Supramolecular hydrogels formed by the conjugates of nucleobases, Arg-Gly-Asp (RGD) peptides, and glycosamine

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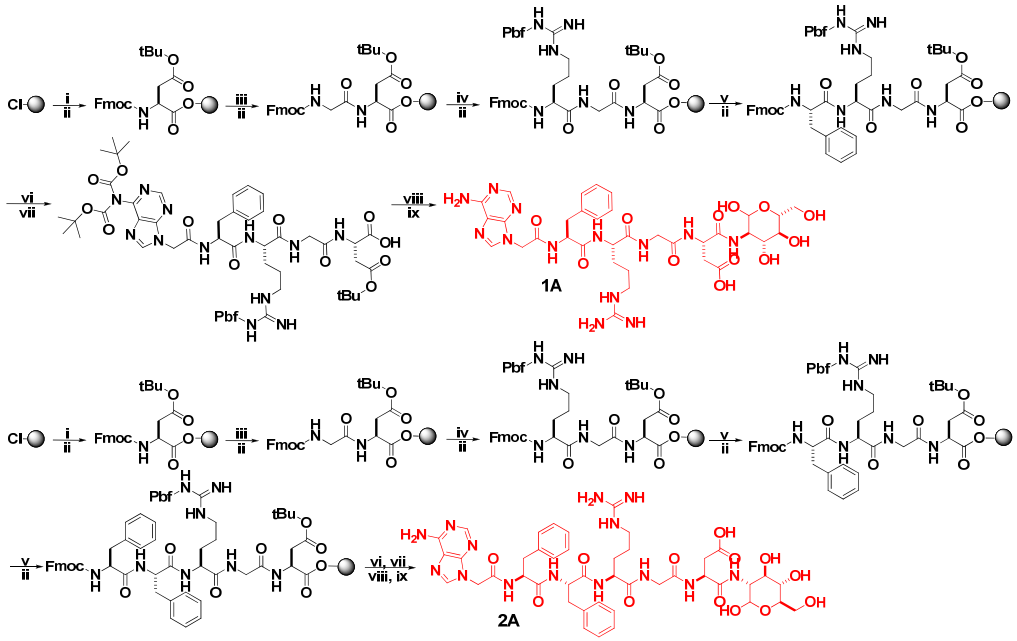
Supporting information

1) Materials and methods

Chemical reagents and solvents were used as received from commercial sources unless otherwise stated. ^{1}H and ^{13}C spectra were obtained on a Varian Unity Inova 400 spectrometer, CD on a JASCO J-810 spectrometer, LC-MS on a Waters Acouity ultra Performance LC with Waters MICROMASS detector, and TEM on a Morgagni 268 transmission electron microscope.

2) Synthesis of hydrogelators of 1A, 2A, 1C, 2C, 1G and 2G.



i) L-Asp(OtBu), DIEA; ii) 20 % piperidine; iii) L-Gly, HBTU, DIEA; iv) L-Arg(Pbf), HBTU, DIEA; v) L-Phe, HBTU, DIEA; vi) Bis-boc adenine acetic acid, HBTU, DIEA; vii) 20 % TFE in DCM; viii) D-glucosamine, HBTU, DIEA; ix) TFA:TIS:water (95:2.5:2.5)

Figure S1. Molecular structures and the typical synthetic routes of hydrogelators **1A** and **2A**.

