Supporting Information

Supramolecular Nanoplatform for Imaging-Guided Phototherapies via Hypoxia Tumour Microenvironment Remodeling

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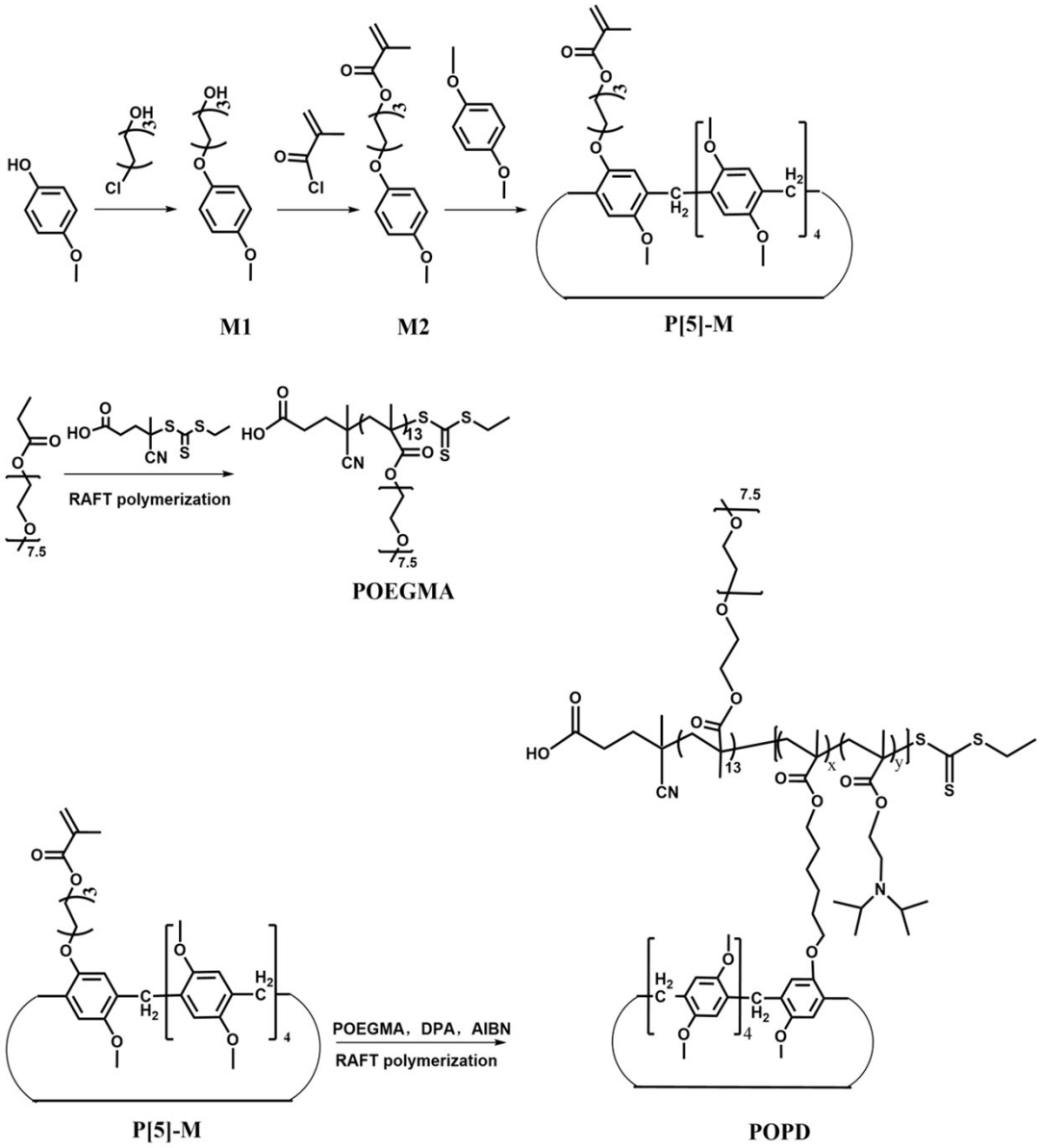
Experimental Section

Materials

4-Methoxyphenol, 6-chloro-n-hexanol, anhydrous potassium carbonate, methacrylic acid chloride, triethylamine TEA, 1,4-dimethoxybenzene, diisopropyl aminoethyl methacrylate (DPA), and azobisisobutyronitrile (AIBN) were all purchased from Aladdin Reagent Co., Ltd. 2,3,3-Trimethyl-3H indole, 2-iodoethanol, acetonitrile, acetone, ether, *N,N*-dimethylformamide (DMF), dichloromethane (DCM), phosphorus oxychloride, cyclohexanone, *n*-butanol, toluene, oligoethylene glycol methacrylate (OEGMA), methanol, 5-bromovaleronitrile, camptothecin (CPT), 6-bromohexanoic acid, 2,4,6-trichlorobenzoyl chloride, 4-dimethylaminopyridine (DMAP) and pyridine were purchased from Titan Technology Co., Ltd.

Methods

1. Synthetic route of POPD



Scheme S1. Synthetic procedure of POPD.

Synthesis of M1: Add 4-methoxy phenol (1.24 g, 10 mmol) into a round-bottom flask, dissolve it with 10 mL DMF, and next add anhydrous potassium carbonate (1.38 g, 10 mmol) under a nitrogen atmosphere, after it is completely dissolved and add 6-chloro-n-hexanol (2.73 g, 20 mmol), then react at 80 ^{o}C for 12 h, remove the solvent, dissolve

the solid with 50 mL ethyl acetate and extract potassium carbonate with water. After removing the ethyl acetate, the product was purified and eluted by silica gel. (ethyl acetate: petroleum ether = 1:3, v/v), and 1 g of white solid is obtained after drying (yield: 44.6%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm: 6.86 (s, 4H), 3.95 (q, 2H), 3.80 (s, 3H), 3.69 (t, 2H), 1.86-1.74 (m, 2H), 1.71-1.57 (m, 2H), 1.57-1.40 (m, 4H).

Synthesis of M2: Add M1 (1.79 g, 8 mmol), triethylamine (1.0 g, 10 mmol) and anhydrous dichloromethane (30 mL) into a 50 mL flask placed in an ice bath. After the solids are dissolved, add 5.0 mL anhydrous dichloromethane which contains methacryloyl chloride (1.67 g, 16 mmol) slowly to the flask and reacted at room temperature for 24 hours. After removing the solvent, the crude product was re-dissolved in ethyl acetate, the organic phase was washed thoroughly with saturated brine, and then use anhydrous sodium sulfate to remove the water in the organic phase and dried to obtain 2.28 g yellow solid product (yield: 97.5%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm: 6.83 (s, 4H), 6.24 (d, 1H), 5.84 (d, 1H), 3.88 (t, 2H), 3.74 (s, 3H), 3.52 (t, 2H), 1.98 (d, 3H), 1.76 (m, 2H), 1.67 (d, 2H), 1.47 (t, 2H).

