Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Supporting Information

Facile Supramolecular Approach to Fabricate Multifunctional Upconversion Nanoparticles as a Versatile Platform for Drug Loading, In Vivo Delivery and Tumor Imaging

Yingying Yuan,[a] Li Xu,[b] Shuyun dai,[a] Min Wang[a] and Hangxiang Wang*[b]*

[a] Institute of Microanalytical Systems, Department of Chemistry, Zhejiang University, Hangzhou, 310058, PR China.

[b] The First Affiliated Hospital, School of Medicine; Key Laboratory of Combined Multi-organ Transplantation, Ministry of Public Health; Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Zhejiang University, Hangzhou, 310003, PR China.

*E-mail: wanghx@zju.edu.cn; minwang@zju.edu.cn

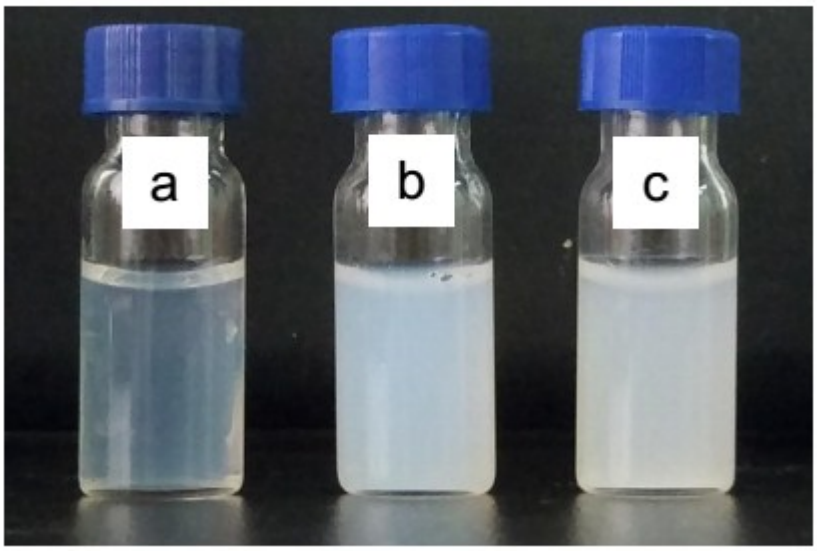

Fig. S1 Photographs of various formulations after injection into deionized (DI) water under ultrasonication. Solutions containing (a) OA-UCNPs+DSPE-PEG_{2000}+prodrug **1**, (b) OA-UCNPs+DSPE-PEG_{2000}+free SN38 and (c) free SN38 in DMSO were injected into DI water. The ratio of OA-UCNP/DSPE-PEG2000/**1**(SN38) was 10:20:1 and the final concentration of SN38 was 0.5 mg/mL. The resultant solution in (a) was transparent, whereas the solutions in (b) and (c) showed large precipitates.

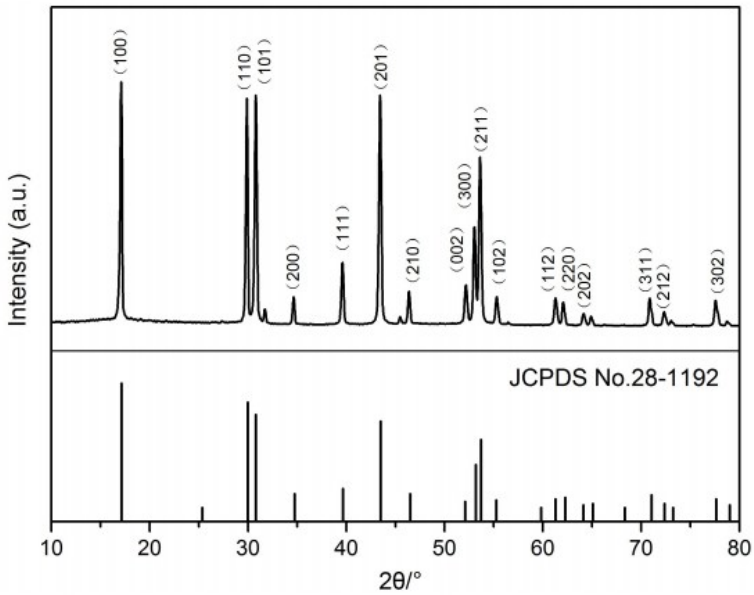

Fig. S2 The powder X-ray diffraction (XRD) pattern of oleic acid-capped $NaYF_4$:Yb^{3+}/Er^{3+} NPs and the standard pattern of hexagonal $NaYF_4$ (JCPDS No.28-1192).

