Supporting Information for

Hierarchical Design of a Polymeric Nanovehicle for Efficient Tumor Regression and Imaging

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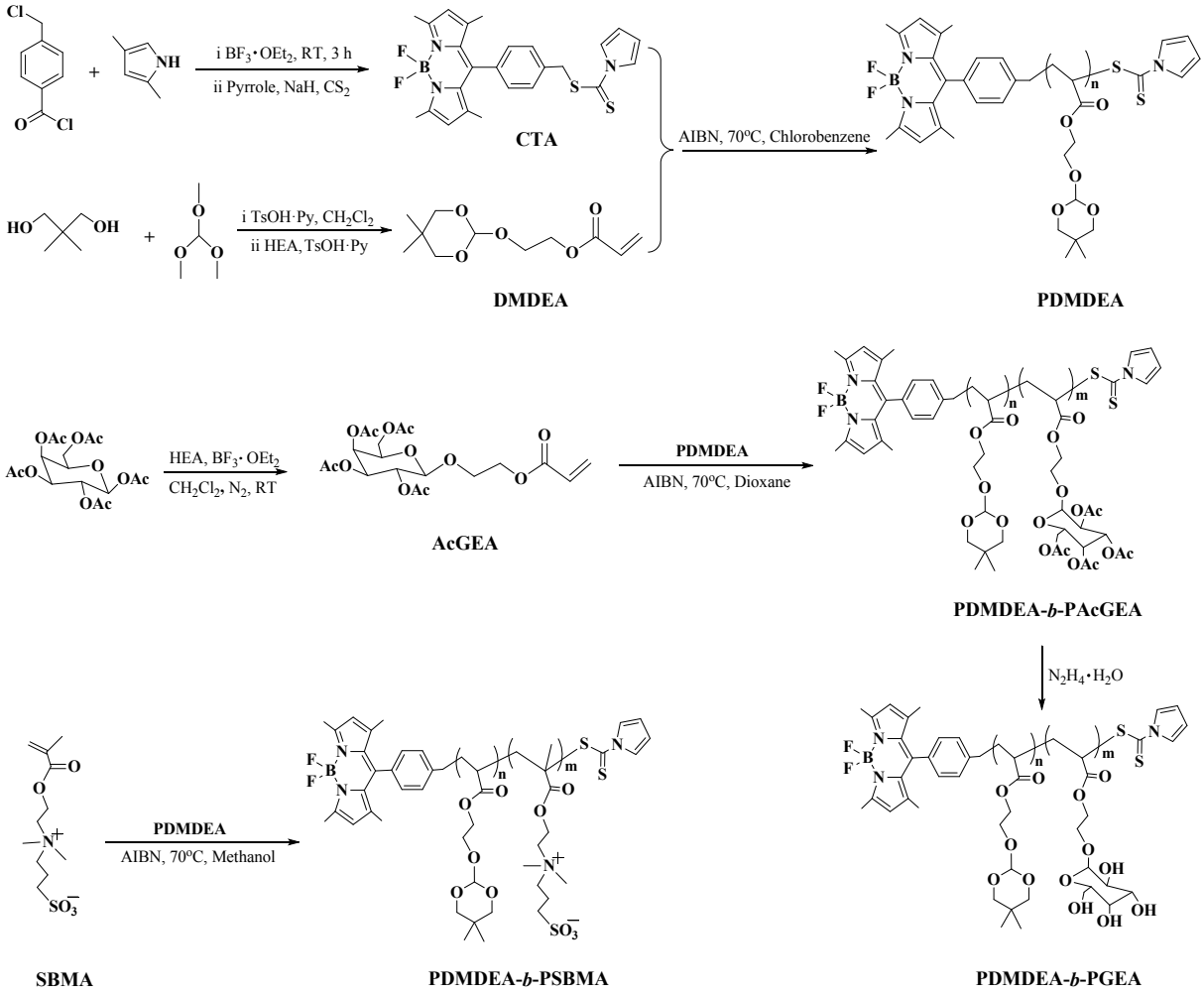
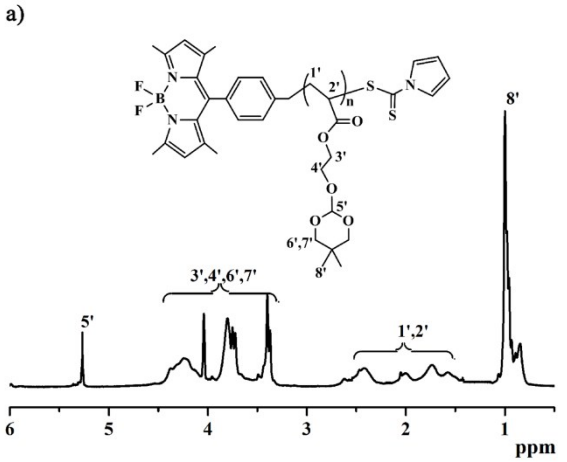
Supplementary Figures