Synthesis of P[5]-M: Add M2 (0.2922 g, 1 mmol) 1,4-dimethoxybenzene (0.6905 g, 5 mmol) and paraformaldehyde (0.1518 g, 5 mmol) into a 100 mL flask containing anhydrous dichloromethane (50 mL), stirring 15 minutes under a nitrogen atmosphere. After all, the solids are dissolved, add boron trifluoride diethyl etherate (0.64 mL, 5 mmol). then stir for three hours at room temperature. After the reaction was completed,

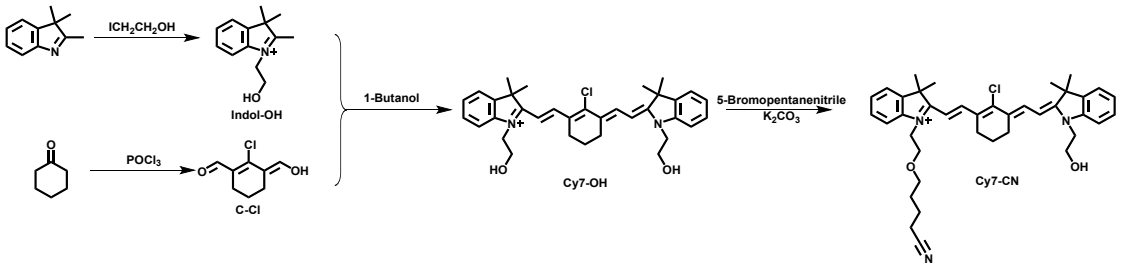
50 mL of methanol was added to terminate the reaction. Then collect solid after filtration, the filter cake was dissolved in 15 mL of dichloromethane, and then added to 200 mL of petroleum ether to get precipitate. After filtrating and drying, 0.75 g of white solid is obtained (yield: 82.1%). ^{1}H NMR (400 MHz, CDCl3): δ ppm: 6.65 (s, 10H), 6.25 (s, 1H), 6.08 (s, 1H), 4.12 (t, 2H), 3.88 (s, 10H), 3.69 (t, 27H), 3.48 (t, 2H), 1.92 (s, 3H), 1.72 (d, 2H), 1.57 (s, 2H), 1.43 (s, 4H).

Synthesis of POEGMA: Dissolve OEGMA (2.0 g, 4.2 mmol), RAFT reagent (42.08 mg 0.16 mmol) and AIBN (5.3 mg 0.032 mmol) with a small amount of 1,4-dioxane, and then add them to the polymerization tube, where the total amount of 1,4-dioxane is 3.0 mL. The polymerization tube was sealed after removing oxygen and moisture, and after polymerization at 75 °C for 48 hours, the reaction terminates. The product was precipitated in petroleum ether three times to obtain 1.8 g of POEGMA (yield: 90%).

Synthesis of POPD: Dissolve POEGMA (0.5 g, 0.08 mmol), P[5]-M (0.2065 g, 0.2 mmol), diisopropyl aminoethyl methacrylate (DPA) (0.4494 g, 2 mmol) and azobisisobutyronitrile (AIBN) (3 mg, 0.018 mmol) with a small amount of DMSO. After dissolving completely, add to the polymerization tube, where the total amount of DMSO in the polymerization tube is 4 mL. After removing oxygen and moisture, the polymerization tube was sealed, and the reaction was terminated after polymerization at 75 °C for 48 hours. The product was added dropwise to petroleum ether. After separation, the precipitate was dissolved with water, and the insoluble matter was

removed by centrifugation. The supernatant was freeze-dried to obtain 0.25 g of compound 5 (yield: 21.6%).

2. Synthetic route of Cy7-CN



Scheme S2. Synthetic method of Cy7-CN.

Synthesis of Indol-OH: Add 2,3,3-trimethyl-3H indole (1.59 g, 10 mmol) and 2-iodoethanol (1.72 g, 10 mmol) into a Schlenk bottle containing 20 mL of acetonitrile, then mix under a nitrogen atmosphere and heat to 80 °C for 8 hours. After evaporating the acetonitrile to obtain a crude product. The crude product was dissolved with a small amount of acetone, and it was added dropwise to a rapidly stirring ice ether solution for precipitation, and then filter and dry to obtain 2.28 g of pink powder (yield: 69%). ^{1}H NMR (400 MHz, d_6-DMSO): δ ppm: 7.92 (m, 1H), 7.82 (m, 1H), 7.63 (m, 2H), 4.60 (m, 2H), 3.89 (m, 2H), 2.83 (s, 3H), 1.56 (s, 6H).

Synthesis of C-Cl: Add anhydrous DMF (10 mL, 136.5 mmol) and 20 mL anhydrous DCM to a 100 mL three-necked flask, mix well, and place in an ice-water bath. Then put the anhydrous DCM solution containing phosphorus oxychloride (8.75 mL, 57.5 mmol) into the constant pressure dropping funnel, and add it to the reaction flask under the nitrogen atmosphere. After the addition is complete, add cyclohexanone (2.5 g, 25

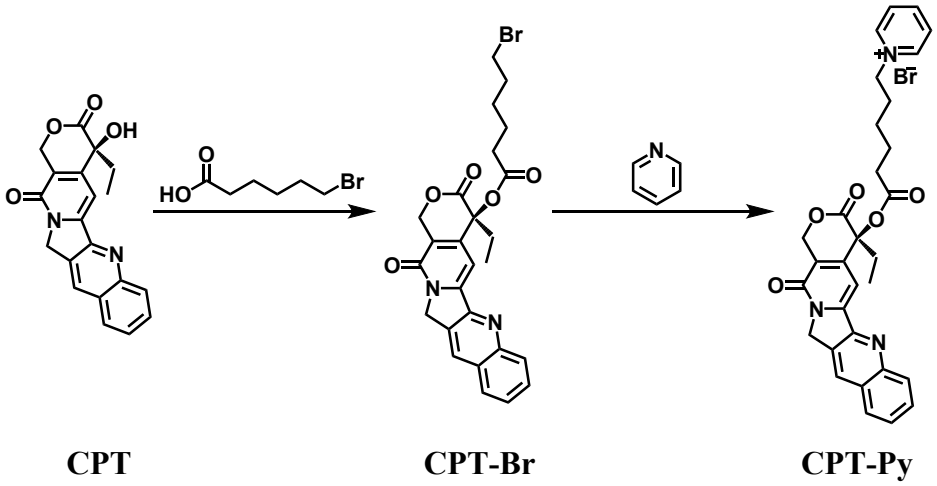
mmol) in a three-necked flask, then heat the solution to 80°C and stir for 6 hours until the reaction is complete. The solution was then poured into ice water and placed overnight at 4 °C. Then the suspension was suction filtered and washed with water several times. After drying, 2.88 g of yellow powder was obtained (yield: 67%).

Synthesis of Cy7-OH: Indol-OH (0.5 g, 1.51 mmol) and C-Cl (0.13 g, 0.755 mmol) were added to a Schlenk bottle containing 10 mL of a mixed solvent of n-butanol and toluene (volume ratio 7:3). then heat to 120 °C and react for 12 hours in the dark. After the solvent was removed, the solid was dissolved with a small amount of DCM, and then it was added dropwise to ice ethyl ether for precipitation. After suction filtration, the crude product was separated and purified by silica gel using DCM/methanol (20:1, v/v). After removing the solvent, get 0.33 g of metal Glossy green powder (yield: 66%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm: 8.25 (t, 2H), 7.39-7.25 (m, 4H), 7.24-7.08 (m, 4H), 6.45 (t, 2H), 4.31(t, 4H), 4.01 (d, 4H), 2.78 (dd, 2H), 1.99-1.86 (m, 2H), 1.67 (s, 12H).

Synthesis of Cy7-CN: Cy7-OH (0.1675 g, 0.25 mmol) and an appropriate amount of anhydrous potassium carbonate were added to a 25 mL flask containing 15 mL of DMF. After stirring for 15 minutes, 5-bromovaleronitrile (0.0041 g, 0.25 mmol) was added under nitrogen atmosphere and the mixture was stirred at 80 °C for 10 hours in the dark. After the reaction was complete, DMF was removed, redissolved in 50 mL of ethyl acetate, and the organic phase was washed several times with deionized water to

remove potassium carbonate. The organic phase was washed with an aqueous pH = 6.0 solution until green. After the removal of ethyl acetate, the crude product was separated by column chromatography with dichloromethane/methanol (20:1, v/v) as the eluent, and the first fraction was collected to give 19 mg of pure Cy7-CN (10% yield). ^{1}H NMR (400 MHz, d_6-DMSO): δ ppm: 8.57 (d, 1H), 8.10 (d, 1H), 7.39-7.25 (m, 8H), 6.96 (d, 1H), 5.91 (d, 1H), 4.64 (t, 4H), 4.55 (t, 2H), 4.16-4.22 (m, 4H), 2.98 (t, 2H), 2.64 (m, 2H), 2.23 (t, 2H), 1.99 (m, 2H), 1.84 (m, 2H), 1.78 (s, 12H), 1,42 (m, 2H).

