Supplementary data

Targeted Delivery of Functionalized Upconversion Nanoparticles for Externally Triggered Photothermal/Photodynamic Therapies of Brain Glioblastoma

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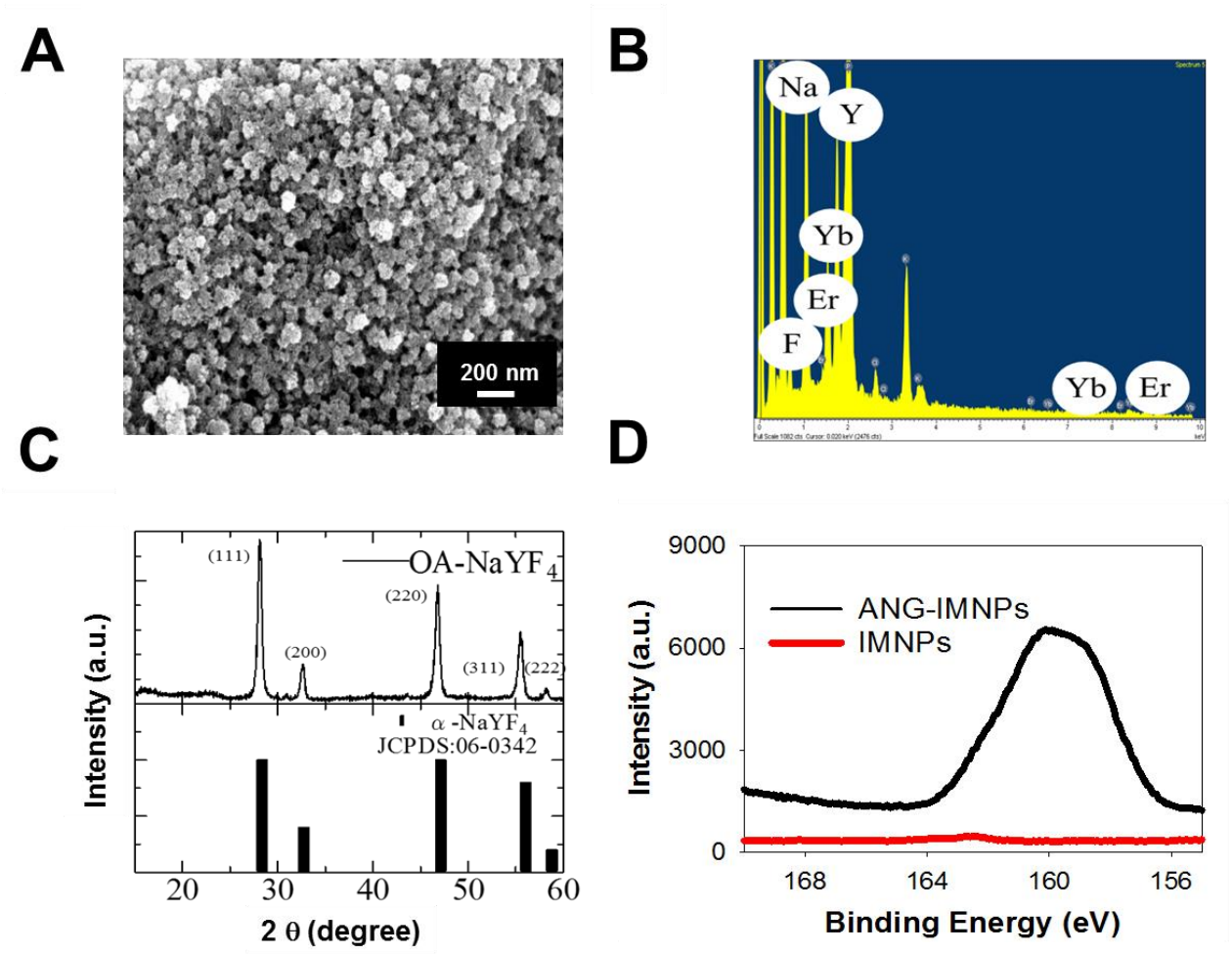

Fig. S1. Characterization of UCNPs. (A) Scanning electron microscopy (SEM) image of UCNPs (B) SEM-EDX measurements, (C) XRD pattern, and (D) XPS spectra of IMNPs and ANG-IMNPs.