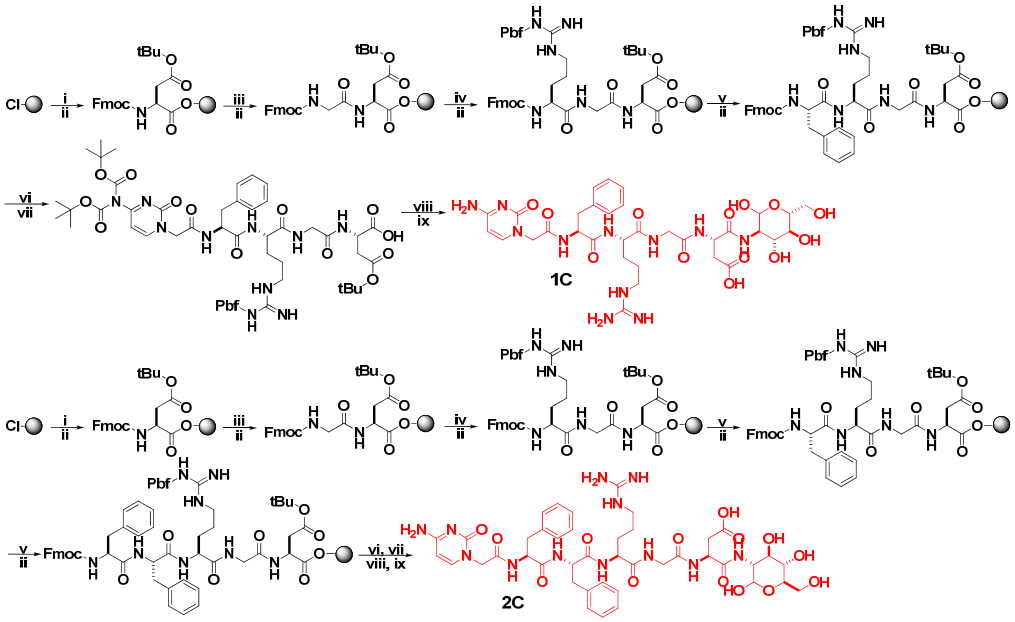


Figure S2. Molecular structures and the typical synthetic routes of hydrogelators **1C** and **2C**.

