# Electronic Supplementary Information

## Amphiphilic BODIPY Dye Aggregates in Polymeric Micelles for Wavelength-Dependent Photo-Induced Cancer Therapy

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## EXPERIMENTAL SECTION

**Materials.** All solvents were purchased from Sinopharm Chemical Reagent Co., Ltd. Other chemicals were purchased from Energy Chemical unless otherwise stated. Acridine orange (AO) was purchased from Amresco. Dihydroethidium (DHE) was obtained from Wusheng Company (Shanghai, China). Lysotracker Green DND-26 was obtained from Invitrogen. UV-vis Absorption spectra were recorded on a UV-Vis Spectrophotometer (UV2600, Shimadzu). Fluorescence spectra were measured by PerkinElmer LS 55. The NMR spectra were performed to characterize the chemical structures using 400 FT-NMR spectrometers. ESI mass spectra were applied using Agilent 1290 UPLC/6540 Q-TOF mass spectrometer. The hydrodynamic diameters of micelles were obtained using Zetasizer ZS90 (Malvern, UK). Furthermore, the morphology was observed using transmission electron microscopy (TEM, Tecnai-G20).

**BDP:**[1] 3,4-Bis(2-(2-(2-methoxyethoxy)ethoxy)ethoxy)benzaldehyde (0.8 g, 1.86 mmol) and 2,4-dimethylporrole (443.0 mg, 4.65 mmol) were dissolved in dried $CH_2Cl_2$ (20 mL) under $N_2$ atmosphere. three drops of trifluoroacetic acid were added into the mixture and stirred for 12 h. Then, 2,3-dicyano-5,6-dichlorobenzoquinone (DDQ, 1.0 g, 1.2 mmol) was added for additional 12 h. Then, excessive triethylamine (6.0 mL, 43.2 mmol) and borontrifluoride etherate (6.0 mL, 43.2 mmol) were further added at 0 ºC. The resultant mixture was allowed to warm up and stirred at room temperature for 12 h. The solution was filtration, concentrated under reduced pressure, extracted by $CH_2Cl_2$ (20.0 mL × 3), washed with brine (20.0 mL × 3), dried over anhydrous $Na_2SO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography ($SiO_2$;

$CH_2Cl_2$/MeOH = 50:1, v/v) to obtain BDP (0.55 g, 44%) as a dark orange oil. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.99 (d, $J$ = 8.4 Hz, 1H, Ar*H*), 6.84 (s, 1H, Ar*H*), 6.80 (d, $J$ = 8.4 Hz, 1H, Ar*H*), 5.97 (s, 2H, pyrrole-*H*), 4.21 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 4.13 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 3.91 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 3.85 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 3.80-3.49 (m, 16H, OC$H_2$), 3.38 (s, 3H, C$H_3$), 3.36 (s, 3H, C$H_3$), 2.54 (s, 6H, C$H_3$), 1.46 (s, 6H, C$H_3$) ppm. ESI-MS (*m*/*z*): 649.4 $[M + H]^+$.

**BDP-I:**[2] The solution of iodic acid (1.0 g, 5.4 mmol) in a minimal water was added into the mixture of BDP (1.8 g, 2.7 mmol) and iodine (1.7 g, 6.7 mmol) in ethanol (50 mL) under $N_2$ atmosphere. The mixture was then warmed up to 60 °C for 2 h. After cooling down, the mixture was evaporated under reduced pressure. The crude product was purified by column chromatography ($SiO_2$; $CH_2Cl_2$/ethyl acetate = 25: 1, v/v) to obtain BDP-I as a bright red solid (0.4 g, 34%). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.01 (d, $J$ = 8.2 Hz, 1H, Ar*H*), 6.78 (d, $J$ = 1.6 Hz, 1H, Ar*H*), 6.75 (dd, $J$ = 8.2, 1.6 Hz, 1H, Ar*H*), 4.22 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 4.12 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 3.93 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 3.85 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 3.79-3.77 (m, 2H, OC$H_2$), 3.74-3.55 (m, 12H, OC$H_2$), 3.53-3.51 (m, 2H, OC$H_2$), 3.38 (s, 3H, OC$H_3$ ), 3.36 (s, 3H, OC$H_3$), 2.63 (s, 6H, C$H_3$), 1.47 (s, 6H, C$H_3$) ppm. ESI-MS (*m*/*z*): 901.4 $[M + H]^+$.