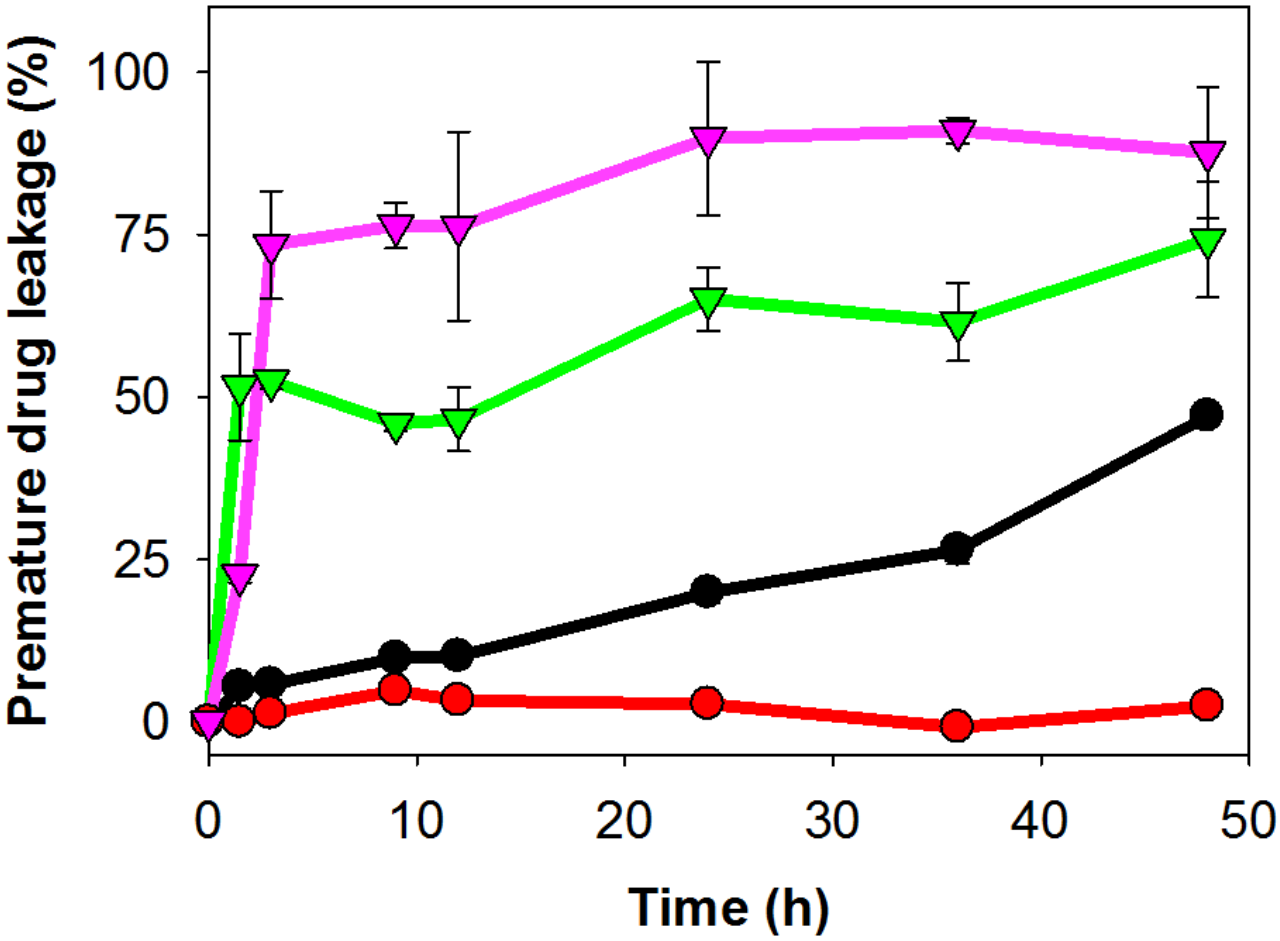

Fig. S2. Release profiles of IR-780 (—●—) and mTHPC (—●—) from ANG-IMNPs at pH 7.4 by the dialysis technique. Free IR-780 (—▽—) and mTHPC (—▽—) were used as controls. The extent of drug release was monitored by UV/vis spectroscopy. (n=3)

