Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Artificial Polymeric Receptors on the Cell Surface Promote the Efficient Cellular Uptake of Quantum Dots

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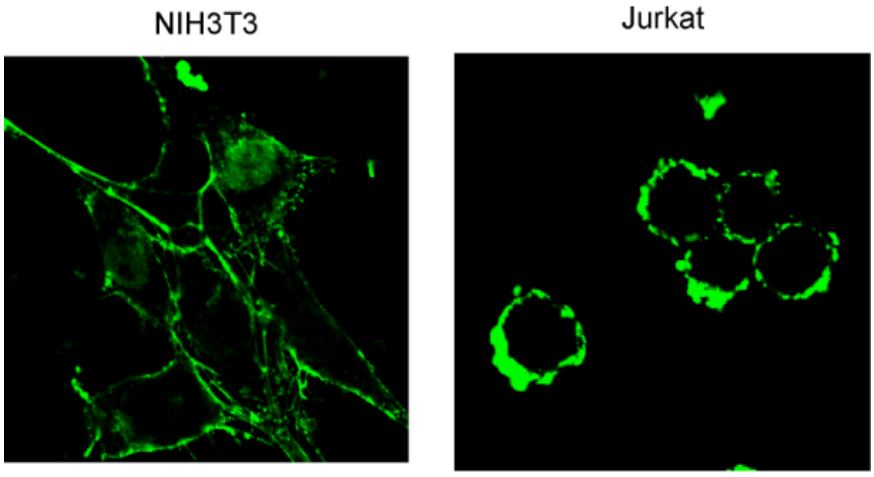

Figure S1 Fluorescence images of NIH3T3 and Jurkat cells treated with polymer **1** (25 μg/mL) for 10 min.

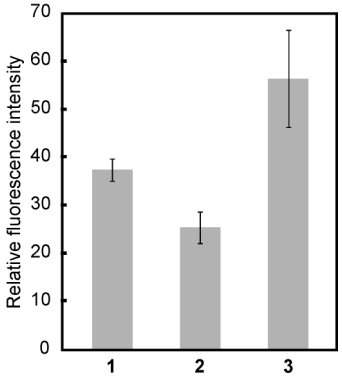

Figure S2 Flow cytometry analysis of HeLa cells treated with polymers **1**-**3**.

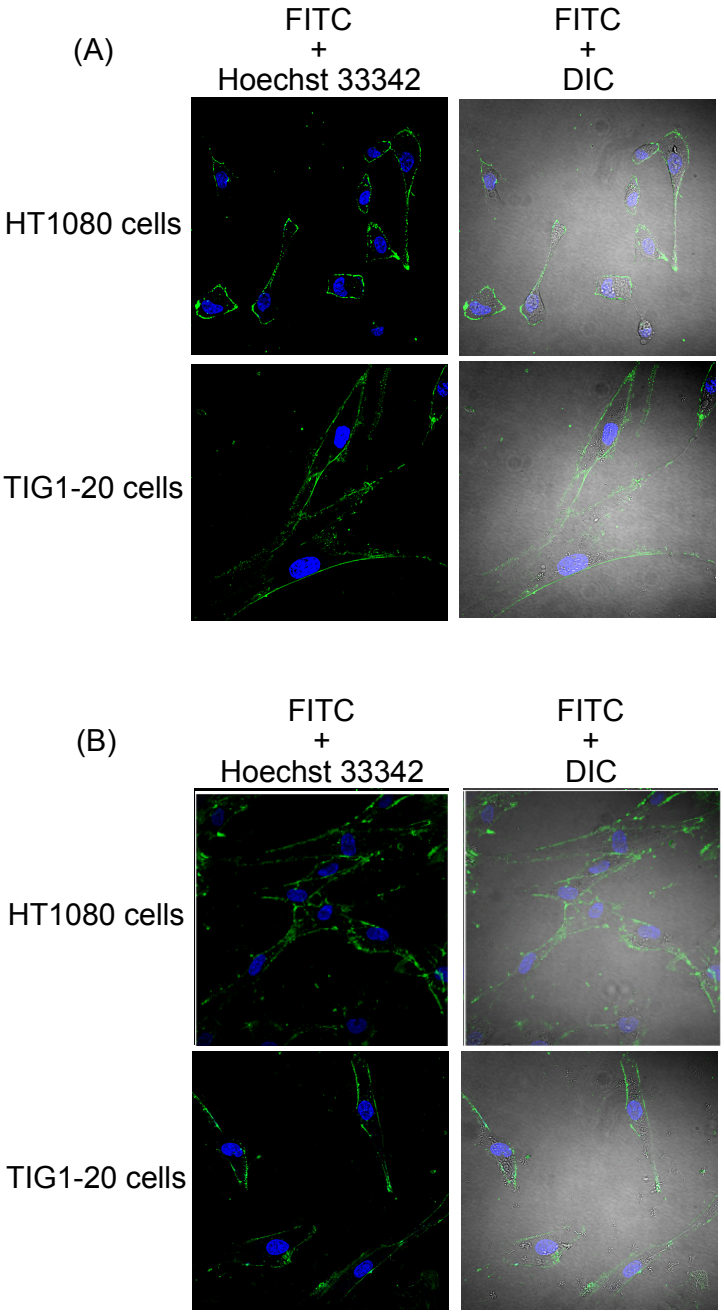

Figure S3 Fluorescence images of HT1080 and TIG1-20 cells (A) after incubation with *s*-amine polymer **6** for 10 min, (B) after incubation with GlcNAc polymer **6** for 10 min, washed with PBS buffer and subsequent culture for 1 hr in serum-free medium at 37 ºC. Green; fluorescence (FITC) from polymer **6**, Blue; Hoechst 33342.

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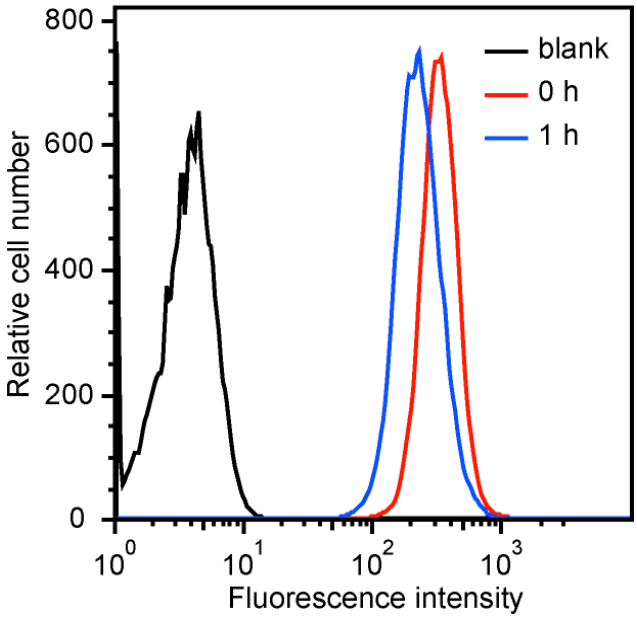


Figure S4 Flow cytometry analysis of HT1080 cells treated with GlcNAc polymer **6** for 10 min, washed with PBS, then incubated with serum reduced medium for 0 (red) or 1 h (blue).

