Chemical Compound Preparation

Instruments. ^{1}H-NMR spectra were recorded in $CDCl_3$ or D_2O on a Varian Merc-300 or Varian Inova-500 spectrometers equipped with Sun workstations at 300K. TMS (δ_H=0.00) or D_2O (δ_H=4.67) was used as the internal reference. ^{13}C-NMR spectra were recorded in $CDCl_3$ or D_2O at 75MHz on Varian Mercury-300 spectrometer, respectively using the central resonance of $CDCl_3$ (δ_C=77.0) as the internal reference. COSY, HSQC, HMBC and TOCSY experiments were used to assist assignment of the products. Mass spectra were obtained on Applied Biosystems Voyager DE-Pro MALDI-TOF. FTIR Spectra were obtained on a Shimadzu IRPrestige-21 spectrophotometer. Size exclusion chromatography (SEC) was performed with Waters 515 fitted with two columns (Styragel® HT3 and HT4 7.8×300mm Columns) connected in series and OPTILAB DSP interferometric refractometer (Wyatt Technology Corporation, USA) with $CHCl_3$ and polystyrene as mobile phase and standard respectively.

Materials. Alexa Fluor® 488 azide **8** (Invitrogen); 1-α-(3-azidopropyl)-*D*-Mannopyranoside **9** was prepared as reported in the literature[1]; 7-ethylcamptothecin (7-Et-CPT, 98%, OChem Incorporation); Fmoc-L-amino acid derivatives and resins were purchased from NovaBioChem and Applied Biosystems; peptide synthesis grade *N, N*- dimethylformamide (DMF) from EM Science and *N*-methylpyrrolidone (NMP) from Applied Biosystems. Chemicals were purchased and used without further purification unless otherwise specified. DCM was distilled from calcium hydride; THF from sodium; CH_3OH from magnesium and iodine. Aqueous solutions are saturated unless otherwise specified. All the reactions were performed under anhydrous conditions under argon and monitored by TLC on Kieselgel 60 F254 (Merck). Detection was by examination under UV light (254 nm), by iodine vapor staining or by charring with 10% sulfuric acid in methanol. Silica gel (Merck, 70-230 mesh) was used for chromatographies. Iatrobeads 6RS-8060 was purchased from Bioscan.

Synthesis of copolymer 4. A one-pot cation ring opening polymerization at 130 ºC under a stream of argon was adapted from a previously reported preparation of PEO-*b*-PCL[2] with some modifications. Briefly, ε-caprolactone monomer (3.5 mL, 31.6 mmol) and MeO-PEG2000-OH **1** (2.5 g, 1.25 mmol) were placed under a nitrogen atmosphere and then a drop of SnOct was added. The mixture was cooled by placing in a bath filled with liquid nitrogen and then evacuated,

sealed off, and kept at 130 °C for 24 h. The resulting polymer was dissolved in THF (20 mL), precipitation by the addition of cold hexane (1000 mL), collected by filtration and then dried *in vacuo* at room temperature to give the product as a white solid (5.4 g, ~90%). The degree of the polymerization of the PCL and the polydispersity was determined by SEC. The degree of polymerization of the PCL was also measured by ^{1}H NMR relative to the degree of polymerization of the PEO. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.10-4.02 (52H, m, $CH_2CH_2CH_2O$), 3.80-3.58 (180H, m, CH_2O), 3.38 (3H, s, CH_3O), 2.26-2.20 (52H, m, $CH_2C{=}O$), 1.65-1.55 (104H, m, CH_2), 1.30-1.22 (52H, m, CH_2). M_n (SEC): 6010 (polydispersity index (PDI) = 1.53).

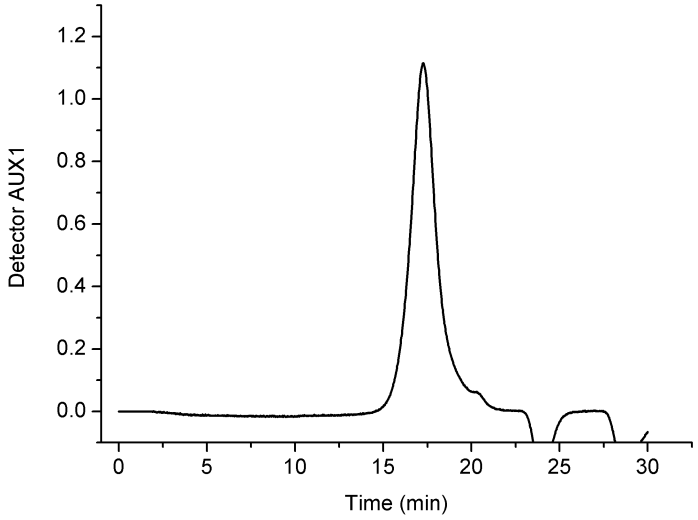

Figure S1. SEC of Polymer **4**.