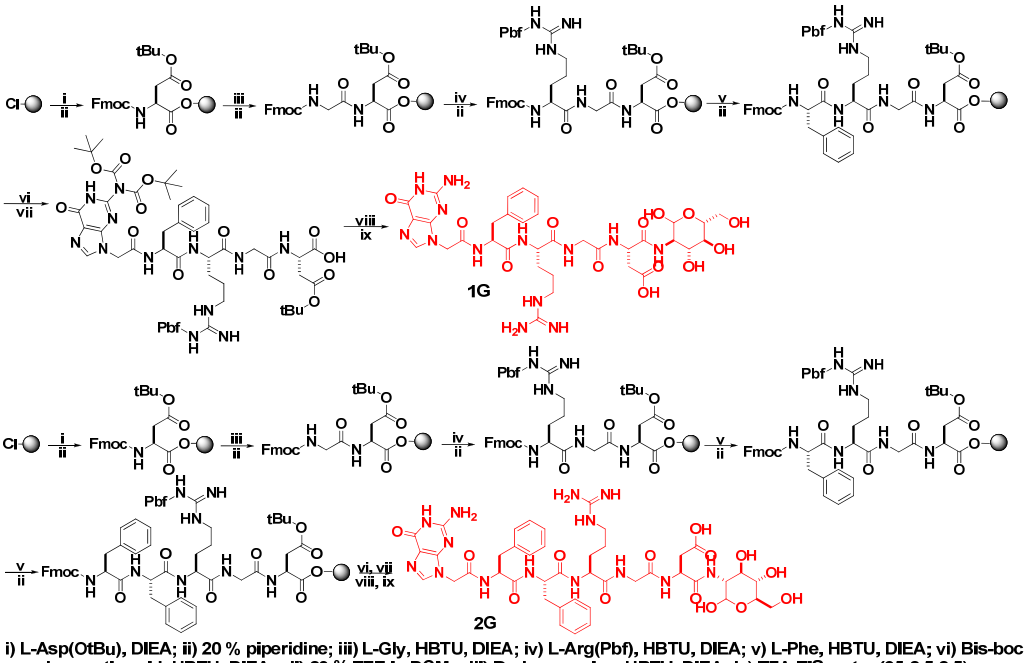
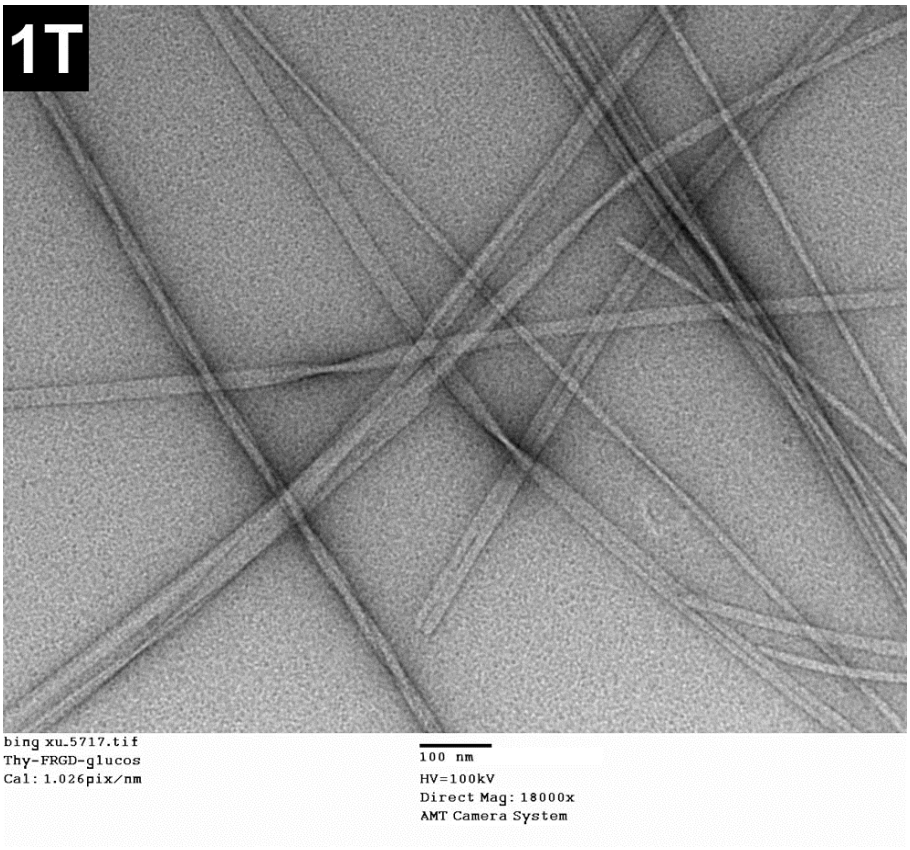
