Supporting Information

Materials and methods

Materials

O-Benzotriazole-N,N,N',N'-tetramethyl-uronium-hexafluorophosphate (HBTU) was obtained from NovaBioChem. Diisopropylethyl amine (DIPEA), 1-Pyrenebutanoic acid andtris(2,2′-bipyridiyl)dichlororuthenium(II) hexahydrate [$Ru(bpy)_3Cl_2 \cdot 6H_2O$] were purchased from Sigma-Aldrich. Graphene oxide sheets (GOS) were obtained from Nanjing XFNANO Materials Tech Co., Ltd. Fmoc-Gly-OH, Fmoc-Ala-OH and Fmoc-Tyr(tBu)−OH were received from GL Biochem (Shanghai). All other chemicals were obtained from Aladdin. All solvents were used directly without further purification. All mice were purchased from laboratory animal center of Academy of Military Medical Sciences (Beijing, China).

Synthesis of PyGAGAGY

PyGAGAGY (**Scheme S1**) was synthesized via the common solid phase peptide synthesis protocol. First, Fmoc-Tyr(^{t}Bu)-OH (1 equiv.) and DIPEA (4 equiv.) were dissolved in CH_2Cl_2(20 mL g^{-1} resin). Then chlorotrityl chloride resin (1 equiv.) was added to the solution and the mixture was stirred at room temperature for 1 h. The reaction was filtered and the unreacted resin was capped with 1: 2: 17 (v/v/v) DIPEA-MeOH-DCM (3 × 20 mL per gram resin). After the capping procedure, the resin was thoroughly washed with CH_2Cl_2, DMF, and CH_2Cl_2, and then dried *in vacuo*. The bead-loading was determined by 2% DBU/DMF method to be ~ 0.5 mmol g^{-1}. The beads were then swollen in DMF for 0.5 h in a sealed spin column and DMF was then removed via filtration. 20% Piperidine/DMF (3 × 5 mL, 5 min each time) was added to remove the Fmoc protecting group. The sequence was elongated with the HBTU coupling reaction: Fmoc-Gly-OH, Fmoc-Ala-OH or 1-Pyrenebutanoic acid (4 equiv.), HBTU (4 equiv.), and DIPEA (8 eq.) were dissolved in DMF (~ 5 mL) and then transferred to the de-Fmoc resin. The mixture was shaken at room temperature for 2 h for elongation of the sequence. Finally, the resin was washed thoroughly with DMF, CH_2Cl_2, and DMF. Reagent K (TFA/thioanisole/water/phenol/EDT = 82.5:5:5:5:2.5, V/V; 75 mL per gram of resin) was incubated with the resin for ~ 3 h at room temperature to cleave the peptide from the resin and to remove the protecting groups on the side chains of the amino acids in the meanwhile. The mixture was filtered and the solution was concentrated *in vacuo*. Then the residue was precipitated with cold diethyl ether. The product was collected by centrifuge, washed with diethyl ether, and then dried under high vacuum. The obtained PyGAGAGY was characterized by HPLC and mass spectroscopy (**Figure S1-2**). HPLC conditions: Alltima^{TM} C18 4.6 x 250 mm column, solvent A: 0.065% TFA in H_2O (v/v), solvent B: 0.05% TFA in CH_3CN (v/v), gradient: 0 to 2.6 min, 1% A, 2.6 to 7.65 min, 1% to 5% A, 7.65 to 17.8 min, 5% to 99% A, 17.8 to 20.15 min, 99% to 100% A, 20.15 to 24 min, 100% to 99% A, 24 to 34 min, 99% A.

Preparation of Hydrogel (Photo-crosslinking reaction by $Ru(bpy)_3Cl_2$ and Ammonium Persulfate (APS).)

PyGAGAGY was dissolved in doubly distilled water (ddH_2O)to make a final concentration of 20 mg mL^{-1}. Then graphene oxide sheets (GOS) were added into the PyGAGAGY solution and dispersed by ultrasonic for 60 minutes to get a GOS final concentration of 10 mg mL^{-1}.Thereafter $Ru(bpy)_3Cl_2$(3.0μL, 1 mM) and APS (15.0 μL, 600 mM) were added into 300μL of the GOS dispersed PyGAGAGY solution. The mixture was vigorously vortex-mixed prior to light irradiation. After irradiation with white light (using a Panasonic PT-UX10 projector with a 220 W lamp as the light source) for 1 minute, the dark brown hydrogel was formed. The formation of PyGAGAGY dimer was confirmed by mass spectrum.

Control experiments for the preparation of the hybrid hydrogels

1. **The Peptide cannot be photocrosslinked into hydrogel without GOS**

In this experiment, PyGAGAGY was first dissolved in ddH_2O to make a final concentration of 20 mg mL^{-1}. Then $Ru(bpy)_3Cl_2$ (3.0 μL,1 mM) and APS (15.0 μL, 600 mM) were added into 300 μL of PyGAGAGY solution. The mixture was vigorously vortex mixed prior to light irradiation. Even after irradiation with white light (using a Panasonic PT-UX10 projector with a 220 W lamp as the light source) for 30 minutes, hydrogel was not formed (**Figure S5**).

2. **GOS cannot self-assembly (or be crosslinked) into hydrogel without the peptide.**

In this experiment, GOS was first dispersed in ddH_2O to make a final concentration of 10 mg mL^{-1} by ultrasonic for 120 minutes (**Figure S6**). Then $Ru(bpy)_3Cl_2$ (3.0 μL, 1 mM) and APS (15.0 μL, 600 mM) were added into 300 μL of GOS dispersed solution. The mixture was vigorously vortex mixed prior to light irradiation. Even after irradiation with white light (using a Panasonic PT-UX10 projector with a 220 W lamp as the light source) for 30 minutes, hydrogel was not formed (**Figure S7**).

3. **The photo-crosslinked peptide cannot form hydrogel when mixed with GOS.**

In this experiment, PyGAGAGY was first dissolved in ddH_2O to make a final concentration of 20 mg mL^{-1}. Subsequently, $Ru(bpy)_3Cl_2$ (3.0 μL, 1mM) and APS (15.0 μL, 600 mM) were added into 300 μL of the PyGAGAGY solution. The mixture was vigorously vortex mixed and irradiated with white light (using a Panasonic PT-UX10 projector with a 220 W lamp as the light source) for 30 minutes to get the photo-crosslinked PyGAGAGY solution. Then GOS were added into the photo-crosslinked PyGAGAGY and dispersed by ultrasonic for 120 minutes to get a GOS final concentration of 10 mg mL^{-1}. However the hydrogel was not formed (**Figure S8**). This result highlights the importance of the formation of peptide-GOS complex in the hierarchical construction approach.