Scheme S1 Synthesis routes of amphiphilic block copolymers PDMDEA-*b*-PGEA and PDMDEA-*b*-PSBMA.



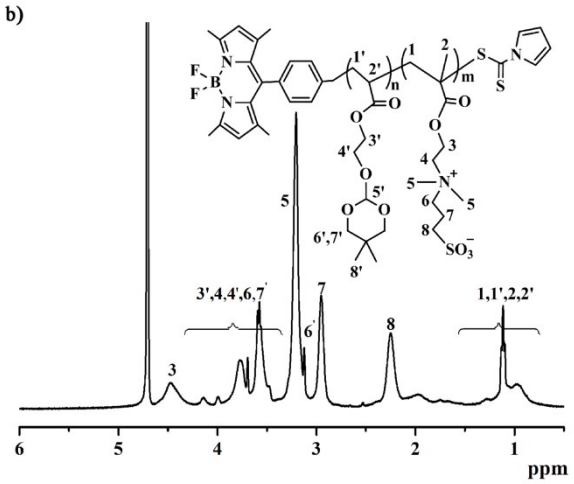


Fig. S1 ^{1}H NMR spectra of (a) PDMDEA in $CDCl_3$ and (b) PDMDEA-*b*-PSBMA in D_2O in the presence of NaCl at 25 °C.

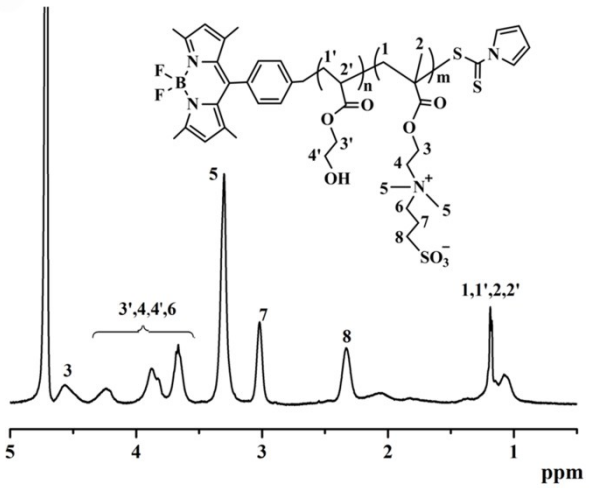
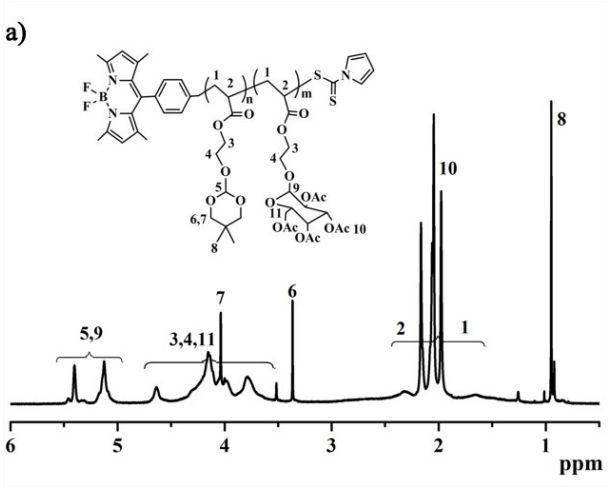


Fig. S2 ^{1}H NMR spectrum of hydrolyzed PDMDEA-*b*-PSBMA in D_2O in the presence of NaCl at 25 °C.

