Electronic Supplementary Information

Self-Assembled Dendron Nanotubes with Surface Peptide-Fluorophore Conjugate as a Sensory Vehicle

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Experimental Section

Materials. N,N-diisopropylethylamine (DIPEA), dicyclohexylcarbodiimide (DCC), N,N-dimethylformamide (DMF), piperidine, N,N'-diisopropylcarbodiimide (DIPC), dansyl chloride, Trifluoroacetic acid (TFA), triisopropylsilane (TIS), N-methyl-2-pyrrolidone (NMP), benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate (PyBOP) from Aldrich were used as received. N-α-Fmoc protected amino acid from novabiochem, 1-hydroxybenzotriazole (HOBt), 2-Cl trityl resin from bead tech and *β*-cyclodextrin (*β*-CD) from TCI were also used as received. Triethylamine (TEA) from Aldrich was purified by distillation under calcium hydride. All the solvents were purified using published procedures.[1]

Synthesis of Dendron 1. The amide dendron 1 with focal pyrene moiety was synthesized as described in previously published article.[2]

Synthesis of mono-6-deoxy-amino-β-CD. The mono-6-deoxy-amino-β-cyclodextrin was synthesized as described in previously published article.[3]

Solid phase peptide synthesis of dans-GGH-COOH. The peptide was synthesized by solid phase synthesis in 2-Cl trityl resin as described in Fig. S1. The coupling reaction in resin was carried out by adding a preactivated solution of N-α-Fmoc protected amino acid (3 eqv.) and DIPEA (6 eqv.) in anhydrous DMF (3 mL) to the resin (1 eqv.) and mixing for 4 hours at room temperature. The unreacted resin was capped by anhydrous MeOH (6 eqv.) in presence of DIPEA (6 eqv.) by 30 minutes stirring at room temperature. The resin was washed with DMF and methanol (1 min, 3 mL, 3 times) respectively. The Fmoc protecting group was removed by using 50 % piperidine in DMF for 20 min. The resin was washed again with DMF and methanol (1 min, 3 mL, 3 times) respectively. Further amino acids were coupled by adding preactivated solution of N-α-Fmoc protected amino acids (3 eqv.), HOBt (3 eqv.),

and DIPC (3 eqv.) in anhydrous DMF (3 mL). The resin was washed with DMF and methanol (1 min, 3 mL, 3 times) respectively and used in subsequent reactions. The coupling of dansyl chloride was performed using the following procedure. To the resin bound peptide (0.05 mmol), dansyl chloride (0.15 mmol) in DMF (3ml) containing TEA (0.15 mmol) was added and the resulting solution containing the resin was kept for 2 hours at room temperature with continuous stirring. Deprotection and cleavage was achieved by treating with a mixture of TFA/TIS/H_2O (9.5/0.5/0.5, v/v/v) at room temperature for 3-4 hrs. After filtration and washing of the resin by TFA, a gentle stream of nitrogen was used to remove the excess TFA. The crude peptide was triturated with diethylether chilled at -20 ^{o}C and then centrifuged at 3,000 rpm for 10 min at -10 ^{o}C.

Synthesis of dans-GGH-CD. The crude peptide (dans-GGH-COOH, 1 eqv.) and mono-6-deoxy-amino-β-CD (2 eqv.) were dissolved in NMP in the presence of PyBOP (3 eqv.), HOBt (3 eqv.), and DIPEA (4 eqv.) and the solution was stirred for 20 hrs. The product was purified by preparative HPLC and then the purity of the product was analyzed by analytical HPLC (Fig. S6). The successful synthesis and purity were confirmed by MALDI-TOF/MS ($[M+H]^+$: cald. 1618.54, obsd. 1618.61; $[M+Na]^+$ cald. 1641.53, obsd. 1640.80) as shown in Fig. S7. ^{1}H NMR (400 MHz, D_2O, Fig. S8) δ 8.53 (d, J = 8.0 Hz, 1H), 8.40 (s, 1H), 8.28 (d, J = 9.2 Hz, 1H), 8.20 (d, J = 6.7 Hz, 1H), 7.72 (t, J = 8.3 Hz, 1H), 7.66 (t, J = 8.3 Hz, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.17 (s, 1H), 5.11 – 4.94 (m, 7H), 3.94 – 3.53 (m, 42H), 3.45 – 3.30 (m, 3H), 3.24 (d, J = 13.1 Hz, 2H), 3.06 (dd, J = 13.9, 9.2 Hz, 2H), 2.89 (s, 6H). ^{13}C NMR (101 MHz, D_2O) δ 174.14, 173.47, 172.20, 153.55, 145.19, 136.64, 135.91, 133.07, 132.28, 132.13, 131.63, 126.53, 121.68, 121.21, 119.80, 118.78, 104.88, 104.68, 83.88, 83.58, 75.83, 75.49, 75.12, 74.88, 74.65, 73.44, 62.62, 55.30, 47.73, 46.77, 45.02, 44.27, 33.60.