Synthesis of N_3-PEG$_{45}$-OH (2). Tosyl chloride (1.9 g, 10.0 mmol) was added to a solution of PEG2000 diol (20.0 g, average molecular weight 2,000 Da, 10.0 mmol) in CH_2Cl_2 (100 mL) and pyridine (4 mL). The resulting mixture was stirred at r.t. for 18 h. The solvent was removed under reduced pressure, the resulting residue was dissolved in DMF (30 mL) and sodium azide (1.3 g, 20.0 mmol) was added and the reaction mixture was stirred at 80 °C for 8 h. CH_2Cl_2 (250 mL) was added and the resulting solution was washed with water (25 mL). The organic layer was dried ($MgSO_4$), and the solvents were removed *in vacuo*. The residue was purified by silica gel chromatography (CH_2Cl_2/CH_3OH, 10/1, v/v) to afford **7** as a white solid (11.74 g, 58% two-

steps). ^{1}H NMR ($CDCl_3$, 300MHz) δ 3.69 (2H, m, CH_2OH), 3.65–3.58 (180H, m, CH_2O), 3.38 (2H, m, CH_2N_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.7, 70.9, 70.9, 70.8, 70.6, 70.3, 61.9, 50.9.

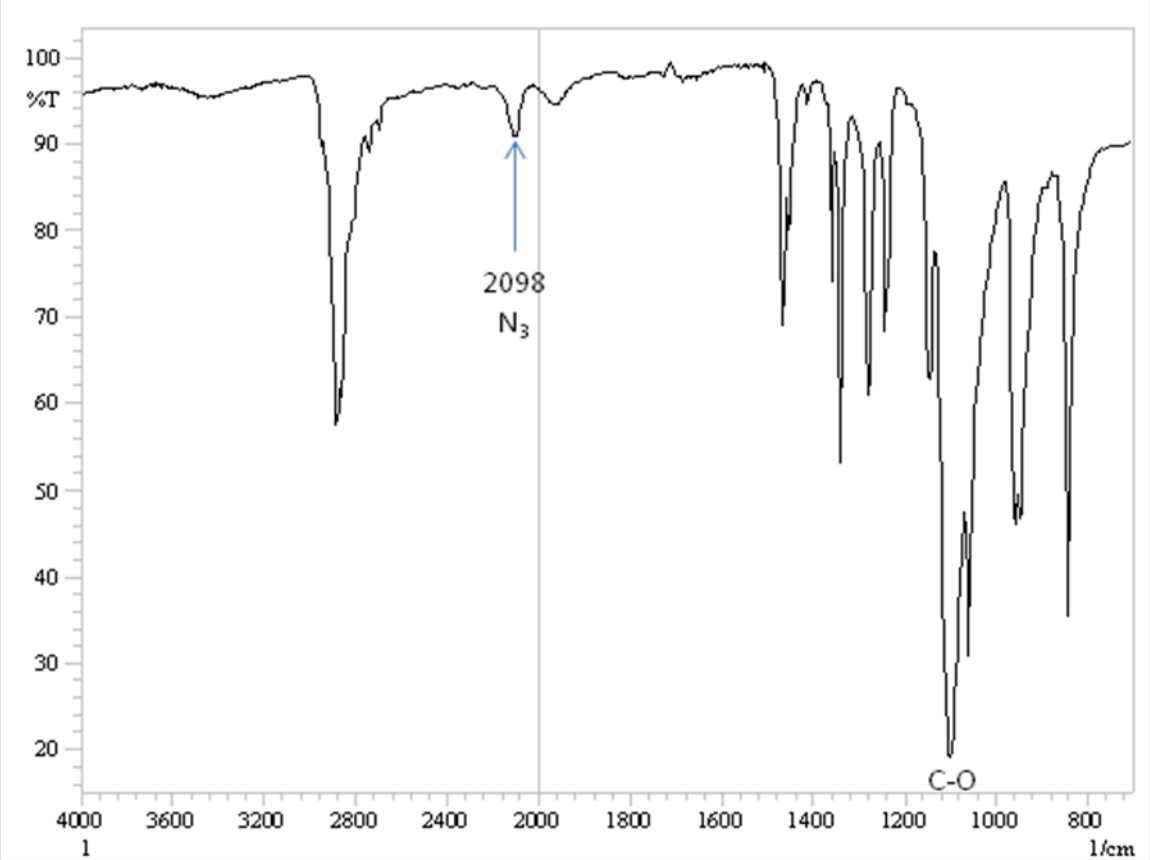

Figure S2. IR spectrum of polymer **2**.

