Supporting Information

Materials and general methods:

Chemicals: L-Tyrosine and Fmoc-OSu were obtained from GL Biochem (Shanghai). All the other Starting materials were obtained from *Alfa*. Commercially available reagents were used without further purification, unless noted otherwise. Nanopure water was used for all experiments. All other chemicals were reagent grade or better.

Proteins: all proteins were from Sigma-Aldrich: Alkali phosphatase (Cat. No. P7640), BSA (Cat. No. A4378), Trypsin (Cat. No. T4799) and gelatin (Cat. No. G9391).

General methods: The synthesized compounds were characterized using ^{1}H NMR (Bruker ARX 300) using DMSO-d_6 as the solvent and ESI-MS spectrometric analyses were performed at the Thermo Finnigan LCQ AD System. HPLC was conducted at LUMTECH HPLC (Germany) system using a C18 RP column with MeOH (0.05% of TFA) and water (0.05% of TFA) as the eluents; Emission spectra were recorded on a Perkin-Elmer LS-55 luminance spectrometer at excitation wavelength of 272 nm; TEM samples were prepared as following: a copper coated with a thin layer of carbon layer was dipped into the hydrogel, and then it was kept in a desicator overnight. The dried sample was performed at the Tecnai G2 F20 system, operating at 200 kV; LC-MS was used to determine the conversion percentage of compound **1** and it was conducted at the LCMS-20AD (Shimadzu) system; And rheology was performed on an AR 2000ex (TA instrument) system using a parallel plates (40 mm) at the gap of 500 μm.

Syntheses and characterizations:

Compound 1 was synthesized by solid phase peptide synthesis:

Peptide Synthesis: The peptide derivative was prepared by solid phase peptide synthesis (SPPS) using 2-chlorotrityl chloride resin and the corresponding

Fmoc-succinated cystamine and N-Fmoc protected amino acids with side chains properly protected by a tert-butyl group. The first amino acid was loaded on the resin at the C-terminal with the loading efficiency about 0.6 mmol/g. 20% piperidine in anhydrous N,N'-dimethylformamide (DMF) was used during deprotection of Fmoc group. Then the next Fmoc-protected amino acid was coupled to the free amino group using O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluroniumhexafluorophosphate (HBTU) as the coupling reagent. The growth of the peptide chain was according to the established Fmoc SPPS protocol. At the final step, the N-terminus of the peptides was coupled with naphthalene acetic aicd to attach the Nap group on the peptides. After the last coupling step, excessive reagents were removed by a single DMF wash for 5 minutes (5 ml per gram of resin), followed by five steps of washing using DCM for 2 min (5 ml per gram of resin). The peptide derivative was cleaved using the solution of TFA: TIS: H_2O = 95: 2.5: 2.5, V/V for 30 min. All the solutions were combined and concentrated, and then 20 mL of ice-cold diethylether was added. The resulting precipitate was centrifuged for 10 min at 2 ^{0}C at 10,000 rpm. Afterward the supernatant was decanted and the resulting solid was dissolved in DMSO for HPLC separation.

Synthesis and Characterization of compound 1: The compound **1** was obtained by general solid phase peptide synthesis (spps). The resulting solid was dissolved in DMSO and purified by HPLC.^{1}H NMR (300 MHz, DMSO-d_6) δ 7.78-7.86 (m, 3H), 7.72 (s, 1H), 7.37-7.47 (m, 3H), 7.14-7.24 (m, 12H), 6.99 (d, J=8.42, 2H), 6.63 (d, J=8.38, 2H), 4.35-4.50 (m, 4H), 4.15-4.23 (m, 4H), 3.65-3.75 (m, 2H), 3.43-6.50 (m, 6H), 3.26-3.30 (m, 3H), 2.65-3.02 (m, 10H), 2.22-2.33 (m, 12H) HR-MS: calc. M^+ = 1321.47, obsvd. $(M+H)^+$ = 1322.4764.

