Electronic Supplementary Information (ESI)

Amyloid peptide hydrogels via formation of coordination polymers with Ag^+ by its core peptide equipped with a C-cysteine

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1. Materials

KLVFFC peptides (L-/D-**KLVFFC**, >98%) and Aβ (1-40) peptide (>95%) were custom synthesized by GL Biochem. Silver nitrate ($AgNO_3$, ≥99.8%) and hydrogen nitrate (HNO_3, 65%~68%) were purchased from Sinopharm Chemical Reagent Ltd. Hexafluoro-2-propanol (HFIP) was purchased from Meryer co. Ltd. Thioflavin T (ThT) was purchased from Energy Chemical Reagent Ltd. All reagents of analytical grade were used without further purification.

2. Methods

Aβ (1-40) sample preparation

Aβ (1-40) peptide was disaggregated and prepared according to a classic protocol as previously described.[1] Briefly, 1 mL HFIP was added into 1 mg Aβ peptide followed by sonication to disaggregate the peptide into monomer form. HFIP was then removed by a slow stream of dry N_2 gas. The procedure was repeated three times and a colorless transparent peptide film was observed on the wall of Eppendorf Protein LoBind tubes. The peptide film was then dried under fume hood overnight and stored at -20 °C.

Thioflavin T aggregation assay

Aβ (1-40) monomer film was suspended in DMSO to a concentration of 2.5 mM, followed by vortex sonication, before diluted with PBS buffer (pH 7.5) to a final concentration of 50 μM. Stock ThT solution was prepared by dissolving ThT powder to 5 mg/mL in water. Prior the fluorescence measurement, the ThT solution was diluted to 25 μM with PBS buffer and added to Aβ (1-40) peptide aggregates at different incubation time.[2] λ_{ex} = 430 nm, the excitation and emission slit width were set at 5 nm and 10 nm, respectively

TEM and SEM imaging

TEM images were obtained by JEM-1400 transmission electron microscope. For sample preparation, drop-casting of 10 μL **KC** or Ag^+-**KC** coordination polymers were applied to carbon film supported copper grid of 400 mesh. The grids were air-dried and applied for TEM imaging. SEM imaging was conducted on Hitachi S-4800 scanning electron microscope. Lyophilized hydrogels at 2 wt% were applied to conductive tape for SEM observation.

Cell Culture and Cytotoxicity

HeLa cells were incubated in DMEM medium with 10% FBS and 1% antibiotic (penicillin–

streptomycin, 10 000 U mL^{-1}) in a humidified atmosphere with 5% CO_2 at 37 °C. The cytotoxicity of Ag^+-L-**KC** against HeLa cells at pH 7.4 was studied by CCK-8 assay. Cells were seeded on 96-well plates with a density of 10000 cells per well. The medium was removed and various concentrations of Ag^+-L-**KC** in DMEM with 10% FBS at pH 7.4 were added. The cells were incubated for 48 h before CCK-8 was added. The optical density (OD) at 450 nm was determined via a microplate reader. The relative cell viability was defined by: cell viability (%) = $OD_{(sample)}$ / $OD_{(control)}$ × 100%. For control experiment, the OD value in the absence of Ag^+-L-**KC** was measured in a similar way.

Absorption spectra were recorded on a Thermo Evolution 300 spectrophotometer. CD spectra were conducted using JASCO J-1500 Circular Dichroism Spectrometer. Fluorescence spectra were recorded using Horiba Fluoromax-4 spectrofluorometer. FT-IR spectra were recorded using Thermofisher Nicolet iS50 FT-IR spectrometer. XRD measurements were obtained using Rigaku Smartlab-SE X-ray diffractometer. Rheometric measurements were obtained using DHR-2 rotary rheometer. ^{1}H NMR spectra were recorded on a Bruker Avance III HD 850 MHz NMR Spectrometer using tetramethylsilane as an internal standard. MALDI-TOF MS spectra were acquired on a Bruker autoflex maX MALDI-TOF Mass Spectrometer.