3.Synthetic route of CPT-Py:



Scheme S3. Synthetic method of CPT-Py.

Synthesis of CPT-Br: Add 6-bromohexanoic acid (0.7760 g, 4 mmol), 2,4,6-trichloro benzoyl chloride (0.9676 g, 4 mmol), triethylamine (0.4048 g, 4 mmol) and DMAP 0.1220 g, 1 mmol) to a round-bottom flask that contains 25 mL dichloromethane, stir to dissolve it, and finally add CPT (0.6962 g, 2 mmol), react at room temperature for 24 hours. After the reaction was completed, the DCM was removed, redissolved with

ethyl acetate, washed three times with water, and finally the organic solvent was removed. After drying, 1.04 g of CPT-Br was obtained (yield: 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm: 8.33 (s, 1H), 8.17-8.14 (d, 1H), 7.89-7.86 (d, 1H), 7.77-7.71 (m, 1H), 7.61-7.56 (m, 1H), 7.24 (s, 1H), 5.65-5.56 (d, 1H), 5.36-5.30 (d, 1H), 5.25-5.20 (m, 2H), 3.35-3.26 (m, 2H), 2.48-2.42 (m, 2H), 2.31-2.19 (m, 1H), 2.12-2.05 (m, 1H), 1.85-1.75 (m, 2H), 1.65-1.57 (m, 2H), 1.48-1.38 (m, 2H), 0.94-0.89 (t, 3H).

Synthesis of CPT-Py: Add CPT-Br (0.1048 g, 0.2 mmol) to a reaction flask containing a mixed solution of pyridine and tetrahydrofuran in equal volumes (5 mL of pyridine and 5 mL of tetrahydrofuran). The reaction was stirred at 70 °C for 12 hours. After the reaction, the suspension was filtered, and the filter cake was washed several times with petroleum ether, and after drying, 0.12 g of pure CPT-Py was obtained (yield: 99.5%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm: 9.03 (s,1H), 8.70-8.69 (d, 2H), 8.19-8.05 (m, 2H), 7.91-7.81 (m, 3H),7.76-7.68 (m, 2H), 7.04 (s, 1H), 5.51 (s, 2H), 5.31 (s, 2H), 4 59-4.51 (m, 2H), 2.58-2.55 (m, 2H), 2.18-2.13 (m, 2H), 1.98-1.88 (m, 2H), 1.66-1.57 (m, 2H), 1.38-1.31 (m, 2H), 0.96-0.85 (t, 3H).

4. Preparation of acid-responsive nanoparticles

The various nanoparticles involved in this article can be prepared by the hydrophilic and hydrophobic self-assembly of polymers. The specific method is described in the preparation of CyCA@POPD nanoparticles. Pillar [5] Aromatic polymer (20 mg) was dissolved in DMF (1.0 mL) solution containing Cy7-CN and

CPT-Py and mixed thoroughly for half an hour until it was combined through the host and guest interactions, and then sucked the solution with a 1 mL syringe and slowly added it to the Atovaquone (dissolve in 4 mL deionized water) and then dialyzed with a dialysis bag with a molecular weight cut-off of 3000 Da. The external dialysate is deionized water, and the dialysate is dialyzed for two days to fully remove the solvent from the dialysis bag. The preparation process of CyA@POPD and Cy7-CN/CPT-Py POPD is similar, just add the corresponding compound in the corresponding solution.

5. Cy7-CN UV-vis absorption standard curve characterization

Accurately weigh the Cy7-CN standard sample, and add DMF solution to dilute Cy7-CN to an appropriate concentration. Then it was diluted gradually and prepared into 0.4875 μg/mL, 0.975 μg/mL, 1.95 μg/mL, 3.9 μg/mL and 7.8 μg/mL sample solutions. Then use DMF as a control reference to measure the UV-vis absorption of Cy7-CN from 300 nm to 900 nm. Taking the mass concentration of Cy7-CN as the independent variable, and taking the UV-vis absorbance of the Cy7-CN standard sample at each concentration at 770 nm as the dependent variable, then drawing the absorbance linear standard curve of Cy7-CN.

6. CPT-Py UV-vis absorption standard curve characterization

Accurately weigh the CPT-Py standard sample of the definite quality, and use deionized water as the solvent to prepare a solution of the appropriate concentration. Then it was diluted gradually and prepared into 3.9 μg/mL, 7.8 μg/mL, 15.6 μg/mL,

31.2 μg/mL and 62.4 μg/mL standard sample solutions. Next use deionized water as a reference to measure the UV-vis absorption from 300 nm to 500 nm. Taking the mass concentration as the independent variable, and the UV-vis absorption of each group of CPT-Py standard samples at 360 nm as the dependent variable, the CPT-Py absorbance linear standard curve was obtained.

7. ATO UV absorption standard curve characterization

Accurately weigh the ATO standard sample, and add DMF solution to dilute ATO to an appropriate concentration. Then it was diluted gradually and prepared into 5.3 μg/mL, 10.6 μg/mL, 15.9 μg/mL, 21.2 μg/mL, 31.8 μg/mL and 42.4 μg/mL sample solutions. Then use DMF as a control reference to measure the UV-vis absorption of ATO from 300 nm to 900 nm. Taking the mass concentration of ATO as the independent variable, and taking the UV-vis absorbance of the ATO standard sample at each concentration at 770 nm as the dependent variable, then drawing the absorbance linear standard curve of ATO.

8. Characterization of particle size and acid response behavior before and after polymer loading

The particle size of the nanoparticles can be measured by laser dynamic scattering scanning technology. In order to test the particle size of the nanoparticles before and after loading the drug, and to compare the particle size changes before and after the acid response, the POPD nanoparticles without guest molecules were dispersed in the PBS

buffer with pH = 7.4, the drug-loaded CyCA@POPD nanoparticles were dispersed in a PBS buffer with pH = 5.5, pH = 6.5 and pH = 7.4, and their particle size was measured after standing for a period of time.

9. In vitro cell culture

The 4T1 cells were cultured at 37℃ with 5% CO_2 in culture flasks with dulbecco's modified eagle medium (DMEM) supplemented with 1% penicillin-streptomycin and 10% fetal bovine serum.

10. Cell uptake experiment

Place 4T1 cells in a glass dish containing 2 mL of culture medium and incubate at 37 °C for 24 hours. Then the original medium was replaced with a new medium that contains samples of each group, the concentration was 10%, and continued incubating at 37 °C for 24 hours. After the incubation, the cells were washed with PBS 3 times. Then, the cells were fixed with 4% paraformaldehyde for 30 minutes. Subsequently, the cells were washed several times to ensure that the excess paraformaldehyde was cleaned, and add 4',6-diamidino-2-phenylindole (DAPI) to the culture dish to stain the nuclei. Finally, wash it and use a confocal microscope to image the 4T1 cells in the culture dish.

11. Detection of ROS generation at different pH conditions

For the sake of investigating the ROS generation of CyCA@POPD assemblies and

other samples in different pH conditions, DPBF was used as a ROS detector by using a UV-vis spectrophotometer. The mixture solution with pH = 7.4 and pH = 5.5 of DPBF (10 μL, 5 mg/mL in DMSO) and CyCA@POPD assemblies or other samples was upon laser irradiation with an 808 nm laser at a power density of 500 mW/cm^2. With light irradiation, the ROS change of CyCA@POPD assemblies could be presented by measuring the UV absorption curve of the DPBF solution at 430 nm.

