

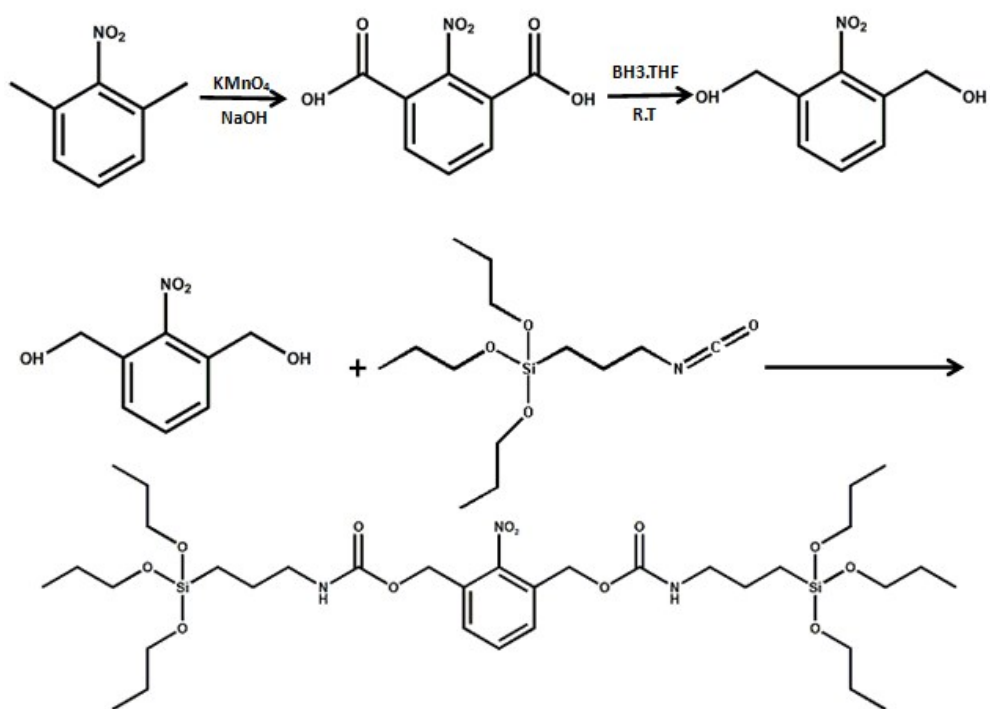
## Supporting Information

### **DOX-UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub> nanocomposites for near-infrared photocontrolled chemo/photodynamic therapy**

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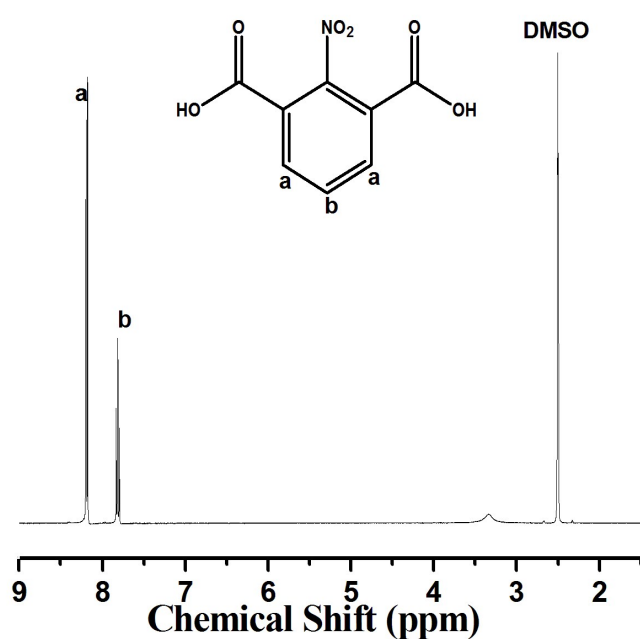
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**Scheme S1.** Synthetic route for the NB linker.

### The Synthesis of 2-nitro-1,3-benzenedicarboxylic acid

1,3-dimethyl-2-nitrobenzene (3.95 g, 0.105 mol), water (200 mL) and sodium hydroxide (1.6 g, 0.16 mol) were added into a three neck flask, which was stirred and heated to 95 °C in oil bath, then  $\text{KMnO}_4$  (16.5 g, 0.418 mol) was added in batches over a period of 3 h. The resulting mixture was refluxed for another 20 h, cooled and filtered, the filtrate was acidified with concentrated HCl and the precipitate was collected and dried.



