

Supplementary Information

Ultralow-intensity near infrared light synchronously activated collaborative Chemo/Photothermal/Photodynamic therapy

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1. Details of process for UCNP synthesis

1.1. Synthesis of NaYF₄:Yb/Er nanoparticles

YCl₃•6H₂O (1.56 mmol), YbCl₃•6H₂O (0.4 mmol), and ErCl₃•6H₂O (0.04 mmol) were added to a 250 mL three-neck round-bottom flask containing oleic acid (12 mL) and 1-octadecene (30 mL). In the presence of argon, the mixture was slowly heated to 160 °C and kept at this temperature for 120 min under vigorous magnetic stirring. After the mixture was cooled down to 50 °C, a solution of ammonium fluoride (8 mmol) and sodium hydroxide (5 mmol) dissolved in methanol (15 mL) was added, then the mixture was stirred at 50 °C for 30 min. After methanol was evaporated, the solution was heated to 300 °C and kept at this temperature for 60 min. When the reaction was completed, the mixture was cooled down to room temperature. The particles were centrifuged and washed 3 times by ethanol, and then the particles were dispersed in 10 mL cyclohexane.

1.2. Synthesis of core-shell structured YF₄:Yb/Er@NaYF₄:Yb:Nd nanoparticles

2.0 mmol as-prepared NaYF₄:Yb/Er@NaYF₄:Yb:Nd nanoparticles (dispersed in cyclohexane), YCl₃•6H₂O (0.5 mmol), YbCl₃•6H₂O (0.1 mmol) and NdCl₃•6H₂O (0.4 mmol) were added to a 250 mL three-neck round-bottom flask containing oleic acid (12 mL) and 1-octadecene (30 mL). The mixture was slowly heated to 160 °C and kept at this temperature for 120 min under vigorous magnetic stirring under argon atmosphere. After the mixture was cooled down to 50 °C, a solution of ammonium fluoride (4 mmol) and sodium hydroxide (2.5 mmol) dissolved in methanol (15 mL) was added, and the mixture was stirred at 50 °C for 30 min. After methanol was evaporated, the solution was heated to 300 °C and kept at this temperature for 90 min. When the reaction was completed, the mixture was cooled down to room temperature.

The particles were centrifuged and washed 3 times by ethanol, and Then the particles used as UCNP cores were dispersed in 10 mL cyclohexane.

1.3. Synthesis of core-shell-shell structured NaYF₄:Yb/Er@NaYF₄:Yb:Nd@NaYF₄ (UCNP) nanoparticles

2.0 mmol as-prepared NaYF₄:Yb/Er@NaYF₄:Yb:Nd nanoparticles (dispersed in cyclohexane), and YCl₃•6H₂O (1.4 mmol) were added to a 250 mL three-neck round-bottom flask containing oleic acid (12 mL) and 1-octadecene (30 mL). The mixture was slowly heated to 160 °C and kept at this temperature for 120 min under vigorous magnetic stirring under argon atmosphere. After the mixture was cooled down to 50 °C, a solution of ammonium fluoride (5.6 mmol) and sodium hydroxide (3.5 mmol) dissolved in methanol (15 mL) was added, and the mixture was stirred at 50 °C for 30 min. After methanol was evaporated, the solution was heated to 300 °C and kept at this temperature for 90 min. When the reaction was completed, the mixture was cooled down to room temperature. The particles were centrifuged and washed 3 times by ethanol, and then the particles used as UCNP cores were dispersed in 20 mL cyclohexane.

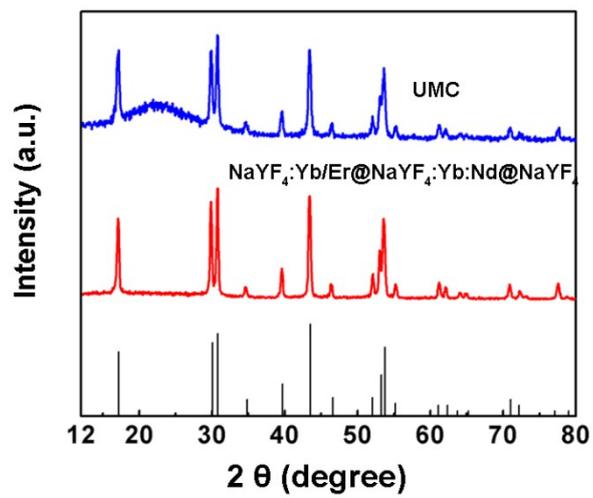


Figure S1. XRD patterns of UCNPs and UMC.

