Supporting Information

Dynamic-Covalent Hydrogel with NIR-Triggered Drug Delivery for Localized Chemo-Photothermal Combination Therapy

Pengfei Sun,[†,⊥] Ting Huang,[†,⊥] Xiaoxiao Wang,[†] Gaina Wang,[†] Zhijia Liu,*[,‡,§] Guosong Chen,[∥] and Quli Fan*[,†]

[†]Key Laboratory for Organic Electronics and Information Displays & Institute of Advanced Materials (IAM), Jiangsu National Synergetic Innovation Center for Advanced Materials (SICAM), Nanjing University of Posts & Telecommunications, Nanjing 210023, China.

[‡]School of Materials Science and Engineering, GD Research Center for Functional Biomaterials Engineering and Technology, Sun Yat-sen University, Guangzhou 510275, China.

[§]Jiangsu Key Laboratory for Biosensors, Institute of Advanced Materials (IAM), Nanjing University of Posts & Telecommunications, Nanjing 210023, China.

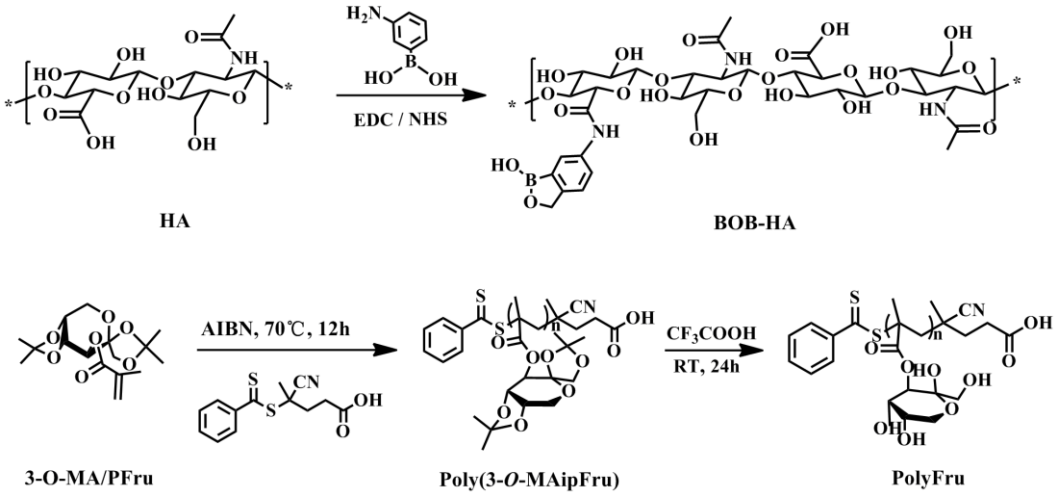
[∥]State Key Laboratory of Molecular Engineering of Polymers, Department of Macromolecular Science, Fudan University, Shanghai 200433, China.

[⊥]Pengfei Sun and Ting Huang contributed equally to this work.

Corresponding Authors

*E-mail: liuzhj9@mail.sysu.edu.cn (Z. Liu)

*E-mail: iamqlfan@njupt.edu.cn (Q. Fan)



Scheme S1. Synthetic procedures for a) BOB-HA and b) PolyFru.

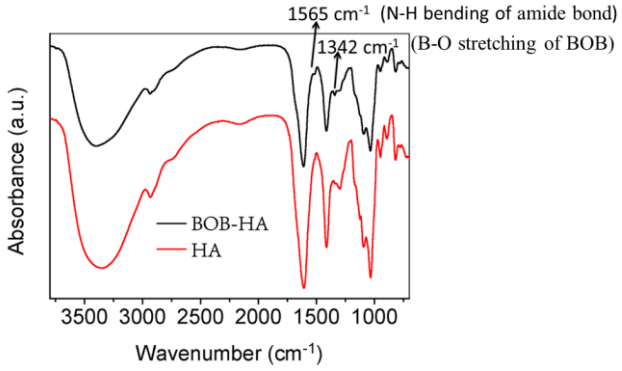


Figure S1. FTIR spectra of BOB-HA and HA.

