Supporting Information

Emitter-Active Shell in $NaYF_4$:Yb,Er/$NaYF_4$:Er Upconversion Nanoparticles for Enhanced Energy Transfer in Photodynamic Therapy

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1. REAGENTS AND INSTRUMENTATION

1.1 Reagents. YCl_3 (99.99%), $YbCl_3$ (99.9%), $ErCl_3$ (99.99%), CF_3COONa (98%), oleic acid (OA, 90%), Oleylamine (80-90%), 1-Octadecene (ODE, 90%), poly(allylamine) solution (PAAM, 20 wt.%, Mw~17,000), rose bengal (RB, 95%), 6-bromohexanoicacid (97%), N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDC, premium), N-hydroxysulfosuccinimide sodium salt (NHS, >98%) and 1,3-diphenylisobenzofuran (DPBF, 97%) were purchased from Sigma-Aldrich. $Y(CF_3COO)_3 \cdot 3H_2O$ (99.9%) and NH_4F (>98.0%) was from Alfa Aesar. $Er(CF_3COO)_3 \cdot 3H_2O$ (99.9%) was purchased from GFS Chemicals. NaOH (>90%) was purchased from Merck KGaA. Dulbecco's modified eagle's medium (DMEM), trypsin and bovine fetal blood serum (FBS) were purchased from Gibco. Cell Counting Kit-8 (CCK-8) reagent was from Dojindo. 2′,7′-Dichlorodihydrofluorescein diacetate (DCFH-DA, ≥ 97%) was purchased from Macklin. Calcein-AM/propidium iodide (PI) Double Stain Kit was obtained from KeyGEN BioTECH. Annexin-V-fluorescein isothiocyanate (FITC) was purchased from Solarbio. All the other solvents were of analytical grade and used as received without further purification.

1.2 Instrumentation. The morphology of the UCNPs was characterized by a transmission electron microscope (TEM, JEM-2100 Plus, Japan). Dynamic light scattering (DLS) results were obtained by using a Malvern Zetasizer Nano system (Nano ZS90). The composition of the rare earth ions in UCNPs were obtained by dissolving them with nitric acid and then analyzing with inductively coupled plasma atomic emission spectrometer (ICP-AES, Prodigy, America). X-ray diffraction (XRD) patterns were acquired using a Rigaku D/MAX-2400 diffractometer with Cu-Kα radiation. Fourier transform infrared (FTIR) transmittance spectra were recorded with Nicolet IS10 spectrometer under the liquid nitrogen environment. Absorption spectra of the centrifugal supernatant were recorded using Shimadzu UV2600 spectrometer to calculate the incorporation amount of RB on the UCNPs. Absorption spectra of the UCNPs were acquired with Hitachi UH-4150 spectrometer. The absorption of Yb sensitizer at ~980 nm was used to adjust the concentration of different samples the

same. Upconversion luminescence spectra of the nanoparticle dispersions were recorded using a fluorescence spectrometer (HORIBA (PTI) QuantaMaster 400) configured with a 980 nm laser diode (Hi-Tech Optoelectronics Company Limited). Temporal behaviors of the upconversion luminescence were monitored by a transient fluorescence spectrometer (JY HORIBA FluoroLog-3, France) configured with a nanosecond tunable laser (Quanta-Ray LAB-170-10H/PR IMOSCAN/ULD-240).