***amp*-BDP:** A mixture of BDP-I (90 mg, 0.1 mmol), glacial acetic acid (0.2 mL, 3.5 mmol), 4-propoxybenzaldehyde (66 mg, 0.4 mmol), and piperidine (0.3 mL, 3.0 mmol) in toluene (40.0 mL) was refluxed for 2 h, and the generated water from the reaction was removed azeotropically using a Dean-Stark apparatus. Then, the mixture was concentrated under reduced pressure, followed by the purification by column chromatography ($SiO_2$; $CH_2Cl_2$/MeOH = 100/3, v/v). The green fraction was collected and evaporated. Next, it

was further purified by size exclusion chromatography with Bio-beads S-X1 beads using THF as the eluent. Finally, the recrystallization in $CHCl_3$ and hexane was carried out to afford a green solid (25 mg, 21%). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.13（d, $J$ = 16.4 Hz, 2H, CH=C*H*), 7.61-7.59 (m, 6H, CH=C*H*, Ar*H*), 7.03 (d, $J$ = 8.4 Hz, 1H, Ar*H*), 6.94 (d, $J$ = 8.4 Hz, 4H, Ar*H*), 6.85 (d, $J$ = 2.0 Hz, 1H, Ar*H*), 6.81 (dd, $J$ = 8.4, 2.0 Hz, 1H, Ar*H*), 4.25 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 4.15 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 3.99-3.93 (m, 6H, OC$H_2$), 3.87 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 3.79 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 3.75-3.56 (m, 12H, OC$H_2$), 3.52 (t, $J$ = 4.8 Hz, 2H, OC$H_2$), 3.39 (s, 3H, OC$H_3$), 3.35(s, 3H, OC$H_3$), 1.85-1.81 (m, 4H, C$H_2$), 1.53 (s, 6H, C$H_3$), 1.05 (t, $J$ = 7.2 Hz, 6H, C$H_3$), $^{13}$C NMR (100.0 MHz, $CDCl_3$): $\delta$ 160.42, 150.49, 149.89, 145.71, 139.22, 138.17, 133.15, 129.43, 127.92, 121.53, 116.67, 114.93, 114.47, 82.67, 72.02, 70.99, 70.78, 70.71, 70.65, 69.85, 69.72, 69.23, 68.76, 59.14, 29.80, 22.64, 17.71, 10.62 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{53}H_{65}BF_2I_2N_2NaO_{10}$: 1215.2687; found: 1215.2711.

## References


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2 H. He, S. Ji, Y. He, A. Zhu, Y. Zou, Y. Deng, H. Ke, H. Yang, Y. Zhao, Z. Guo, H. Chen, Photoconversion-tunable fluorophore vesicles for wavelength-dependent photoinduced cancer therapy, *Adv*. *Mater*., 2017, **29**, 1606690.

