Supporting Information

Acid Degradable Poly(vinylcaprolactam)-based Nanogel with Ketal Linkage for Drug Delivery

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**Fig. S1** $^1$H NMR spectrum of DMAEP. $^1$H NMR (500 MHz, CDCl3): $\delta$ (ppm) 1.38 (6H, s, (COOCH$_2$CH$_2$O)$_2$C(CH$_3$)$_2$), 1.94 (6H, s, (OCOCCH$_3$CH$_2$)$_2$), 3.70 (4H, m, (COOCH$_2$CH$_2$O)$_2$C(CH$_3$)$_2$), 4.27 (4H, m, (COOCH$_2$CH$_2$O)$_2$C(CH$_3$)$_2$), 5.57 (2H, s, (OCOCCH$_3$CH$_2$)$_2$ – syn to methyl), 6.11 (2H, s, (OCOCCH$_3$CH$_2$)$_2$ – anti to methyl).

**Fig. S2** $^1$H NMR spectra of cross-linker DMAEP before and after degradation.
Fig. S3 Representative TEM images (×5W) of P(VCL-ketal-HPMA) nanogels with different HPMA contents: (a) 3 wt%, (b) 5 wt%, (c) 8 wt% and (d) 10 wt%.

Fig. S4 $^1$H NMR spectrum of P(VCL-ketal-HPMA) nanogel in D$_2$O.
**Fig. S5** Hydrolysis kinetics of acid-cleavable cross-linker DMAEP at pH 5.0, 6.5 and 7.4, respectively.

**Fig. S6** TEM image of P(VCL-ketal-HPMA-8) nanogels after degradation.
Fig. S7 The molecular weight of copolymer P(VCL-co-HPMA) by GPC measurement.

Fig. S8 DOX release profiles of acid-degradable P(VCL-ketal-HPMA) nanogel in the medium of pH 5.0 at 37 °C and 45 °C.
**Fig. S9** CLSM images of the intracellular DOX release of free DOX. (a) 2 h, (b) 6 h and (c) 12 h incubation of free DOX. In each column, images from top to down: differential interference contrast microscopy, fluorescence microscopy, and overlays of both images.

**Fig. S10** Hemolysis assay of the P(VCL-ketal-HPMA-8) nanogel. RBC suspension to make the final particle concentration 0.1, 0.2, 0.5 and 1 mg/mL, respectively. Distilled water served as positive control and normal saline as negative control.