Supporting Information

Materials and general methods:

Chemicals: Fmoc-amino acids 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.

General methods: The synthesized compounds were characterized using ^{1}H NMR (Bruker ARX 400) using DMSO-d_6 or CD_3OD 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 methanol (1‰ of TFA) and water (1‰ of TFA) as the eluents. 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 conducted at the LCMS-2020 (Shimadzu) system, and rheology was performed on an ARES 1500ex (TA instrument) system using a parallel plates (40 mm) at the gap of 500 μm. ARES 1500ex can not control the strain when the mechanical strength (G' value) of the sample is low. For example, for a solution sample with low viscosity, though we set the strain value to 1%, the machine can not control the strain and sometimes the strain will be 100% which will destroy the gels.

Syntheses and characterizations:

Preparation of Fmoc-NPhe-OH: The synthesis of Fmoc-NPhe-OH was described by John et al.[1] And we got the white solid of the product in a yield of 84% by using the same method. ^{1}H NMR (400 MHz, DMSO-d_6) δ7.92-7.85 (d, 2H), 7.65 (d, 1H), 7.53 (d, 1H), 7.46-7.37 (m, 2H), 7.35-7.31 (m, 1H), 7.30-7.20 (m, 5H), 7.03-6.98 (m, 1H), 4.50-4.45 (d, 2H), 4.38-4.35 (d, 1H), 4.29-4.24 (m, 2H), 3.83 (d, 2H). MS: calc. $M^+ = 387.1$, obsvd. $(M+1)^+ = 387.7$.

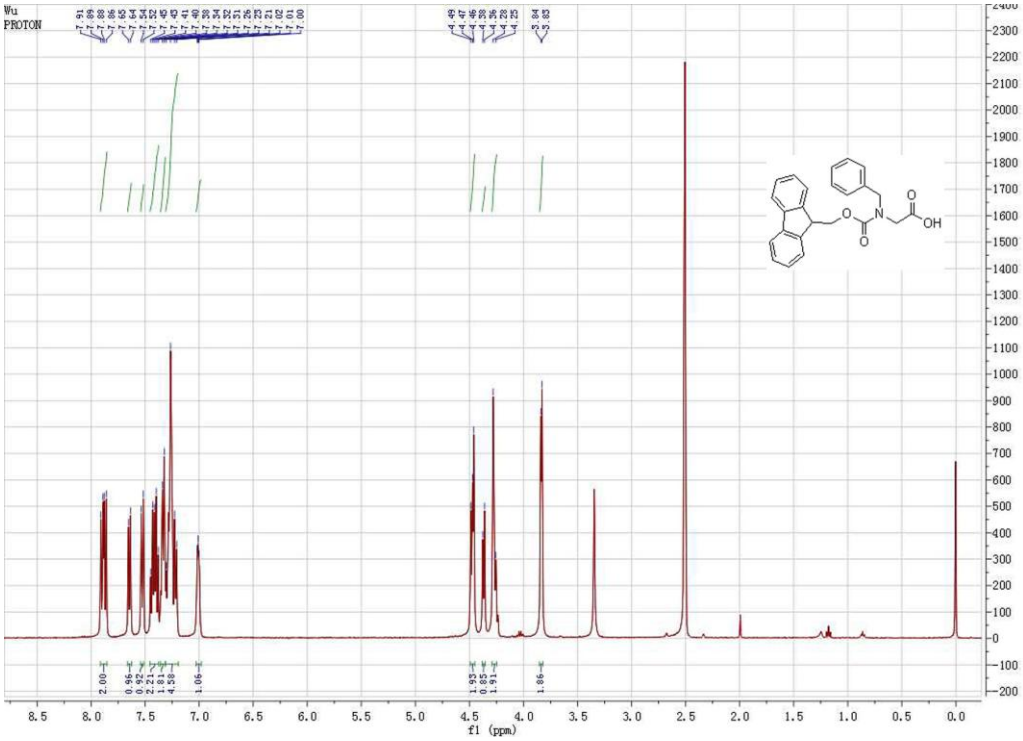


Figure S-1. ^{1}H NMR of Fmoc-NPhe-OH

Preparation of F'F'F'F'-GGGG: The F'F'F'F'-GGGG was prepared by solid phase peptide synthesis (SPPS) using 2-chlorotrityl chloride resin, the corresponding N-Fmoc protected amino acids with side chains properly protected by a tert-butyl group, Fmoc-succinated cystamine and Fmoc-protected N-substituted glycine. The first amino acid was loaded on the resin at the C-terminal with the loading efficiency of about 0.6 mmol/g in anhydrous dichloromethane (DCM). After 2 hours, the reaction solution was drained and the resin was washed by dimethyl Formamide (DMF) for 5 minutes. Afterwards, 20% piperidine in DMF was used to deprotect Fmoc group. Then the next Fmoc-protected amino acid was coupled to the free amino group on the resin using HBTU as the coupling reagent and DIPEA as the catalytic agent. The growth of the peptoid-peptide chain was according to the established Fmoc SPPS protocol.[1] After the last coupling step, excessive reagents were removed by DMF washing one time 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 peptoid-peptide conjugates were cleaved from resin using 95% of TFA with 2.5% of TIS and 2.5% of H_2O for 30 minutes, then washed the resin 5 times with DCM. After combining these solutions together and concentrated by the rotary evaporator, diethyl ether was then added to concentrate the solution. The resulting precipitate was centrifuged for 10 min at room temperature at 10,000 rpm and further purified by reverse phase HPLC. ^{1}H NMR (400MHz, DMSO-d_6) δ 7.54-7.45(m, 2H), 7.45-7.36 (m, 4H), 7.38-7.20 (m, 12H), 7.18-7.01 (m, 2H), 4.61-4.19 (m, 6H), 4.31-4.11 (m, 6H), 3.99-3.89 (m, 2H), 3.78-3.74 (m, 6H). MS: calc. M^+ = 834.4, obsvd. $(M+1)^+$ = 835.3. HR-MS: obsvd. $(M+1)^+$ =835.4

