Supporting Information

NIR-Absorbing Water-Soluble Conjugated Polymer Dots for Photoacoustic Imaging-Guided Photothermal/Photodynamic Synergetic Cancer Therapy

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Experimental Section

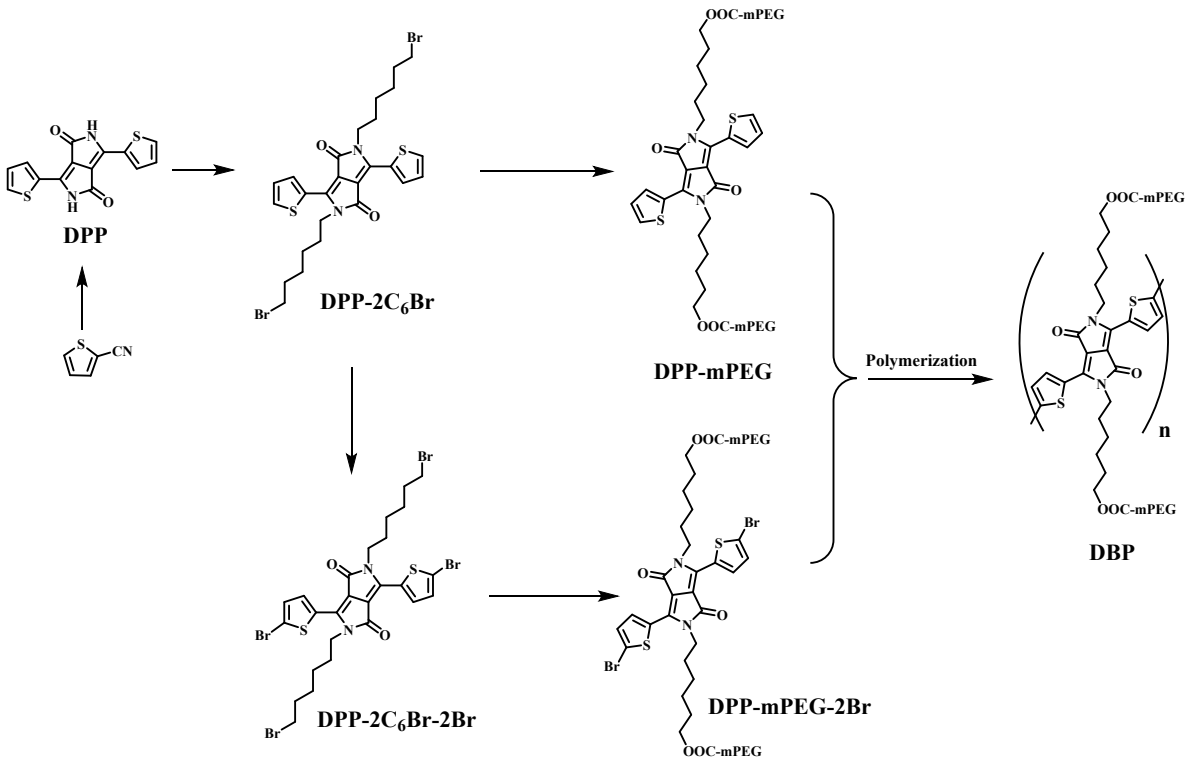

Figure S1. Structure of DPP-mPEG, DPP-mPEG-2Br, WSCP and synthetic route of WSCP.

Synthesis of DPP. Typically, potassium tert-butoxide (4.0 g, 35.71 mmol) was added into reactive containers with the protection of N_2. Then, 25 ml 1, 1-dimethyl-1-propanol was added into the container and heated up to 108 ˚C to make the potassium tert-butoxide dissolved into amylene alcohol. 2-Thiophenecarbonitrile (3.24 g, 29.71 mmol) and methyl succinate (1.46 g, 11.16 mmol) were added into the above reaction and keep the reaction for 1 h. Decrease the reaction temperature to 65 ˚C. And then, 50 ml methanol and 2-3 ml acetic acid were added into the reaction and keep the reaction under reflux for 10 min. Cooling down the system to room temperature, filtrate and wash to get the powder. ^{1}H-NMR (400 MHz, DMSO-d6) δ 11.22 (d, 2H), 8.20 (d, 2H), 7.95 (d, 2H), 7.29 (m, 2H); ^{13}C-NMR (100 MHz, DMSO-d6) δ 162.16, 133.41, 131.66, 131.28, 129.11, 109.12; MS (EI) calcd for $[M]^{+}$: 301.01, found 300.73.