Synthesis of dans-CD. Mono-6-deoxy-amino-β-CD (100 mg, 1 eqv.) and dansyl chloride (48 mg, 2 eqv.) were dissolved in NMP (2 mL) in presence of TEA (37 µL, 3 eqv.) and the solution was stirred for 12 hrs at room temperature. The resulting solution was poured into anhydrous acetone (10 mL) with

vigorous stirring, and the resultant mixture was stored in refrigerator to produce a pale yellow precipitate. The product was purified by preparative HPLC and then the purity of the product was analyzed by analytical HPLC (Fig. S9). The successful synthesis and purity were confirmed by MALDI-TOF/MS ([(M +Na)$^+$]: cald. 1391.50, obsd. 1389.87) as shown in Fig. S10. ^{1}H NMR (400 MHz, D_2O) δ 8.50 (d, *J* = 8.2 Hz, 1H), 8.27 (d, *J* = 8.2 Hz, 1H), 8.08 (d, *J* = 7.4 Hz, 1H), 7.69 (t, *J* = 6.5 Hz, 1H), 7.60 (t, *J* = 6.6 Hz, 1H), 7.44 (d, *J* = 7.4 Hz, 1H), 5.15 – 4.85 (m, 7H), 4.15 (d, *J* = 13.0 Hz, 1H), 4.04 – 3.22 (m, 38H), 3.13 (d, *J* = 12.1 Hz, 1H), 2.99 (d, *J* = 12.2 Hz, 1H), 2.91 (d, *J* = 2.5 Hz, 6H), 2.34 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, D_2O) δ 153.23, 138.26, 136.56, 132.21, 131.96, 130.79, 129.37, 128.69, 118.68, 104.89, 104.38, 86.18, 83.49, 75.80, 75.49, 74.85, 74.64, 74.27, 62.62, 60.92, 47.69, 46.51.

Synthesis of Ac-GGH-CD. To the resin bound GGH peptide (0.1 mmol), 3 mL of DMF solution containing acetic acid (0.6 mmol, 6 eqv.), DCC (0.6 mmol, 6 eqv.), HOBt (0.6 mmol, 6 eqv.), and DIEA (0.6 mmol, 6 eqv.) was added and then the solution was stirred at room temperature for 1 hr. Deprotection and cleavage of Ac-GGH-COOH from resin was achieved by treating with a mixture of TFA/TIS/H_2O (9.5/0.5/0.5, v/v/v) at room temperature for 3-4 hrs. The crude peptide (Ac-GGH-COOH, 1 eqv.) and mono-6-deoxy-amino-β-CD (2 eqv.) were dissolved in NMP in the presence of PyBOP (3 eqv.), HOBt (3 eqv.), and DIPEA (4 eqv.) and the solution was stirred for 20 hrs. The product was purified by preparative HPLC and then the purity of the product was analyzed by analytical HPLC (Fig. S11). The successful synthesis and purity were confirmed by MALDI-TOF/MS ([M +H]$^+$: cald. 1427.12, obsd. 1427.57; [M+Na]$^+$: cald. 1450.11, obsd. 1449.72) as shown in Fig. S12. ^{1}H NMR (400 MHz, D_2O) δ 8.35 (s, 1H), 7.18 (s, 1H), 5.15 – 4.95 (m, 7H), 4.94 – 4.86 (m, 1H), 4.71 – 4.64 (m, 1H), 4.01 – 3.49 (m, 40H), 3.45 – 2.97 (m, 7H), 2.07 (d, *J* = 3.9 Hz, 3H). ^{13}C NMR (101 MHz, D_2O) δ 177.69, 174.94, 174.31, 174.05, 136.97, 132.59, 119.75, 104.86, 104.76, 85.68, 83.81, 82.23, 75.82, 75.68, 75.08, 74.79, 73.51, 62.68, 57.00, 45.21, 45.08, 44.77, 33.51, 24.41.

