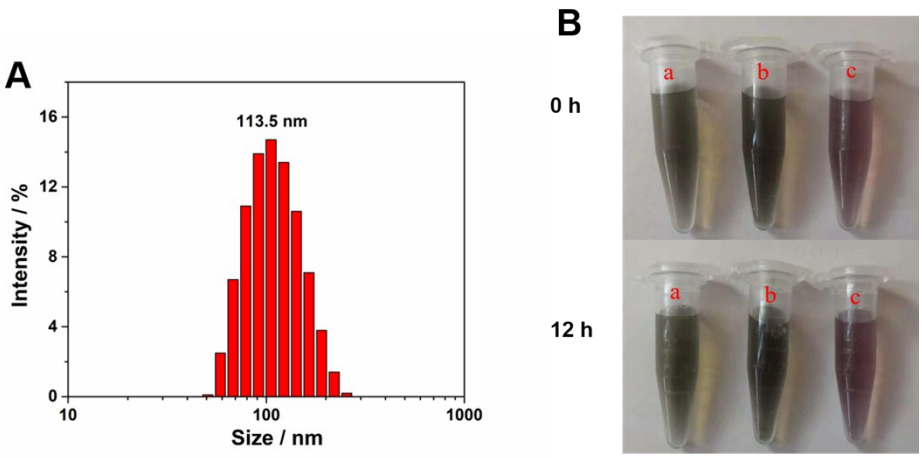

Figure S3. (A) Size distribution of Pt-DMSNs-TPP/Ce6. (B) Stability test of Pt-DMSNs-TPP/Ce6 in water (a), PBS (b) and F-12K medium (c).

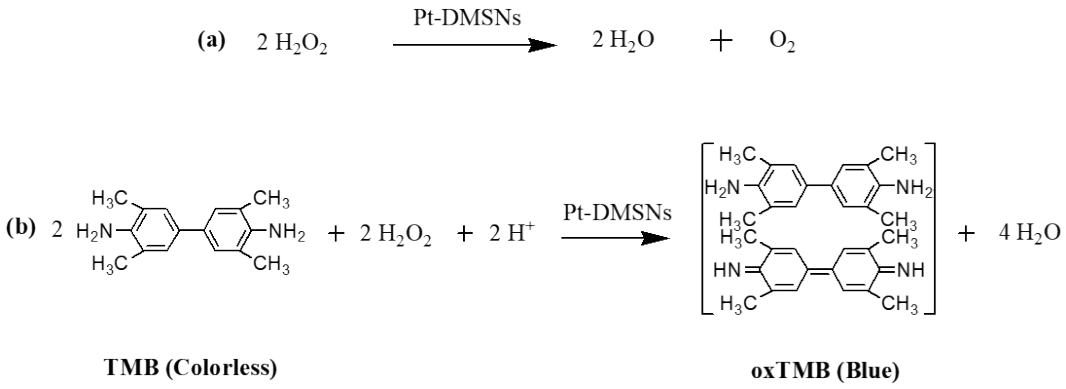

Figure S4. (a) The equation of peroxidase-like reaction between Pt-decorated DMSNs-based system and H_2O_2. (b) The equation of peroxidase-like reaction between Pt-decorated DMSNs-based nanoparticles and TMB in acidic solution.

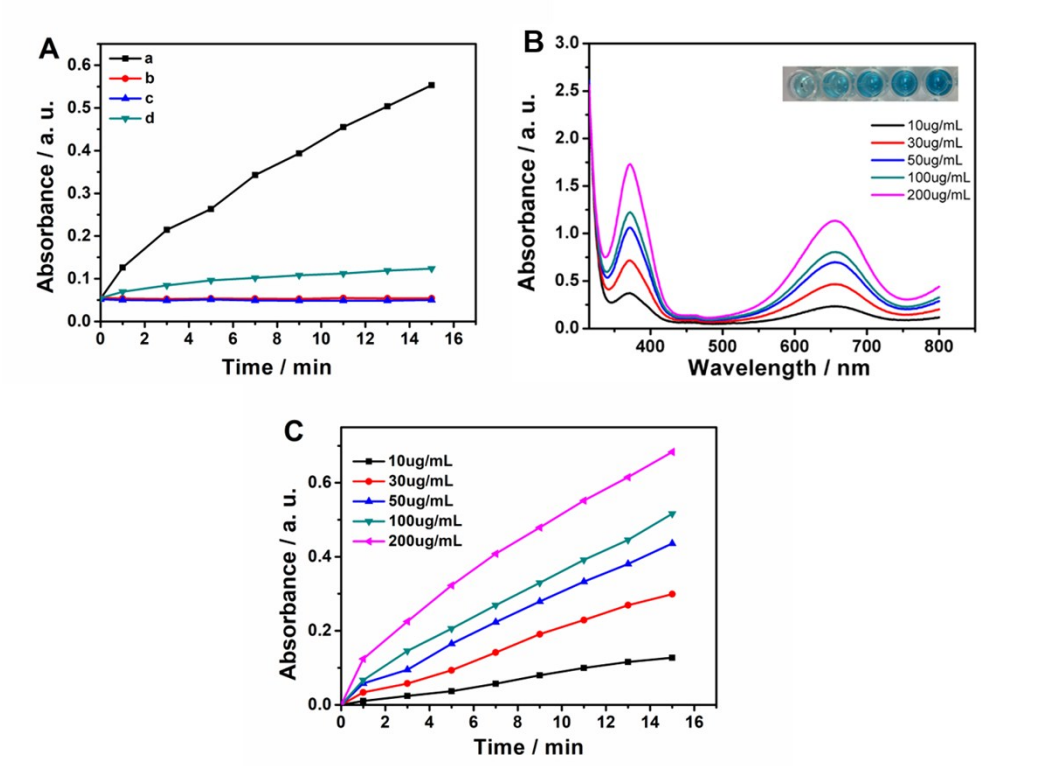

Figure S5. (A) Time-dependent absorbance changes at 652 nm of TMB solutions in different system: (a) TMB+H_2O_2+Pt-DMSNs/Ce6, (b) TMB+H_2O_2+DMSNs/Ce6, (c)