3. References

1 W. B. Stine, K. N. Dahlgren, G. A. Krafft and M. J. LaDu, *J. Biol. Chem.*, 2003, **278**, 11612-11622.

2 D. Shea, C.-C. Hsu, T. M. Bi, N. Paranjapye, M. C. Childers, J. Cochran, C. P. Tomberlin, L. Wang, D. Paris, J. Zonderman, G. Varani, C. D. Link, M. Mullan and V. Daggett, *Proc. Nat. Acad. Sci. U.S.A.*, 2019, **116**, 8895-8900.

4. Experimental Data

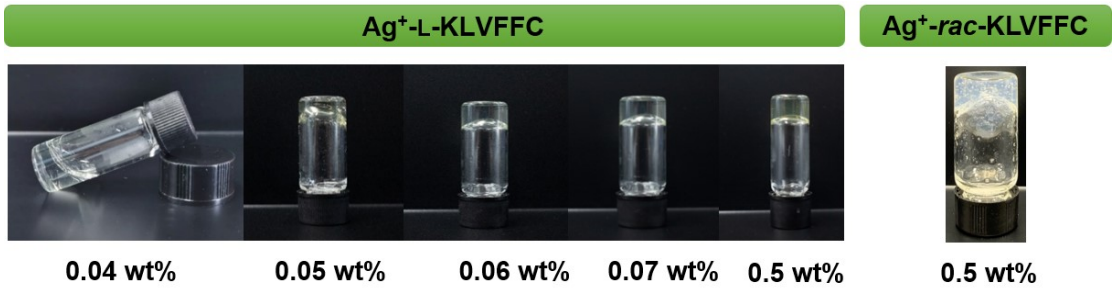

Fig. S1 Photographs of Ag^+-L-**KLVFFC** hydrogels at 0.04 wt% - 0.5 wt% and Ag^+-*rac*-**KLVFFC** hydrogels at 0.5 wt%.

Fig. S2 Left to right are TEM image, photograph of self-assembled L-**KLVFF** peptide and Zn^+-L-**KLVFFC** at 1.0 wt%.

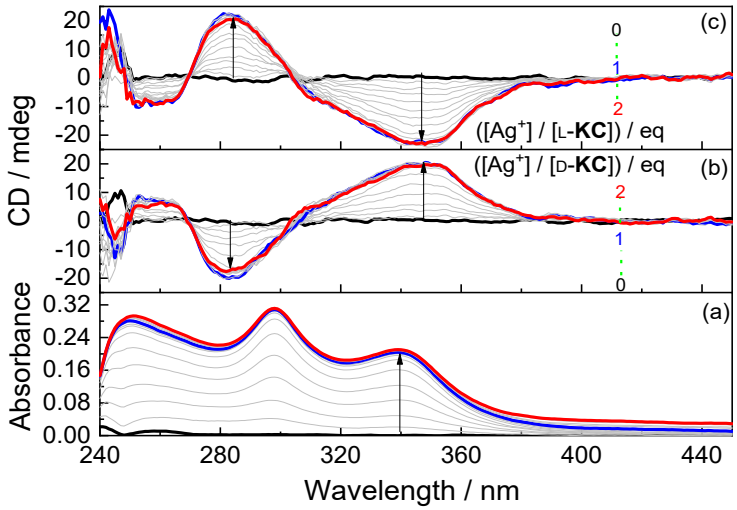

Fig. S3 Absorption (a) spectra of L-**KC** and CD (b, c) spectra of L-**KC** and D-**KC** peptide in the presence Ag^+ in pH = 5.0 buffer. [L-**KC**] = [D-**KC**] = 50 μM (0.0038 wt%), [Ag^+] = 0 – 100 μM.

