Supporting Information

CO_2-based amphiphilic polycarbonate micelles enable a reliable and efficient platform for tumor imaging

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Experimental section

General characterizations

^{1}H NMR and COSY NMR spectra were detected on Bruker Avance DMX400 spectrometer using $CDCl_3$, DMSO-d6 or D_2O as solvent at 25 °C with TMS as internal reference (400 MHz). The M_n and PDI of the polymers were performed with a Waters 410 GPC (USA) installing WAT044222 and WAT044234 tandem double columns using polystyrene as standard. CH_2Cl_2 was used as eluent and the flow rate was set at 1.0 mL/min. MALDI-TOF mass spectroscopy was carried out on a Brukerauto flex III mass spectrometer in positive ion mode. DSC measurements were carried out on a PerkinElmer DSC-7 instrument. The glass transition temperature (T_g) and the thermal decomposition (T_d) temperature were measured from the second heating process and PerkinElmer 7 thermo gravimetric analyzer under N_2, respectively. Inductively coupled plasma-optical emission spectrometer (ICP-OES) analysis was detected by PerkinElmer ICP instrument. The longitudinal (T1) relaxation times of the samples were acquired from Brukeravance III 400 MHz nuclear magnetic resonance spectrometer (9.4 T, Germany).

Synthesis of (Salen) Co-TFA catalyst

The (Salen) Co-TFA catalyst was synthesized in high yield (93%) according to our previous report [1].

Synthesis of bis(triphenylphosphine) iminium trifluoroacetic (PPN-TFA)

The PPN-TFA complex was synthesized in high yield (97%) according to our previous report [1].

The synthetic route of PAGEC-*b*-PPC-*b*-PAGEC triblock polycarbonate

The triblock polycarbonate was synthesized according to previous report [2]. In order to synthesize triblock polycarbonate in a controlled manner, we selected sebacic acid as starter. (Salen) Co-TFA/PPN-TFA (0.025 mmol), propylene oxide (1.74 mL, 25 mmoL) and 1.4 mL CH_2Cl_2/toluene (1/1,V/V) with sebacic acid (20 equiv., 101 mg) were transferred into a 15 mL autoclave, and charged to 2 Mpa CO_2 pressure. By reaction of 48 h, allylglycidyl ether was put in after carefully releasethe CO_2 pressure. Then the autoclave was regulated to CO_2 pressure of 2 MPa. After 48 h, the reaction was stoped. The resulting product was dissolved in CH_2Cl_2 and precipitated into methanol, and recycled for 3 times to remove the residual catalyst. The resulting polymers were subjected to vacuum drying under room temperature.

Synthesis of Boc-L-Cysteine

Boc-L-cysteine (70% of yield) was synthesized without column purification according to literature [2].

Thiol-Ene clikc reaction of triblock Polycarbonate with boc-L-Cysteine

0.5 g ABA triblock polymer (M_n = 10200 g moL^{-1}, A:B = 1:1, 2 mmoL alkenes), 8.8 g boc-L-Cysteine (20 equiv.) and 50 mg DMPA (0.1 equiv.) were dissolved in 30 mL THF and was degased for 10 min. After refilling with N_2, the mixture was exposed to

UV light (365 nm) for 2 h. The product was obtained by precipitation into diethyl ether, and then dried by vacuum.

Bocdeprotection of boc-L-Cysteine based APC

0.5 g boc-L-cysteine based APC was dissolved in 1 mL THF, then added 25 mL HCl saturated THF under stirring at room temperature. Until no precipitation was formed, the product was isolated and dissolved in water, then lyophilized.

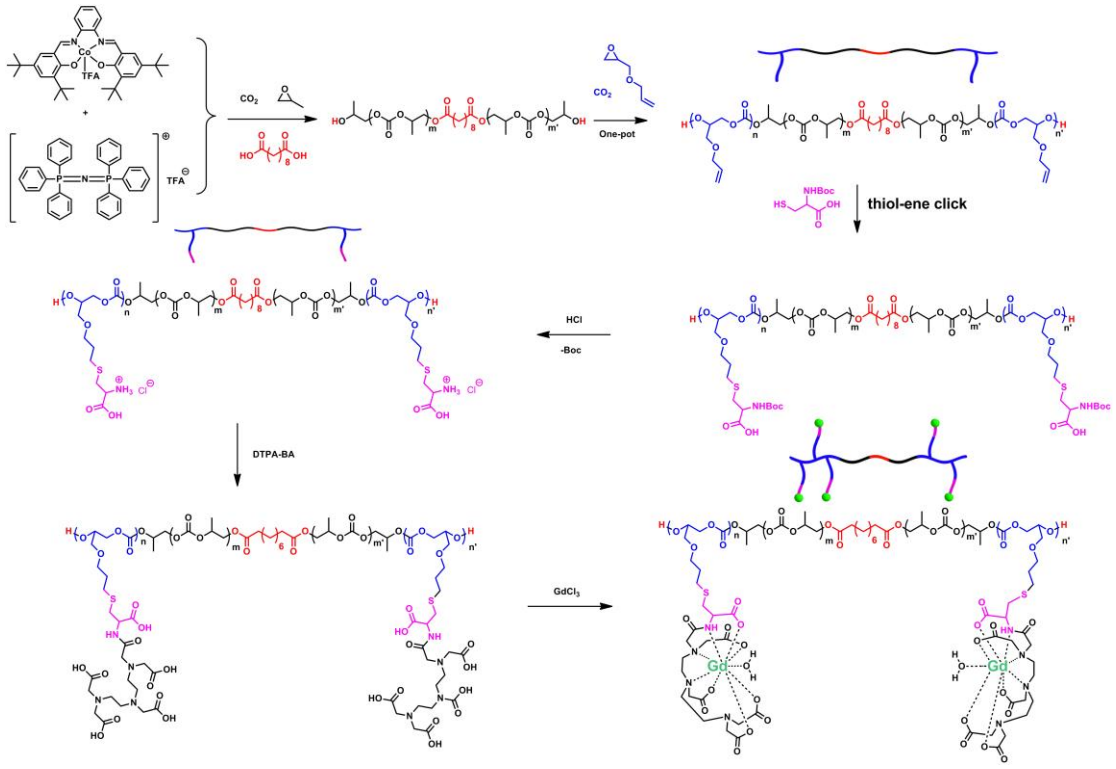

Figure S1. Synthetic procedure of APC-DTPA/Gd conjugate.

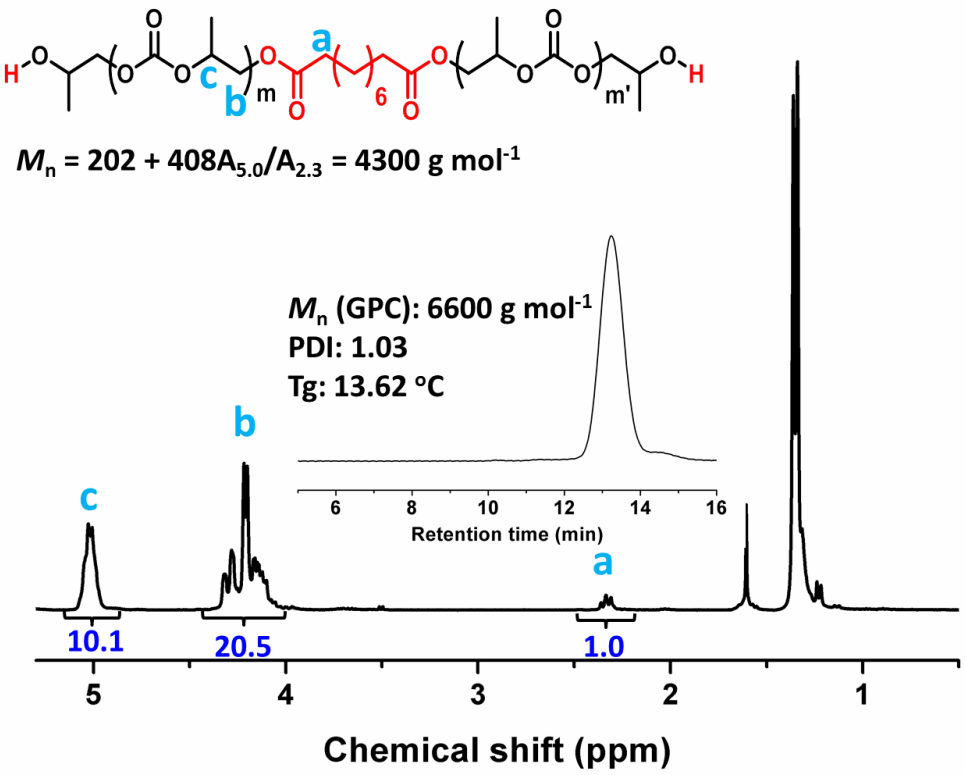

Figure S2. ^{1}H NMR of polymer PPC-diol (m+m' = 40) (d-Chloroform).