## SUPPORTING FIGURES

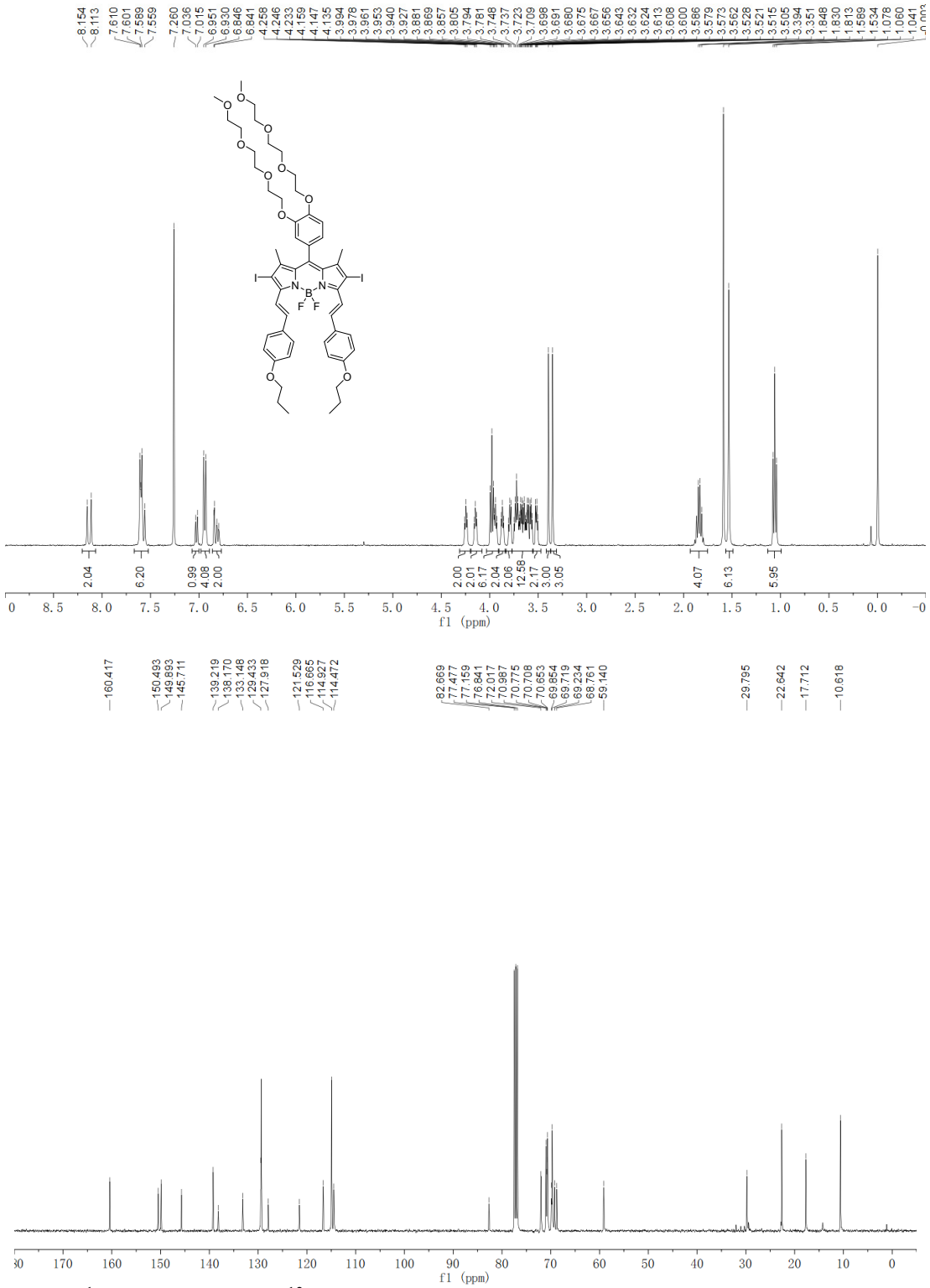

**Fig. S1.** $^{1}$H NMR (top) and $^{13}$C NMR (bottom) spectra of *amp*-BDP.

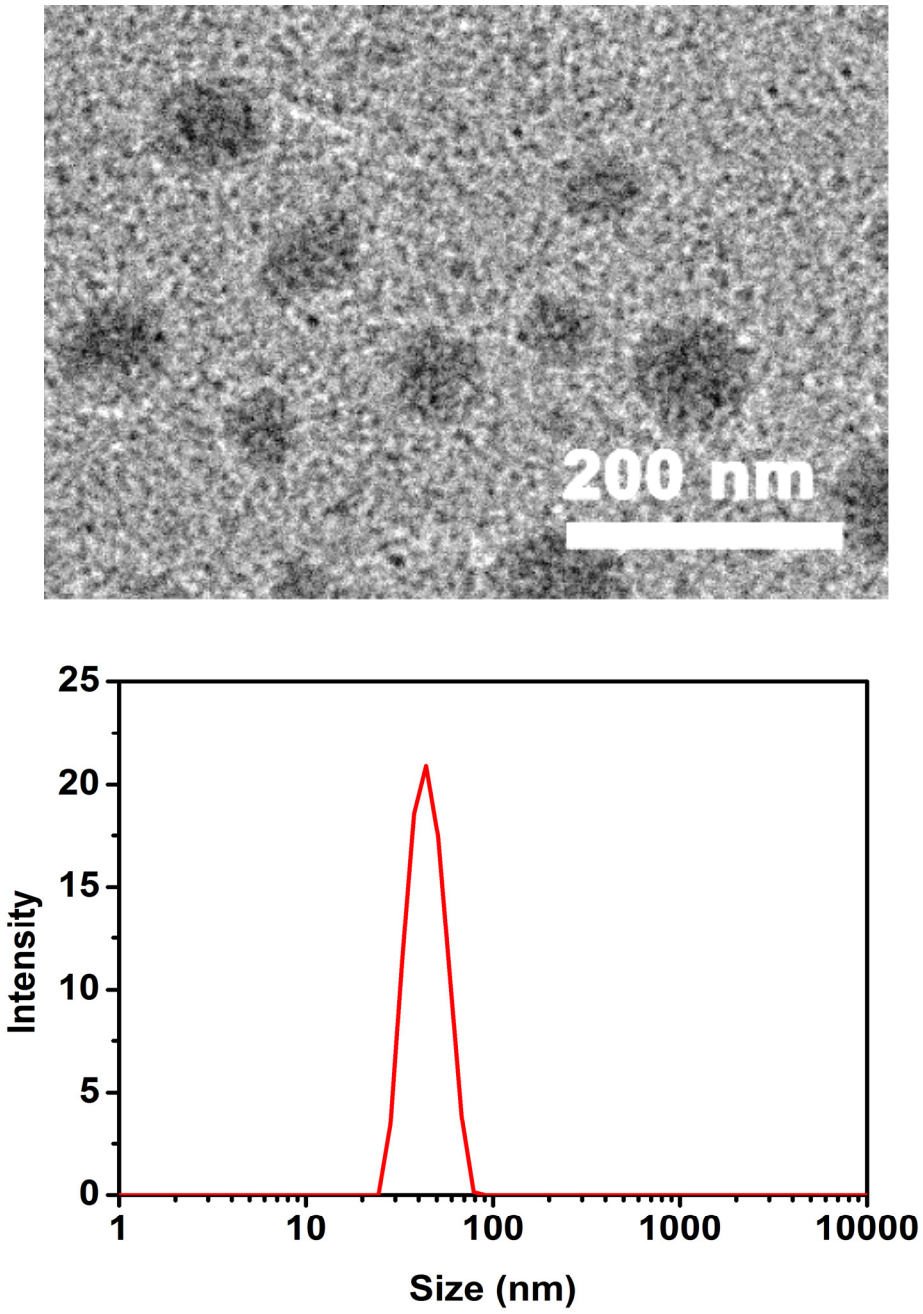


**Fig. S2.** TEM (top) and size distributions (bottom) of 5% Micelles.