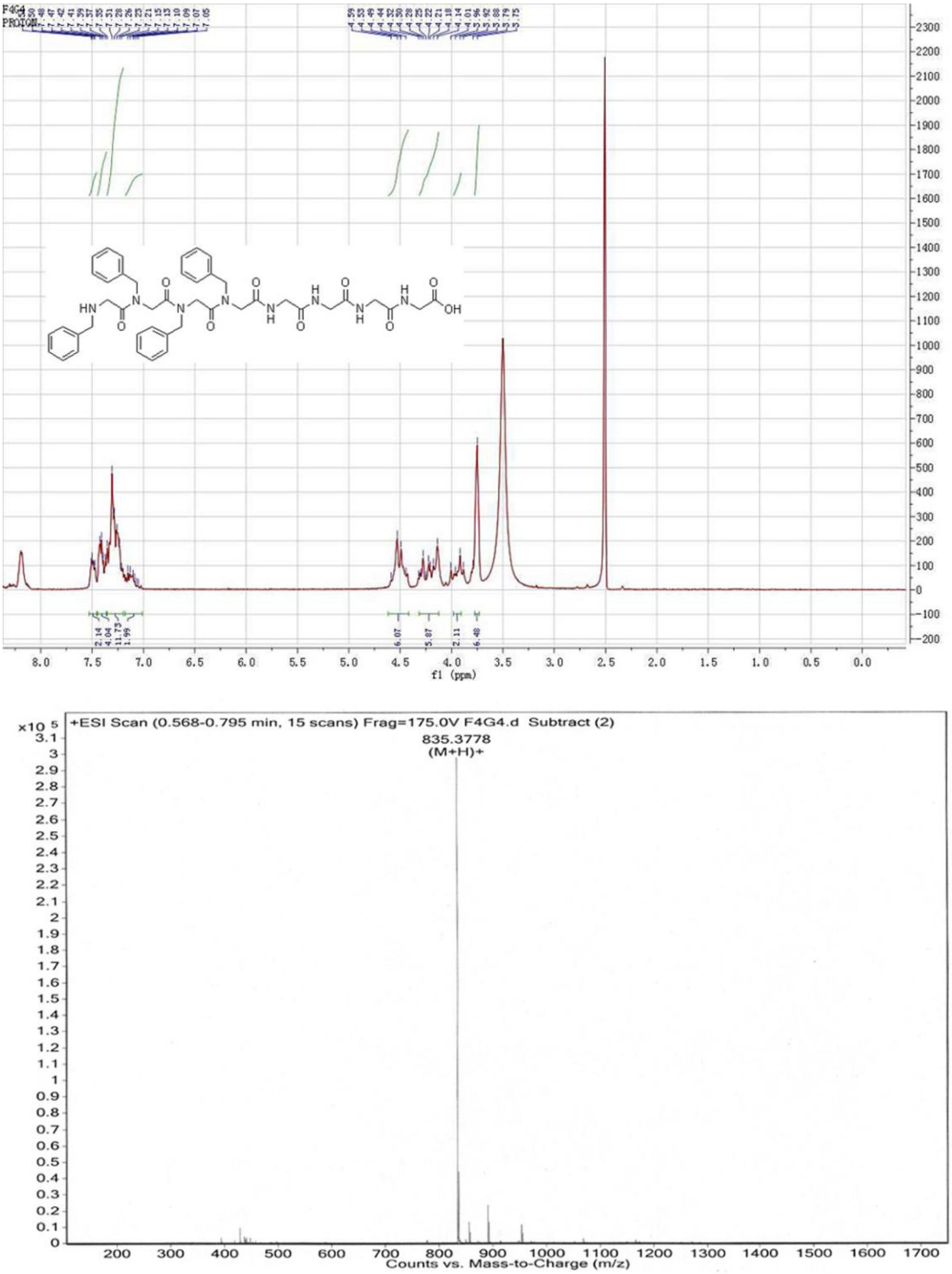


Figure S-2. ^{1}H NMR and HR-MS of F'F'F'F'-GGGG

Preparation of F'F'F'F'-GRGD: The same procedure for preparation of **F'F'F'F'-GGGG** was used. ^{1}H NMR (400 MHz, DMSO-d_6) δ7.51-7.47 (m, 2H), 7.44-7.38 (m, 3H), 7.35-7.21 (m, 12H), 7.19-7.08 (m, 3H), 4.58-4.45 (m, 6H), 4.29-4.12 (m, 6H), 4.02-3.83 (m, 6H), 3.81-3.77 (m, 2H), 3.16-3.03 (m, 2H), 2.73-2.55 (m, 2H), 1.76-1.42 (m, 4H). MS: calc. M^+ = 991.5, obsvd. $((M+2)/2)^+$ = 495.6. HR-MS: obsvd. $(M+1)^+$ =992.5