Synthesis of copolymer 5. N_3-PEO-*b*-PCL was synthesized by a one-pot cation ring opening polymerization at 130 °C under a stream of argon as previously reported[2] for the preparation of PEO-*b*-PCL with some modifications. Briefly, ε-caprolactone monomer (3.5 mL, 31.6 mmol) was added to a flask containing N_3-PEG-OH (**2**) (2.5 g, 1.235 mmol) and the resulting mixture was placed under a nitrogen atmosphere and then a drop of SnOct was added. The mixture was cooled by placing it in a bath of liquid nitrogen and then evacuated, sealed off, and kept at 130 °C for 24 h. The resulting polymer was dissolved in THF (20 mL), precipitated by the addition of ice-cold hexane (1,000 mL), collected by filtration and then dried *in vacuo* at room temperature to give **5** as a white solid (5.5 g, ~91%). The degree of the polymerization of PCL and the polydispersity was determined by SEC. The degree of polymerization of the PCL was also

measured by ^{1}H NMR relative to the degree of polymerization of PEO. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.10-4.02 (52H, m, $CH_2CH_2CH_2O$), 3.80-3.58 (178H, m, CH_2O), 3.36 (2H, m, CH_2N_3), 2.26-2.20 (52H, m, $CH_2C{=}O$), 1.65-1.55 (104H, m, CH_2), 1.30-1.22 (52H, m, CH_2). M_n (SEC): 6070 (polydispersity index (PDI) = 1.46).

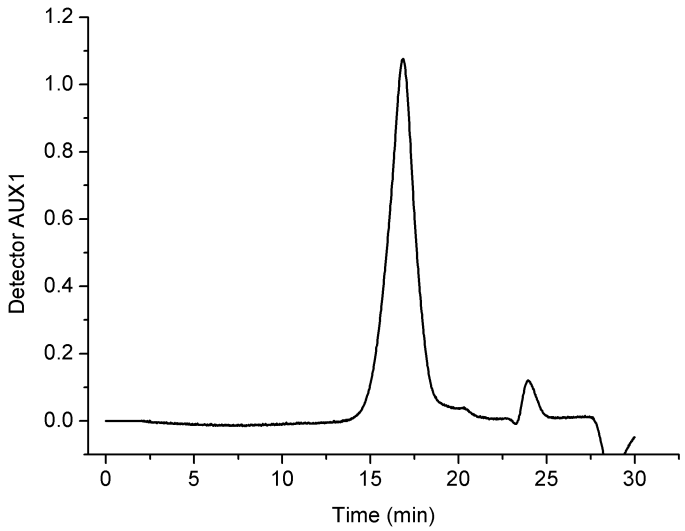

Figure S3. SEC of polymer **5**.