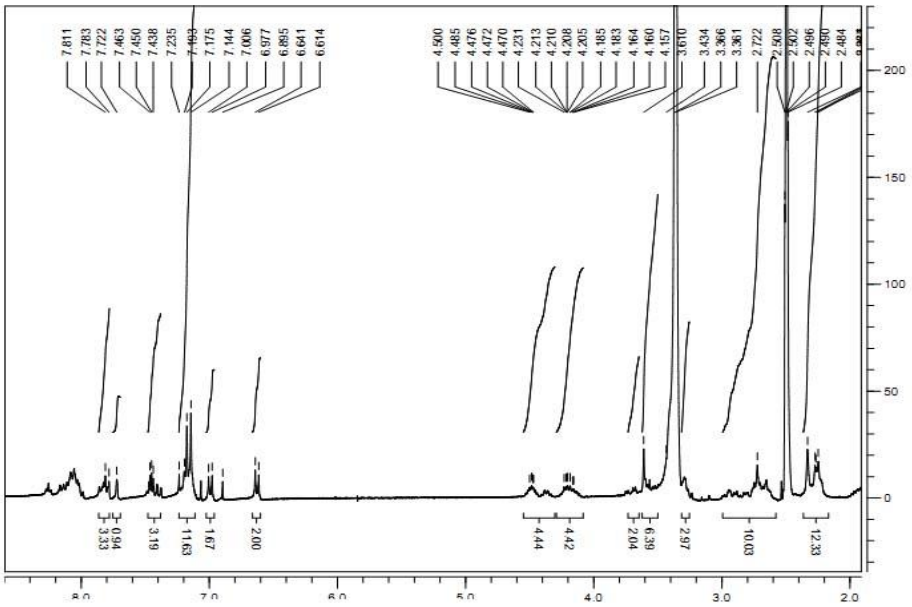

Figure S-1. ^{1}H NMR of compound 1

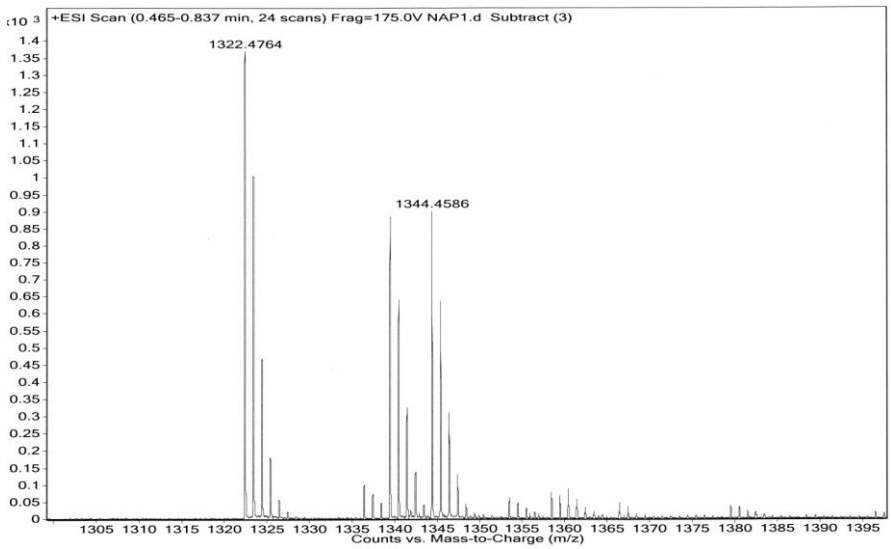

Figure S-2. HR-MS of compound 1

Formation of gel Nap-GFFY-OMe: 1.0 mg of Nap-GFFpY-OMe were dissolved in 1 mL of PBS buffer solution containing 0.13 mg (1 equiv. to Nap-GFFpY-OMe) of Na_2CO_3 and the final pH value of the resulting solution to about 7.4. Alkali phosphatase was added to the above solution (final enzyme concentration = 60 U/mL).

Details procedure to isolate self-assembled structures from gel of Nap-GFFY-OMe: 24 hours after the formation of 0.5 mL gel of Nap-GFFY-OMe, 2 mL of PBS was added, vortex-mixed and centrifuged at 10000 rpm for 10 minutes. The supernatant was taken out and a fresh PBS solution (2 mL) was added to wash the self-assembled structures again. This process was repeated for 9 times. The clear supernatants and the final precipitation were used to detect the activity of alkaline phosphatase in the presence of 10 μM of 4-Nitrophenyl phosphate as the substrate of alkali phosphatase.