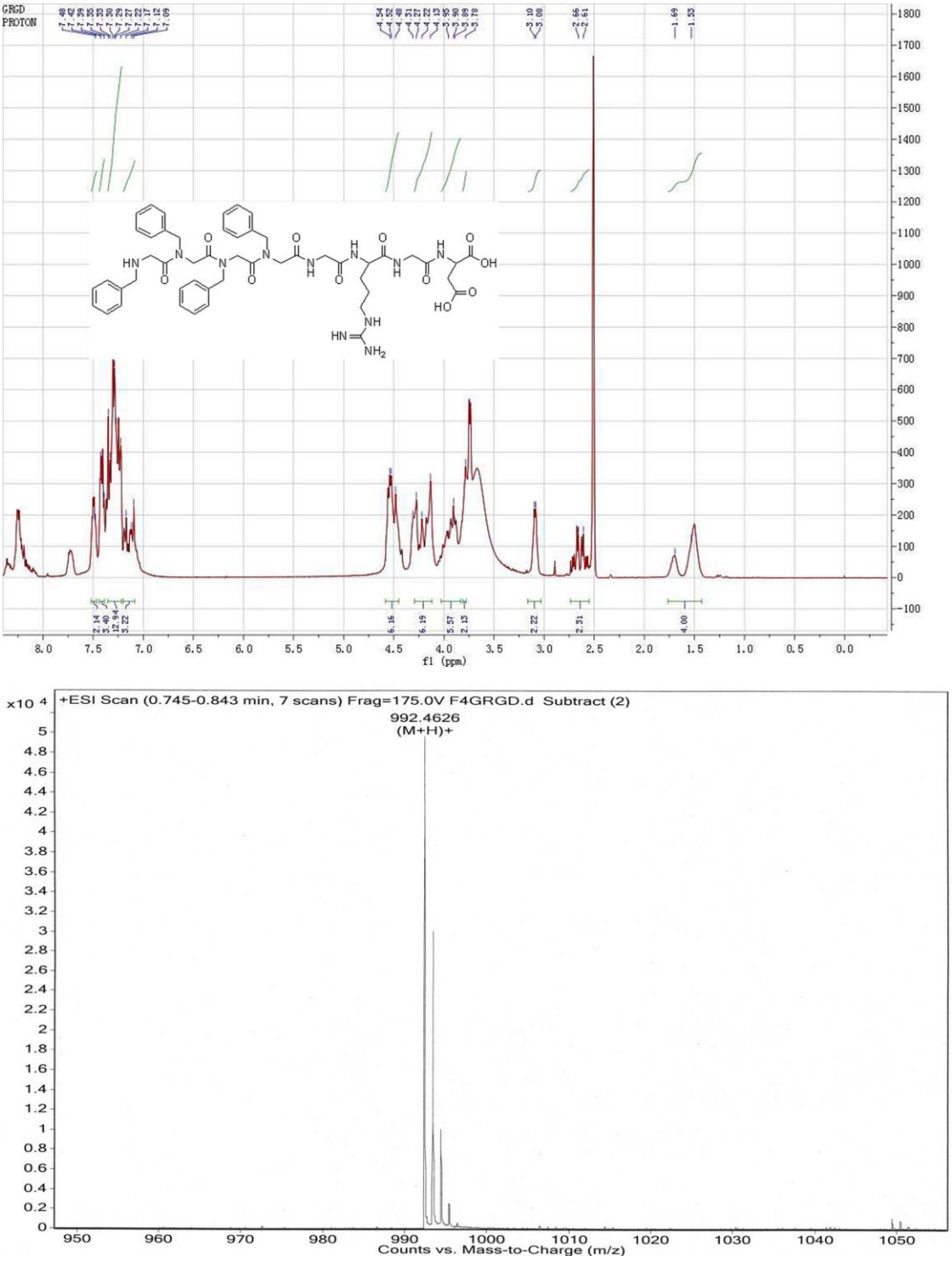
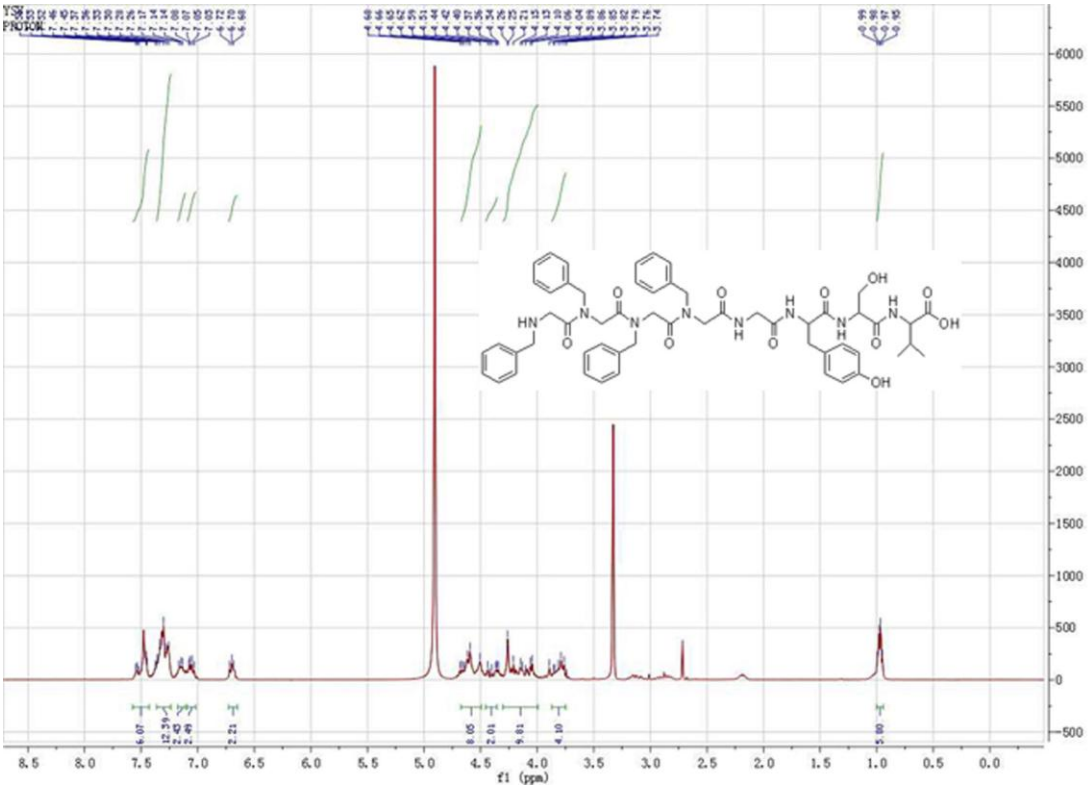


Figure S-3. ^{1}H NMR and HR-MS of F'F'F'F'-GRGD

Preparation of F'F'F'F'-GYSV: The same procedure for preparation of **F'F'F'F'-GGGG** was used. ^{1}H NMR (400 MHz, CD3OD) δ 7.57-7.43 (m, 6H), 7.36-7.23 (m, 12H), 7.15-7.10 (m, 2H), 7.09-7.01 (m, 2H), 6.72-6.65 (m, 2H), 4.67-4.49 (m, 8H), 4.45-4.35 (m, 2H), 4.30-4.99 (m, 10H), 3.87-3.74 (m, 4H), 1.00-0.94 (dd, 6H). MS: calc. M^{+} = 1012.5, obsvd. $(M+1)^{+}$ = 1013.4. HR-MS: obsvd. $(M+1)^{+}$ =1013.5