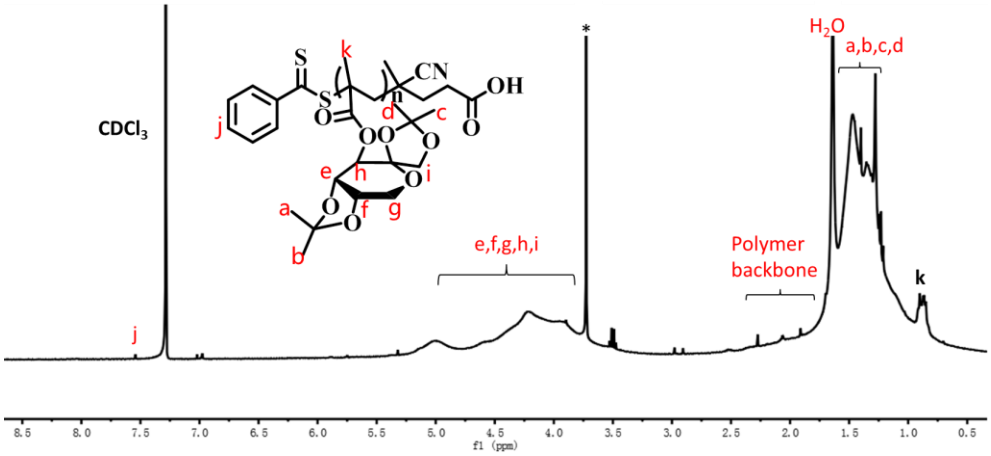


Figure S2. ^{1}H NMR spectra of Poly(3-O-MAipFru) in $CDCl_3$. The characteristic peaks (-CH_3: 1.0-1.5 ppm) of fructose and the peaks of phenyl ring on the RAFT (d: ~7.5 ppm) appeared obviously.

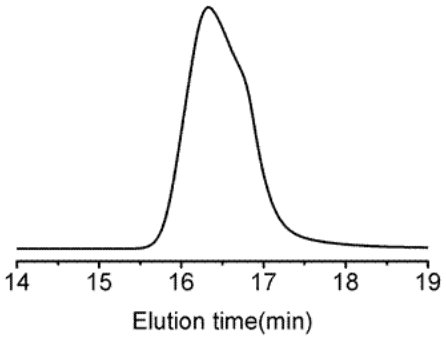


Figure S3. GPC curve of Poly(3-O-MAipFru).

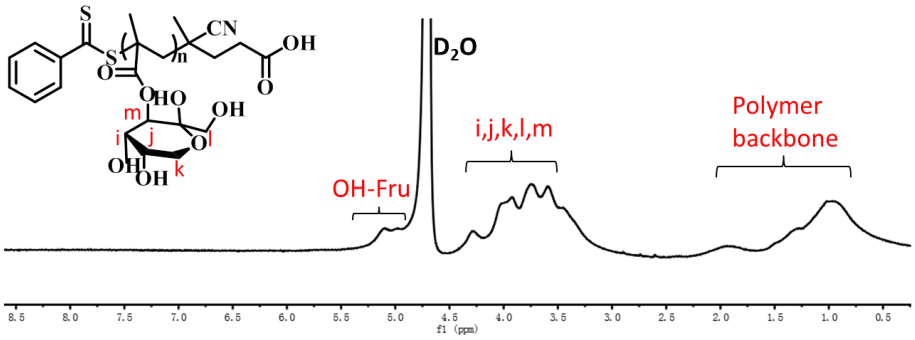


Figure S4. ^{1}H NMR spectra of PolyFru in D_2O. The hydroxyl peaks (*d*: 4.5~5.0 ppm) of fructose appeared in PolyFru.

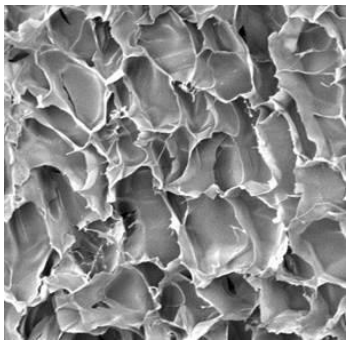


Figure S5. SEM image of the Gel.