Fluorescence Measurements. All of the fluorescence measurements were performed using a Shimadzu RF-5301PC spectrofluorometer.

Transmission electron microscopy experiments. Transmission electron microscopy (TEM) was performed using a Philips CM 200, operated at an acceleration voltage of 80 kV. Field emission transmission electron microscopy (FE-TEM) experiments were performed using a JEOL JEM-2100F, operated at an acceleration voltage of 200 kV. For the preparation of dispersed samples in water, a drop of sample solution (50 mg/L) was placed onto a 300-mesh copper grid coated with carbon. About 15 min after deposition, the grid was tapped with filter paper to remove surface water, followed by air-drying. Negative staining was performed by using a droplet of a 2 wt% phosphotunstate solution. The samples were air-dried before measurement. EDX spectra and scanning transmission electron microscopy (STEM) images were also collected using the above described JEM 2100F.

Field-Emission Scanning electron microscopy experiments. Field-Emission Scanning electron microscopy (FE-SEM) experiments were carried out using a Hitachi S-4300. The FE-SEM samples were prepared by transferring a drop of sample solution onto a silicon wafer or an aluminum foil and dried in vacuo.

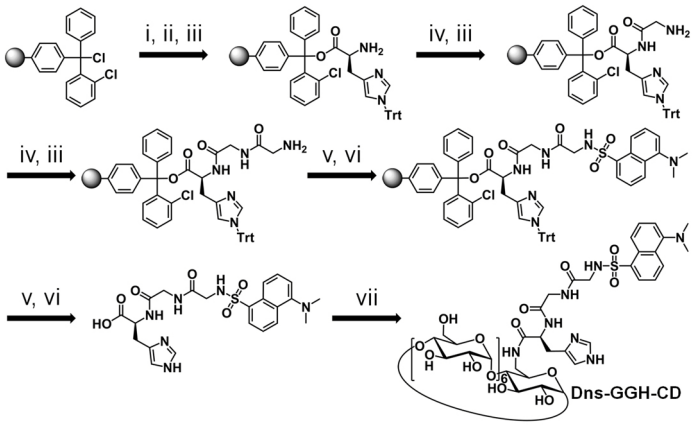

Fig. S1. Synthetic routes to dans-GGH-CD. Conditions: i) Fmoc-His(Trt)-OH, DIPEA; ii) MeOH, DIPEA; iii) 50 % Piperidine/DMF; iv) Fmoc-Gly-OH, DIPC, HOBt; v) Dansyl chloride, TEA; vi) TFA/TIS/H_2O; vii) mono-6-deoxy-amino-β-CD, PyBop, HOBt, DIPEA.

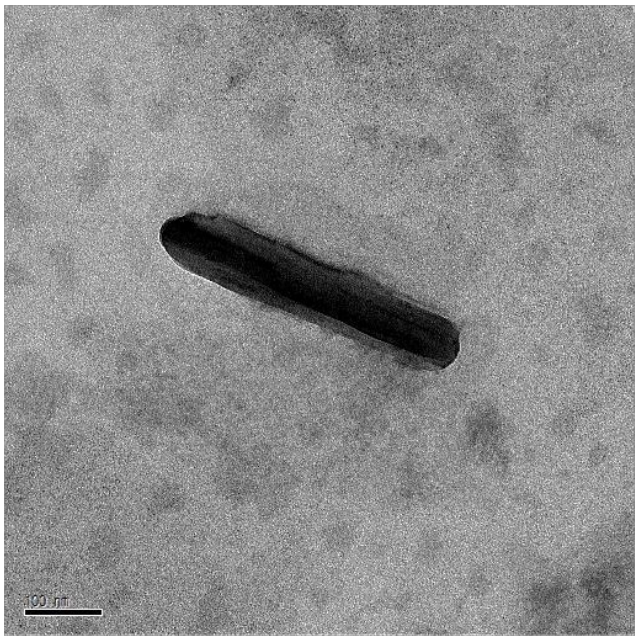

Fig. S2. TEM image of Den-Ac-GGH-CD-NT (stained with 2 wt% phosphotungstic acid).

