# Supplementary Data

## 1. Supplementary Methods

*Materials:* The β-cyclodextrin (β-CD) was kindly gifted by International Specialty Products (ISP) Inc. (NJ., USA). N,N-diisopropylethylenediamine (DPA) was supplied by TCI (Shanghai) Development Co. Ltd. (Shanghai, China). The mPEG-COOH (Mw 5000) was purchased from Beijing Jenkem Technology Co. Ltd (Beijing, China). D-luciferin was provided by Perkin-Elmer (MA, USA). Succinobucol (SCB, purity 99.2%) was derived from probucol as previously described methods. Matrigel$^{TM}$ matrix gel was supplied by BD bioscience (San Jose, USA). Primary monoantibody against VCAM-1 (Ab174279, AB19569) was purchased from Abcam® (Cambridge, UK). Hoechst 33342, $DiIC_{18}(3)$ (DiI) and secondary antibody were purchased from Beyotime Institute of Biotechnology (Jiangsu, China). Adamantane methylamine, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI), N-hydroxysuccinimide (NHS), nile red and indocyanine green (ICG) were supplied by J&K scientific Co. Ltd (Shanghai, China).Other chemicals and reagents were of analytic grade.

The metastatic 4T1 cells were supplied by Shanghai Cell Bank, Chinese Academy of Sciences (CAS), while the 4T1-luc cells with stable expression of luciferase were purchased from Keyuandi Biotech Co. Ltd (Shanghai, China).Cells were cultured in RPMI 1640 containing 10% FBS, 2.5 g/L glucose, 0.11 g/L Sodium Pyruvate, 100 U/mL penicillin G sodium and 100 μg/mL streptomycin sulfate (Invitrogen, USA).Cells were incubated at 37 °C in a humidified and 5% $CO_2$ incubator.

The monocyte/macrophage RAW 264.7 cells were provided by Shanghai Cell Bank, CAS. Cells were cultured in Dulbecco's modified Eagle's medium (DMEM) 10% fetal bovine serum (FBS), 100 U/mL penicillin G sodium and 100 μg/mL streptomycin sulfate (Invitrogen, USA). Cells were kept at 37 °C in a humidified and 5% $CO_2$ incubator.

BALB/c nude mice (18～22g, ♀) were used to develop the lung metastatic breast cancer model, which was induced by injection of 4T1-luc cells via tail vein. Animals were provided by the Shanghai Laboratory Animal Center, CAS, and kept under the animal care facility for at least 5 day prior to the experiments. The in vivo experimental protocols were approved by the Institutional Animal Care and Use Committee (IACUC) of Shanghai Institute of Materia Medica, CAS.

*Synthesis of βCD-DPA*: Prior to the reaction, β-CD was dried under vacuum at 110 °C for 12 h to remove the water content. The synthesis processes of βCD-DPA were showed in Figure S1.The β-CD-I was synthesized as previously described method. In brief, iodine (20.25g) was added to a solution of tripenylphosphine (20g, Ph3P) in dry DMF (80 mL) in 15 min with the temperature rising from room temperature to 50 °C. Then, 5.8 g of dry β-CD was added to the red solution with the temperature rising from 50 °C to 80 °C under stirring, and the reaction was continued for further 24 h. At the end, the reaction solution was concentrated under reduced pressure to half of its original volume, and cooled in ice-colded bath. Then, 20 mL of newly prepared sodium methoxide in methanol was added to the solution, stirred at 0 °C for 30 min, and added to 500 mL of ice-colded methanol to collect the precipitate by filtration. The resulted precipitate was rinsed with methanol by Soxhlet extraction and dried under vacuum to obtain the product of β-CD-I.

Then, for the synthesis of βCD-DPA, 3.5 mL of DPA and 2.5 mL of triethylamine (TEA) were dissolved in anhydrous DMF solution. Then, 1.0 g of β-CD-I was dissolved in 15 mL of anhydrous DMF, dropped into the solution of DPA and TEA at room temperature, and stirred at 60 °C for 48 h. The reaction solution was mixed with 200 mL of double-distilled water under agitation. The precipitate was collected by centrifugation, and purified by extensive dialysis against double-distilled water (MWCO, 3500). The final product of βCD-DPA was

lyophilized and characterized by 1H-NMR spectroscopy. The measured results indicated that 6 arms of DPA were conjugated to the β-CD molecules (Figure S3).