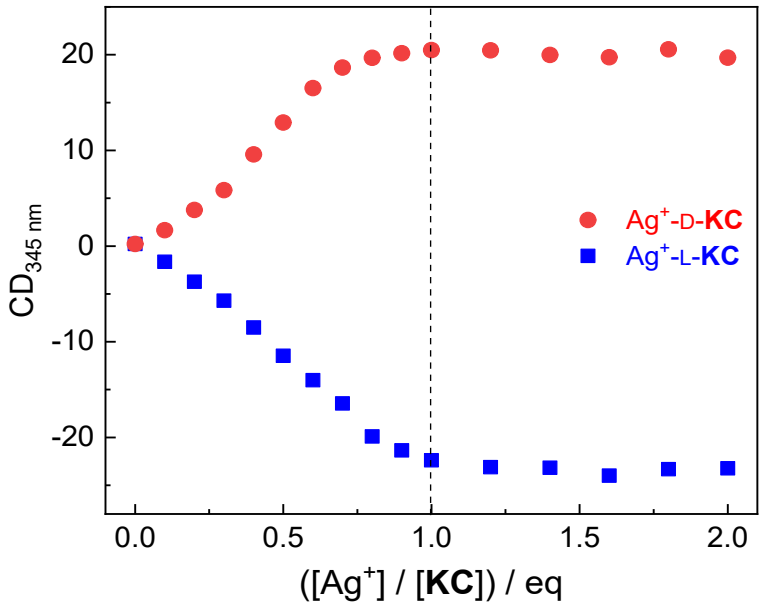

Fig. S4 Plots of CD signal at 345 nm of L-**KC** or D-**KC** peptide versus concentration of Ag^+. [L-**KC**] = [D-**KC**] = 50 μM (0.0038 wt%), [Ag^+] = 0 – 100 μM.

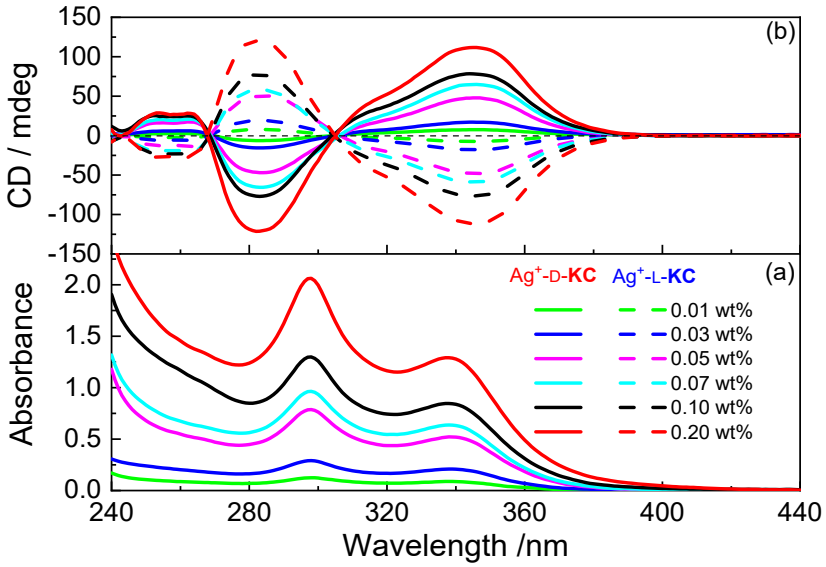

Fig. S5 Absorption (a) and CD (b) spectra of Ag^+-L-**KC** and Ag^+-D-**KC** coordination polymers of increasing concentration showing hydrogelation at high concentration. Spectra were all measured using a 1-mm cuvette.

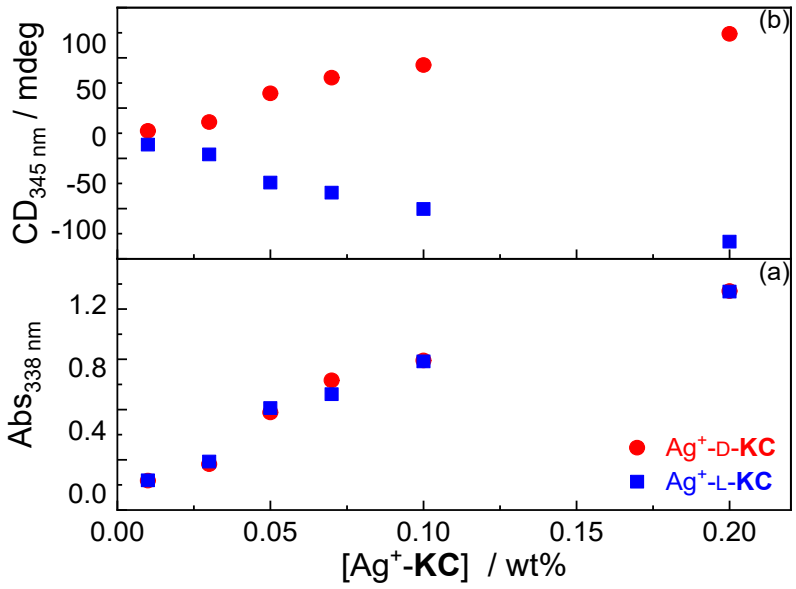

Fig. S6 (a) Absorbance at 338 nm and (b) CD signal at 345 nm of Ag^+-**KC** coordination polymers of increasing concentration.