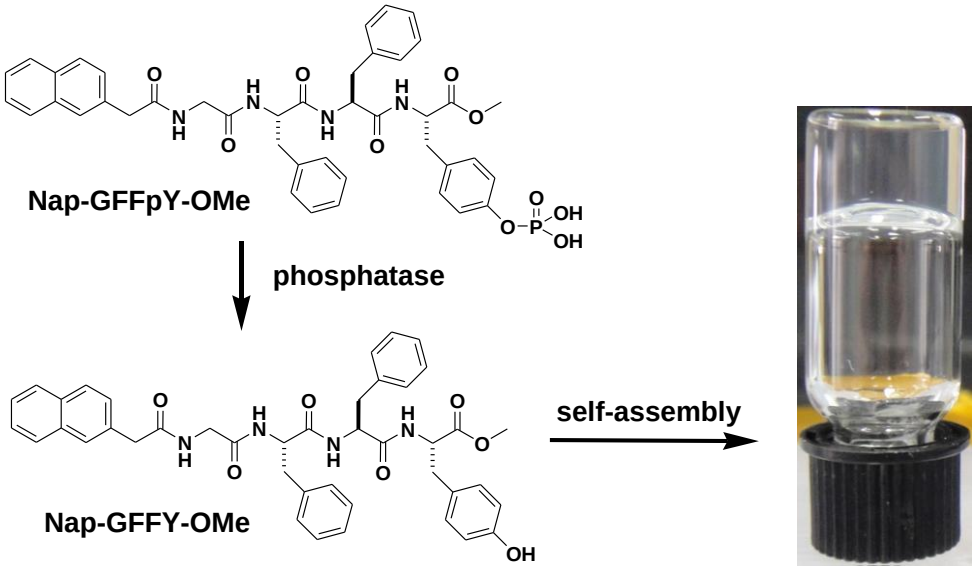

Figure S-3. Phosphatase-triggered conversion from Nap-GFFpY-OMe to Nap-GFFY-OMe and the formation of a molecular hydrogel

Formation of gel of 1 without or with different concentrations of BSA:

Formation of gel of 1: 2.0 mg of **1** (1.51 μmol) was dissolved in 0.45 mL of PBS buffer solution containing 0.8 mg (5 equiv. to **1**) of Na_2CO_3 (3 equiv. of Na_2CO_3 were used to neutralize the carboxylic acids on **1** and the additional 2 equiv. of Na_2CO_3 were used to neutralize DTT to make the final pH value of the resulting gel to about 7.4). And then 0.05 mL of PBS buffer solution containing 0.47 mg of DTT (3.02 μmol, 2.0 equiv. to **1**) was added. Gels would form after being kept at room temperature (22-25^{0}C) for about 30 minutes.

Formation of gel of 1 in the presence of different kinds of proteins: the same procedure was used to prepare gels with 20% of different kinds of proteins (gelatin, alkali phosphatase, trypsin and BSA).

Formation of gel of 1 with different concentrations of BSA: the same procedure was used to prepare gels with different concentrations of BSA (0.2, 0.3, 0.4 and 0.8 mg of BSA for gels containing 10, 15, 20 and 40% of BSA, respectively).

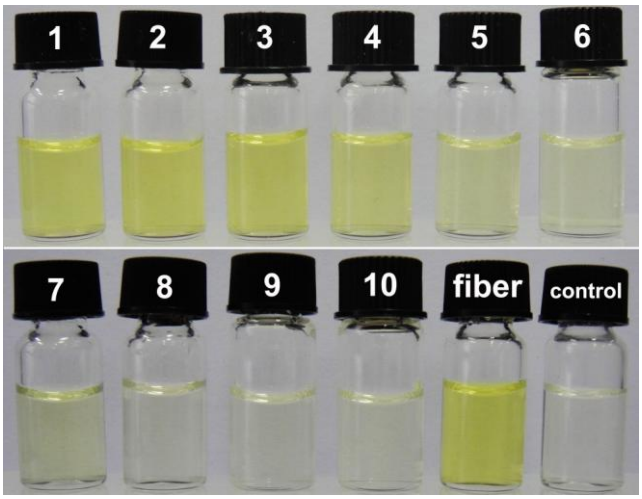

Figure S-4. Optical images of 1-10) supernatants obtained by washing a gel of Nap-GFFY-OMe (0.5 mL) with 2 mL of PBS following by centrifugation and fiber) the resulting fibers after 10 times of washing in solutions of 10 μM of 4-Nitrophenyl phosphate (control: a PBS solution containing 10 μM of 4-Nitrophenyl phosphate) (the intensity of yellow colour represents the activity of phosphatase)