**Fig.S1** The  $^1\text{H}$ NMR spectrum of 2-nitro-1,3-benzenedicarboxylic acid.

### The Synthesis of 2-nitro-1,3-benzenedimethanol

A solution of 2-nitro-1,3-benzenedicarboxylic acid (1.6 g, 38 mmol) in 10 mL anhydrous THF (dried with molecular sieve) was added to three neck flask and cooled to 0 °C in the presence of N<sub>2</sub>. Besides, 1.0 M borane-tetrahydrofuran (40 mL) was added dropwise over about 1 h with constant pressure drop funnel. The reaction mixture was allowed to warm slowly to room temperature and stirred as well as refluxed for another 48 h. Afterwards, Methanol (8 mL) was added into the reaction system slowly by constant pressure drop funnel, then the mixture was evaporated with a rotary evaporator at 40 °C. The residue was redissolved in ethyl acetate and washed three to four times with water ( 100 mL). The organic layer was dried with anhydrous MgSO<sub>4</sub> overnight, the next day the solvent was evaporated once again with a rotary evaporator at 40 °C. The resulting yellow solid was further purified by silica gel chromatography (hexane:ethyl acetate=1:1) to obtain 2-nitro-1,3-benzenedimethanol.

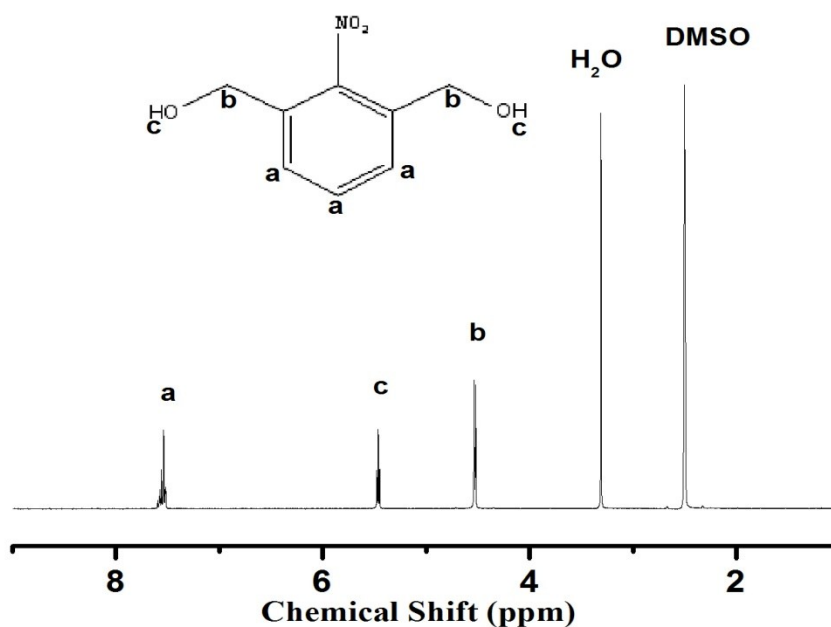


Fig.S2 The <sup>1</sup>H NMR spectrum of 2-nitro-1,3-benzenedimethanol.

