Using Matrix Metalloprotease-9 (MMP-9) to Trigger Supramolecular Hydrogelation

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Electronic Supporting Information

General. Chemical reagents and solvents were used as received from commercial sources. ¹H NMR spectra were obtained on a 300 MHz Varian XL-300 using DMSO-d₆ as the solvent; Mass spectra were measured on Finnigan TSQ7000 System; HPLC analysis were performed on Waters 600E Multi-solvent Delivery System using XTerra MS C_{18} RP column with CH₃CN (0.1% of TFA) and water (0.1% of TFA) as the eluent. Transmission electron micrograph (TEM) was done on JEOL 2010 transmission electron microscope, operating at 200 kV. The rheology test was performed on Rheometrics ARES with a cone and a plate (25 mm diameter plate and 0.0999 rad cone angle), and the gap opening at the apex of the cone and plate was set to be 0.0483 mm. The cryo-dried samples were prepared as following: a copper grid coated with carbon was dipped into the hydrogel and placed into a vial, which was plunged into liquid nitrogen. Then, water was removed from the frozen specimen by a freeze-drier.

Rheology experiment. 0.6 mL of Gel I or Gel II was sandwiched between the cone and the plate to obtain the dynamic frequency curve at the strain of 0.5%. For the dynamic time sweep, 0.6 mL of solution of 1 containing MMP-9 was sandwiched between the cone and the plate at the frequency of 2 rad/s and strain of 0.5%. All rheological measurements were carried out at room temperature (25-26 $^{\circ}$ C).

Solid phase peptide synthesis: peptides of **1** and **2** were synthesized by solid phase peptide synthesis using trityl chloride resin. The crude product was dissolved in DMSO and purified by HPLC.

¹H NMR of FFFFCGLDD (1) (300MHz, DMSO- d_6) δ (ppm): 8.77-8.82 (1H), 8.48-8.52 (3H), 8.02-8.14 (4H), 7.26-8.50 (22H), 4.72-4.80 (3H), 4.45-4.62 (3H), 4.10 (1H), 3.88 (2H), 3.50-3.60 (5H), 3.10-3.27 (3H), 2.82-3.04 (5H), 2.73-2.76 (2H), 2.58 (2H), 2.55-2.80 (3H), and 0.95-1.05 (6H). MS: calc. M⁺ = 1109.5, obsvd. (M+1)⁺ = 1110.5.

¹H NMR of FFFFCG (**2**) (300MHz, DMSO- d_6) δ (ppm): 8.70 (1H), 8.42-8.52 (4H), 7.25-7.50 (20H), 4.70-4.82 (3H), 4.60-4.70 (1H), 4.01 (1H), 3.92 (2H), and 2.88-3.25 (10H). MS: calc. M⁺ = 766.3, obsvd. (M+1)⁺ = 767.3.



Figure S-1. Optical image of the hydrogel of **2** in water (0.35 wt%, pH = 7.4).

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Time (minute)	Flow (ml/min.)	H ₂ O %	CH ₃ CN %
0	5.0	100	0
35	5.0	20	80
40	5.0	20	80
41	5.0	100	0
45	5.0	100	0

Table S-1. Eluting gradient for HPLC purifications of compound 1 and 2.