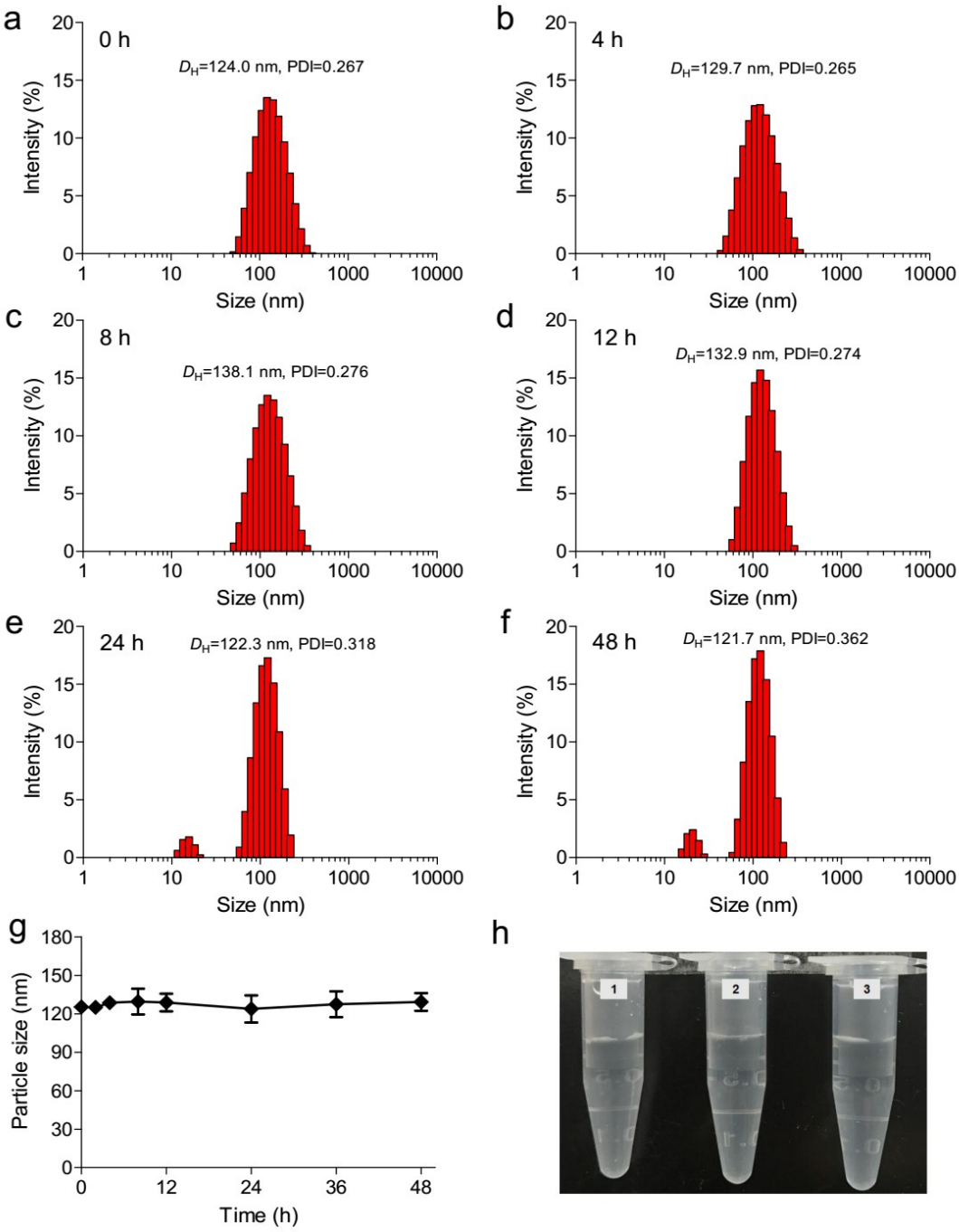

Fig. S3 The stability of **1**@pUCNP in PBS (0.5 mg mL^{-1}) measured by dynamic light scattering (DLS). (a-f) The size distribution of **1**@pUCNP after incubation in PBS at 4°C. (g) Particle size variation of **1**@pUCNP in PBS at different time points post-incubation. The data are presented as the means ± SD (n = 3). (h) Photographs of three parallel samples of **1**@pUCNP incubated in PBS (0.5 mg mL^{-1}) for 48 h. No obvious aggregation was observed.