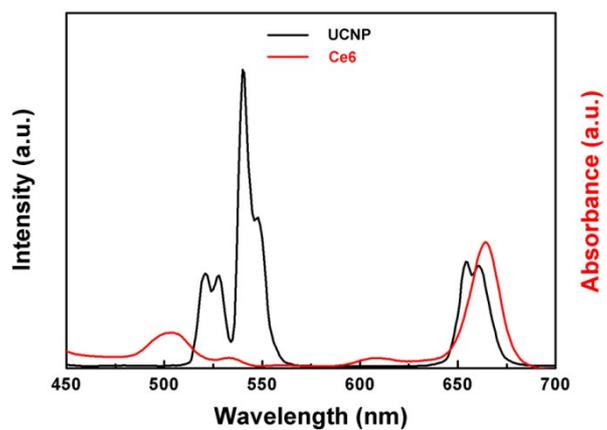


Figure S2. Upconversion fluorescent spectra of $\text{YF}_4:\text{Yb}/\text{Er}@\text{NaYF}_4:\text{Yb}:\text{Nd}@\text{NaYF}_4$ (black) under NIR light excitation ($\lambda = 808 \text{ nm}$, 2.0 W cm^{-2}) and UV-vis absorption of Ce6 (red).

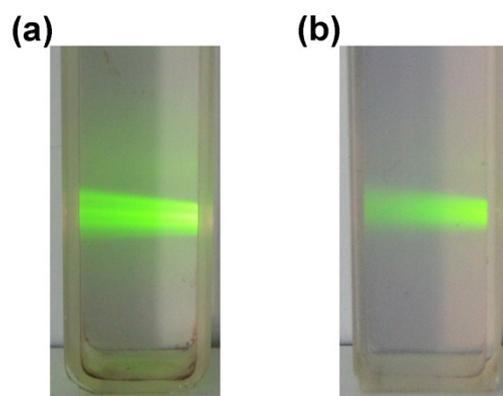


Figure S3. (a) Upconversion fluorescent photographs of core-shell-shell structured $\text{NaYF}_4:\text{Yb}/\text{Er}@\text{NaYF}_4:\text{Yb}:\text{Nd}@\text{NaYF}_4$ under ultralow-power 808 nm light excitation (0.3 W). (b) The widely used $\text{NaYF}_4:\text{Yb}/\text{Er}$ under high-power 980 nm light excitation (2.0 W).

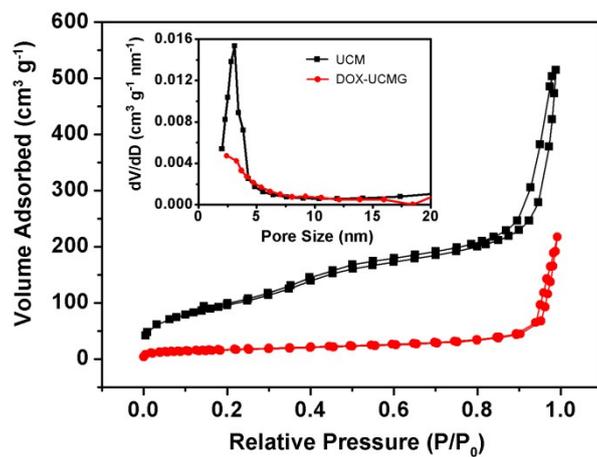


Figure S4. N₂ adsorption–desorption isotherm and pore distribution of UCM and DOX-UCMG.

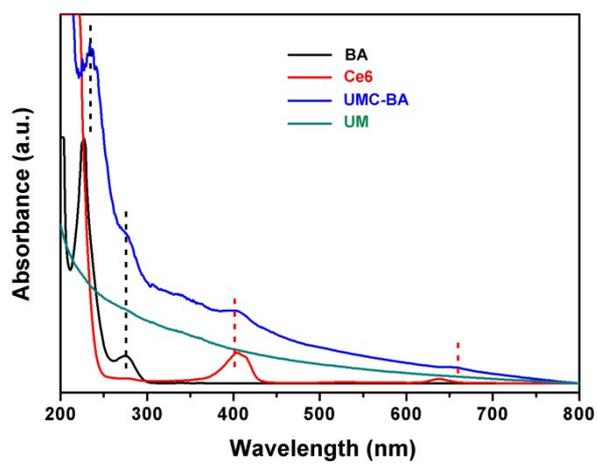


Figure S5. UV-vis spectra of BA, Ce6, UMC-BA and UM.