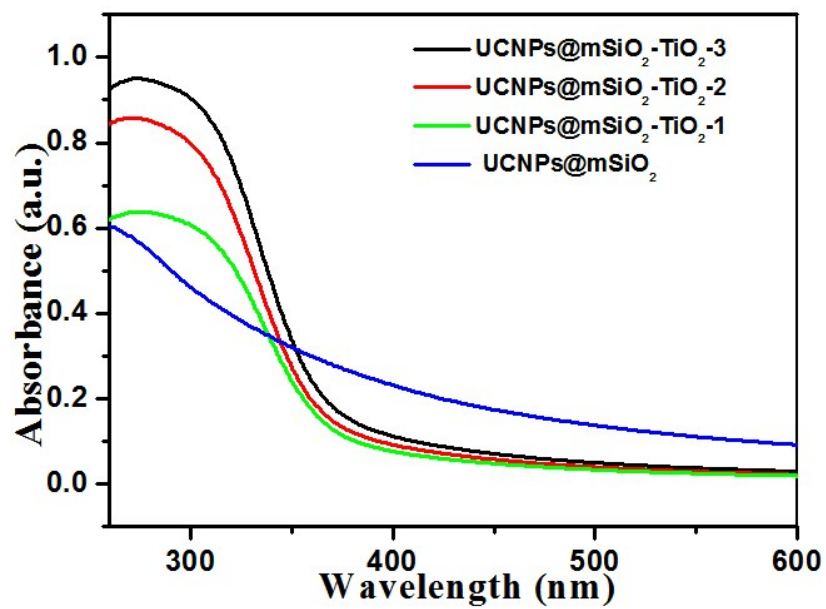
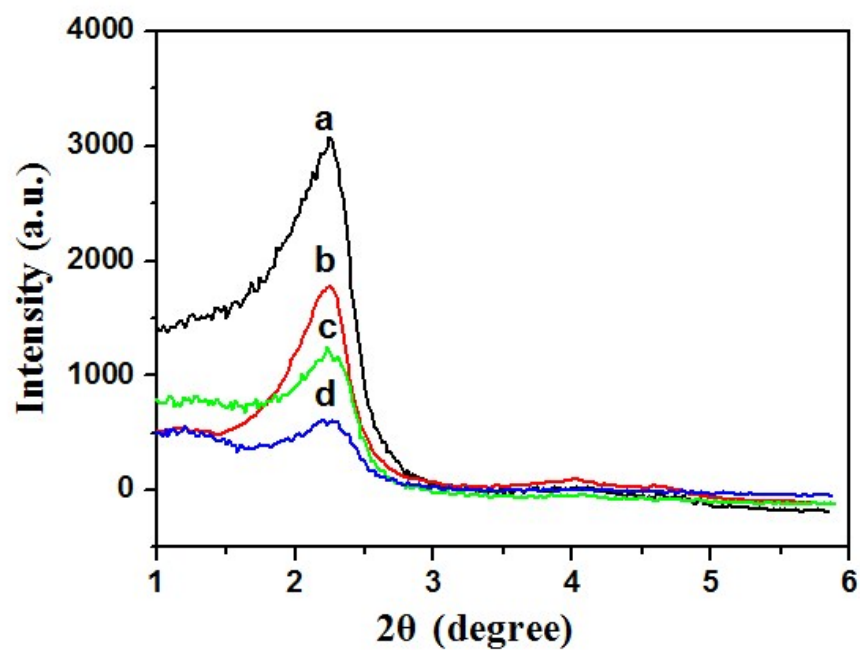


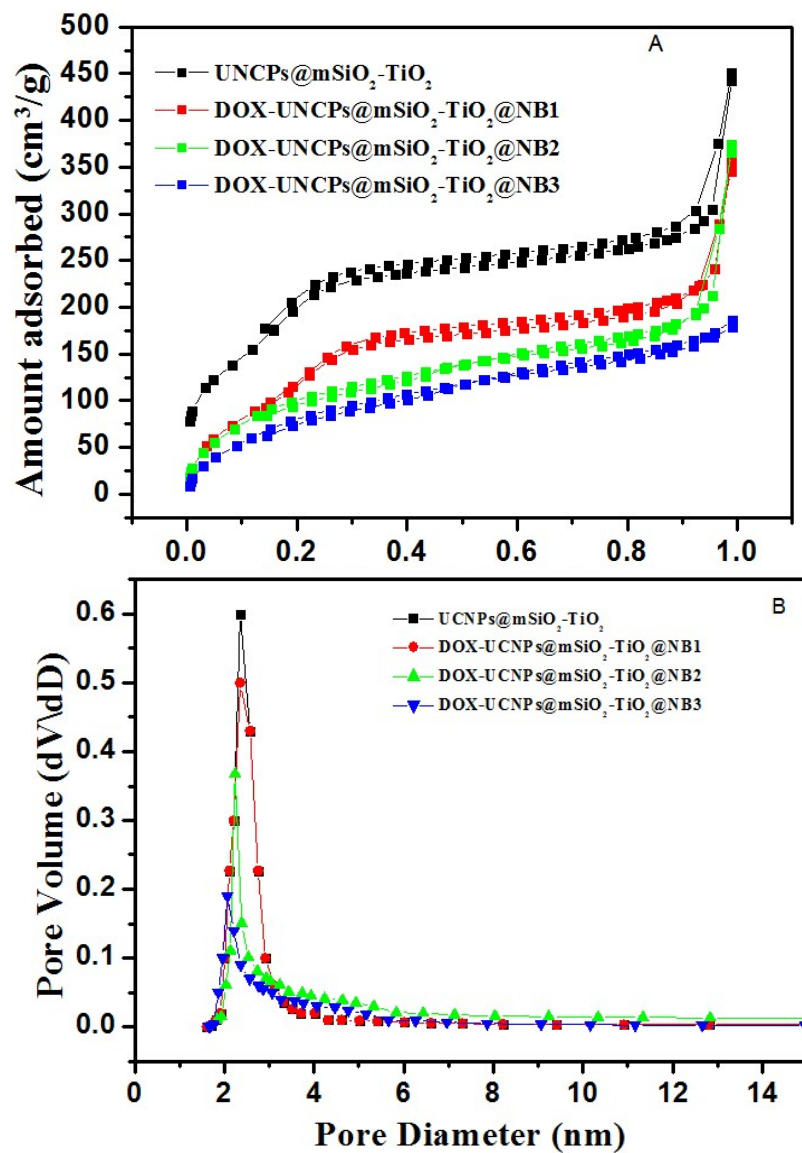
Fig.S3 The UV-Vis absorption spectra of the samples with different amounts of doped-TiO<sub>2</sub>.