Homopolymer PDMDEA was first prepared by RAFT polymerization. Then PSBMA-*b*-PDMDEA and PDMDEA-*b*-PAcGEA copolymers were synthesized using PDMDEA as macro-CTA at 70 °C. The ^{1}H NMR results of homopolymer PDMDEA and copolymer PSBMA-*b*-PDMDEA were shown in Fig. S1. Compared with PDMDEA, peaks at 2.3, 2.9 and 3.6 assigned to methylene of sulfobetaine emerged in the spectrum of PSBMA-*b*-PDMDEA. This result confirmed successful synthesis of amphiphilic copolymer PSBMA-*b*-

PDMDEA. Nevertheless, due to the subsequent micellization of amphiphilic PSBMA-*b*-PDMDEA copolymer in the aqueous solution, the observed peaks of PDMDEA in the ^{1}H NMR was partial. The amphiphilic PSBMA-*b*-PDMDEA copolymer was hydrolyzed to obtain hydrophilic block copolymer in acidic aqueous solution, which could accurately show the molar composition of PSBMA-*b*-PDMDEA copolymer. As shown in Fig. S2, compared with PSBMA-*b*-PDMDEA, peak at 3.2 ppm assigned to methylene of ortho ester unit disappeared and the peak intensity at 4.2-4.4 ppm attributed to methylene of -CH_2CH_2OH strengthened, indicating successful hydrolysis of copolymer PSBMA-*b*-PDMDEA. The ratio of polymerization degree for PDMDEA and PSBMA blocks was 24:14, determined by comparison of the area of the peak at 4.2-4.4 ppm (2H, -CH_2-) assigned to the hydrolyzed DMDEA unit, the peak at 2.8-3.1 ppm (2H, -$CH_2CH_2SO_3$) assigned to the SBMA unit, to the peak at 2.5-2.6 ppm (6H, 2 × -CH_3-) corresponding to the chain transfer agent unit, respectively. And the molecular weight of PSBMA-*b*-PDMDEA was 10.3 kDa.



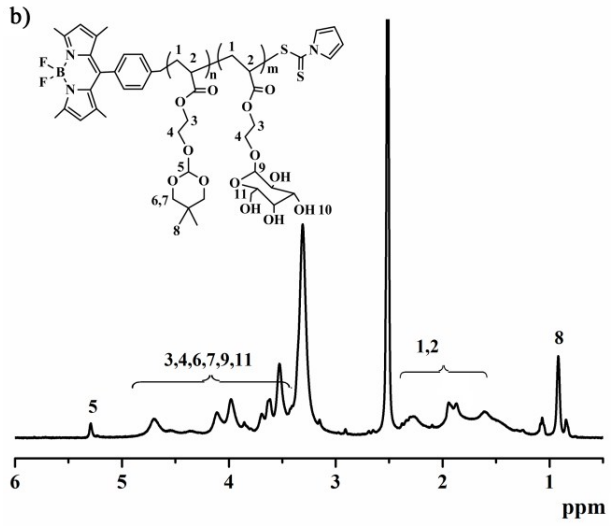


Fig. S3 ^{1}H NMR spectra of (a) PDMDEA-*b*-PAcGEA copolymer in $CDCl_3$ and (b) PDMDEA-*b*-PGEA copolymer in DMSO-d_6 at 25 °C.

The structure of PDMDEA-*b*-PAcGEA and PDMDEA-*b*-PGEA copolymers was further measured using ^{1}H NMR spectroscopy (Fig. S3). Compared with PDMDEA, new peaks at 1.9-2.2 and 5.1 ppm assigned to AcGEA unit emerged in the spectrum of PAcGEA-*b*-PDMDEA. Peaks, however, at 1.9-2.2 ppm of the acetyl group disappeared after treatment of PAcGEA-*b*-PDMDEA with hydrazine hydrate. Strong peaks at 3.5-4.5 ppm of PGEA-*b*-PDMDEA were assigned to galactose residues, signifying successful deacetylation reaction. These results collectively confirmed successful synthesis of the amphiphilic copolymer PGEA-*b*-PDMDEA. The molecular weight of PAcGEA-*b*-PDMDEA based on ^{1}H NMR spectrum was 13.9 kDa. After deacetylation with hydrazine hydrate, the molecular weight of PGEA-*b*-PDMDEA was 10.0 kDa and the corresponding molar composition was 23:14 which was determined by comparison of the area of the peak at 5.3-5.5 ppm (1H, -CHO_3-) attributed to the DMDEA unit,4.9-5.2 ppm (1H, -$O_2CHCHOAc$-) attributed to the AcGEA unit, to the peak at 2.5-2.6 ppm (6H, 2 × -CH_3-) corresponding to the chain transfer agent unit, respectively.