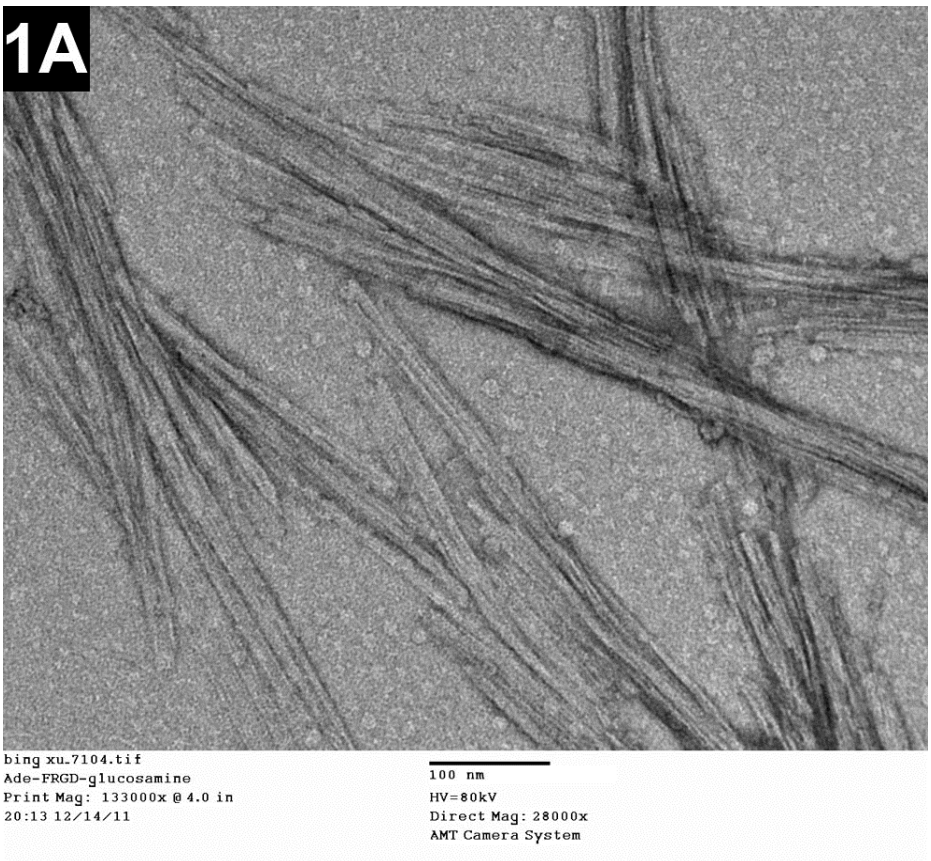
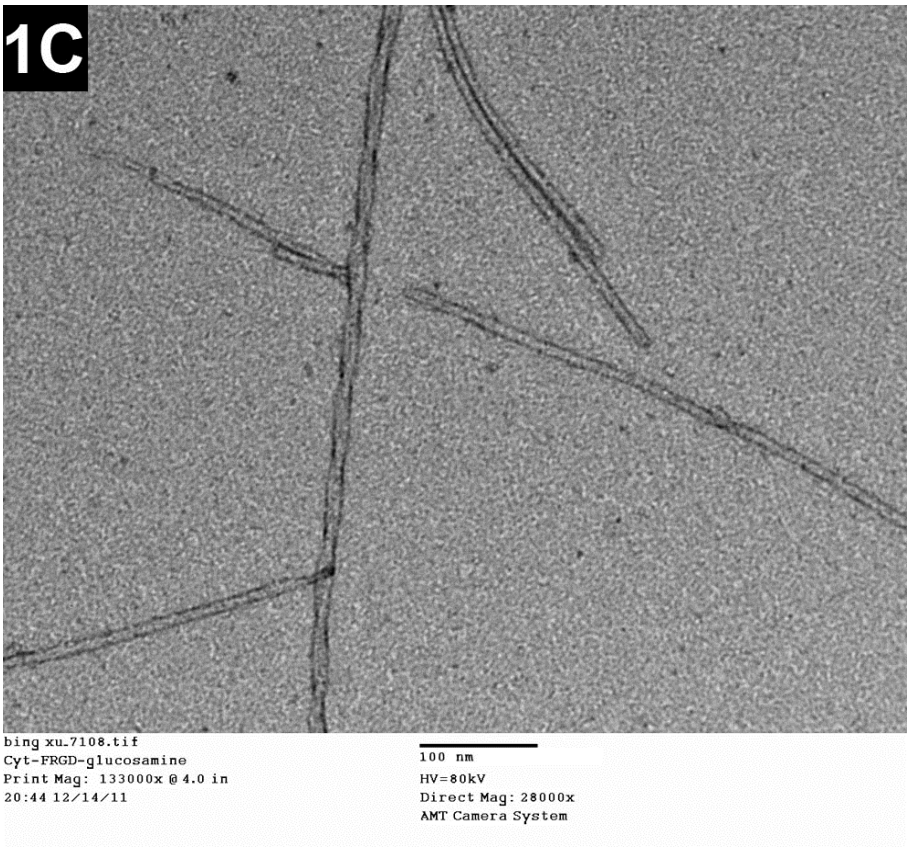