12. Photothermal performance in vitro

To investigate the photothermal effect of CyCA@POPD assemblies and other samples, the aqueous PBS solution with pH = 7.4 or pH = 5.5 of CyCA@POPD assemblies (1 mL) and other samples (1 mL) was added into a 2 mL centrifuge tube. After that, the centrifuge tube was continuously subjected to 808 mn laser for 5 min. The solution temperature was monitored ad recorded every 30 seconds by thermometer and Thermal imager.

Additionally, the photothermal conversion efficiency (η) was calculated according to the following equation which was from previous reports:

$$\eta_T = \frac{hs(T_{max} - T_{sur}) - Q_{dis}}{I(1 - 10^{-A})}$$

$$hs = \frac{m \cdot c}{\tau_s}$$

$$t = -\tau_s ln(\frac{T - T_{sur}}{T_{max} - T_{sur}})$$

Where h represents the heat transfer coefficient, s is the surface area of the sample container, T_{max} is the maximum steady state temperature of the solution and T_{sur} represents the room temperature of the surrounding. Q_{dis} is the heat input by the solvent

and container without samples in the same condition. *I* is the power density of the laser and *A* is the absorption value of samples at 808 nm. *C* is the specific heat capacity of the solvent (C_{water} = 4.2 J/(g·°C)), m is the mass of the solution, and τ_s is the associated time constant.

13. Detection of intracellular ROS

In order to figure out the level of ROS produced by CyCA@POPD assemblies in cells, The cell culture method is the same as in the cell uptake experiment. The difference is that after the culture is completed, add the sample and incubate for 24 hours, then add DCFH-DA (5 μM), incubate for 30 minutes, and irradiated with 808 nm laser (0.2 W/cm^2) for 5 minutes, then the ROS production in the cells of each group of samples was recorded by a confocal microscope. In this intracellular ROS detection, the following three experimental groups are set for comparison: (1) PBS group; (2) Cy@POPD group; (3) CyCA@POPD group.

14. In vitro dark toxicity test

Add 4T1 cells to a 96-well plate. Each well contains approximately 5000 cells and 200 μL of DMEM. After incubating for 24 hours, replace the DMEM with the medium containing the sample (the sample concentration is 10%). After incubating for another 24 hours, wash the well plate with PBS and replace it with DMEM containing 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) MTT (5 mg/mL, 10%). After incubating for 4 hours, use 150 μL Dimethyl sulfoxide (DMSO) to replace the

medium, and then record the absorbance with a microplate reader. The above operation is the dark toxicity under normal oxygen conditions. The dark toxicity under hypoxic conditions can be cultured by putting the 96-well plate in a sealed bag.

15. *In vitro* phototoxicity test

Add 4T1 cells to a 96-well plate. Each well contains about 5000 cells and 200 μL of DMEM. After incubating for 24 hours, replace the DMEM with the medium containing the sample (the sample concentration is 10%). Incubate for another 24 hours and irradiate with an 808 nm laser for 10 minutes (0.5 W/cm^2). After incubating for another 24 hours, wash the well plate with PBS and replace it with DMEM containing MTT (5 mg/mL 10%). After incubating for 4 hours, use 150 μL DMSO instead of the culture medium, and then use a microplate reader to record the absorbance. The operation is the phototoxicity under normal oxygen conditions, and the phototoxicity under hypoxic conditions can be cultured by putting the 96-well plate in a sealed bag.

16. *In vivo* imaging in mice

All animal experimental procedures were carried out in accordance with Chinese legislation on the Use and Care of Research Animals (Document No. 55, 2001), and institutional guidelines for the Care and Use of laboratory animals established by the East China University of Science and Technology Animal Studies Committee.

In order to test whether the sample can be targeted at the lesion through the EPR effect, When the tumor volume of the mouse reaches 100 mm^3, CyCA@POPD

nanoparticles are delivered by tail vein injection (200 μL). After anesthetizing the mice, they were imaged with the mouse imaging system at different time points to observe the distribution of CyCA@POPD in the body.

17. *In vivo* anti-tumor studies

When the size of the solid tumor in the mouse reaches 50-60 mm^3, the mice are subjected to in vivo experiments. Randomly divide all mice into five groups (four mice per group): (1) PBS group, (2) CyCA@POPD group, (3) CyA@POPD + light group, (4) CyC@POPD + light group, (5) CyCA@POPD + light group. On the first day, each group was injected with the corresponding solution through a tail vein injection. In each group, the mice were treated on the first day, and the corresponding solution was injected into the mouse body. Group 3, Group 4, and Group 5 were irradiated with an 808 nm laser. Then, the volume and weight of the solid tumor were measured every other day for a total of fourteen days. In order to evaluate the size of the tumor, the tumor volume was calculated according to the following formula: $0.5\times L\times W^2$ (L: the length of the tumor; W: the width of the tumor), and the relative tumor volume is calculated according to V/V_0 (V_0: the tumor volume on the first day). After the treatment on the 14th day, the mice were dissected and the tumors were removed. The tumors and main organs of the mice were removed, processed and stained, and fixed with 4% paraformaldehyde, then embedded in paraffin blocks for sectioning, stained with hematoxylin and eosin (H&E) for further observation of tissue damage condition.

Figures and Tables

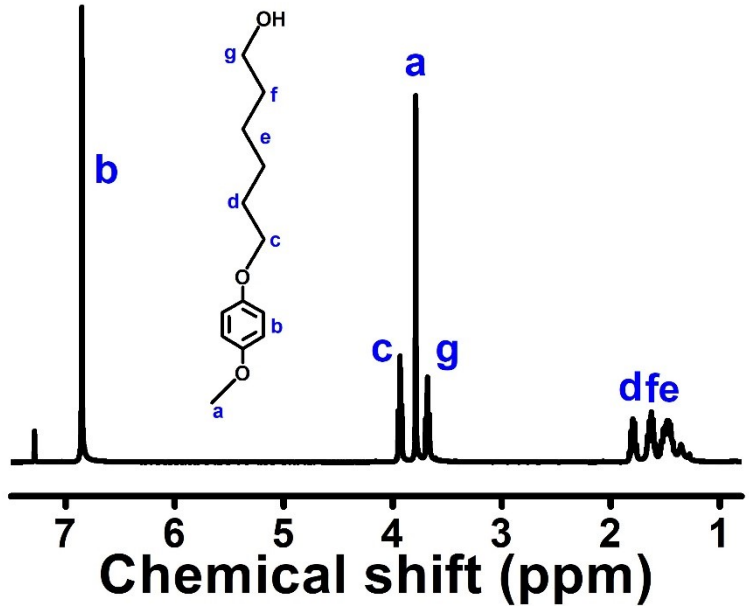


Fig. S1 ^{1}H NMR spectrum of M1 in $CDCl_3$.

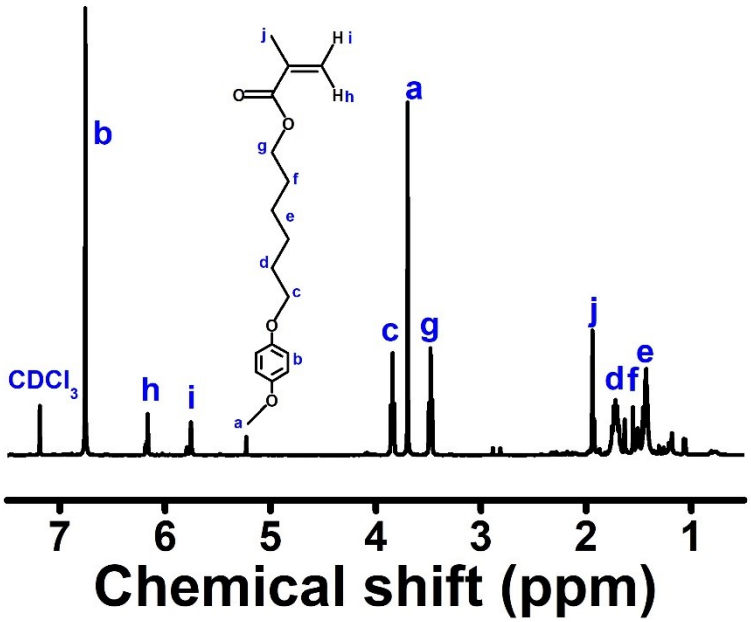


Fig. S2 ^{1}H NMR spectrum of M2 in $CDCl_3$.