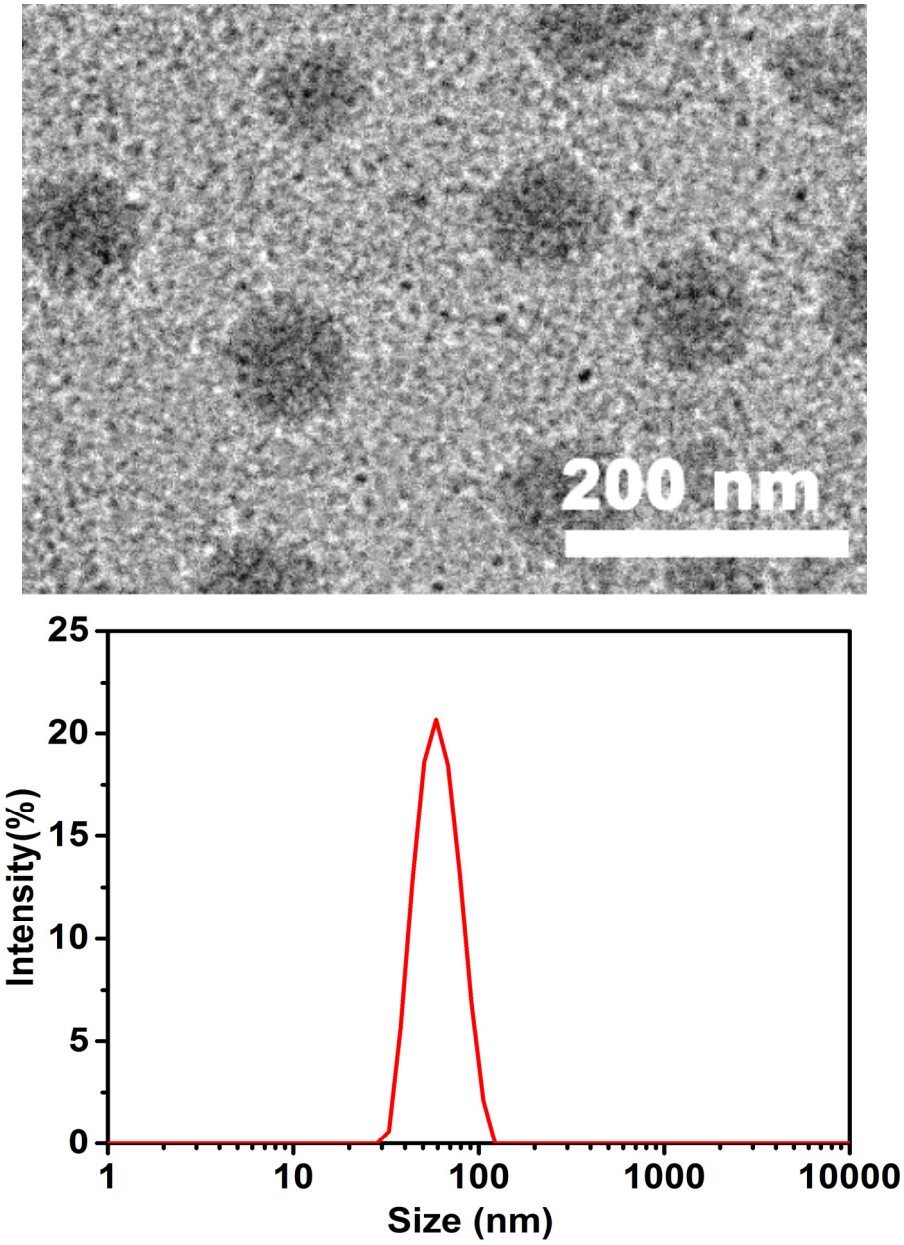


**Fig. S3**. TEM (top) and size distributions (bottom) of 10% Micelles.

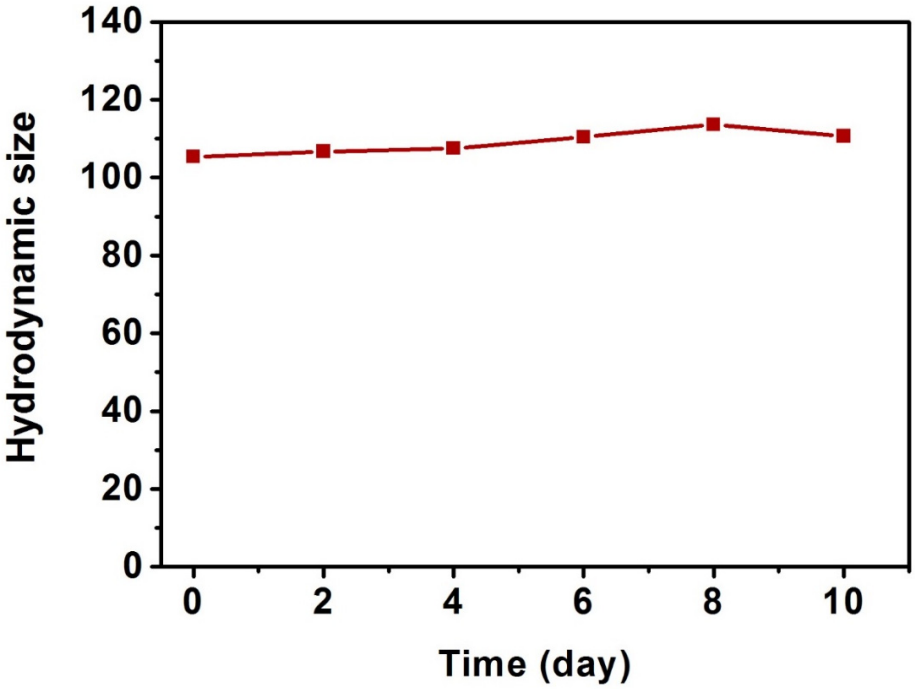


**Fig. S4.** Size distributions of 20% Micelles at aqueous solutions at different times.

