## **Electronic Supplementary Information for**

Novel Multifunctional NaYF<sub>4</sub>:Er<sup>3+</sup>,Yb<sup>3+</sup>/PEGDA Hybrid Microspheres: NIR-Light-Activated Photopolymerization and Drug Delivery<sup>+</sup>

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## **Experimental Section**

Synthesis of PAA Modified  $NaYF_4:Er^{3+},Yb^{3+}$  UCNPs: Hexagonal phase NaYF<sub>4</sub>:Er<sup>3+</sup>,Yb<sup>3+</sup> UCNPs were synthesized by thermal decomposition of trifluoroacetate precursors in the solvents of 1-octadecene (ODE) and oleic acid (OA). In a typical procedure, CF<sub>3</sub>COONa (2 mmol), Y(CF<sub>3</sub>COO)<sub>3</sub> (0.78 mmol), Yb(CF<sub>3</sub>COO)<sub>3</sub> (0.2 mmol), and Er(CF<sub>3</sub>COO)<sub>3</sub> (0.02 mmol) were dissolved in ODE (12 mL) and OA (6 mL) at room temperature (RT) , the obtained mixture was heated under vigorouis stirring in N<sub>2</sub> atmosphere to remove water and oxygen (120 °C, 1 h). Thereafter, the mixture was heated at 320 °C for 1 h and then cooled to RT naturally. The resulting  $NaYF_4:Er^{3+},Yb^{3+}$  UCNPs were precipitated by addition of ethanol (20 mL), collected via centrifugation, washed with ethanol several times and then dried in a vacuum oven.

In order to obtain PAA modified UCNPs, the oleic-capped UCNPs were surface modified by PAA using a general ligand exchange procedure. Typically, diethylene glycol (15.0 mL) solution containing PAA (Mw≈1800) (0.4 g) was heated to 110 °C with vigorous stirring in N<sub>2</sub> atmosphere. Cyclohexane solution (10 mL) of NaYF<sub>4</sub>:Er<sup>3+</sup>,Yb<sup>3+</sup> UCNPs (0.4 mmol) was injected into the above hot solution and then the system was heated at 240 °C for 30 min. After the solution was cooled down to RT, excess dilute hydrochloric aqueous solution (0.10 M) was added to precipitate the PAA modified UCNPs. The precipitates were collected by centrifugation, washed several times with pure water, neutralized with a diluted solution of NaOH (0.01 M), and finally re-dispersed in D-PBS.

Synthesis of UCNPs/PEGDA Hybrid Microspheres Using NIR Light Photoinitiation: Typically, PEGDA (mol wt 2000) (40 mg) were dissolved in D-PBS (1 mL) containing triethanolamine (TEOA) (120 mM). Acrylic acid and N-vinylpyrrolidone (NVP) with equal number of moles as PEGDA molecules were added to PEGDA solutions. Then, D-PBS solution (1 mL) of Eosin Y (120  $\mu$ M), sodium sulfate (800 mM) and NaYF<sub>4</sub>:Er<sup>3+</sup>,Yb<sup>3+</sup> UCNPs (20 mg) was added to the PEGDA solution. The solution was maintained at 37 °C for 20 min and photopolymerized for 4 h upon laser irradiation at 980 nm (3W, Inter-Diff Optoelectronics Technology Co., Ltd, Shanghai) with proper stirring at RT. To avoid possible overheating effect from NIR laser, the NIR light was irradiated for 10 min with each interval of 10 min in dark. To monitor growth of UCNPs/PEGDA composites, small aliquots (~0.1 mL) of reaction mixture were taken at different growth periods. The obtained composites were then buffer-exchanged by centrifugation in D-PBS to remove the sodium sulfate.

*Cytotoxicity Assay*: MTT (thiazolyl blue tetrazolium bromide) assays were carried out to evaluate the potential cytotoxicity of PAA capped UCNPs and UCNPs/PEGDA hybrid microspheres in L929 (mouse fibroblast cell) cells. L929 cells were cultured with 1640 medium supplemented with 10% fetal bovine serum, 100 IU/ml penicillin, and 100 µg/ml streptomycin at 37 °C with 5% CO2. Cells of  $10^5$ /ml overnight and then incubated with 200 µL of 0 µg/mL, 20 µg/mL, 100 µg/mL, 200 µg/mL, 300 µg/mL, 400 µg/mL and 500 µg/mL of PAA capped UCNPs and UCNPs/PEGDA hybrid microspheres, respectively (n=3). After 24 h, MTT was added to each well of cells (final concentration 0.5mg/ml) and incubated for 4 h at 37 °Cin a humidified atmosphere of 95% air and 5% CO<sub>2</sub>. DMSO was added to solubilize the blue MTT-formazan product and the sample was incubated for a further 30 min at room temperature. Absorbance of the solution was read at a test wavelength of 490nm.