2. SUPPORTING FIGURES

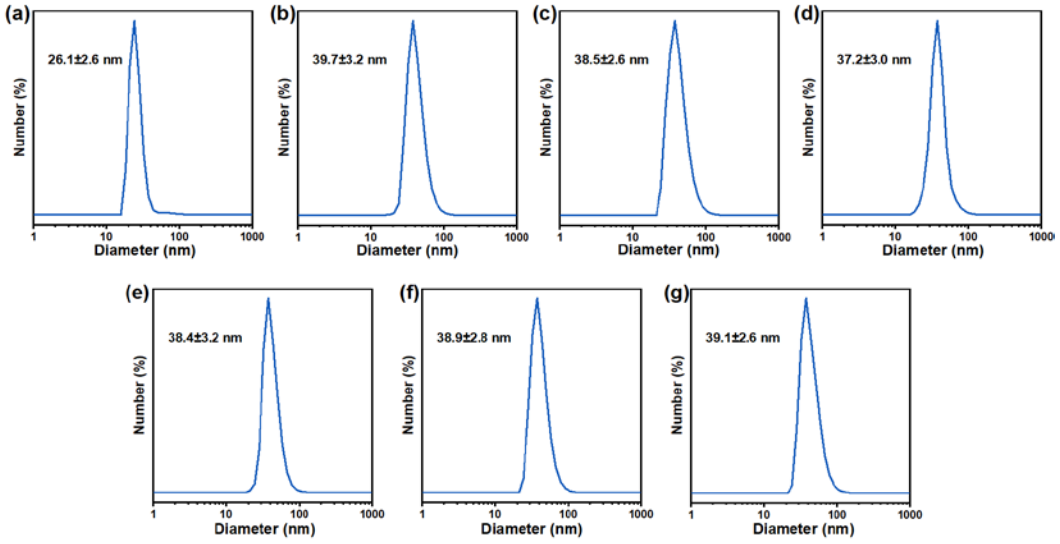

Figure S1. DLS results of (a) $NaYF_4$:Yb,Er/oleate and $NaYF_4$:Yb,Er/$NaYF_4$:Er/oleate UCNPs with (b) 0.0%, (c) 0.2%, (d) 0.5%, (e) 1.0%, (f) 2.0% and (g) 5.0% Er^{3+} in the shell.

Table S1. Relative contents of Yb^{3+}, Er^{3+} and Y^{3+} in $NaYF_4$:Yb,Er core and $NaYF_4$:Yb,Er/$NaYF_4$:Er core/shell UCNPs obtained by ICP analyses.

	Core	$CS_{0.0\%Er}$	$CS_{0.2\%Er}$	$CS_{0.5\%Er}$	$CS_{1.0\%Er}$	$CS_{2.0\%Er}$	$CS_{5.0\%Er}$
Yb^{3+}	0.190	0.142	0.167	0.169	0.170	0.167	0.167
Er^{3+}	0.021	0.008	0.012	0.015	0.021	0.050	0.073
Y^{3+}	0.789	0.850	0.821	0.816	0.809	0.783	0.760

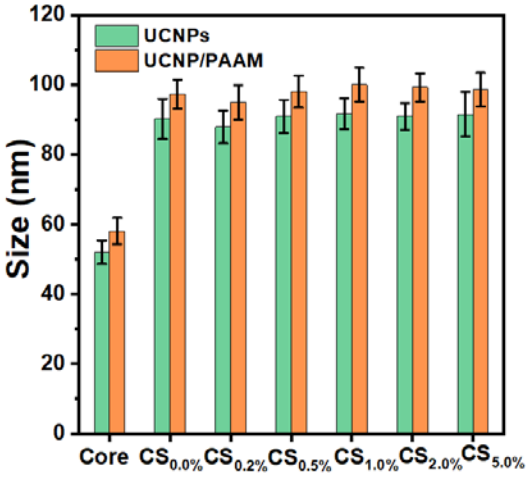

Figure S2. DLS results of bare and PAAM-modified $NaYF_4$:Yb,Er core and $NaYF_4$:Yb, Er/$NaYF_4$:Er core/shell with various doping concentrations of Er in the shell.