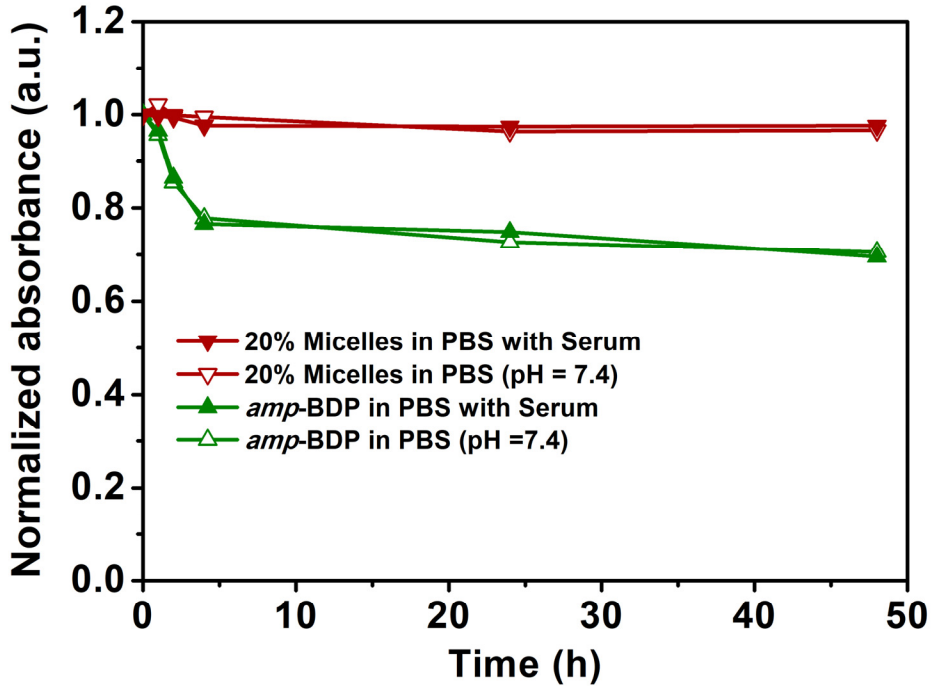


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**Fig. S5.** Normalized absorbance of *amp*-BDP and 20% Micelles in PBS at pH 7.4, and PBS containing 10% serum (pH 7.4) at various time, respectively.