Scanning electron microscopy (SEM) and Transmission electron microscopy(TEM)
SEM image was performed on a field emission scanning electron microanalyzer (Zeiss Supra 40) at an acceleration voltage of 5 kV. The tested samples were obtained by lyophilization of GOS (**Figure S4**). Transmission electron microscopy images were obtained using a JEOL JEM-200CX transmission electron microscope operating at an acceleration voltage of 200 kV.

Fourier Transform Infrared (FTIR) Spectroscopy
FTIR spectra were recorded on Bruker VERTEX 80V spectrometers using lyophilized hydrogel, the peptide and GOS samples.

Rheology experiments
The hydrogels were carefully transferred to the rheometer plate using a spatula prior to the measurement. The rheology experiments were then carried out with a strain-sweep mode at 1 Hz and/or a frequency-sweep mode at 0.1% strain on a Haake RheoStrss 6000 rheometer (geometry: 1° /20 mm of cone and plate; gap: 0.2 mm; temperature: 20 °C).The strain-sweep experiments were carried out at 1 Hz from strain amplitude range of 0.01% to 100% (**Figure S9**). The recovery experiments were carried out in the time-sweep mode with an initial oscillation frequency of 1 Hz and strain of 0.1% for 240 s to measure the mechanical properties of the hydrogel before being destroyed. Then, the gel was destroyed by an ossilation at the frequency of 100 Hz and the strain of 100% for 60 s. The recovery of the gel was subsequently monitored at a low frequency of 1 Hz and a strain of 0.1% for 1200 s. Mechanical properties of the hybrid hydrogel with different GOS concentration were measured by the dynamic frequency sweep mode (**Figure S10**).

Melting Temperature of PyGAGAGY
The melting temperature of PyGAGAGY was measured by circular dichroism spectroscopy (CD). Far-UV CD measurements were carried out on the Jasco J-815 CD spectrometer. Before the experiment, the instrument was flushed with nitrogen gas. The CD spectra were recorded in a cuvette with a path length of 1.0 cm at a scan rate of 10 nm min^{-1}. For each peptide sample, an average of 5 scans were reported. CD spectra of PyGAGAGY, which was designed and sythesized according to the procedure described above were measured. The molar ellipticity of PyGAGAGY was calculated according to the following equation: $[\theta_M]=[\theta_{exp}]/(d*C)$, where $[\theta_M]$ and $[\theta_{exp}]$ are the molar and observed ellipticity, respectively; d is the pathlength; and C is the molar concentration. T Variable CD measurements were carried out in the same condition. During the experiment, temperature changed from 10 to 90 °C, and the ellipticity at 215 nm wavelength was recorded and then converted to the molar ellipticity by the formula described above. The fitting was based on the following equation: $[\theta_M]=[\theta_0]+A/(1+\exp((T_m-T)/r)$, where T_m is the melting temperature of the peptide, and $[\theta_0]$, A, r were the fitting parameters independent of T_m, T is the temperature of the peptide solution recorded during the T variable CD measurement experiment.

Photothermal effect triggered in vitro drug release

1. **Drug Loading after the Formation of Hydrogels**

   In the present experiment, doxorubicin was used as the model drug. After the 100 μL hydrogel (with 20 mg mL^{-1} PyGAGAGY and 10 mg mL^{-1} GOS) was prepared in an AXYGEN MCT-200-C microtube, 1.0 ml PBS (pH=7.4) with 0.2 mg mL^{-1} DOX was added into the tube. Then let the tube in dark at room temperature. 2 μL of PBS with DOX above the hydrogel in the above mentioned tube was taken out at different time after 1.0 ml PBS (pH=7.4) with 0.2 mg mL^{-1} DOX was added into the tube. The amount of DOX left in the PBS was calculated through UV-vis spectrophotometric measurement on NanoDrop 2000 (Thermo Scientific) at 480 nm. The percentage of the loaded DOX=(1- the amount of DOX left in the PBS/total DOX in the PBS before loading) ×100%. It is worth mentioning that exposure of the hydrogel to the light source for photo-crosslinking or the NIR laser for photothermal-triggered drug release does not cause measurable decomposition of DOX, as estimated from the UV-vis spectra of DOX (data not shown).

2. **Photothermal Irradiation**

   To examine the photothermal heating ability of the hydrogel, 100 μL hybrid hydrogel (containing 20 mg mL^{-1} PyGAGAGY and 10 mg mL^{-1} GOS) was prepared in an AXYGEN MCT-200-C microcentrifuge tube (2 mL). Then 1.0 mL PBS (pH=7.4) was added into the tube before the hydrogel was exposed to laser irradiation. The source of irradiation was an optical fiber coupled 808 nm high power diode-laser (Hi-Tech Optoelectronics Co., Ltd. Beijing, China) with a spot diameter of~5 mm, and was placed ~3 cm above the gel surface. The photothermal heating ability was validated by measuring the temperature of the hydrogel with an infrared thermometer (OMEGA ENGINEERING, INC. Shanghai, China) immediately upon removal of the laser source. In the control experiment, 1.1 mL water in the same microcentrifuge tube without hydrogel was used as blank.

3. **In vitro Drug release experiment**

   In our experiment, DOX was used as the model drug. DOX (2.0 mg mL^{-1}) was incorporated in the hydrogel after the formation of the hydrogel. One hundred μL of DOX-loaded hydrogel (with 20 mg mL^{-1}PyGAGAGY and 10 mg mL^{-1} GOS) was settled at the bottom of an AXYGEN MCT-200-C microcentrifuge tube. Then, 1.0 mL PBS (pH=7.4) was filled into the tube. Immediately, the hydrogel was subjected to laser irradiation at different power and for different time using the experimental scheme depicted in **Figure 4A**. An optical fiber-coupled 808-nm high power diode-laser (Hi-Tech Optoelectronics Co., Ltd. Beijing, China) with a spot diameter of ~5 mm was used as the irradiation source. The irradiation pulses were applied hourly and the system was set still after each irradiation pulse. To measure the released DOX, 2 μL of supernatant was taken out immediately before,

8 min and 30 min after each irradiation pulses. The amount of released DOX was calculated based on the UV-vis absorbance of the supernatant at 480 nm measured using UV-vis spectrometer (NanoDrop 2000, Thermo Scientific).

Cytotoxicity of hydrogel on normal human hepatocytes cell line L02

1. Cell culture and treatment

Hydrogel was prepared in an AXYGEN MCT-200-C microcentrifuge tube according to the method described in supporting information. The volume of the hydrogel was 0.1 mL and hydrogels could be taken out as a whole easily. Before added to the cell culture medium, all the hydrogels were sterilized by ultraviolet for 15 min. Normal human hepatocytes cell line L02 was purchased from Xiangya Central Experiment Laboratory, Central South University, China. These cells were grown in RPMI 1640 medium with 10% FBS in the presence of 100 UmL^{-1} penicillin and 100 μgmL^{-1} streptomycin and maintained at 37 °C in a humidified atmosphere containing 5% (v/v) CO_2.

