Supporting information

Degradable pH-responsive NIR-II imaging probes based on polymer-lanthanide composite for chemotherapy

Miao Feng, [a] Yanxing Wang, [a] Bi Lin, [a] Xiangrong Peng, [a] Ying Yuan,[b] Xiaofeng Tao,[b,*] and Ruichan Lv, [a,*]

[a]Engineering Research Center of Molecular and Neuro Imaging, Ministry of Education, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710071, China

[b]Department of Radiology, School of Medicine, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University, Shanghai 200011, China.

Corresponding author:

E-mail: cjr.taoxiaofeng@vip.163.com (X. Tao); rclv@xidian.edu.cn (R. Lv)

Experiments and Materials

Phase Transfer of UCNP@mSiO$_2$. Typically, a beaker containing 30 mL of deionized water and 0.15 g of CTAB was placed in an ultrasonic cleaner to obtain a transparent solution. Then, 3 mL of cyclohexane solution containing UCNP (20 mg mL^{-1}) was added. The mixture was then stirred vigorously under room temperature over night to obtain a homogeneous UCNP-CTAB solution. After that, the UCNP-CTAB aqueous solution, 6 mL of ethanol, and 200 μL of NaOH (2 M) were mixed, and the mixture was heated to 70 °C under stirring. Then, 150 μL of TEOS mixture was added slowly into the solution and stirred vigorously for 10 min. The precipitation was centrifuged and washed with ethanol several times, and the UCNP@SiO$_2$ was obtained.

The CTAB template was extracted by ion exchange process. Typically, UCNP@SiO$_2$ was added into 30 mL of ethanol solution together with 0.08 g of NH_4NO_3, and the mixture was heated and kept at 60 °C for 2 h. Then, the UCNP@mSiO$_2$ were obtained after centrifugation with deionized water for three times.

Animal model. The female BALB/c mice (aged 5-6 weeks) used in these experiments were obtained from the School of Pharmacy' s Ethics Committee of Xi' an Jiaotong University. The tumor passage was by the mince-trocar technique. The tumor, designated 4T1, was derived from a mice breast cancer. 4T1 tumor model was injection of 4T1 cells in PBS (1*10^6, 50 μL) into the right buttock of mice. When the tumor size reached 0.045 cm^3, the in vivo assays were performed.

In vivo **Toxicity of DMDN.** The tumor-bearing mice were randomized into two groups (n=3, each group) and were treated by intratumoral injection with DMDN and PBS (blank control). The injected material is 100 μL (1 mg/mL) every 2 days. The tumor sizes of all BALB/c mice were monitored by a digital caliper and calculated by the equation:

$V_{tumor} = LW^2/2$ (*L*: tumor length, *W*: tumor width).

In each injection, the weight of nude mice and tumor volume were measured. After two weeks of treatment, the BALB/c mice were sacrificed. The main organs and tumor tissues were extracted for histological examination. Tumor tissues and main organs were fixed with formalin (10 %), embedded with paraffin and sliced into thin sections. The sections were stained with hematoxylin and eosin (H&E) and observed by an optical microscope.

***In vivo* NIR-II imaging.** *In vivo* NIR-II imaging experiments were performed using a commercial NIR-II imaging system (Grand-Imaging, China). 100 μL (1 mg mL^{-1}) of DMDN solution was injected into the mice intravenously, and then NIR-II signals of vessels of the right hind limb of mice.

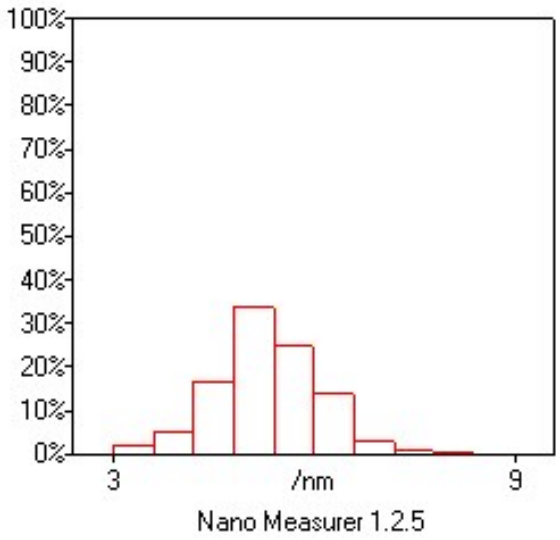

Fig. S1. Size distribution of $NaGdF_4$:2%Nd@$NaLuF_4$ nanocrystal.