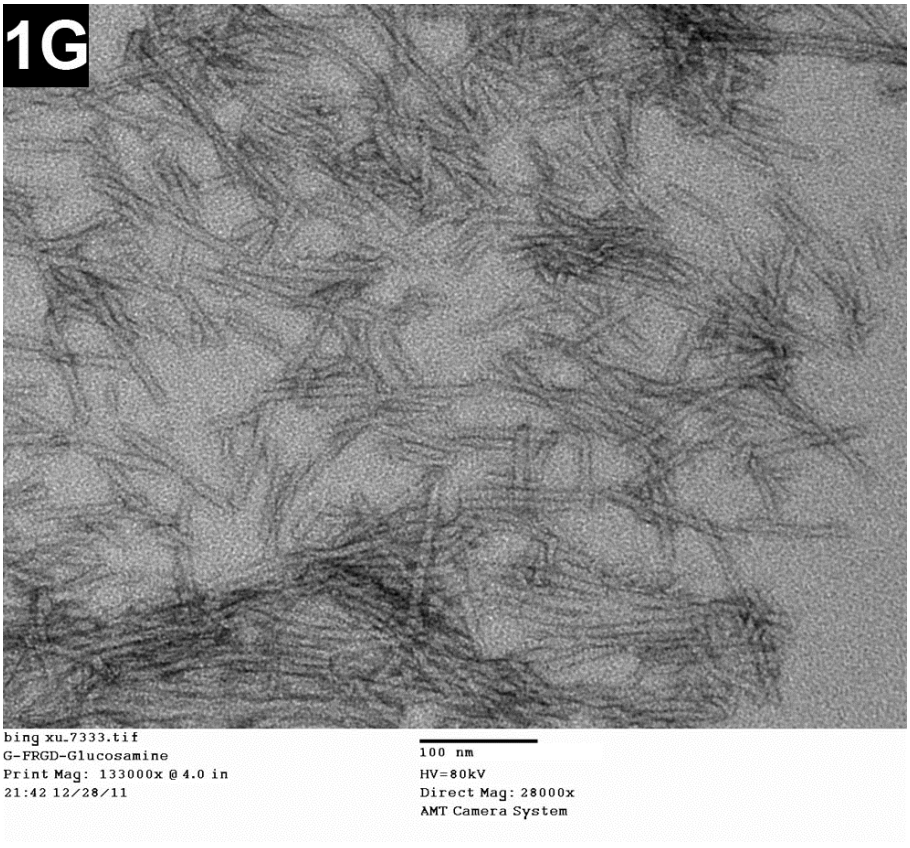
Figure S3. Molecular structures and the typical synthetic routes of hydrogelators **1G** and **2G**.

