Supporting Information

Experimental Section

Materials.

Cis-1,2-dichloroethylene (97%) and poly (ethylene glycol) methyl ether methacrylate (OEGMA, M_n = 500) were purchased from Sigma-Aldrich. Cumyl dithiobenzoate (CDB) was synthesized according to the previous literature.[1] Ethanol (Standard for GC, > 99.8%), *tert*-butyl methacrylate (*t*BMA, Aladdin, 99%), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) and 4-dimethylaminopyridine (DMAP) were obtained from Aladdin Reagents of China. Tetrahydrofuran (THF) and *N, N*-dimethylformamide (DMF) were dried over with calcium hydride (CaH_2) and distilled before use. All other chemicals were utilized as received without further purification.

Characterization

^{1}H NMR spectra in $CDCl_3$ and DMSO-d_6 were determined by a Bruker AVANCE III HD 400 Spectrometer with tetramethyl silane as the internal standard. Mass spectrum was recorded on a Waters LCT Premier XE spectrometer with methanol as the solvent. The UV-Vis spectra of the samples were measured over different irradiation time intervals using a Thermo Scientific Evolution 220 spectrophotometer. Dynamic light scattering was performed on Anton Paar Litesizer 500 particle analyzer at room temperature. TEM samples were prepared by dropping the nanoparticles solution (1 mg/mL) on to a carbon coated copper grid, and the images were observed on a JEOL JEM1400 electron microscope operated at 100 kV.

Synthesis of poly [oligo (ethylene glycol) methyl ether methacrylate] (POEGMA) via RAFT homopolymerization (macro-CTA)

OEGMA (1 mL, 2 mmol), CDB (10.8 mg, 0.04 mmol), AIBN (1.3 mg, 0.008 mmol) and 1 mL anhydrous THF were charged in a reaction vial equipped with a magnetic stir bar. The mixture was degassed by several freeze-thaw cycles and sealed in vacuum. Then the reaction was carried out in a preheated oil bath at 70 °C. After 2.25 h, the flask was plunged into liquid nitrogen. The reaction solution was precipitated with ice-cold diethyl ether and dried overnight under vacuum. $M_{n,\ NMR}$ = 10, 272 g/mol, $M_{n,\ GPC}$ = 6900 g/mol, M_w/M_n = 1.05.

Synthesis of POEGMA-*b*-P*t*BMA block copolymers

POEGMA (100 mg, 10 μmol), *t*BMA (0.35 mL, 2.15 mmol), AIBN (0.1 mL, 3 μmol) and 1 mL anhydrous THF were charged in a reaction vial equipped with a magnetic stir bar. The mixture was degassed by several freeze-thaw cycles and sealed in vacuum. Then the reaction was carried out in a preheated oil bath at 70 °C. After 3.75 h, the flask was plunged into liquid nitrogen. The solution was transferred to a dialysis bag (MWCO, 8000-14000) and dialyzed for 72 h against a mixture of methanol/water (1:4, v/v). Finally, the product-containing solution was frozen and lyophilized under vacuum to afford the white powder. $M_{n,\ NMR}$ = 22, 472 g/mol, $M_{n,\ GPC}$ = 14, 200 g/mol, M_w/M_n = 1.15.

Synthesis of POEGMA-*b*-PMAA block copolymers

POEGMA-*b*-PMAA was obtained by hydrolyzing the POEGMA-*b*-P*t*BMA block copolymers with an excess of trifluoroacetic acid. POEGMA-*b*-P*t*BMA (50 mg) and dichloromethane (5 mL) were added into a round-bottom flask and stirred to dissolve the polymer. After 2 mL trifluoroacetic acid was added, the solution was stirred at room temperature for 4 h. Then the solvent was removed by a rotary evaporator and the product was dried overnight. (Yield: 90%).

Synthesis of 2, 2'-[(1Z)-1,2-ethenediylbis(thio)] bisethanol

2, 2'-[(1*Z*)-1,2-ethenediylbis(thio)] bisethanol (vinyldithioether) was synthesized according to the previous literature.[2] Nitrogen was purged in EtOH (15 mL) for 30 min. NaOH (4.5 g, 112.5 mmol) and 2-mercaptoethanol (8 g, 7.5 mL, 102.5 mmol) were added and the reaction was stirred at 0 °C for 30 min. Then, *cis*-1, 2-dichloroethylene (1 g, 0.78 mL,10.3 mmol) in degassed EtOH (2 mL) was dropwise added and the resulting solution was heated at 80 °C for 20 h. After cooling the solution to ambient temperature, deionized water (30 mL) was added. The mixture was washed with diethyl ether (3 × 30 mL) and then the organic layers were collected, washed with deionized water (2 × 30 mL). After the organic layer was dried over $MgSO_4$, the solvent was evaporated under reduced pressure to give the crude product. The product was purified by silica gel column chromatography using the mixture of ethylacetate/hexane (50:50, v/v) to obtain the desired pure 2, 2'-[(1*Z*)-1, 2-ethene-diylbis(thio)] bisethanol (Yield: 70%).^{1}H NMR (400 MHz, $CDCl_3$): δ ppm: 6.10 (s, 2H), 3.71 (t, J = 5.8 Hz, 4H), 2.84 (t, J = 5.8 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm: δ 124.63, 61.28, 37.16. $[M+Na]^+$, calculate: 203.0176, find: 203.017.

Synthesis of (*Z*)-2,3-dimethylbut-2-ene-1,4-diol

(*Z*)-2,3-dimethylbut-2-ene-1,4-diol was synthesized *via* the reduction of 2,3-dimethylmaleic anhydride. $LiAlH_4$ (1 g, 26 mmol) was dissolved into anhydrous diethyl ether under N_2. And then 2,3-dimethylmaleic anhydride (1 g, 7.9 mmol) was added in small portions. After the mixture was refluxed for 5 h, the reaction was terminated by dropwise adding 1 M hydrochloric acid and washed with DCM to obtain the product. Silica gel column chromatography was used to purify the product using the mixture of ethylacetate/petroleum ether (50:50, v/v) (Yield: 50%).^{1}H NMR (400 MHz, $CDCl_3$): δ ppm: 4.12 (s, 4H), 1.78 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm: 132.78, 63.24, 17.65. $[M+K]^+$, calculate: 155.0474, find: 155.05706.

Synthesis of VSPpa-OH

2, 2'-[(1*Z*)-1, 2-ethenediylbis(thio)] bisethanol (100 mg, 0.555 mmol), pyropheophorbide-a (100 mg, 0.187 mmol) and 4-dimethylaminopyridine (DMAP) (22.8 mg, 0.187 mmol) were dissolved in 2 mL of anhydrous DMF under a N_2 atmosphere. After the solution was cooled to 0 °C in an ice-water bath, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) (80 mg, 0.417 mmol) in DMF (3 mL) was added dropwise, and the mixture was stirred at room temperature for 48 h. Then the solution was diluted with DCM (20 mL) and washed with brine (3 × 50 mL) and DCM (2 × 50 mL). The combined organic layers were dried with Na_2SO_4 and concentrated under reduced pressure. The product was purified on a silica gel column with ethyl acetate/dichloromethane (1:4, v/v) as the eluent. (Yield: 64%). OCPpa-OH and DMEPpa-OH were separately synthesized in a similar manner as the synthesis of VSPpa-OH. VSPpa-OH, ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm: 9.41 (s, 1H), 9.30 (s, 1H), 8.48 (s, 1H), 7.93 (dd, J = 17.8, 11.5 Hz, 1H), 6.28 – 6.02, (m, 2H), 5.86 (d, J = 1.1 Hz, 2H), 5.20 (d, J = 19.8 Hz, 1H), 5.05 (d, J = 19.8 Hz, 1H), 4.47 – 4.36 (m, 1H), 4.25 (d, J = 8.5 Hz, 1H), 4.10 – 3.98 (m, 2H), 3.60 (d, J = 10.4 Hz, 5H), 3.49 (t, J = 5.8 Hz, 2H), 3.33 (s, 3H), 3.16 (s, 3H), 2.66 (t, J = 6.6 Hz, 2H), δ 2.53 – 2.23 (m, 2H)., 2.19 (td, J = 9.5, 4.7 Hz, 2H), 1.75 (d, J = 7.3 Hz, 3H), 1.62 (t, J = 7.6 Hz, 3H), -1.75 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm: 196.22, 172.85, 171.58, 162.59, 151.78, 150.30, 149.74, 144.82, 141.80, 137.88, 136.45, 135.67, 131.97, 130.64, 129.10, 124.42, 124.00, 122.98, 106.52, 104.15, 97.20, 93.86, 63.27, 61.19, 51.74, 50.07, 48.16, 37.07, 36.56, 32.48, 31.04 , 23.26, 19.52, 17.41, 12.23, 11.30. $[M+H]^+$, calculate: 697.2882, find: 697.2068. OCPpa-OH, ^{1}H NMR (400 MHz, $CDCl_3$) : δ ppm: 9.44 (s, 1H), 9.32 (s, 1H), 8.48 (s, 1H), 7.94 (dd, J = 17.9, 11.6 Hz, 1H), 6.22 – 6.08, (m, 2H), 5.20 (d, J = 19.9 Hz, 1H), 5.04 (d, J = 19.8 Hz, 1H), 4.42 (q, J = 7.3 Hz, 1H), 4.23 (d, J = 8.6 Hz, 1H), 3.90 (q, J = 6.9 Hz, 2H), 3.69 – 3.55 (m, 5H), 3.48 (t, J = 6.6 Hz, 2H), 3.34

(s, 3H), 3.17 (s, 3H), 2.65-2.30 (m, 2H), 2.32 – 2.13 (m, 2H), 1.74 (d, J = 7.3 Hz, 3H), 1.63 (t, J = 7.6 Hz, 3H), 1.25 – 1.07 (m, 12H), -1.73 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm: 196.28, 173.20, 171.56, 160.57, 152.33, 150.15,149.14, 144.82, 141.60, 137.78, 136.23, 135.87, 131.67, 130.43, 129.12, 122.63, 106.17, 104.00, 97.08, 93.30, 64.75, 62.87, 51.72, 49.99, 48.10, 32.66, 31.18, 29.87, 29.17, 29.09, 28.49, 25.76, 25.57, 23.20, 19.42, 17.42, 12.16, 12.10, 11.20. $[M+H]^+$, calculate: 663.3910, find:663.30051. DMEPpa-OH,^{1}H NMR (400 MHz, $CDCl_3$): δ ppm: 9.41 (s, 1H), 9.30 (s, 1H), 8.47 (d, J = 3.2 Hz, 1H), 7.93 (dd, J = 17.9, 11.5 Hz, 1H), 6.28 – 6.02 (m, 2H), 5.18 (dd, J = 19.9, 9.0 Hz, 1H), 5.03 (dd, J = 19.8, 10.2 Hz, 1H), 4.54 (s, 2H), 4.39 (d, J = 7.9 Hz, 1H), 4.26 – 4.10 (m, 2H), 4.02 (s, 1H), 3.60 (d, J = 11.5 Hz, 5H), 3.33 (s, 3H), 3.16 (s, 3H), 2.69 – 2.39 (m, 2H), 2.34 – 2.11 (m, 2H), 1.81 – 1.67 (m, 6H), 1.60 (q, J = 7.9 Hz, 3H), 1.53 (s, 3H), -1.74 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm: 195.37, 172.43, 170.387, 159.13,154.21, 149.71, 147.95. 143.97, 140.55, 136.78, 135.18, 134.81, 131.387, 130.55, 129.85, 128.44, 128.13, 121.54, 104.89, 103.08, 96.13, 92.00, 66.72, 64.00, 50.54, 48.99, 47.03, 29.53, 28.66, 22.69, 21.94, 18.41, 16.42, 15.83, 13.03, 11.07. $[M+H]^+$, calculate: 633.3441, find: 633.21421.

Synthesis of Ppa-based block copolymers

POEGMA-*b*-PMAA (30 mg, 0.0013 mmol), VSPpa-OH (84 mg, 0.12 mmol) and DMAP (15 mg, 0.12 mmol) were charged in a flask and dissolved with 2 mL of DMF under a N_2 atmosphere. After the solution was stirred for 30 min in an ice-water bath, EDC (115 mg, 0.6 mmol) in 3 mL of anhydrous DMF was added dropwise, and the mixture was stirred at room temperature for 48 h. Then the solution was transferred to a dialysis bag (MWCO = 3500) and dialyzed for 72 h against water. Finally, the product-containing solution was frozen and lyophilized under vacuum. (Yield: 66%). POEGMA-*b*-P(MAA-*co*-OCPpaMA) (**OCP**), (POEGMA-*b*-P(MAA-*co*-VSPpaMA))2 (**VSP2**) and POEGMA-*b*-P(MAA-*co*-DMEPpaMA) (**DMEP**) as the control samples were separately synthesized in a similar approach of POEGMA-*b*-P(MAA-*co*-VSPpaMA) (**VSP**).

Preparation of nanoparticles in aqueous solution

VSP, **OCP**, **VSP2** and **DMEP** were separately dissolved in THF at a concentration of 1 mg/mL. Under vigorous stirring, 1 mL of the sample-containing solution was added dropwise to deionized water (9 mL) at room temperature. After stirring for 1 h, the organic solvent was removed by dialysis against deionized water for 24 h using a dialysis membrane (MWCO = 3500). The control samples, **P@Ppa** and **P@VPpa** nanoparticles were also prepared in the similar approach by dissolving Ppa and VSPpa-OH in block copolymer-containing THF solution, respectively.

The critical micelle concentration (CMC) of polymer was determined by using pyrene as a fluorescent probe at a fixed concentration of 6.0×10^{-7} mol/L. A predetermined amount of polymer solutions was added into a series of volumetric flasks, and different concentration solutions was obtained after adding deionized water. The fluorescence spectrum was acquired using a F-4500 fluorescence spectrometer at an excitation wavelength of 335 nm. The CMC was estimated as the cross-point when the intensity ratio of I_{372}/I_{383} was plotted at low and high concentration regions.