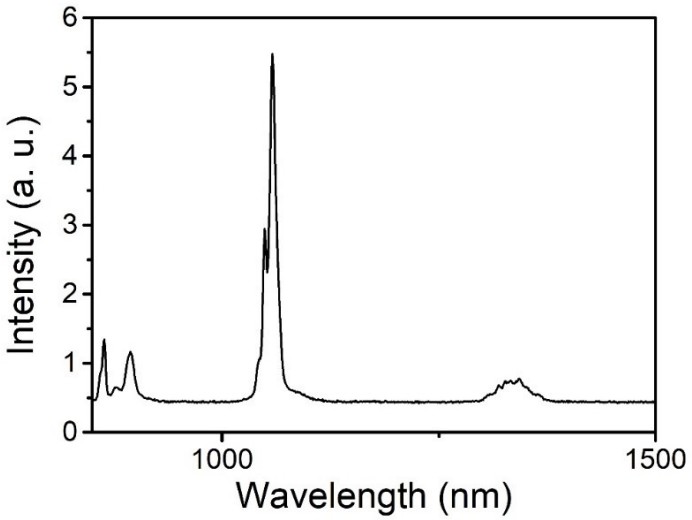

Fig. S2. NIR-II luminescence spectra of $NaGdF_4$:2%Nd@$NaLuF_4$ nanocrystal.

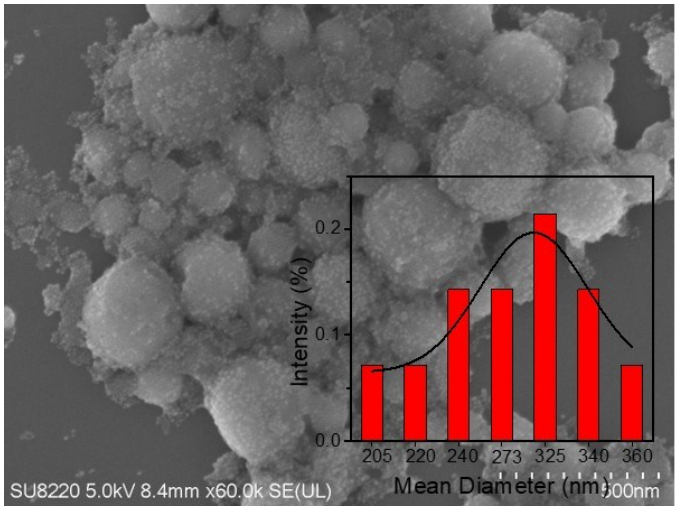

Fig. S3. SEM image of DMDN and particle size distribution.

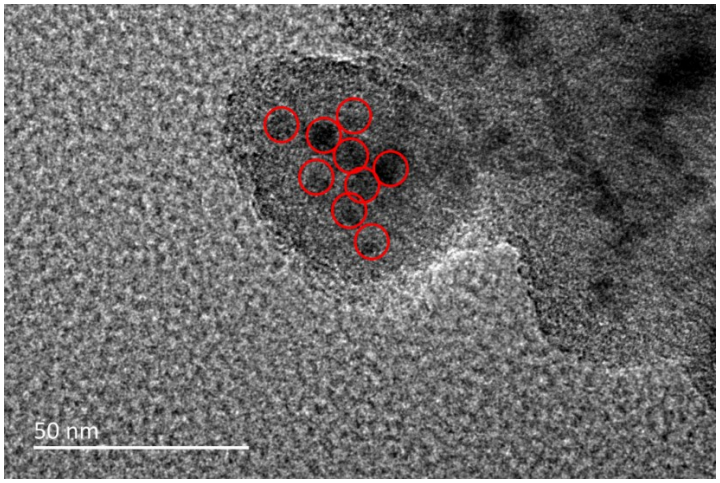

Fig. S4. TEM image of ultra-small DCNP@SiO_2.