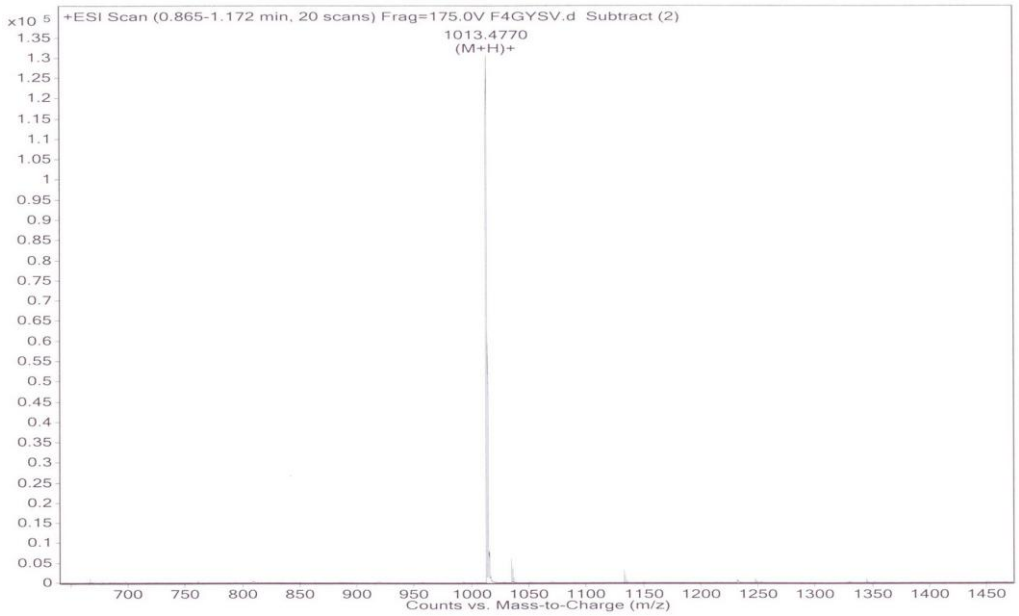


Figure S-4. ^{1}H NMR and HR-MS of F'F'F'F'-GYSV

Preparation of F'F'F'F'-GVPP: The same procedure for preparation of **F'F'F'F'-GGGG** was used. ^{1}H NMR (400 MHz, DMSO-d_6) δ.53-7.47 (m, 2H), 7.44-7.38 (m, 3H), 7.35-7.21 (m, 12H), 7.20-7.01 (m, 3H), 4.59-4.46 (m, 6H), 4.32-4.13 (m, 9H), 4.01-3.93 (m, 2H), 3.91-3.88 (m, 2H), 3.62-3.48 (m, 4H), 2.14-2.08 (m, 2H), 1.95-1.74 (m, 7H), 0.93-0.80 (dd, 6H). MS: calc. M^+ = 956.5, obsvd. $(M+1)^+$ = 957.5. HR-MS: obsvd. $(M+1)^+$ =957.5

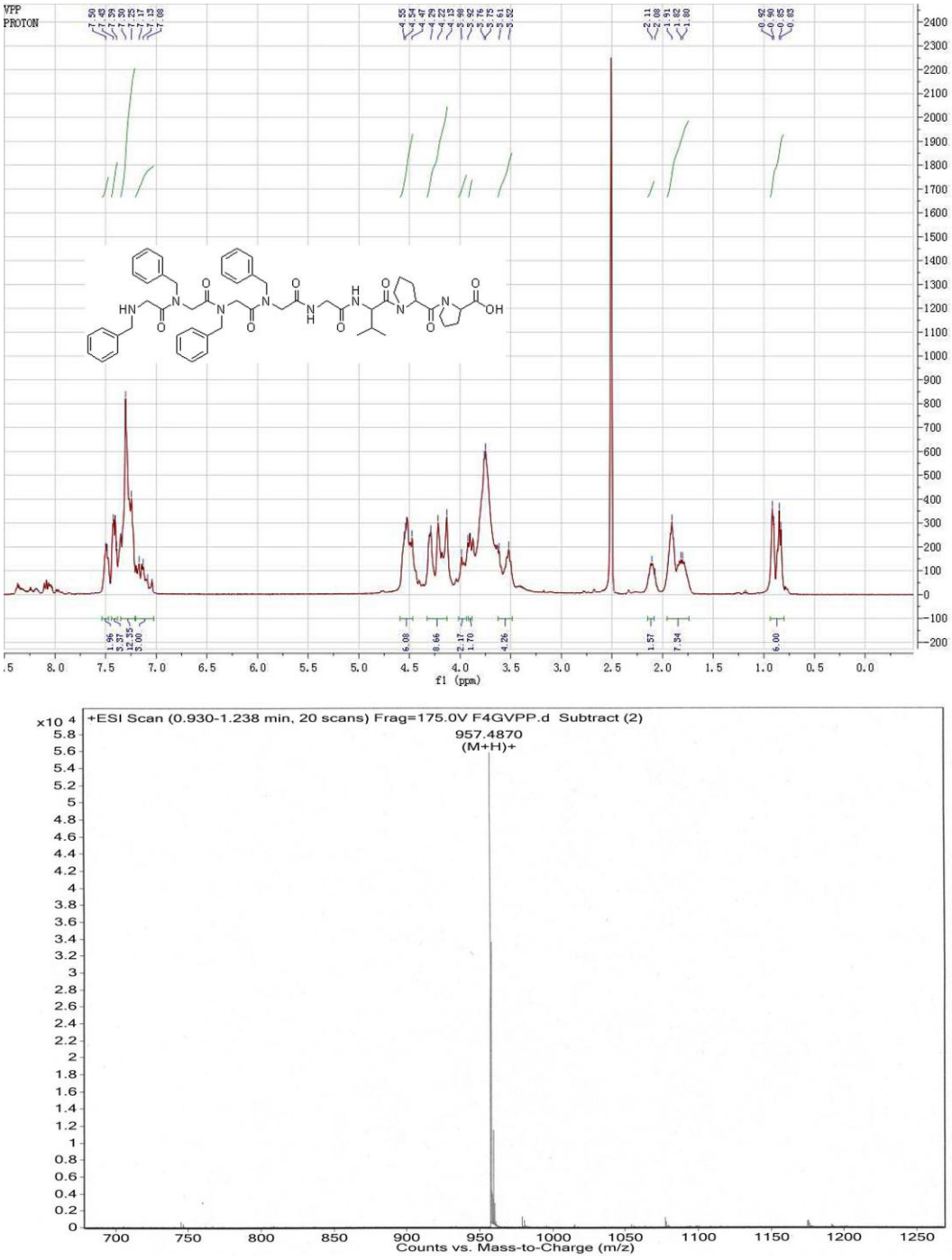


Figure S-5. ^{1}H NMR and HR-MS of F'F'F'F'-GVPP

Preparation of the hydrogels (1.0 wt%):

2 mg of pepoid-peptide conjugates was dissolved in 0.19 mL of PBS buffer solution (pH = 7.4). Na_2CO_3 (0.4 M) was then added to the above solution to make the final pH=7.4. The solution was heated to dissolve the powders completely and gel was formed after the hot solution being kept at room temperature (22-25 ℃) for less than 15 minutes.