TMB+H_2O_2, (d) TMB+Pt-DMSNs/Ce6. H_2O_2: 10 mM, TMB: 1 mM. (B) UV-vis absorption spectra of different concentrations of Pt-DMSNs/Ce6 nanoparticles containing 10 mM H_2O_2 and 1 mM TMB. (C) Comparison of the time-dependent absorbance evolution at 652 nm for different concentration of Pt-DMSNs/Ce6 nanoparticles.

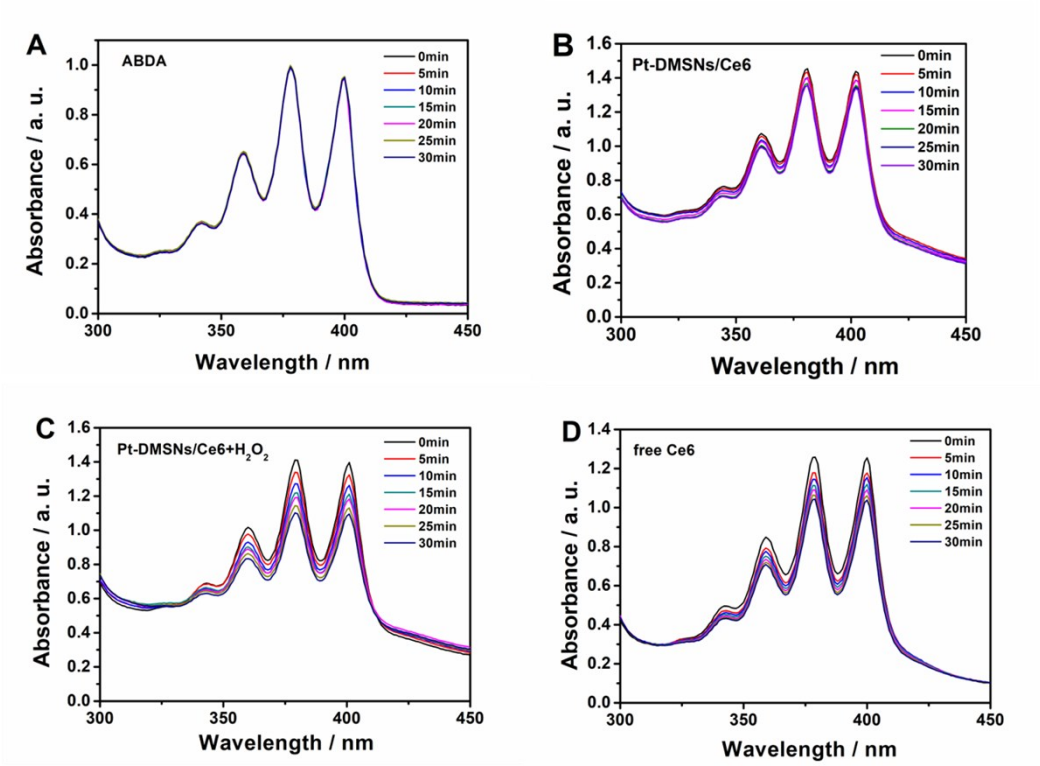

Figure S6. UV-vis absorption spectra of ABDA (A) under 660 nm laser irradiation for different time in the presence of (B) Pt-DMSNs/Ce6, (C) Pt-DMSNs/Ce6+H_2O_2 and (D) free Ce6.

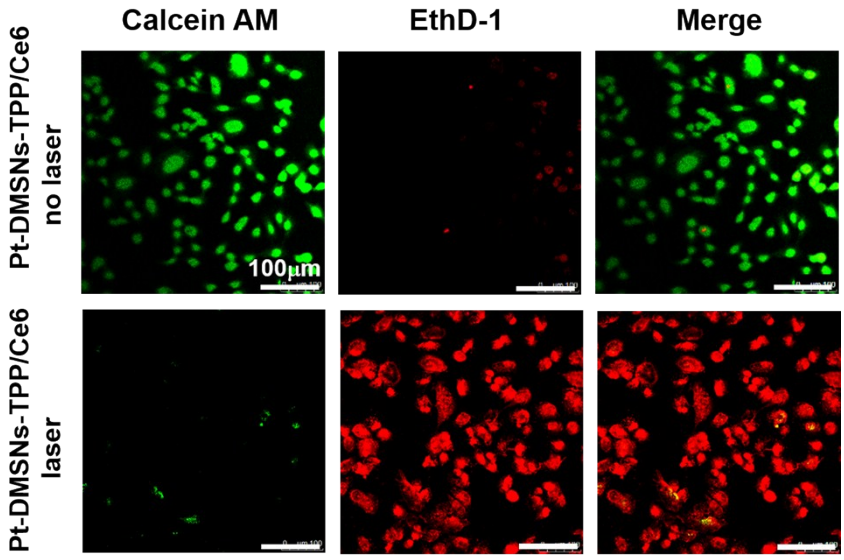

Figure S7. CLSM images of cell viability treated with Pt-DMSNs-TPP/Ce6 with and without laser irradiation. The cells were stained with live/dead viability (green: live cells, red: dead cells). All laser irradiation was 5 min (660 nm, 50 mW cm^{-2}).