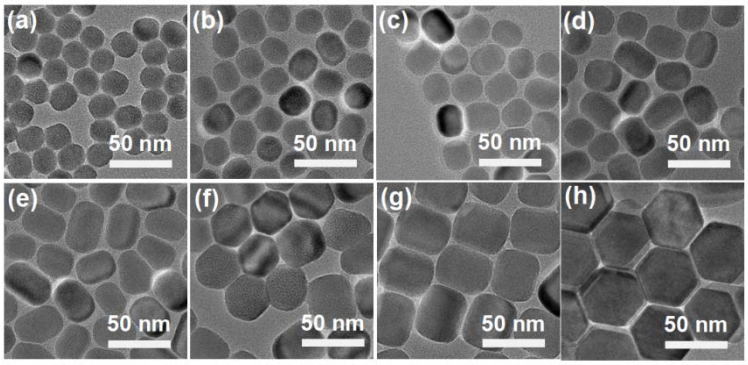

Figure S3. TEM images of $NaYF_4$:Yb,Er/$NaYF_4$: 0.5% Er/oleate with increasing shell thickness from (a) CS1 to (h) CS8.

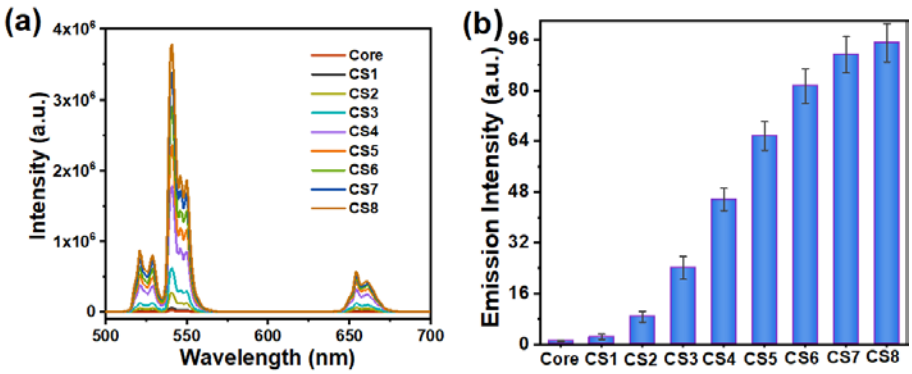

Figure S4. (a) Emission spectra and (b) integrated emission intensities of $NaYF_4$:Yb,Er/PAAM and $NaYF_4$:Yb,Er/$NaYF_4$:0.5% Er/PAAM with different shell thicknesses under 980 nm excitation.

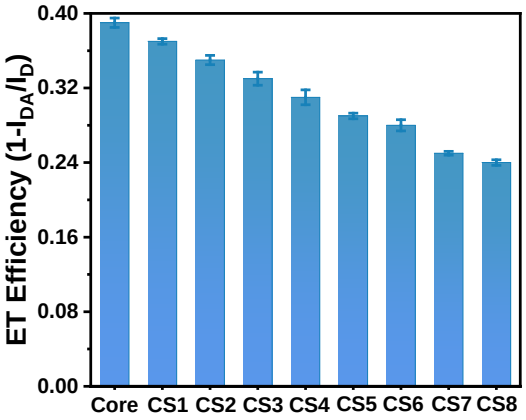

Figure S5. ET efficiency of the UCNP/RB therapeutic agents with different thicknesses of $NaYF_4$: 0.5% Er emitter-active shell.