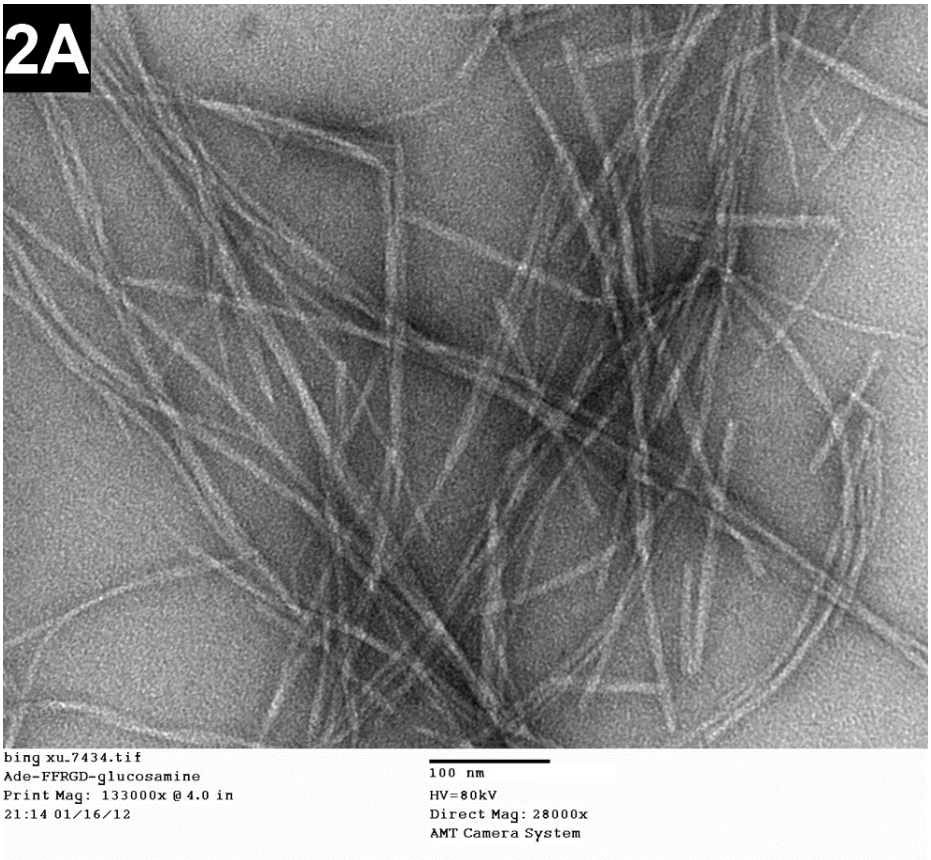
3) Transmission electron micrograph (TEM) of hydrogels of 1T, 1A, 1C, 1G, 2A and 2C, and solution of 2G.

