Supplement information

Modular Synthesis of Folate Conjugated Ternary Copolymer Polyethylenimine-Graft-Polycaprolactone-Block-Poly (ethylene glycol)-Folate for Targeted Gene Delivery

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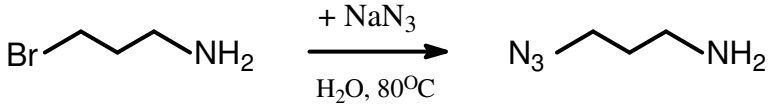
1. Synthesis of 1-azido-3-aminopropane



A solution of 3-Bromopropylamine hydrobromide (5 g, 22.8 mmol) and sodium azide (4.45 g, 68.4 mmol, 3equiv) in water (30 mL) was heated at 80 °C for 18 h. After most of the water was removed by distillation under vacuum, the reaction mixture was cooled in an ice bath. Diethyl ether (50 mL) and then KOH pellets were added keeping the temperature below 10 °C. After separation of the organic phase, the aqueous layer was further extracted with diethyl ether. The combined organic layers were dried over Na_2SO_4 and concentrated to give oil which was purified by quick distillation at 160°C.

^{1}H NMR ($CDCl_3$):

δ 3.3 (t, 2H, CH_2N_3), 2.75 (t, 2H, CH_2NH_2), and 1.65 (q, 2H, $CH_2CH_2CH_2$).

^{13}C NMR ($CDCl_3$):

δ 49.0 (CH_2N_3), 39.2 (CH_2NH_2), and 32.5 ($CH_2CH_2CH_2$).

2. Characterization of azido-folate

In Figure S-1, sharp peak appeared in 2095 cm-1 due to the introduction of -N_3 to folate. ^{1}H NMR analysis (Figure S-2) revealed that folate was functionalized into azido-folate via the γ-carboxylate of the glutamic acid moiety mostly. Taken together, these results confirmed the successful synthesis of azido-folate.

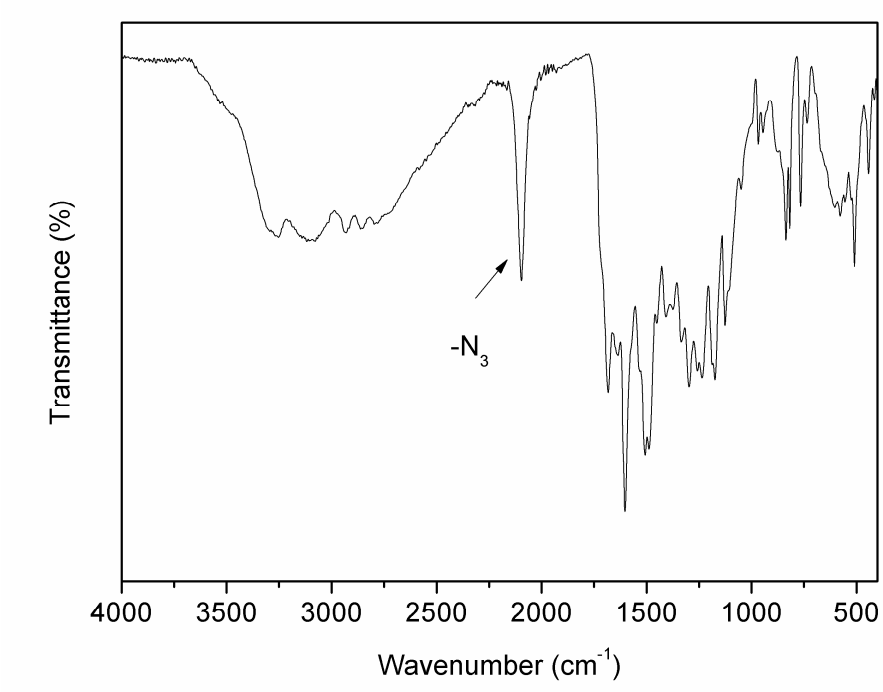


Figure S-1. IR spectra of azido-folate.