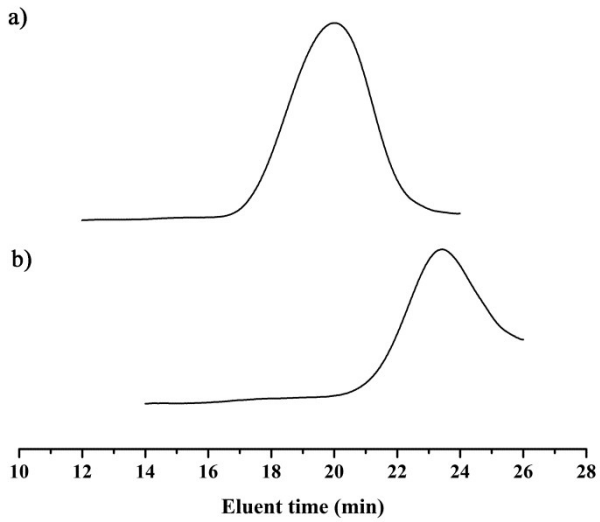


Fig. S4 GPC curves of (a) PDMDEA macro-CTA (M_n = 3.9 kDa, M_w/M_n = 1.18) and (b) PDMDEA-*b*-PAcGEA (M_n = 14.1 kDa, M_w/M_n = 1.26). THF was used as the eluent (1.0 mL/min), and polystyrenes were used as a standard.

The molecular weights obtained from GPC characterization were nearly consistent with the ^{1}H NMR results, where the molecular weight of PDMDEA and PAcGEA-*b*-PDMDEA were 3.9 kDa and 14.1 kDa with narrow molecular weight distribution (Fig. S4). Since the charged polymers easily interacts with the stationary phase of the chromatographic column,[1] it is still a challenge to measure the gel permeation chromatography of PSBMA-*b*-PDMDEA.

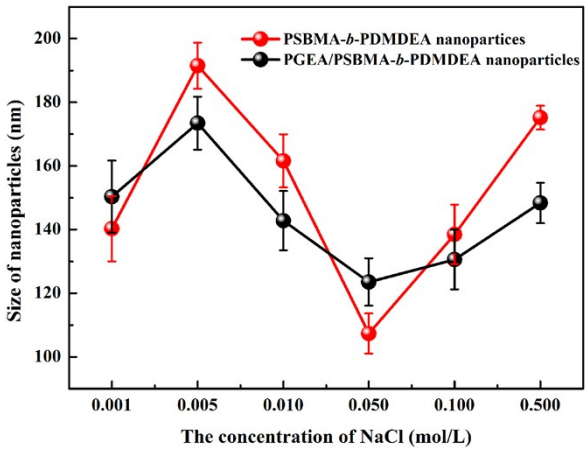


Fig. S5 Size of nanoparticles in different concentrations of NaCl solution.

For most like-charged polymers, hydrodynamic diameter of the nanoparticles is dependent

on the concentration of electrolytes e.g. NaCl.[2] In this work, PSBMA-*b*-PDMDEA copolymer easily aggregate in pure water, due to the formation of intra and inter chain ionic contacts between ammonium and sulfonate of the inter- or intra-polymer chains. However, they can form nanoparticles in the presence of NaCl during the preparation process of nanoparticles. This can be attributable to the fact that the electrolyte NaCl crosses the ionic network, interacts with charges, destroys the attractive electrostatic interactions between ammonium and sulfonate of the inter- or intra-polymer chains, and thus promotes swelling of PSBMA.[2-5] We also explored the size change of PSBMA-*b*-PDMDEA nanoparticles in aqueous solution with different concentrations of NaCl by DLS (Fig. S5). The result shows that the size of the PSBMA-*b*-PDMDEA nanoparticles was susceptible to the concentration of NaCl, which is consistent with the previous report.[6] The similar result is obtained for PGEA/PSBMA-*b*-PDMDEA nanoparticles.

References

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