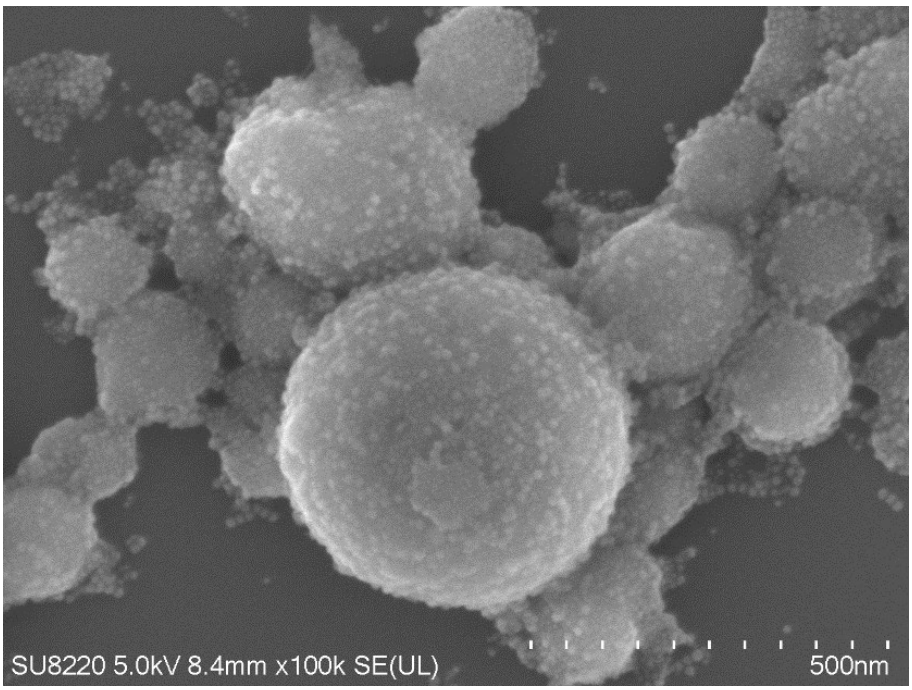

Fig. S5. SEM image of UCNP@mPEG-PLGA.

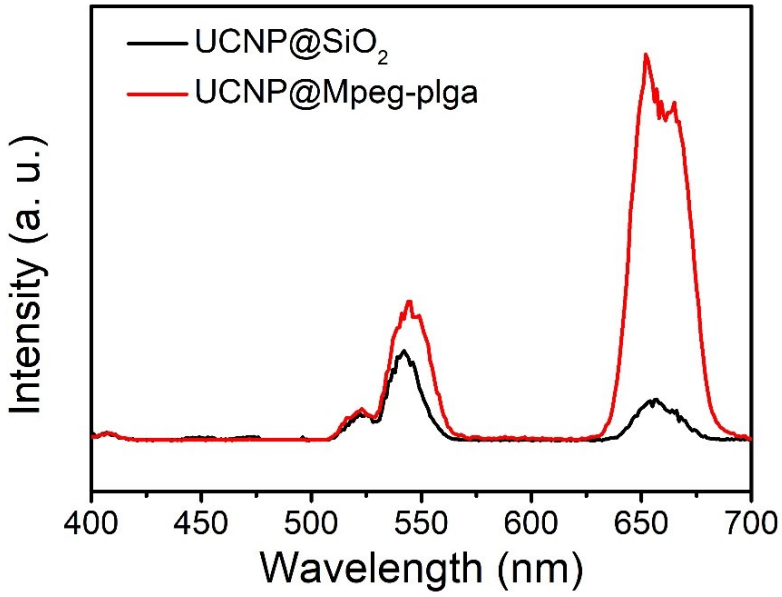

Fig. S6. The upconversion luminescence spectra of UCNP@SiO_2 and UCNP@mPEG-PLGA.