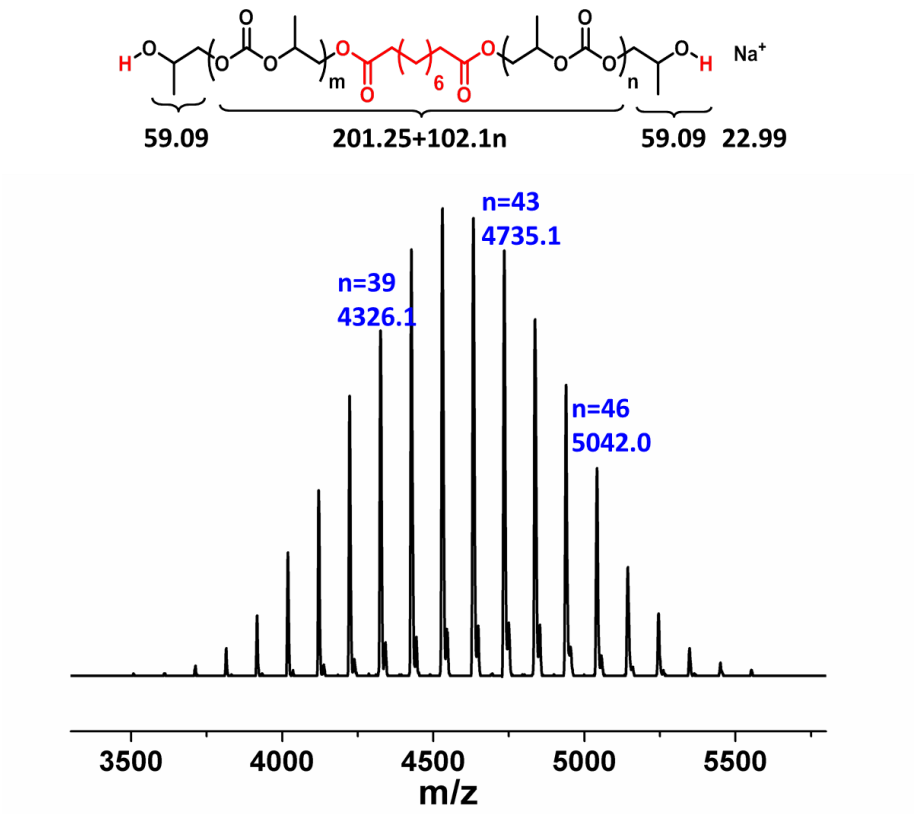

Figure S3. MALDI-TOF-MS spectrum of triblock copolymer PAGEC-b-PPC-b-PAGEC.

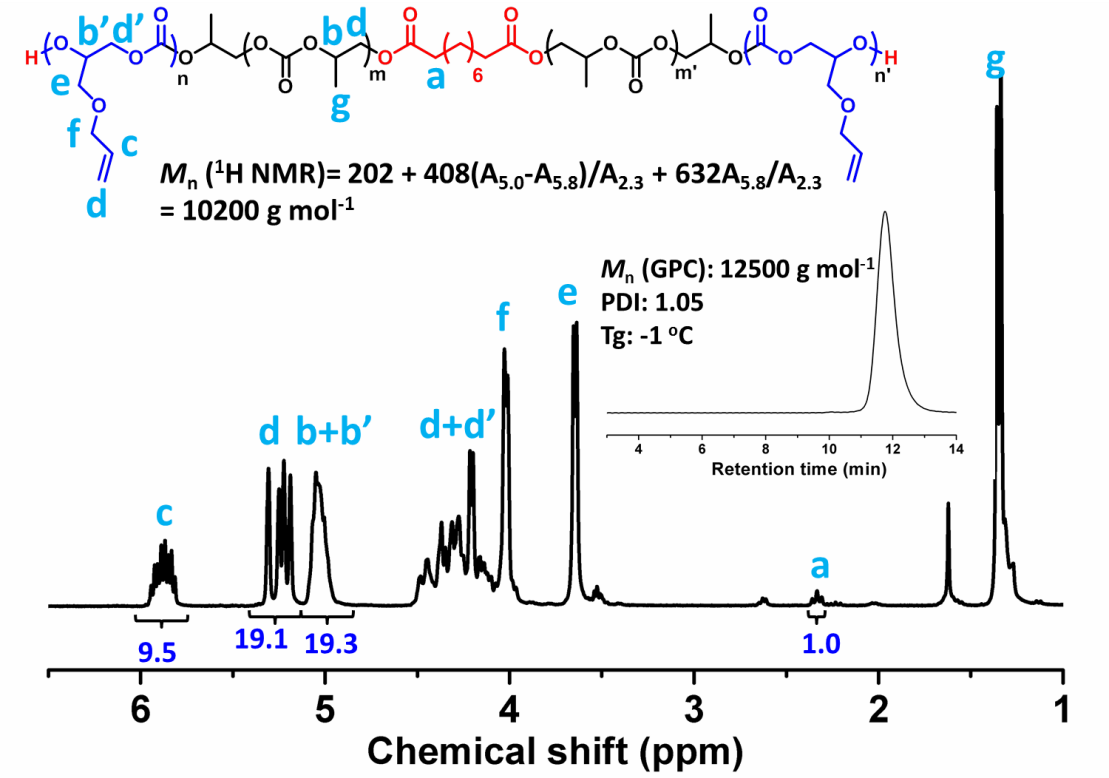

Figure S4. ^{1}H NMR of triblock copolymer PAGEC-b-PPC-b-PAGEC (m+m')/(n+n') = 40/40) (d-Chloroform).