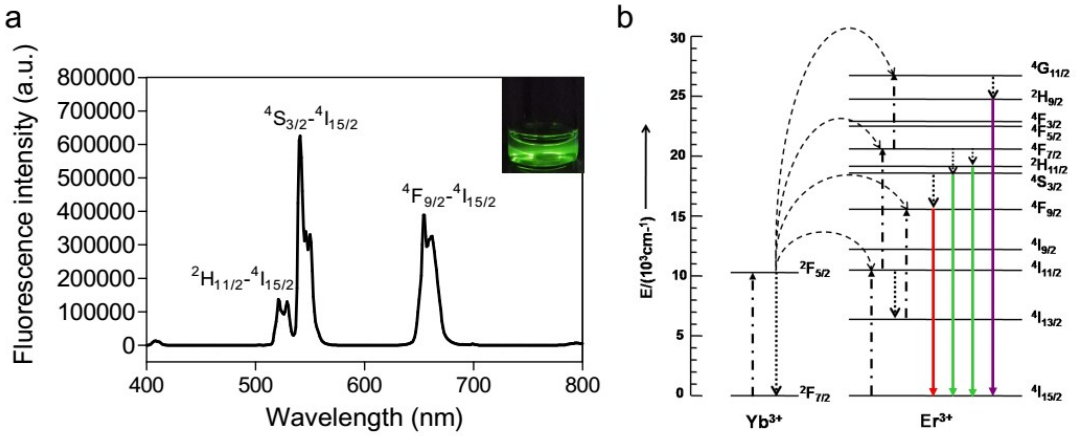

Fig. S4 (a) UCL spectrum of as-synthesized $NaYF_4$:Yb^{3+}/Er^{3+} NPs dispersed in cyclohexane under the excitation of 980 nm laser. The inset shows the corresponding photograph of $NaYF_4$:Yb^{3+}/Er^{3+} colloidal solution (1.5 mg/mL) in cyclohexane upon excitation at 980 nm. (b) Upconversion mechanism of $NaYF_4$:Yb^{3+}/Er^{3+} NPs under excitation at 980 nm. The UCL bands at 525, 541 and 655 nm are corresponding to the $^2H_{11/2}\rightarrow{}^4I_{15/2}$, $^4S_{3/2}\rightarrow{}^4I_{15/2}$ and $^4F_{9/2}\rightarrow{}^4I_{15/2}$ transitions of Er^{3+}, respectively.