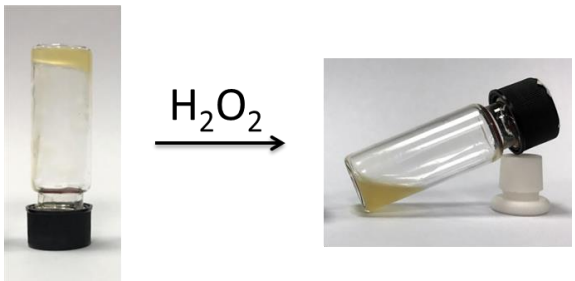


Figure S6. Photograph of gel-sol transition of the Gel after treatment with hydrogen peroxide.

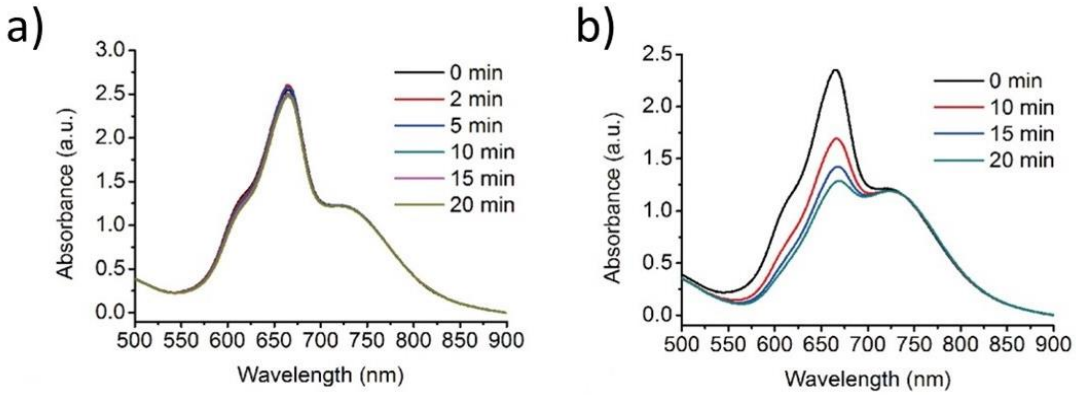


Figure S7. Absorbance of methylene blue (MB) in water upon laser irradiation (660 nm, 0.5 W cm^{-2}) a) in the presence of photosensitizer PDS (0.25 mg mL^{-1}) and b) in the presence of both photosensitizer PDS and Vc.