Table S1 The porous parameters of the samples

Sample	Surface area (m <sup>2</sup> g <sup>-1</sup> )	Pore volume (cm <sup>3</sup> g <sup>-1</sup> )	Pore size (nm)
UCNPs@mSiO <sub>2</sub>	724	0.7	2.57
UCNPs@mSiO <sub>2</sub> -TiO <sub>2</sub> -1	599	0.68	2.46
UCNPs@mSiO <sub>2</sub> -TiO <sub>2</sub> -2	573	0.66	2.35
UCNPs@mSiO <sub>2</sub> -TiO <sub>2</sub> -3	333	0.35	1.65

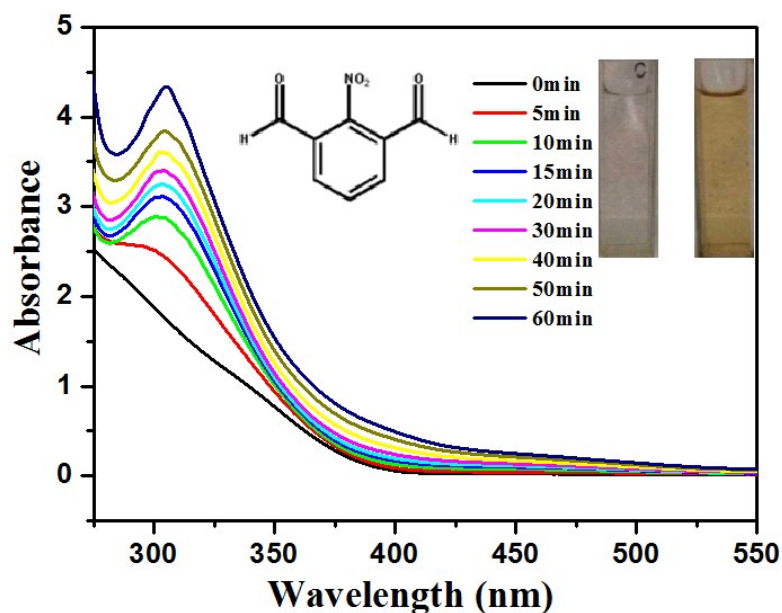
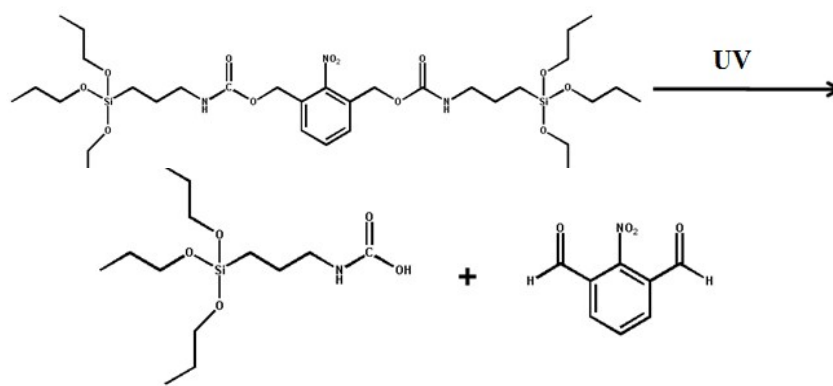


**Fig.S4** Low-angle XRD patterns of (a) UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub>, (b) DOX-UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub>@NB1, (c) DOX-UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub>@NB2, and (d) DOX-UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub>@NB3.