In experiment, L02 cells were seeded in a 24-well plate at a density of 1×10^4 cells per well (with 1.0 mL DMEM medium). After 24 h incubation, 0.1 mL hydrogel was added to the wells with L02 cells. Then all the cells were cultured for 24h and then all the immersed hydrogels were removed from the RPMI 1640 medium thoroughly. Then all the cells were cultured for another 20 h and the photos of the cells were taken.

2. Cell viability assay

After the photos had been taken, cell viability was assessed by the MTT method. Briefly, cells were incubated with MTT (0.5 $mgmL^{-1}$) for 4 h at 37 °C. During this incubation period, water-insoluble formazan crystals were formed, which were dissolved by the addition of 100 μL DMSO per well. The optical densities (*A*) at 570 nm were measured using an enzyme-linked immunosorbent assay plate reader. Wells containing culture medium and MTT but no cells acted as blanks. The percentage of cell viability was calculated as follows: $A_{drug\text{-}blank}/A_{control\text{-}blank} \times 100\%$.

Cytotoxicity of $Ru(bpy)_3Cl_2$ and APS on normal human hepatocytes cell line L02

1. Cell culture and treatment

Normal human hepatocytes cell line L02 was purchased from Xiangya Central Experiment Laboratory, Central South University, China. These cells were grown in RPMI 1640 medium with 10% FBS in the presence of 100 UmL^{-1} penicillin and 100 μgmL^{-1} streptomycin and maintained at 37 °C in a humidified atmosphere containing 5% (v/v) CO_2. $Ru(bpy)_3Cl_2$ and APS were dissolved in RPMI 1640 mediumas a stock solution at 10 mM and 3 M, respectively. Before use, the stock solution was diluted to the desired concentration with fresh medium immediately. Cells grown in RPMI 1640 media served as the control.

2. Cell viability assay

Cell viability was assessed by the MTT method. Briefly, cells were seeded in a 96-well plate at a density of 1×10^4 cells per well. After 24 h incubation, $Ru(bpy)_3Cl_2$

and APS at different concentrations were added to the cells. In the negative control, only RPMI 1640 medium was added. After growing for 24h, cells were incubated with MTT (0.5 $mgmL^{-1}$) for 4 h at 37 °C. During this incubation period, water-insoluble formazan crystals were formed, which were dissolved by the addition of 100 μL DMSO per well. The optical densities (*A*) at 570 nm were measured using an enzyme-linked immunosorbent assay plate reader. Wells containing culture medium and MTT but no cells acted as blanks. The percentage of cell viability was calculated as follows: $A_{drug\text{-}blank}/A_{control\text{-}blank} \times 100\%$.

Cytotoxicity of leachable components from hydrogel on normal human hepatocytes cell line L02

The hydrogel was dried on a lyophilizer and the freeze-dried product was soaked in 300 μLRPMI 1640 media and shaken at 300 rpm for 30 min. Then the supernatant was obtained by centrifugation at 10, 000 rpm for 5 min and filtered using a celluloseacetate membrane filter (0.22 μm pore diameter) for sterilization. Cytotoxicity of leachable components from the hydrogel was assessed also by MTT method as described above.

Cytotoxicity of hydrogel, DOX-loaded hydrogel and DOX-loaded hydrogel irradiated by NIR on hepatocarcinoma cell line SMMC-7721

1. Cell culture and treatment

Hydrogel and DOX-loaded hydrogel (with 0.2 or 2.0 mg/ml DOX) were prepared in an AXYGEN MCT-200-C microcentrifuge tube according to the method described above.

Before added to the cell culture medium, all the hydrogels were sterilized by ultraviolet for 15 min. DOX was dissolved in DMEM medium as a stock solution and DOX stock solution was diluted to the desired concentration with fresh medium right before the experiments.

Hepatocarcinoma cell line SMMC-7721 was purchased from Xiangya Central Experiment Laboratory, Central South University, China. These cells were grown in DMEM medium with 10% FBS in the presence of 100 UmL^{-1} penicillin and 100 μg mL^{-1} streptomycin and maintained at 37 °C in a humidified atmosphere containing 5% (v/v) CO_2.

In experiment, SMMC-7721 cells were seeded in a 24-well plate at a density of 1×10^4 cells per well (with 1.0 mL DMEM medium). After 24 h incubation, DOX solution, 0.1 mL hydrogel or 0.1 mL DOX-loaded hydrogel was added to the wells with SMMC-7721 cells. Then half of the wells with hydrogels or DOX-loaded hydrogels which were immersed in medium were irradiated by 808 nm NIR with a spot diameter of ~14 mm at 1.5 W for 2 min and the NIR light spots were controlled for thoroughly covering the hydrogels or DOX-loaded hydrogels. The wells with only DMEM medium and cultured SMMC-7721 cells also were irradiated by 808 nm NIR with a spot diameter of ~14 mm at 1.5 W for 2 min. Then all the cells were cultured for 4h and then all the immersed hydrogels or DOX-loaded hydrogels were removed from the DMEM medium thoroughly. Then all the cells were cultured for another 20

h and the photos of the cells were taken.

2. Cell viability assay

After the photos had been taken, cell viability was assessed by the MTT method. Briefly, cells were incubated with MTT (0.5 mgmL^{-1}) for 4 h at 37 °C. During this incubation period, water-insoluble formazan crystals were formed, which were dissolved by the addition of 100 μL DMSO per well. The optical densities (*A*) at 570 nm were measured using an enzyme-linked immunosorbent assay plate reader. Wells containing culture medium and MTT but no cells acted as blanks. The percentage of cell viability was calculated as follows: $A_{drug\text{-}blank}/A_{control\text{-}blank} \times 100\%$.

Photothermal effect triggered in vivo drug release

In our experiment, DOX was used as the model drug. DOX (2.0 mg mL^{-1} hydrogel) was incorporated in the hydrogel after the formation of hydrogel as described above. Then DOX-loaded hydrogel (50 μL) was subcutaneously injected into mice (BALB/C nude mice, Laboratory Animal Center of the Academy of Military Medical Science, Beijing, China) followed by NIR fluorescence imaging using a Maestro Dynamic Lumina system (CRI, Woburn, MA). The excitation and emission wavelength was 465 nm and 570 nm respectively, and the exposure time was 1 s. Scans were carried out at 0, 10, 60 and 120 min post subcutaneous injection (**Figure S20A-D**). And 120 minutes after subcutaneous injection, the 808 nm NIR with a spot diameter of ~8 mm at 2.0 W for 1 min was applied for the irradiation of the raised skin caused by subcutaneous injection in one of the mice (the right one in **Figure S20**) and the NIR light spots were controlled for thoroughly covering the raised skin above the injected DOX-loaded hydrogel. Then scans were carried out at 0, 10, 60 and 120 min post irradiation (**Figure S20E-H**). The animal experiments were performed with animal experimental permission.