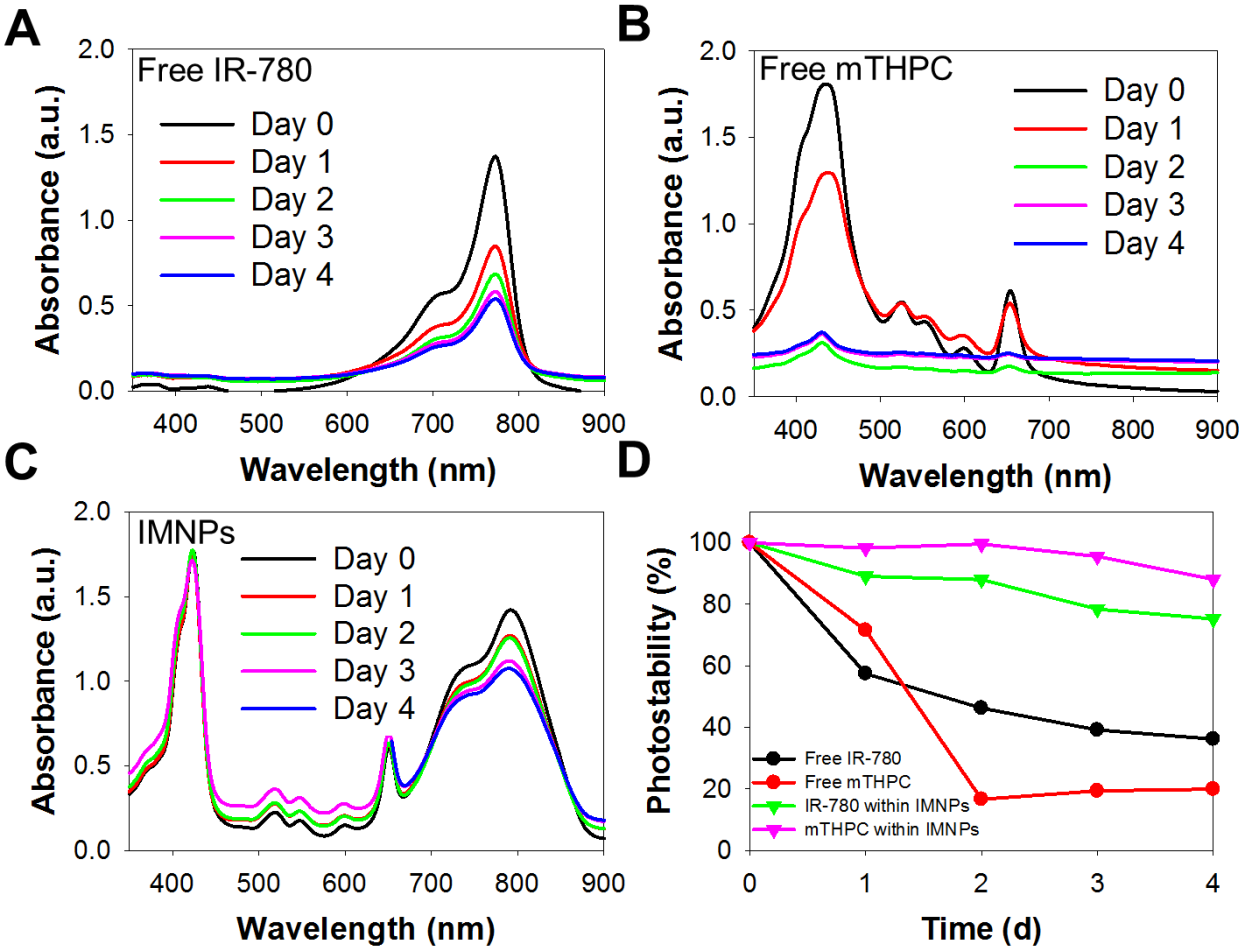

Fig. S3. Photostability of (A) IR-780, (B) mTHPC and (C) IMNPs in PBS at different time intervals measured by UV/vis spectrometer. (D) A plot of photostability *versus* time with respect to free IR-780, free mTHPC and IR-780, and mTHPC within IMNPs.