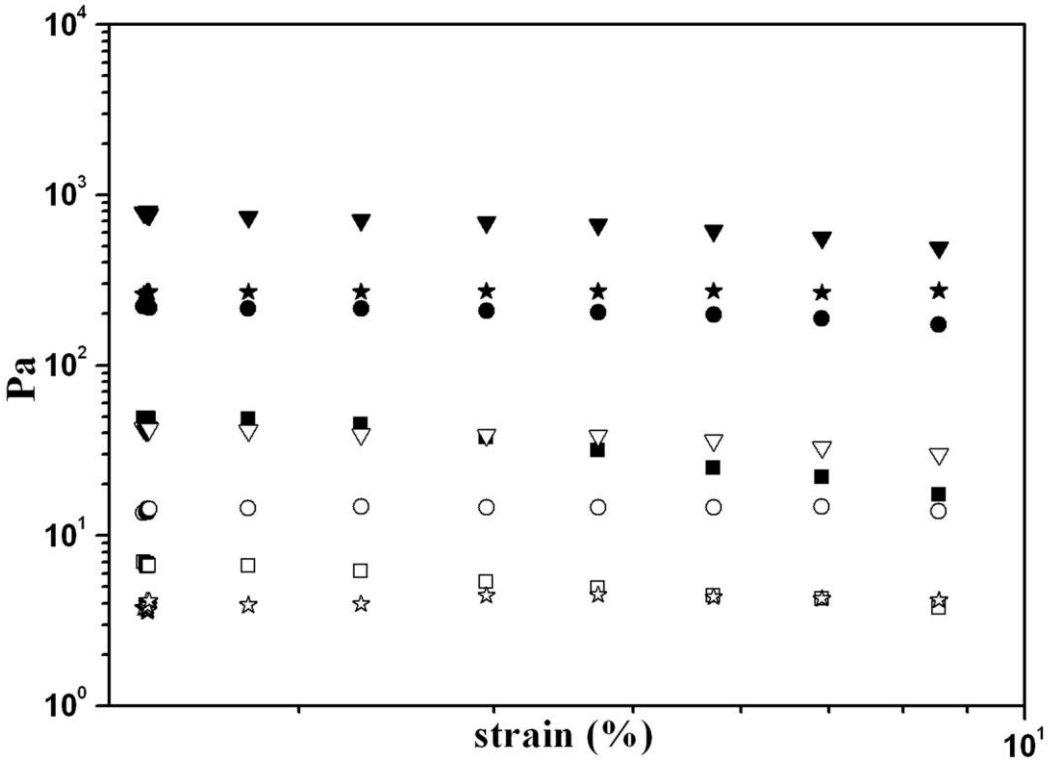


Figure S-6. Dynamic stain sweep at the frequency of 1 rad/s of four hydrogels at 1.0 wt% (triangles: GGGgel, circles: RGDgel, squares: YSVgel, and stars: VPPgel, filled symbols: storage modulus (G') and open symbols: loss modulus (G")).

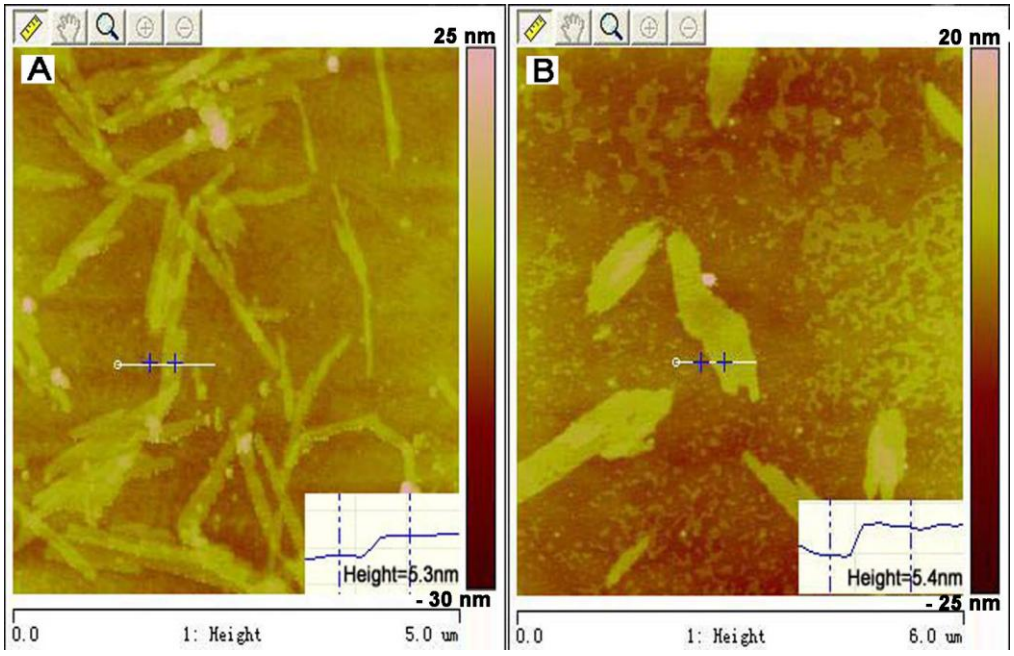


Figure S-7. AFM of (A) GGG gel and (B) RGD gel.