Three, five, seven, ten and twelve days after first NIR irradiation, the irradiation was performed in the same mouse (the right mouse in **Figure S21**) as described above and scans were carried out before and immediately after the irradiation (**Figure S21**).

In vivo tumor inhibition study

Four-week-old female BALB/C nude mice (Laboratory Animal Center of the Academy of Military Medical Science, Beijing, China) were used as animal models and bred in the specific-pathogen-free facility. The animal experiments were conducted according to the Regulation on Experimental Animals of Nanjing University.

SMMC-7721 cells (5×10^6 cells/mouse) were subcutaneously injected in the left flank region of mice. Tumor-bearing mice were randomly divided into 6 groups (n = 5). Treatments were started 15 days after inoculation of SMMC-7721 cells, which was designated as day 0.

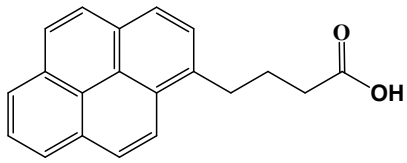
In our experiment, DOX was used as the model drug. DOX was incorporated in the hydrogel after the formation of hydrogel as described above. Hydrogel or DOX-loaded hydrogel was subcutaneously injected near the tumor at day 0. Irradiation was

performed as described above and repeated six times at day 0-5 respectively.
Tumor-bearing mice (n = 5) without treatment were used as control. Tumor-bearing mice (n = 5) with subcutaneous injection of 50 μL hydrogel and 808 nm NIR irradiation were used as gel-irradiation group. Tumor-bearing mice (n = 5) with subcutaneous injection of 50 μL DOX-loaded hydrogel (hydrogel containing DOX of 1.0 mg mL^{-1}) were used as DOX-L-gel group. Tumor-bearing mice (n = 5) with subcutaneous injection of 50 μL DOX-loaded hydrogel (hydrogel containing DOX of 1.0 mg mL^{-1}) and 808-nm NIR irradiation were used as DOX-L-gel-irradiation group. Tumor-bearing mice (n = 5) with subcutaneous injection of 50 μL DOX-loaded hydrogel (hydrogel containing DOX of 5.0 mg mL^{-1}) were used as DOX-H-gel group. Tumor-bearing mice (n = 5) with subcutaneous injection of 50 μL DOX-loaded hydrogel (hydrogel containing DOX of 5.0 mg mL^{-1}) and 808 nm NIR irradiation were used as DOX-H-gel-irradiation group.
The tumors were measured by caliper every 3 days. Tumor volume and tumor volume ratio were calculated using the following equations:
Tumor volume, $V = (a \times b^2)/2$, where a and b were the largest and the smallest diameter of the tumor.
Tumor volume ratio $= V/V_0$, where V_0 was the tumor volume when the treatment was initiated.
At day 23, all the tumor-bearing mice were sacrificed and tumors were taken from mice carefully and tumor weight was measured by balance (**Figure S22**). Then tumors from mice of the same group were arranged in the same row and photos were taken.

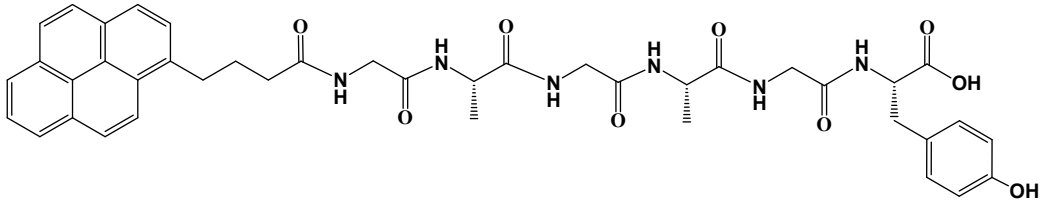
Statistical analysis

All data were expressed as mean ± SD. Difference between two groups was analyzed by two-tailed Student's t-test. $P < 0.05$ or $P < 0.01$ was considered statistically significant.

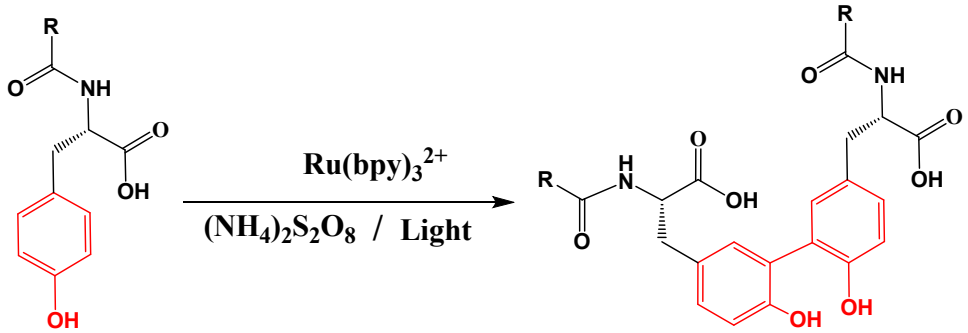
Supporting Figures



1-Pyrenebutanoic acid (Py)



PyGAGAGY



PyGAGAGY
R=PyGAGAG

PyGAGAGY-YGAGAGPy

Scheme S1 Schematic illustration of the structures of Py and PyGAGAGY and the $Ru(bpy)_3Cl_2$-catalyzed photo-crosslinking reaction.

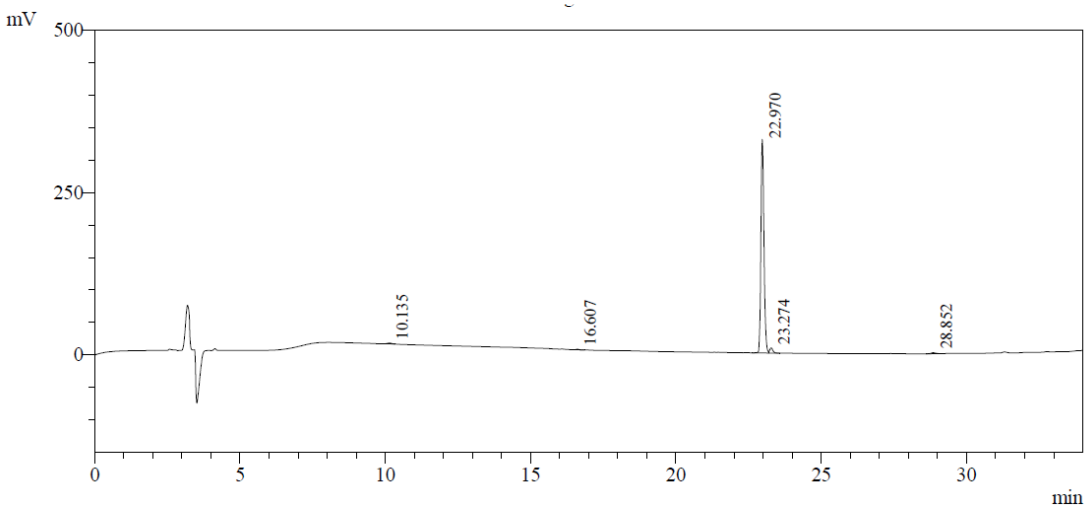


Figure S1 HPLC chromatogram of PyGAGAGY.