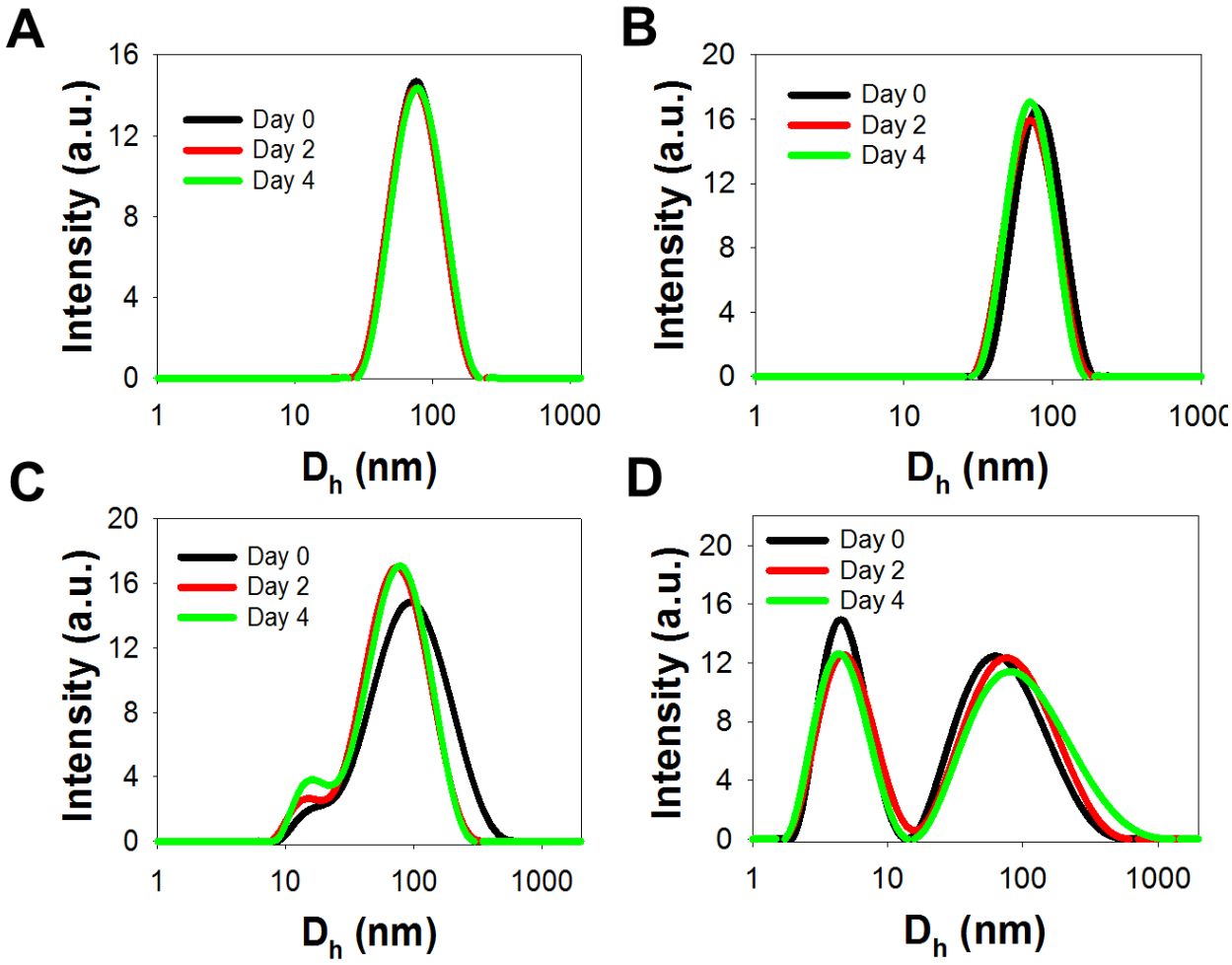

Fig. S4. Colloidal stability of ANG-IMNPs in (A) PBS, (B) DMEM, (C) 1% IgG and (D) 4% BSA at different time intervals by DLS measurements. The appearance of small particles with the sizes < 20 nm in (C) and (D) is most likely caused by the aggregation of proteins in media.