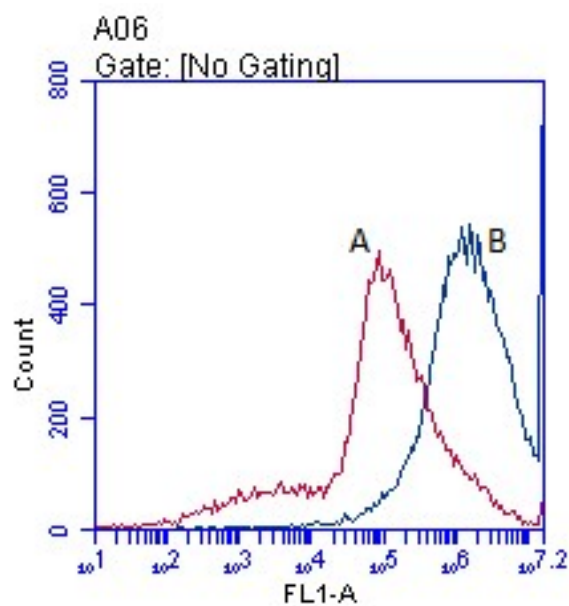
**Fig.S5** Nitrogen adsorption–desorption isotherms (A) and the pore size distribution curves of (B) UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub>, DOX-UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub>@NB1, DOX-UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub>@NB2 and DOX-UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub>@NB3.



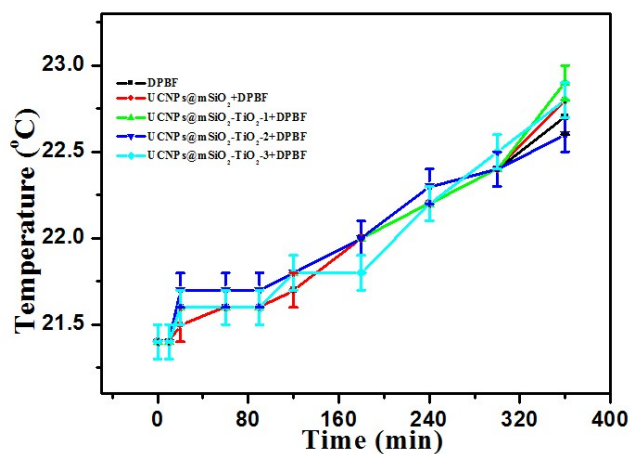


**Fig.S6** UV-Vis spectra of NB linker solution after treated with UV irradiation for different time.

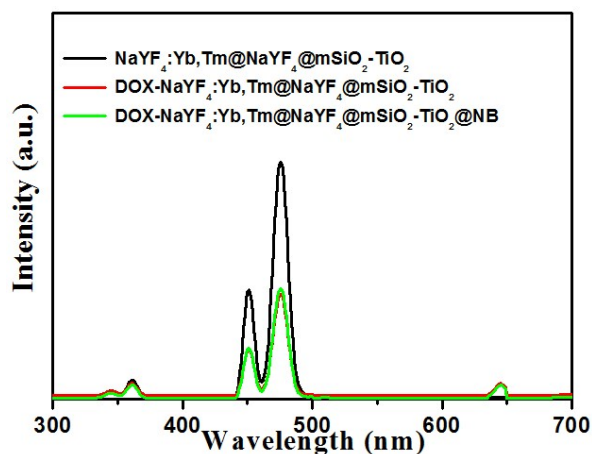
Based on the above equation, NB linker could be broken under UV irradiation, and UV-Vis adsorption was used to survey photolysis of NB. Fig S6 shows the UV-Vis spectra of NB linker (30  $\mu$ L, 0.26 M) dissolved in PH 6.5 PBS (3 mL) treated by UV irradiation for different time. The increased absorbance at about 300~350 nm owing to the 2-nitro-1,3-benzenedialdehyde fall off from NB linker. And the inset photo exhibits the color change for NB linker solution before and after the UV irradiation.



**Fig.S7** Flow cytometry analysis of the HeLa cells incubated with FITC modified DOX-UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub>@NB2 (red) and DOX-UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub>@NB2-FA (blue).



**Fig. S8** The temperature changes of each sample after 980 nm irradiation for different time. (the irradiation power density of 1.5 W cm<sup>-2</sup>)



**Fig.S9** The upconversion fluorescence spectra of DOX-UCNPs@SiO<sub>2</sub>-TiO<sub>2</sub> and DOX-UCNPs@SiO<sub>2</sub>-TiO<sub>2</sub>@NB linker under 980 nm excitation.



**Fig. S10** DCF fluorescence images of HeLa cells incubated with UCNPs@mSiO<sub>2</sub>-TiO<sub>2</sub> under NIR irradiation (1.5 W cm<sup>-2</sup>) for 0, 20, 30 min.

ROS generation was detected using DCFH-DA, which is oxidized to form (2',7'-dichlorofluorescein, DCF) a green fluorescent substance inside cells, as indicator. After excited by 980 nm light, the green fluorescence enhances with the prolonging of irradiation time, owing to the ROS generation.