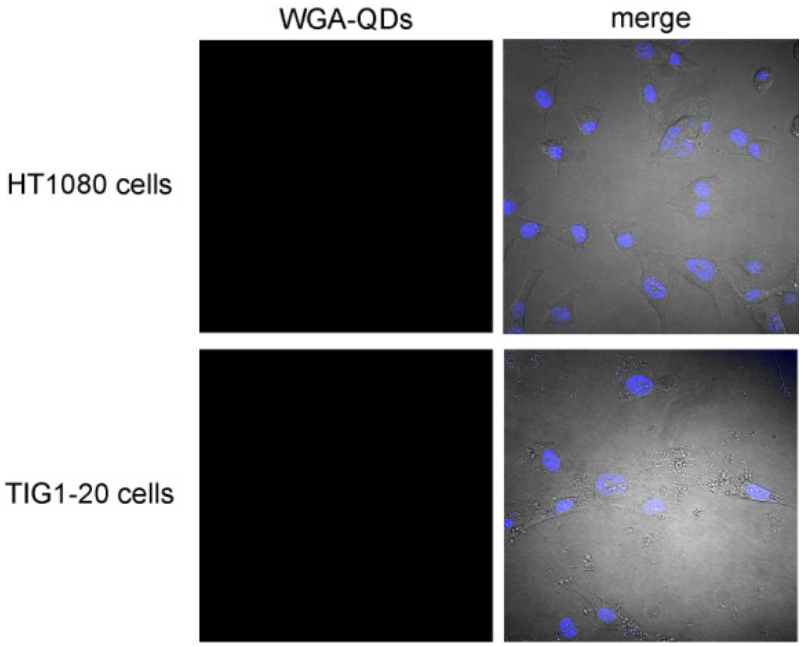


Figure S5 Fluorescence images of HT1080 and TIG1-20 cells treated with WGA-QDs for 1 h in the absence of polymers.

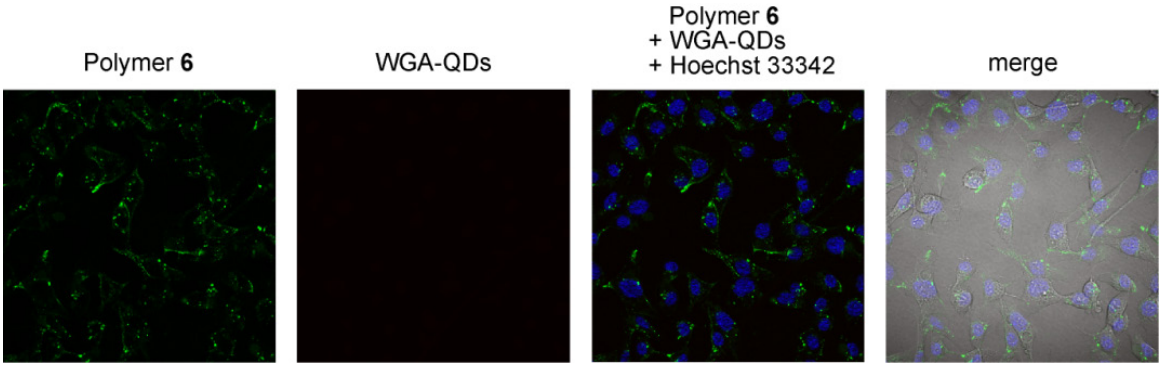


Figure S6 Fluorescence images of HT1080 cells after 1hr incubation with the premixed solution of GlcNAc polymer **6** and WGA-QDs. No fluorescence from QDs was observed.

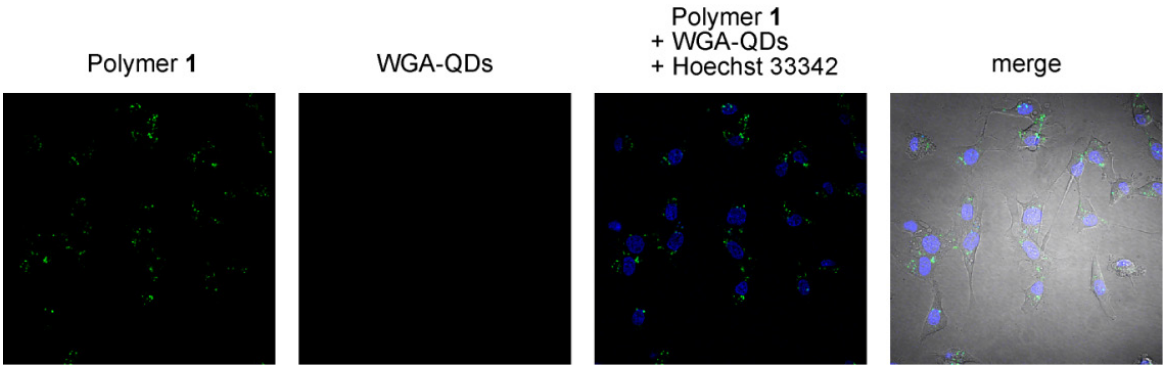


Figure S7 Fluorescence images of HT1080 cells treated with *s*-amine polymer **1** for 10 min, washed with PBS, and incubated with WGA-QDs for 1h. Green: FITC, Blue: Hoechst33342

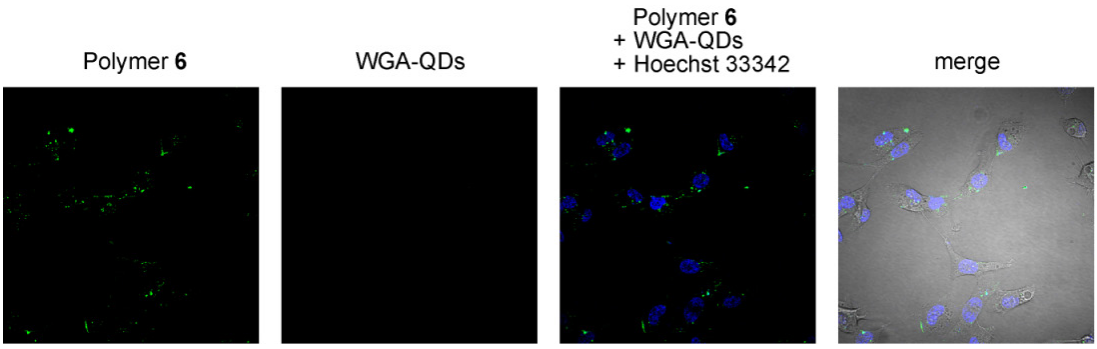
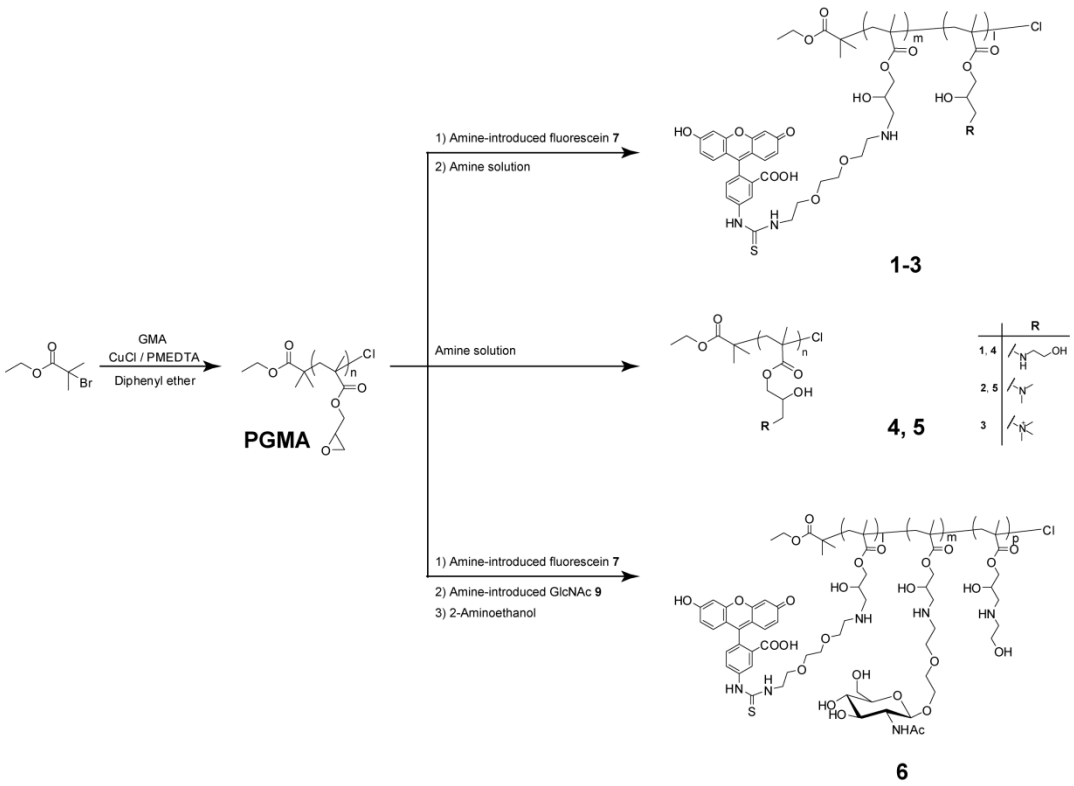