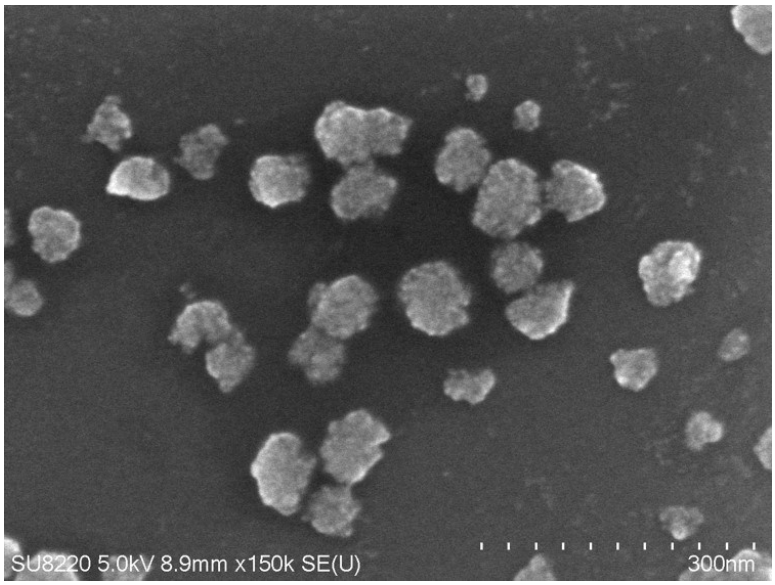

Fig. S7. SEM image of hydrolyzed DMDN.

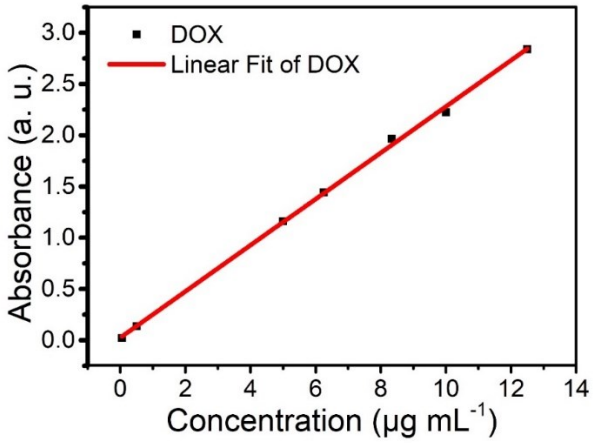

Fig. S8. Standard absorbance curve of pure DOX.

Abs (Wave length / Concentration)	414 nm	541 nm
31.25	0.35	0.319
62.5	0.206	0.186
125	0.226	0.205
250	0.355	0.31

Table S1. Hemolytic experiment results of DMDN.

