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Supporting Information

Poly(ε-caprolactone) with pH and UCST responsiveness as a 5-fluorouracil carrier

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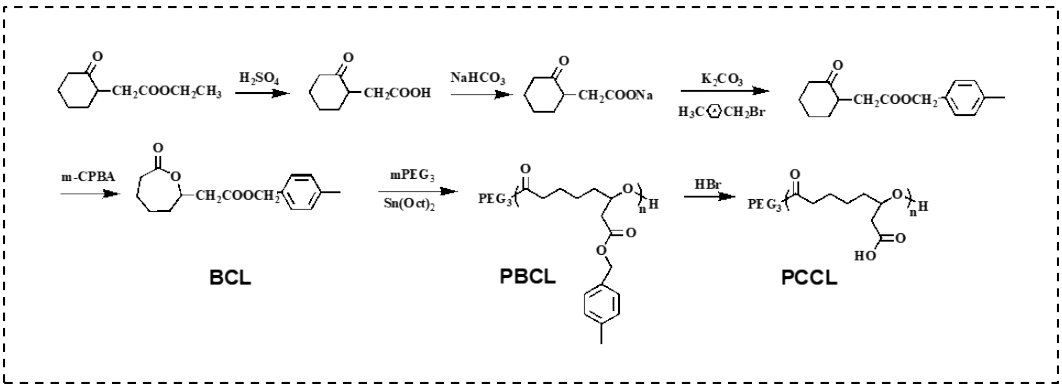

Fig. S1 Synthesis route for PCCL.

PCCL was obtained *via* reported three steps which contained the synthesis of monomer, the ring-opening polymerization (ROP) of monomer and the deprotection of *p*-methylbenzyl groups. The synthetic procedures were displayed as follows (Fig. S1).

Synthesis of 6-(*p*-methylbenzyl acetate)-*ε*-caprolactone (BCL).

BCL was prepared as followed: Ethyl 2-cyclohexanone acetate (18.4 g) was hydrolyzed in 300 ml 2 wt% H_2SO_4 for 4 h, After cooling to room temperature, the reaction mixture was extracted by dichloromethane and the organic layer was washed by $NaHCO_3$ solution to obtain 2-carbethoxy cyclohexanone sodium salt. Then 2-carbethoxy cyclohexanone sodium salt was reacted with *p*-methylbenzyl bromide (18.4 g) and K_2CO_3 (2.0 g) in acetone (300 ml) to obtain *p*-methylbenzyl-2-cyclohexanoneacetate. After that, the resulted carboxyl protected cyclohexanone was reacted with *m*-CPBA (40.92 g) in dry dichloromethane (400 ml) for 24 h. The resulted product was purified by

column chromatography.

Synthesis of poly(6-(*p*-methylbenzyl acetate)-*ε*-caprolactone) (PBCL).

PBCL was prepared as followed: 0.5 g BCL was reacted with appropriate catalyst $Sn(Oct)_2$ and initiator $mPEG_3$ at 130 ºC. After reaction for 24 h, the product was received by precipitation with ether.

Synthesis of poly(6-acetoxyl-*ε*-caprolactone) (PCCL).

PCCL was prepared as followed: PBCL (0.2 g) was dissolved into 10 ml dried dichloromethane with excess HBr (35 wt% in acetic acid). After stirring at room temperature for 2 h, the mixture was precipitated with ether. After removing the solvent by vacuum drying, the viscous yellow product PCCL was obtained.

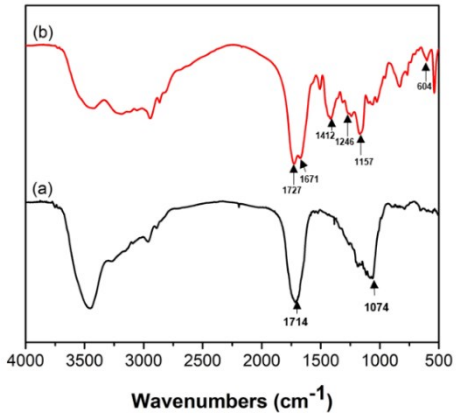

Fig. S2 FT-IR spectra of (a) PCCL and (b) $PCCL_{40}$-*g*-MU_{25}.

The peaks at 1714 cm^{-1} and 1074 cm^{-1} which were attributed to the C=O and C-C & C-O stretching of ester bonds of PCCL, shifted to 1727 cm^{-1} and 1157 cm^{-1} after modification. Besides, the signals of 1671 cm^{-1} and 1246 cm^{-1} were assigned to the C=O and C-N stretching of amide bonds and the signals at 1412 cm^{-1} and 604 cm^{-1} were corresponded to bending vibrations of =C-H on uracil groups. These results demonstrated that MU was successfully incorporated into PCCL side chains.

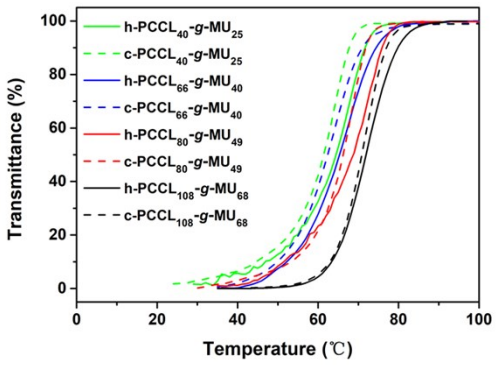

Fig. S3 Temperature-dependent transmittance curves of PCCL-*g*-MUs aqueous solutions measured by UV-VIS spectrophotometer at a wavelength of 500 nm with the heating/cooling rate of 1 °C /min. (2 mg/ml).