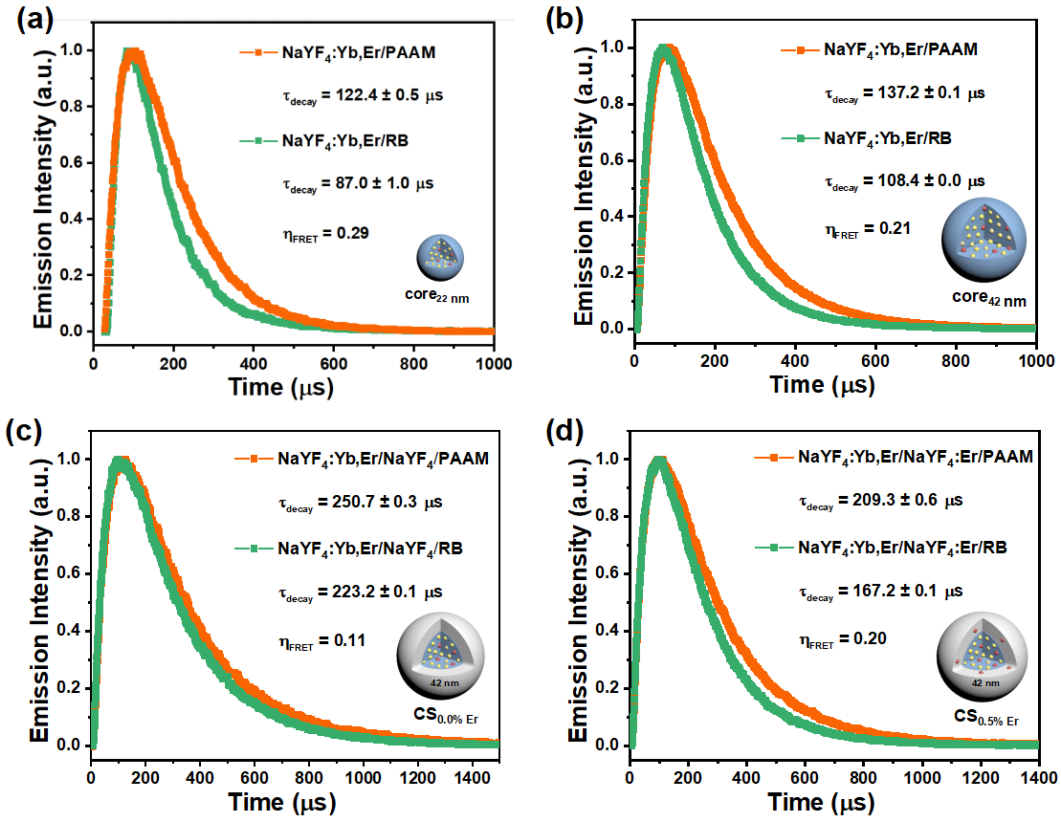

Figure S6. Temporal behaviors of the green upconversion luminescence (540 nm) from (a) ~22 nm $NaYF_4$:Yb,Er/PAAM, (b) ~42 nm $NaYF_4$:Yb,Er/PAAM, (c) ~42 nm $NaYF_4$:Yb,Er/$NaYF_4$/PAAM and (d) ~42 nm $NaYF_4$:Yb,Er/$NaYF_4$: 0.5% Er/PAAM with and without RB attached under 980 nm excitation.

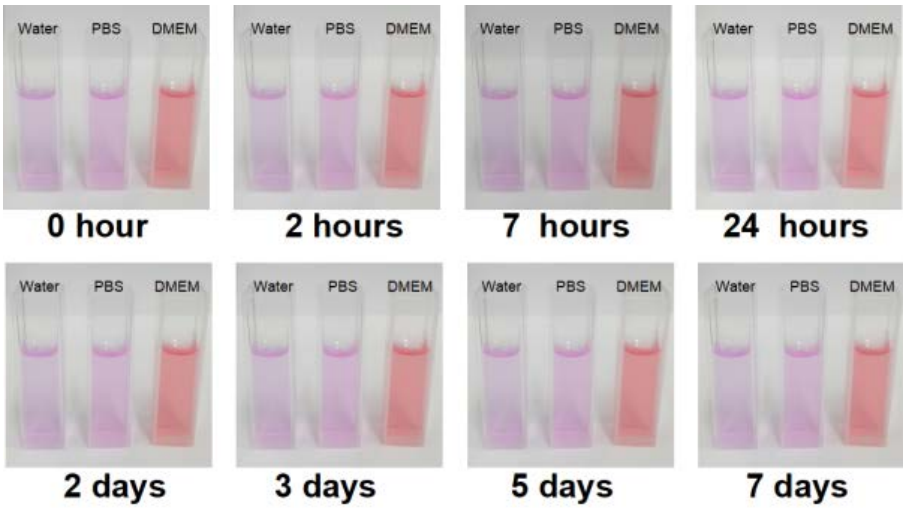

Figure S7. Digital photographs of the $NaYF_4$:Yb,Er/$NaYF_4$:Er/RB therapeutic agents dispersed in water, PBS and DMEM for varied durations.