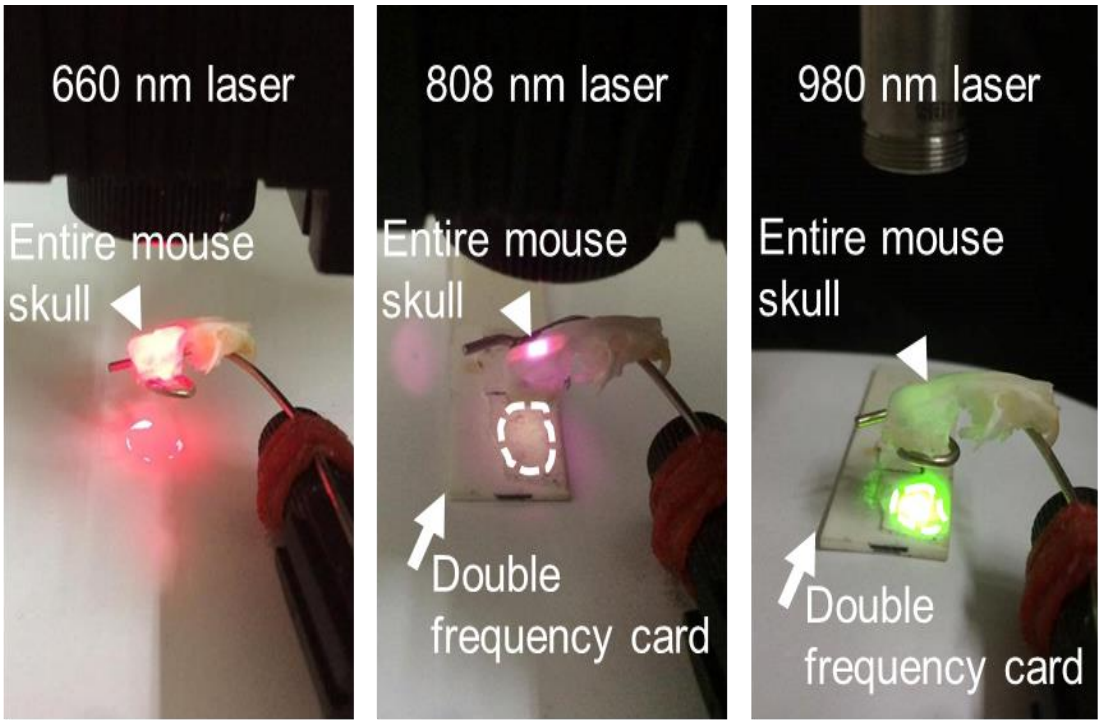

Fig. S5. Penetration of laser lights with different wavelengths through mouse skull. Photographs of the mouse skulls irradiated with 660, 808, and 980 nm lasers to demonstrate the improved penetration efficacies of 808 nm and 980 nm NIR light, whereas the penetration is severely limited with the laser light at 660 nm. Light penetration is indicated by dotted white line.