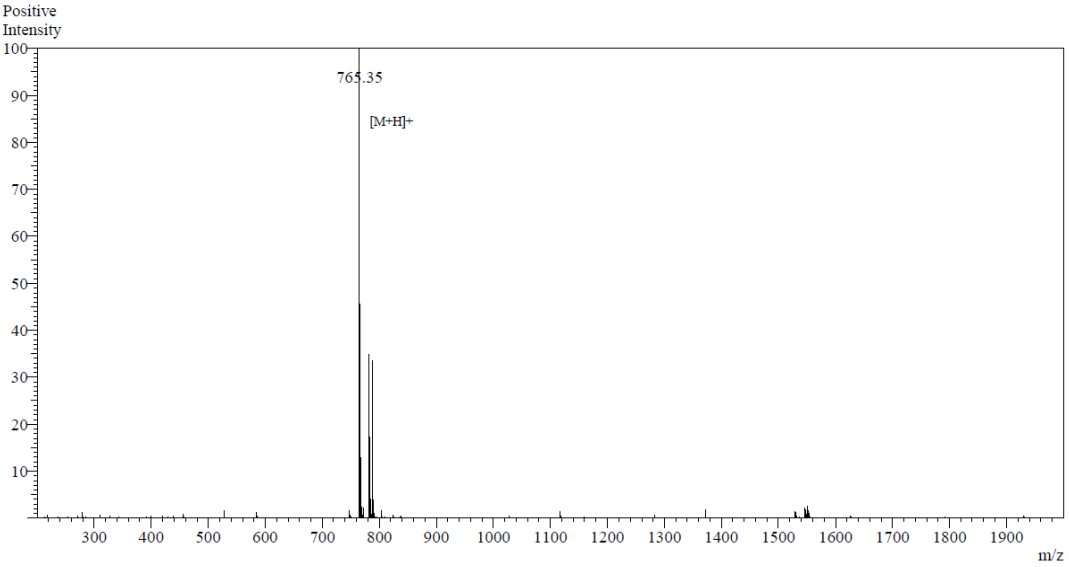


Figure S2 Mass spectrum of PyGAGAGY.

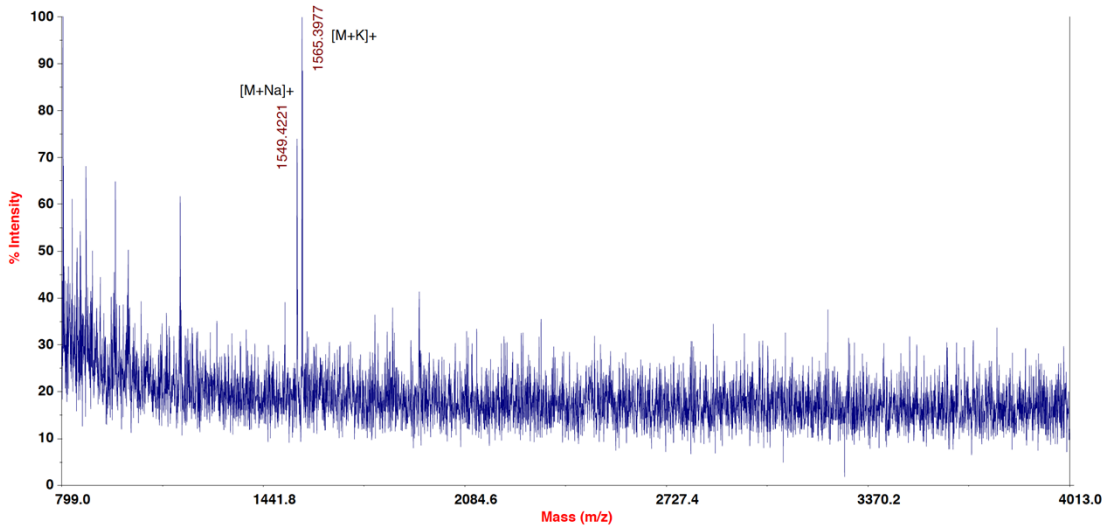


Figure S3 Mass spectrum of crosslinked PyGAGAGY dimer.

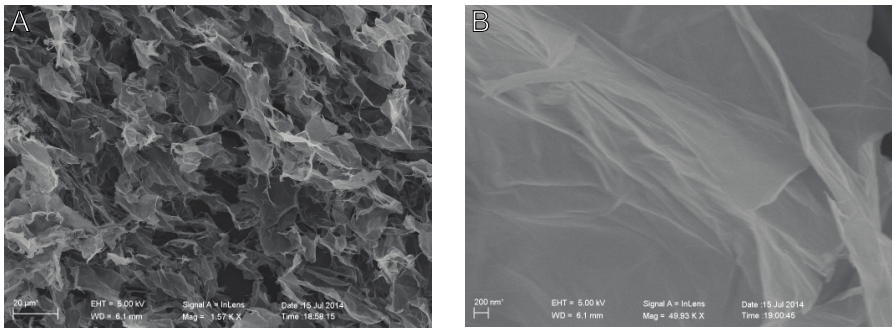


Figure S4 SEM images of the lyophilized GOS solution. (A) low magnification. (B) high magnification.

Figure S5 The image for PyGAGAGY solution photo-crosslinked by $Ru(bpy)_3Cl_2$ and APS.

Figure S6 The image for GOS dispersed solution.

Figure S7 The image for GOS dispersed solution photo-crosslinked by $Ru(bpy)_3Cl_2$ and APS.

Figure S8 The images for GOS dispersed PyGAGAGY solution which was photo-crosslinked by $Ru(bpy)_3Cl_2$ and APS before the addition of GOS.