*Synthesis of mPEG-Ad*: The mPEG-Ad was synthesized according to the previously described method. In brief, mPEG-COOH (5.0 g) was dissolved in 10 mL of dimethylacetamide (DMA), and mixed with 0.955g of EDCI and 0.575 g of NHS in 3 mL of DMA, and reacted at room temperature for 2 h. Then, 0.7 mL of adamantane methylamine was dropped into the mixed solution, and stirred at room temperature for 24 h. The resulted product was precipitated in 10 volumes of ice-cooled ether, and the precipitation was re-dissolved in methanol and precipitated twice in ice-cooled ether. The product was dried under vacuum overnight and characterized by $^{1}$H-NMR spectroscopy.

*Characterization of the supramolecular polymer of PCD*: The formation of PCD was determined by 2D NOSEY NMR spectroscopy. In brief, βCD-DPA and mPEG-Ad (1:1, molar ratio) was dissolved in 50 μL of methanol-D4 and sonicated for 30 min. Then, the mixed solution was added to 950 μL of $D_2O$ under agitation, and then characterized by 2D NOSEY NMR analysis.

*Histological Evaluation of toxicity of PHN in Mice.* The systemic toxicity of PHN was measured in healthy mice by histological examination. Mice were divided into three groups and respectively treated with saline control and PHN (40 mg/kg of SCB). Mice were intravenously administered every two days for two weeks. At the end point, mice were autopsied and the major organs including heart, liver, spleen, lung and kidney were carefully removed. These tissues were fixed overnight in 10% buffered formaldehyde and embedded in paraffin. Afterwards, samples were sectioned at 4.0 μm, and then stained with the H&E kit for visualization under light microscopy (Leica, Germany).