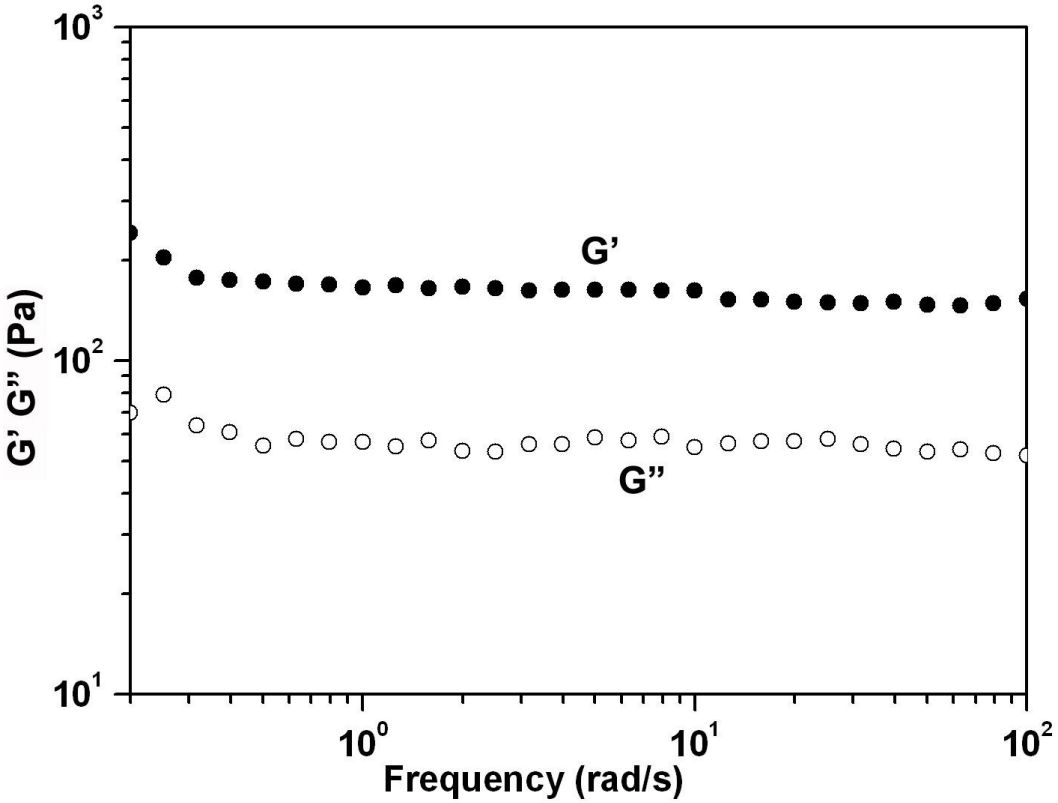


Figure S-8. Dynamic frequency sweep at the strain of 1% of DFDFDFDF-GRGD gel

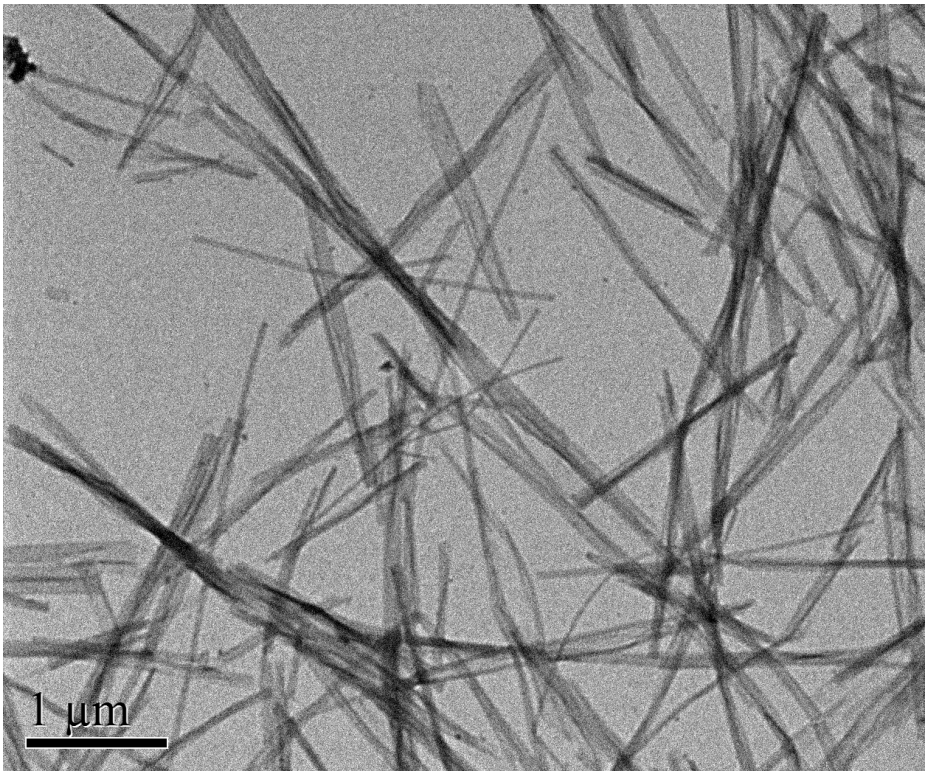


Figure S-9. The TEM image of DFDFDFDF-GRGD gel

Biostability test with proteinase K:

1 mg of each compound was dissolved in 5 mL PBS buffer solution and adjusted it to a final pH at 7.5. Then proteinase K were added in the concentration of 3.2 units/mL and incubated at 37℃ for 24 hours.

Afterwards 500 μl of sample were taken out each time and analyzed by LC-MS.