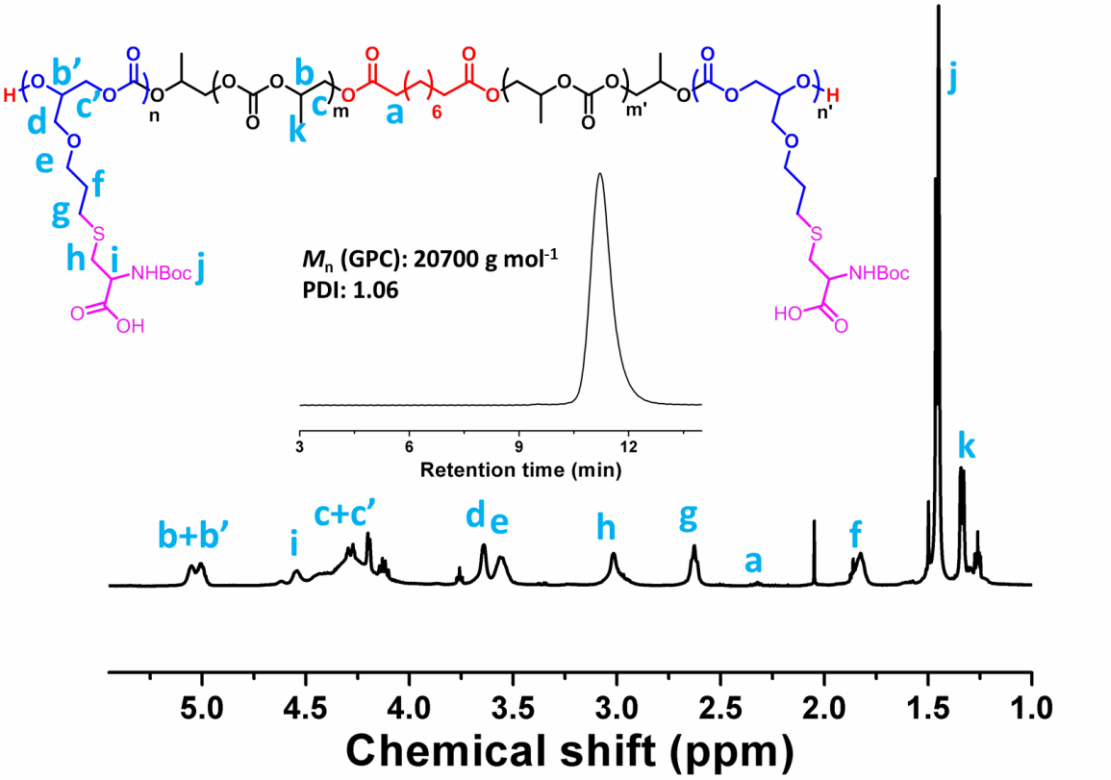

Figure S5. ^{1}H NMR of Boc-protected triblock copolymer PAGEC-b-PPC-b-PAGEC (m+m')/(n+n') = 40/40) (d-Chloroform).

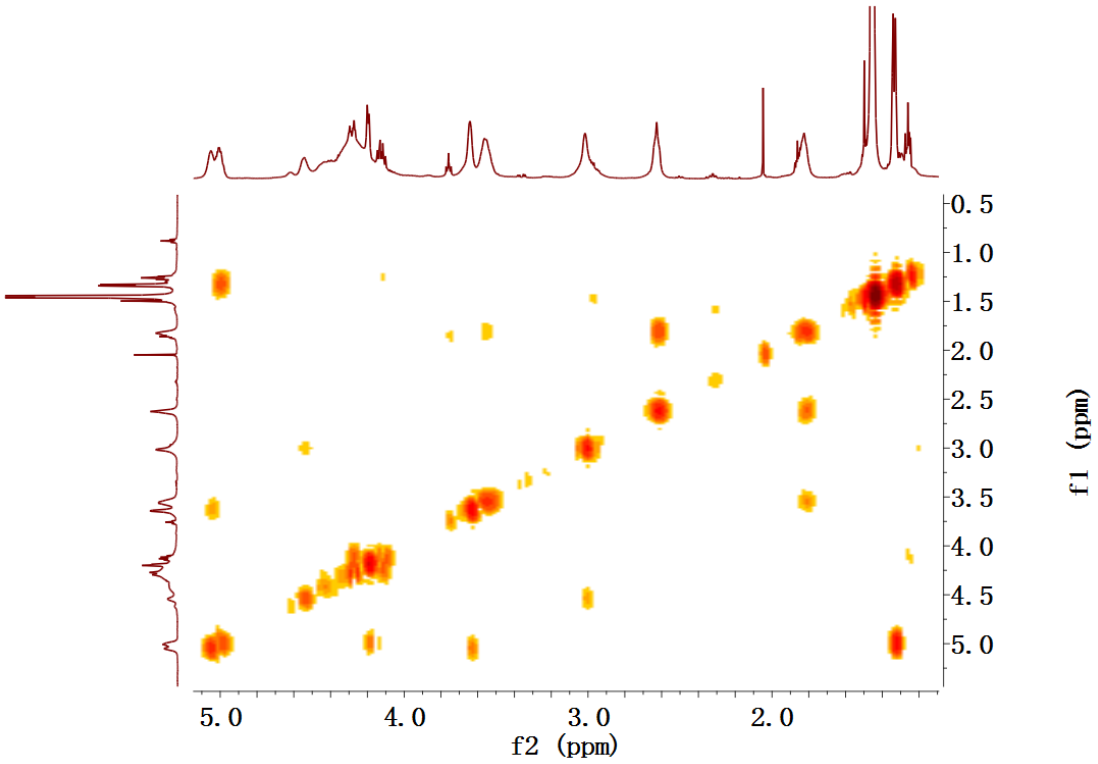

Figure S6. COSY NMR of Boc-protected triblock copolymer PAGEC-b-PPC-b-PAGEC (m+m')/(n+n') = 40/40) (d-Chloroform).

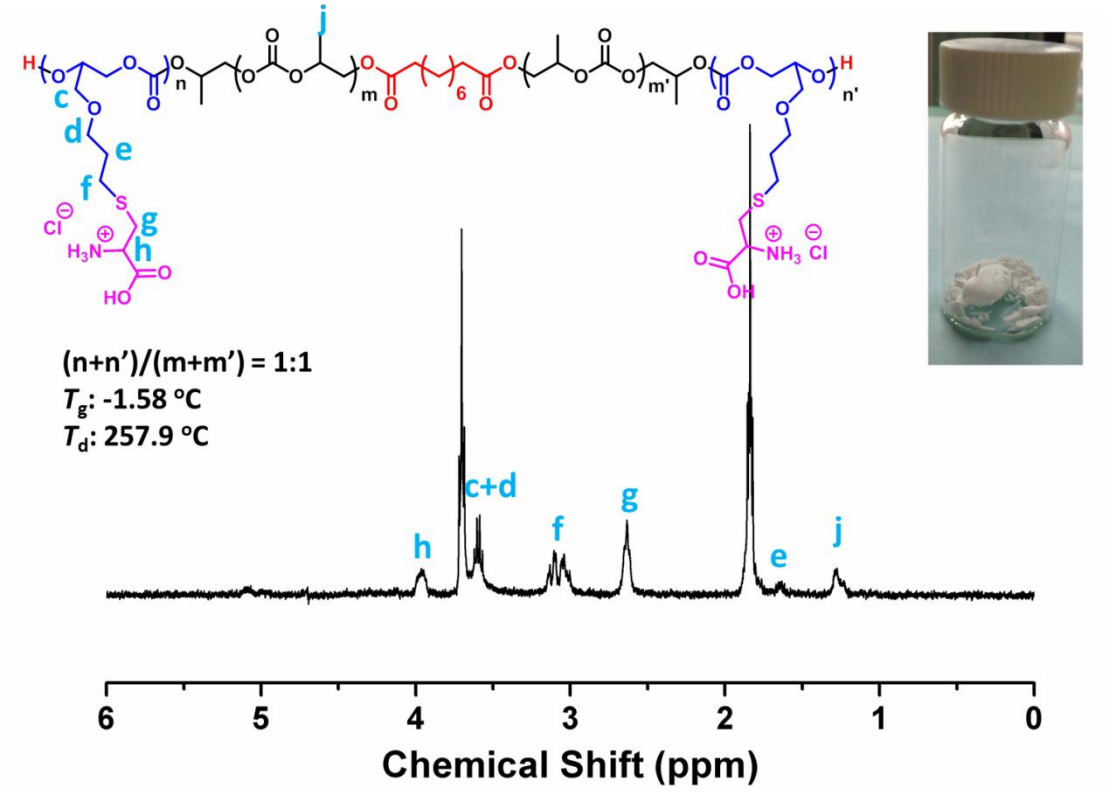

Figure S7. ^{1}H NMR of cysteine-based triblock copolymer PAGEC-b-PPC-b-PAGEC in D_2O (The inset picture is the product of cysteine-based triblock copolymer PAGEC-b-PPC-b-PAGEC).