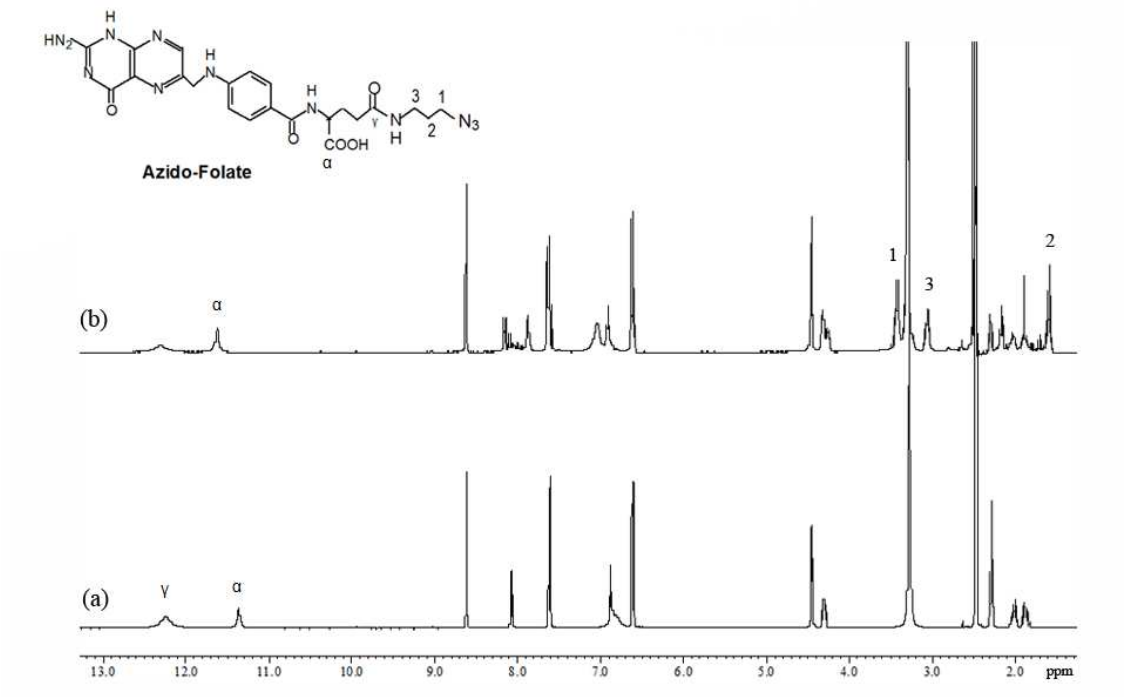


Figure S-2. ^{1}H NMR spectra of folate (a) and azido-folate (b) in *d_6-DMSO*.

3. Characterization of heterobifunctional PCL-*b*-PEG at different stage.

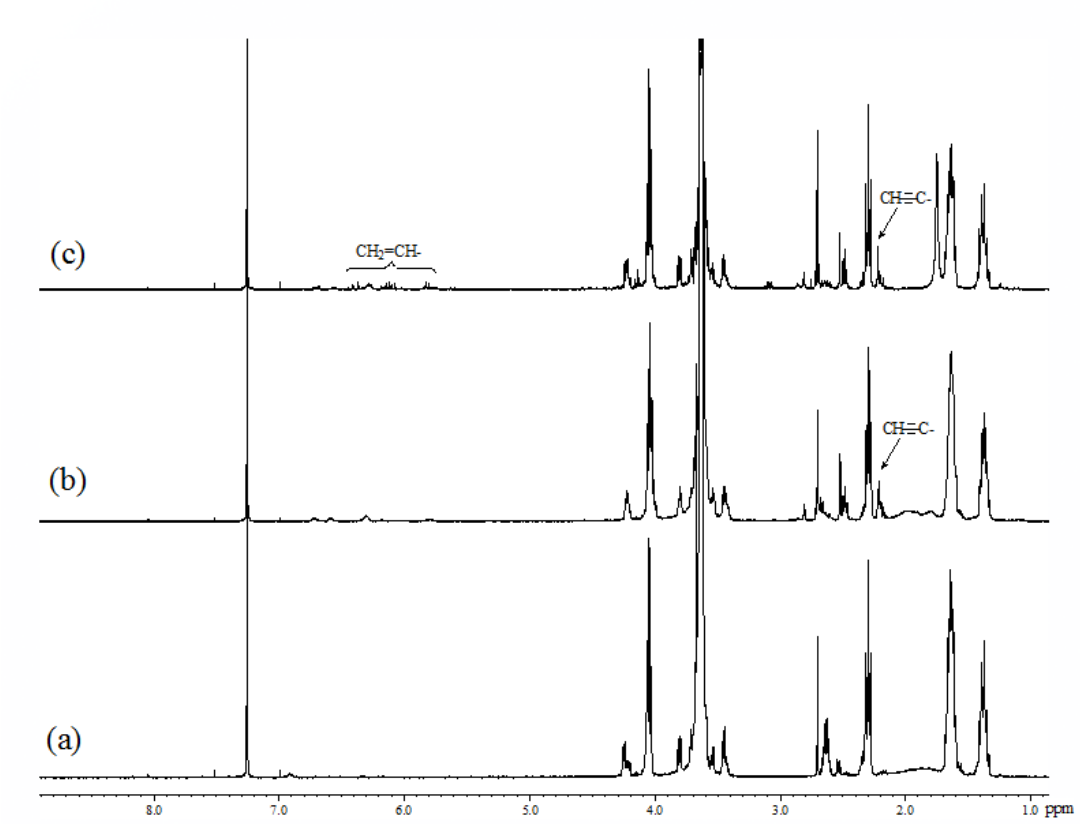


Figure S-3. ^{1}H NMR spectra of di-block polymer PEG-PCL (a), alkyne-functionized PEG-PCL (b) and bi-functional alkyne-PEG-PCL-acrylate (c) in $CDCl_3$.