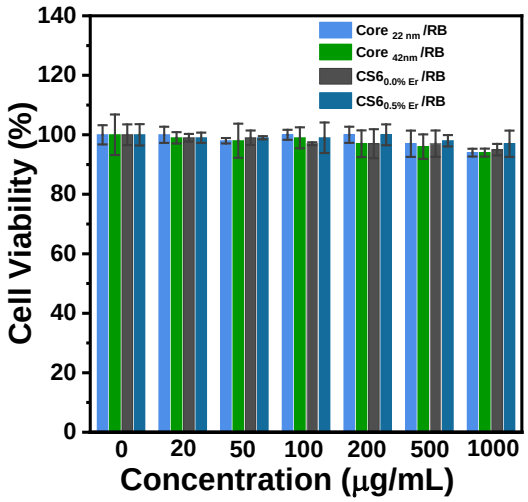

Figure S8. Viability of U87MG cells obtained by CCK-8 method. The cells were treated with the UCNP/RB therapeutic agents at different concentrations.

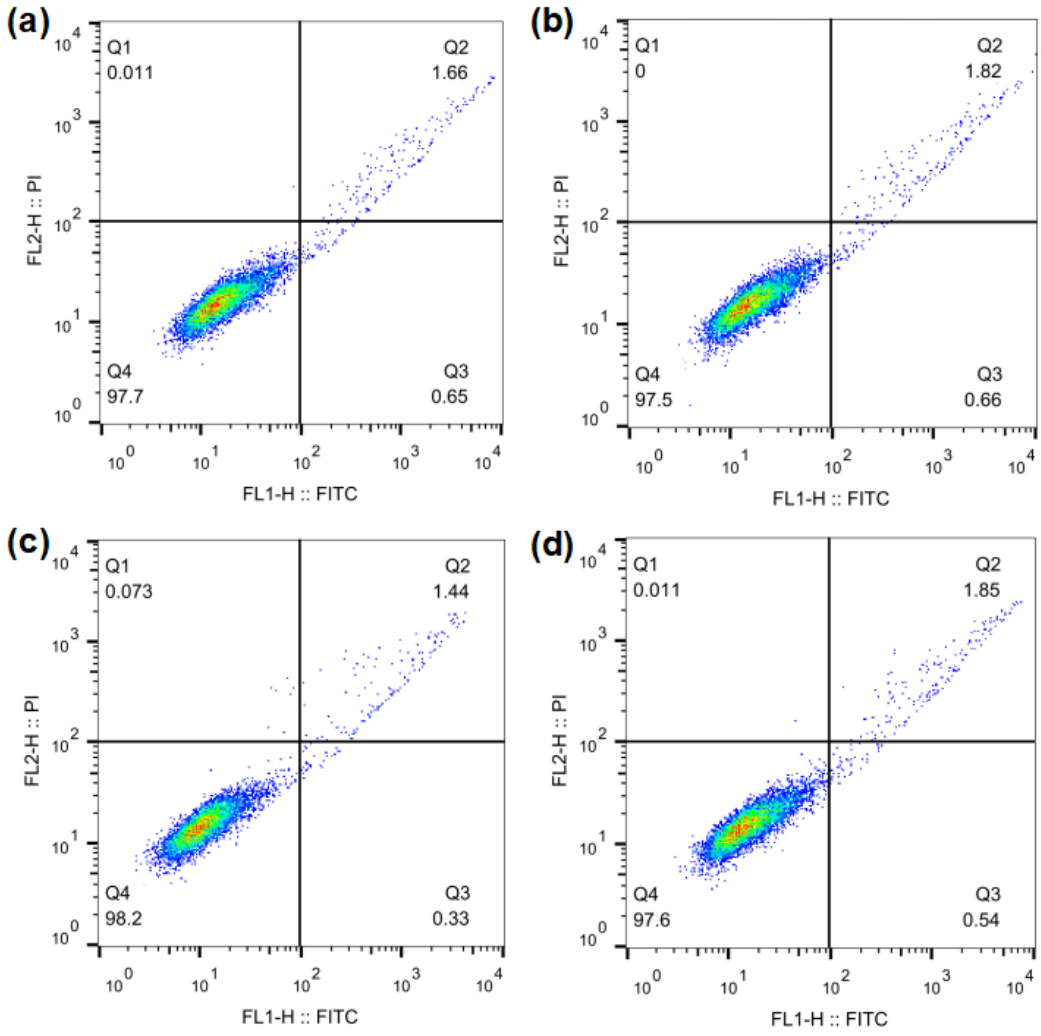

Figure S9. Flow cytometry analyses of U87MG cells after incubation with (a) ~22 nm $NaYF_4$:Yb,Er/RB, (b) ~42 nm $NaYF_4$:Yb,Er/RB, (c) ~42 nm $NaYF_4$:Yb,Er/$NaYF_4$/RB and (d) ~42 nm $NaYF_4$:Yb,Er/$NaYF_4$: 0.5% Er/RB. All of these therapeutic agents are 500 μg/mL.

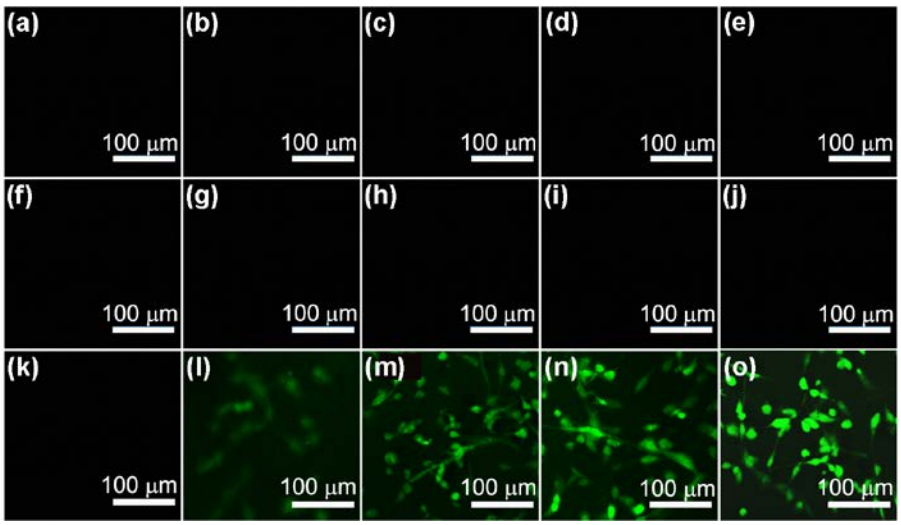