Synthesis of DPP-2C_6Br. The obtained DPP and potassium hydroxide were dissolved in DMF and heated at 120 ˚C for 30 min. Then, hexamethylene dibromide was added into above solution, and the mixture was stirred until completely consumption of DPP. After that, the solvent was evaporated under reduced pressure. The residual was purified by column chromatography (silica gel, pure PE) to give a black solid. ^{1}HNMR (400 MHz, DMSO-d6) δ 8.94-8.91 (m, 2H), 7.67-7.64 (m, 2H), 7.31-7.28 (m, 2H), 4.13-4.04 (m, 4H), 3.43-3.36 (m, 4H), 1.92-1.82 (m, 4H), 1.81-1.72 (m, 4H), 1.53-1.41 (m, 8H); ^{13}CNMR (100 MHz, DMSO-d6) δ 161.13, 139.93, 135.34, 130.84, 129.65, 128.78, 42.02, 33.56, 32.46, 29.69, 27.63, 25.81; MS (EI) calcd for [M] $^+$: 626.01, found 626.12.

Synthesis of DPP-2C_6Br-2Br. Typically, DPP-2C_6Br (0.627 g, 1 mmol) and N-bromobutanimide (NBS, 0.356 g, 2 mmol) were added into trichloromethane at room temperature without light for 48 h. And then, the above solution was heated to 40 ˚C for 3 h. After that, the reaction was terminated and large amount of PE was added into the final mixture while keeping stirring, followed by filtrating. The residual was purified by column chromatography (silica gel, PE/DCM, v/v, 1/3) to give a black brown solid (0.65 g, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.67 (d, J = 4.2 Hz, 2H), 7.25 (s, 2H), 4.08 - 3.93 (m, 4H), 3.40 (t, J = 6.7 Hz, 4H), 1.94 - 1.82 (m, 4H), 1.79 - 1.67 (m, 4H), 1.49 (d, J = 12.8 Hz, 8H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.03, 138.95, 135.44, 131.72, 130.97, 119.26, 107.80, 42.05, 33.64, 32.55, 29.82, 27.77, 26.01.

Synthesis of DPP-mPEG. Firstly, mPEG-COOH (M_W = 2,000 KDa) and tetrabutylammonium hydroxide (10% in water) were added into 30 ml double distilled water (DDW) and kept stirring for a day. After the reaction, the mPEG$^+$COO$^-$ were

obtained followed by freezing-dry without further purification. Next, DPP-2C_6Br and mPEG$^+$COO$^-$ were dissolved into THF: acetone (v/v, 3:1) and kept stirring for a day. After evaporating the solvent under reduced pressure, 50 ml DDW was added into the above crude product under the ultrasound and filtered to get the filtrate. The as-obtained filtrate was further purified by dialyzing with dialysis membrane (molecular weight cut-off: 3.5 kDa) for 2 days. And the final product, TDPP-mPEG, was yielded by freeze-drying.

Synthesis of DPP-mPEG-2Br. The synthetic route of DPP-mPEG-2Br is similar to DPP-mPEG described above. Firstly, mPEG-COOH (M_W = 2,000 KDa) and tetrabutylammonium hydroxide (10% in water) were added into 30 ml double distilled water (DDW) and kept stirring for a day. After the reaction, mPEG$^+$COO$^-$ was obtained followed by freezing-dry without further purification. Next, DPP-2C_6Br-2Br and mPEG$^+$COO$^-$ were dissolved into THF: acetone (v/v, 3:1) and kept stirring for a day. After evaporating the solvent under reduced pressure, 50 ml DDW was added into the above crude product under the ultrasound and filtered to get the filtrate. The as-obtained filtrate was further purified by dialyzing with dialysis membrane (molecular weight cut-off: 3.5 kDa) for 2 days. And the final product, TDPP-mPEG, was yielded by freezing-dry.