In vitro Ppa Release

For evaluating the Ppa release, nanoparticles were in buffer solution contained Tween-80 (0.8 w/w %). The solution was dialyzed in the relevant dispersion medium and gently shacked at 110 cycles per minute at 37 °C in a temperature-controlled incubator. After 24 h, the solution of **VSP**, **OCP**, **P@Ppa** and **P@VPpa** nanoparticles was irradiated with 660 nm laser to generate singlet oxygen. One milliliter of solution outside the dialysis bag was withdrawn at appointed time points and supplemented with fresh buffer. The cumulative drug release curves were assessed based on the fluorescence concentration of Ppa.

$^1O_2$ production of nanoparticles

As a singlet oxygen scavenger, 1, 3-diphenylisobenzofuran (DPBF) was used to determine the singlet oxygen production of nanoparticles. A solution containing a fixed concentration **VSP** nanoparticles and DPBF was added into a quartz cuvette and irradiated at 660 nm for 180 s. The $^1O_2$ generation of **VSP** nanoparticles can be directly correlated with the decrease of the DPBF absorbance in the UV-vis spectrum, thus the absorbance of DPBF at 415 nm was measured every 20 s. **OCP** nanoparticles at the same photosensitizer concentration was tested as a control.

^{64}Cu-labeling.

^{64}Cu was produced with an onsite cyclotron (GE PETrace) at the University of Wisconsin-Madison. $^{64}CuCl_2$ (150 MBq) was diluted in 0.1 M sodium acetate buffer (pH = 5, 7, 10) and mixed with 100 μL of **VSP** and **OCP** nanoparticles. The reaction was conducted at 37 or 70 °C for 120 min with constant shaking. TLC determined the labeling yield at different time points using 50 mM EDTA solution as the mobile phase. The resulting product was purified using a PD-10 column with PBS as the mobile phase.

Cell culture

Human malignant melanoma cell line (A375 cells) were cultivated in Dulbecco's modified Eagle's medium (DMEM) supplemented with 1% antibiotics (penicillin and streptomycin) and 10% fetal bovine serum (FBS) in a humidified standard atmosphere of 5% CO_2 at 37 °C.

Intracellular uptake and photoactivity

The cellular uptake of **VSP** and **OCP** nanoparticles were separately observed by using confocal laser scanning microscopy (CLSM) and flow cytometry. For flow cytometry measurement, 4×10^5 cells of A375 in 2 mL culture medium were cultured in a well of 6-cell plate for 24 h. Then the cells were treated with free Ppa, **VSP** and **OCP** nanoparticles at the same concentration 5 μg/mL of Ppa for 20 h. After that, cells were washed carefully and irradiated respectively by 660 nm laser (200 mW/cm^2) for 1 min or 0 min under fresh medium. Finally, the cells were collected and washed for analysis after further 4 h incubation.

For CLSM, A375 cells (2×10^4 cells/well) were seed on glass bottom cell culture dish for 24 h, and then the cells were treated with fresh medium containing free Ppa, **VSP** and **OCP** nanoparticles at the same concentration 5 μg/mL of Ppa for 20 h. After that, cells were washed carefully and irradiated respectively with or without 660 nm laser (200 mW/cm^2) for 1 min under fresh medium. After further 4 h incubation, the cells were treated with PBS, 4% paraformaldehyde, and PBS. Then the cells nuclei were stained with Hoechst for 3 min and washed three times with PBS. Finally, intracellular fluorescence of Ppa was observed by CLSM with excitation at 404 nm and emission at 700 nm.

Intracellular ROS generation was also detected by CLSM. Tumor cells were seed on glass bottom cell culture dish for 24 h, then treated with **VSP** and **OCP** nanoparticles at the same concentration 5 μg/mL of Ppa for 24 h. Then **VSP** nanoparticles treated cells were irradiated for 1 plus 5 min with a 0, 1, 2, 3, 4, 5 h interval, respectively. **OCP** nanoparticles treated cells were irradiated 6 min or 1 plus 5 min with 4 h interval. The DCFH-DA were incubated with cells for 20 min and then washed 3 times by PBS before final irradiation.

In vitro dark cytotoxicity and phototoxicity of nanoparticles.

200 μL of A375 cell suspension (2.5 × 10^4 cells/mL) was seeded in a 96-well plate and then incubated for 24 h at 37 °C. Different concentrations of free Ppa, **VSP**, **OCP**, **P@Ppa**, **P@VPpa VSP2** and **DMEP** nanoparticles (Ppa concentration at 0-5 μg/mL) in fresh DMEM media were added into the wells and co-cultured for another 24 h. The cells were washed and irradiated with 660 nm laser (200 mW/cm^2) for 6 min or 1 min, after 4 h, the cells were irradiated for 0 min or 5 min (the total time was 6 min). Before the media was replaced with 200 μL of MTT solution (0.5 mg/mL in DMEM) and cultured for 4 h, the cells were incubated for further 24 h. Finally, 150 μL of DMSO per well was added to replace the MTT solution and dissolve the formazan, and the absorbance value was recorded with a SpectraMax spectrometer at the wavelength of 492 nm. The in vitro dark cytotoxicity of nanoparticles or free Ppa was checked using the same procedure described above but without illumination.

Tumor models.

Tumor-bearing BALB/c mice were established and used for in vivo performance: A375 cells (10^6 in 200 μL PBS) were subcutaneously injected into the mice, respectively. Once the tumors reached the required volume, the tumor-bearing mice were used for imaging or therapy.

In vivo imaging and biodistribution studies

For fluorescence imaging, 200 μL of **VSP** or **OCP** nanoparticles (1 mg/mL of Ppa) were injected into tumor bearing mice through the tail vein. After the nanoparticles successfully accumulated at tumor site, 1 min light irradiation was carried. Fluorescence imaging data at designed times were obtained by in vivo multispectral imaging system (Kodak FX).

For normal PET imaging, B16F10 tumor bearing BALB/c mice were injected with ^{64}Cu-labelled nanoparticles via the tail vein before serial PET scans. Quantitative PET data was presented as a percentage of the injected dose per gram (%ID/g). For biodistribution studies, major organs were collected and wet-weighed at designed time points. The radioactivity uptake by the tissue was measured by using a gammacounter (Perkin-Elmer) and presented as %ID/g (mean ± SD).

In vivo self-amplified photodynamic cancer therapy of nanoparticles

In vivo photodynamic therapy of nanoparticles was evaluated in tumor bearing mice. When the tumor volume reached ~ 200 mm^3, the mice were divided into several groups: (1) control, (2) **OCP**, (3) **VSP**, (4) **OCP** with 6 min laser irradiation (**OCP/6** min), (5) **VSP** with 6 min laser irradiation (**VSP/6** min), (6) **DMEP** with 6 min laser irradiation (**DMEP/6** min), (7) **VSP2** with 6 min laser irradiation (**VSP2/6** min), (8) **OCP** with 1 plus 5 min laser irradiation (**OCP/1+5** min) and (9) **VSP** with 1 plus 5 min laser irradiation (**VSP/1+5** min), (10) **DMEP** with 1 plus 5 min laser irradiation (**DMEP/1+5** min) and (11) **VSP2** with 1 plus 5 min laser irradiation (**VSP2/1+5** min). Each mouse was injected with 200 μL PBS or nanoparticles (Ppa concentration at 1mg/mL). Groups of **OCP/6** min, **VSP/6** min, **DMEP/6** min and **VSP2/6** min were treated with consecutive 6 min laser irradiation while groups of **OCP/1+5** min, **VSP/1+5** min, **DMEP/1+5** min and **VSP2/1+5** min were irradiated 1 plus 5 min laser irradiation with a 4 h interval after the injection of 24 h. The tumor volumes and mice weights were measured twice a week and the program was end when the mice in the control group were all dead. Then all tumors were carefully harvested, weighed, and photographed.

Statistical analysis.

Statistical analysis was performed by Student's t-test for two groups. All results were expressed as the mean ± s.d. unless otherwise noted. A value of $P < 0.05$ was considered statistically significant.

References

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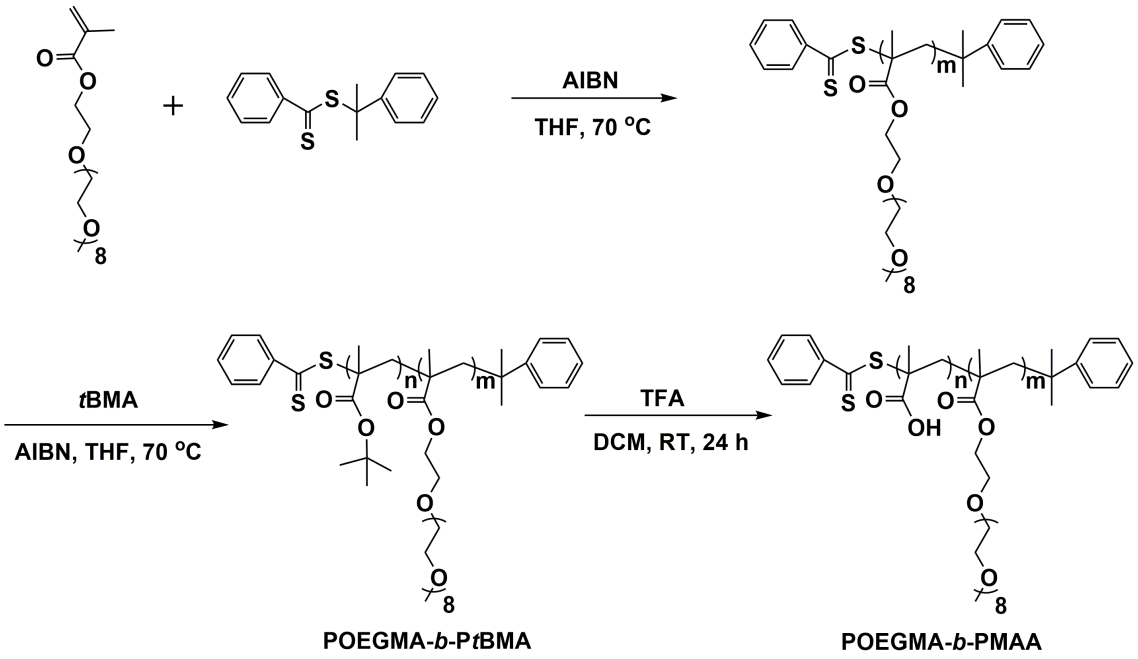
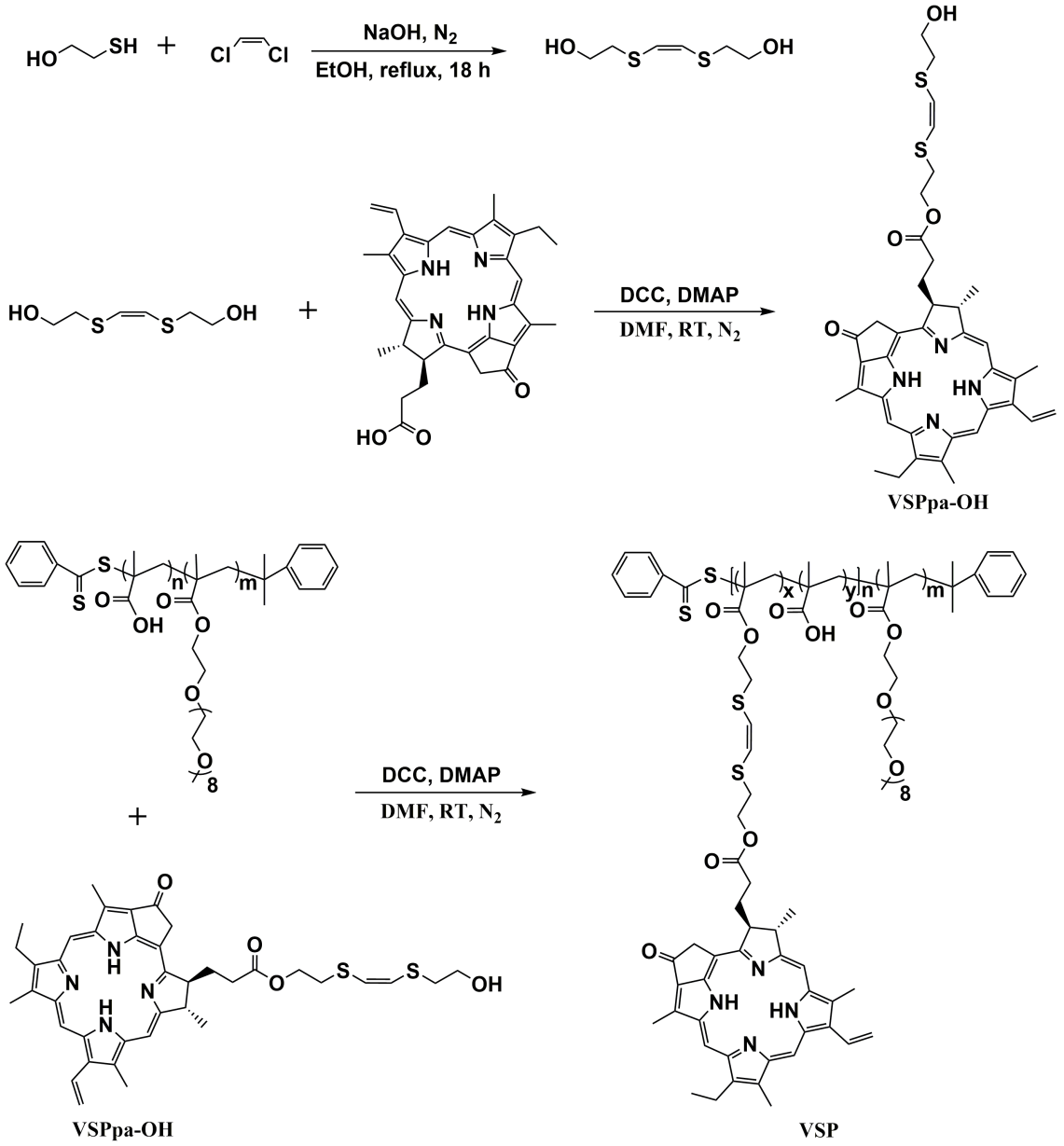
[2] S. Erbas-Cakmak, E. U. Akkaya, *Angew. Chem. Int. Ed.* **2013**, *52*, 11364-11368.