## 2. Supplementary Results

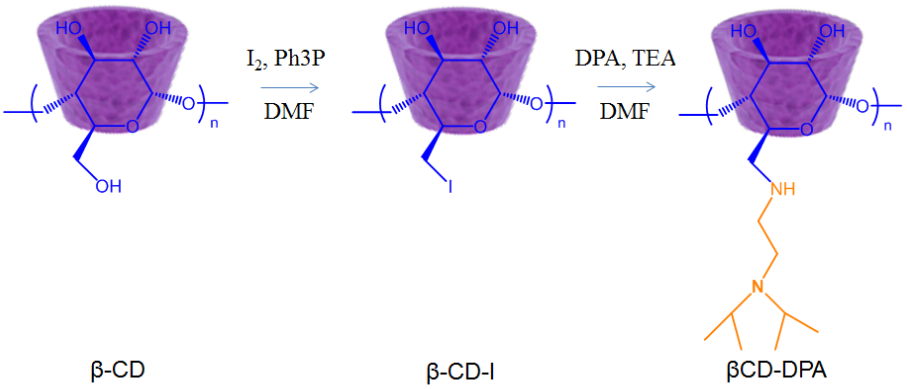



**Figure S1** The synthesis procedure of βCD-DPA.

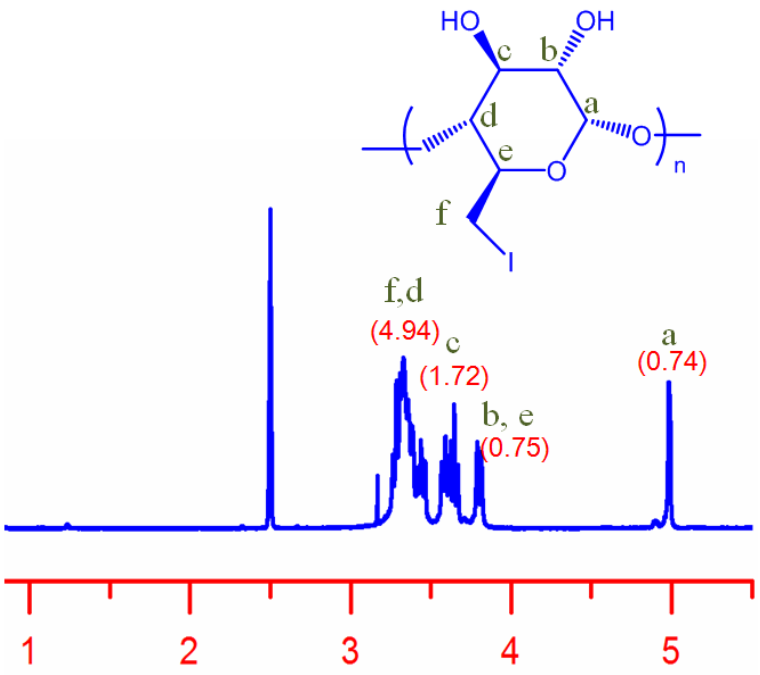
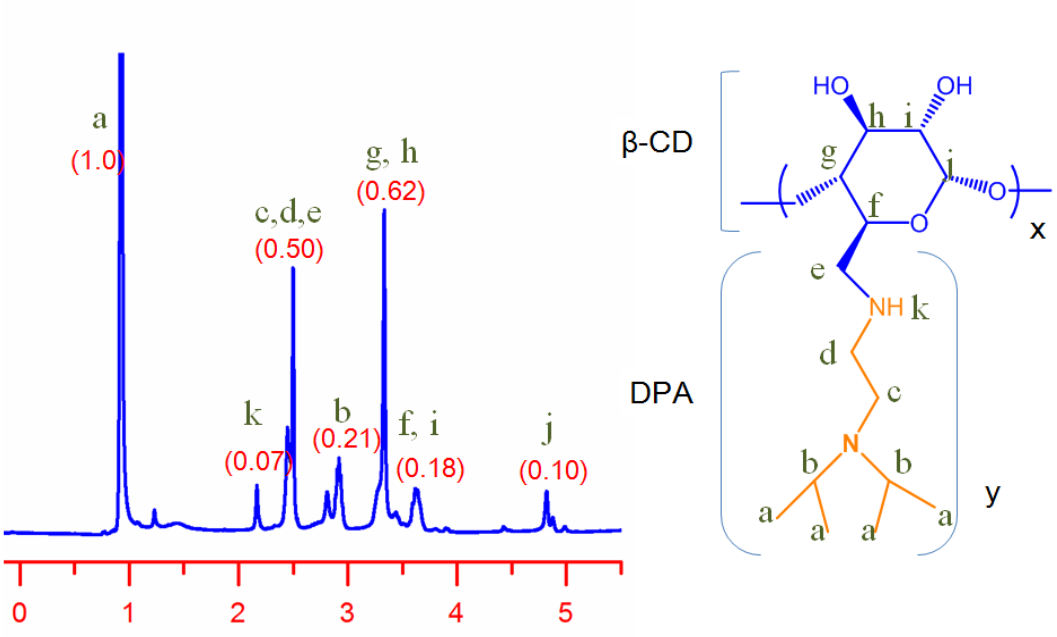



**Figure S2** The typical $^{1}$H-NMR spectrum of β-CD-I




Calculated as
j: x=0.10/7; a: y=1.0/(3*4)=1/12; n1=y/x=(1*7)/(12*0.10)=5.83
f,i: x=0.18/(7*2)=0.09/7; a: y=1.0/(3*4)=1/12; n2=y/x=6.48
n= (n1+n2)/2=6.15≈6