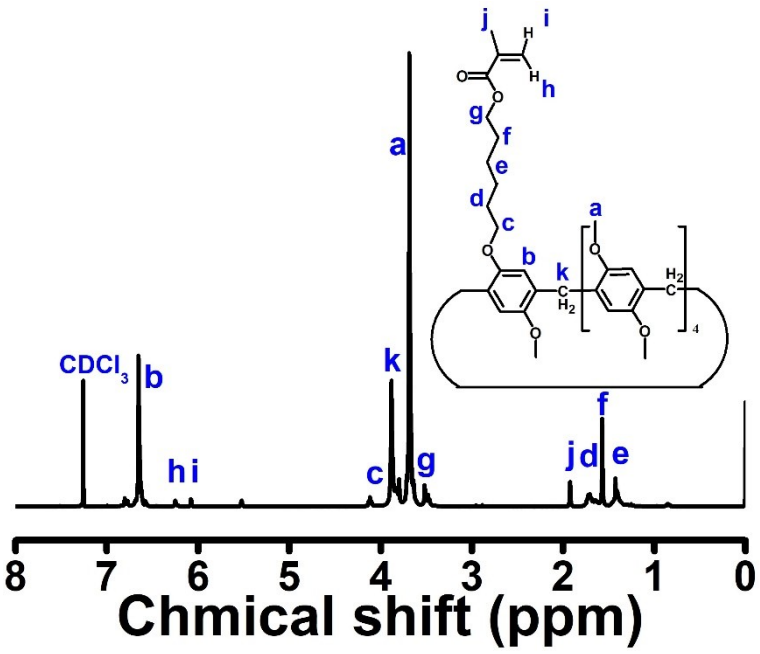


Fig. S3 ^{1}H NMR spectrum of P[5]-M in $CDCl_3$.

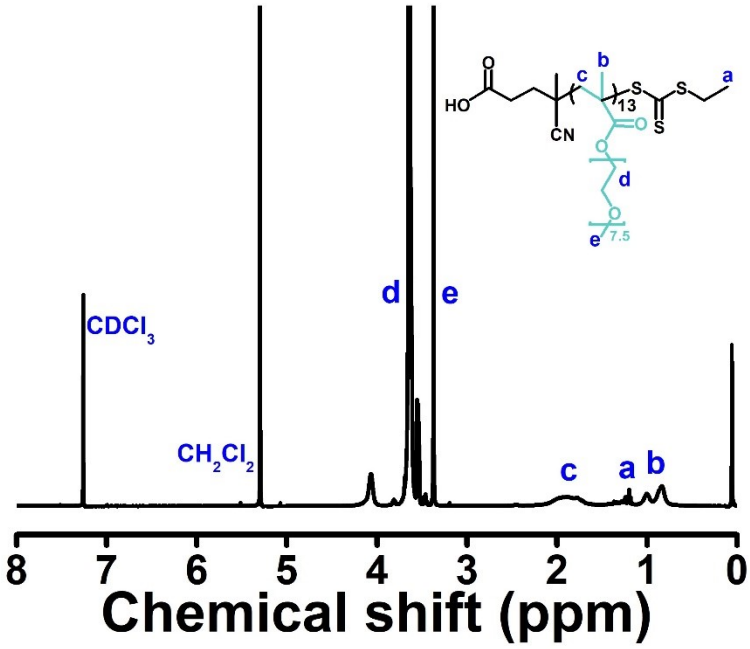


Fig. S4 ^{1}H NMR spectrum of POEGMA in $CDCl_3$.

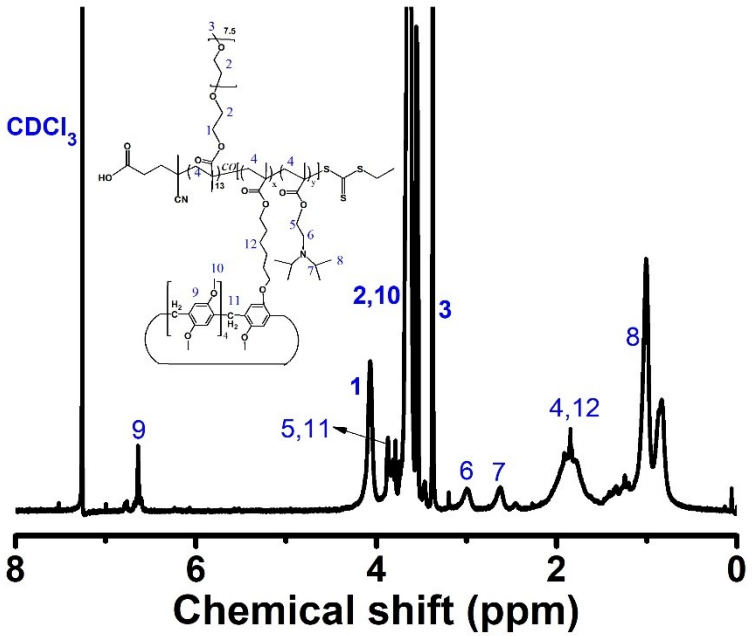


Fig. S5 ^{1}H NMR spectrum of POPD in $CDCl_3$.

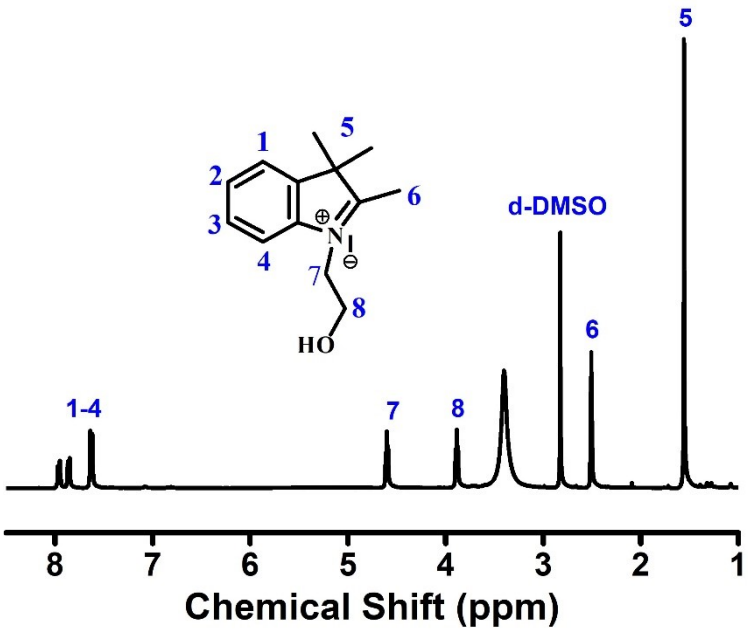


Fig. S6 ^{1}H NMR spectrum of Indol-OH in d_6-DMSO.