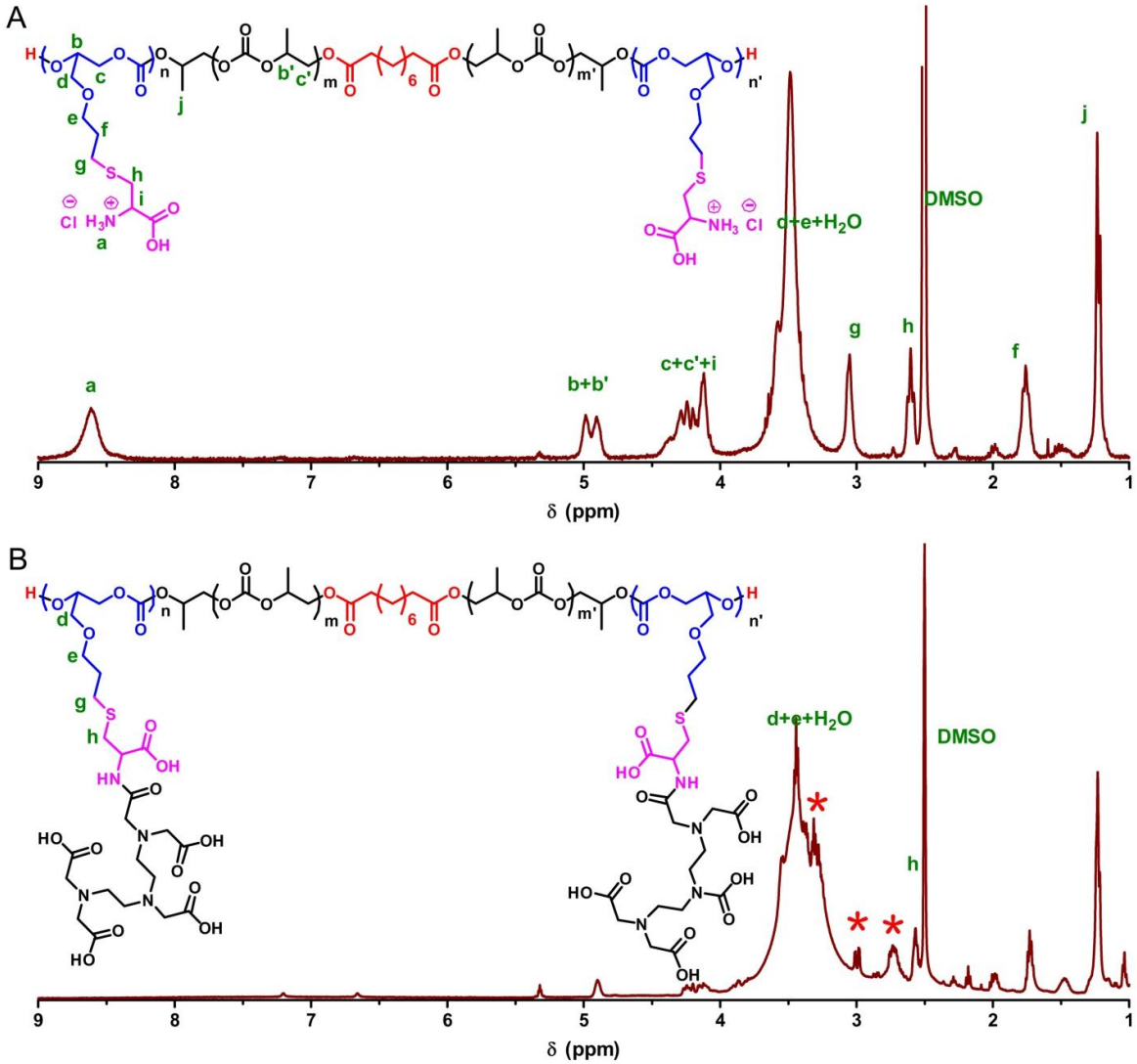

Figure S8. The ^{1}H NMR spectra of APC (A) and APC-DTPA (B) (d6-DMSO). The peak labeled by asterisks was attributed to the DTPA.

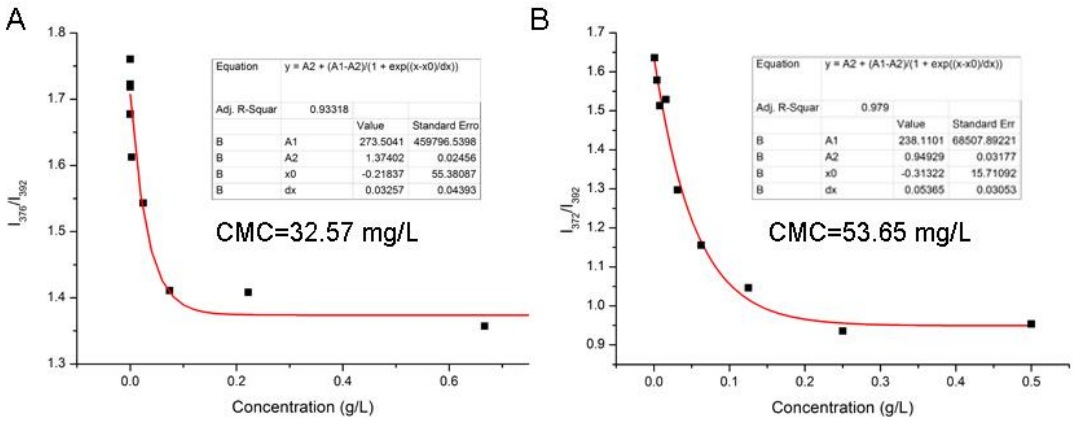

Figure S9. CMC measurement of (A) APC and (B) APC-DTPA/Gd determined by pyrene fluorescent probe method.

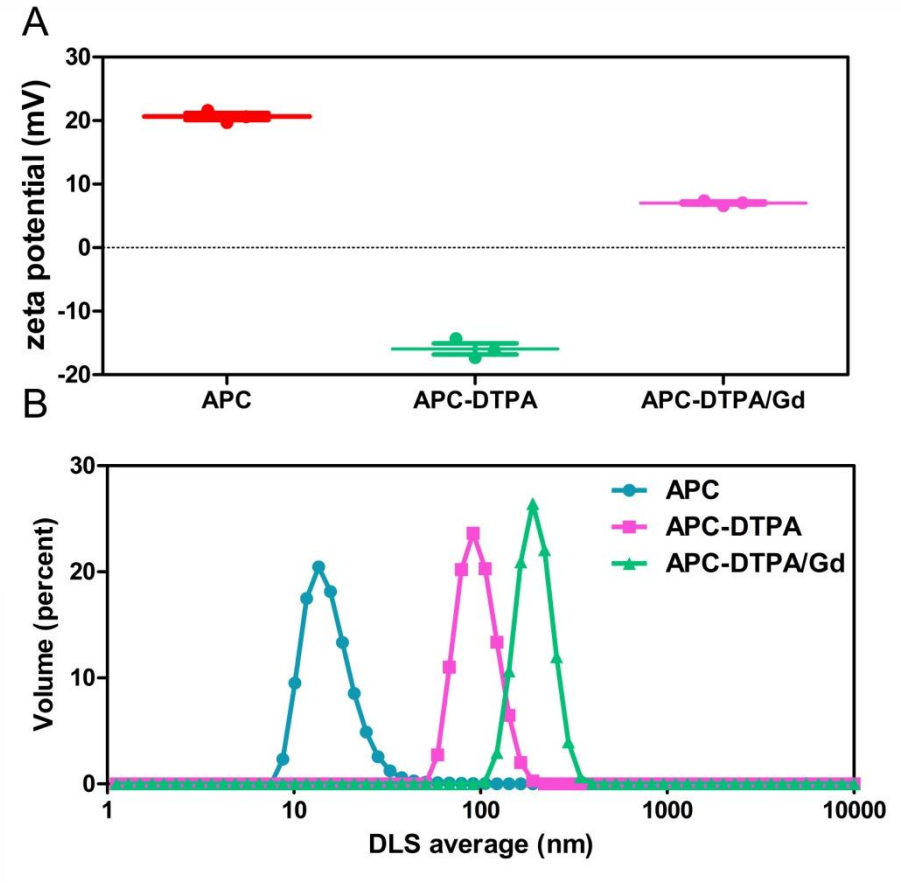

Figure S10. Zeta potential and DLS of APC, APC-DTPA and APC-DTPA/Gd.