Figure S10. Detection of ROS produced in U87MG cells stained by DCFH-DA: (a) Blank; (b) NIR irradiation; (c) RB, (d) ~22 nm $NaYF_4$:Yb,Er/PAAM, (e) ~42 nm $NaYF_4$:Yb,Er/PAAM, (f) ~42 nm $NaYF_4$:Yb,Er/$NaYF_4$/PAAM and (g) ~42 nm $NaYF_4$:Yb,Er/$NaYF_4$:Er/PAAM under NIR irradiation; (h) ~22 nm $NaYF_4$:Yb,Er/RB, (i) ~42 nm $NaYF_4$:Yb,Er/RB, (j) ~42 nm $NaYF_4$:Yb,Er/$NaYF_4$/RB and (k) ~42 nm $NaYF_4$:Yb,Er/$NaYF_4$:Er/RB without NIR irradiation; (l) ~22 nm $NaYF_4$:Yb,Er/RB, (m) ~42 nm $NaYF_4$:Yb,Er/RB, (n) ~42 nm, $NaYF_4$:Yb,Er/$NaYF_4$/RB and (o) ~42 nm $NaYF_4$:Yb,Er/$NaYF_4$:Er/RB under NIR irradiation. The power density of 0.70 W/cm^2 and the exposure time of 10 min were adopted for the NIR irradiation.