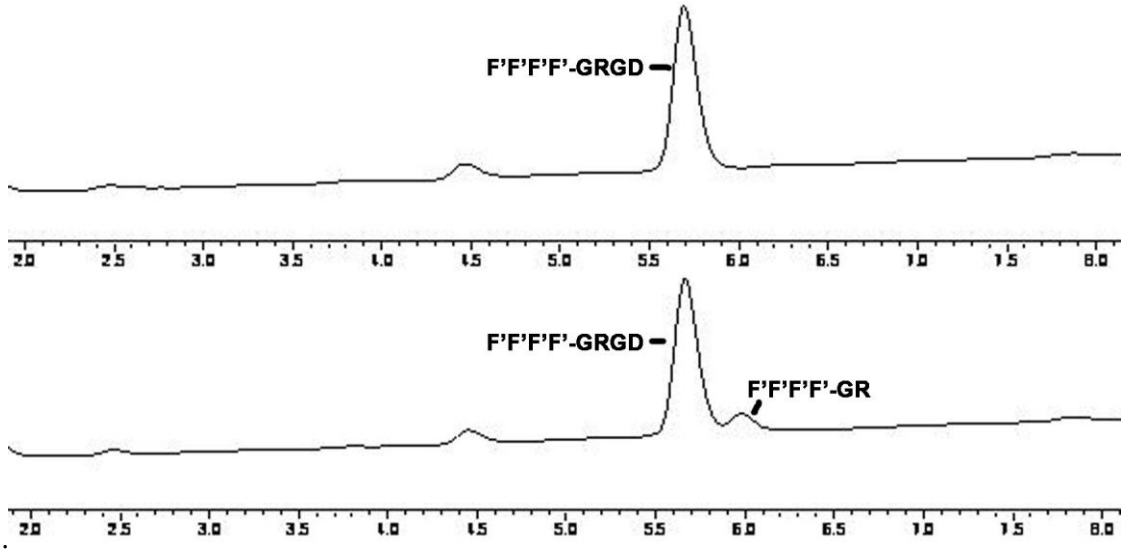


Figure S-10. HPLC traces of F'F'F'F'-GRGD digested by proteinase K (top: no proteinase K, bottom: 24 hours after added proteinase K)

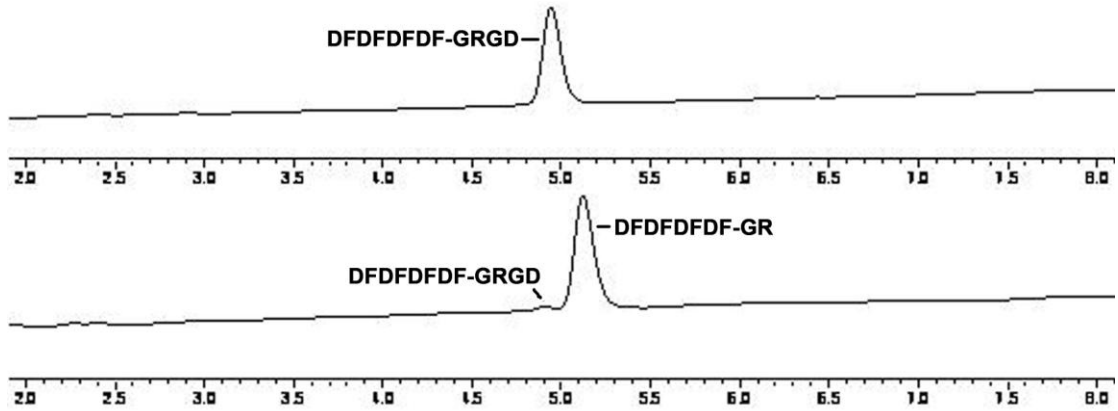


Figure S-11. HPLC traces of DFDFDFDF-GRGD digested by proteinase K (top: no proteinase K, bottom: 24 hours after added proteinase K)

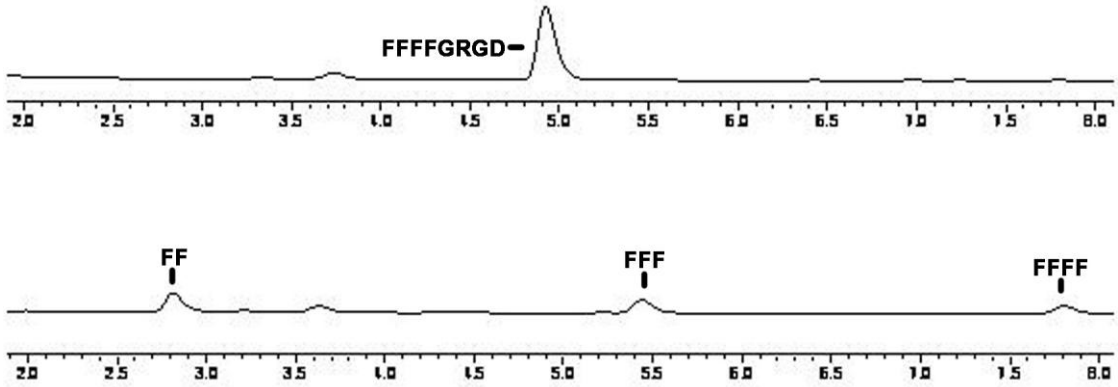


Figure S-12. HPLC traces of FFFF-GRGD digested by proteinase K (top: no proteinase K, bottom: 24 hours after added proteinase K).

Determination of the biocompatibility of the compounds by the MTT assay:

Four cells are tested to determine the biocompatibility of the compounds. They are Hela cells, HepG2 cells, A549 cells and NIH 3T3 cells. Each kind of cells were seeded in a 96-well plate with a density of 5000 cells per well (total medium volume of 100 mL). 24 hr post-seeding, the medium was replaced with solutions with a series of concentrations (5 concentrations) of different compounds were added to each well (five wells for each concentration). The MTT assays were performed after a culture time of 48 hr. Cells without treatment with the compounds were used as the control.