Author Contributions

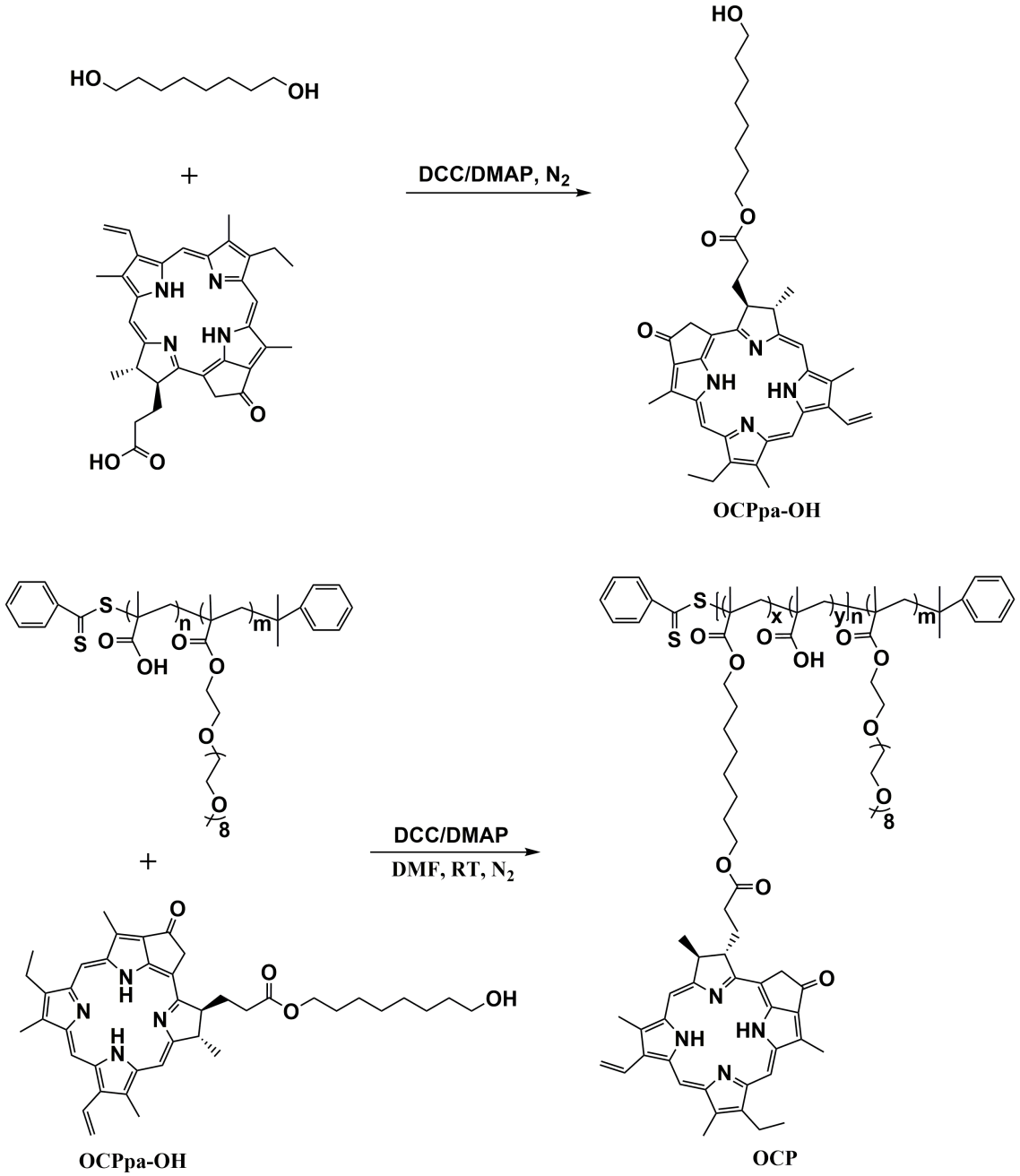
Z. Liu conceived the project and designed the experiments. Z. liu, Y. Xue, M. Wu, T. Cao and M. Li performed the sample preparation, characterization and biological experiment. Z. Liu and T. Cao wrote the paper and contributed equally. All authors discussed the results and commented on the manuscript.



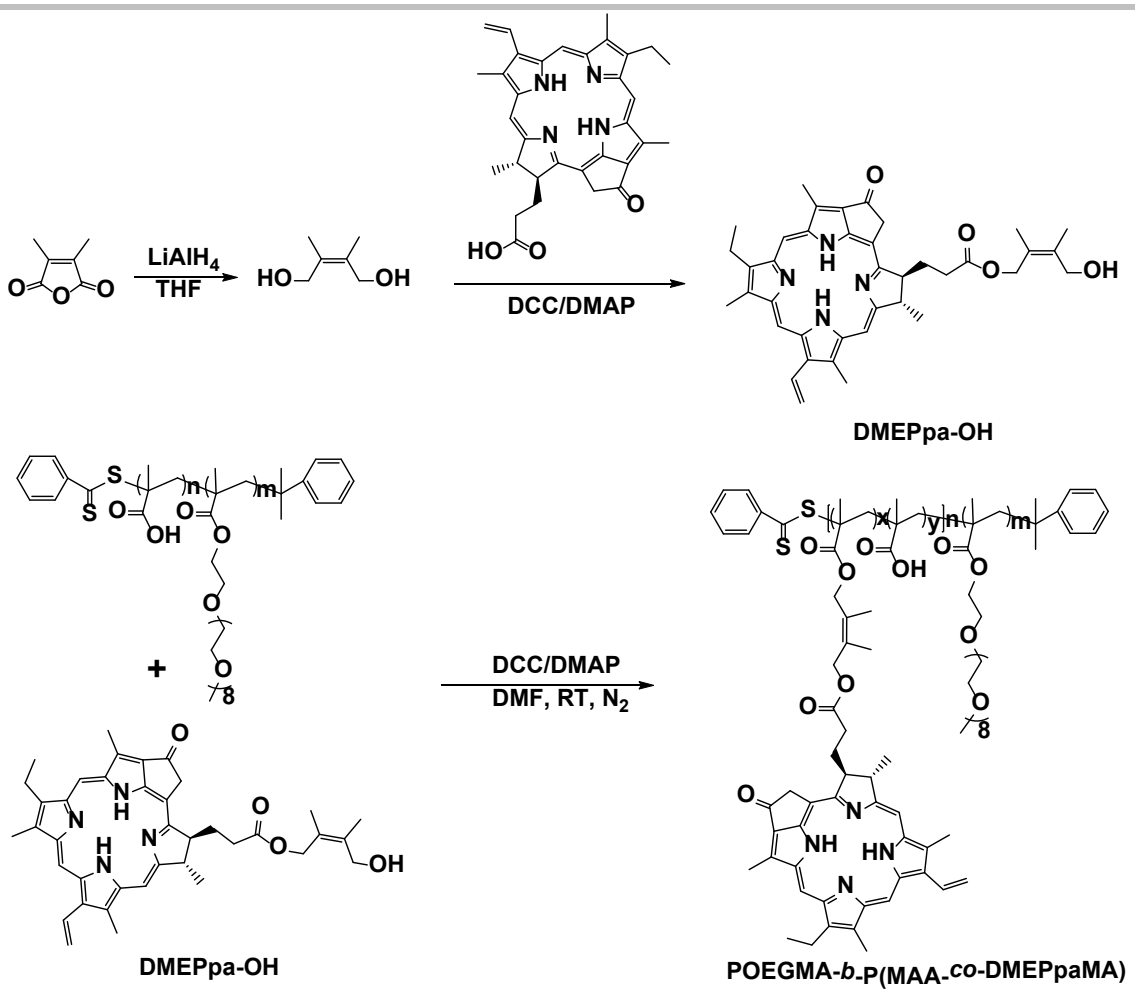
Scheme S1. Synthesis of POEGMA-*b*-PMAA block copolymer.



Scheme S2. Synthesis of POEGMA-*b*-P(MAA-*co*-VSPpaMA) block copolymer.



Scheme S3. Synthesis of POEGMA-*b*-P(MAA-*co*-OCPpaMA) block copolymer.



Scheme S4. Synthesis of POEGMA-*b*-P(MAA-*co*-DMEPpaMA) block copolymer.

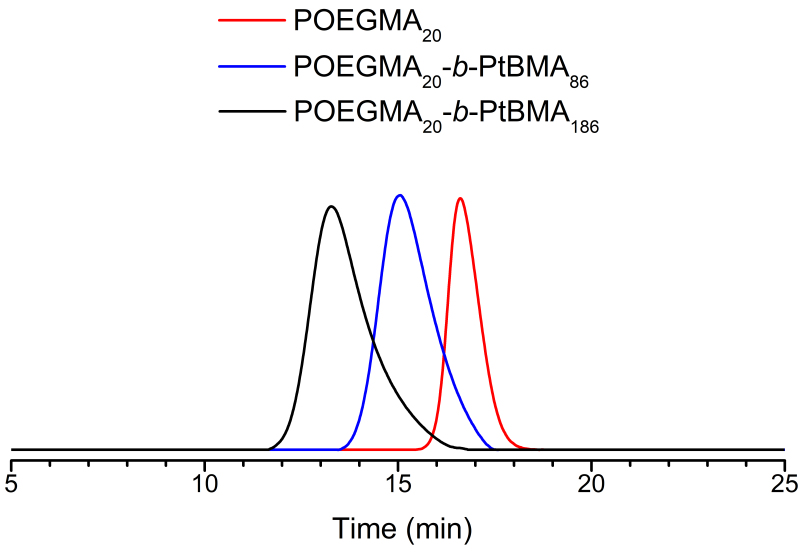


Figure S1. GPC traces of POEGMA homopolymer and POEGMA-*b*-P*t*BMA block copolymers.

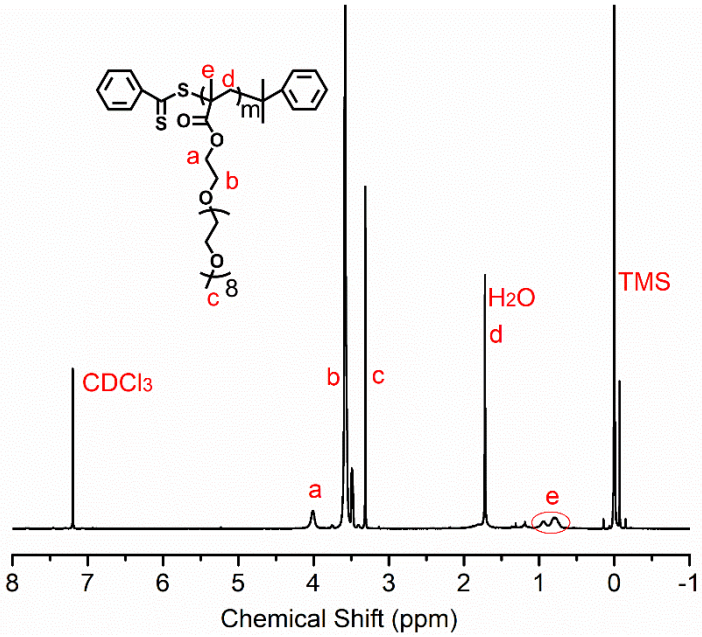


Figure S2. ^{1}H NMR spectrum of POEGMA homopolymer.

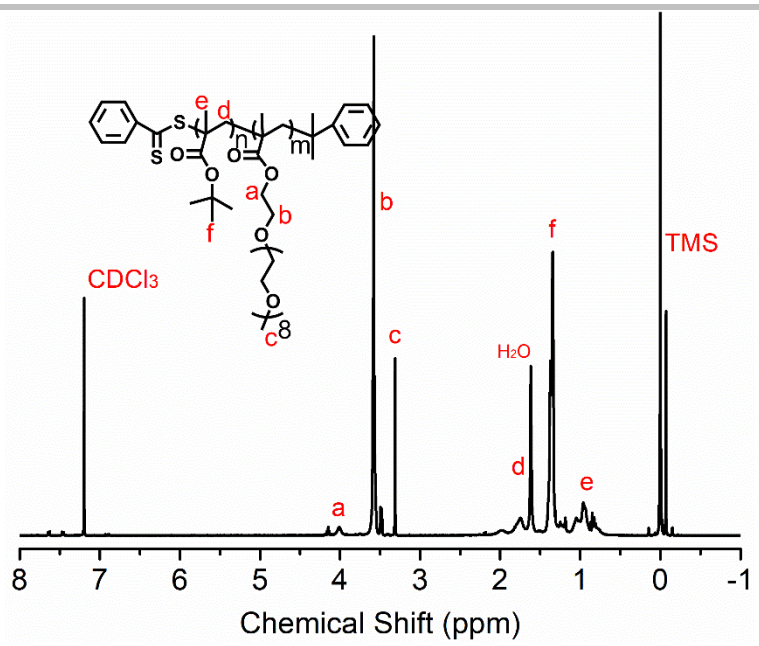


Figure S3. ^{1}H NMR spectrum of POEGMA-*b*-P*t*BMA$_{86}$ block copolymer.