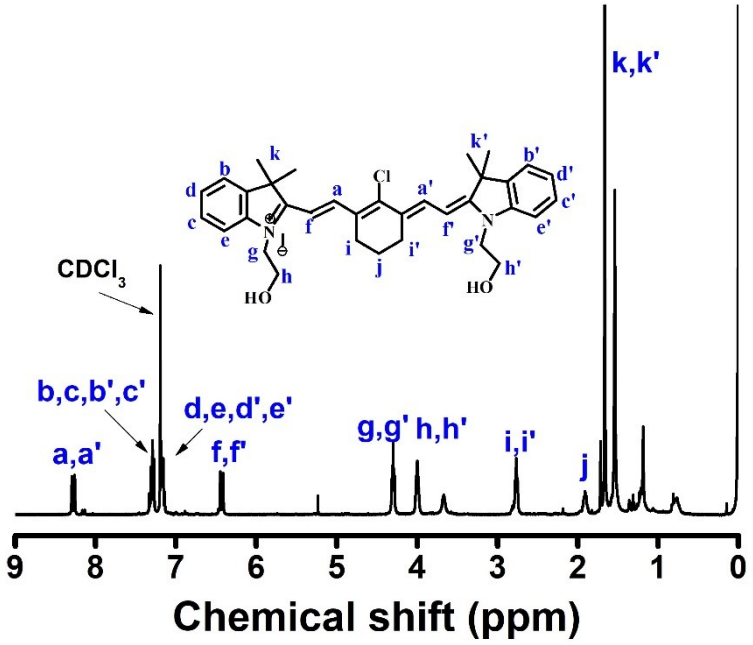


Fig. S7 ^{1}H NMR spectrum of Cy7-OH in $CDCl_3$.

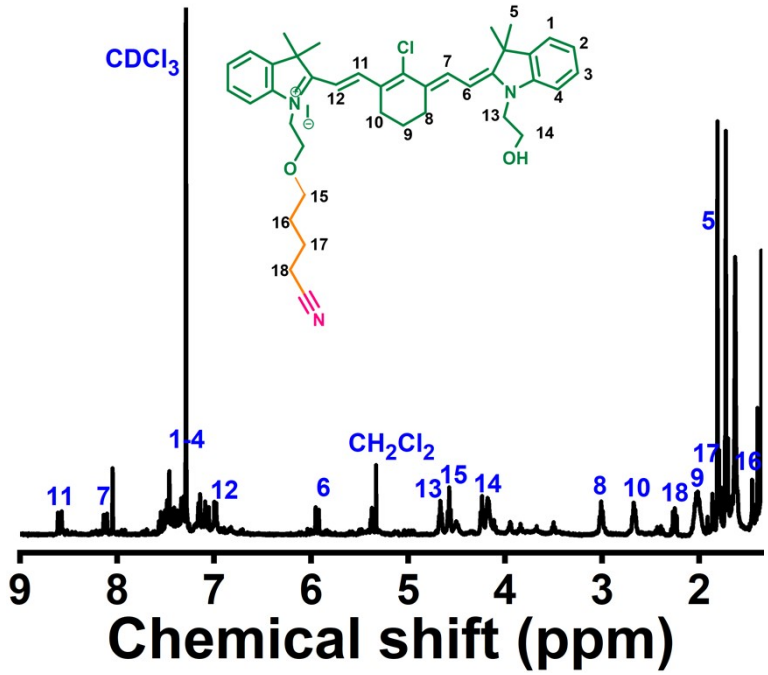


Fig. S8 ^{1}H NMR spectrum of Cy7-CN in $CDCl_3$.

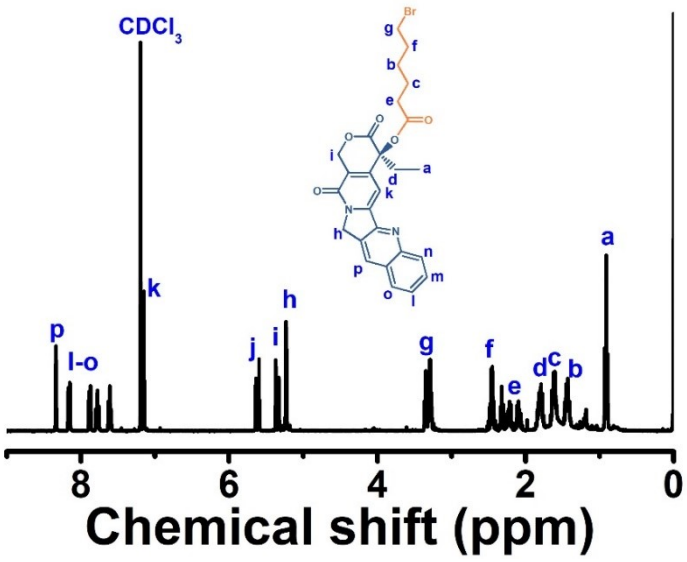


Fig. S9 ^{1}H NMR spectrum of CPT-Br in $CDCl_3$.

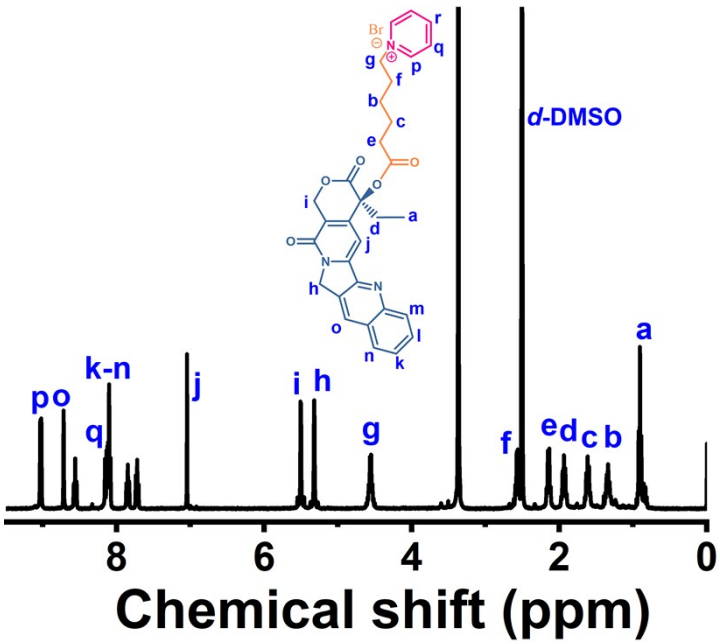


Fig. S10 ^{1}H NMR spectrum of CPT-Py in d_6-DMSO.

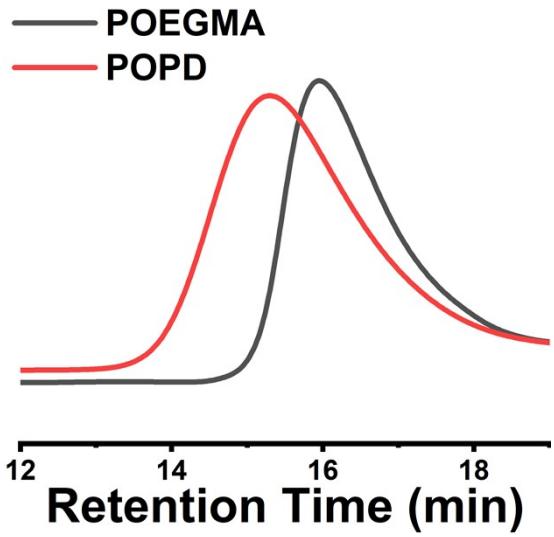


Fig. S11 GPC traces of POEGMA homopolymer and POPD copolymer.

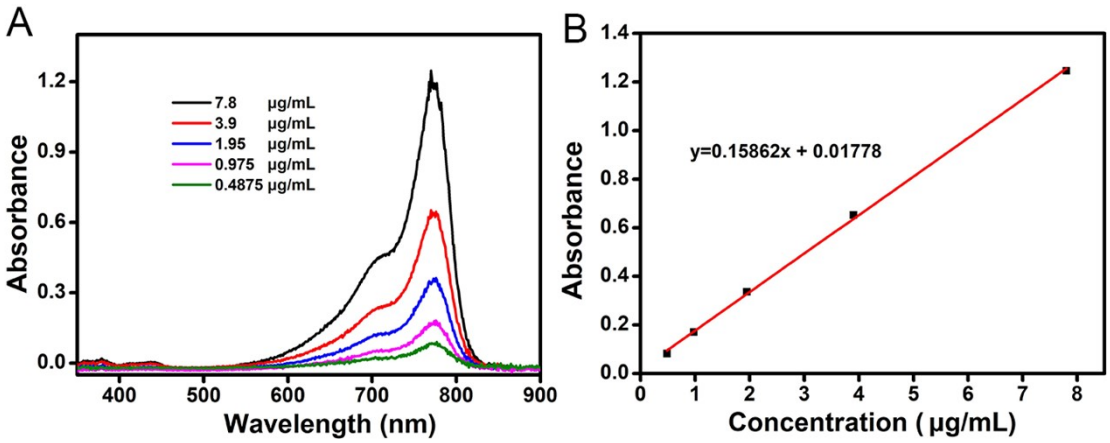


Fig. S12 (A) UV-vis absorption of different concentrations of Cy7-CN in DMF solution. (B) Standard absorption curve of Cy7-CN in DMF.