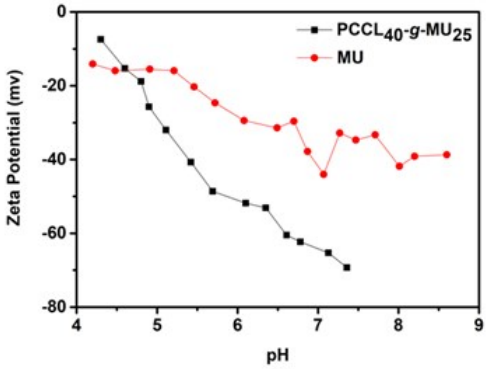

Fig. S4 Zeta potentials of $PCCL_{40}$-*g*-MU_{25} and MU aqueous solutions at 25 °C with different pHs measured by DLS.

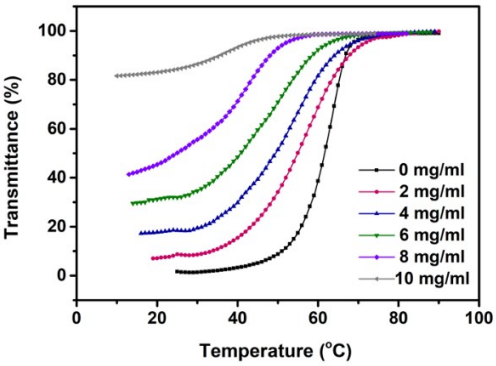

Fig. S5 Temperature-dependent transmittance curves of $PCCL_{40}$-*g*-MU_{25} aqueous solution at pH 5.2 with different concentrations of NaSCN measured by UV-VIS spectrophotometer.

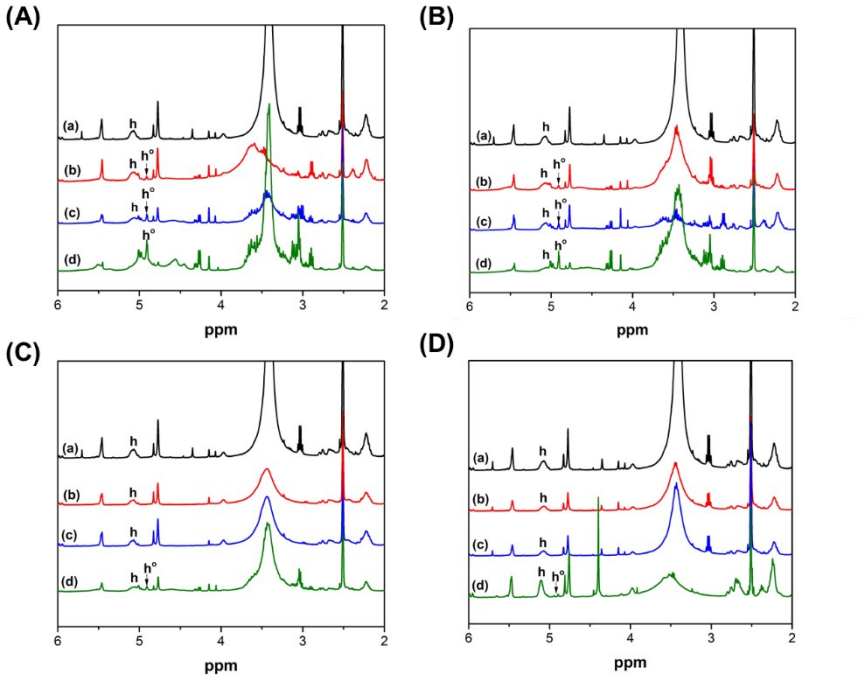

Fig. S6 ^{1}H NMR spectra for PCCL$_{40}$-*g*-MU$_{25}$ in PBS solution at 37 °C: (A) with lipase at pH 6.5, (B) with lipase at pH 7.4, (C) without lipase at pH 6.5 and (D) without lipase at pH 7.4. The black line (a), red line (b), blue line (c) and green line (d) were referred to the spectrum of PCCL$_{40}$-*g*-MU$_{25}$ after degradation for 0 week, 1 week, 3 weeks and 7 weeks respectively.

Taking the ^{1}H NMR spectrum A(a) in Fig. S6 as an example, it was observed that the peak **h** appearing at 5.08 ppm was attributed to the methine proton of PCL backbone. While after degradation for 1 week (spectrum A(b)), the appearance of new peak **h^{o}** at 4.90 ppm revealed the hydrolysis of polymer mainchain. And after 7 weeks (spectrum A(d)), the peak **h** was almost completely replaced by **h^{o}**, which indicated the almost complete degradation of PCCL$_{40}$-*g*-MU$_{25}$. The percentage of polymer remaining was determined as the integral decrement of methine proton of PCL backbone (**h**), which was calculated as:

$$Polymer\ remaining\ (mol\%) = \frac{integral\ area\ of\ h^{o}}{integral\ area\ of\ h^{o}\ and\ h} \times 100\%$$