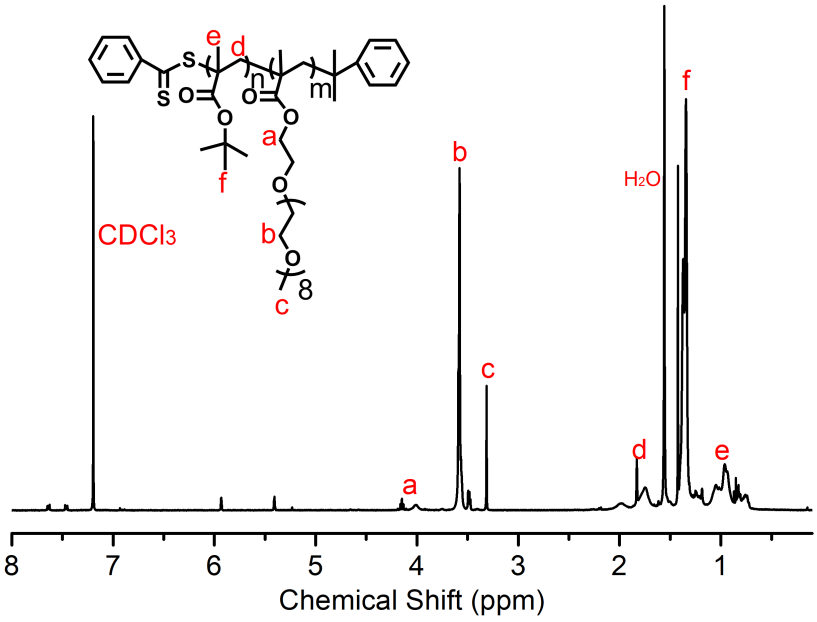


Figure S4. ^{1}H NMR spectrum of POEGMA-*b*-P*t*BMA$_{186}$ block copolymer.

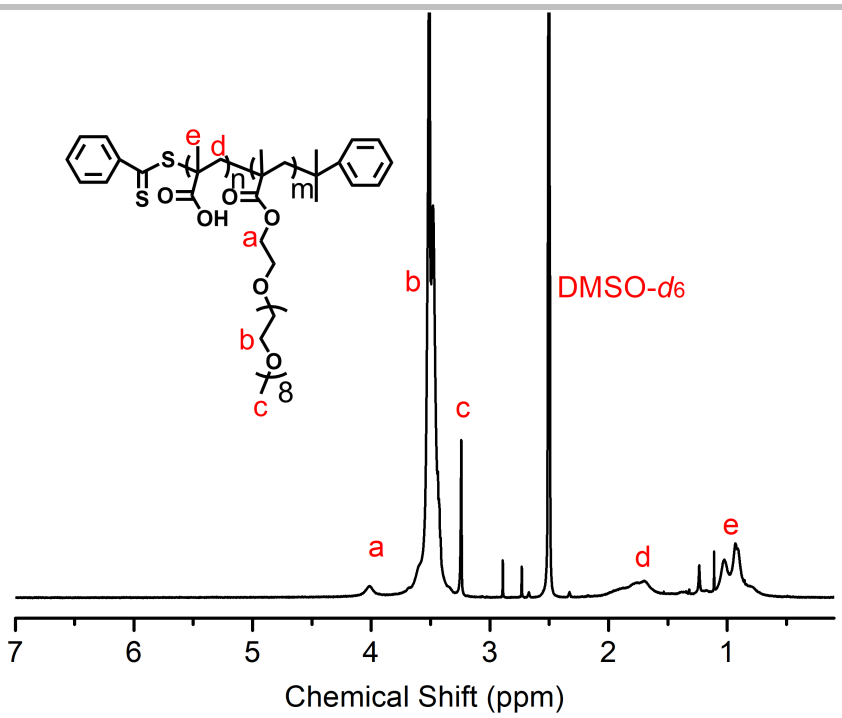


Figure S5. ^{1}H NMR spectrum of POEGMA-*b*-PMAA$_{86}$ block copolymer.

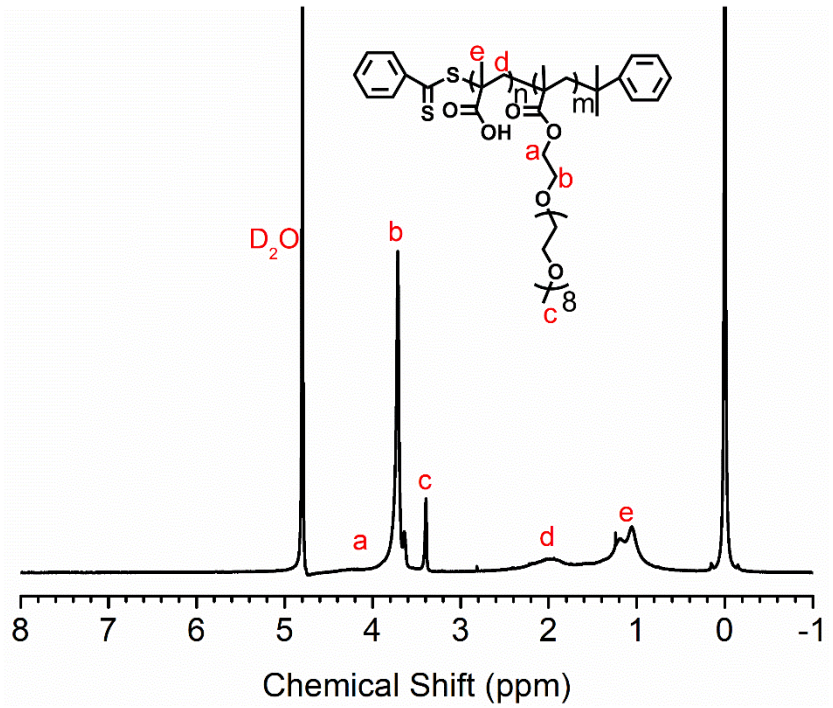


Figure S6. ^{1}H NMR spectrum of POEGMA-*b*-PMAA$_{186}$ block copolymer.

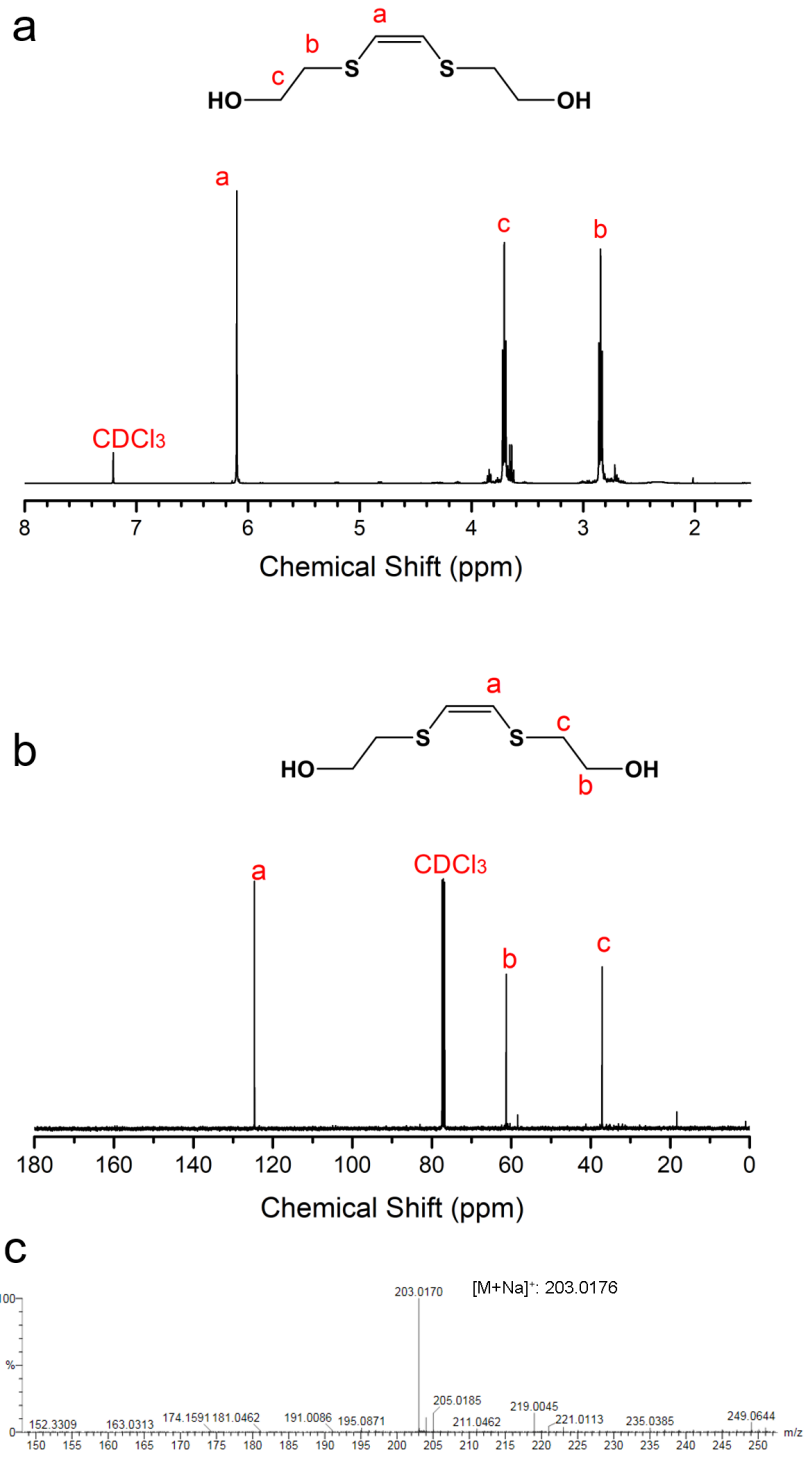


Figure S7. (a) ^{1}H NMR, (b) ^{13}C NMR and (c) Mass spectrum of 2, 2'-[(1Z)-1, 2-ethenediylbis(thio)]bisethanol.

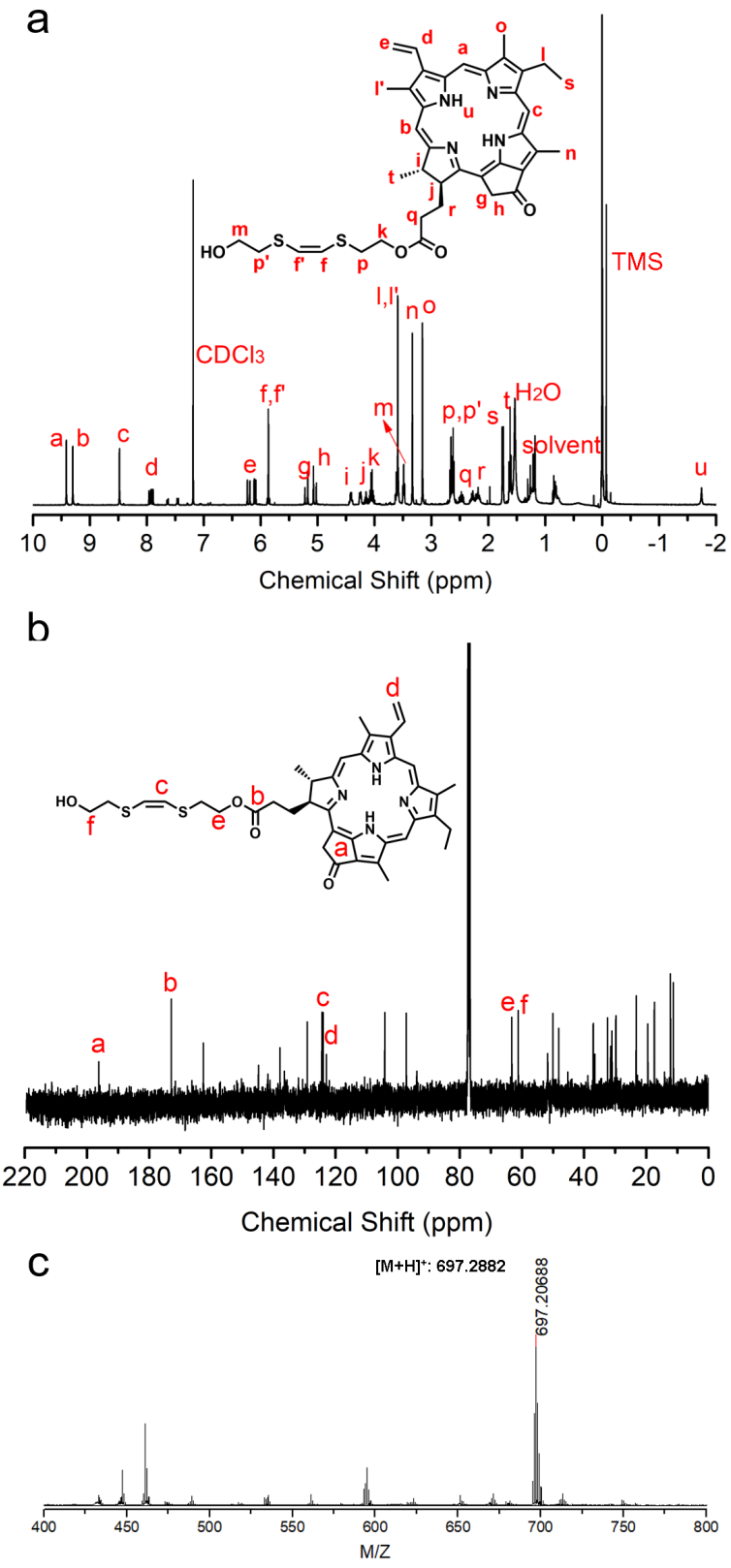


Figure S8. (a) ^{1}H NMR, (b) ^{13}C NMR and (c) Mass spectrum of VSPpa-OH.