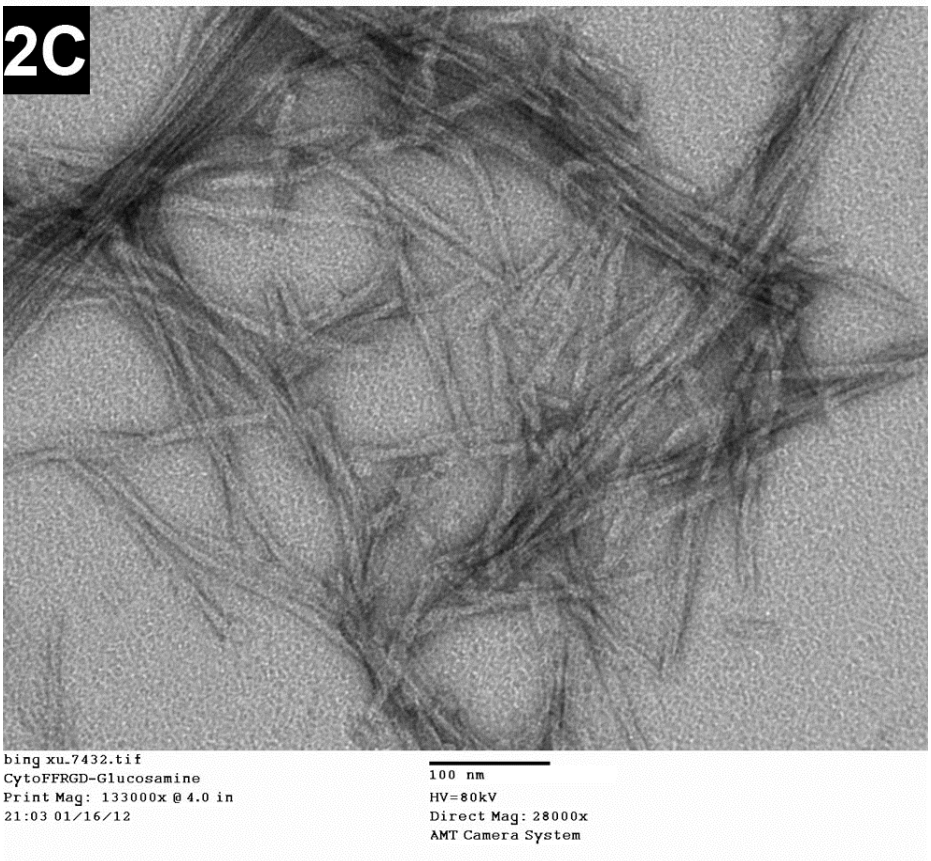












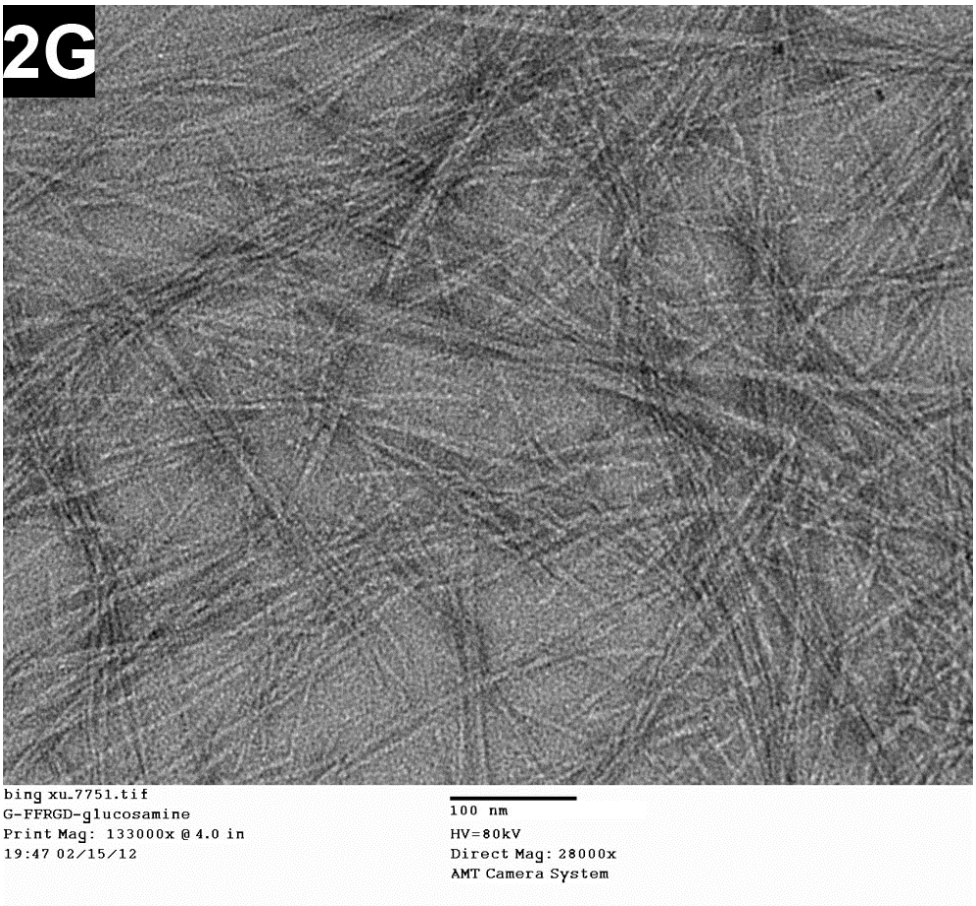


Figure S4. High magnification TEM images of hydrogels 1T, 1A, 1C, 1G, 2A and 2C, and solution of 2G.

4) Rheological measurement

Rheological tests were conducted on a TA ARES G2 rheometer (with TA Orchestrator Software). 25 mm cone-plates were used during the experiment. 0.3 mL of hydrogel sample was placed on the cone-plate.

i) Dynamic Strain Sweep Test

Test range (0.1 to 10 % strain, frequency =10 $rads^{-1}$), 10 points per decade. Sweep mode is "log" and temperature was carried out at 25 ^{o} C.

ii) Critical strain determination

The critical strain (γ_c) value was determined from the storage-strain profiles of the hydrogel sample. The strain applied to the hydrogel sample increased from 0.1 to 10 % (10 rad/s and 25 ^{o}C). Over a certain strain, a drop in the elastic modulus was observed, and the strain amplitude at the onset of decrease to 5 % decrease from its maximum value was determined and taken as a measure of the critical strain of the hydrogels, which correspond to the breakdown of the cross-linked network in the hydrogel sample.

i) Dynamic Frequency Sweep Test
Test range (0.1 to 200 rad/s, strain =0.4%), 10 points per decade. Sweep mode is "log" and was carried at 25 ^{o}C.