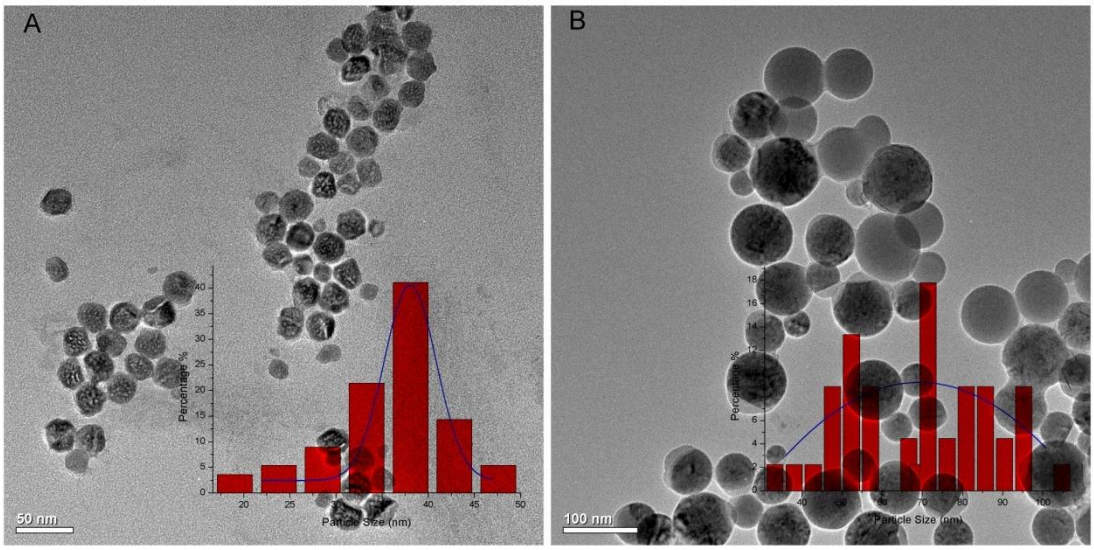

Figure S11. TEM and size distribution histograms of (A) APC and (B) APC-DTPA/Gd.

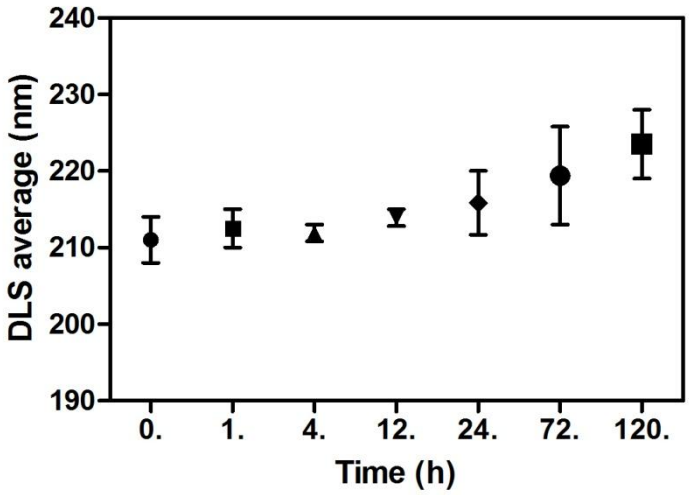

Figure S12. The DLS of APC-DTPA/Gd in water for 120 h.

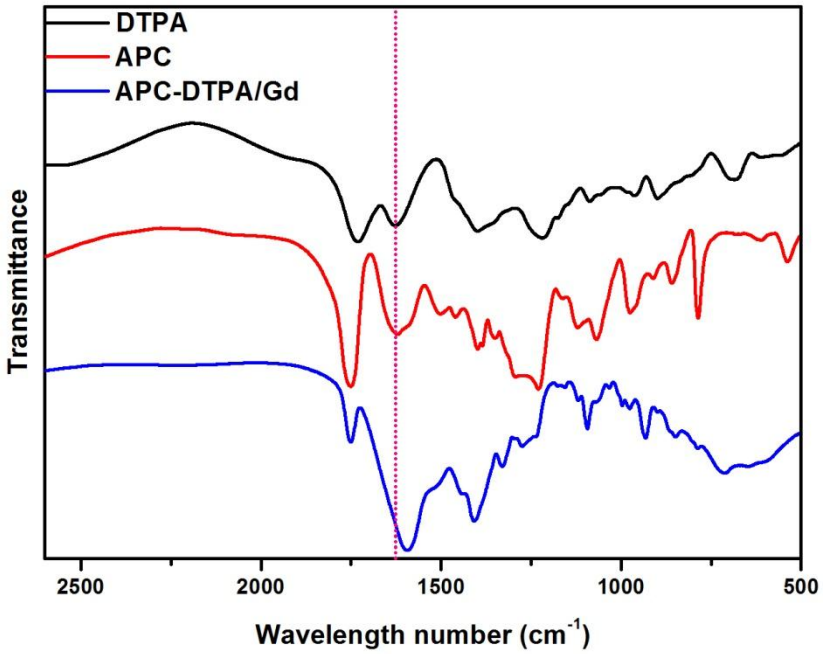

Figure S13. FTIR of APC after Gd^{3+} chelation.

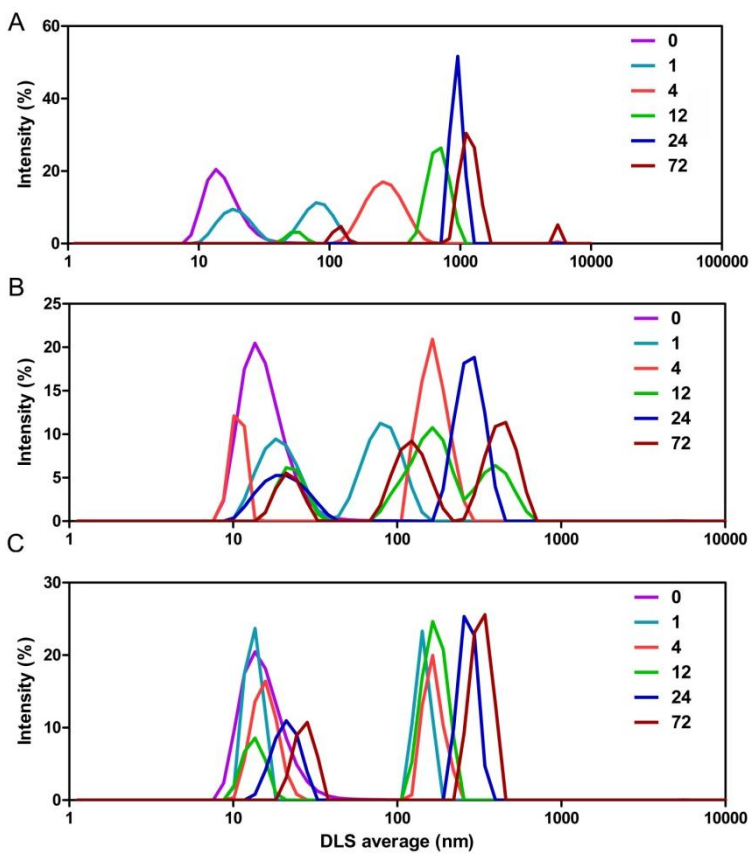

Figure S14. DLS changes of APC after incubation under (A) pH=5.0, pH=9.0 (B), or (C) in the presence of esterase.