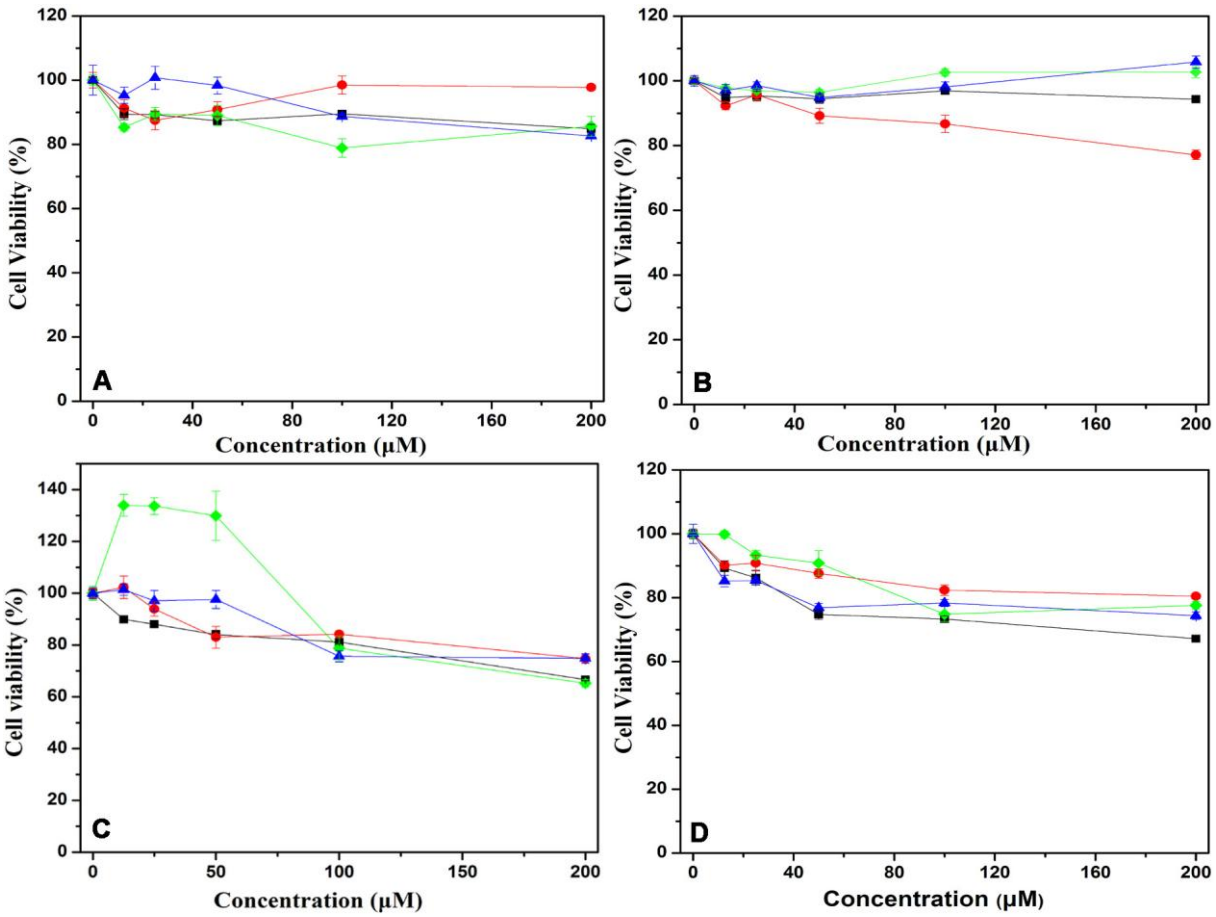


Figure S-13. 48hr cytotoxicity of four peptoid-peptide conjugates: (A) GGG, (B) RGD, (C) YSV, (D) VPP hydrogelators on fibroblast 3T3, HeLa, HepG2, and A549 cells (blue: fibroblast 3T3, black: HeLa, red: HepG2, green: A549.)

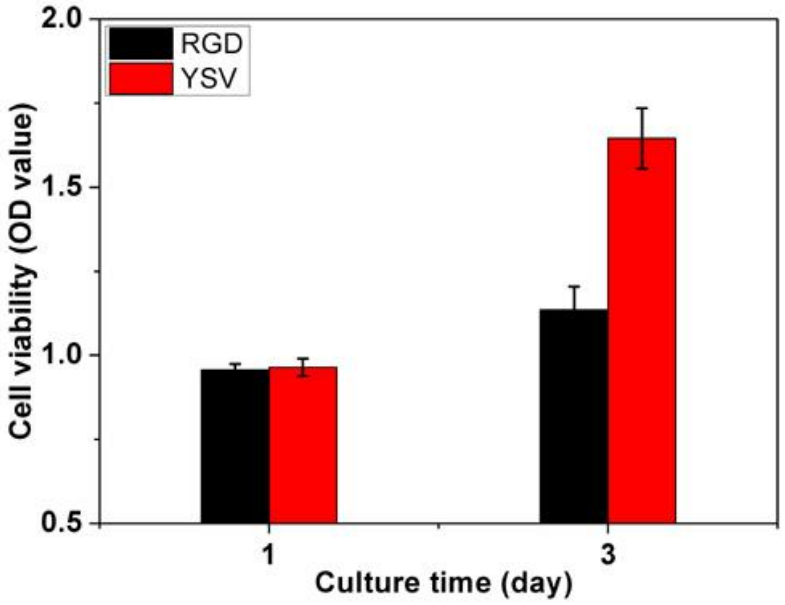


Figure S-14. Proliferation rates of 3T3 cells cultured on RGDgel and YSVgel

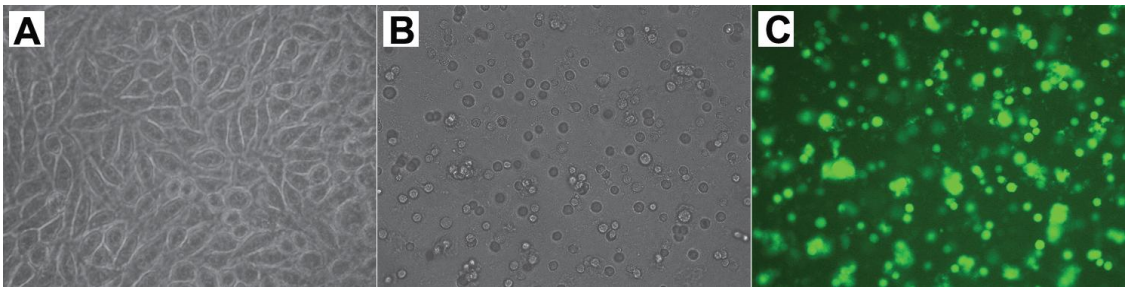


Figure S-15. Bright field images of 3T3 cells cultured on A) YSVgel and B) RGDgel and C) live-dead assay of cells in B)

Reference:

1. J. A. W. Kruijtzer, L. J. F. Hofmeyer, W. Heerma, C. Versluis, R. M. J. Liskamp, *Chem-Eur J*. **1998**, *4*, 1570-1580.