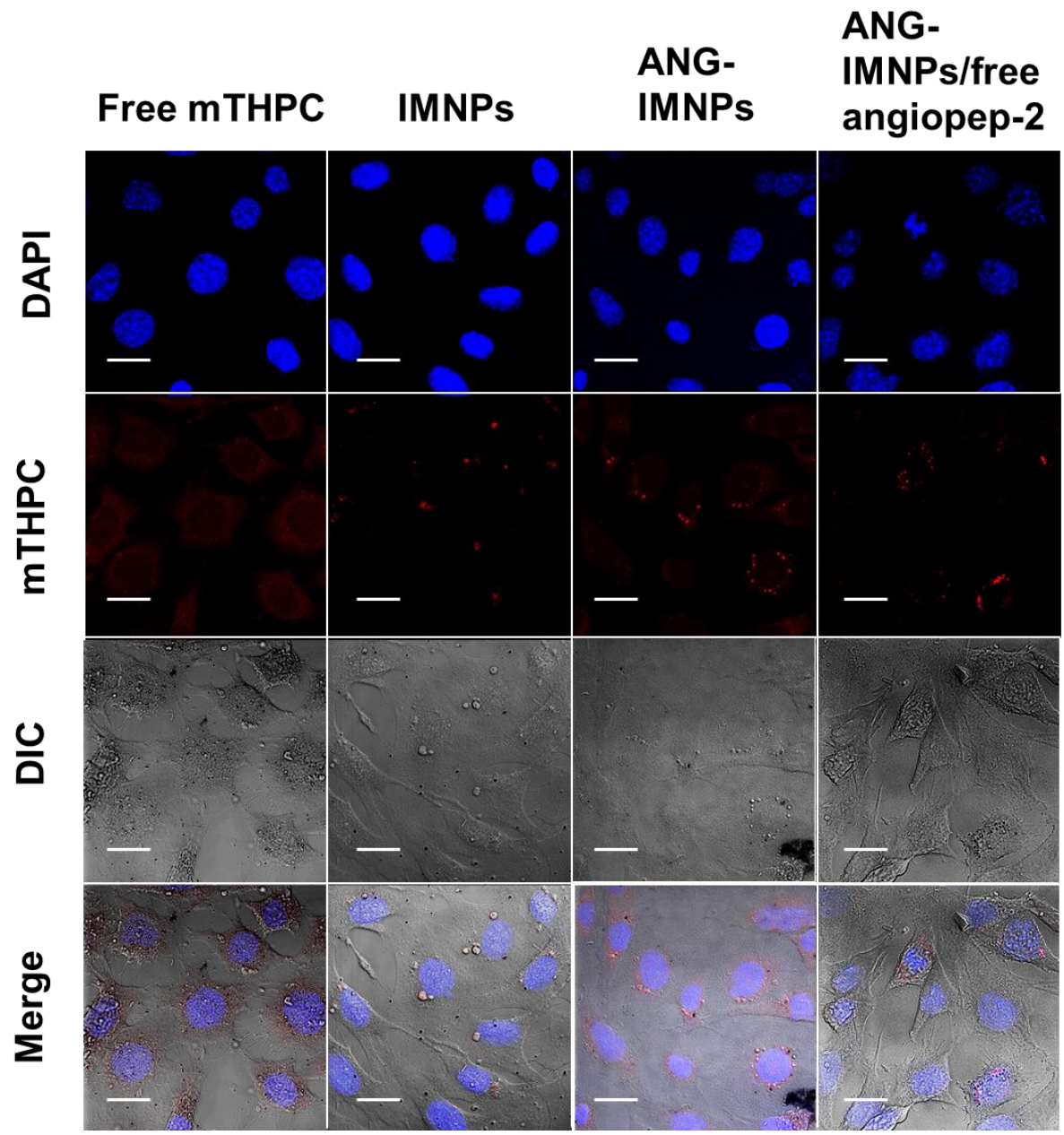

Fig. S6. LSCM images of the *in vitro* cellular uptake of free mTHPC, IMNPs, ANG-IMNPs, and ANG-IMNPs/free angiopep-2 by ALTS1C1 cells. The cell nuclei were stained with DAPI (λ_{ex} = 405 nm, λ_{em} = 450-500 nm) and uptake was monitored from the fluorescence channel for mTHPC (λ_{ex} = 633 nm, λ_{em} = 640-670 nm). Scale bar: 20 μm.

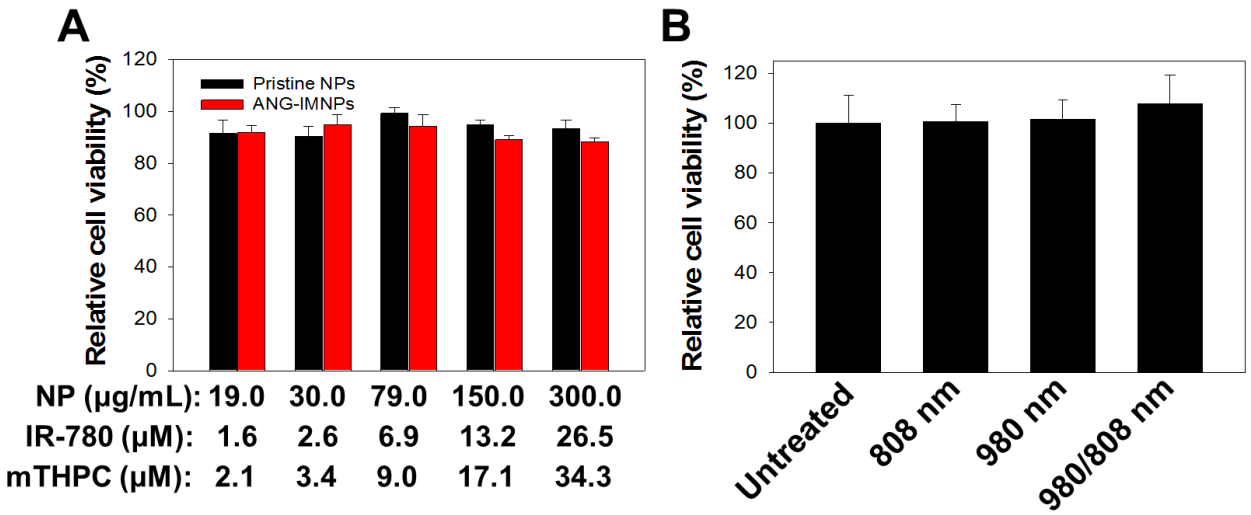

Fig. S7. (A) *In vitro* cytotoxicity of ANG-IMNPs of varying concentrations without irradiation on ALTS1C1 cells by MTT assay. (B) Cell viability of ALTS1C1 cells after laser irradiation at either 980 or 808 nm or both (980 nm laser, 0.8 W/cm^2; 808 nm laser, 0.36 W/cm^2).