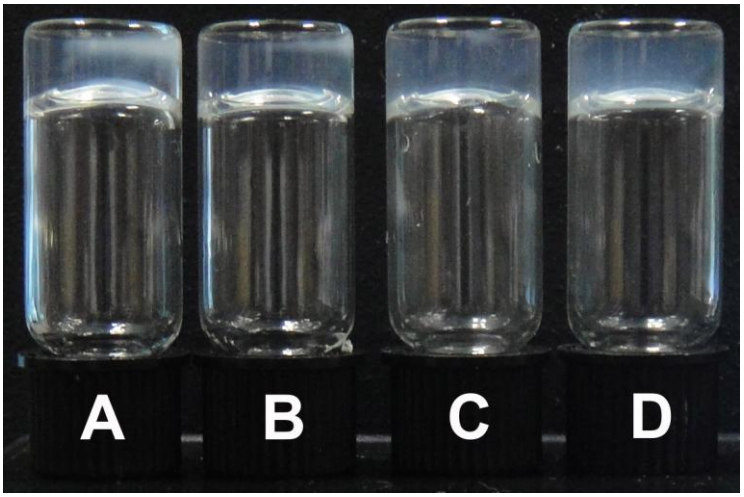

Figure S-5. Optical images of gels from treating solutions of **1** (0.4 wt%) with 2 equiv. of DTT in the presence of different concentrations of BSA at 24h time point: A) 10%, B) 15%, C) 20% and D) 40% of BSA

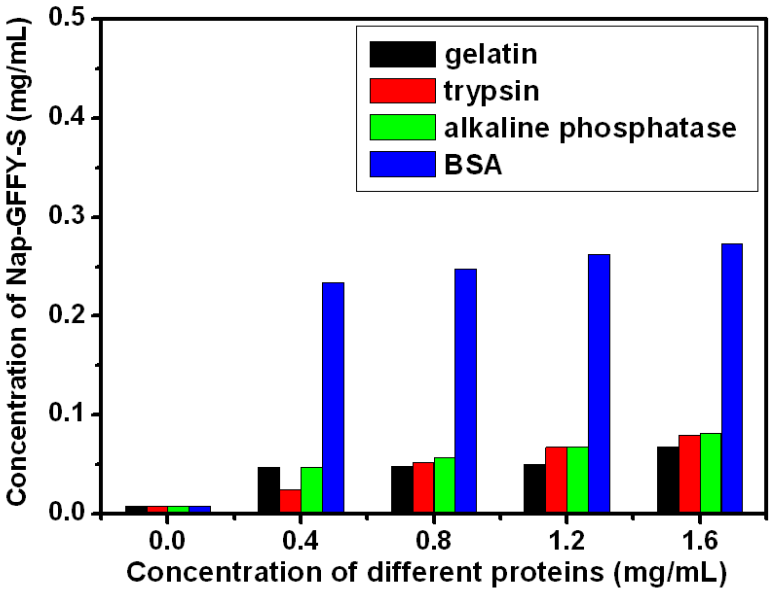

Figure S-6. The saturated concentration of **2** in PBS solutions with different kinds of proteins at different concentrations

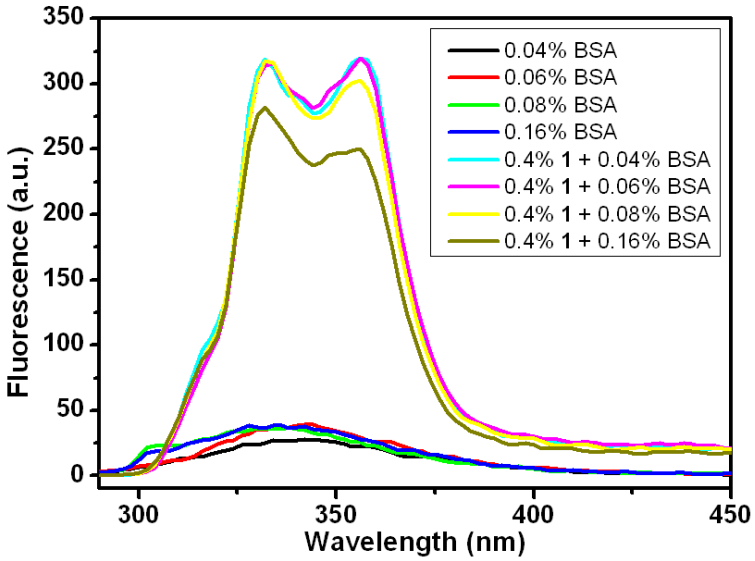

Figure S-7. Emission spectra of solutions of **1** without and with different concentrations of BSA and emission spectra of solutions of BSA ($\lambda_{exc.}$ = 272 nm)