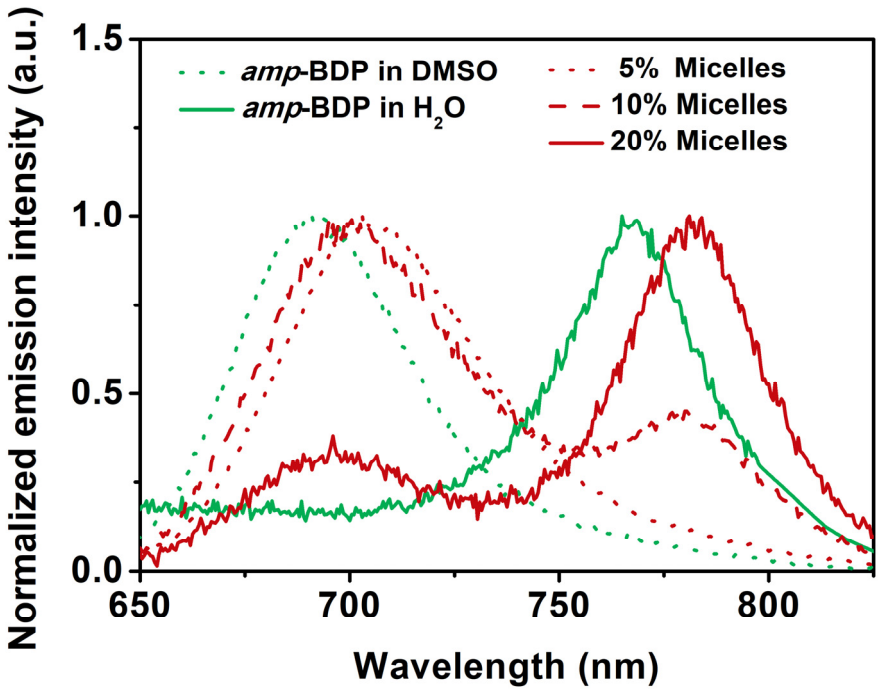


**Fig. S6.** Normalized emission spectra of *amp*-BDP and micelles at different conditions.

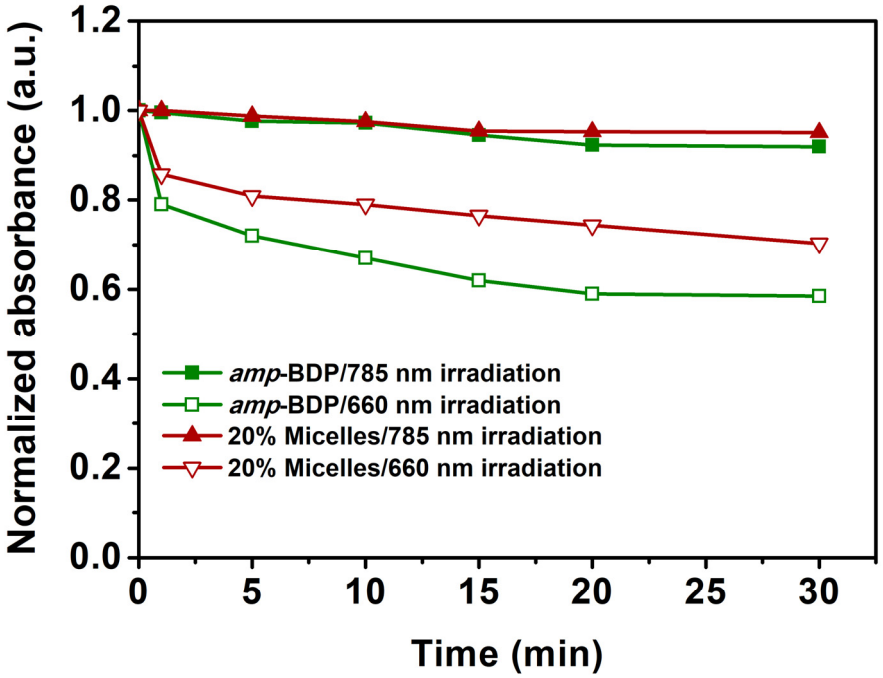


**Fig. S7.** Normalized absorbance of *amp*-BDP and 20% Micelles in aqueous medium at a different time under 660 nm and 785 nm light exposure at 0.5 W $cm^{-2}$, respectively.