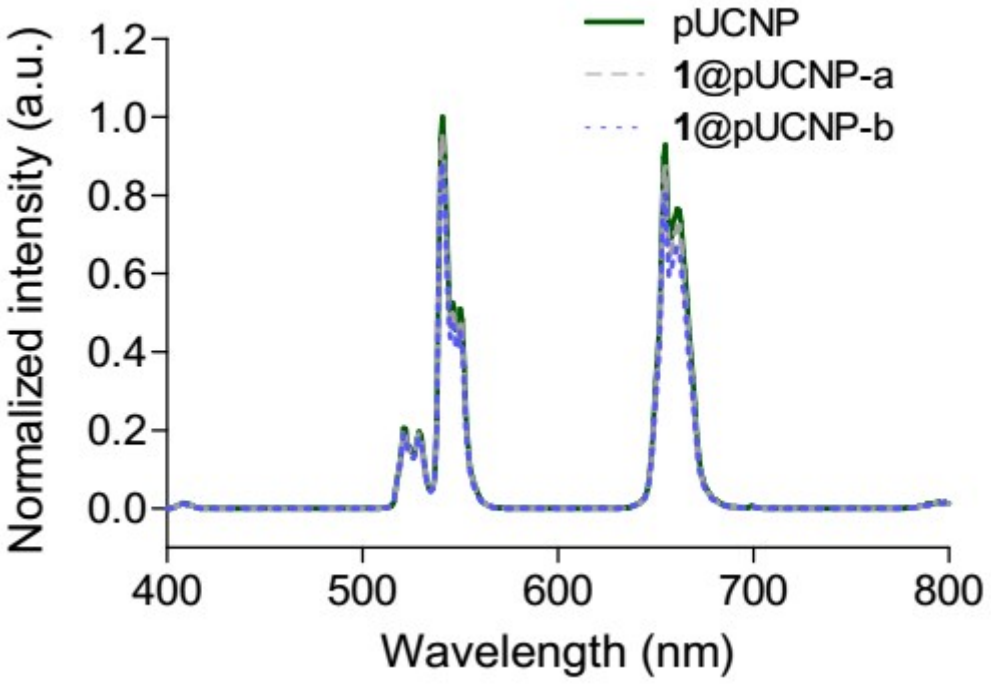

Fig. S5 UCL spectra of pUCNP with different prodrug **1** loading contents, the drug loading capacity was 2.5 wt % in **1**@pUCNP-a (grey dashed line) and 6.25 wt % in **1**@pUCNP-b (purple dotted line). The corresponding quenching efficiency (541 nm) was 4.5 % and 10.5% respectively.