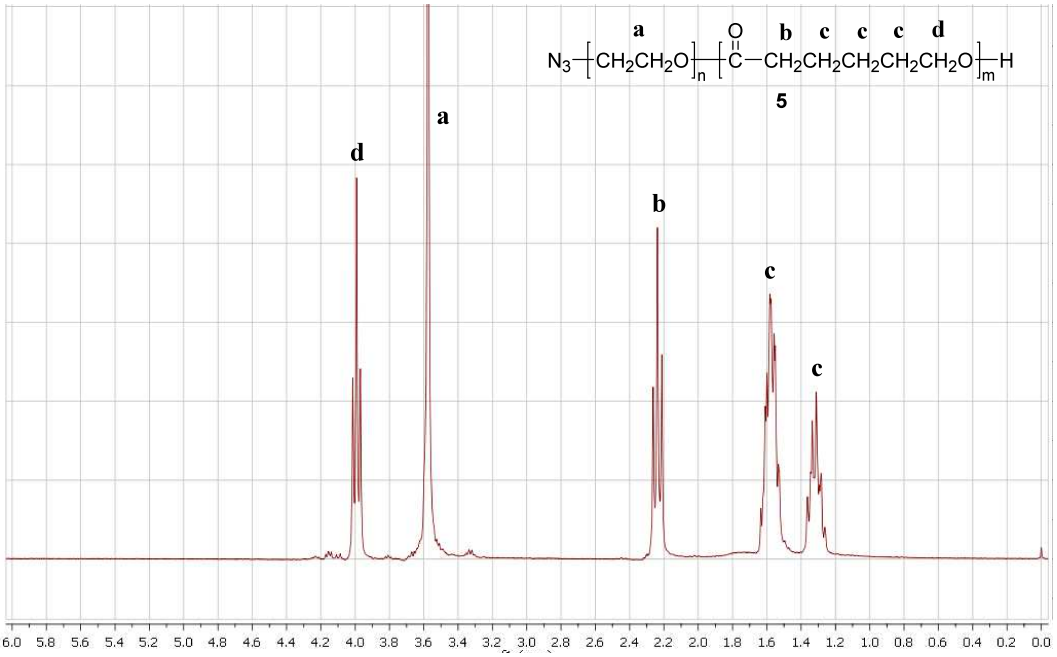

Figure S4. ^{1}H-NMR spectrum of N_3-PEO_{45}-*b*-PCL_{26} **5** in $CDCl_3$.

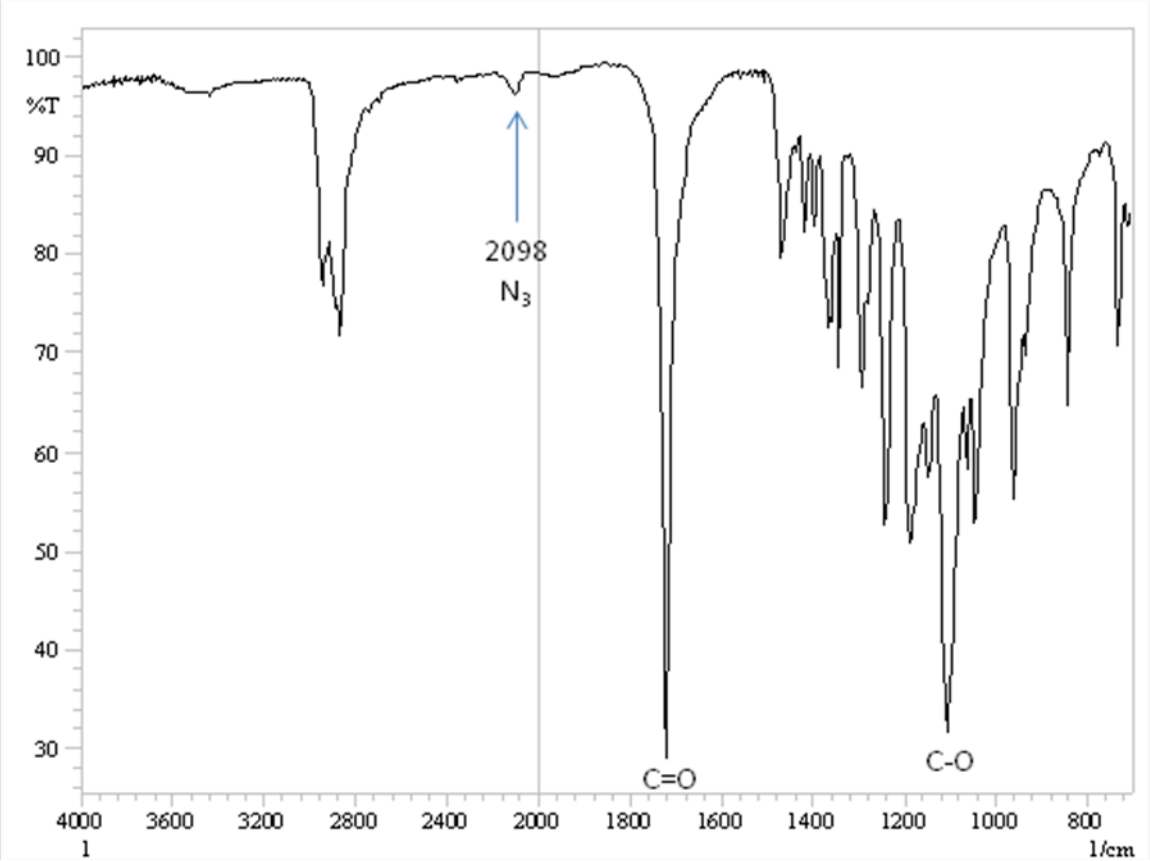

Figure S5. IR spectrum of copolymer **5**.