*Loading of ZnPc into UCNPs/PEGDA Hybrid Microspheres:* To load hydrophobic photosensitizer ZnPc into UCNPs/PEGDA hybrid microspheres, different amounts of ZnPc in dimethylformamide (DMF) solution (40-500 mM) were added into aqueous solution (2 mL) containing hybrid microspheres (10 mg) and stirred for 24 h. After removing free ZnPc by centrifugation, the obtained precipitate was washed with distilled water for several times and resuspended in D-PBS by sonication. To evaluate

the ZnPc loading amount, ZnPc was extracted from the UCNPs/PEGDA hybrid microspheres by ethanol, and the residual ZnPc content was determined using the calibration curve of ZnPc standard solutions by the UV-vis measurement at 650-680 nm. For comparison, ZnPc was loaded into submicro-flakes counterparts following the same procedure as the UCNPs/PEGDA hybrid microspheres.

*Production of Singlet Oxygen upon NIR Light Irradiation:* Singlet oxygen production from ZnPc loaded UCNPs/PEGDA hybrid microspheres as well as submicro-flakes counterparts were determined by the DPBF bleaching method. An ethanol solution of DPBF (300 ml, 2 mM) was added to ZnPc (100 mM) loaded UCNPs/PEGDA hybrid microspheres and submicro-flakes counterparts aqueous solution. The samples were continuously irradiated by 980 nm light (3W, Inter-Diff Optoelectronics Technology Co., Ltd, Shanghai) for 40 min under proper magnetic stirring, and the absorbance of DPBF around 350-500 nm was collected. For comparison, the absorbance of DPBF in solution of UCNPs/PEGDA hybrid microspheres with no ZnPc loaded was measured upon 980 nm excitation.

*Characterization:* XRD patterns were carried out on a BRUKER D8 Discover power diffractometer with Cu-Ka1 radiation ( $\lambda$ =0.154 nm). Both TEM and HRTEM measurements were performed using a Tecnai G<sup>2</sup> F20 S-Twin field-emission TEM. SEM measurements were performed using Quanta400 FEG field emission SEM and Inspect S tungsten filament SEM. TGA were performed with TG/DTA 6200 (SII EXSTAR 6000 of Seiko Instrument) under N<sub>2</sub> atmosphere in the temperature range from 80-580 °C at a rate of 5 °C min<sup>-1</sup>. UCL spectra were recorded on a Princeton Instruments (SP-2500i) spectrofluorimeter equipped with a 3W semiconductor laser (Inter-Diff Optoelectronics Technology Co., Ltd, Shanghai). Absorption spectra were recorded using PerkinElmer's Lamda 25 UV/vis spectrophotometer in the range of 190-1100 nm.

Figures



**Fig. S1.** (a) XRD pattern before and after ligand exchange with PAA and (b) TEM and HRTEM (inset) images of  $NaYF_4$ : $Er^{3+}$ ,  $Yb^{3+}$  UCNPs.



**Fig. S2.** (a) The absorption spectrum of Eosin Y (dotted line) and UCL spectra of NaYF<sub>4</sub>: $Er^{3+}$ ,Yb<sup>3+</sup> UCNPs in D-PBS (red line) and D-PBS containing Eosin Y (60  $\mu$ M) (blue line). (b) Photographs of NaYF<sub>4</sub>: $Er^{3+}$ ,Yb<sup>3+</sup> UCNPs in D-PBS (I-II) and D-PBS containing Eosin Y (III-IV) in D-PBS with and without 980 nm excitation, respectively.



**Fig. S3.** UCL spectra of NaYF<sub>4</sub>: $Er^{3+}$ ,Yb<sup>3+</sup> UCNPs in D-PBS with the presence of different concentrations of Eosin Y upon 980 nm excitation.



Fig. S4. TEM image for the edge of UCNPs/PEGDA hybrid microspheres.



**Fig. S5.** Cytotoxicity assays of the PAA capped UCNPs and UCNPs/PEGDA hybrid microspheres on L929 cells.



**Fig. S6.** TGA curves of UCNPs capped with PAA, UCNPs/PEGDA submicro-flakes and hybrid microspheres. The measurements were performed under N<sub>2</sub> atmosphere.



**Fig. S7.** Absorption of DPBF in solutions of ZnPc loaded UCNPs/PEGDA hybrid microspheres with NIR light irradiation from 0 to 40 min.