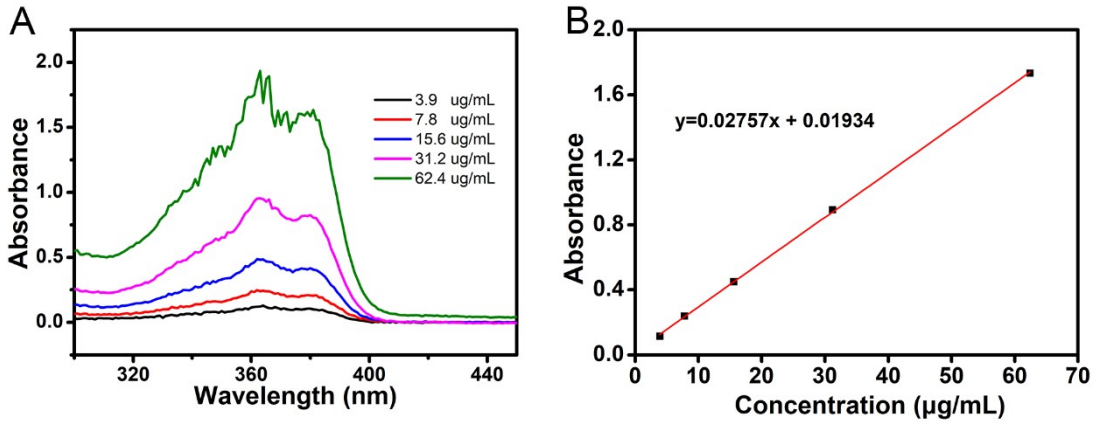


Fig. S13 (A) UV-vis absorption of different concentrations of CPT-Py in DMF solution. (B) Standard absorption curve of CPT-Py in DMF.

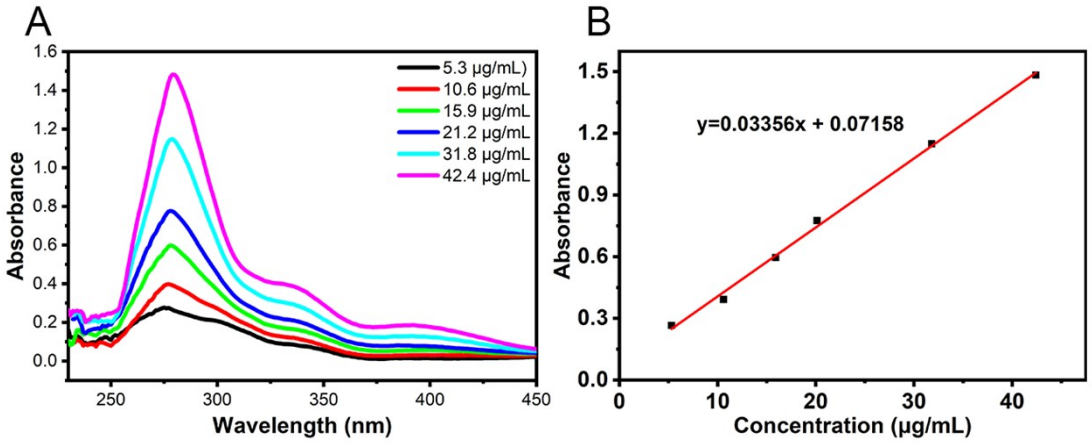


Fig. S14 (A) UV-vis absorption of different concentrations of ATO in DMF solution. (B) Standard absorption curve of ATO in DMF.

Table S1. the LC and EE of Cy7-CN, CPT-Py and ATO in CyCA@POPD nanoparticles

	Cy7-CN	CPT-Py	ATO
LC (%)	4.5	4.2	2.0
EE (%)	39.0	34.4	20.2

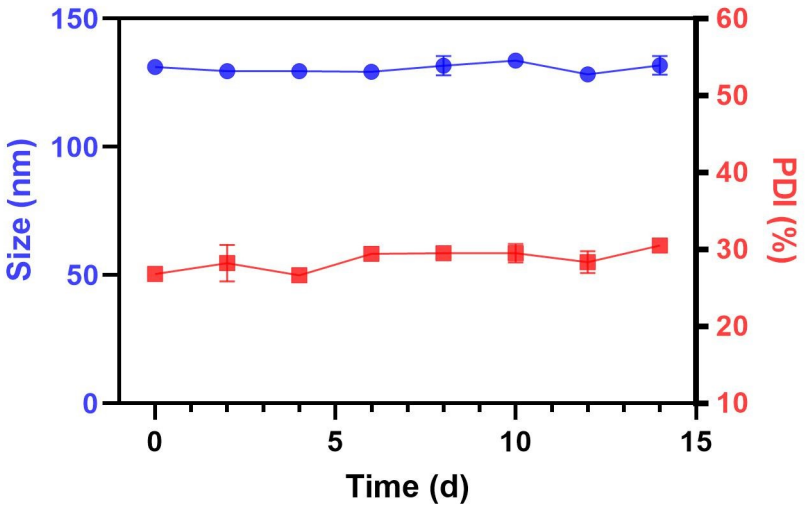


Fig. S15 The physical stability of CyCA@POPD in the mixture of RPMI-1640 Medium and fetal bovine serum. Each data point was expressed as mean standard deviation (n = 3).

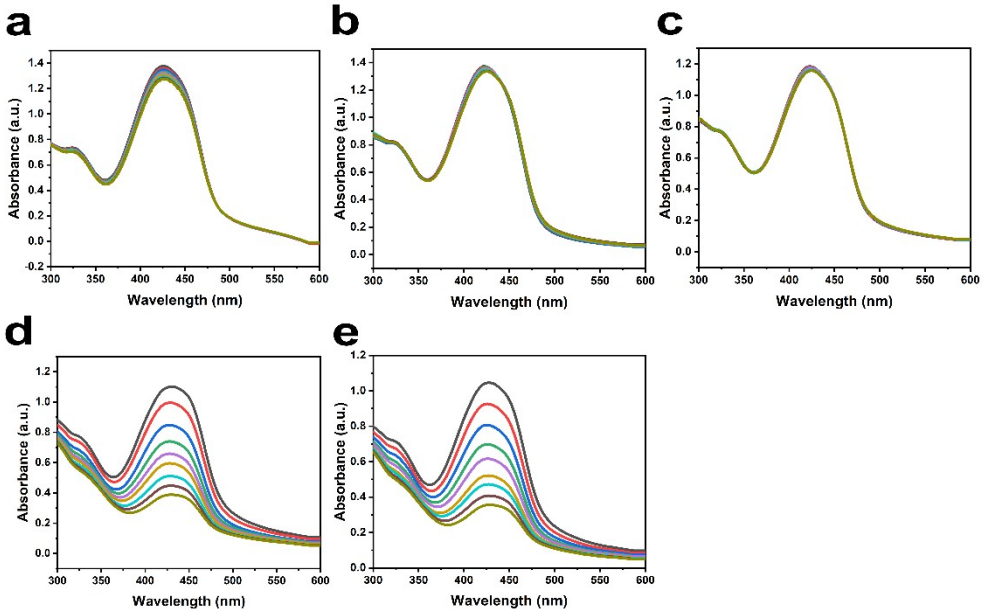


Fig. S16 UV-vis spectra of DPBF with (a) PBS, (b) POPD, (c) C@POPD, (d) Cy @POPD and (e) CyCA@POPD assemblies under light irradiation (808 nm 500 mW/cm^2) for predetermined time point.