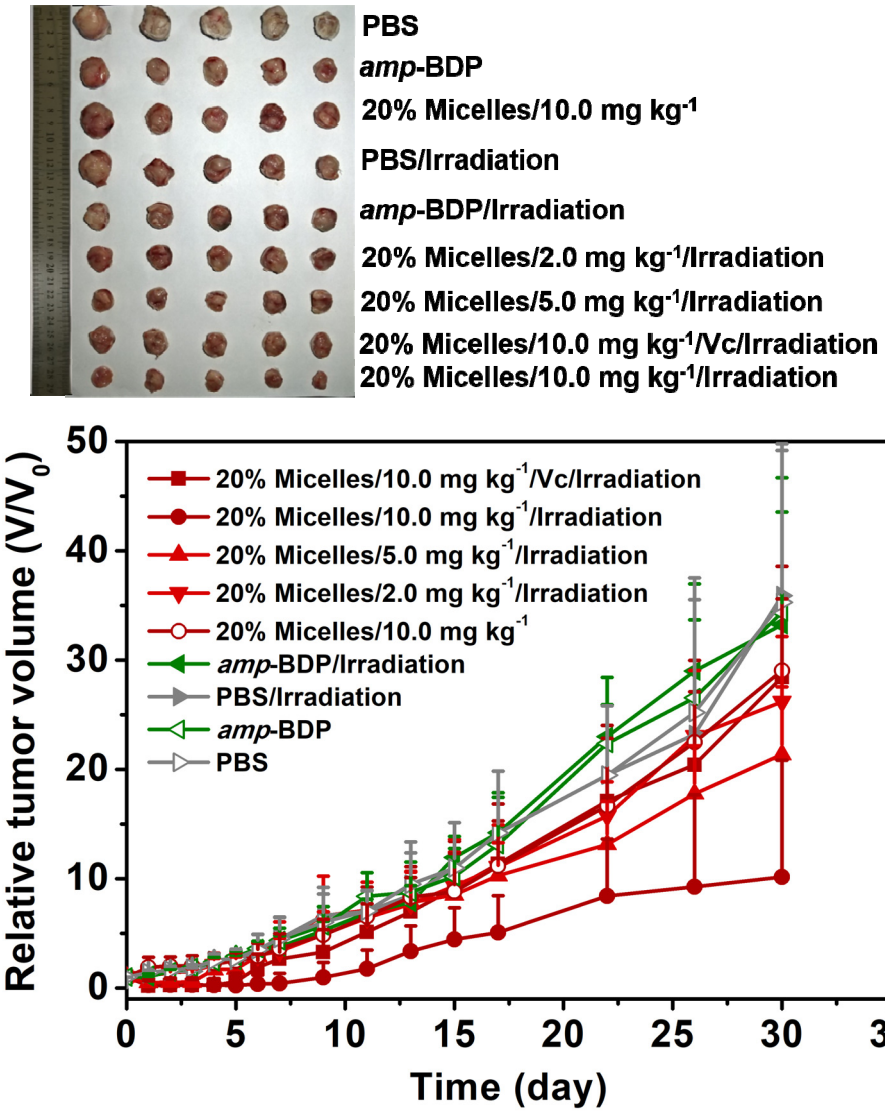


**Fig. S8.** Tumor growth profile of the mice treated with 20% Micelles in the presence or absence of Vc under 660 nm light exposure at 0.5 W $cm^{-2}$ for 5 min or not (student's t-test, *$p < 0.05$ and **$p < 0.01$).