Synthesis of WSCP. The polymerization is based on "C-H" activation. Typically, under the protection of N_2, DPP-mPEG (0.12 g, 0.026 mmol), DPP-mPEG-Br (0.12 g, 0.026 mmol), potassium carbonate (0.24 g, 0.17 mmol), 2, 2-dimethylpropanoic acid (0.061 g, 0.6 mmol) and palladium acetate (0.012 g, 0.053 mmol) were added into N, N-dimethylacetamide (80 ml), followed by heating to 110 °C and keeping for 10 min. After the polymerization, the solvent was removed under reduced pressure. And then, 30 ml

double distilled water was added under the sonication, followed by filtering to get the filtrate. The as-obtained filtrate was further purified by dialyzing with dialysis membrane (molecular weight cut-off: 8-14 kDa) for 3 days. And the final product, black WSCP, was yielded (0.17 g, 71%) by freeze-drying.

Preparation of WSCP dots. Due to the structurally amphiphilic property of WSCP, we prepared WSCP dots from WSCPs directly without any other nano-technology. Typically, 50 mg WSCPs was dissolved into double distilled water (DDW, 0.5 mL). Then, the above WSCP solution was added into 10 mL DDW drop by drop under the ultra-sonication. After that, the WSCP dots were obtained by freeze-drying.

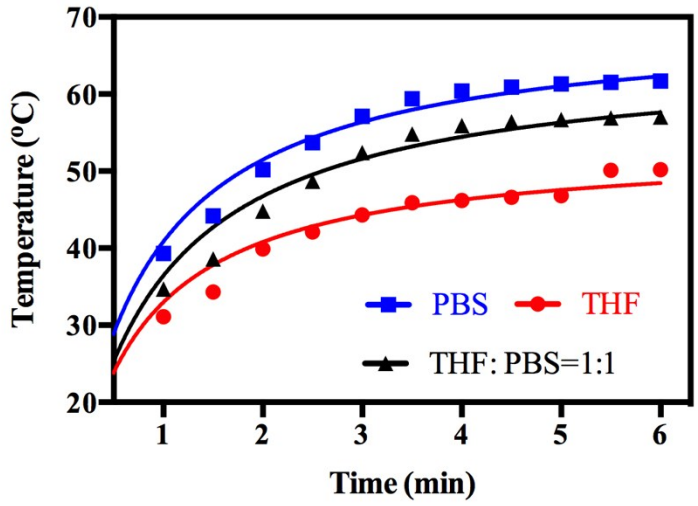

Figure S2. Photothermal profiles of WSCP dots in PBS, THF, and PBS: THF = 1:1 (v/ v), respectively.

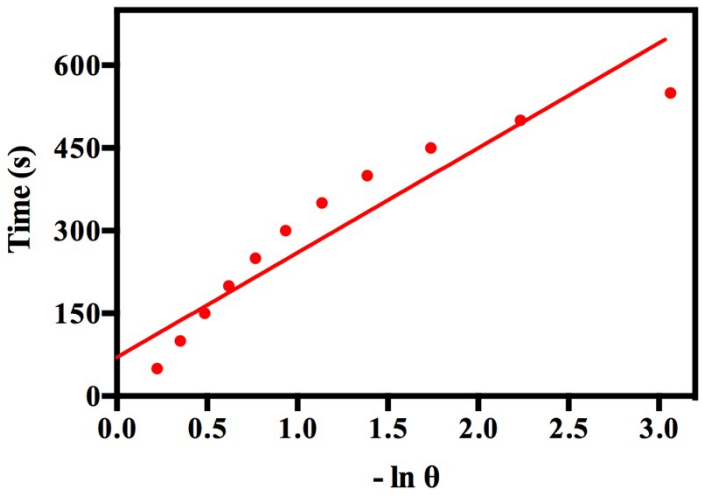

Figure S3. Linear time versus -ln θ obtained from the cooling period of Figure 2d.