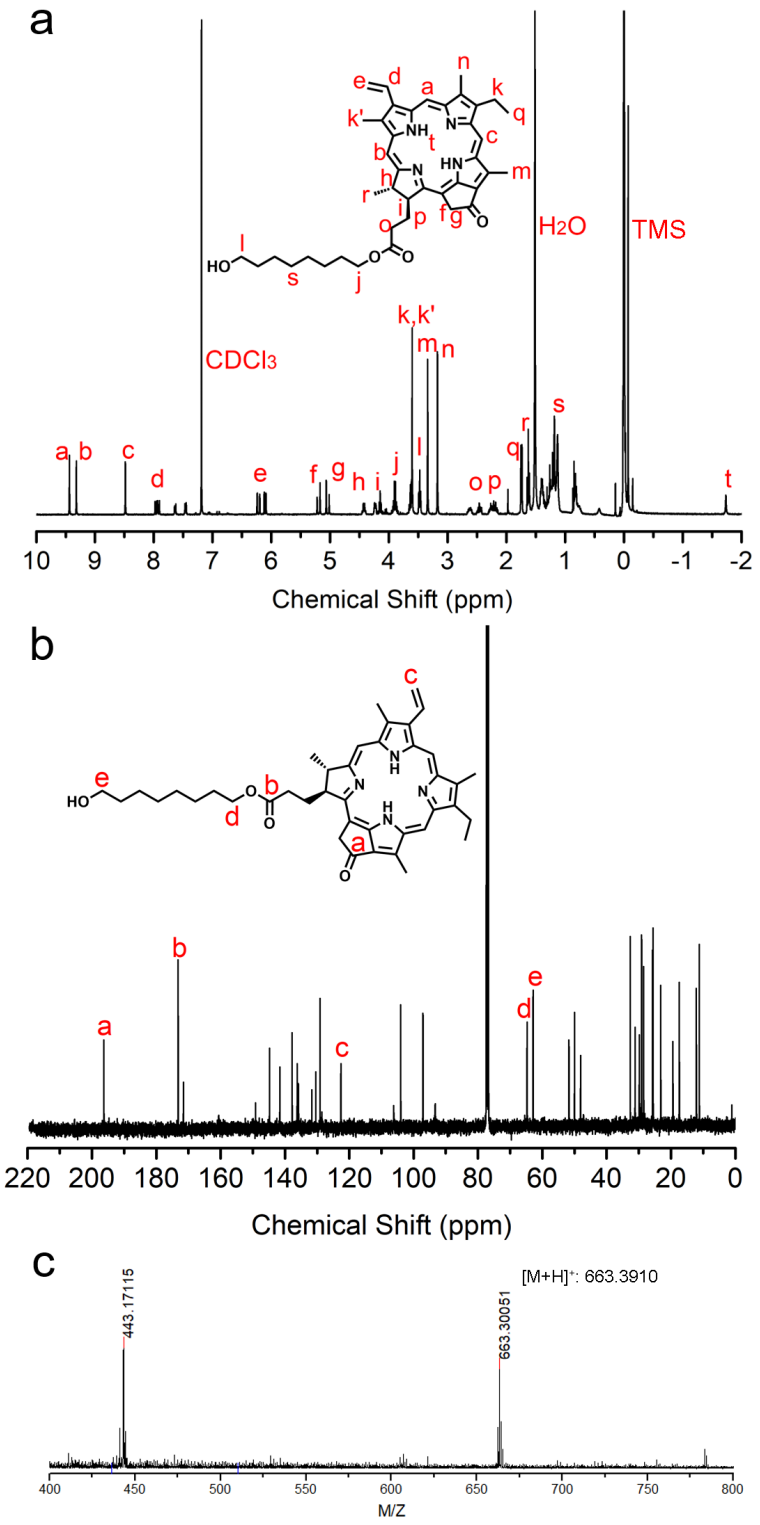


Figure S9. (a) ^{1}H NMR, (b) ^{13}C NMR and (c) Mass spectrum of OCPpa-OH.

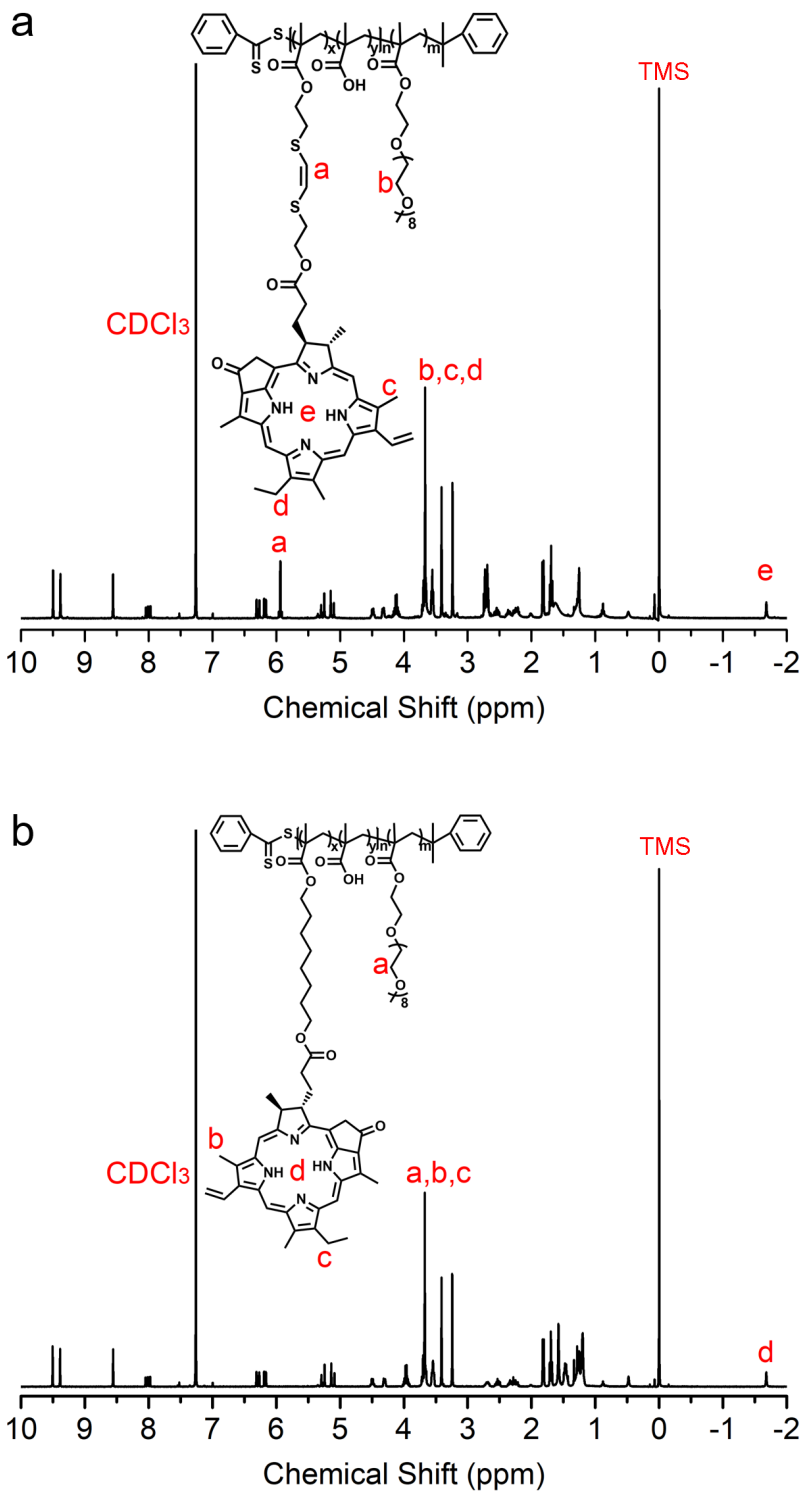


Figure S10. ^{1}H NMR spectra of (a) POEGMA-*b*-P(MAA-*co*-VSPpaMA) and (b) POEGMA-*b*-P(MAA-*co*-OCPpaMA).

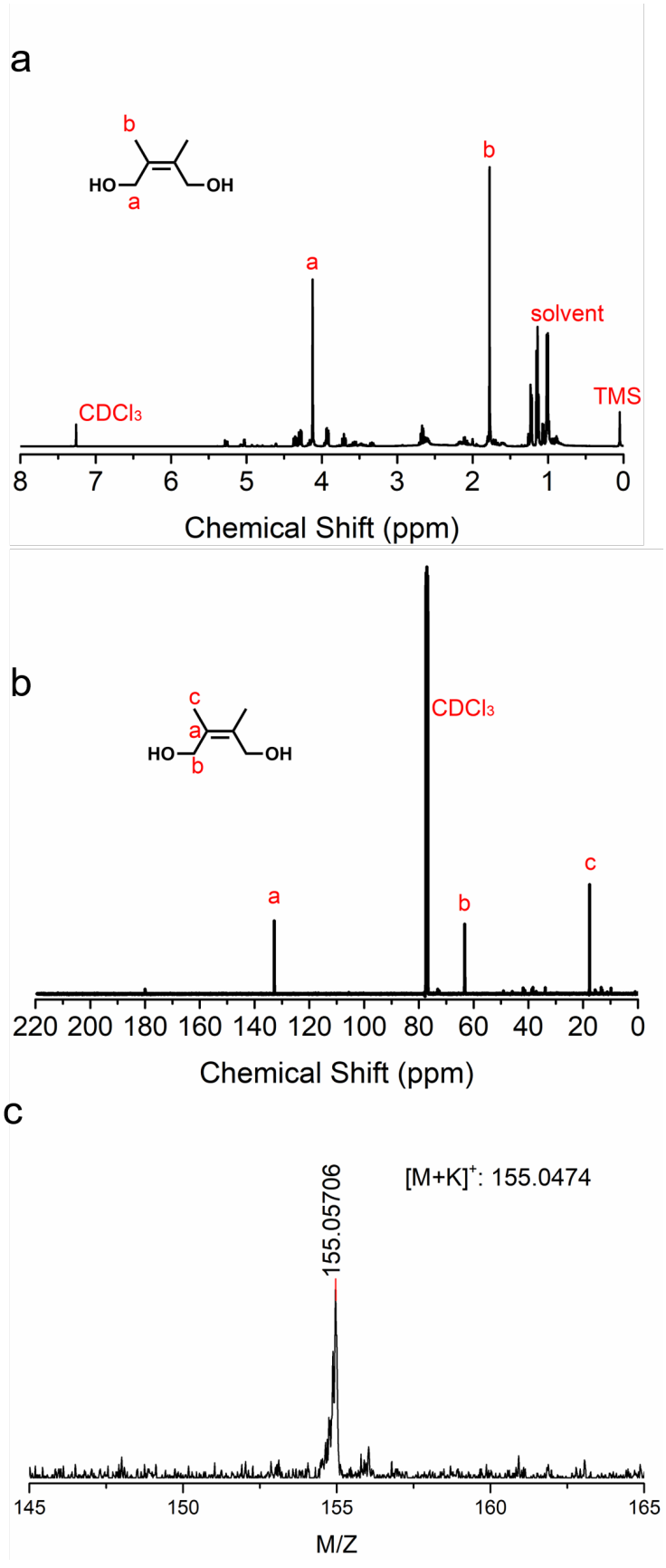


Figure S11. (a) ^{1}H NMR, (b) ^{13}C NMR and (c) Mass spectrum of (Z)-2,3-dimethylbut-2-ene-1,4-diol.

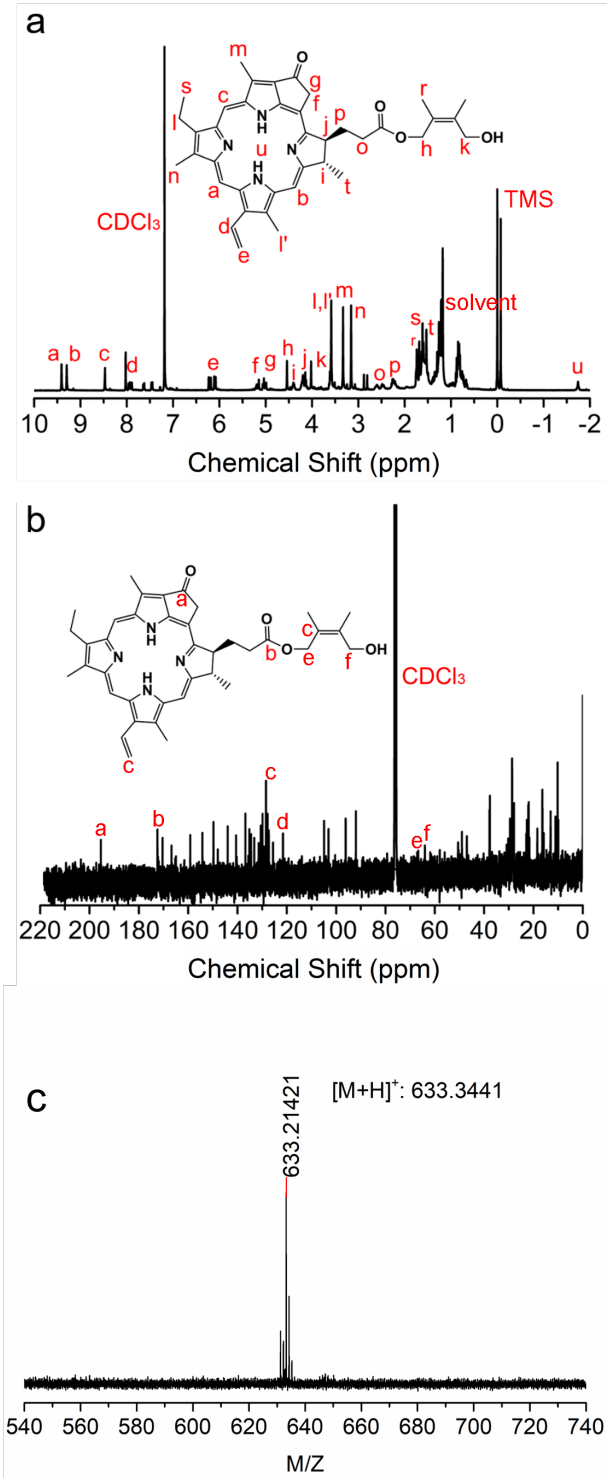


Figure S12. (a) ^{1}H NMR, (b) ^{13}C NMR and (c) Mass spectrum of DMEPpa-OH.