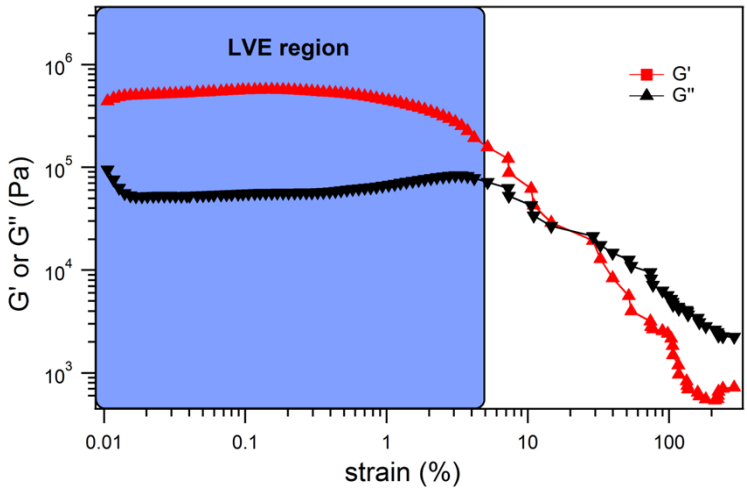


Figure S9 The strain-sweep experiment of the hybrid hydrogel at a constant sweep frequency of 1 Hz**.** The linear viscoelastic (LVE) regions are shaded in light blue.

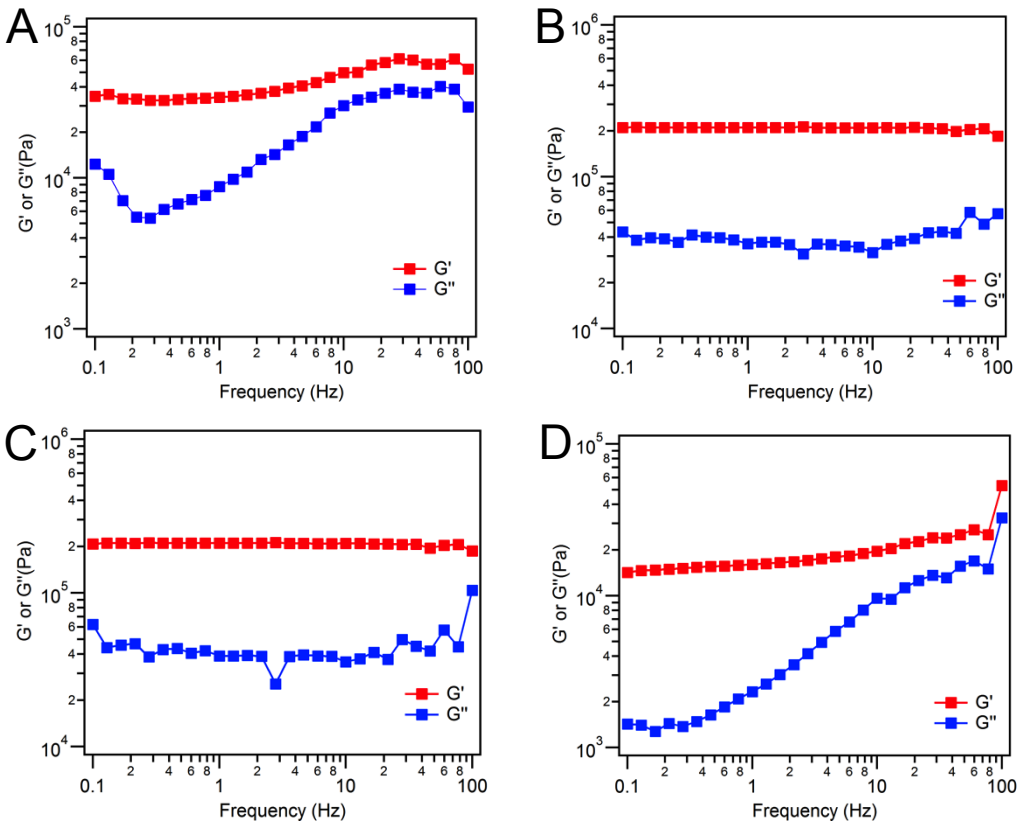


Figure S10 Mechanical properties of the hybrid hydrogel. (A-D) The rheological measurement in the dynamic frequency sweep mode for the hydrogel with the GOS concentrations of 5, 10, 15 and 20 mg mL^{-1}, respectively.

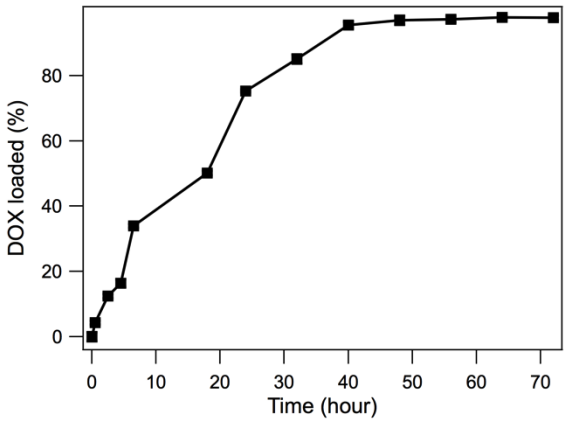


Figure S11 DOX Loading into the hybrid hydrogel at different incubation time. The percentage of the loaded DOX=(1-the amount of DOX left in the PBS/total DOX in the PBS before loading) ×100%.

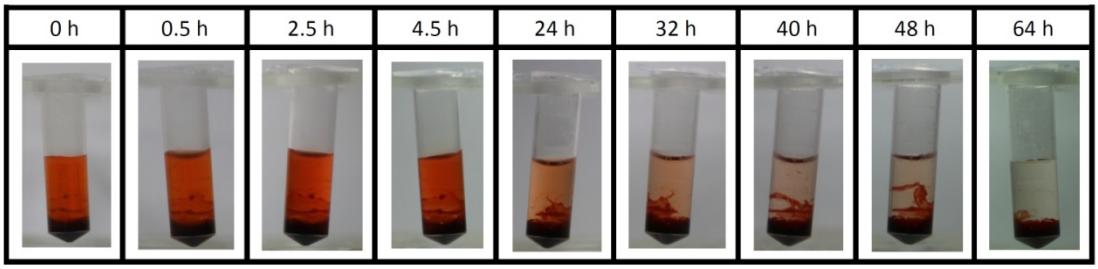


Figure S12 Image of DOX loading at the indicated time.