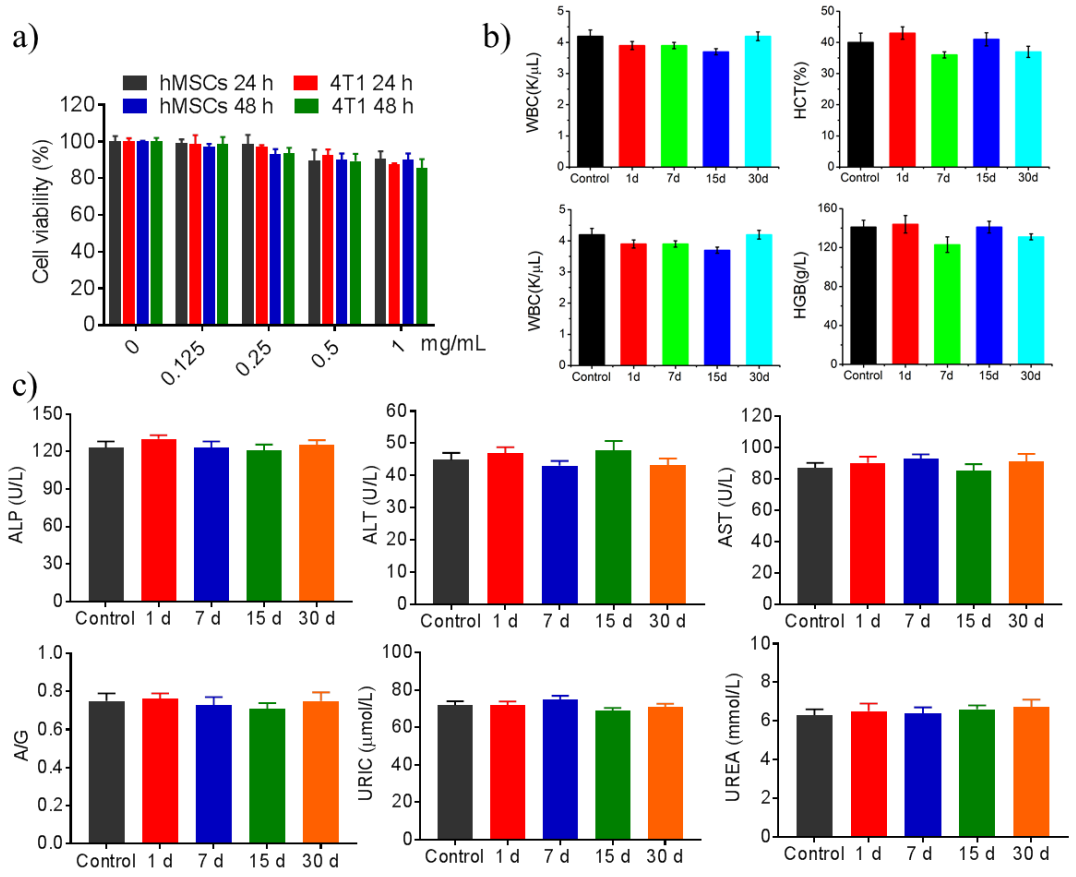


Figure S8. a) *In vitro* cytotoxicity of GelPV co-incubated with hMSCs and 4T1 cells for 24 h or 48 h, b) Hematological indicators and c) Clinical biochemistry indexes analysis of SD rats after subcutaneous injection of GelPV or untreated.

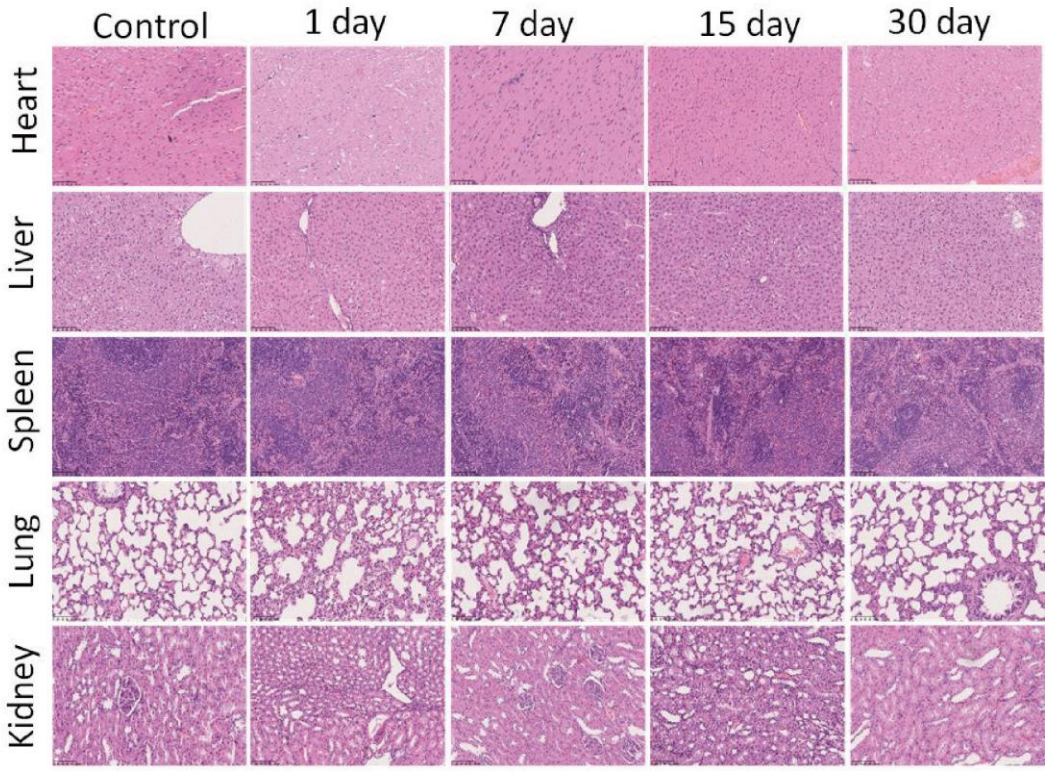
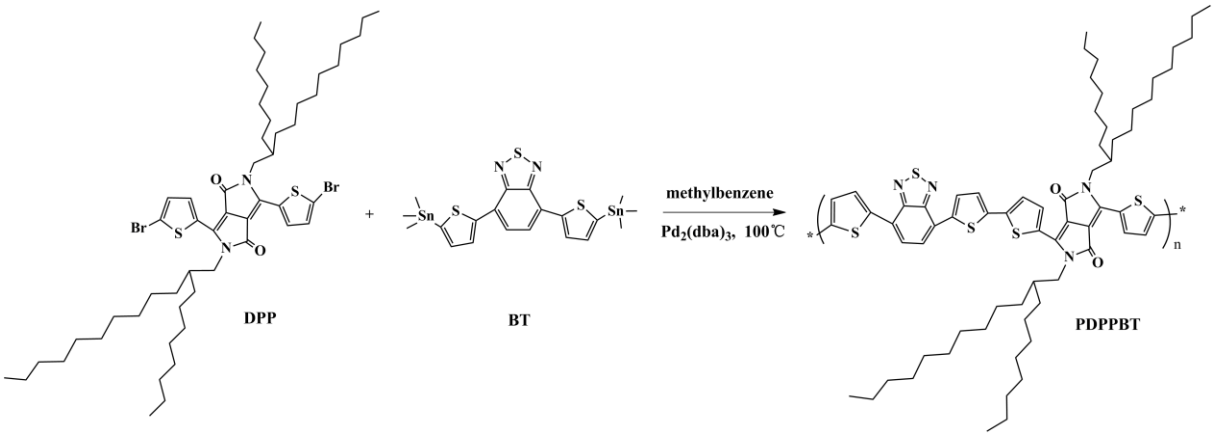