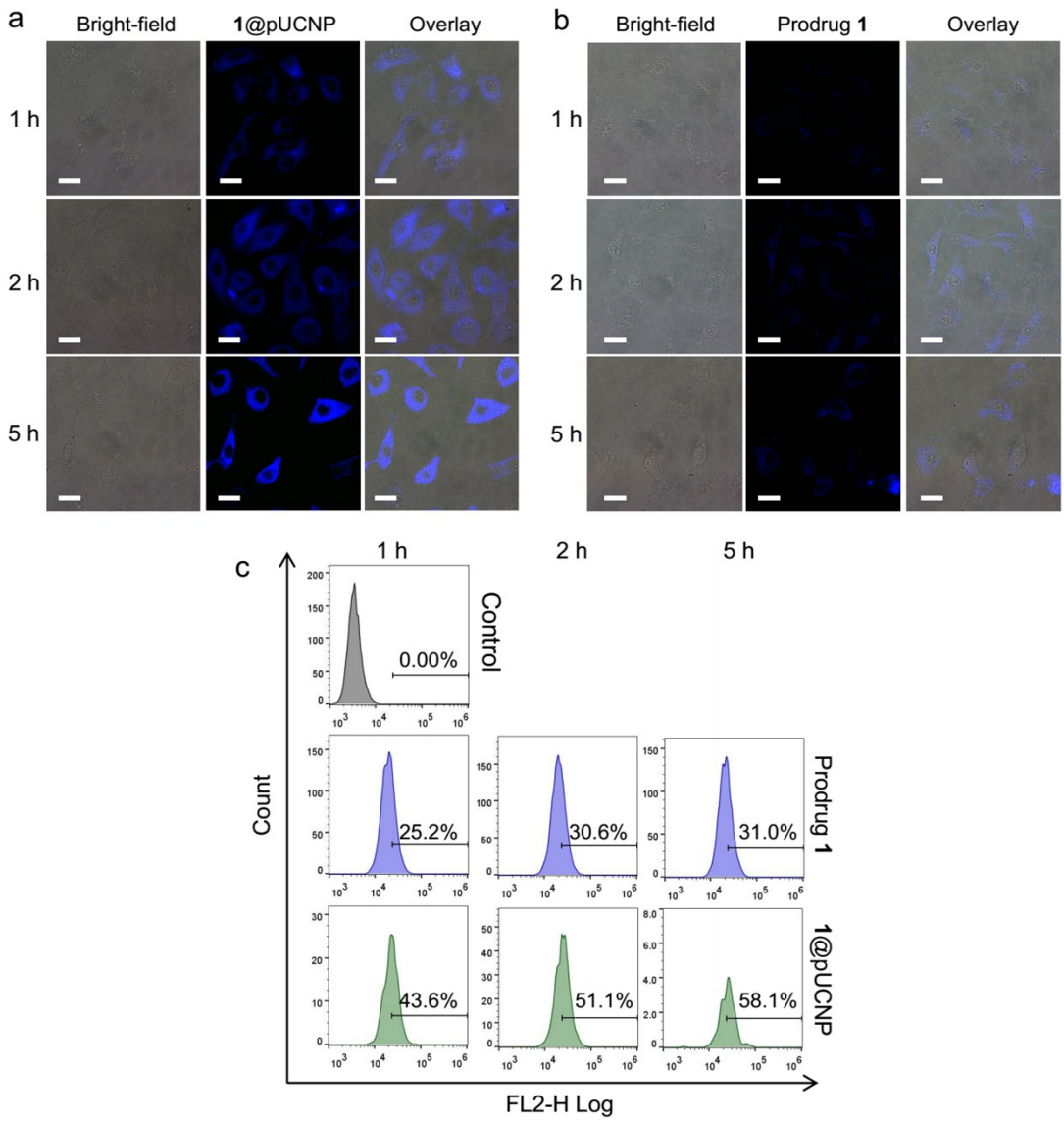

Fig. S6 Fluorescence microscope images of Bcap-37 cells incubated with **1**@pUCNP (a) and prodrug **1** (b) for 1 h, 2 h, and 5 h with 405 nm laser excitation. All scale bars are 20 μm. (c) Flow cytometry analysis of Bcap-37 cells incubated with prodrug **1** and **1**@pUCNP for 1 h, 2 h, and 5 h, respectively. Both **1**@pUCNP and prodrug **1** were at an SN38-equivalent concentration of 15 μM.

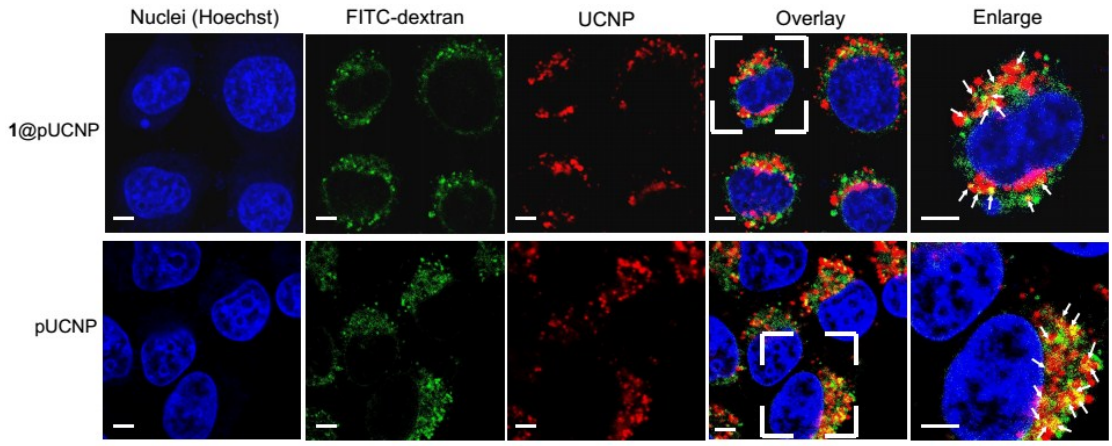

Fig. S7 Confocal laser scanning microscopy (CLSM) images of Bcap-37 cells at 4 h post-incubation with pUCNP and **1**@pUCNP. Each series shows the nuclei of cells stained with Hoechst 33258 (blue), the endosomes/lysosomes stained with FITC-dextran (green), the upconversion luminescence (UCL) images, the overlay and the enlargement of regions of interest (ROI) in overlay images. The arrows show the signal (yellow pots) overlay of the endosomes/lysosomes and drug loaded pUCNP (or empty pUCNP). The blue Hoechst fluorescence was collected from 425 to 475 nm, green FITC fluorescence was collected in the range of 500-600 nm, and the red UCL emission was collected at 575-650 nm. All scale bars are 5 μm.