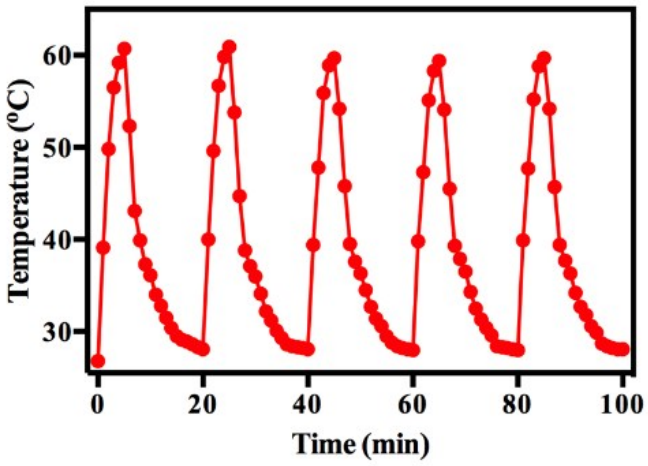

Figure S4. Photothermal profiles of WSCP dots aqueous solution for five ON/OFF cycles (730 nm, 1.0 W/cm^2, 1 μM).

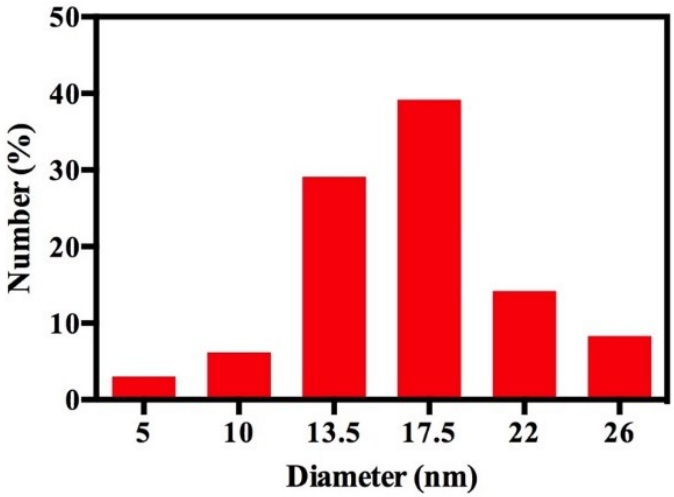

Figure S5. DLS size distribution histogram of WSCP dots after five ON/OFF cycles irradiation (730 nm laser).

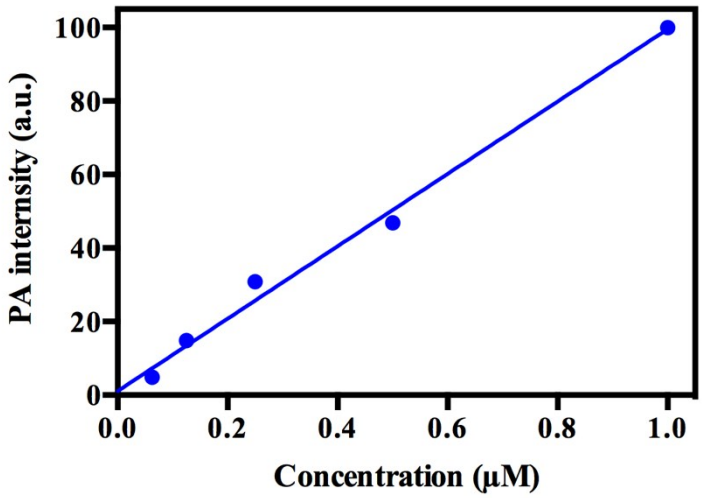

Figure S6. PA intensity-concentration plot shows the relationship between concentration of WSCP dots and PA intensity.