Synthesis of polymer 7. A suspension of copolymer **5** (250 mg) and 10% Pd/C (50 mg) in ethanol (15 mL) was stirred under an atmosphere of H_2 at room temperature for 15 h. The catalyst was removed by filtration and the filtrate was concentrated in *vacuo* to give **6**. To a solution of **6** (82 mg, 0.016 mmol) in dry CH_2Cl_2 (15 mL) was added **3** (12.7 mg, 0.033 mmol) and Et_3N (10.1 mg, 0.1 mmol). After stirring the reaction mixture for 18 h at ambient temperature, the mixture was concentrated under reduced pressure and the residue was purified by LH-20 size exclusion column chromatography (CH_2Cl_2/CH_3OH, 35/1, v/v) to afford **7** (350 mg, 71%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40-6.90 (8H, m, Aromatics), 5.43 (1H, m, C*H*OC=O), 4.20-3.90 (52H, m, $CH_2CH_2CH_2O$), 3.85-3.30 (180H, m, CH_2O), 3.08-291 (2H, m, ArCH_2), 2.32-2.18 (52H, m, CH_2C=O), 1.72-1.50 (104H, m, CH_2), 1.40-1.22 (52H, m, CH_2).

Synthesis of peptide AzGRGD (10). The synthesis of **10** was carried out on a Rink amide resin (0.25 mmol) using Fmoc chemistry. The first four amino acids, Gly-Arg-Gly-Asp were coupled on the peptide synthesizer using a standard protocol [on a Applied Biosystems, ABI 433A peptide synthesizer equipped with UV-detector using N^{α}-Fmoc-protected amino acids and 2-(1H-bezotriazole-1-yl)-oxy-1,1,3,3-tetramethyl hexafluorophosphate (HBTU)/1-Hydroxybenzotriazole (HOBt) as the activating reagents]. After the completion of the synthesis, a manual coupling of 2-azido-acetic acid (prepared as reported in the literature[2]) was carried out. 2-Azido-acetic acid (1.0 mmol, 101 mg) was dissolved in DMF (5 mL) and benzotriazole -1-yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate (PyBOP; 1.0 mmol, 520 mg), 1-hydroxybenzotriazole (HOBt; 1.0 mmol, 135 mg), and diisopropylethylamine (DIPEA; 2.0 mmol, 348 μL) were added to the solution and the resulting mixture was added to the resin. The coupling reaction was monitored by standard Kaiser test. After 4 h, the reaction was completed, and the resin was thoroughly washed with DMF, CH_2Cl_2 and methanol, and dried in vacuum. The resin was treated with cleavage solution [5 mL; TFA (95%), water (2.5%), TIS (2.5%)] for 1 h. The resin was filtered, washed with TFA (5 mL), and the filtrate was then concentrated in vacuum to approximately 1/3 of its original volume. The peptide was precipitated by using diethyl ether (0 °C, 100 mL) and recovered by centrifugation at 3000 rpm for 15 min. The crude peptide was purified by RP-HPLC on a semipreparative C-18 column using a linear gradient solvent (0-95% CH_3CN in H_2O, 0.1% TFA in 40 min; flow: 1 mL min^{-1}) and the appropriate fractions were lyophilized to afford **10**. MALDI HRMS: m/z 486.2157 [M + H^+]. Calcd for $C16H28N11O7^+$ 486.2168.