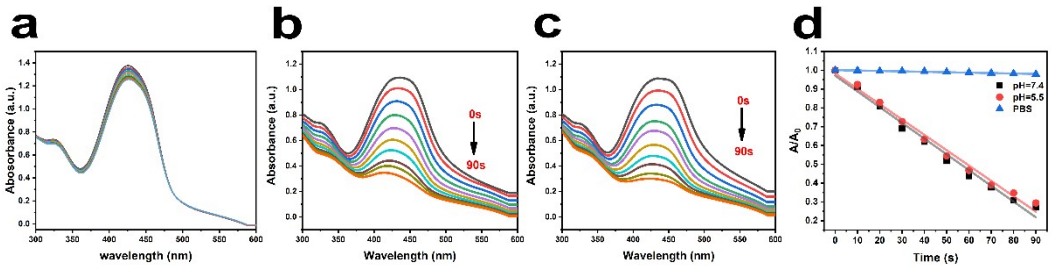


Fig. S17 UV-vis spectra of DPBF with (a) PBS and CyCA@POPD assemblies under light irradiation (808 nm, 500 mW/cm^2) for predetermined time points at (b) pH = 7.4 and (c) pH = (5.5). (d) The maximum absorbance variation at different pH conditions.

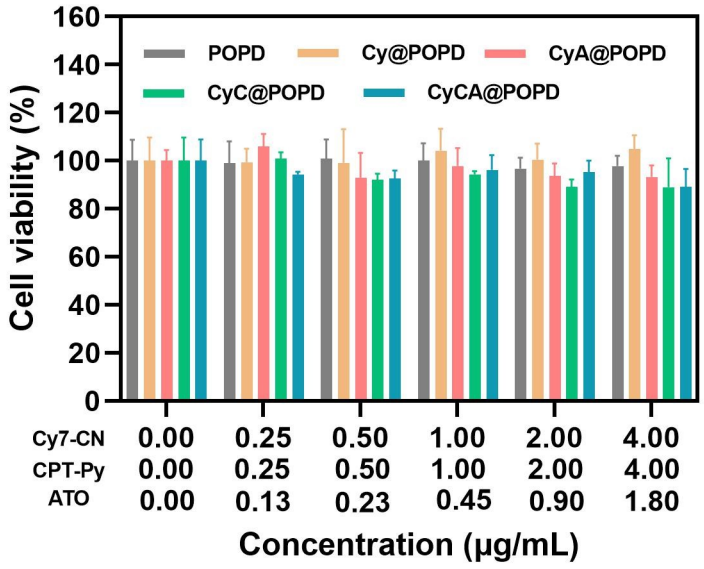


Fig. S18 The cell viability of L929 cells treated by different samples with various concentrations in the dark.

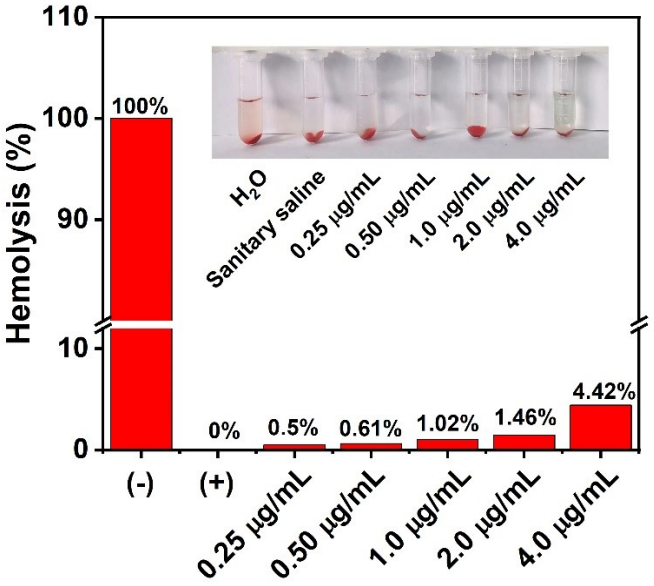


Fig. S19 Hemolysis of CyCA@POPD nanoparticles (the concentration on the horizontal axis refers to the concentration of Cy7-CN in the nanoparticles).

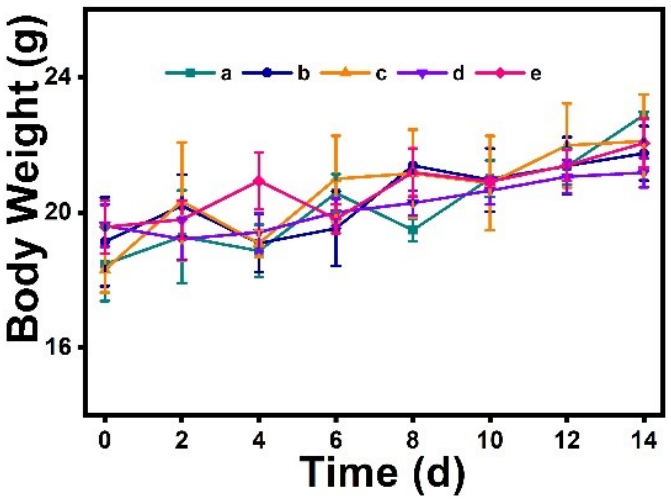


Fig. S20 Body weight variation of the mice after receiving different treatments.

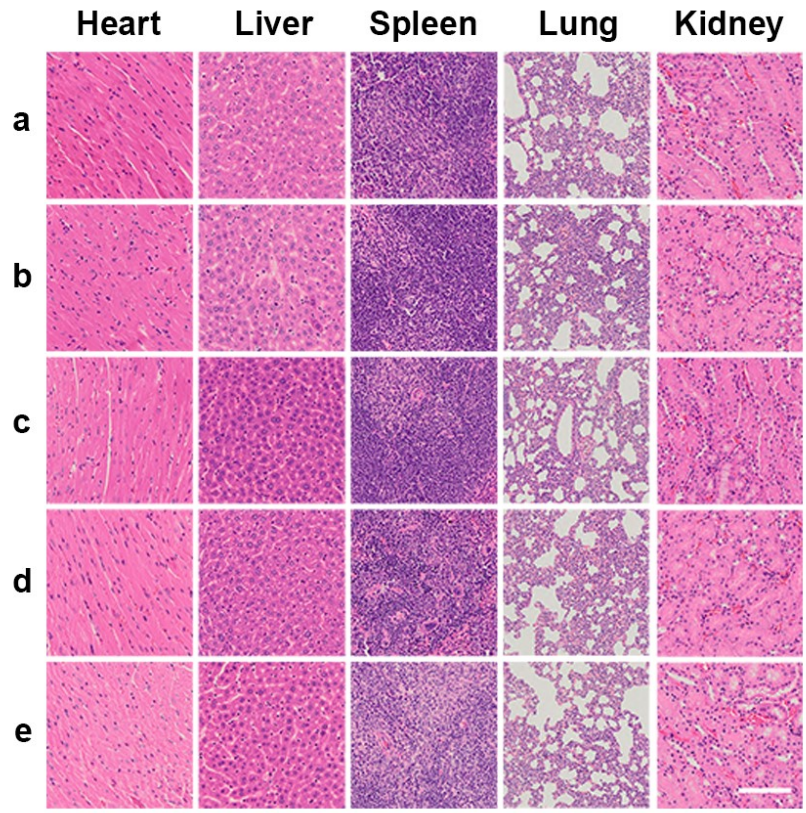


Fig. S21 H&E staining images of major organs of different treatment groups on the 14th day. Scale bar 200 μm.