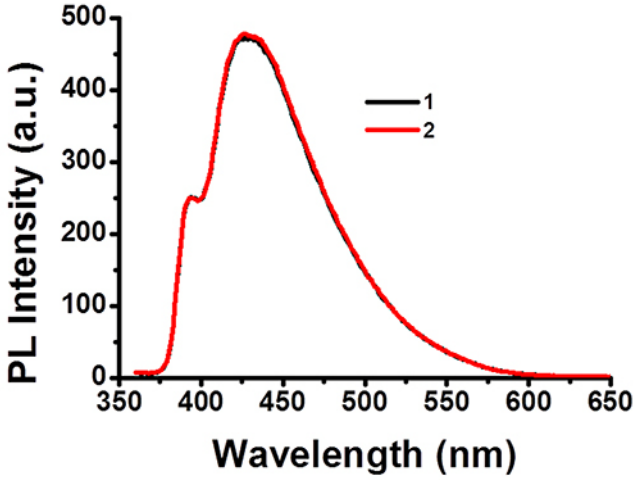

Fig. S3. PL spectra of Den-Ac-GGH-CD-NT without (1) and with (2) Cu(II). The excitation wavelength was 345 nm.

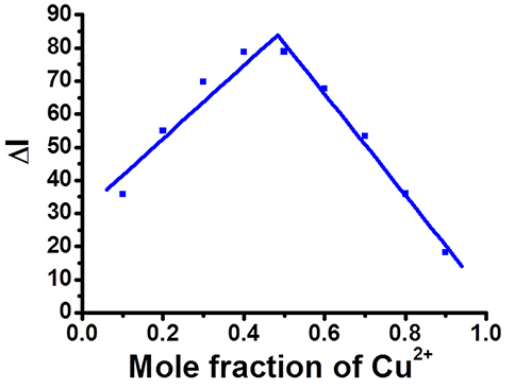

Fig. S4. Job's plot of Den-dans-GGH-CD-NT with Cu(II). ΔI means the PL intensity change of Den-dans-GGH-CD-NT before and after addition of Cu(II).

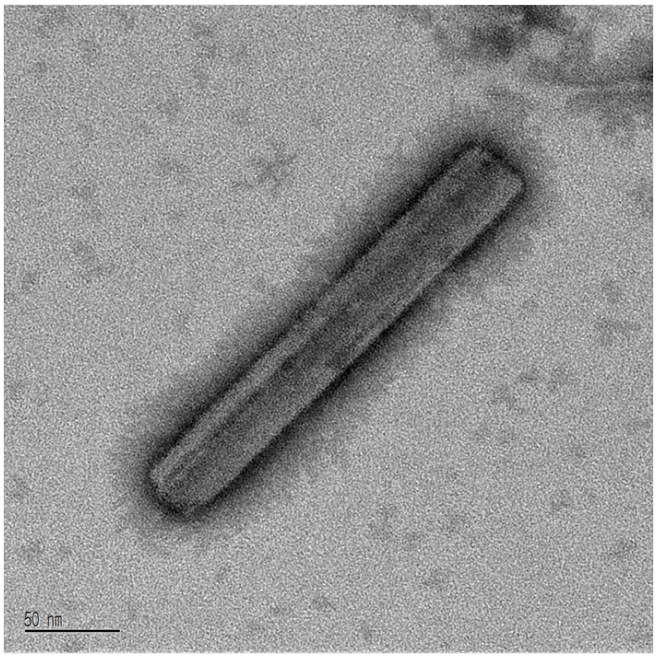

Fig. S5. TEM image of Den-dans-CD-NT (stained with 2 wt% phosphotungstic acid).