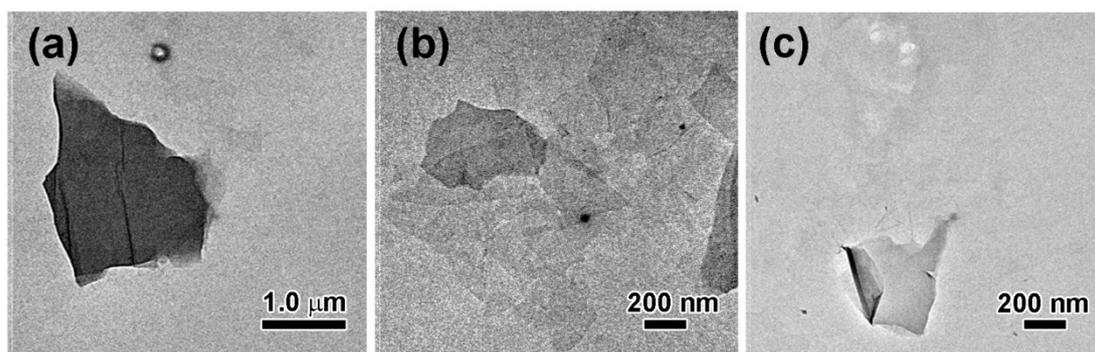


Figure S6. TEM images of (a) GO flake, and (b, c) a single layer GO sheet.

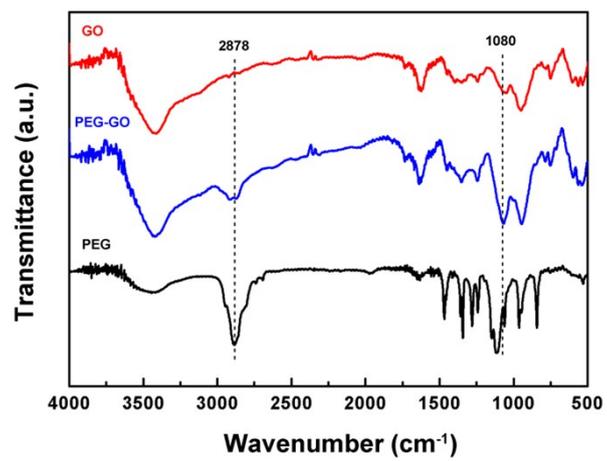


Figure S7. FT-IR of GO, PEG-GO and PEG.

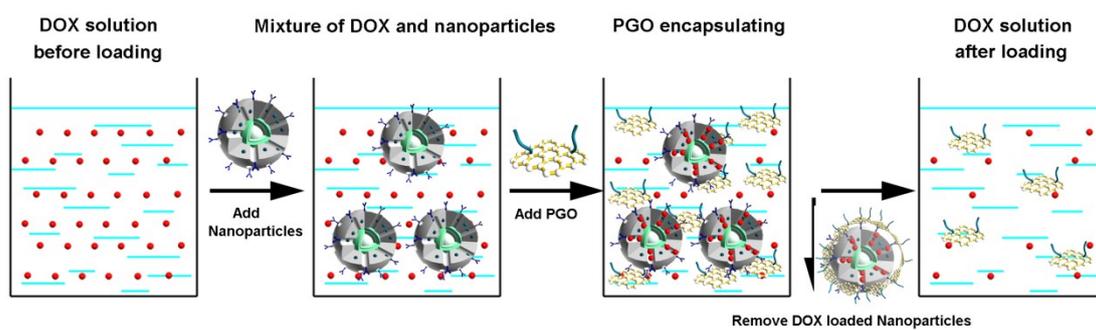


Figure S8. Schematic illustration of DOX loading and PGO encapsulating.