Synthesis of *N*-(2-azido-acetyl)-*N'*-biotinyl-3,6-dioxaoctane-1,8-diamine (11). To a solution of *N*-biotinyl-3,6-dioxaoctane-1,8-diamine (0.500 g, 1.335 mmol; prepared as reported in the literature[3]), 2-azido-acetic acid (0.162 g, 1.60 mmol; prepared as reported in the literature[2]) and DIPEA (0.345 g, 2.67 mmol) in DMF (60 mL) was added 2-(7-aza-1H-bezotriazole-1-yl)-oxy-1,1,3,3-tetramethyl hexafluorophosphate (HATU; 0.609 g, 1.60 mmol). The reaction mixture was stirred at ambient temperature for 2 h. The solvent was removed at reduced pressure, and the residue was purified by flash chromatography on silica gel (5-12% v/v MeOH/CH_2Cl_2) to give **11** as a yellowish solid (0.420g, 69%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.20 (1H, br, N*H*), 6.83 (1H, br, N*H*), 6.69 (1H, br, N*H*), 6.05 (1H, br, N*H*), 4.44 (1H, m, C*H*), 4.25(1H, m, C*H*), 3.90

(2H, s, N_3CH_2), 3.63-3.43 (8H, m), 3.42-3.29 (4H, m), 3.08 (1H, m, C*H*), 2.84 (1H, m), 2.68 (1H, m), 2.16 (2H, t), 1.88-1.59 (4H, m), 1.42 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7, 167.4, 164.5, 70.4, 70.2, 70.1, 69.7, 62.0, 60.5, 55.9, 52.6, 40.7, 39.4, 39.3, 36.2, 28.5, 28.3, 25.8. MALDI HRMS: m/z 480.1990 [M + Na^+]. Calcd for $C18H31N7O5SNa^+$ 480.2000.

Lipoic acid-modified ConA. A solution of ConA (5 mg) in PBS buffer (1 mL) was mixed with of a solution of lipoic acid-NHS active ester (prepared by a reported procedure[4]) in DMSO (58.3 μL of 5 mg mL^{-1}) and the resulting reaction mixture was kept at room temperature for 2 h. The mixture was dialyzed at 4 ºC for 12 h using the Tris buffer (0.01 M Tris.HCl, 0.09 M NaCl, 1 mM $CaCl_2$, and 1 mM $MnCl_2$, pH 7.2) containing 1% DMSO (200 mL) and then with Tris buffer alone (200 mL). The lipoic acid-modified ConA solution was aliquoted and stored at -20 ºC.