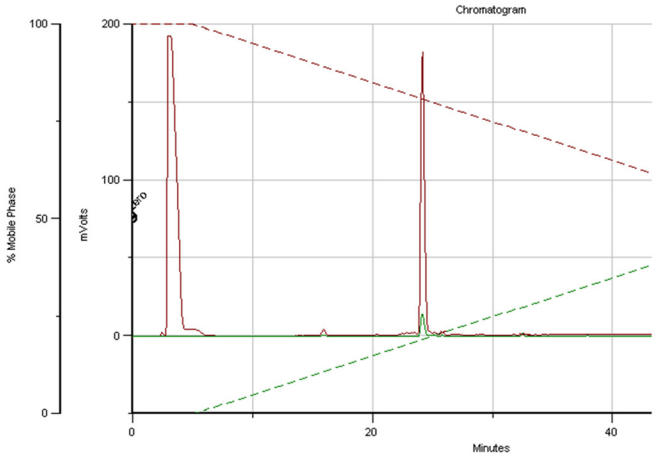

Fig. S6. HPLC chromatogram of dans-GGH-CD.

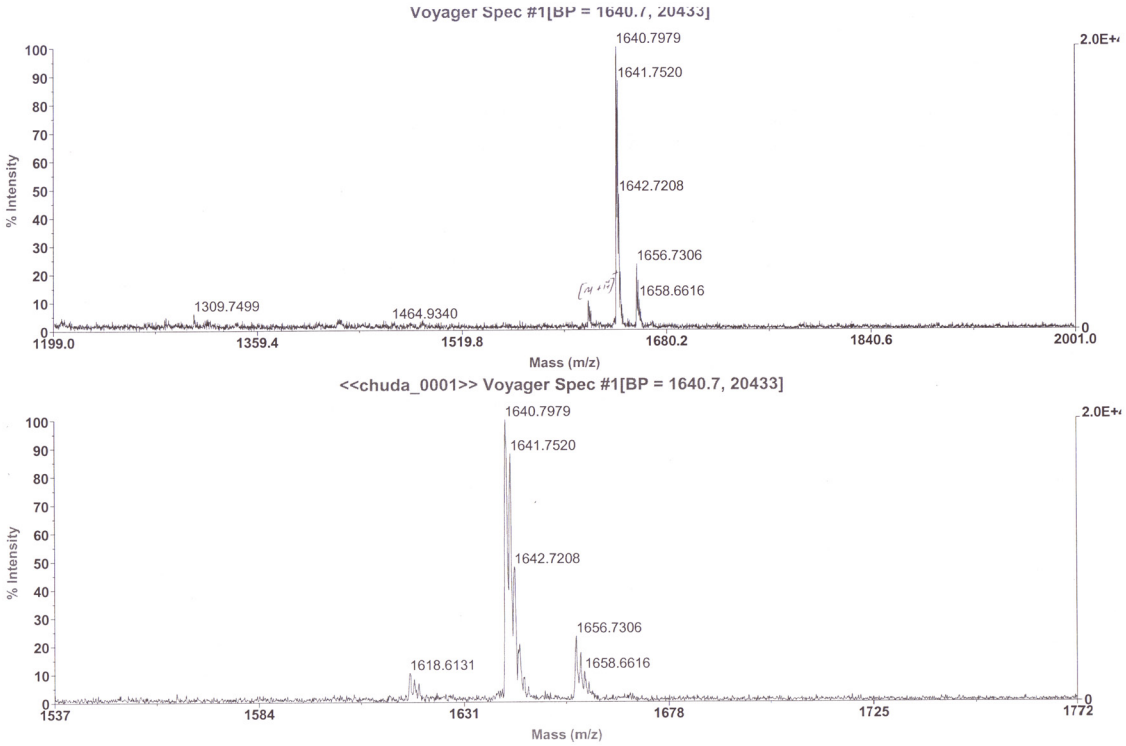

Fig. S7. MALDI-TOF mass spectrum of dans-GGH-CD.

