Electronic Supplementary Material (ESI) for Chemical Communications

Supporting information

Magnetic/Upconversion Luminescent Mesoparticles of Fe_3O_4@LaF_3: Yb^{3+}, Er^{3+} for Dual-Modal Bioimaging

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1. EXPERIMENTAL SECTION

1.1 Reagents. Polyacrylic acid (PAA), iron (III) chloride anhydrous ($FeCl_3$), diethylene glycol (DEG) and tetraethyl orthosilicate (TEOS, 98%) were purchased from Sigma-Aldrich. Sodium hydroxide (NaOH), ethonal and aqueous ammonia ($NH_3 \cdot H_2O$, 28%) ~~cetyltrimethylammoniumbromide (CTAB)~~ were obtained from Beijing Chemical Reagent Factory. Lanthanum nitrate ($La(NO_3)_3.6H_2O$, >99.99%), ytterbium nitrate ($Yb(NO_3)_3.6H_2O$, >99.99%), erbium nitrate ($Er(NO_3)_3.6H_2O$, >99.99%) were purchased from National Engineering Research Centre of Rare Earth Metallurgy and Function Materials. Soldium fluoride (NaF, 98.0%) was purchased from Tianjin Guangfu Fine Chemical Research Institute, China. Thiazolyl Blue Tetrazolium Bromide (MTT) and sodium dodecyl sulfate (SDS) were purchased from Sigma-Aldrich. All reagents were used as received without further purification.

1.2 Preparation of magnetic nanoparticles. The Fe_3O_4 NPs were produced by using a high temperature hydrolysis reaction.[1] A stock NaOH solution was prepared by dissolving 2.0 g of NaOH in 20 mL of DEG. $FeCl_3$ (0.8 mmol), PAA (8 mmol), and DEG (34 mL) were added into a three-necked flask, and the mixed solution was heated to 220 °C for 30 min under nitrogen. The NaOH solution obtained beforehand was then dropped rapidly into the mixture with vigorous mechanical stirring for an additional 1 h. The products were cooled to room temperature and, thereafter, washed with deionized water and ethanol three times via centrifugation.

1.3 Preparation of magnetic/upconversion luminescent mesoparticles (M/UCL MPs). 0.55 mmol $La(NO_3)_3.6H_2O$, 0.096 mmol $Yb(NO_3)_3.6H_2O$, and 0.024 mmol $Er(NO_3)_3.6H_2O$ were first dissolved in 10 ml aqueous water under stirring at room temperature. After about 10 min, 0.5～3 ml Fe_3O_4 NPs solution (8.6 mg/ml) was added into the lanthanide nitrate solution for 30 min stirring. The stock solution of 1.6 mmol NaF in 15 ml aqueous water was injected dropwise into the round-bottomed flask at a rate of 1 ml per minute, and the mixture was kept at 75°C for 2 h under vigorous stirring. Subsequently, the resulting M/UCL MPs

were collected by centrifugation and washed by water for several times. Finally, MUCNPs were heated to 400 °C at a rate of 20 °C per minute, and were kept at this temperature for 1 hour under N_2 atmosphere. After naturally cooling down to room temperature, the up-conversion fluorescent shell was thus formed.

1.4 Cytotoxicity test. Human lung adenocarcinoma epithelial cell line A549 were cultured in RPMI-1640 medium (Invitrogen, USA), supplemented with 10% heat-inactivated fetal bovine serum (FBS) and antibiotics at 37 °C in the humidified atmosphere with 5% CO_2. The Cells were seeded in 96-well plates at a density of 7×10^3 cells/well and grew overnight. Cells of 80% confluent were incubated with fresh media containing M/UCL MPs with different concentrations (v/v) (from 1% to 10%). After 24 hours, 10 μL of MTT solution of 5 mg/mL was added to each well of the 96-well plate for incubation another 4 h. Then cells were lysed with 10% acid SDS solution. The absorbance of supernatants was measured at 600 nm, and the experiment was repeated at least three times.

1.5 MRI imaging in vitro and vivo. The MR imaging experiments were performed on a 1.5-T clinical MRI instrument (GE Signa 1.5 T), and the pulse sequence used was a T_2-weighted fast-recovery fast spin-echo sequence with the following parameters: TR=4000 ms, slice thickness=3.0 mm, TE=98 ms, echo length=15 ms, FOV=200 mm, matrix = 256×256. M/UCL MP solutions of different concentrations (0, 15.6, 31.2 62.5, 125~250 μg/mL) were placed in centrifuge tubes for T_2-weighted MR imaging. The concentration of Fe was determined by inductively coupled plasma–mass spectrometry (ICP). T_2 relaxivities were calculated through the curve of $1/T_2$ relaxation time versus the Fe concentration. The solution of M/UCL MP (125 μg/mL, 200 μl) was injected into the mouse via tail vein injection, and the mice of pre- and post-injection were scanned.