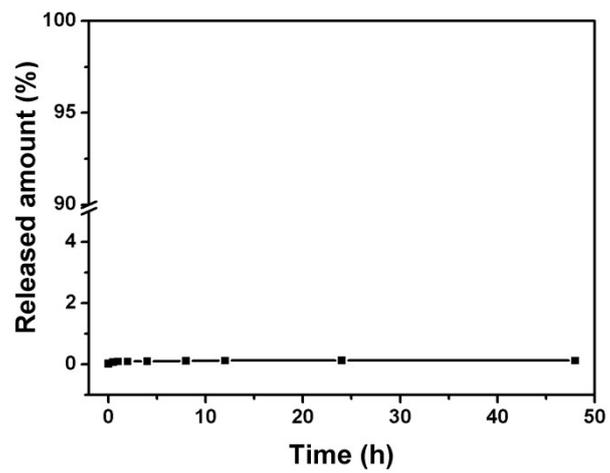


Figure S9. Release profile of Ce6 from DOX-UMCG nanoparticles.

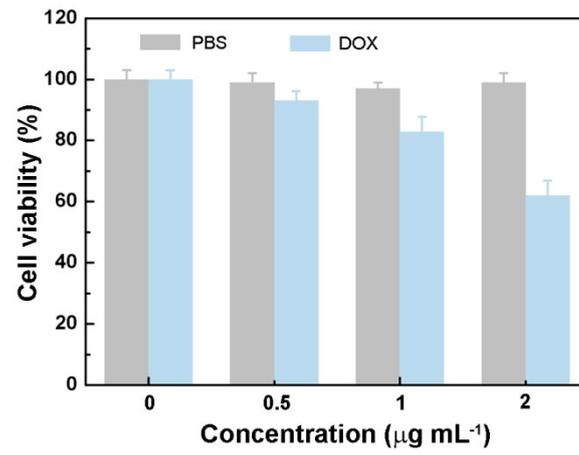


Figure S10. Viabilities of HeLa cells treated with the same DOX dosage.



Figure S11. Photodamage of the mice after continuous 10 min of 808 nm light irradiation with 2.0 W/cm², which suggests the employment of ultralow-intensity NIR light for phototherapy to avoid photodamage is quite essential.

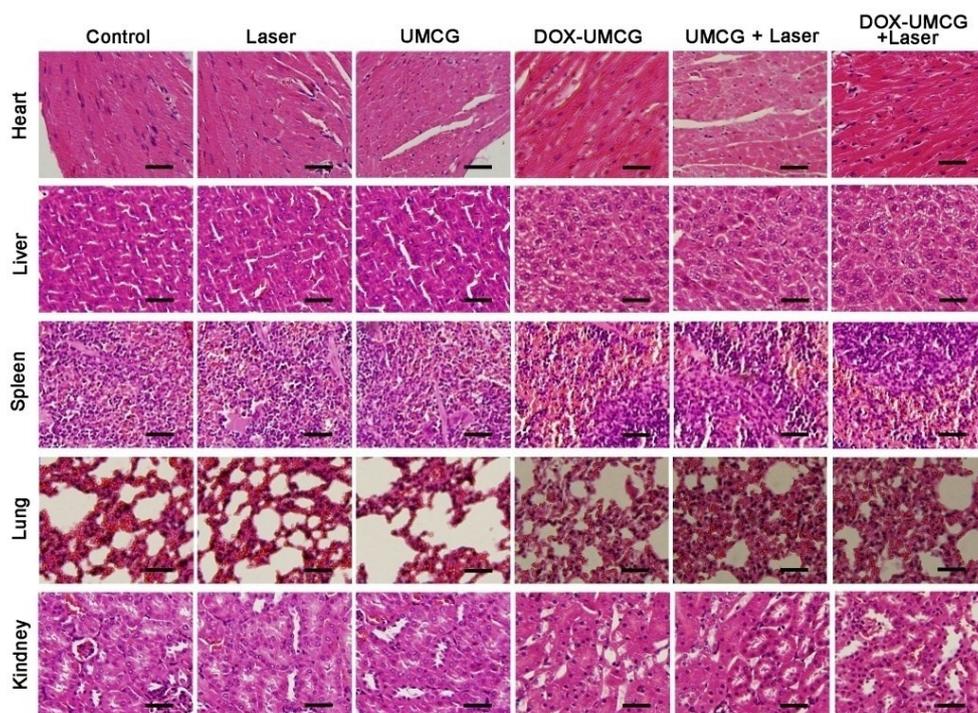


Figure S12. H&E staining of major organs collected from mice after various treatments.

Scale bars for all images are 50 μm.