**Figure S3** The typical [1]H-NMR spectrum of β-CD-DPA.

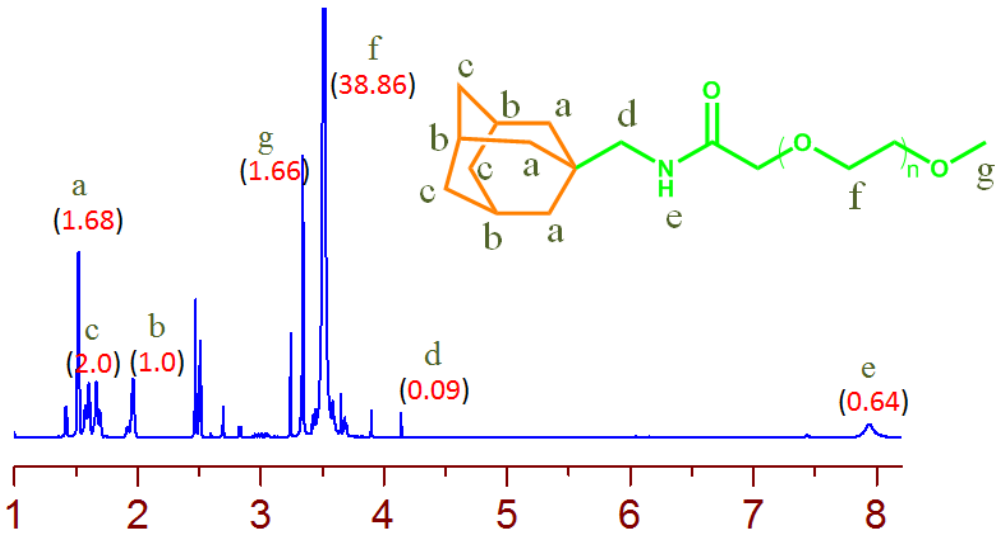



**Figure S4** The typical [1]H-NMR spectrum of mPEG-Ad.

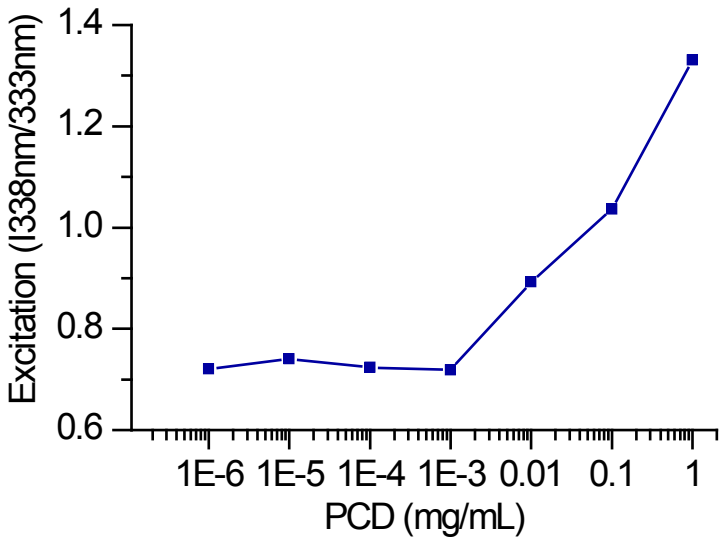



**Figure S5** The determination of the critical aggregation concentration of PCD by pyrene fluorescence measurements.

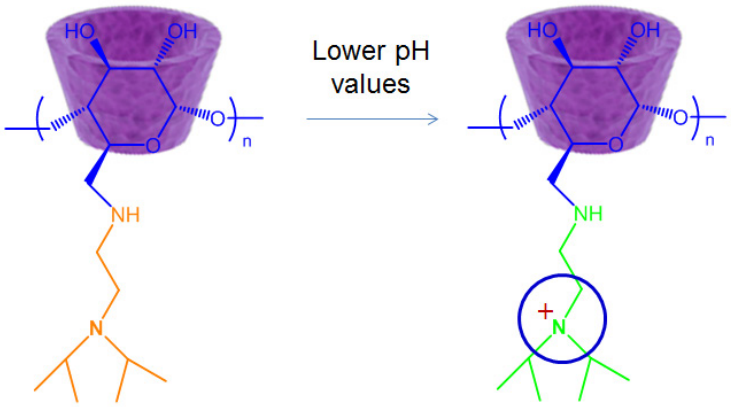



**Figure S6** The conversion of β-CD-DPA from hydrophobic polymer to hydrophilic polymer at intracellular acidic environments.