1.6 UCL imaging in vitro and vivo. Up-conversion fluorescent spectra were measured on an LS-50B fluorescence spectrometer (Perkin-Elmer Corp., Forster City, CA, USA) with an external 980 nm laser (260 mW, Beijing Hi-Tech Optoelectronic Corp., Beijing, China) as the excitation source in place of the

xenon lamp in the spectrometer. A fluorescence detection device equipped with digital camera and 980 nm laser was built in the laboratory. The mouse was killed at 30 min after the vein tail injection of M/UCL MP solution. The liver was collected and frozen immediately to obtain a 50 μm-thick frozen section. The digital photos of the liver section were taken.

1.7 Characterizations. TEM images were used to investigate the morphology of the MUCNPs taken with a Hitachi H-8100IV Transmission Electron Microscope operated at 200 kV. The crystal structure was characterized by X-ray diffraction (XRD) (Philips X'pert PRO) analysis. Magnetic measurements were carried out using a TDM-B vibrating sample magnetometer (VSM) at 300 K. The elemental ratio of the prepared nanocomplex was characterized by energy dispersive X-ray spectrometry (EDX). Inductively coupled plasma spectrometry (ICP, X-7, Thermo Elemental, USA) was used to determine the silver concentrations of the nanorods. Bacterial cultures were measured by optical density measurements at 600 nm (OD600) using a UV/Vis spectrophotometer (Hitachi).

Reference

1 H. Xia, L. Zhang, Q. D. Chen, L. Guo, H. H. Fang, X. B. Li, J. F. Song, X. R. Huang, H. B. Sun, *J. Phys. Chem. C.*, 2009, **113**, 18542.

Figure S1. Square-wave curve of the changes in UV-Vis absorption peak intensity of Fe_3O_4@LaF_3:Yb^{3+},Er^{3+} MPs solution before and after magnetic separation for 10 times.

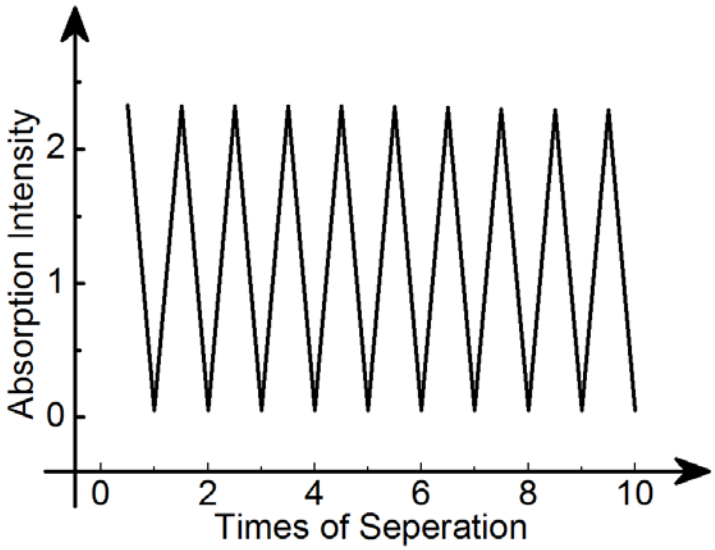

Figure S2. Simplified energy level diagram and possible up-conversion mechanisms for the Fe_3O_4@LaF_3:Yb^{3+},Er^{3+} MPs.

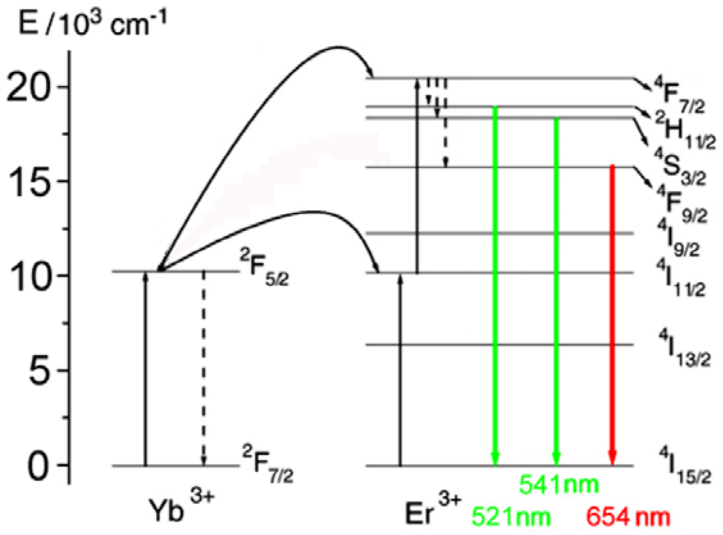

Figure S3. Up-conversion fluorescence spectra of Fe_3O_4@LaF_3:Yb^{3+},Er^{3+} MPs with varying doping concentration of Er^{3+} versus Yb^{3+} (mass ratio) after excitation at 980 nm after annealing at 400 °C for 1 h.