4. Standard line of UV absorbance of folate solution.

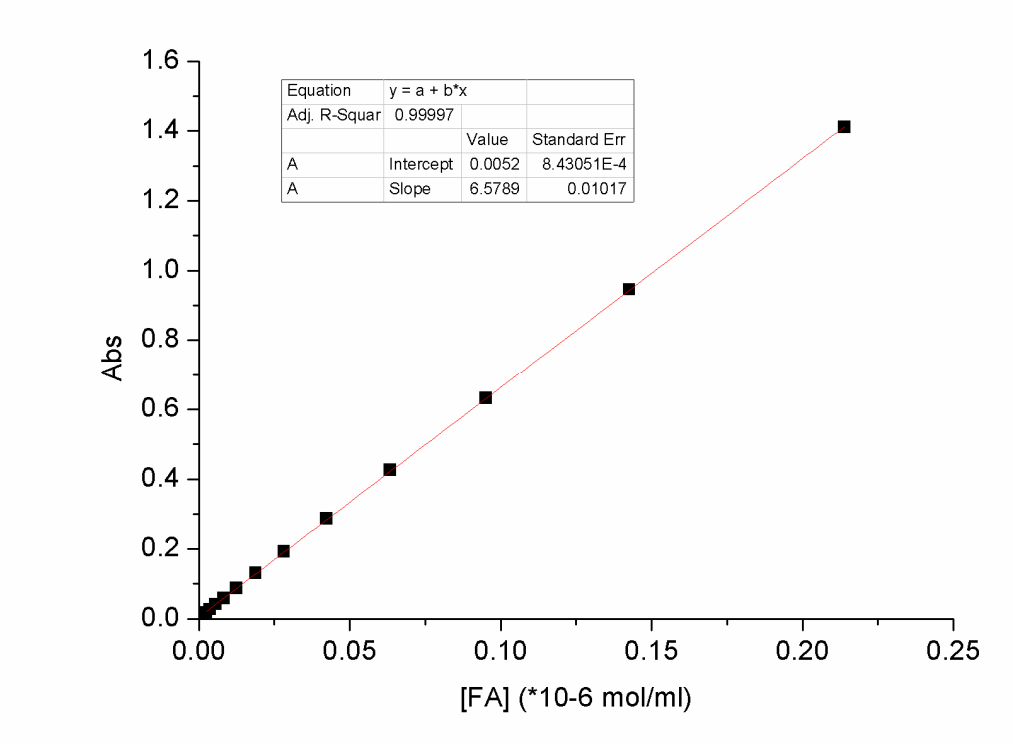


Figure S-4. Fit line of UV absorbance vs folate concentration.

5. FACS data of polyplexes with YOYO-1 labeled pDNA in KB cells.

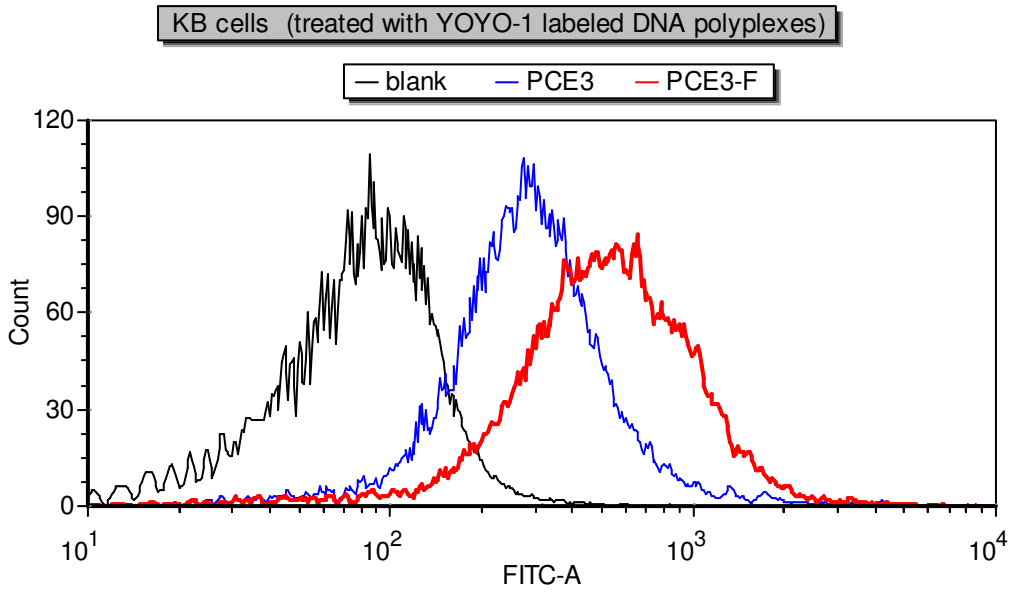


Figure S-5. FACS analysis of cellular uptake of polyplexes. KB cells were incubated with polyplexes using YOYO-1 labeled pDNA for 4 h.