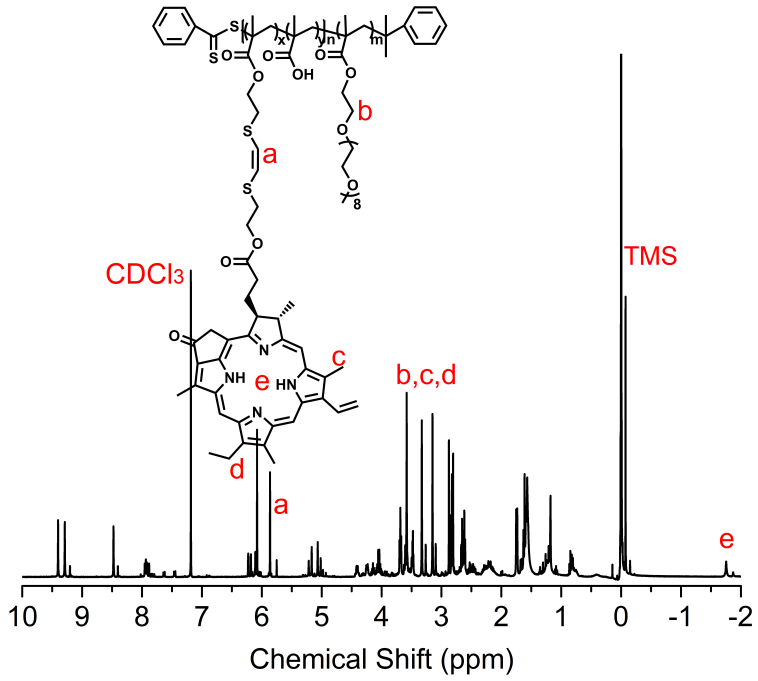


Figure S13. ^{1}H NMR spectra of (POEGMA-*b*-P(MAA-*co*-VSPpaMA))2.

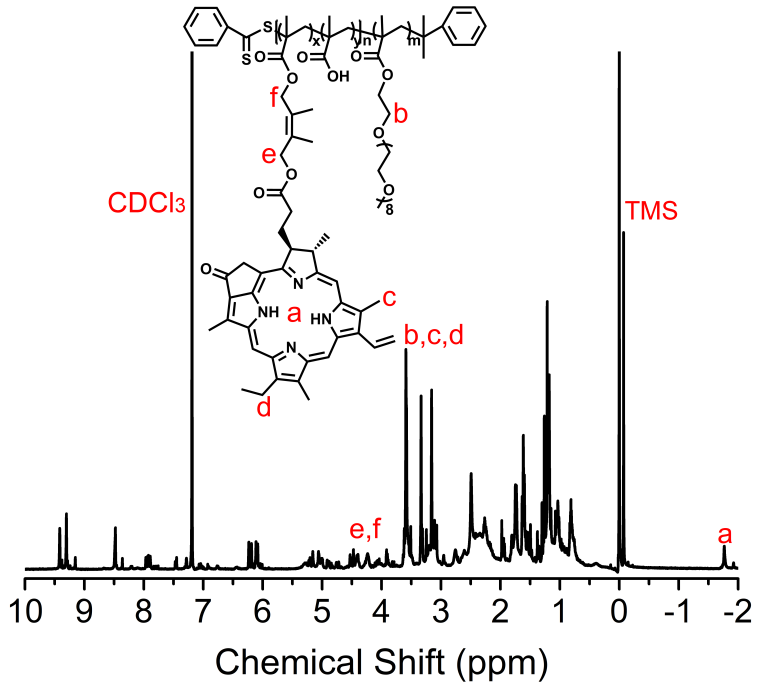


Figure S14. ^{1}H NMR spectra of POEGMA-*b*-P(MAA-*co*-DMEPpaMA).

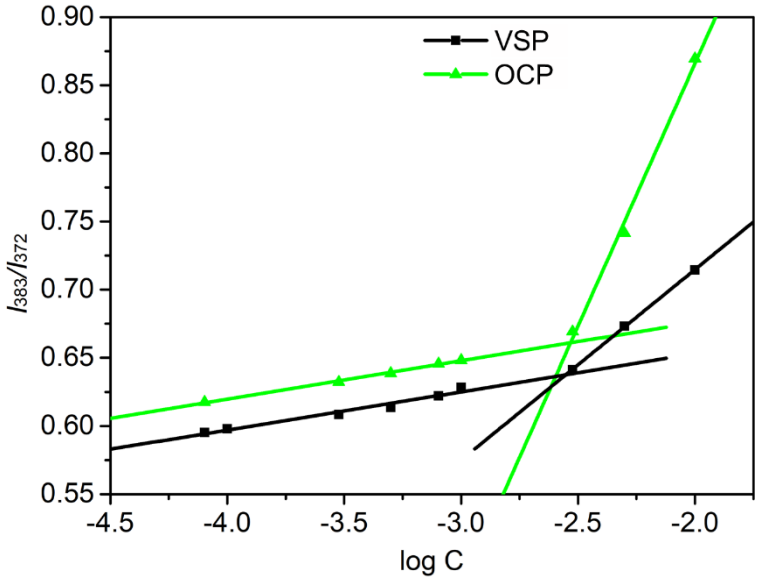


Figure S15. Plot of the I_{383}/I_{372} ratio against log C of **VSP** and **OCP**.

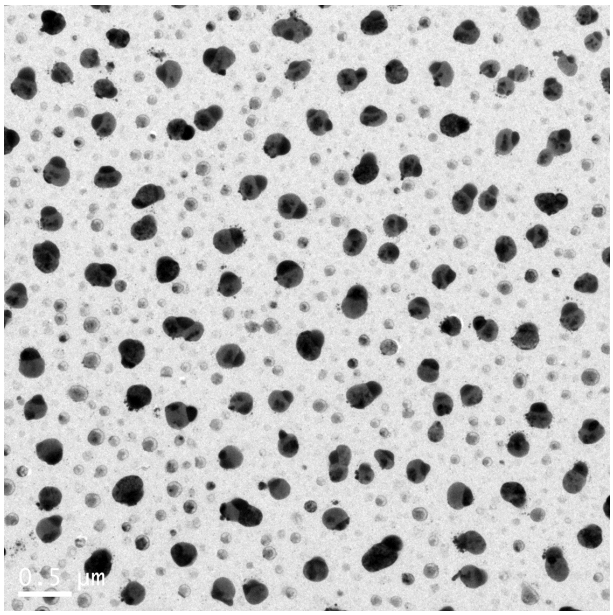


Figure S16. TEM image of **OCP** nanoparticles.

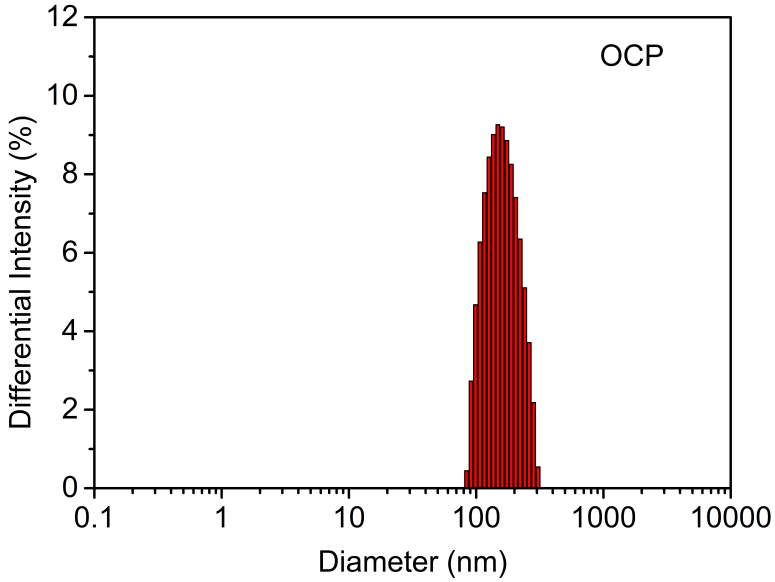


Figure S17. Size distribution of **OCP** nanoparticles determined by DLS.

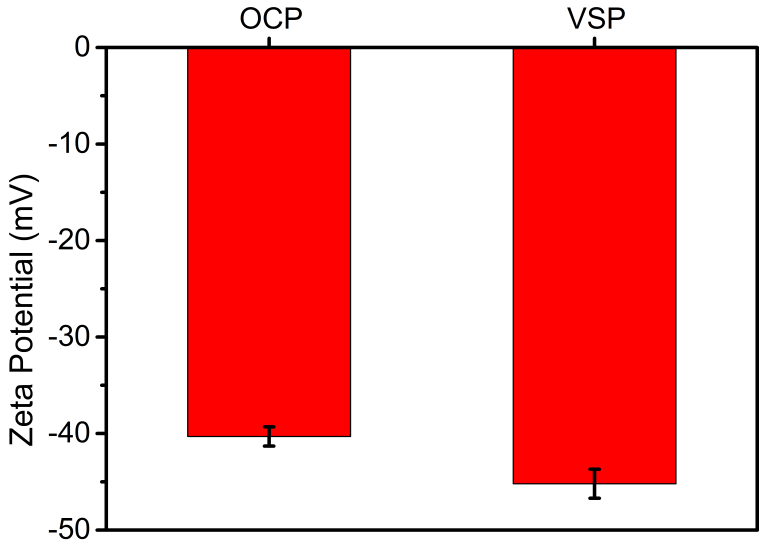


Figure S18. Zeta potential of nanoparticles in water.

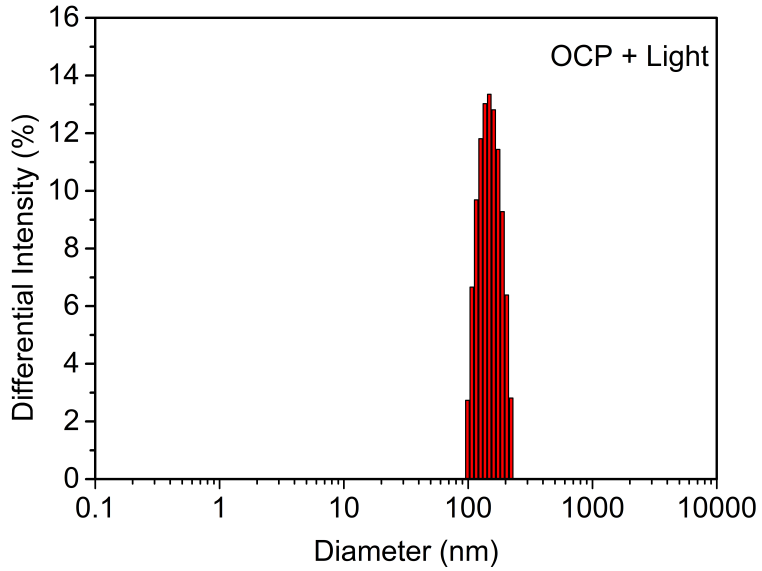


Figure S19. Size distribution of **OCP** nanoparticles after light irradiation determined by DLS.

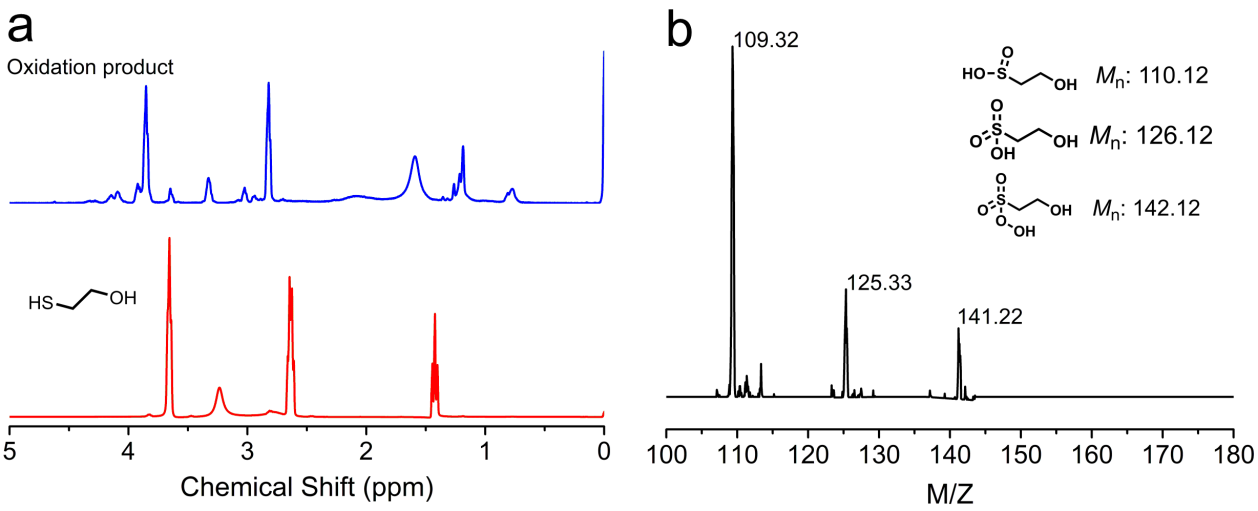


Figure S20. (a) ^{1}H NMR spectra of mercaptoethanol before (red) and after (blue) oxidization and (b) Mass spectra of mercaptoethanol after oxidization.