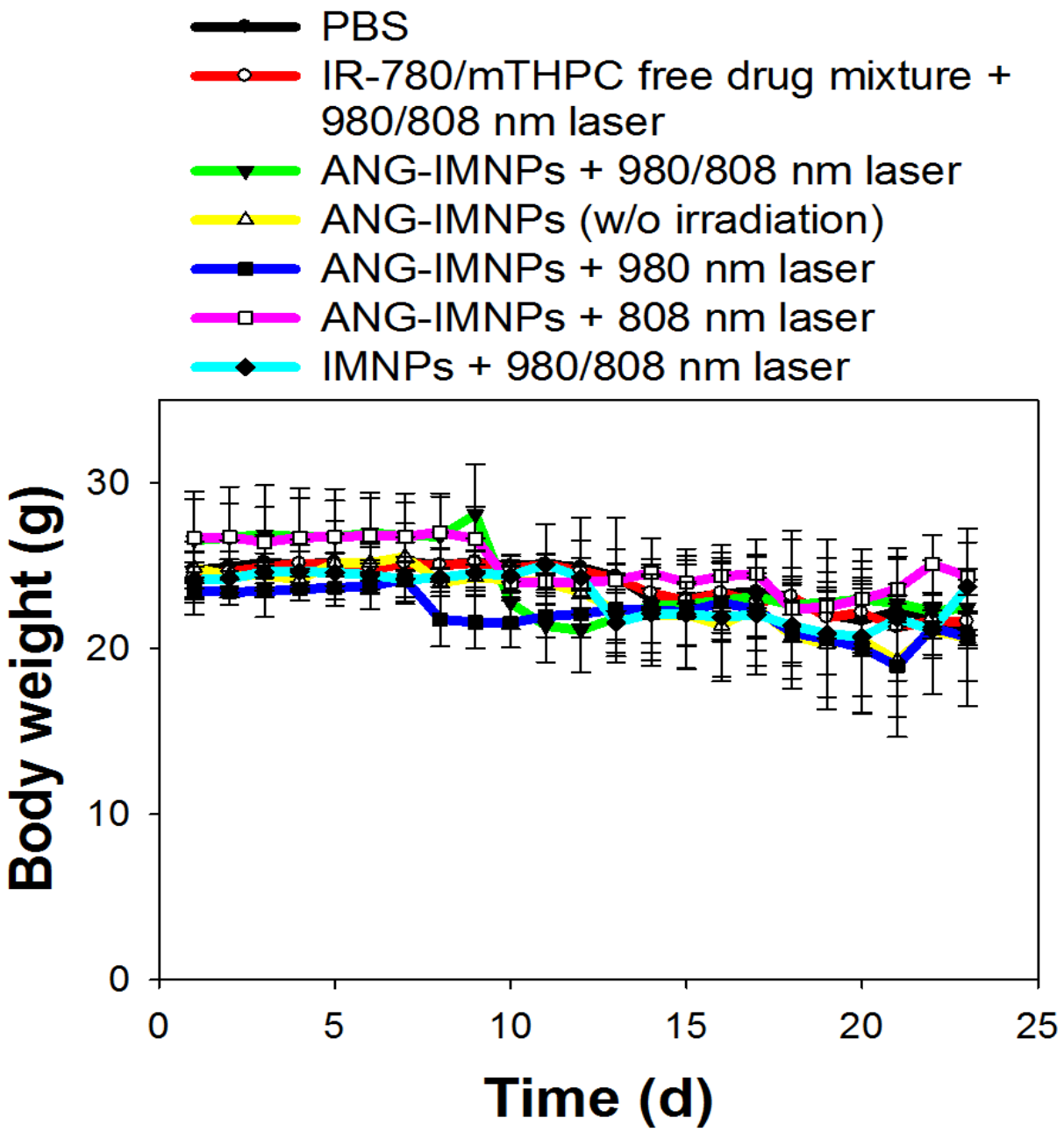

Fig. S8. Change of body weight of tumor-bearing mice following PDT/PTT treatments. Mice in each group were injected with PBS (control), IR-780/mTHPC free drug mixture + 980/808 nm laser, ANG-IMNPs + 980/808 nm laser, ANG-IMNPs (w/o irradiation), ANG-IMNPs + 980 nm laser, ANG-IMNPs + 808 nm laser, or IMNPs + 980/808 nm laser. (n = 5, mTHPC dose = 1.4 mg/kg and IR-780 dose = 1.1 mg/kg).