Figure S8 Fluorescence images of HT1080 cells treated with GlcNAc-polymer **6** for 10 min, washed with PBS, and incubated with WGA-QDs for 1h in the presence of GlcNAc (10mM) in the culture medium.

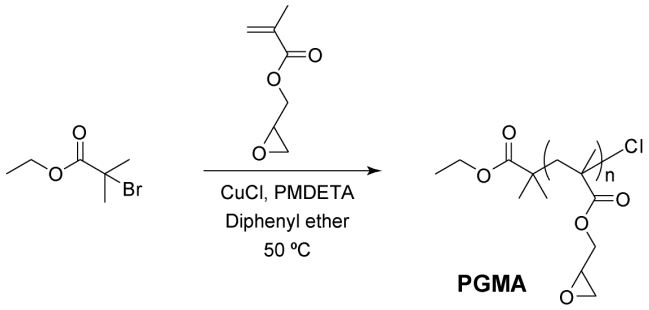
Materials and Methods

NMR spectra were recorded on a JEOL 400 spectrometer. MALDI-TOF-MS spectra were measured with a Voyager-DE STR-H spectrometer (Applied Bio Systems) using 2,5-dihydroxybenzoic acid (Bluker, Germany) as the matrix. Gel permeation chromatography (GPC) analysis was carried out at 40 °C on the HLC-8220 GPC system (TOSOH, Japan) equipped with the TSK gel Super HM-M column (TOSOH, Japan). Chloroform was used as an eluent at a flow rate of 0.3 mL/min. Polystyrene standards (Polymer Laboratories, USA) were used to calibrate the GPC system. Infrared reflection absorption spectra were measured using an FT/IR-660 fourier transform infrared (FT-IR) spectrometer (JASCO, Japan) equipped with a MCT detector. Single-channel transmittance spectra (256 scans) were collected at a spectral resolution of 4 cm^{-1}. Confocal laser scanning microscopy (CLSM) employed an Olympus FV300 microscope. Hoechst 33342 was excited with a 405 nm argon ion laser and emitted photons were collected through 445/15 nm band pass filter. Fluorescein isothiocyanate isomer I (FITC) was excited with a 488 nm argon ion laser and emitted photons were collected through 510 nm long pass filter. Texas Red was excited with a 543 nm argon ion laser and emitted photons were collected through 560 nm long pass filter. WGA-QDs (Invitrogen, Q12021MP, USA) were excited with a 405 nm laser and emitted photons were collected through 610 nm long pass filter. All images were processed with Adobe Photoshop 7.0.



Scheme S1 Synthetic scheme and chemical structures of polymers used in this study.

Synthesis of poly (glycidyl methacrylate) (PGMA)



Glycidyl methacrylate monomer (2.50 mL, 18.8 mmol) was dissolved in diphenyl ether (2.5 mL) and the solution was bubbled with dry nitrogen gas for 15 min. Purified CuCl (9.4 mg, 95 μmol) and pentamethyl-diethylenetriamine (PMDETA, 19.9 μL, 95 μmol) were added. After bubbling with dry nitrogen gas for 30 min, the ethyl-2-bromo-2-methylpropanoate (13.9 μL, 95 μmol) was added to start the polymerization. Reaction was carried out for the 120 min at 50 °C. After filtration through a short neutral alumina column to remove the copper complexes, the PGMA was precipitated from ethanol. Precipitation was collected by centrifugation and dried under reduced pressure.

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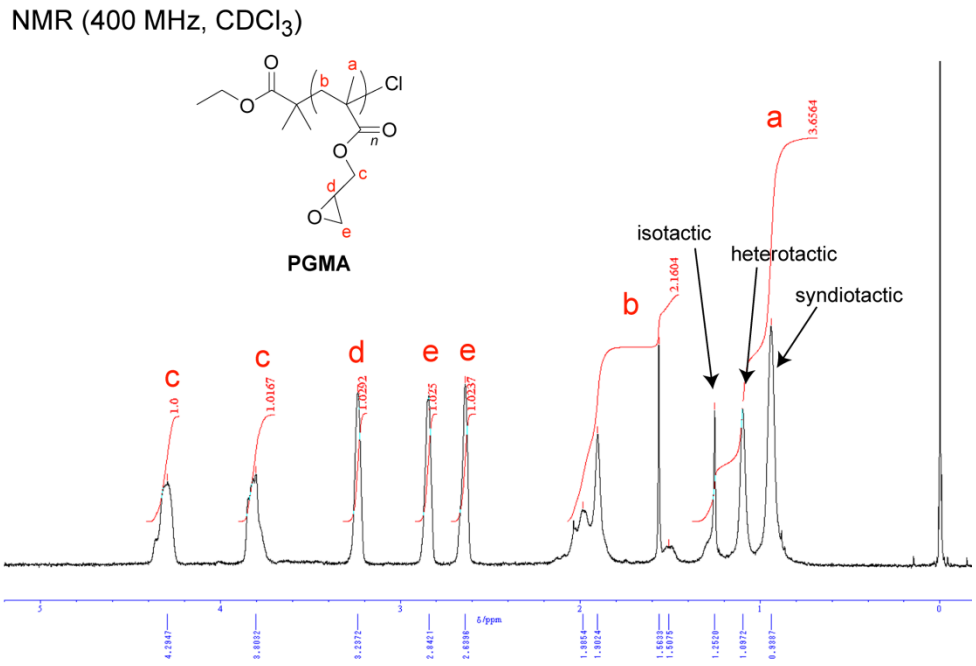
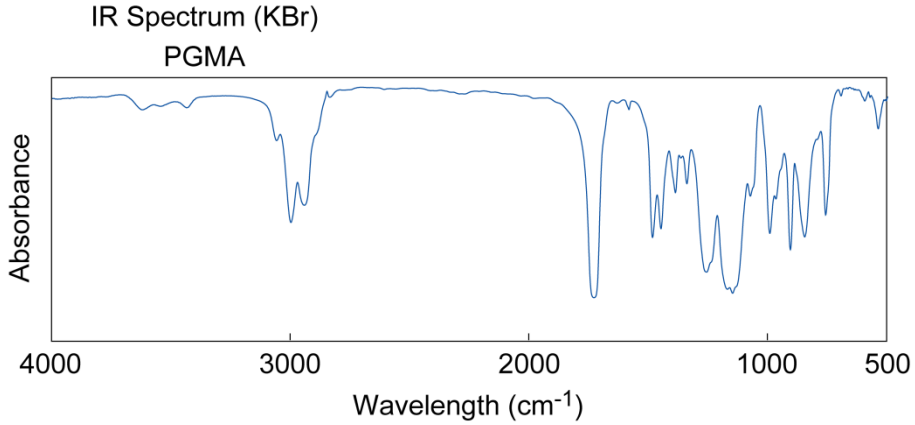
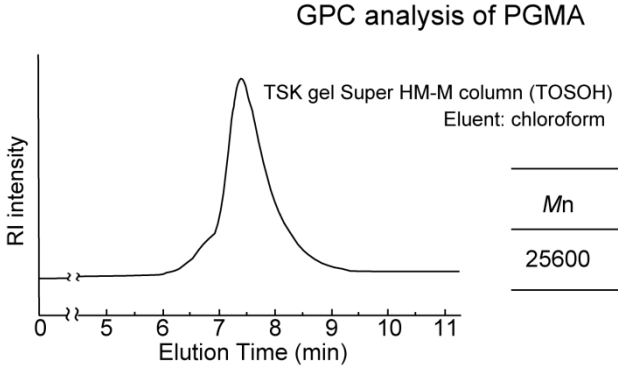