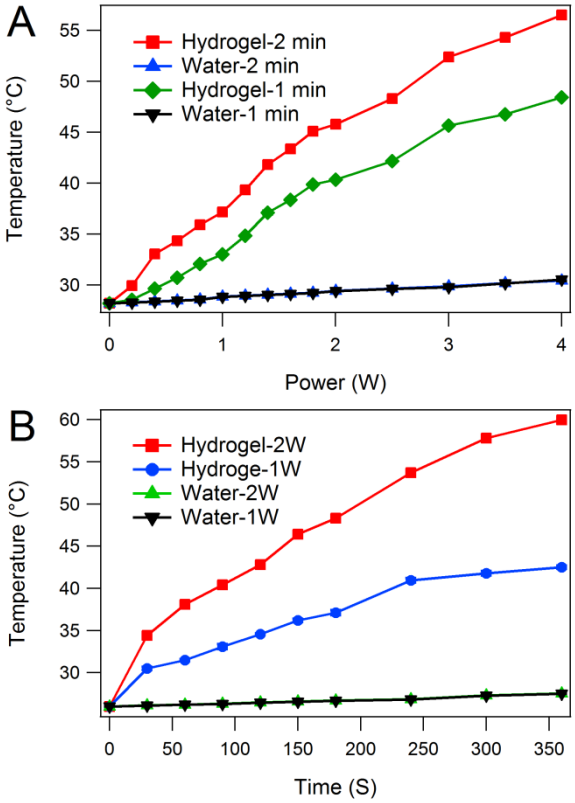


Figure S13 Temperature response of the hybrid hydrogels after NIR laser irradiation. The temperature was measured immediately after the removal of the NIR laser irradiation. (A) Temperature changes of the hydrogels after being irradiated for 1 or 2 minutes at different power. (B) Temperature changes of the hydrogels after being irradiated at the power of 1 or 2W for different time.

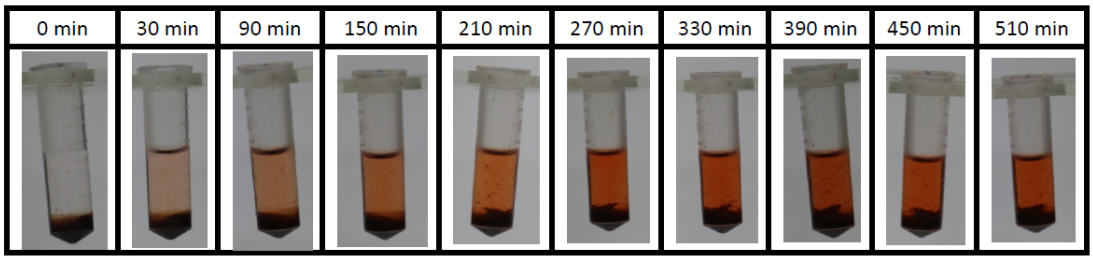


Figure S14 Snapshots of laser irradiation-triggered release of DOX (power: 1.5 W; irradiation time: 2 min; frequency: hourly). The time that each picture was taken was shown on the top.

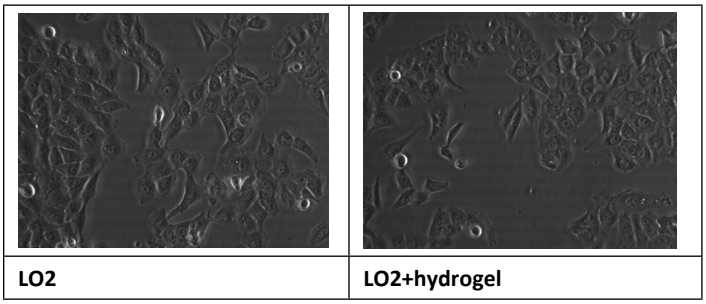


Figure S15 Cytotoxicity of hydrogel on normal human hepatocytes cell line L02.

Photographs of the normal human hepatocytes cell line L02 grown on a 24-well plate at a density ~1 × 10^4 cells per well in 1.0 mL of DMEM medium (10%FBS, 100U mL^{-1} penicillin, and 100 μg mL^{-1} streptomycin) at 37 °C in a humidified atmosphere containing 5% (v/v) CO_2. After growth for 24 h, 0.1 mL of fractured hydrogel was added to the desired wells. Then the cells were cultured for additional 24 h and the floating fractured hydrogels were removed by rinsing with DMEM medium before taking the photographs.

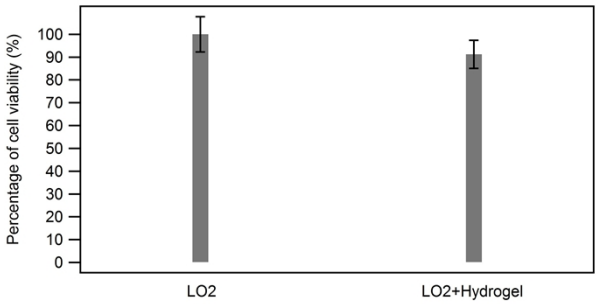


Figure S16 Cytotoxicity of hydrogel on normal human hepatocytes cell line L02.

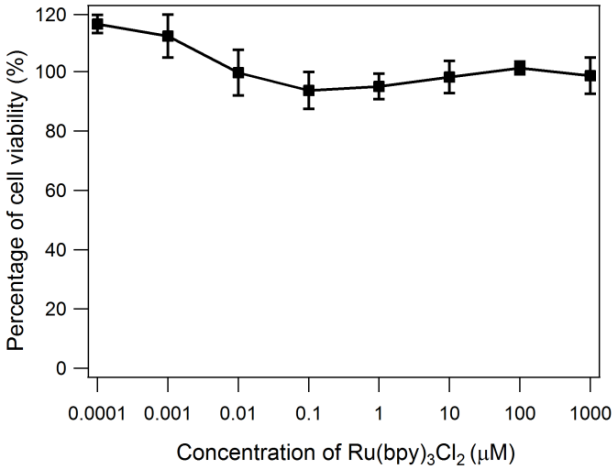


Figure S17 Cytotoxicity of $Ru(bpy)_3Cl_2$ on normal human hepatocytes cell line L02. In the hydrogel, the $Ru(bpy)_3Cl_2$ concentration is ~ 10μM, which is certainly safe for cell growth.

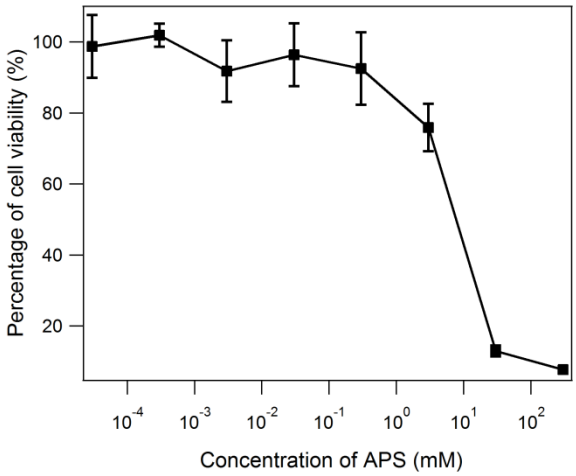


Figure S18 Cytotoxicity of APS on normal human hepatocytes cell line L02. In the hydrogel, most of APS added during the preparation was decomposed upon light-triggered photo-crosslinking reaction. The residual APS was estimated to be safe for cell growth.