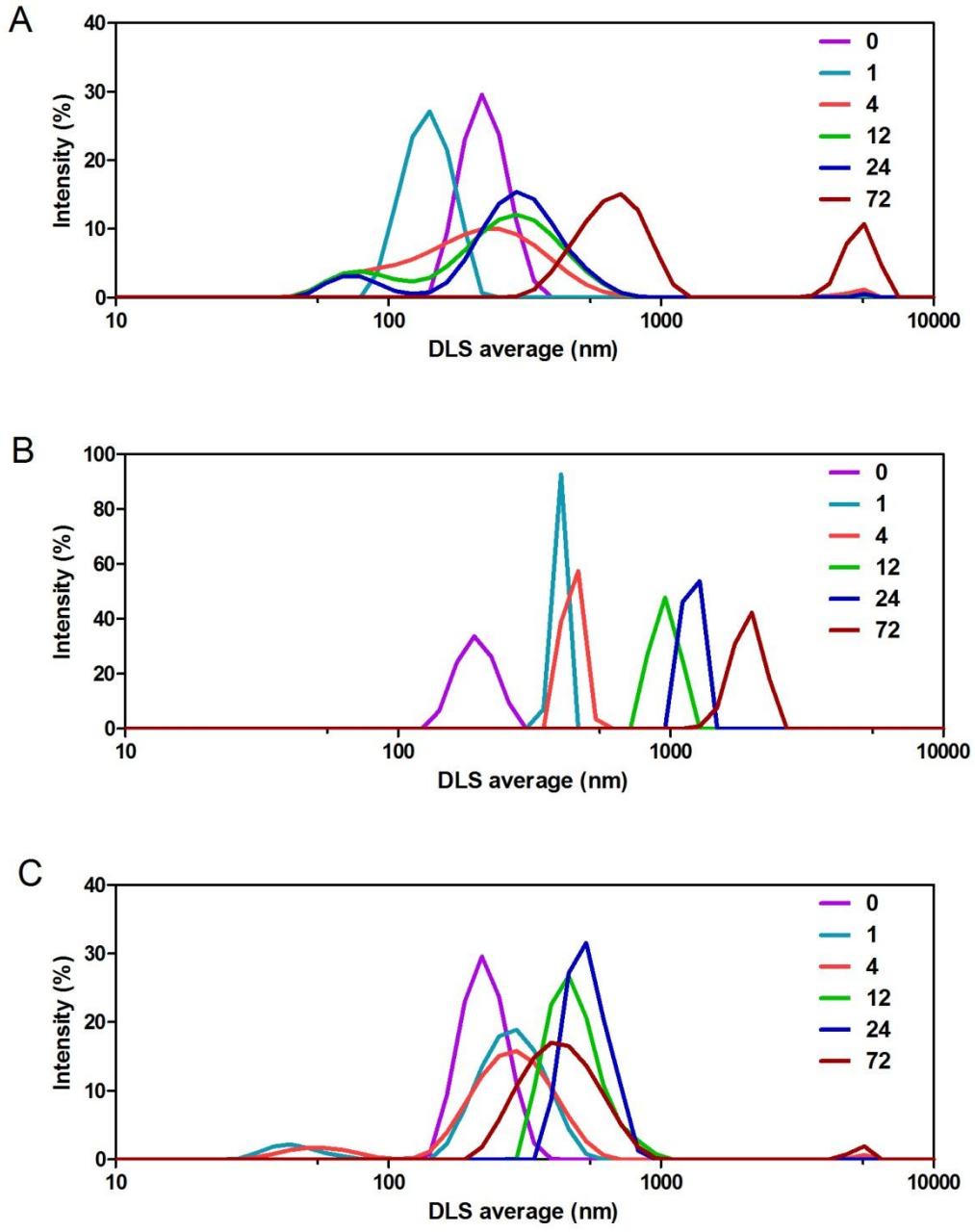

Figure S15. DLS changes of APC-DTPA/Gd after incubation under (A) pH=5.0, (B) pH=9.0, or (C) in the presence of esterase.

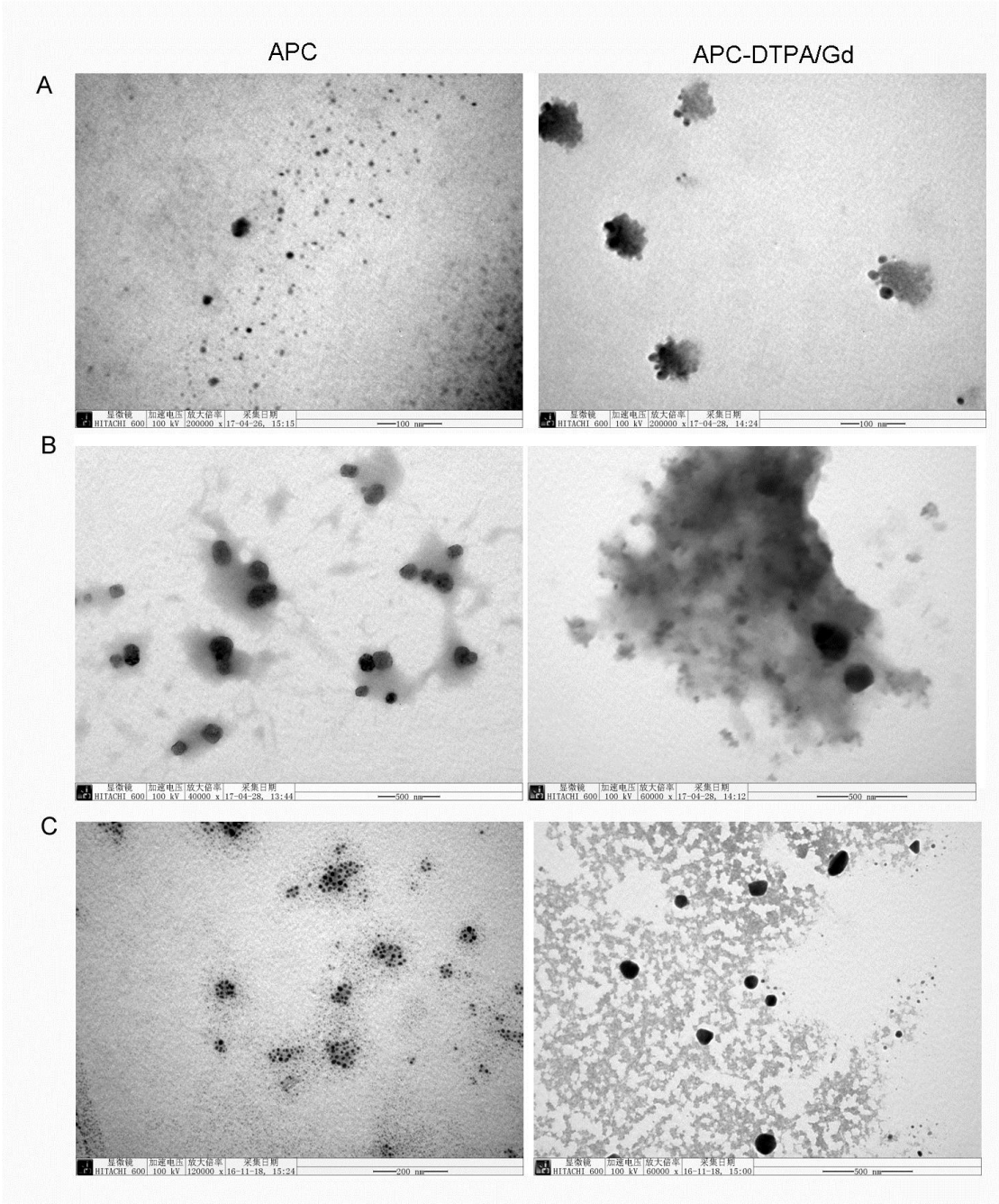

Figure S16. The TEM of APC and APC-DTPA/Gd after incubation under (A) pH=5.0, (B) pH=9.0, or (C) in the presence of esterase.

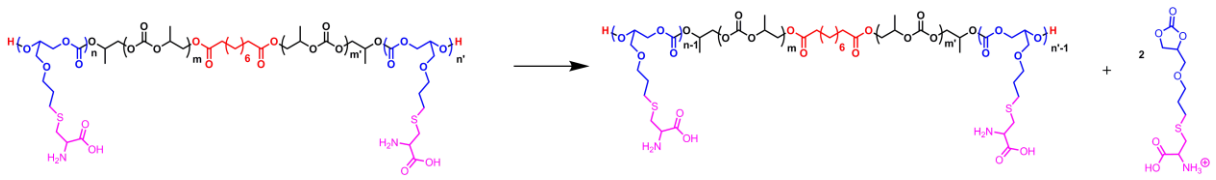

Figure S17. The depolymerization process of APC.