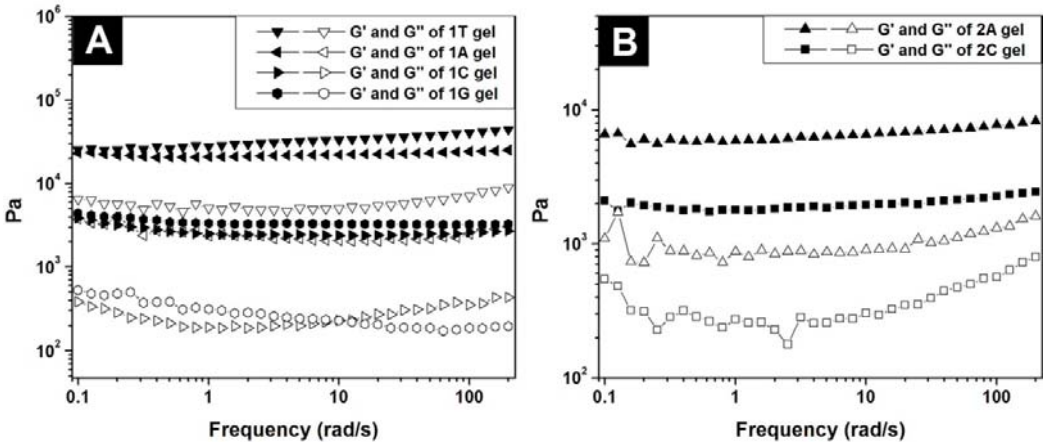


Figure S5. Frequency dependence of dynamic storage moduli (G') and loss moduli (G'') of (**A**) the hydrogels of **1T**, **1C**, **1A**, and 1**G**, (B) the hydrogels of **2A,** and **2C** shown in Fig. 1.

5) Biostability test with proteinase K
1 mg of each compound was dissolved in 5 mL of HEPES buffer at pH 7.5. Then 3.2 units/mL of proteinase K were added and incubated at 37 ^{o}C for 24 hr, then 100 µL of sample were taken out at 2, 4, 8, 12, and 24h and analyzed by HPLC.

For the control experiment, 1 mg of Thymine-FRGD and 1 mg of thymine-FFRGD (nucleopeptides without glucosamine in conjugation) were dissolved in 5 mL of HEPES buffer at pH 7.5 respectively. Then 3.2 units/mL of proteinase K were added and incubated at 37 ^{o}C for 24 hr, then 100 µL of sample were taken out each time and analyzed by HPLC.

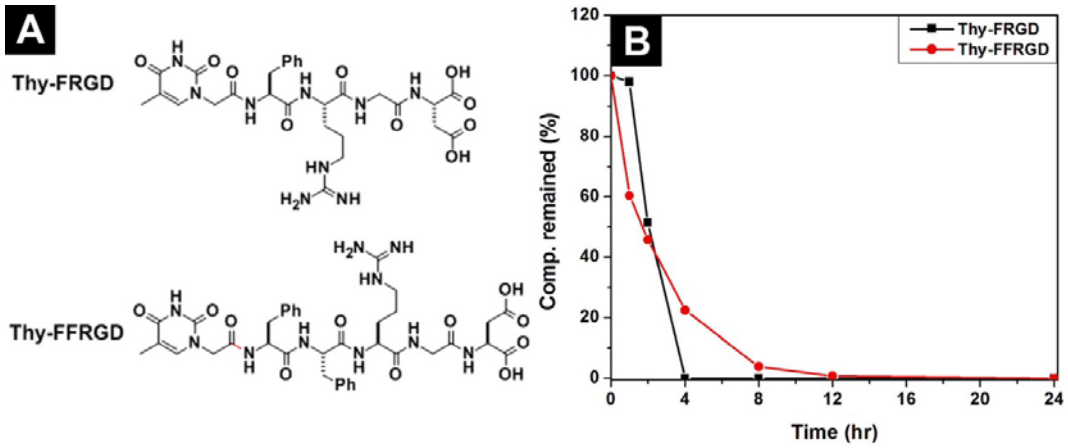


Figure S6. (A) The molecular structures of Thymine-FRGD and thymine-FFRGD, and (B) their time-dependent course of the digestions by proteinase K as control experiment, in which

Thymine-FRGD and thymine-FFRGD are the nucleopeptides without D-glucosamine in conjugation.