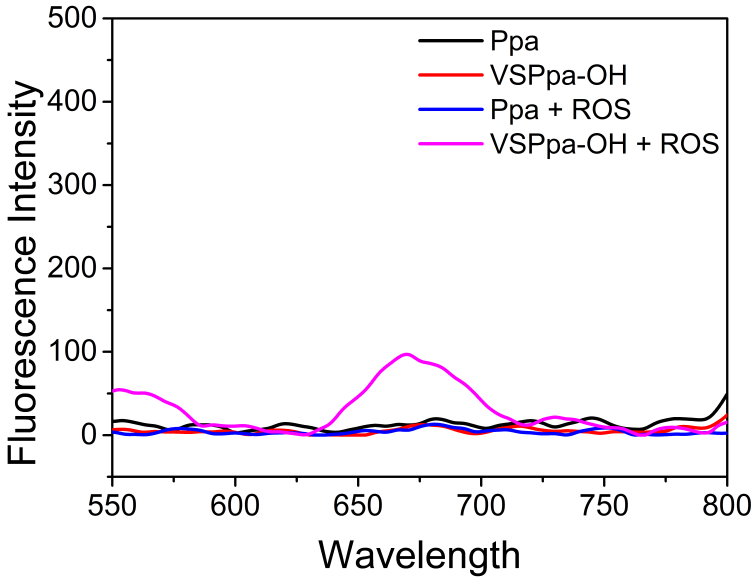


Figure S21. Fluorescence emission spectra of Ppa and VSPpa-OH after oxidization by ROS.

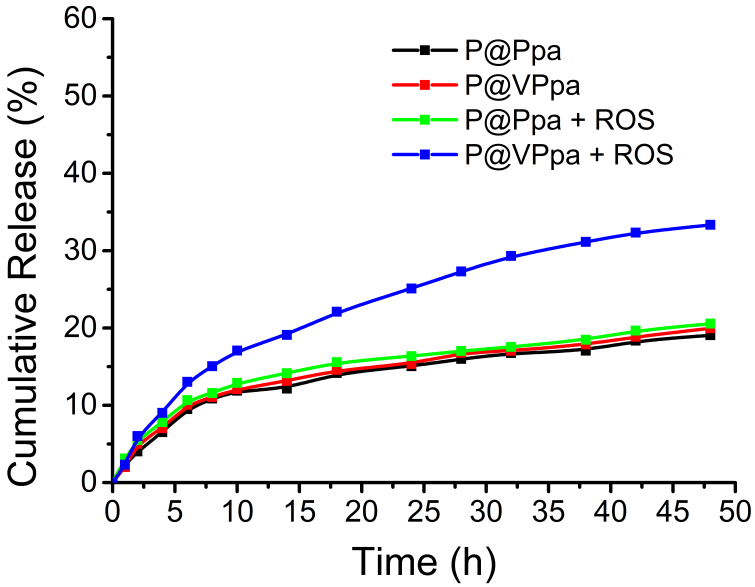


Figure S22. Ppa release curves of **P@Ppa** and **P@VPpa** nanoparticles in buffer incubated with or without ROS.

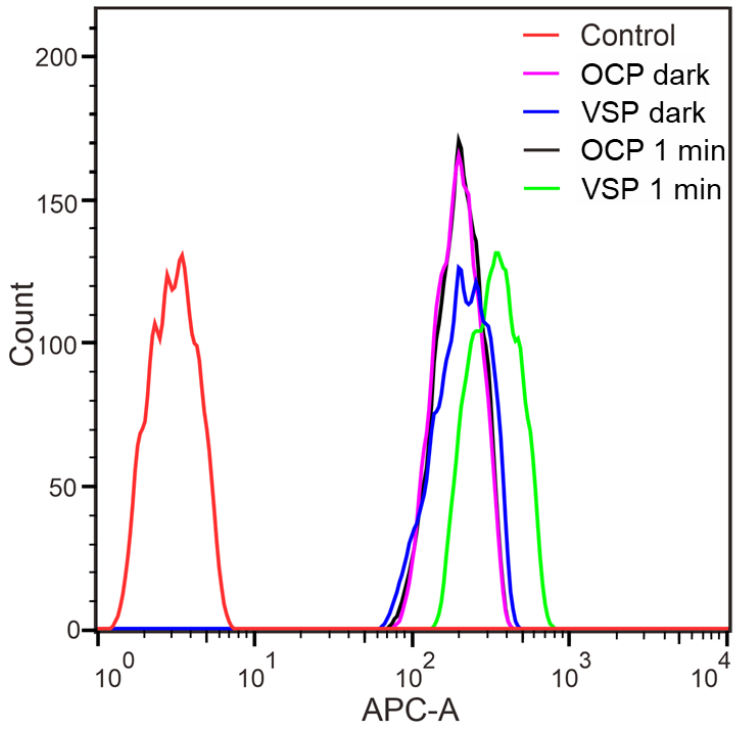


Figure S23. Intracellular release of Ppa from **VSP** and **OCP** nanoparticles at different conditions (Ex: 640 nm, Em: 670 nm).

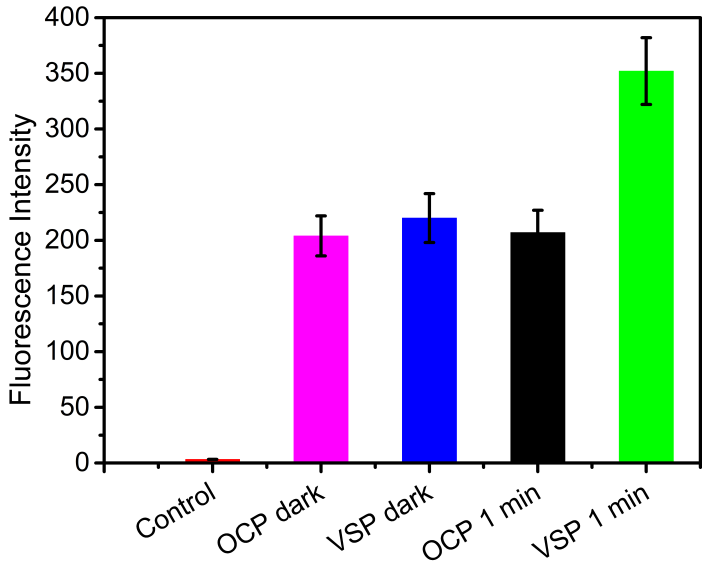


Figure S24. Intracellular quantitative analysis of Ppa released from **VSP** and **OCP** nanoparticles at different conditions (Ex: 640 nm, Em: 670 nm).

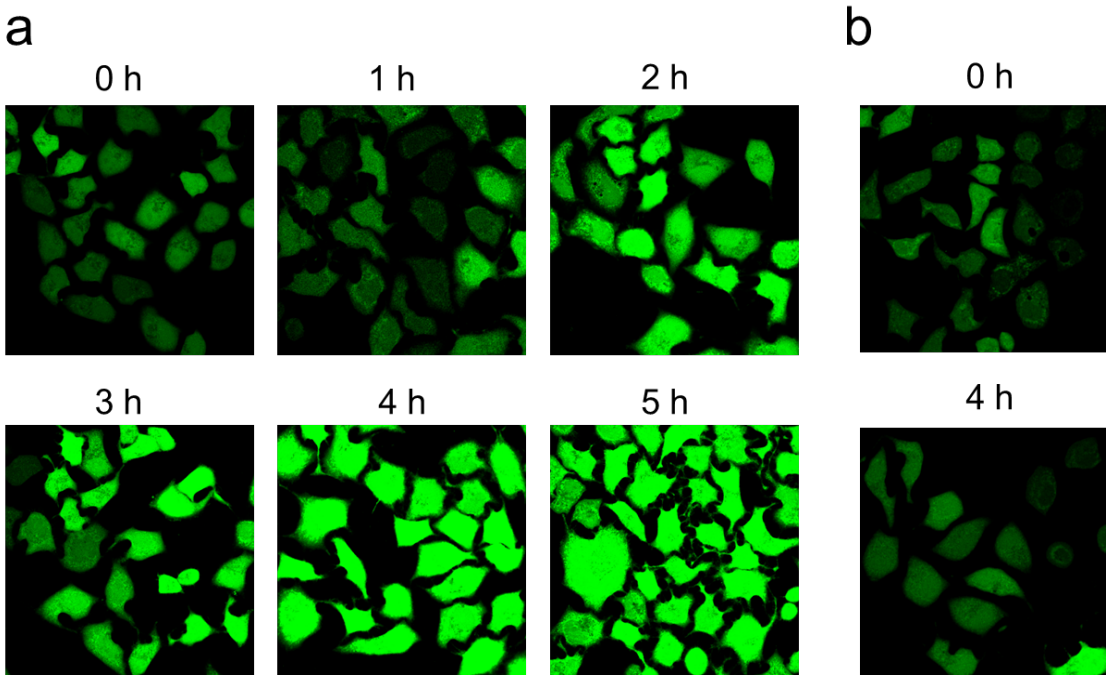


Figure S25. Intracellular ROS generation of nanoparticles. (a) **VSP** nanoparticles under light radiation with 0, 1, 2, 3, 4 and 5 h interval between 1 min irradiation and subsequent 5 min irradiation and (b) **OCP** nanoparticles irradiated with laser for 1 + 5 min with 0 or 4 h interval.

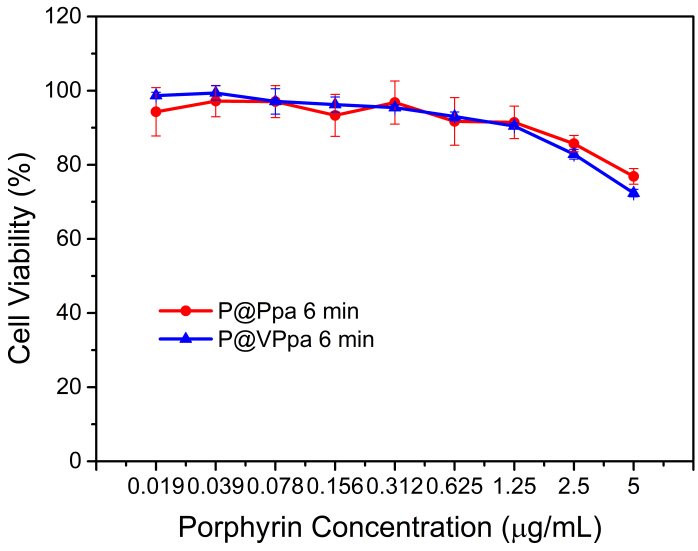


Figure S26. In vitro cellular toxicity of **P@Ppa** and **P@VPpa** nanoparticles irradiated with laser for 6 min.

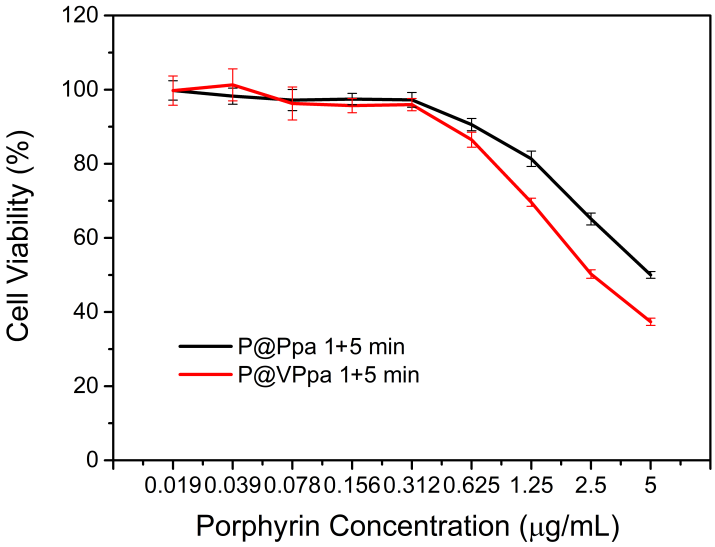


Figure S27. In vitro cellular toxicity of **P@Ppa** and **P@VPpa** nanoparticles irradiated with laser for 1 + 5 min with an interval of 4 h.

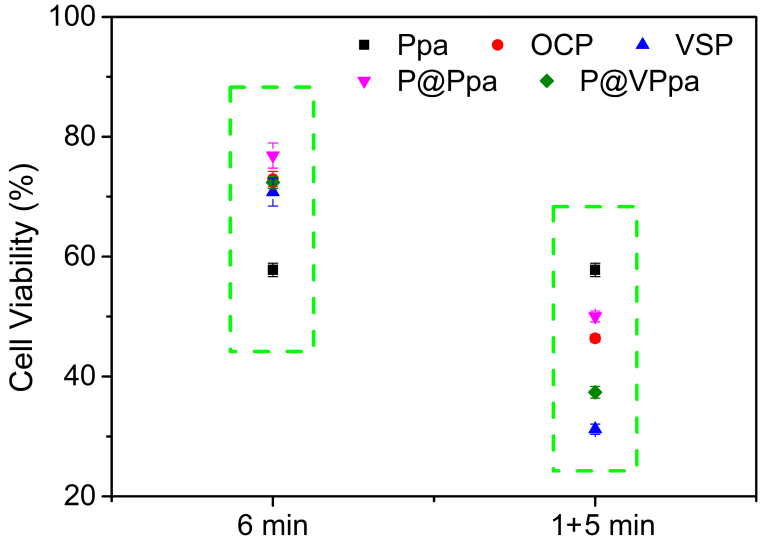


Figure S28. In vitro cellular toxicity contrast of different nanoparticles at 5 μg/mL of Ppa concentration.