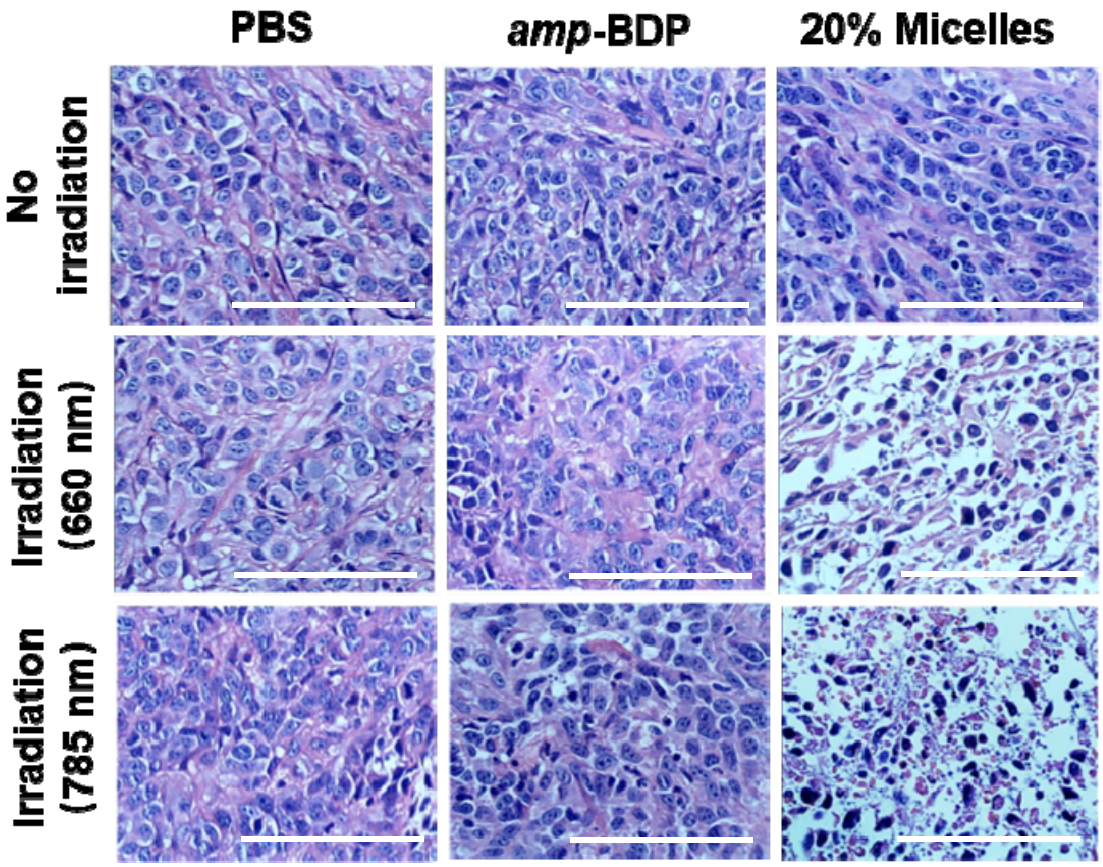


**Fig. S9.** Image of H&E-stained tumor sections harvested from the mice treated with *amp*-BDP and 20% Micelles at the dose of 10.0 mg $kg^{-1}$ at 24 h post-irradiation under 660 nm or 785 nm light exposure at 0.5 W $cm^{-2}$ for 5 min (Scale bar: 250 μm).

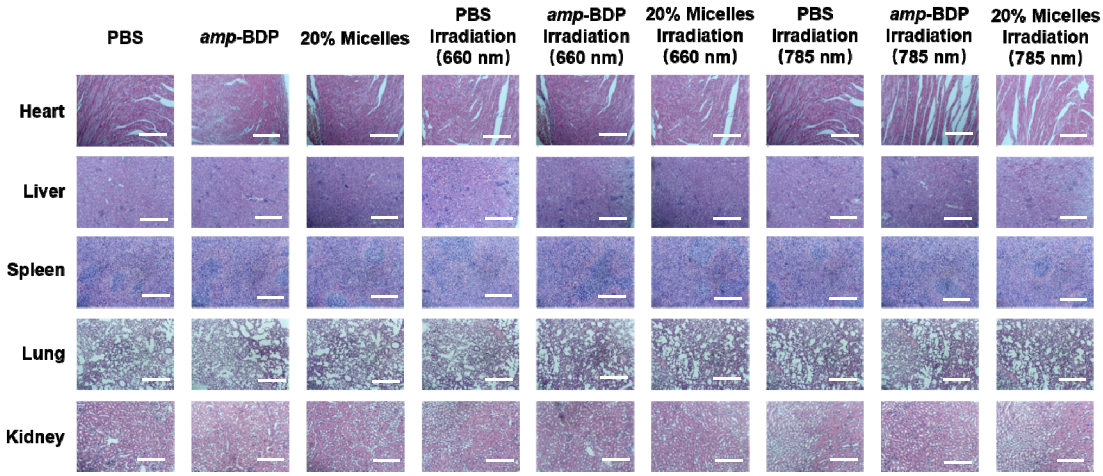


**Fig. S10.** Image of H&E-stained normal tissue sections harvested from the mice treated with *amp*-BDP and 20% Micelles at the dose of 10.0 mg $kg^{-1}$ at 24 h post-irradiation under 660 nm or 785 nm light exposure at 0.5 W $cm^{-2}$ for 5 min (Scale bar, 500 μm).