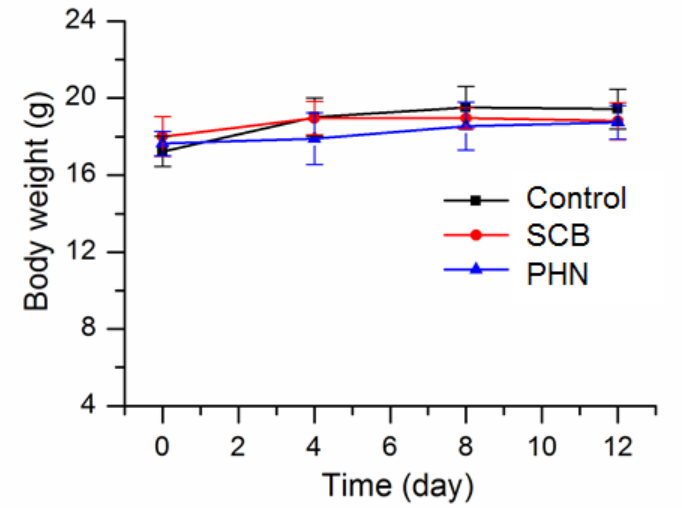



**Figure S7** The body changes of lung metastatic breast cancer model during the treatment of saline, SCB and PHN.

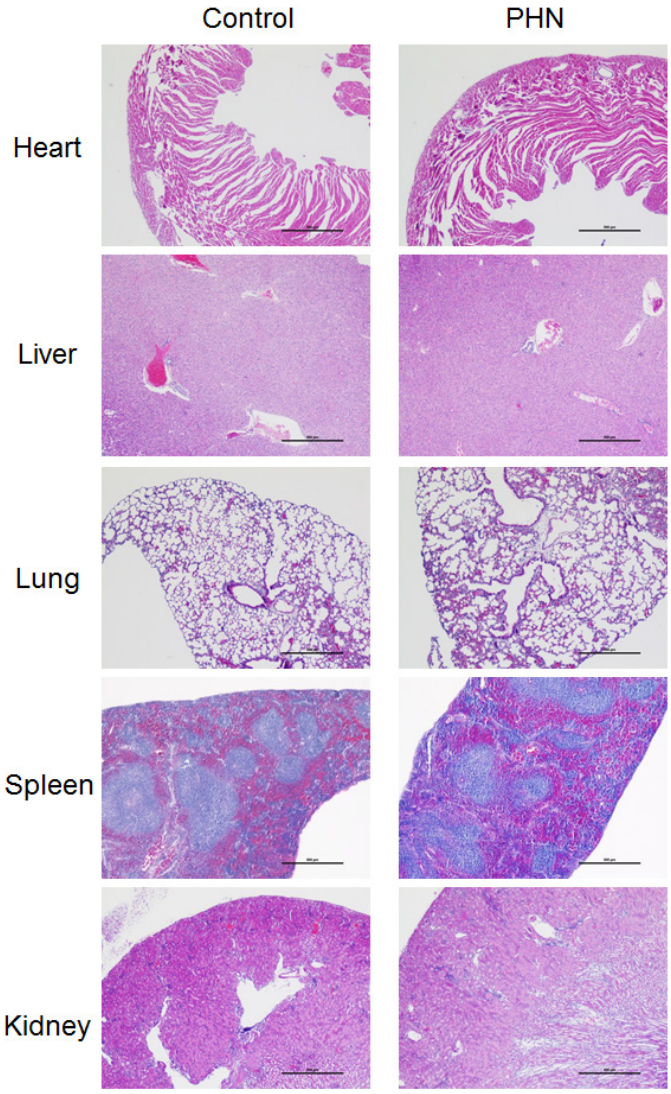



**Figure S8** H&E staining of the major organs (i.e., heart, liver, lung, spleen and kidney) separated from healthy mice injected intravenously with saline and PHN every three days for two weeks, Scale bar = 500 μm.