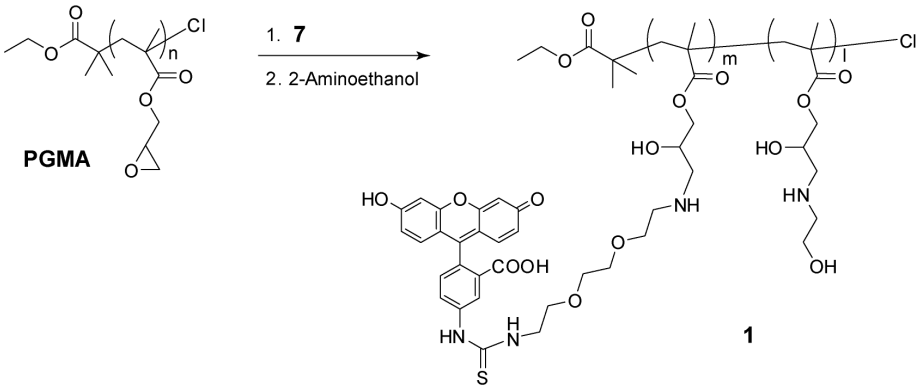




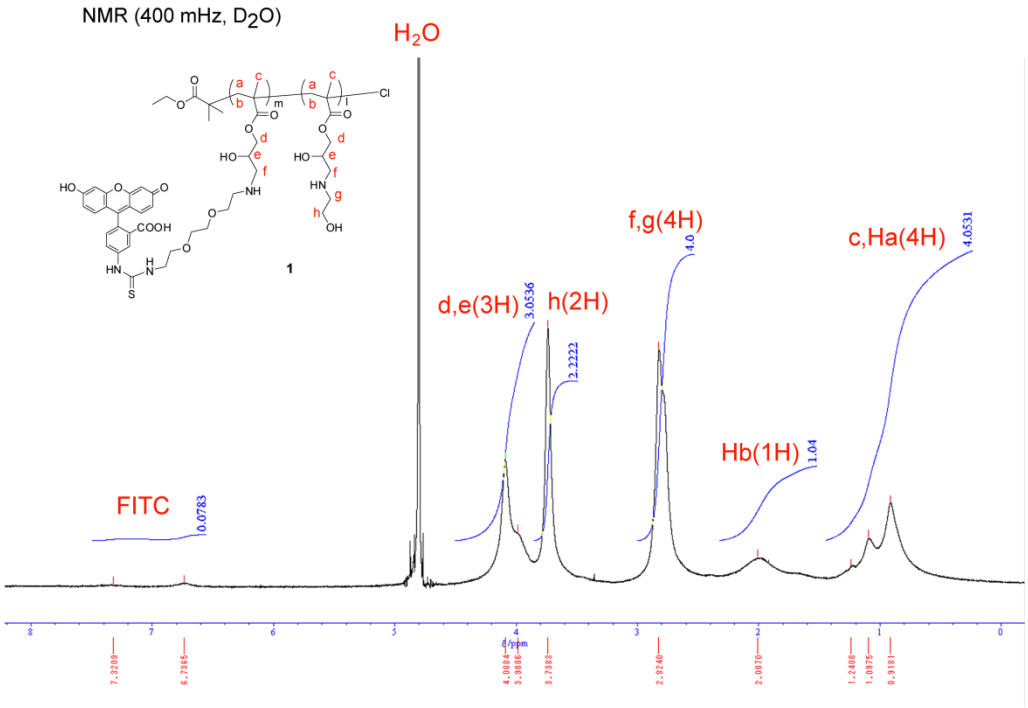
*M*n	*M*w	PDI (*M*w / *M*n)	polymerization degree (n)
25600	33000	1.29	180

Figure S9 NMR, IR, GPC analysis of **PGMA**.

Synthesis of FITC-appended secondary amine-polymer (1)



To a solution of PGMA (20.0 mg) in DMF/MeOH (1:1 v/v, 1.0 mL) were added amine-introduced fluorescein **8** (15.2 mg, 28.3 μmol). The mixture was stirred for 12 hours at 50 °C. 2-Aminoethanol (2 mL) was added and stirred for 1 day at room temperature. The solution was dialyzed using a 11,000 MWCO membrane in distilled water for 3 days and lyophilized to give **1** as a yellow solid; IR (KBr, cm^{-1}): 3390, 2944, 1727, 1636, 1577, 1459, 1277, 1164, 1057.



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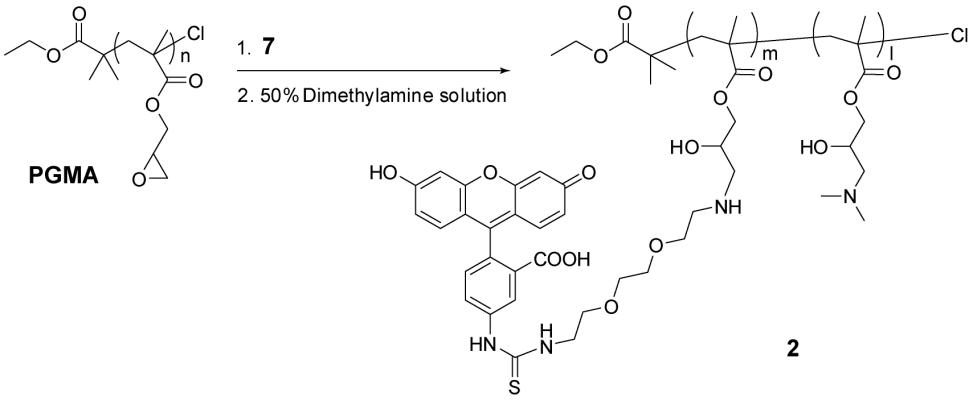
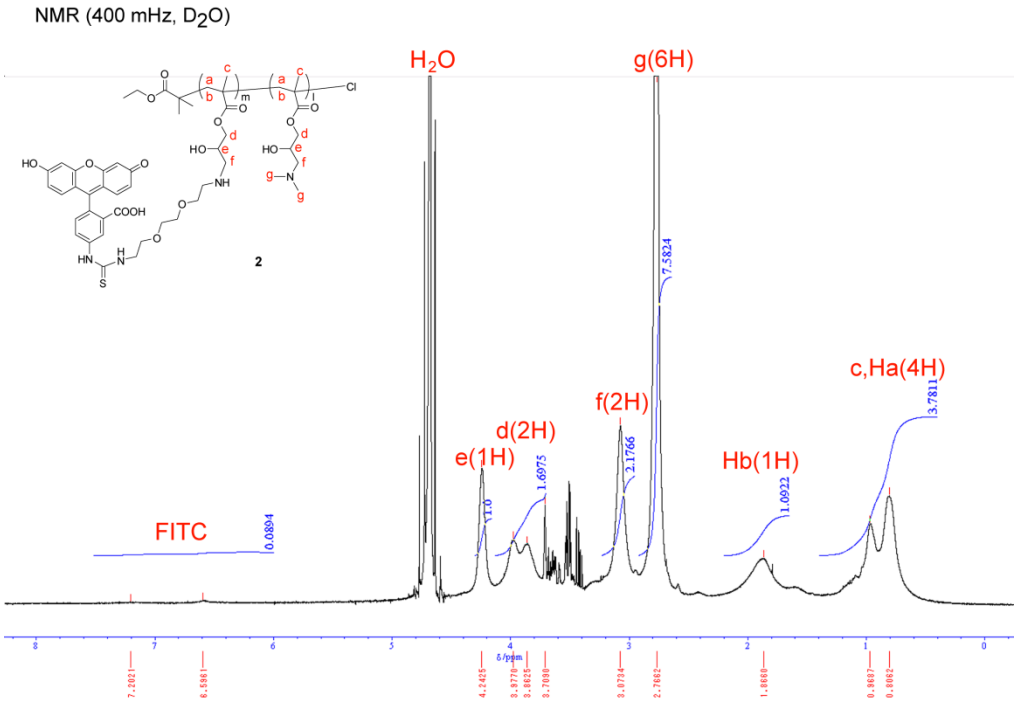
Synthesis of FITC-appended tertiary amine-polymer (2)