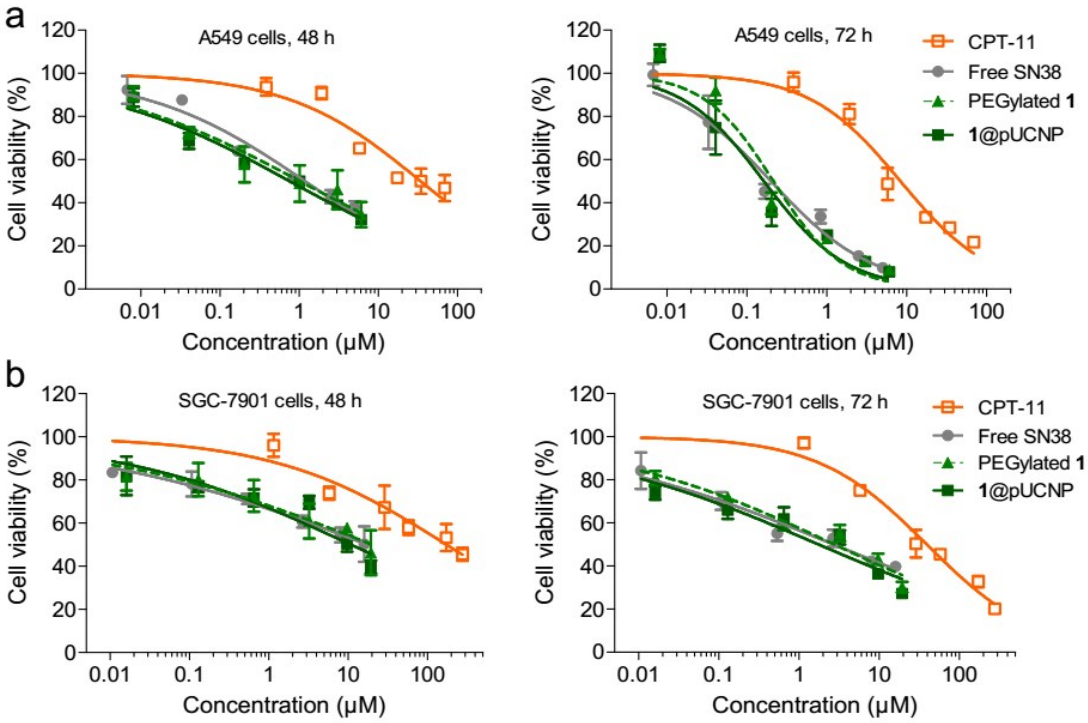

Fig. S8 In vitro cell viability for CPT-11, free SN38, PEGylated **1** and **1**@pUCNP in (a) A549 cells and (b) SGC-7901 cells after incubation for 48 h or 72 h measured by CCK-8 assay (Means ± SD).