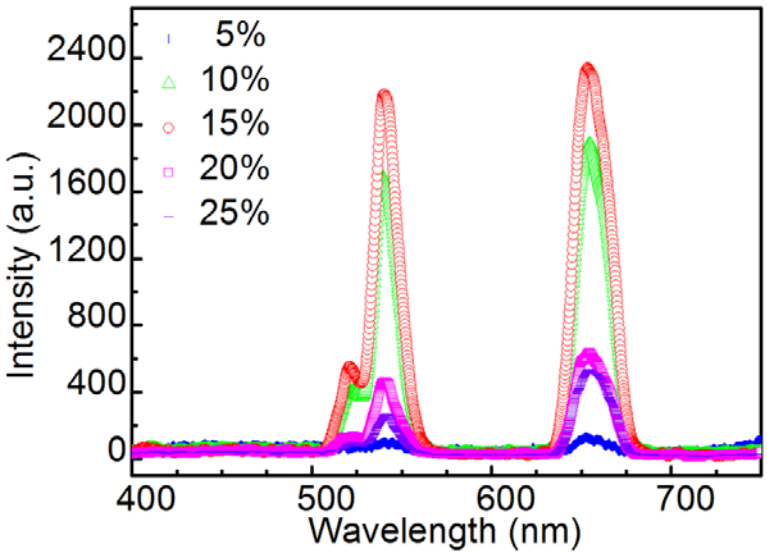

Figure S4. Cytotoxicity of Fe_3O_4@LaF_3:Yb^{3+},Er^{3+} MPs. The viability of A549 cells incubated with different concentrations of Fe_3O_4@LaF_3:Yb^{3+},Er^{3+} MPs for 24 h.

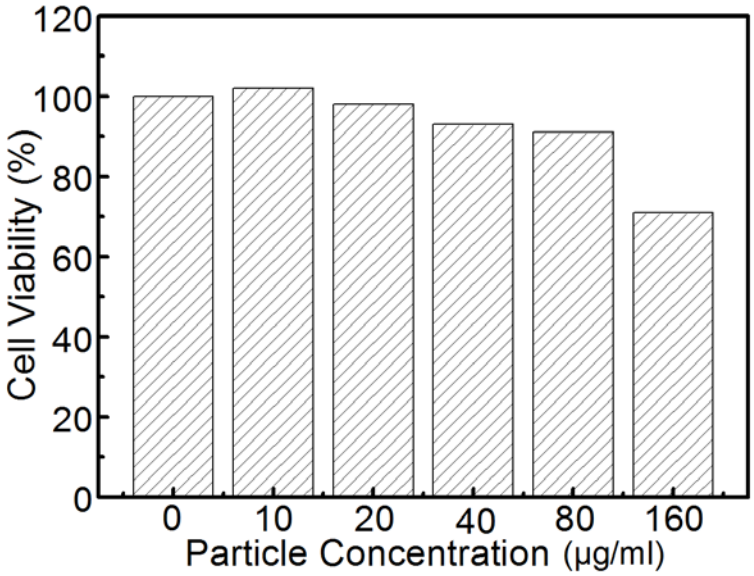

Figure S5. (a) Pre- and (b) post-injection MR imaging of a transplanted tumor on the shoulder of a mouse. Fe_3O_4@LaF_3:Yb^{3+},Er^{3+} MPs were injected into the tumor site.

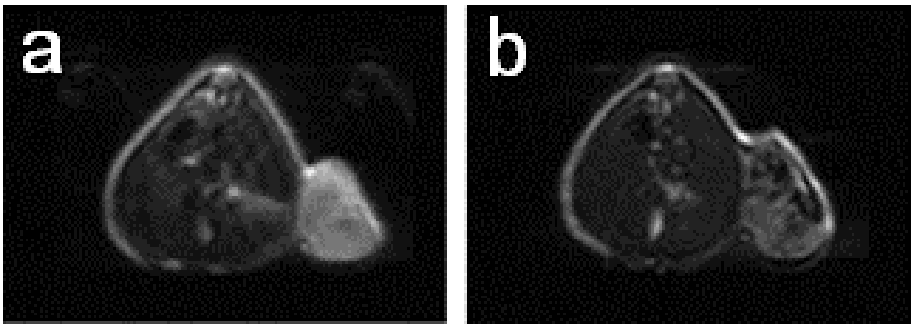

Figure S6. Digital photography of the frozen section of Fe_3O_4@LaF_3:Yb^{3+},Er^{3+} MPs loaded liver without (a) and with (b) 980 nm laser excitation.