To a solution of PGMA (20.0 mg) in DMF/MeOH (1:1 v/v, 1.0 mL) were added amine-introduced fluorescein **7** (15.2 mg, 28.3 μmol). The mixture was stirred for 12 hours at 50 °C. 50% dimethylamine solution (2 mL) was added and stirred for 1 day at room temperature. The solution was dialyzed using a 11,000 MWCO membrane in distilled water for 3 days and lyophilized to give **2** as a yellow solid.



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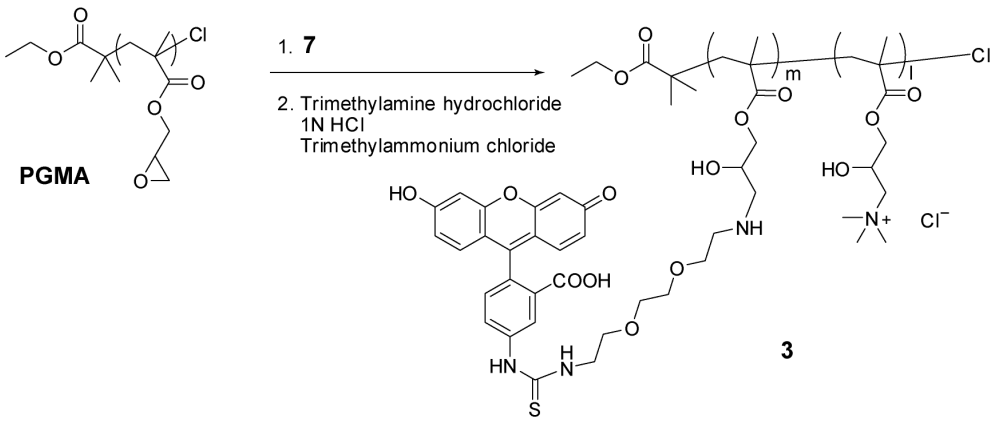
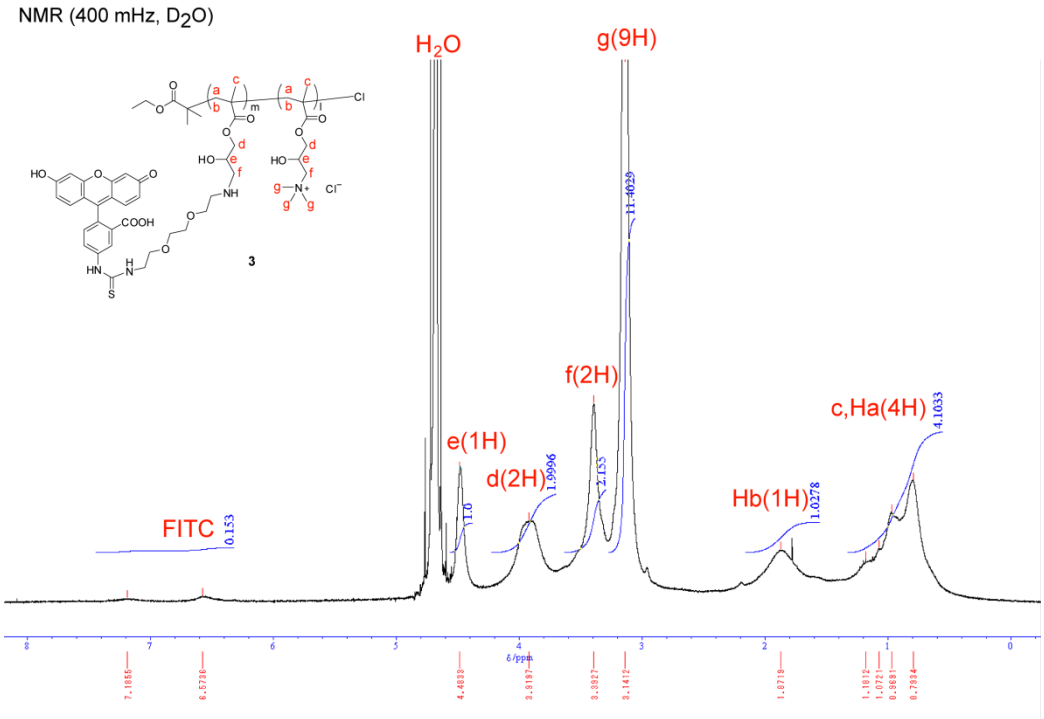
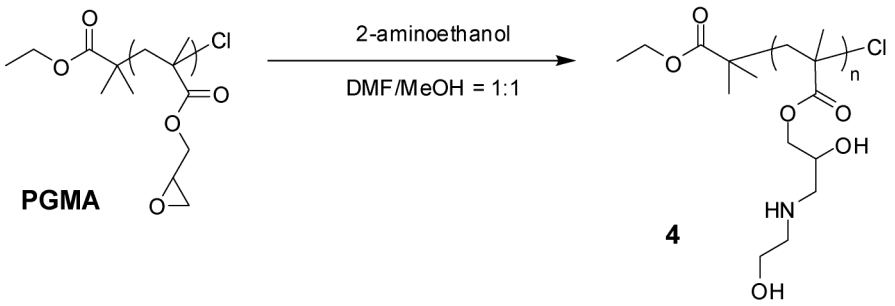
Synthesis of FITC-appended quaternary amine-polymer (3)



To a solution of ethyl-PGMA **1** (20.0 mg) in DMF/MeOH (1:1 v/v, 1.0 mL) were added amine-introduced fluorescein **7** (15.2 mg, 28.3 μmol). The mixture was stirred for 12 hours at 50 °C. Equimolar amount of 70% trimethylammonium solution, 1N HCl aq. (total 4 mL) and a catalytic amount of trimethylammonium chrolide were added and stirred for 1 day at 70 °C. The solution was dialyzed using a 11,000 MWCO membrane in distilled water for 3 days and lyophilized to give **3** as a yellow solid.