Figure S9. H&E staining images of different tissues from SD rats after subcutaneous injection of GelPV or untreated.



Scheme S2. Synthetic procedure of PDPPBT.

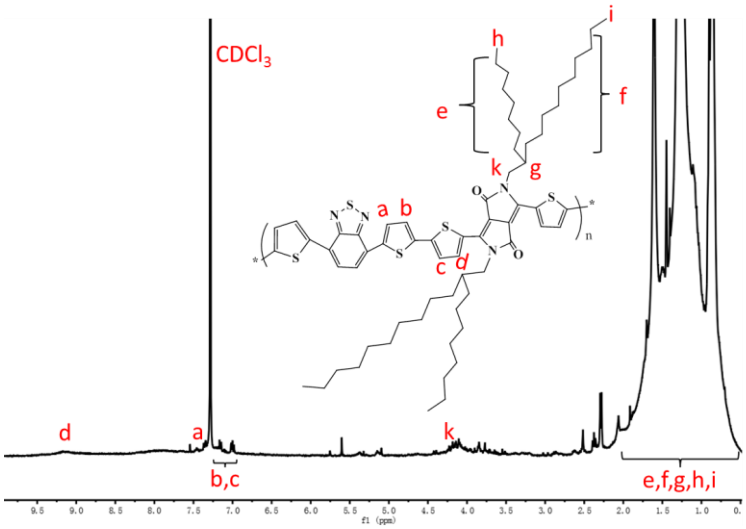


Figure S10. ^{1}H NMR spectra of PDPPBT in $CDCl_3$.

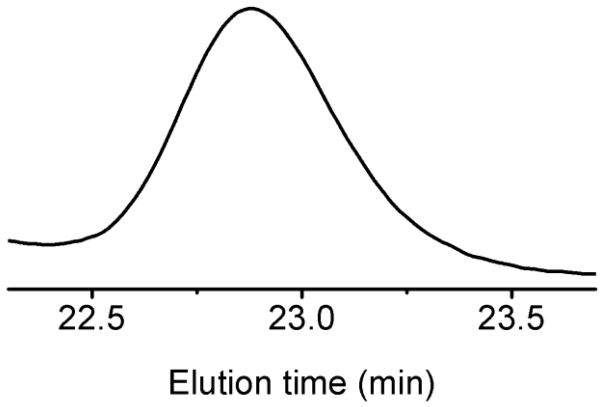


Figure S11. GPC curve of PDPPBT.