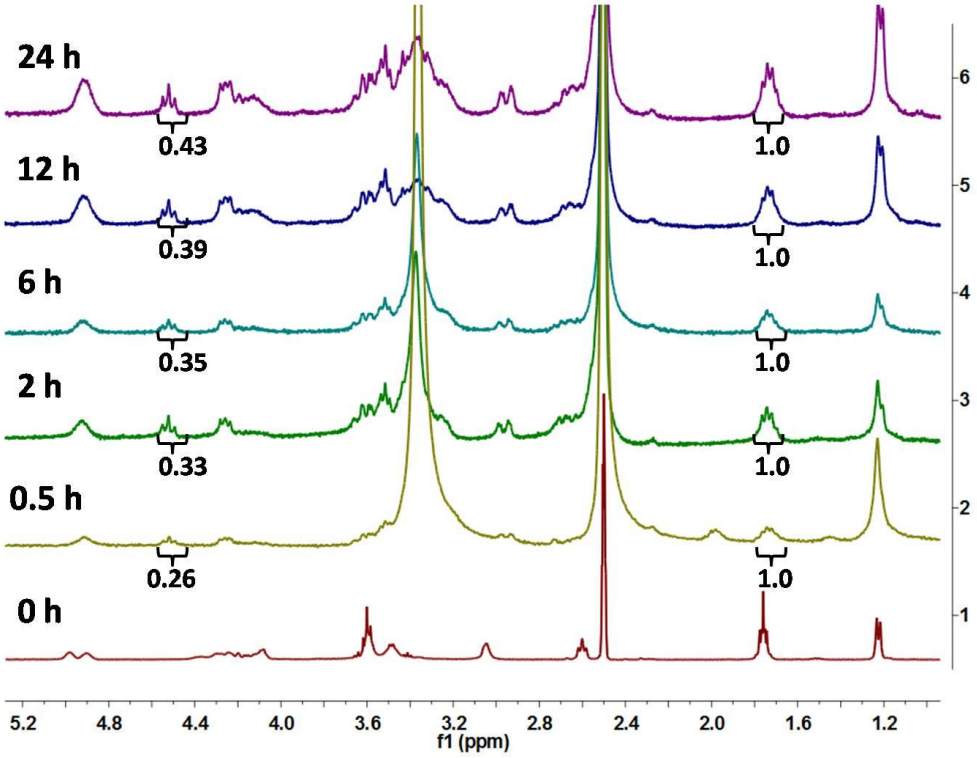

Figure S18. ^{1}H NMR of APC in pH = 5.0 at 0, 0.5, 2, 6, 12 and 24 h (1-6) (d6-DMSO).

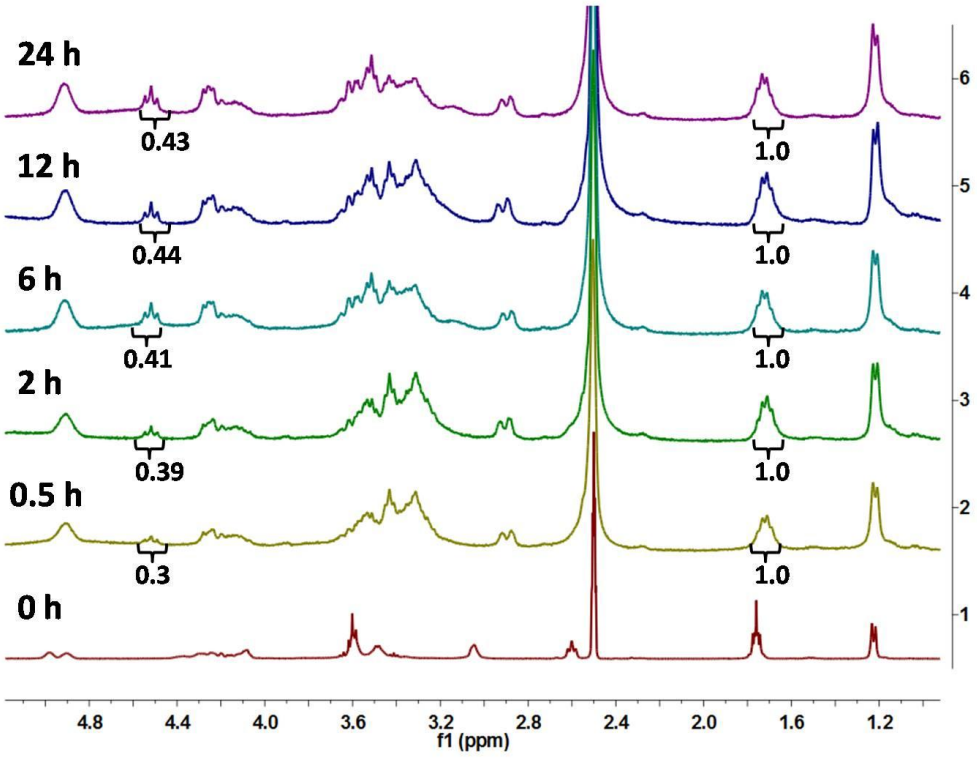

Figure S19. ^{1}H NMR of APC in pH = 9.0 at 0, 0.5, 2, 6, 12 and 24 h (1-6) (d6-DMSO).

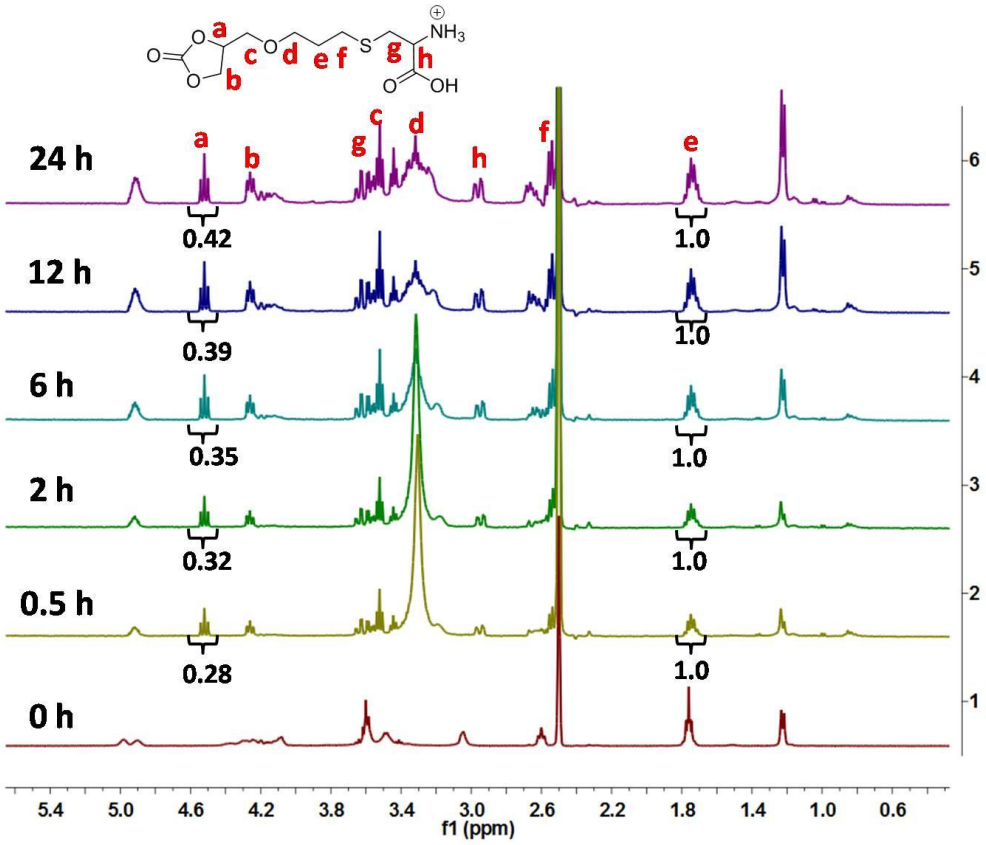

Figure S20. ^{1}H NMR of APC in esterase at 0, 0.5, 2, 6, 12 and 24 h (1-6) (d6-DMSO).