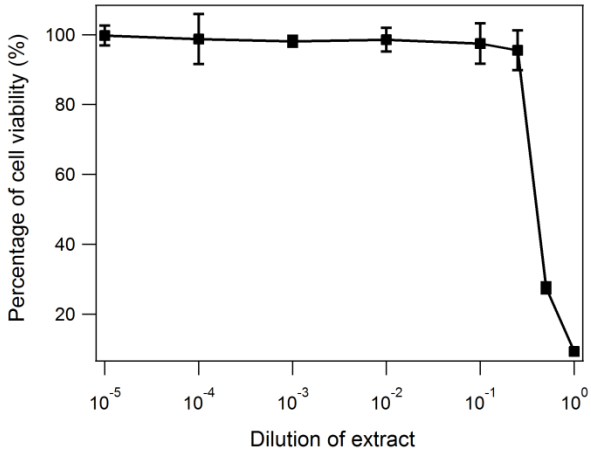


Figure S19 Cytotoxicity of leachable components on normal human hepatocytes cell line L02. The hydrogel is safe even only in the presence of medium of 3 times gel volume.

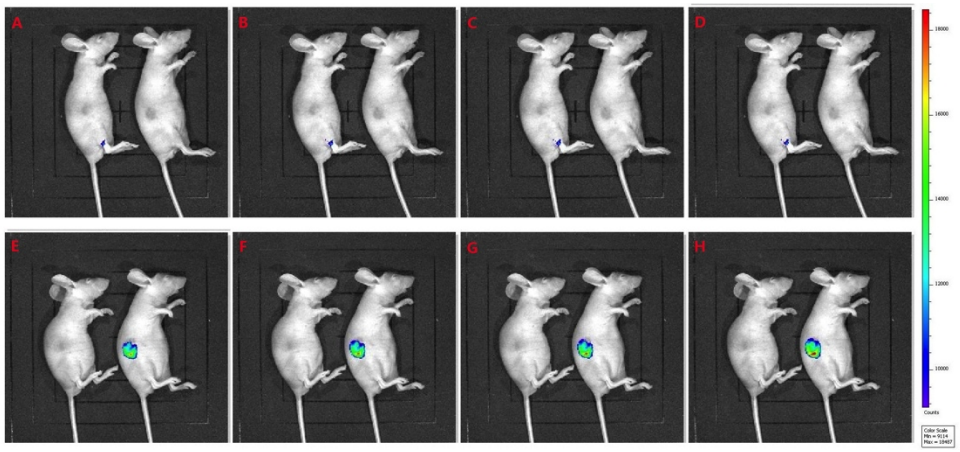


Figure S20 The fluorescence photos of mice at 0, 10, 60 and 120 min post subcutaneous injection of DOX-loaded hydrogel and at 0, 10, 60 and 120 min post the first 808 nm NIR irradiation (120 minutes after subcutaneous injection) on raised skin above the injected DOX-loaded hydrogel in one of the mice (the right mouse in Figures). (A-D): At 0, 10, 60 and 120 min post subcutaneous injection of DOX-loaded hydrogel, respectively. (E-H): At 0, 10, 60 and 120 min post the first 808 nm NIR irradiation (120 minutes after subcutaneous injection of DOX-loaded hydrogel) on raised skin above the injected DOX-loaded hydrogel in one of the mice (the right mouse in Figures), respectively.

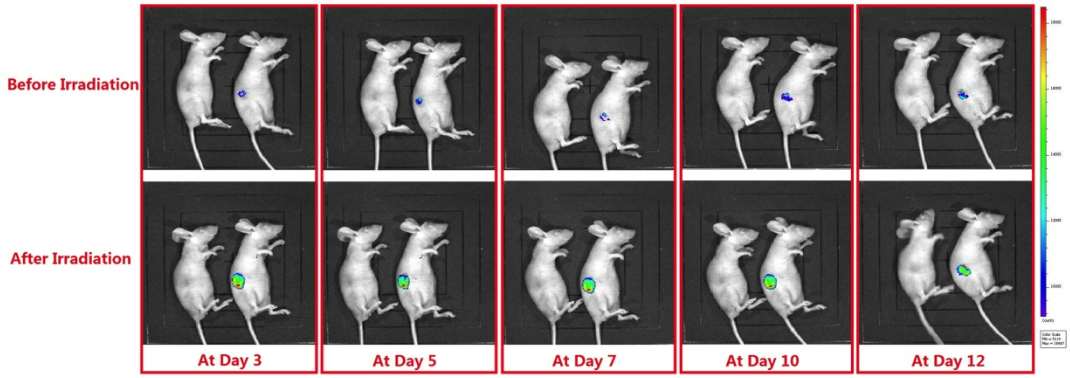


Figure S21 The fluorescence photos of mice at day 3, 5, 7, 10 and 12 after first NIR irradiation. Three, five, seven, ten and twelve days after first NIR irradiation, the irradiation was performed in the same mouse (the right mouse in Figures) as described above and scans were carried out before and immediately after the irradiation.

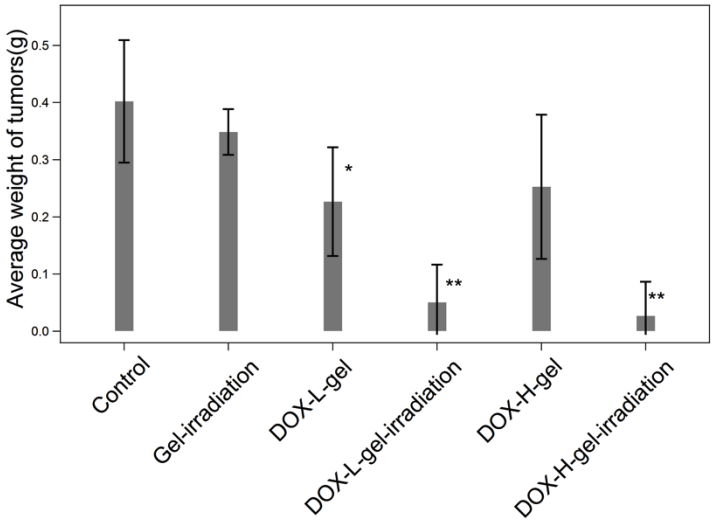


Figure S22 Average weight of tumors from tumor-bearing mice with different treatments. Each data point was denoted as mean ± SD. *P < 0.05, compared with control; **P < 0.01, compared with control.