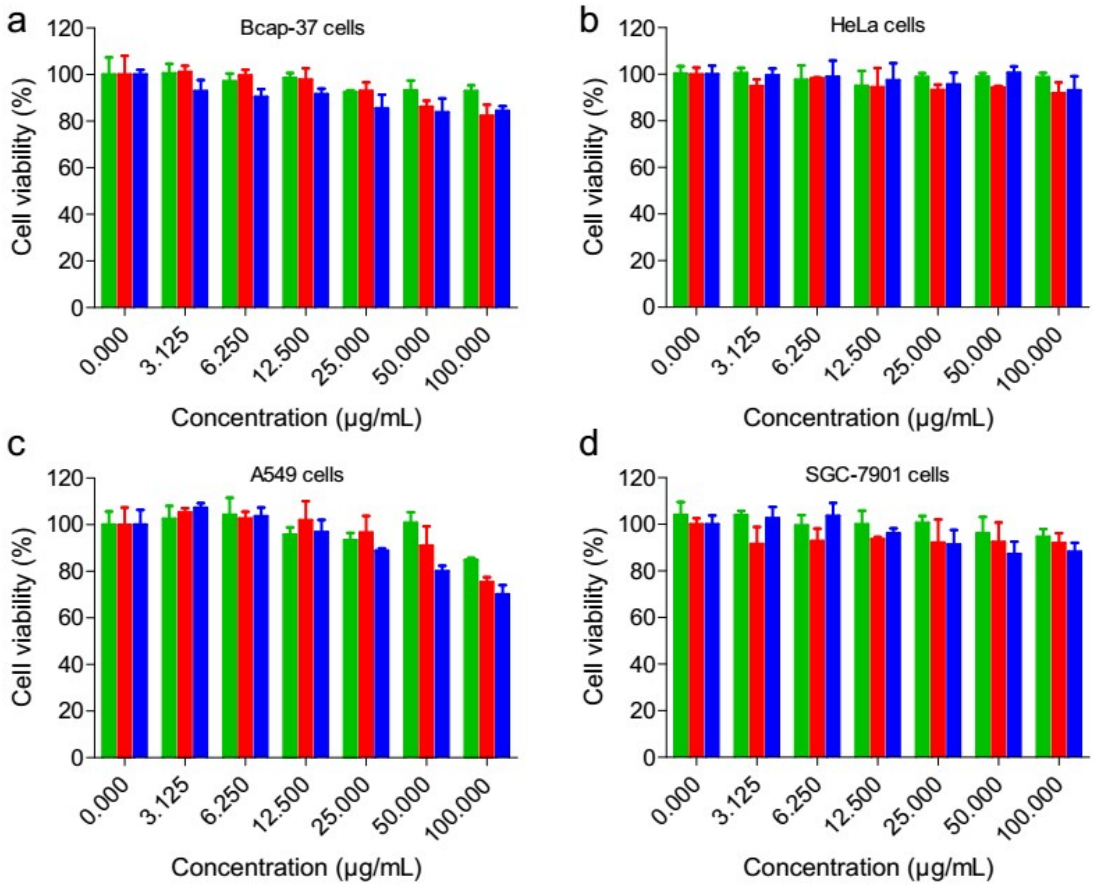

Fig. S9 In vitro cell viability of (a) Bcap-37 cells, (b) HeLa cells, (c) A549 cells and (d) SGC-7901 cells upon treatment with various concentrations of pUCNP for 24 h (green columns), 48 h (red columns) and 72 h (blue columns) using CCK-8 assay (Means ± SD).