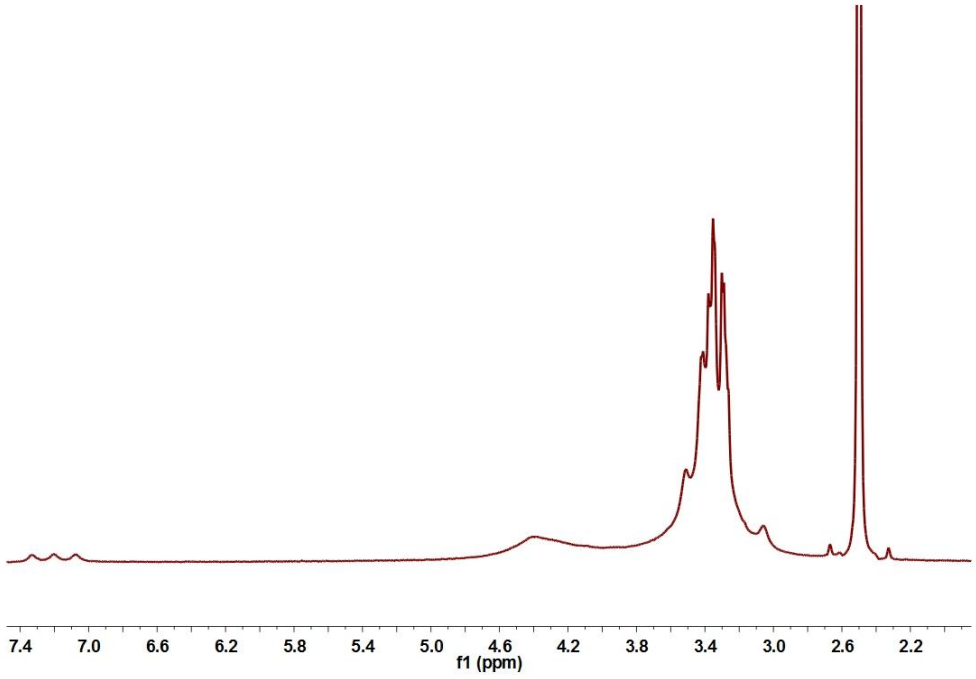

Figure S21. ^{1}H NMR of hydrolysis product from APC-DTPA/Gd (d6-DMSO).

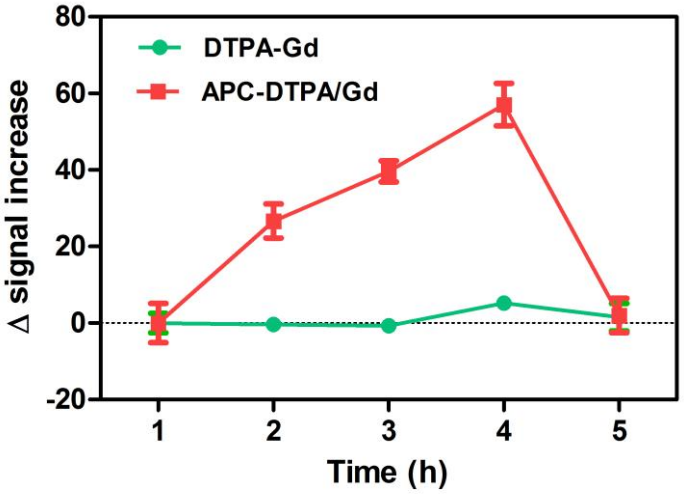

Figure S22. *In vivo* T_1-weighted MR signal enhancement of large 4T1 tumor-bearing mouse before and after intravenous injection of DTPA-Gd and APC-DTPA/Gd.

Table S1 Copolymerization results for the synthesis of ABA triblock amphiphilic polycarbonates.[a]

Entry	sample	M_n[b] (^{1}H NMR) (g mol^{-1})	M_n (GPC) (g mol^{-1})	PDI	T_g (^{o}C)	T_g (de-Boc) (^{o}C)	T_d (de-Boc) (^{o}C)
1	PPC diol	4300	6600	1.03	13.62	-	-
2	M/N=1:0.6	8600	9500	1.05	3.9	41.16	273.6
3	M/N=1:0.8	9000	13300	1.04	1.9	4.71	260.4
4	M/N=1:1.0	10200	16500	1.05	-1	-1.58	257.9

[a] See the experimental section for the exact procedure, M = m + m', N = n + n'. [b] Calculated by ^{1}H NMR.

	APC	SD	APC-Gd	SD	Control	SD	Normal range
ALT(U/L)	45.4	18.95521	44.4	9.581232	50	14.21267	40-170
AST(U/L)	158.2	66.55599	131.6	28.86694	129.6	45.87265	67-381
TP(g/L)	50.28	2.376342	48	2.421776	45.58	2.341367	49-73
ALB(g/L)	31.7	0.770281	31.46	1.112654	30.66	1.675709	31-53
ALP(U/L)	117	27.98214	122.6	17.92484	197.8	39.92117	108-367
WBC(K/μL)	4.32	1.681368	4.78	2.029039	5.4	1.911805	5.69-14.84
RBC(M/μL)	8.55	0.578835	8.466	0.409976	8.676	0.155016	8.16-9.98
HGB(g/L)	144	4.795832	145.6	4.219005	133.6	5.899152	125-189
HCT(%)	44.56	1.429336	44.84	1.813284	45.68	2.270903	43.5-67
MCV(fL)	52.2	2.145926	53.02	2.01544	54.28	2.662142	50.8-64.1
MCH(pg）	16.92	0.645755	17.2	0.632456	17.44	0.60663	13.0-17.6
MCHC(g/L)	323.8	4.266146	324.6	6.348228	321.4	5.59464	239-331
RDW(%)	16.16	0.589915	15.42	0.535724	15.8	0.367423	16.9-23.5
PLT(K/μL)	570.4	72.67255	596.8	42.65208	647.4	46.3875	476-1611

Table S2 Blood chemistry in mice after 30 days intravenous injection of APC, APC-Gd or PBS *(n=5)*. The normal data range for 8-10 week Balb/c female mice was provided by Charles River Data outside the normal range are highlighted in red. The

WBC and RDW were low in animals treated with either APC, APC-Gd or PBS, with no difference between groups.

		ICP-OES (ppm)				**ICP-MS (ppb)**			
		Liver		Spleen		Liver		Spleen	
		Mean	Stdev	Mean	Stdev	Mean	Stdev	Mean	Stdev
Test result	5 day	0.0115	0.0026	0.0043	0.001	9.2355	1.366	5.235	1.326
	10 day	0.0052	0.003	0.002	0.001	3.541	0.558	3.891	0.819
% ID/g	5 day	0.1517	0.053	0.1844	0.029	0.0541	0.014	0.0614	0.016
	10 day	0.0492	0.026	0.0857	0.029	0.010	0.002	0.038	0.010

Table S3 The ICP of Gd detected in liver and spleen in 5 day and 10 day via ICP-OES and ICP-MS.

References

1. Liu S, Zhao X, Guo H, et al. Construction of well-defined redox-responsive CO_2-based polycarbonates: combination of immortal copolymerization and prereaction approach. Macromol Rapid Commun. 2017; 38: 1600754 (1-5).
2. Wang Y, Fan J, Darensbourg DJ. Construction of versatile and functional nanostructures derived from CO_2-based polycarbonates. Angew Chem Int Ed. 2015; 54: 10206-10.