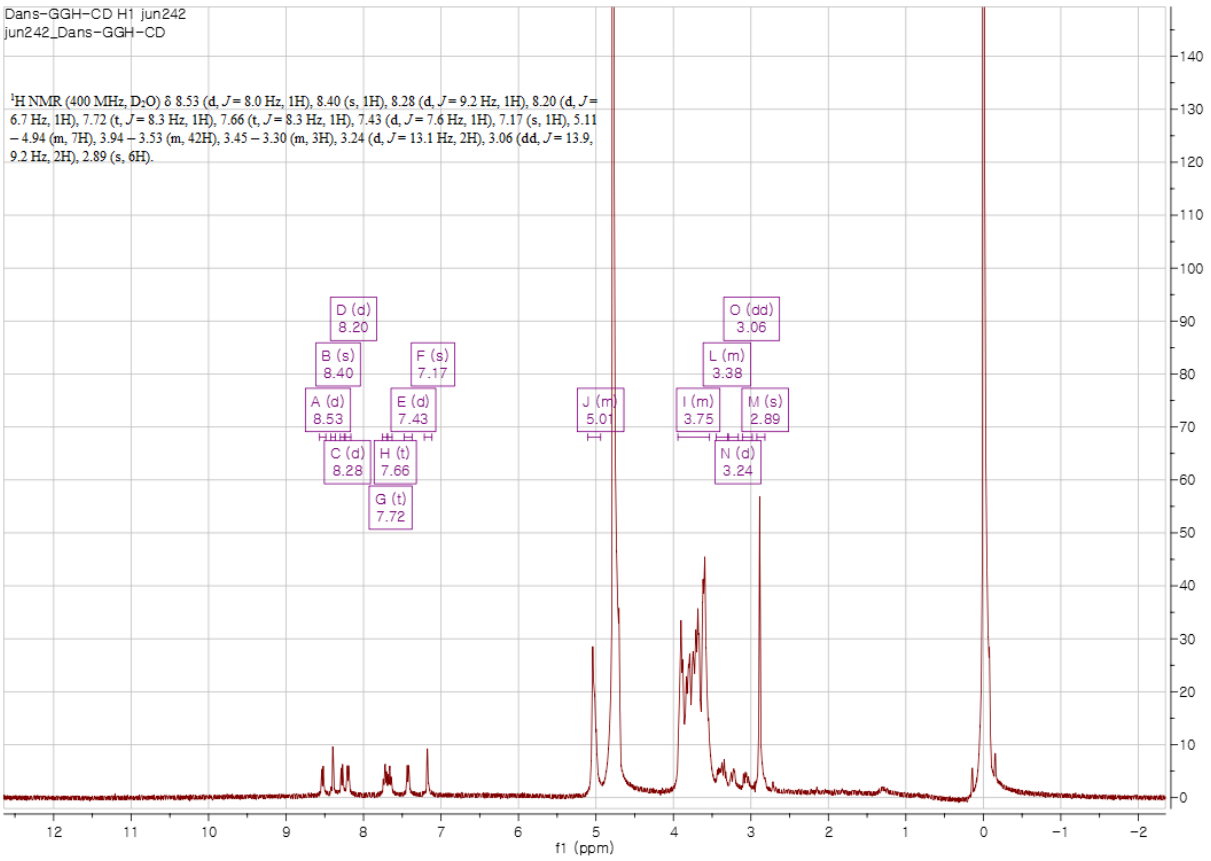

Fig. S8. ^{1}H NMR spectrum of dans-GGH-CD.

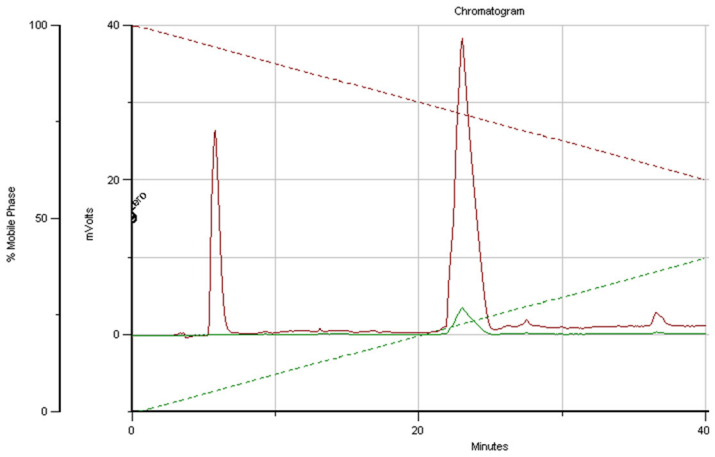

Fig. S9. HPLC chromatogram of dans-CD.