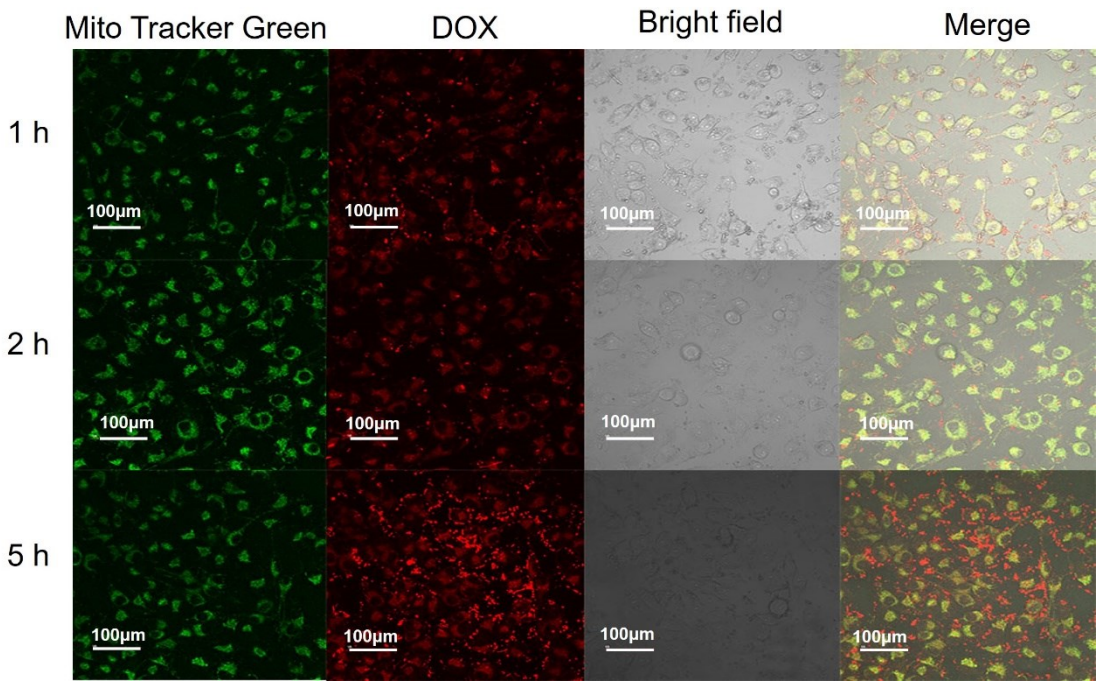

Fig. S9. CLSM images of cells incubated with DMDN and marked with Mito-tracker for different time points.

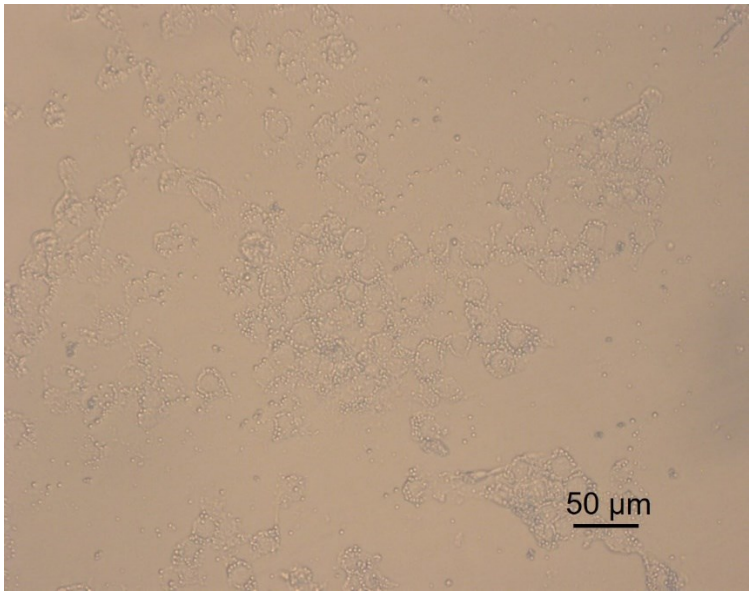

Fig. S10. Microscopy images (bright field) of 4T1 cells incubated with DMDN for 48 h.