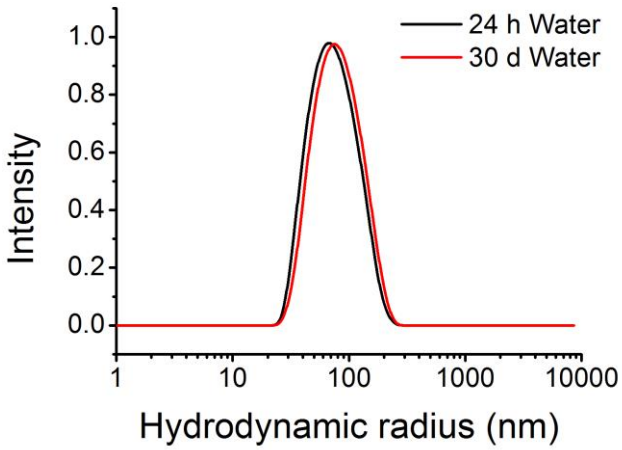


Figure S12. R_h of DB-NPs dispersed in water after storage for 24 h and 30 day, respectively.

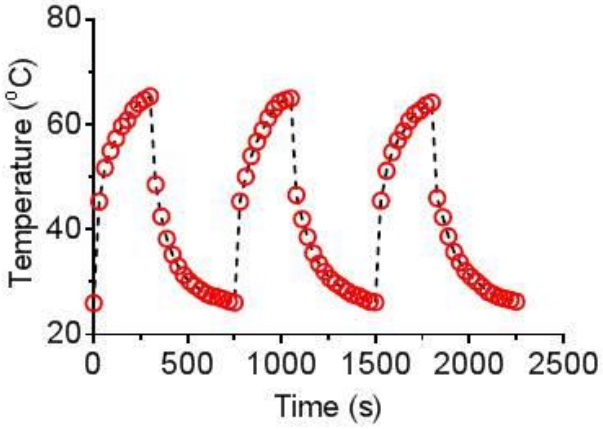


Figure S13. Thermal cycling of DB-NPs aqueous solution (915 nm, 0.5 W cm^{-2}).

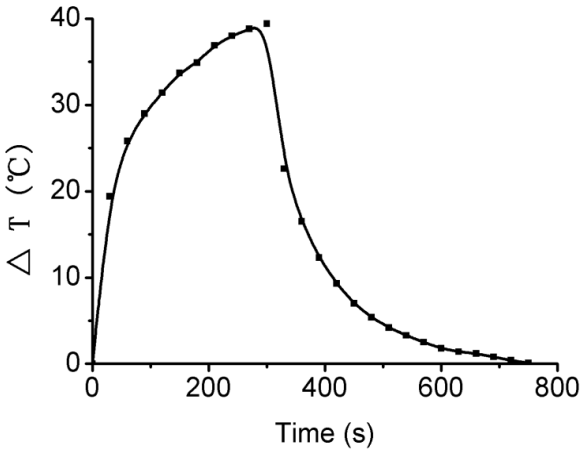


Figure S14. Photothermal response of DB-NPs aqueous dispersion for 750 s with a NIR laser (915 nm, 0.5 W cm^{-2}) and then the laser was shut off.

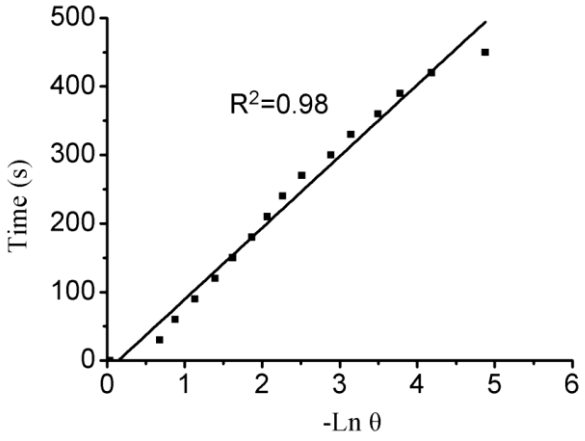


Figure S15. Linear time data versus -Ln θ obtained from the cooling period of Figure S14.