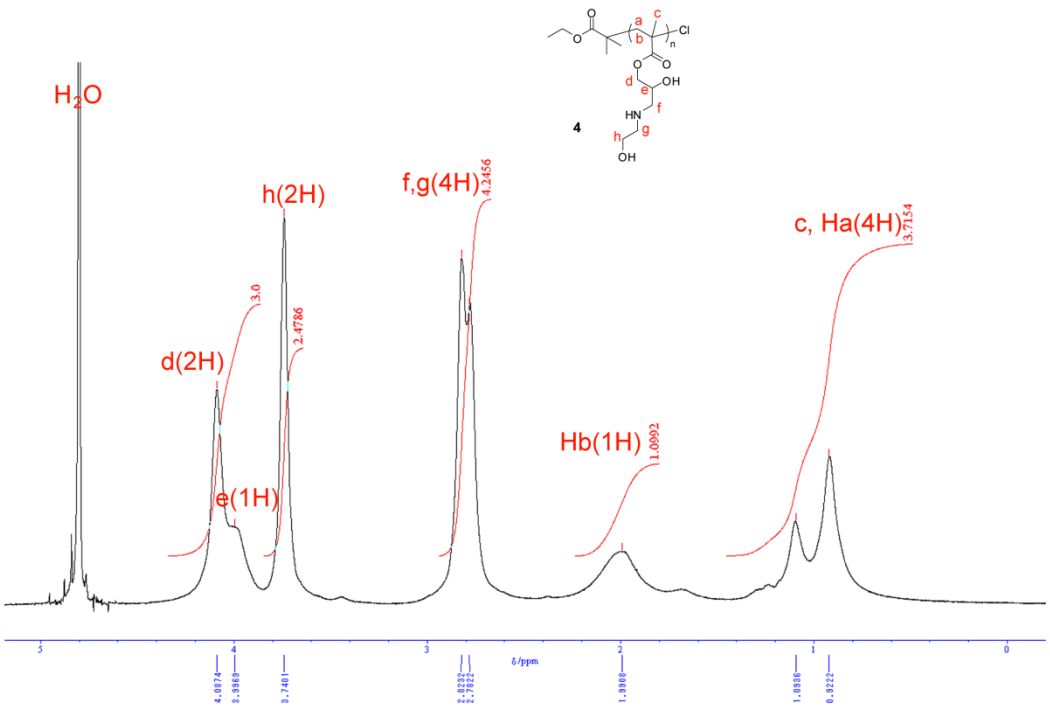


Synthesis of secondary amine-polymer (4)

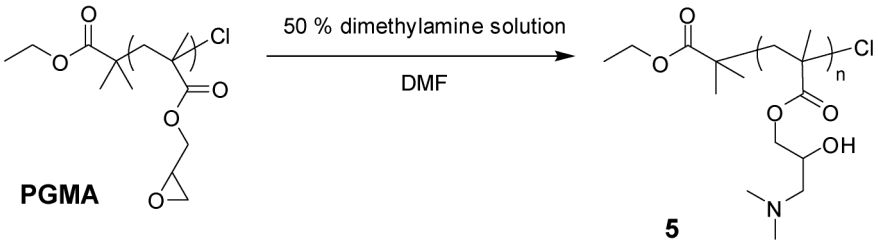


To a solution of PGMA (20.0 mg) in DMF/MeOH (1:1 v/v, 1.0 mL), 2-aminoethanol (2 mL) was added and stirred for 1 day at 50 °C. The solution was dialyzed using a 11,000 MWCO membrane in distilled water for 3 days and lyophilized to give **4** as a white solid; IR (KBr, cm^{-1}): 3421, 2944, 1732, 1653, 1457, 1276, 1164, 1056, 1276.

NMR (400 mHz, D_2O)

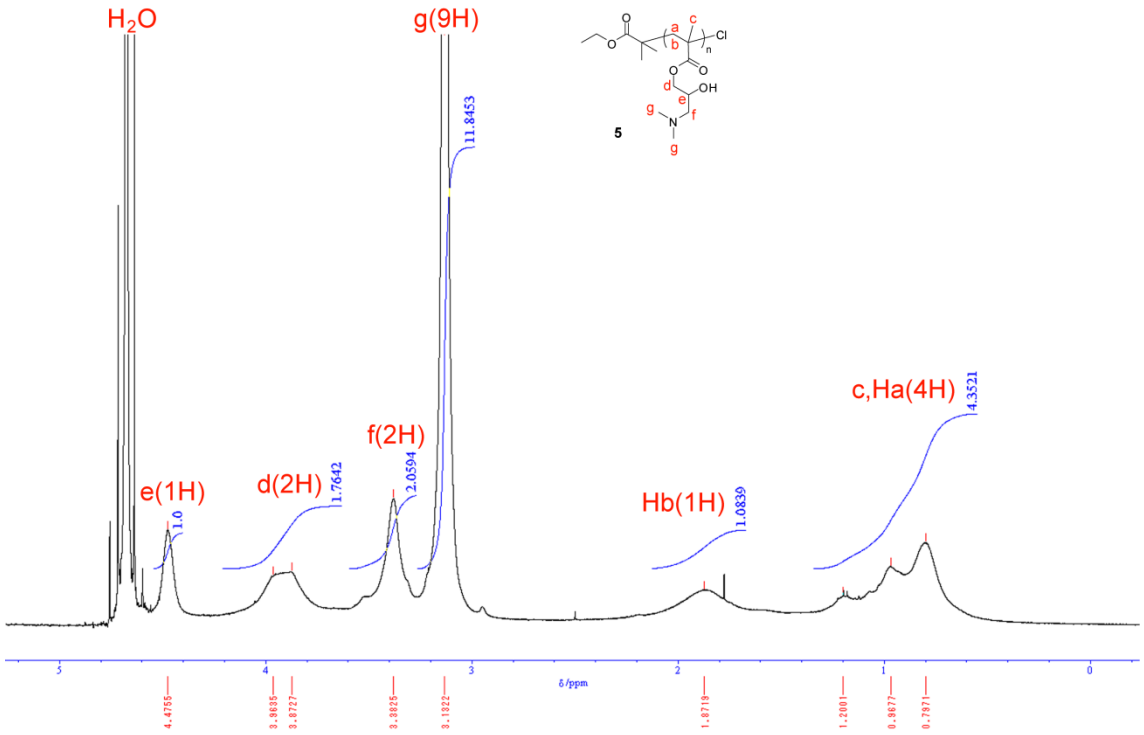


Synthesis of tertiary amine-polymer (5)



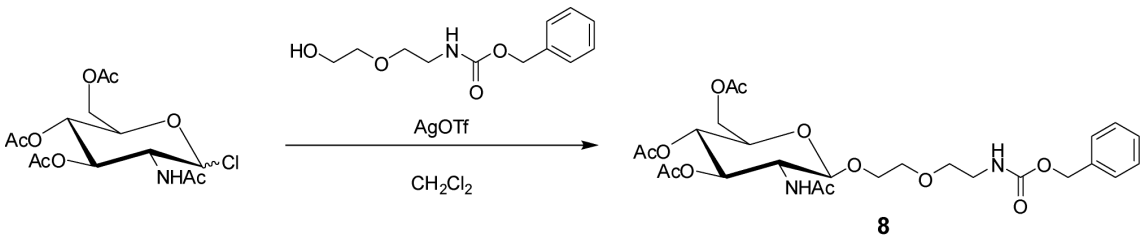
To a solution of PGMA (20.0 mg) in DMF (10 mL), 50% dimethylamine solution (2 mL) was added and stirred for 1 day at 50 °C. The solution was dialyzed using a 11,000 MWCO membrane in distilled water for 3 days and lyophilized to give **5** as a white solid.