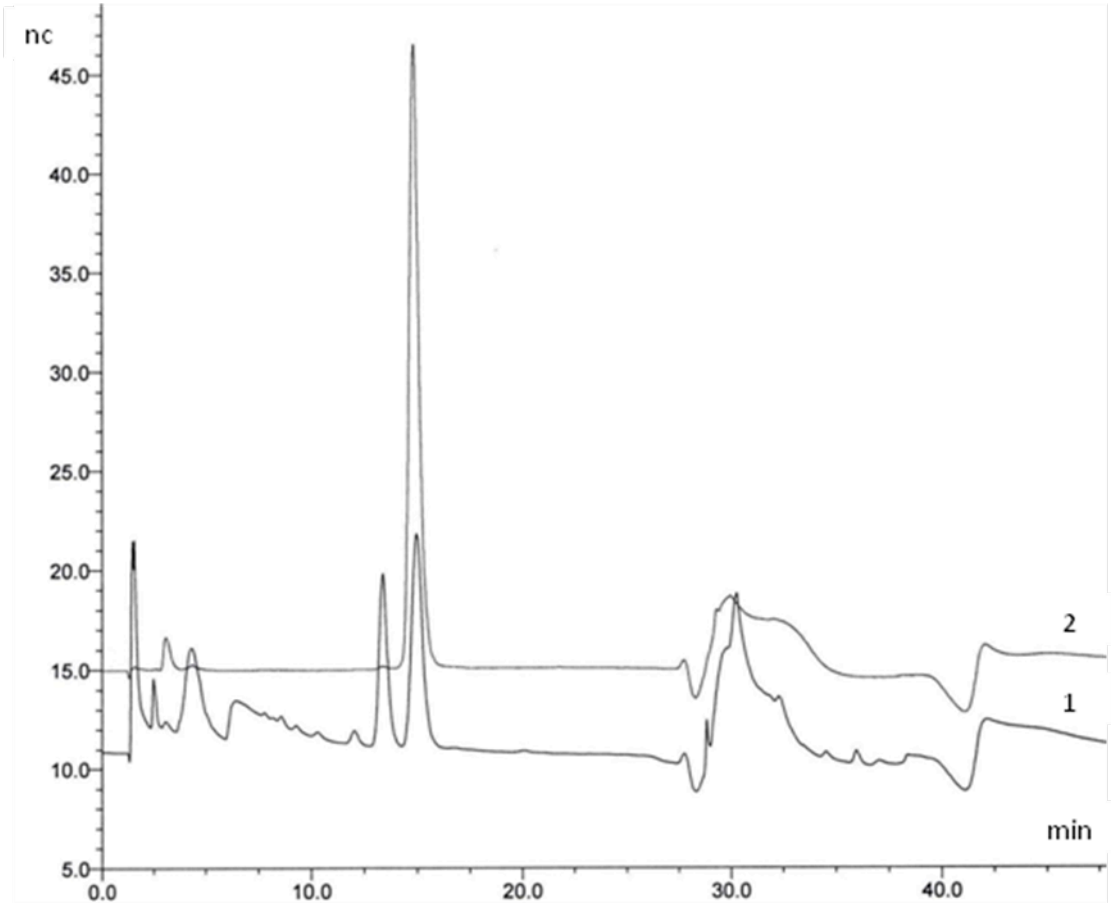

Figure S6. Quantification of conjugated mannoside. Trace **1**: Micelles **D** functionalized with mannose; Trace **2**: Mannose standard.

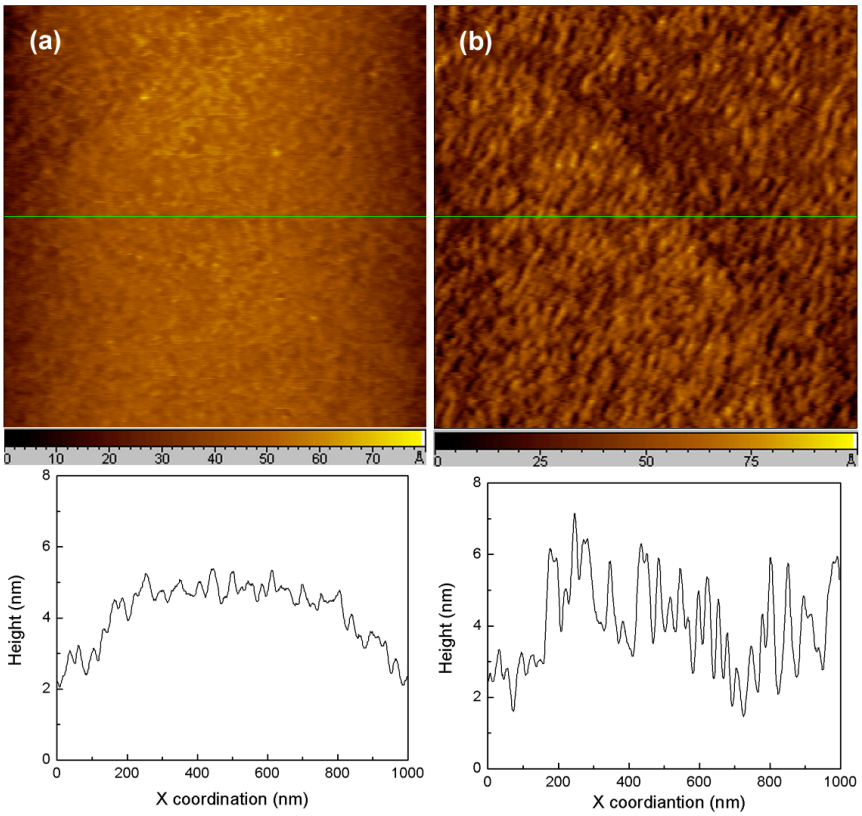

Figure S7. (a) Pure gold surface topographical image and its corresponding cross-section analysis, (b) ConA covered gold surface topographical image and its corresponding cross-section analysis. It is clear that pure gold surface is much flatter than the one modified by ConA, and it is very different in topography between them. Besides, figure (b) indicates that ConA formed a very dense layer on the gold surface.

References

1. V. Ladmiral, G. Mantovani, G. J. Clarkson, S. Cauet, J. L. Irwin, and D. M. Haddleton. *J. Am. Chem. Soc.* **2006**, *128*, 4823-4830.

2. L. A. Banaszynski, C. W. Liu, and T. J. Wandless. *J. Am. Chem. Soc.* **2005**, *127*, 4715-4721.

3. X. H. Ning, J. Guo, M. A. Wolfert and G.-J. Boons. *Angew. Chem. Int. Ed.* **2008**, *47*, 2253-2255.

4. M. M. Ponpipom, R. L. Bugianesi, and T. J. Blake. *J. Med. Chem.* **1987**, *30*, 705-710.