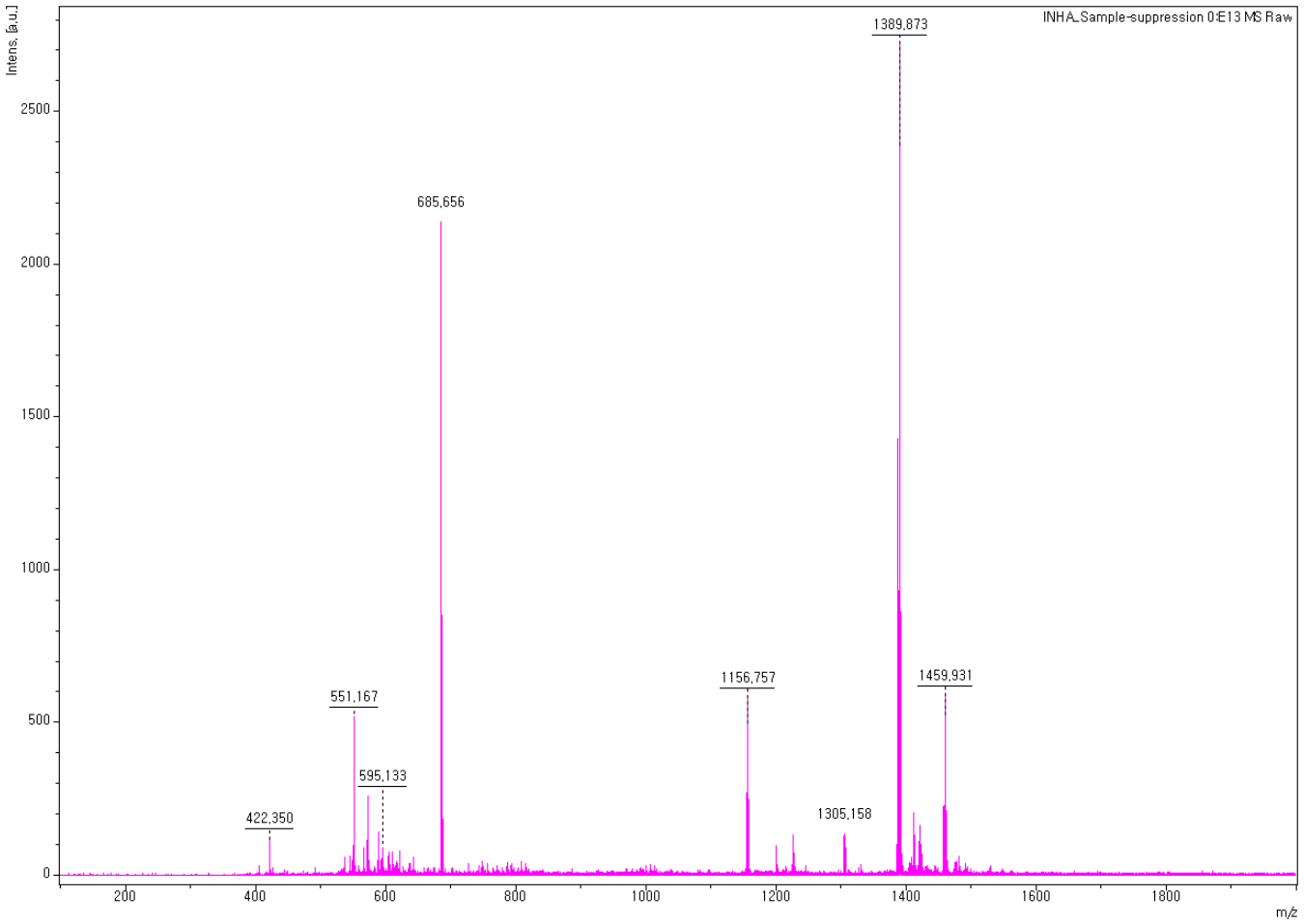

Fig. S10. MALDI-TOF mass spectrum of dans-CD.