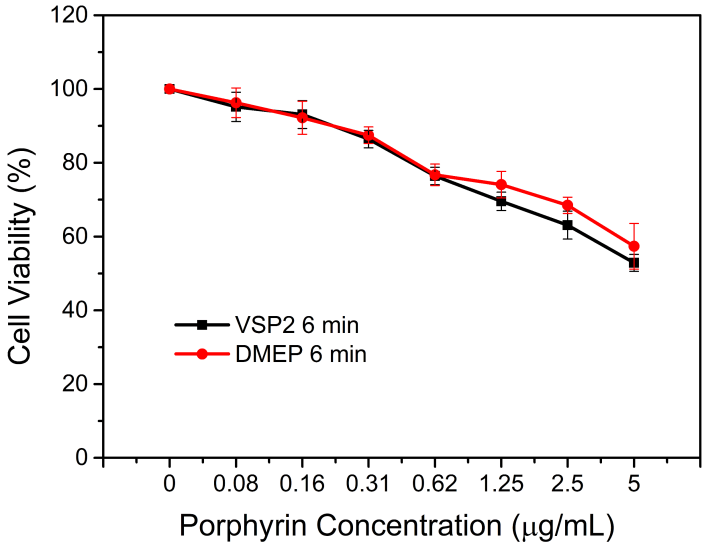


Figure S29. In vitro cellular toxicity of **VSP2** and **DMEP** nanoparticles irradiated with laser for 6 min.

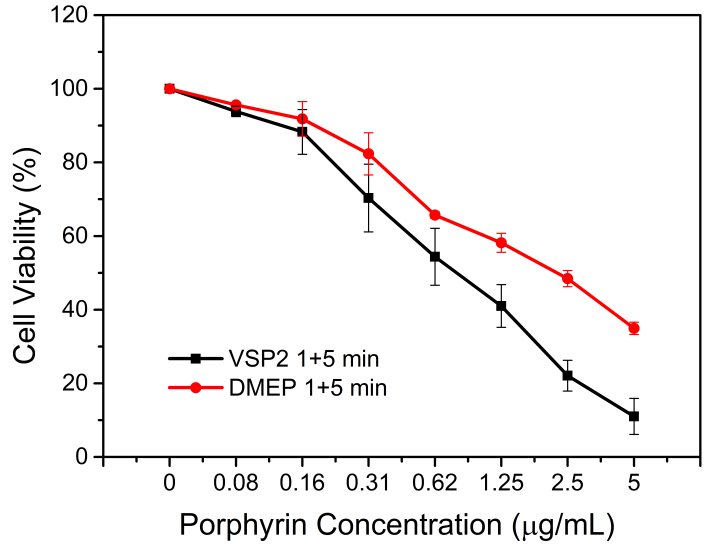


Figure S30. In vitro cellular toxicity of **VSP2** and **DMEP** nanoparticles irradiated with laser for 1 + 5 min with an interval of 4 h.

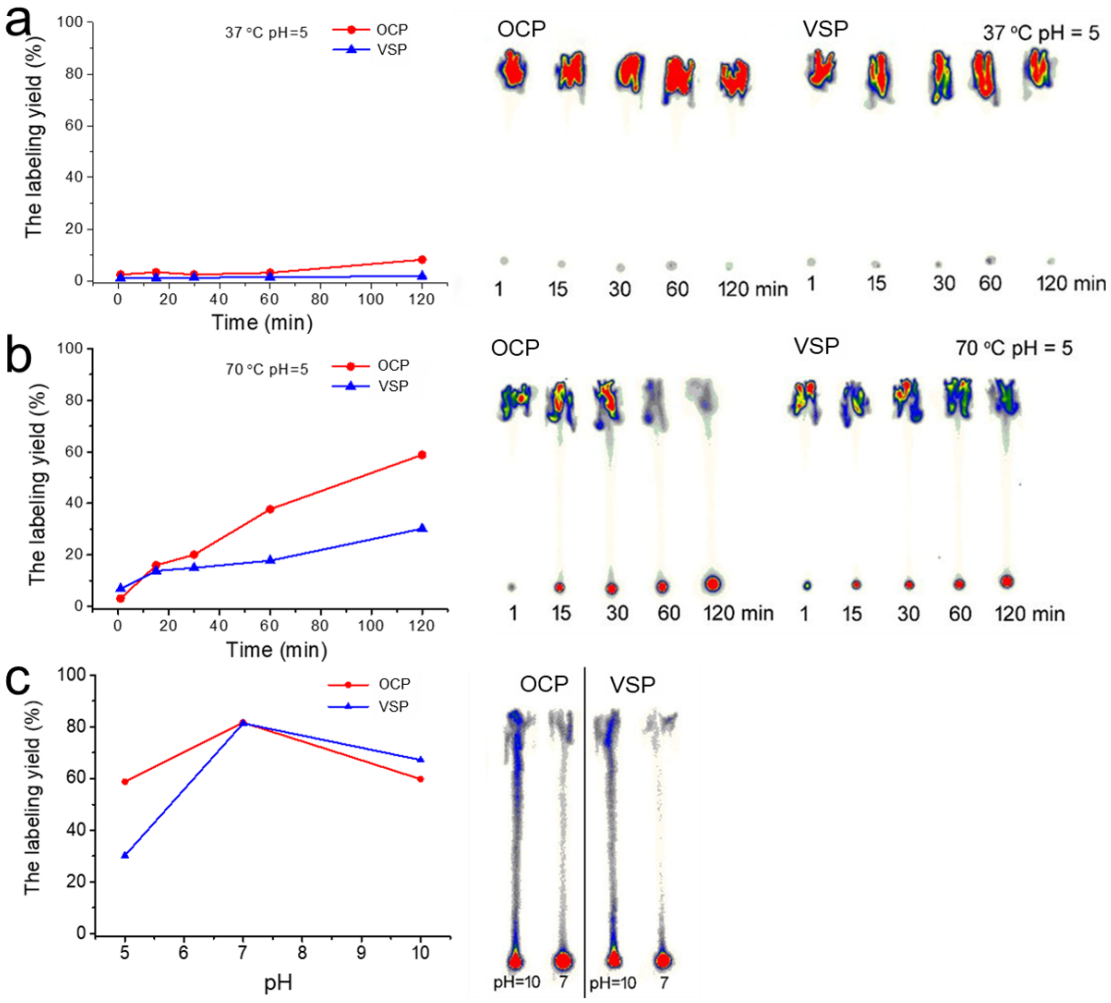


Figure S31. The labeling yield of polymers (**OCP** and **VSP**) with $^{64}Cu^{2+}$ and corresponding TLC autoradiograph imaging were shown at different conditions: labeling at pH = 5 with time-dependent (1, 15, 30, 60 and 120 min) in (a) 37 °C or (b) 70 °C, and (c) labeling at different pH = 5, 7, 10 in 70 °C for 120 min.

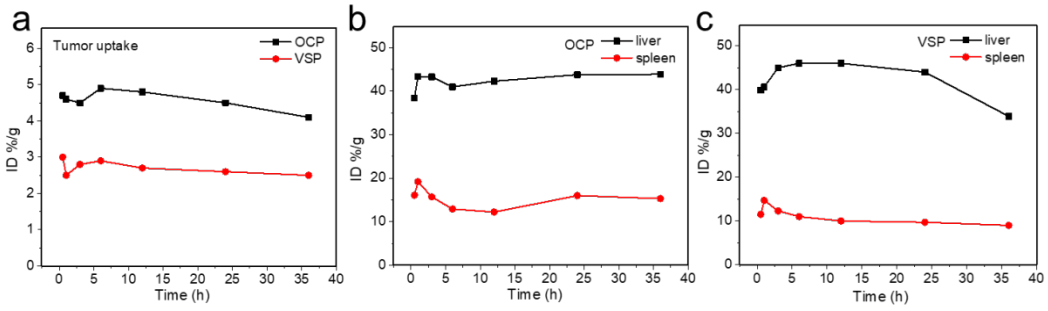


Figure S32. (a) Quantitative PET imaging-based accumulation kinetics of **OCP** and **VSP** nanoparticles in tumor. Quantitative biodistribution of **OCP** nanoparticles (b) and **VSP** nanoparticles (c) obtained from ROI analysis of PET images.

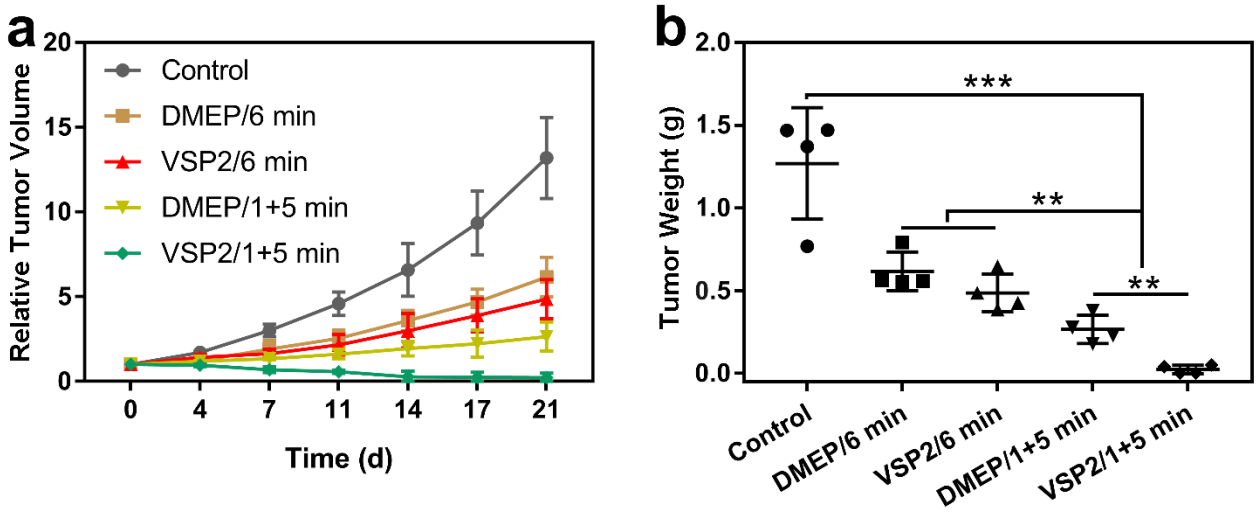


Figure S33. In vivo antitumor performance of **VSP2** and **DMEP** nanoparticles. (a) tumor inhabitation efficiency; (b) tumor weight. (n = 4, mean ± s.d., **P < 0.01, ***P < 0.001).

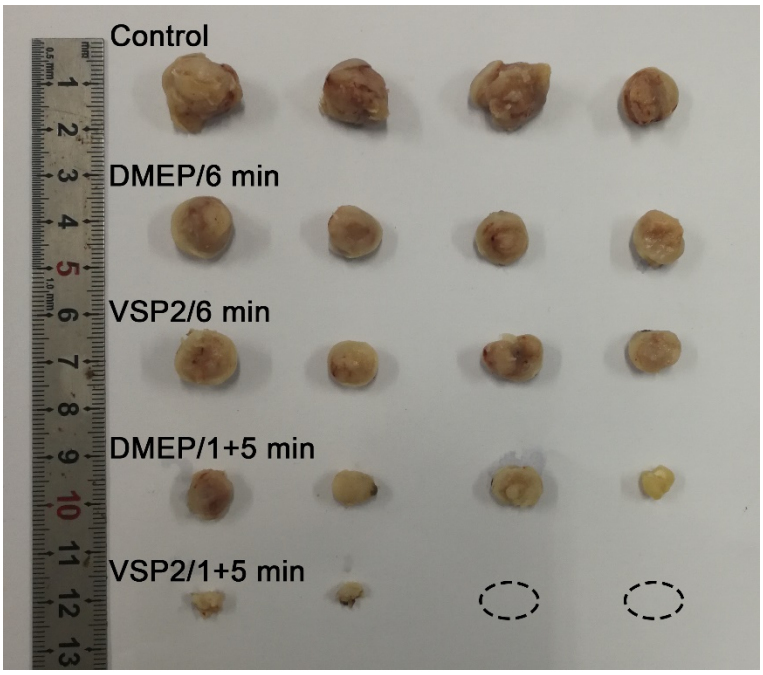


Figure S34. Images of the tumors in different groups after 21-days PDT treatment of **VSP2** and **DMEP** nanoparticles.

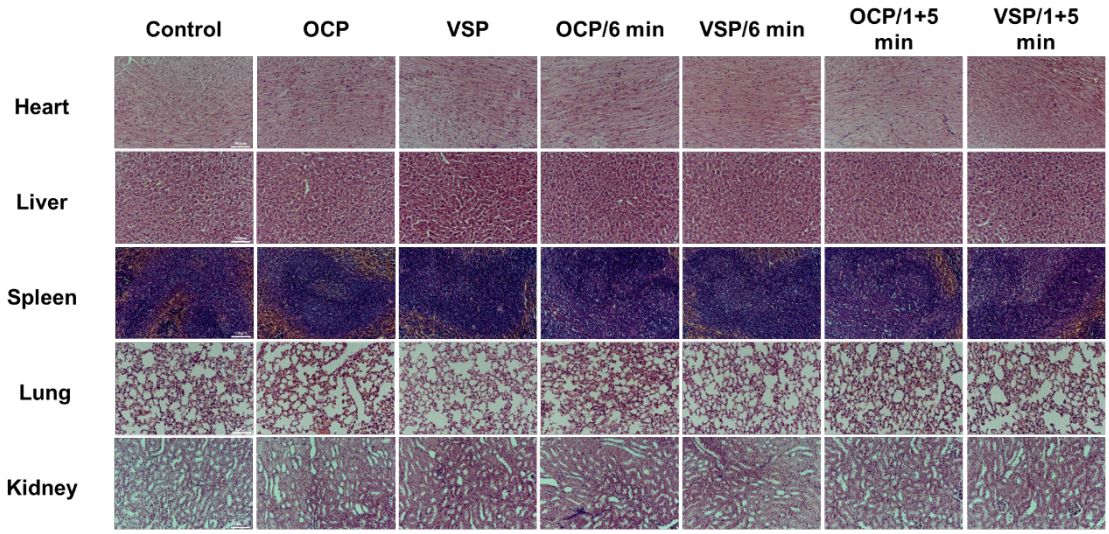


Figure S35. H&E staining images of major organs （400 X, scale bar: 100 nm）.