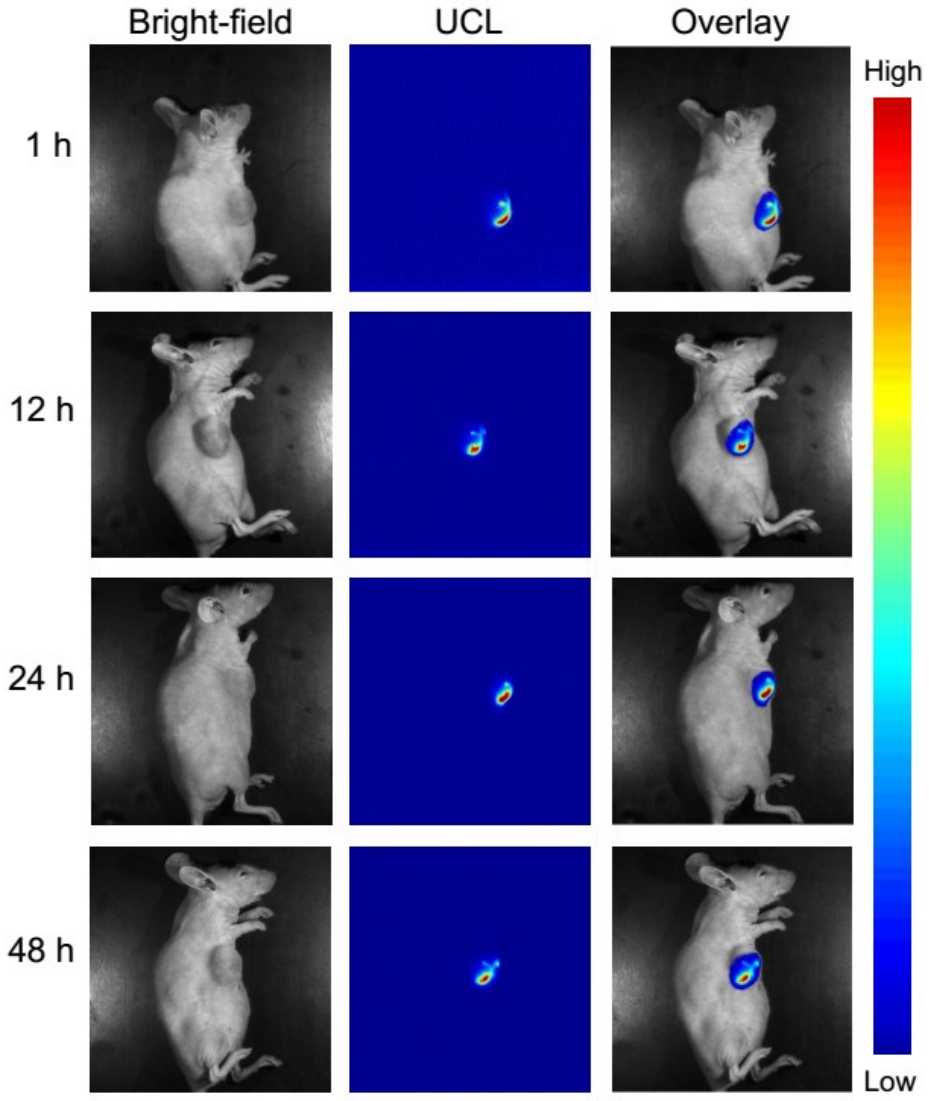

Fig. S10 In vivo UCL imaging of the Bcap-37 xenograft-bearing Balb/c mouse after intratumoral injection with pUCNP (20 μL, 2 mg/kg) into the tumor site. All images were acquired under the same conditions with a power density of ~0.12 W/cm^2. Representative images were taken from the same mouse, and the distance between light source and the tumor was kept constant at each time point.

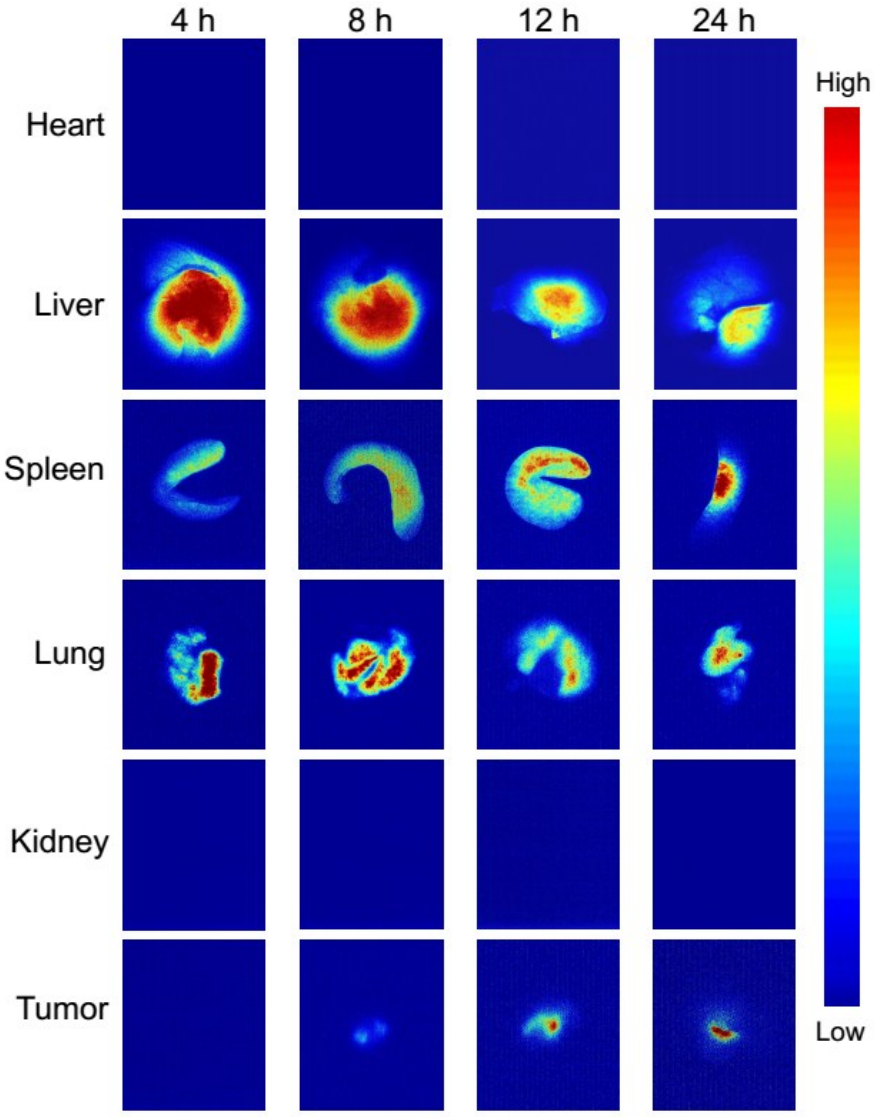

Fig. S11 Representative ex vivo UCL images obtained from heart, liver, spleen, lung, kidney and tumor. After intravenous (IV) injection of pUCNP (200 μL, 20 mg/kg), the mice were sacrificed at different time points, and major organs and tumors were imaged immediately. All images were acquired under the same conditions with a power density of ~0.2 W/cm^2.