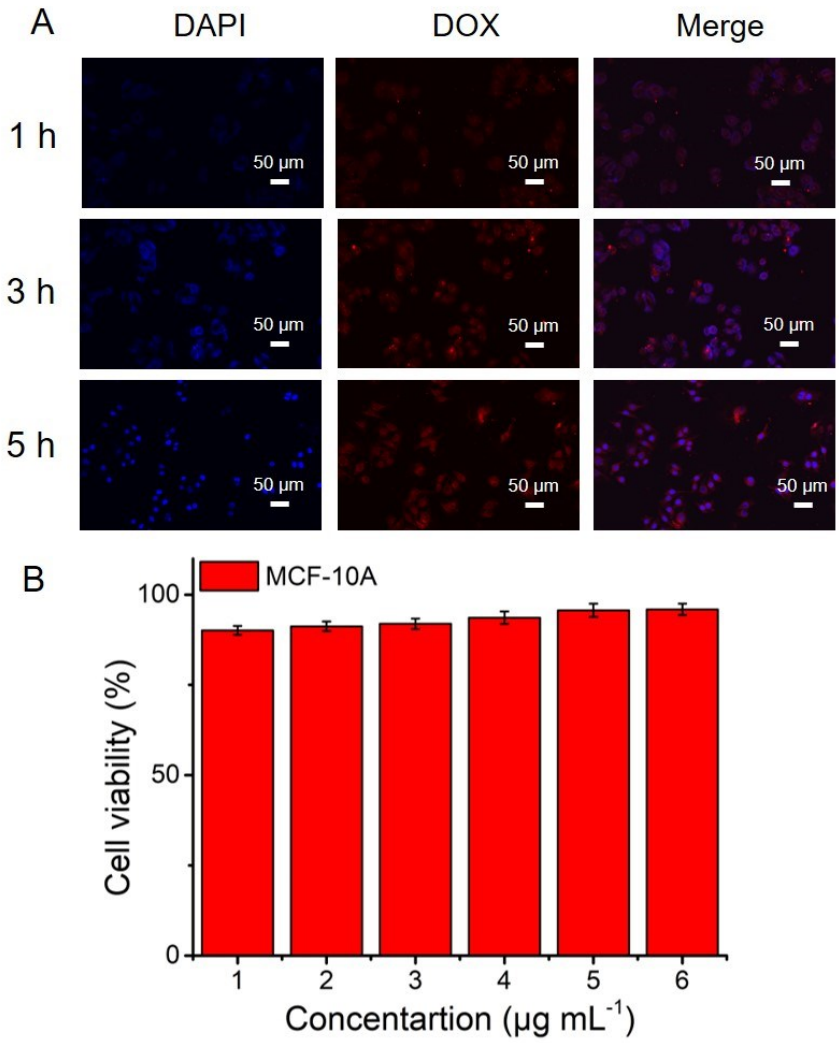

Fig. S11. (A) CLSM images (marked with DAPI) and (B) the cell viability of MCF-10A cell incubated with DMDN.