NMR (400 mHz, D_2O)



Synthetic scheme of amine-introduced GlcNAc

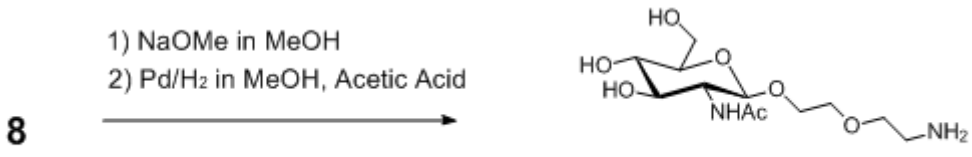
5-Benzyl-3-oxa-pentyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (8)



8

A solution of 1-chloro-2-acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-α-D-glucose (1.34 g, 3.66 mmol, Tokyo Kasei Co., Japan), 2-[2-*N*-(benzyloxycarbonyl)aminoethoxy]ethanol (0.70 g, 2.93 mmol) and silver trifluoromethanesulfonate (940 mg, 3.66 mmol) in anhydrous CH_2Cl_2 were stirred for 15 h under a nitrogen atmosphere at 40 °C. The reaction was quenched by addition of TEA, filtered with $CHCl_3$. The filtrate was washed with aqueous $NaHCO_3$ and brine. The organic layer dried with Na_2SO_4. After filtration, the solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel, $CHCl_3$/EtOAc 1:1) to give 1.35 g (81%) of **8** as a white solid; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.37 (br, 5H, aromatic), 5.90 (br, 1H, CH-N*H*-CO), 5.44 (br, 1H, CH_2-N*H*-CO), 5.31 (dd, 1H, *J* =9.7 and 10.2 Hz, H-3), 5.15 (s, 2H, Ph-CH_2-O), 5.04 (dd, 1H, *J* =9.7 and 9.7 Hz, H-4), 4.74 (d, 1H, *J* =8.3 Hz, H-1), 4.23 (dd, 1H, *J* =4.7 and 12.9 Hz, H-6), 4.12 (m, 1H, H-6), 3.92 (m, 1H, CH-O-C*H*H), 3.81 (m, 1H, H-2), 3.71-3.53 (m, 6H, H-5, CH*H*-CH_2-O-CH_2-CH_2-NH), 3.45-3.30 (m, 2H, O-CH_2-CH_2-NH), 2.07 (s, 3H, CH_3-CO), 2.03 (s, 3H, CH_3-CO), 2.02 (s, 3H, CH_3-CO), 1.90 (s, 3H, CH_3-CO); ^{13}C-NMR(150 MHz, $CDCl_3$): 170.78, 170.46, 169.39, 156.93, 135.52, 128.54, 128.13, 128.05, 100.75, 77.21, 77.00, 76.79, 72.23, 71.72, 70.23, 70.11, 68.61, 68.57, 66.64, 62.04, 54.64, 40.95, 23.18, 20.74, 20.68, 20.62; Elemental analysis: calcd: C, 54.92; H, 6.38; N, 4.93. Found: C, 54.77; H, 6.34; N, 4.92; MALDI-TOF-MS (pos) calcd. for $C_{26}H_{36}N_2NaO_{12}$ $[M+Na]^+$: 591.22; found 591.37; HR-FAB-MS calcd. for $C_{26}H_{37}N_2O_{12}[M+H]^+$: 569.2348, found: 569.2346.

2-(2-Aminoethoxy)ethyl 2-(acetylamino)-2-deoxy-β-D-glucopyranoside (9)



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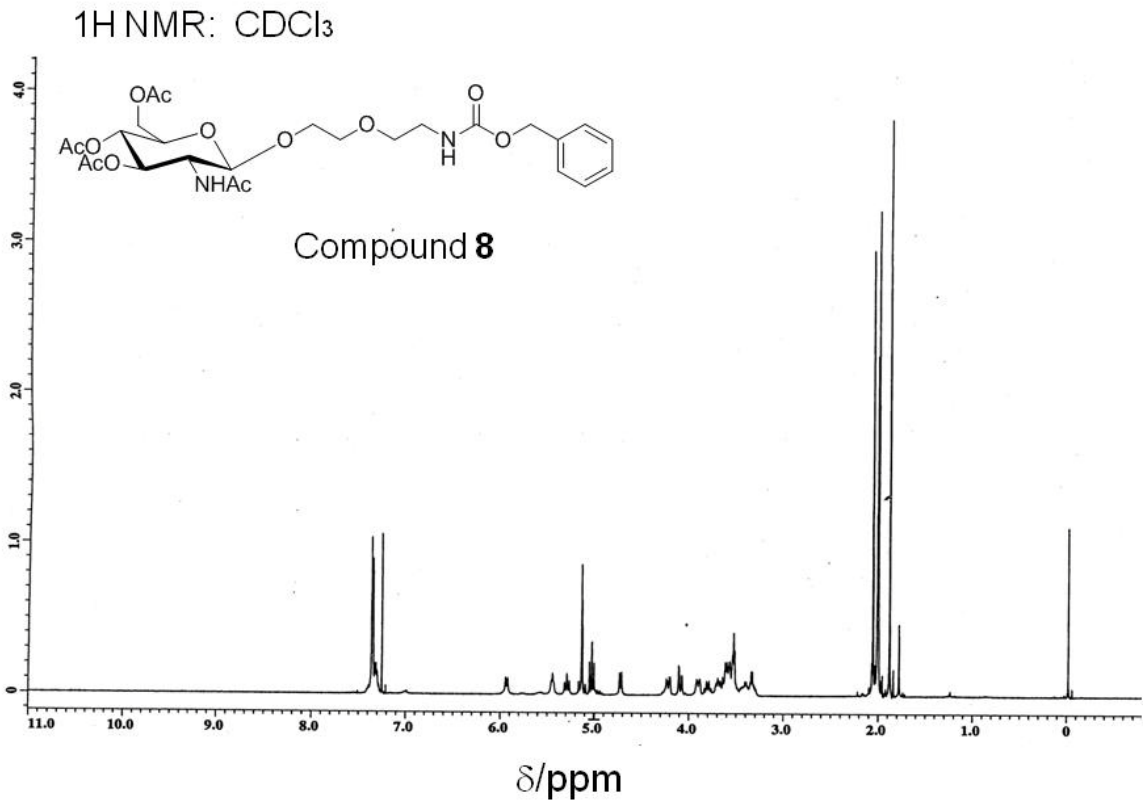
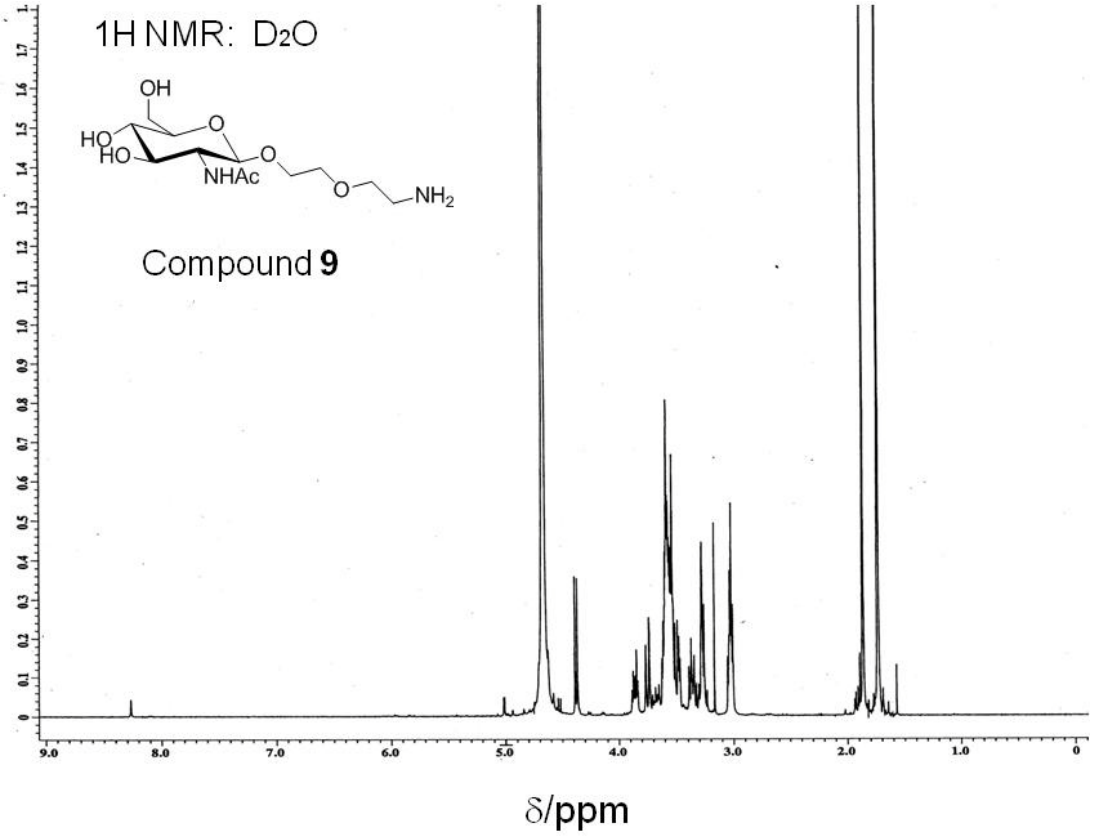
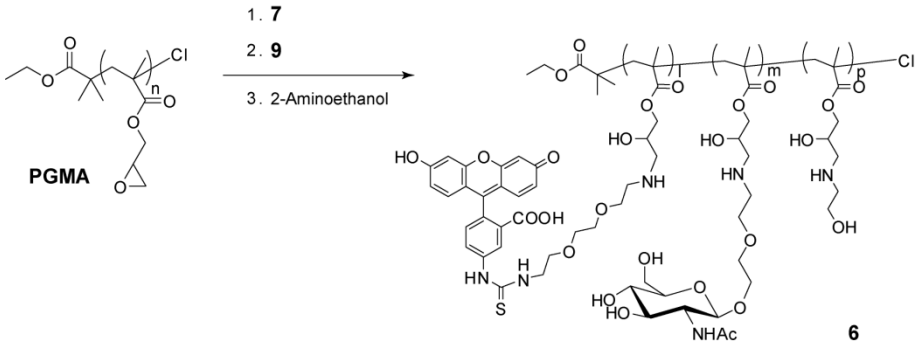
9