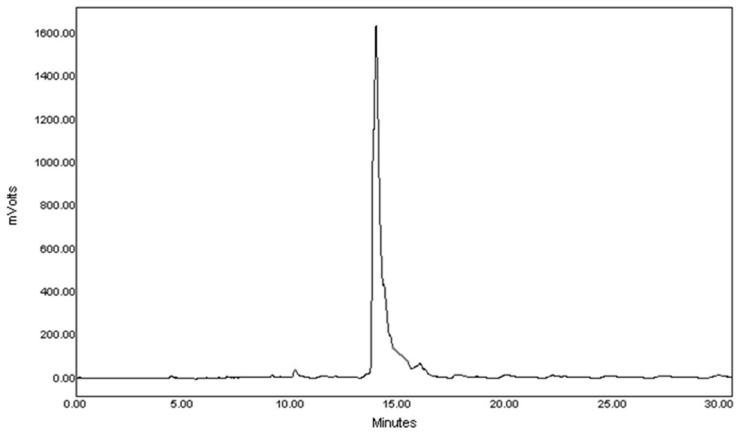

Fig. S11. HPLC chromatogram of Ac-GGH-CD.

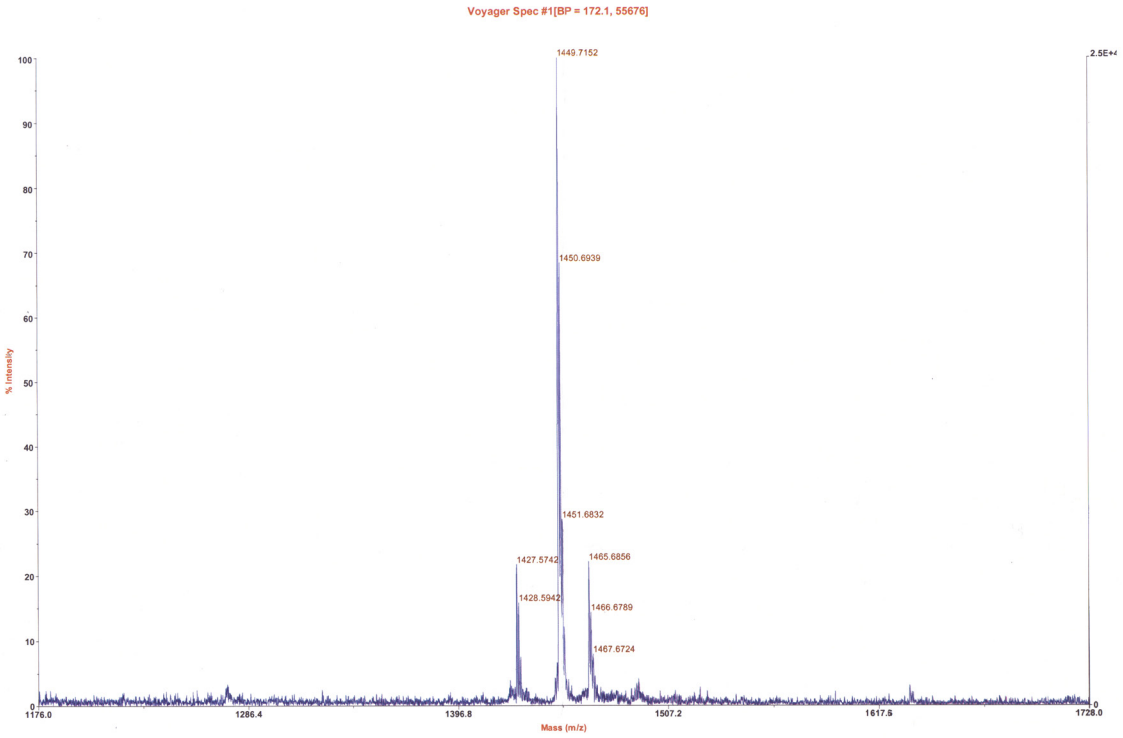

Fig. S12. MALDI-TOF mass spectrum of Ac-GGH-CD.

References

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