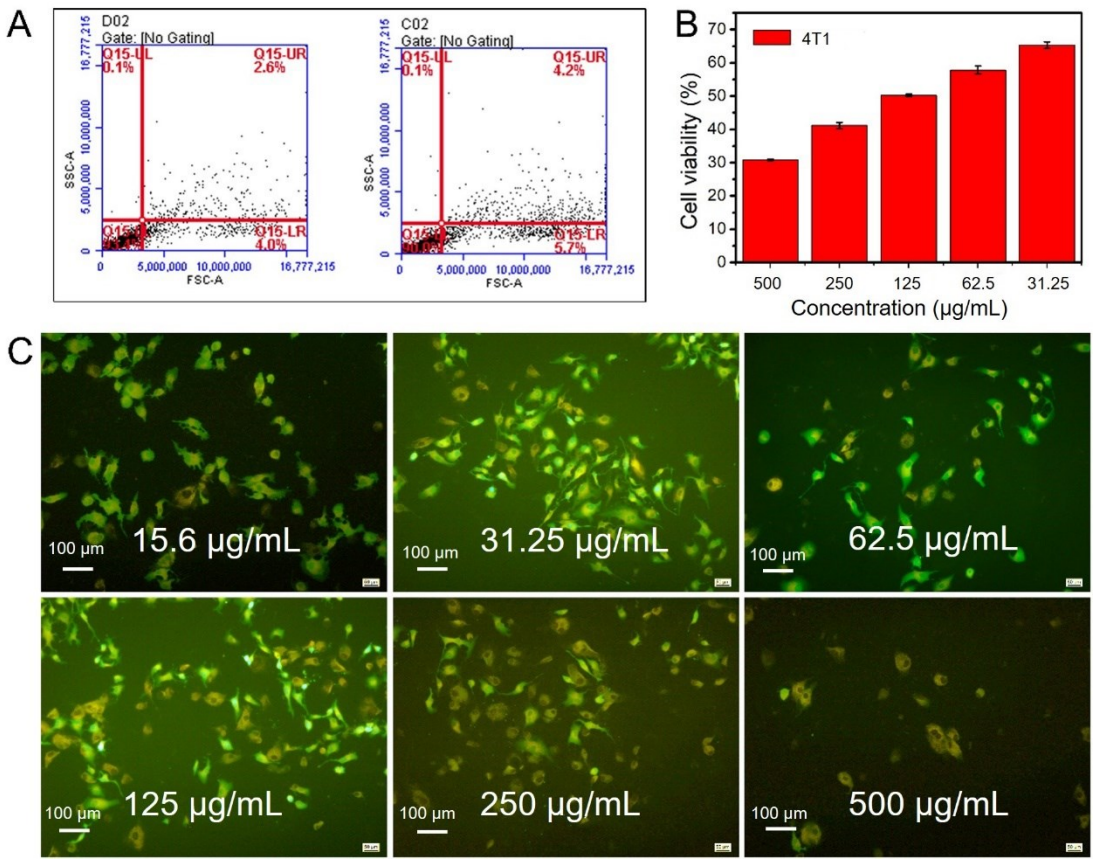

Fig. S12. (A) Flow cytometry results of cancer cells incubated with DOX for different incubation time points of 3 h and 6 h, (B) Cell viability and (C) Calcein AM/PI stained microscopy images of cells incubated with different concentrations of DOX.

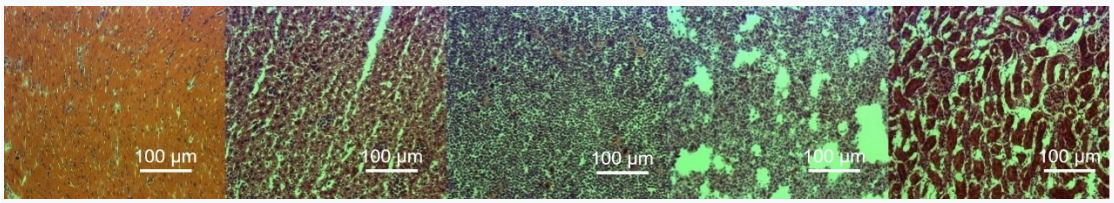

Fig. S13. H&E staining microscopy images of heart, liver, spleen, lung, and kidney of mice injected intravenously with DMDN.

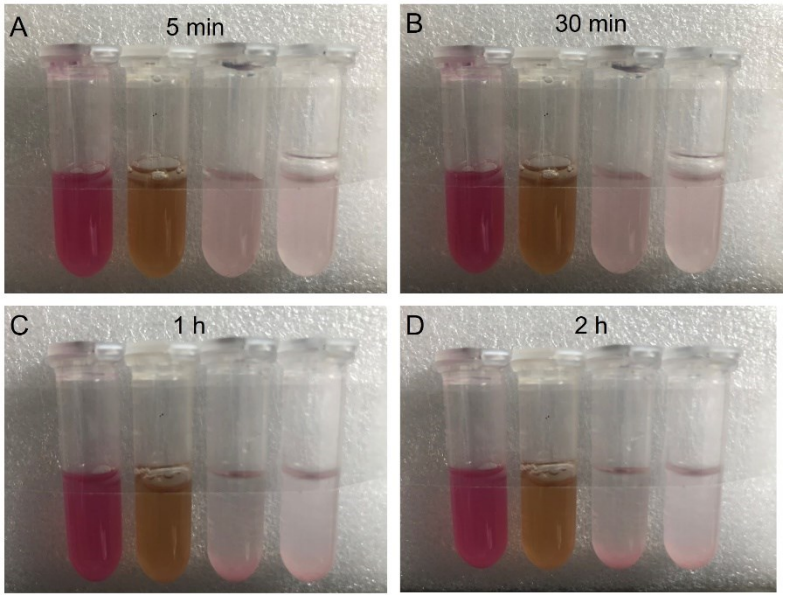

Fig. S14. The stability of DMDN in four solutions (FBS, medium, water, and PBS).