GlcNAc derivative **8** (1.35 g, 2.38 mmol) was dissolved in methanol. Sodium methoxide (33.6 mg, 621 µmol) was added to the solution and stirred for 2 h at room temperature. After neutralized with DOWEX-50 (H^+ form) resin, the solvent was evaporated. The residue was dissolved in methanol (20 mL), H_2O (5 mL) and acetic acid (500 µL). The solution was stirred in the presence of 20% $Pd(OH)_2/C$ (cat.) for 24 h under H_2. The mixture was filtered and concentrated under reduced pressure to give 594 mg (81%) of **9** as a white solid; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 4.53 (d, *J* =8.3 Hz, H-1), 4.02 (m, 1H, CH-O-C*H*H), 3.91 (dd, 1H, *J* =1.9 and 12.5 Hz, H-6), 3.78-3.65 (m, 7H, H-6, CH*H*-CH_2-O-CH_2), 3.53 (m, 1H, H-3), 3.42 (m, 2H, H-4, H-5), 3.18 (m, 2H, -CH_2-NH), 2.02 (s, 3H, CH_3-CO); ^{13}C-NMR(150 MHz, D_2O): 173.85, 100.44, 75.12, 73.05, 69.09, 68.81, 68.37, 66.99, 59.90, 54.74, 38.51, 21.39; Elemental analysis(monohydrate as a Cl^- form): calcd: C, 39.73; H, 7.50; N, 7.72. Found: C, 40.17; H, 7.18; N, 7.80; MALDI-TOF-MS (pos) calcd. for $C_{12}H_{24}N_2O_7$ $[M+H]^+$: 309.17; found 309.34; HR-FAB-MS calcd. for $C_{12}H_{24}N_2O_7$: 309.1662, found: 309.1650.





Synthesis of FITC-appended GlcNAc-polymer (6)



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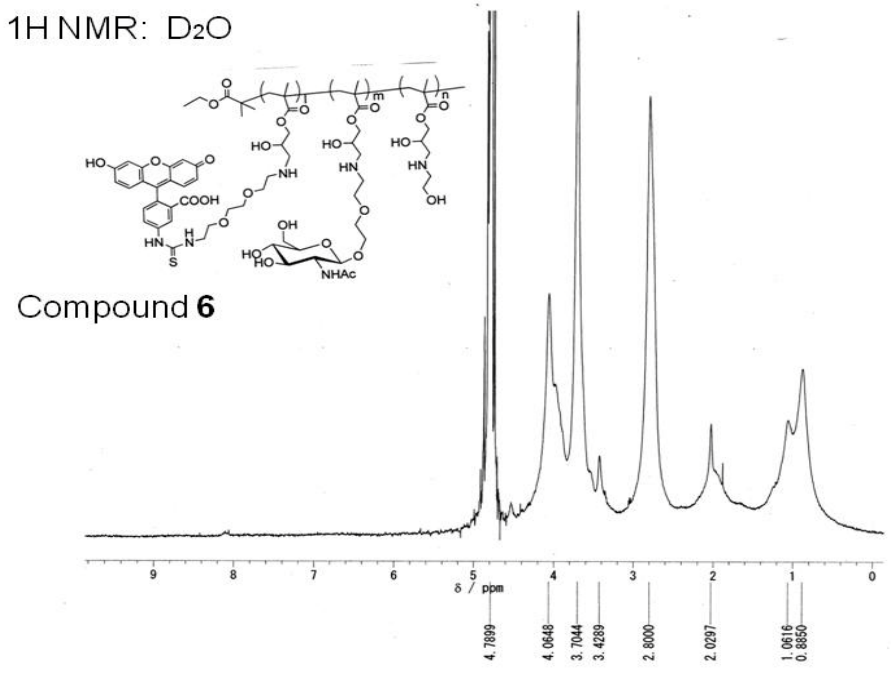
To a solution of PGMA (55.2 mg) in DMF/MeOH (1:1 v/v, 1.0 mL) were added amine-introduced fluorescein **7** (1.50 mg, 2.79μmol). The mixture was stirred for 24 hours at 50 °C. Amine-introduced GlcNAc **9** (25.6 mg, 83.2 μmol) were added and stirred for 1 day at 50 °C. 2-aminoethanol (100 μL, 3.31 mmol) was added and stirred for 1 day at 50 °C. The solution was dialyzed using a 11,000 MWCO membrane in H_2O for 3 days and lyophilized to give 40.0 mg of **6** as a yellow solid; IR (KBr, cm^{-1}): 3369, 2941, 1726, 1559, 1457, 1269, 1160, 1061.



Compound **6 (IR)**