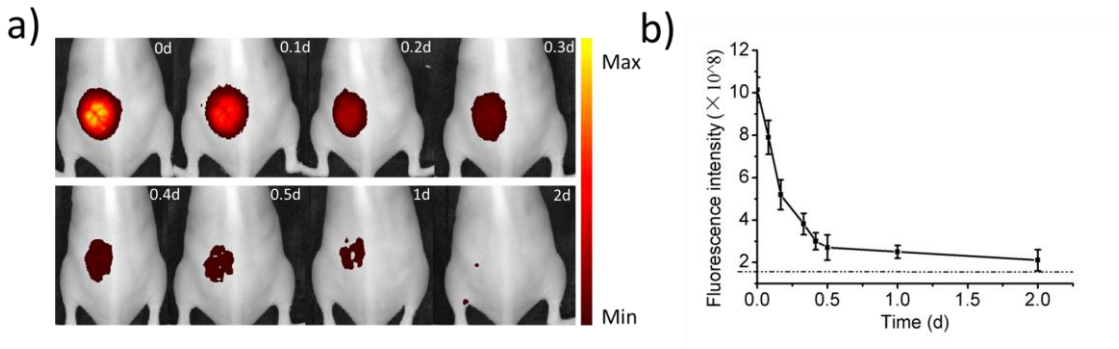


Figure S16. a) Fluorescence signal changes of DOX in the back of mice using *in vivo* imaging system. b) Quantified results of DOX fluorescence signal intensity relative to figure a. BALB/c mice were injected with free DOX solution (0.5 mg mL^{-1}, 0.1 mL) on the back space (n = 3 per groups).

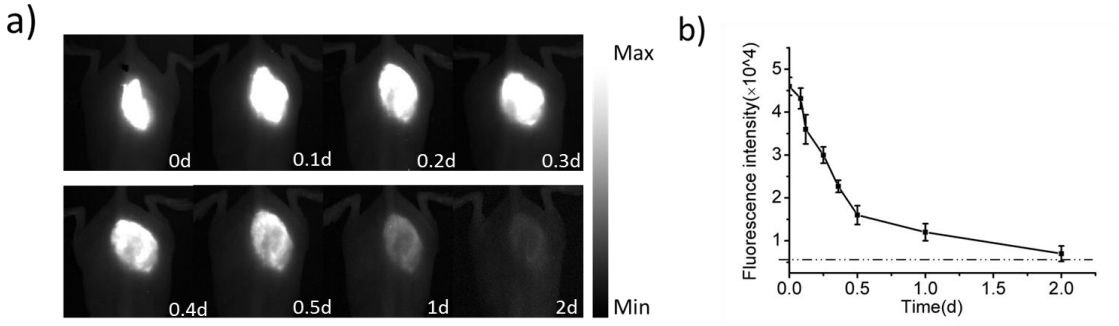


Figure S17. a) Fluorescence signal changes of DB-NPs in the back of mice using in vivo imaging system. b) Quantified results of DB-NPs fluorescence signal intensity relative to figure a. BALB/c mice were injected with free DB-NPs solution (1.0 mg mL^{-1}, 0.1 mL) on the back space (n = 3 per groups).

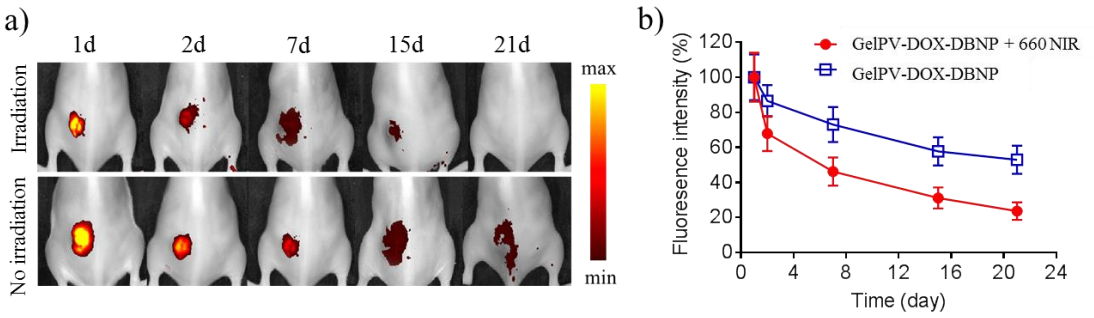


Figure S18. a) Changes of DOX fluorescence signals monitored by *in vivo* imaging. b) Quantified results of DOX fluorescence signals relative to figure a, fluorescence signals were detected at 1, 2, 7, 15, and 21 days of post-treatment. BALB/c mice were injected with