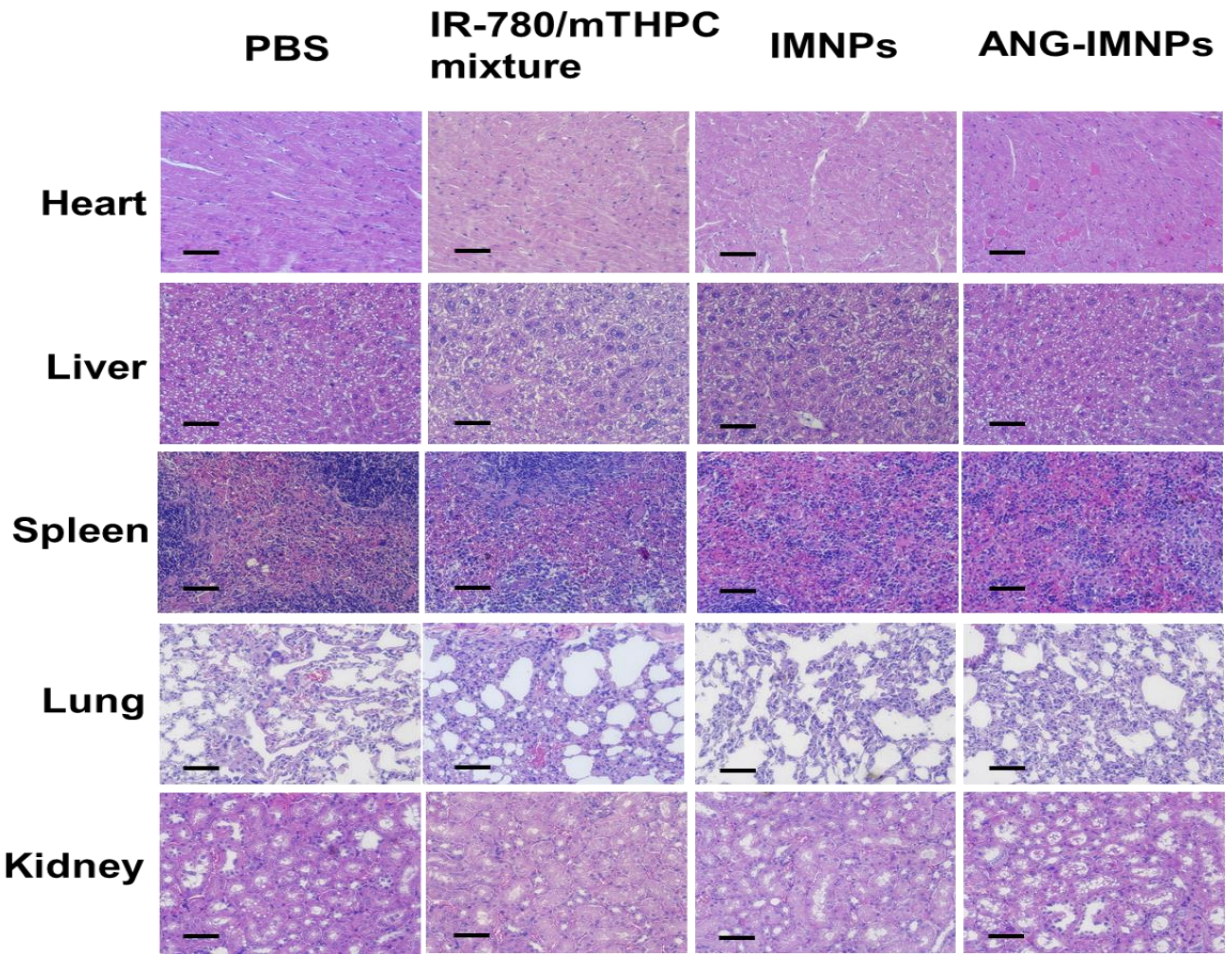

Fig. S9. H&E staining of tissue sections from major organs following PDT/PTT treatments. No noticeable differences were seen among the animal groups receiving different treatments. Scale bar: 50 μm.