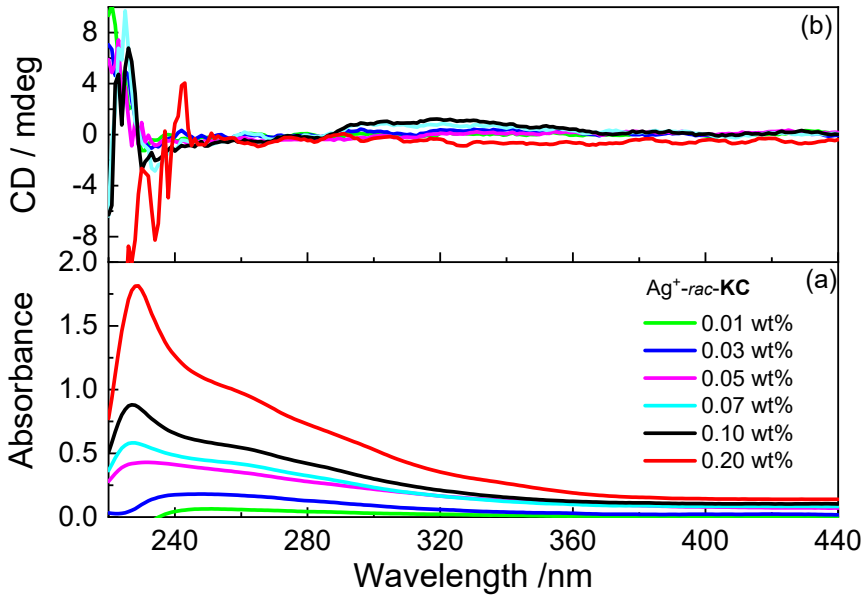

Fig. S7 Absorption (a) and CD (b) spectra of Ag^+-*rac*-**KC** coordination polymers of increasing concentration. Spectra were all measured using a 1-mm cuvette.

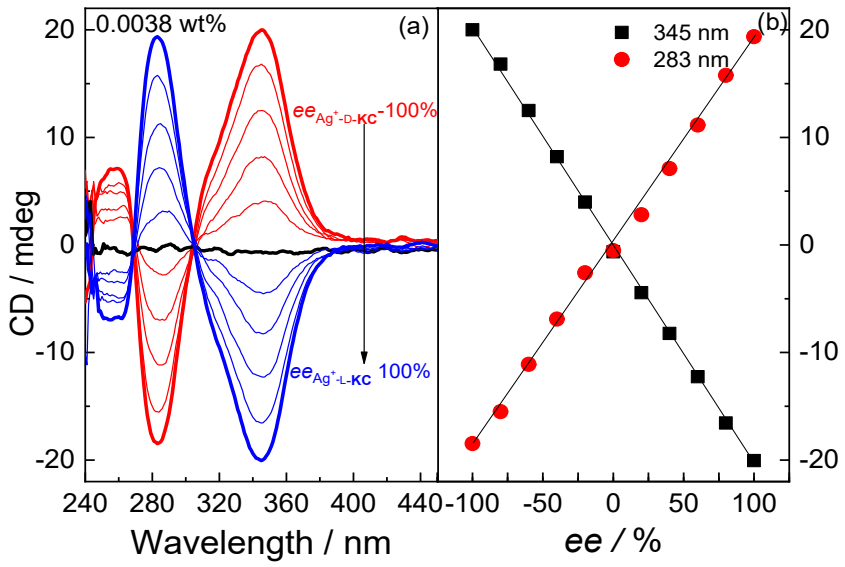

Fig. S8 (a) CD spectra and (b) plot of CD signals of Ag^+-**KC** coordination polymers of varying *ee* of **KC** in pH = 5 buffer. Spectra were all measured in a 10-mm cuvette. [L-**KC**] + [D-**KC**] = [Ag^+] = 50 μM (0.0038 wt%).