GelPV-DOX-DBNP (50 μL) on the back space with light irradiation (660 nm, 0.5 W cm^{-2}, 20 min) (n = 3 per groups).

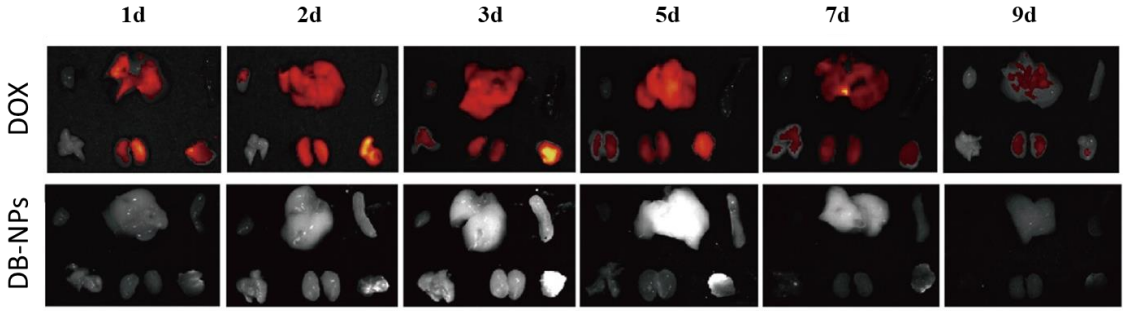


Figure S19. *Ex vivo* fluorescence imaging of DOX (up-line) and DB-NPs (down-line) in major organs (heart, liver, spleen, lung, and kidney) and tumors after subcutaneous injection of GelPV-DOX-DBNP with 660 nm laser irradiation (0.5 W cm^{-2}, 20 min).

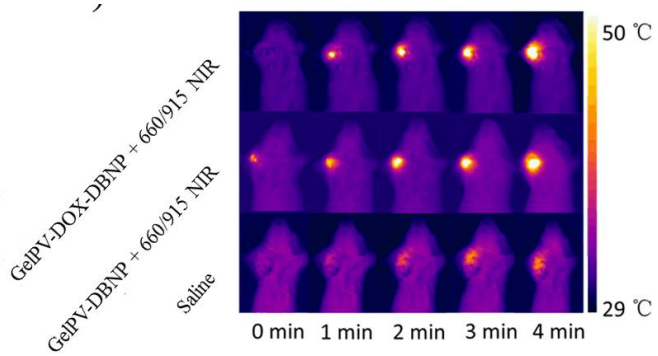


Figure S20. *In vivo* photothermal effects. Thermal images of 4T1 tumor-bearing mice of saline-treated group, GelPV-DOX-DBNP +660/915 NIR group, and GelPV-DBNP+660/915 NIR group under 915 nm laser irradiation (0.5 W cm^{-2}, 10 min).

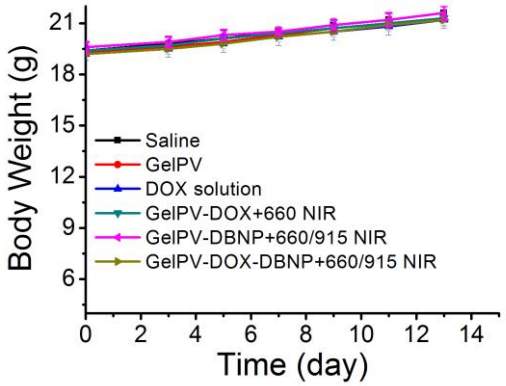


Figure S21. Body weight curves of 4T1 tumor-bearing mice after treatment with different therapy modalities.