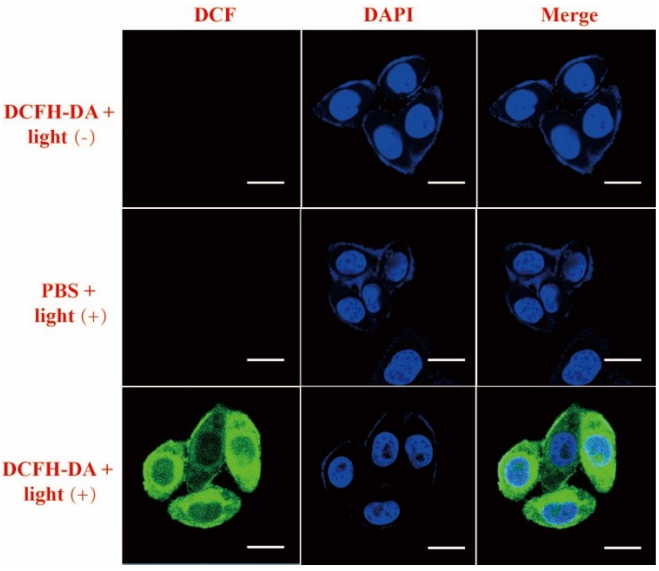

Figure S7. Fluorescence imaging of DCFH-DA (ROS probe) and DAPI in each group. The first row, DCFH-DA without light irradiation; the second row, no DCFH-FA but PBS with 730 nm light irradiation; the third row, DCFH-DA with 730 nm light irradiation. Fluorescent emission from DCF (green, left). Fluorescent emission from DAPI (blue, middle). Merged fluorescence of DCF and DAPI (right). Scale bar is 20 μm.

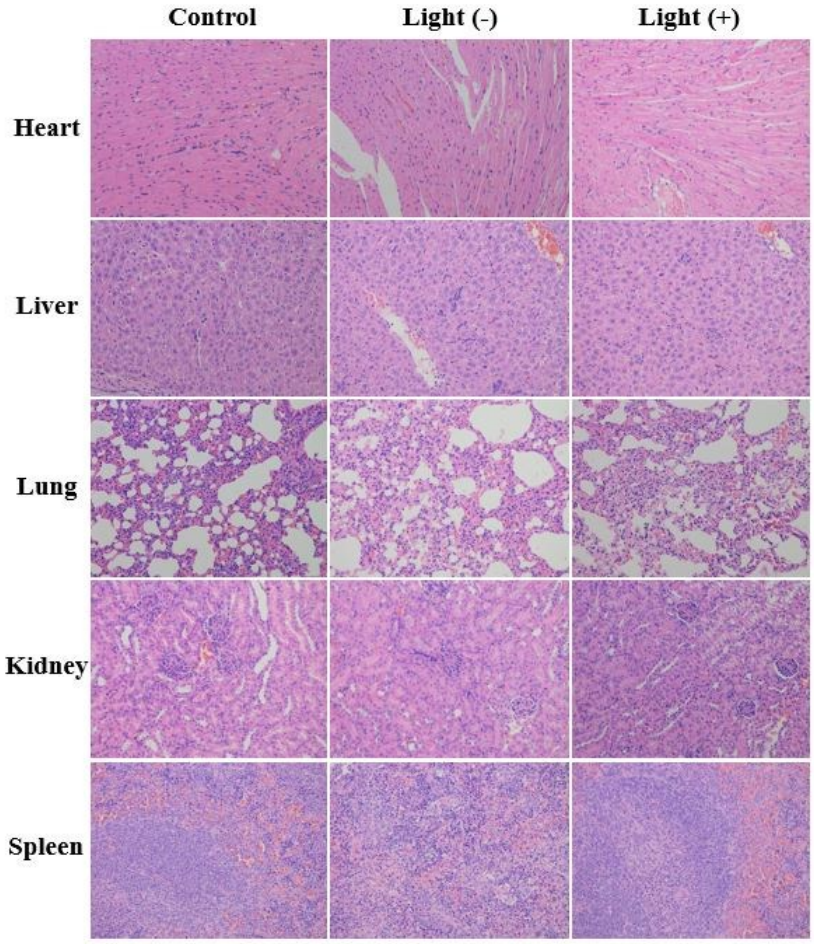

Figure S8. H&E stained images of major organs (heart, liver, spleen, lung, and kidney) for each group after treatment.

Table S1. Molecular weights, polydispersity index (PDI) and photophysical properties of DPP-mPEG, DPP-mPEG-2Br and WSCP, respectively.

	Number-average molecular weight, Mn (g/ mol) [a]	**Polydispersity index (PDI), Mw/ Mn** [b]	**$\lambda_{Max, abs}$ (nm)**	**ε ($M^{-1}cm^{-1}$)**
DPP-mPEG	4, 555		515, 544	28, 398
DPP-mPEG-2Br	4, 715		532, 559	25, 207
WSCP [c]	65, 762	1.21	750	39, 982

Notice: a and b, Both Mn and Mw/Mn were measured by gel permeation chromatography (GPC) with polystyrene calibration. All samples were dissolved in PBS. c, no fluorescence signal can be detected in PBS.