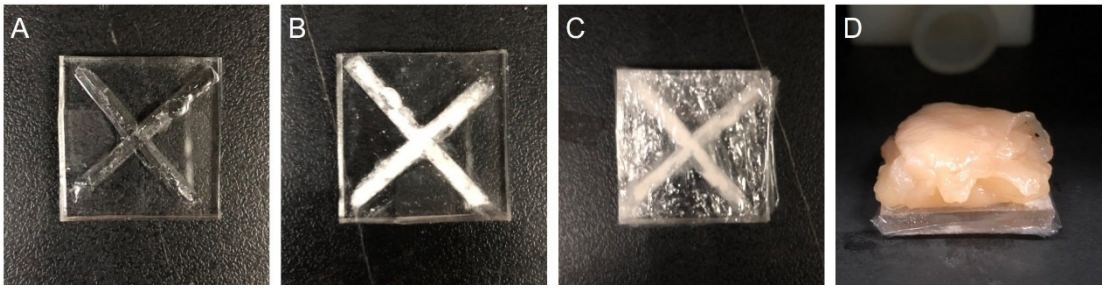

Fig. S15. The fabrication process of PDMS substrate with chicken breasts (thickness: 7 mm).

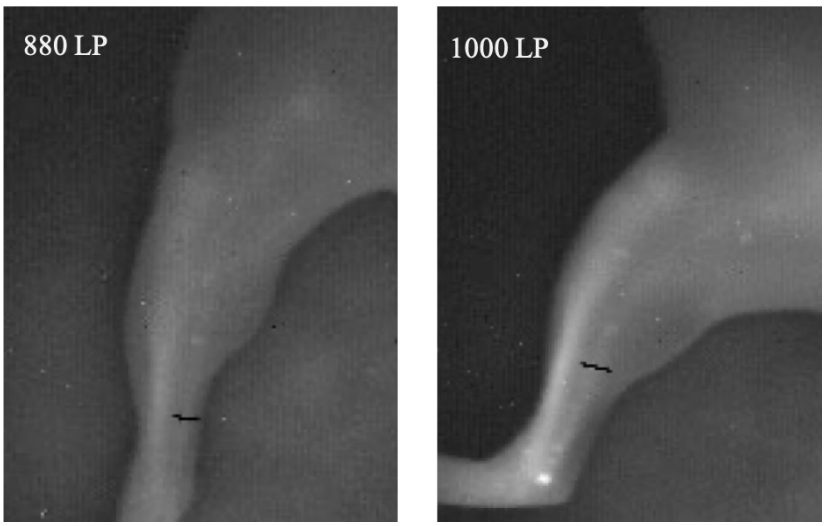

Fig. S16. The enlarged view of NIR-II imaging of blood vessels.

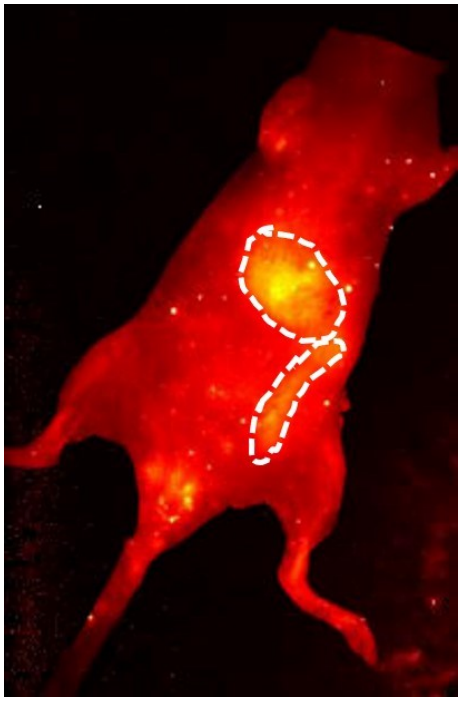

Fig. S17. NIR-II imaging of the whole mice after intravenous injection of DMDN.