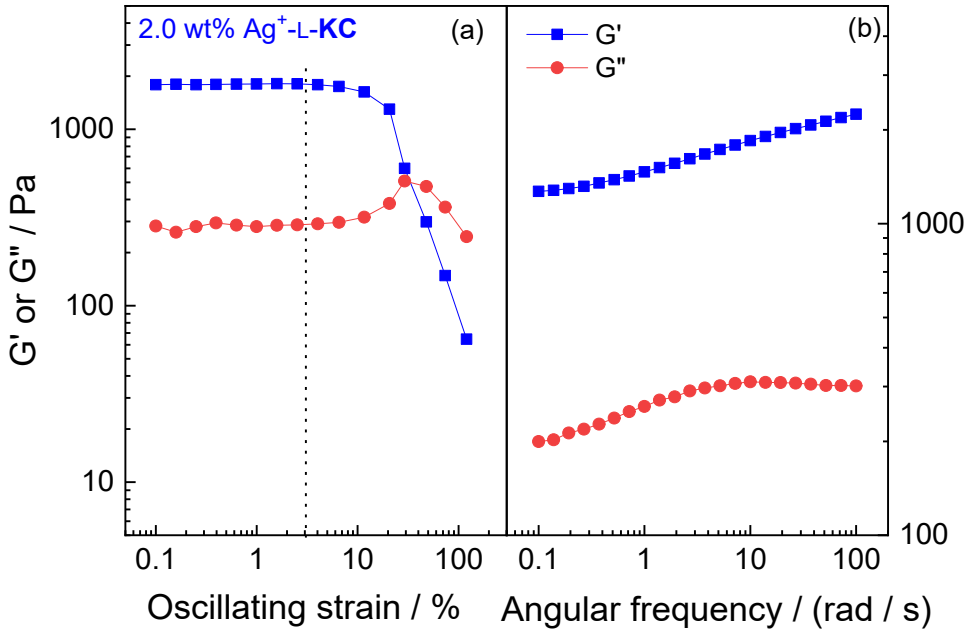

Fig. S9 Storage modulus (G′) and loss modulus (G″) of 2.0 wt% Ag^+-L-**KC** hydrogel (a) at different oscillating strain and (b) at different frequencies under a strain of 3%.

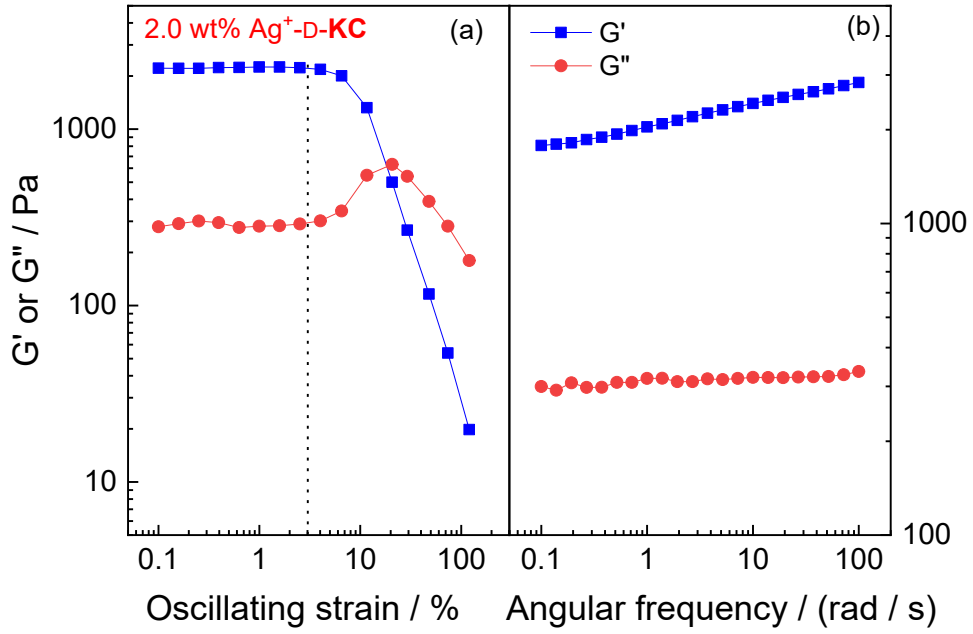

Fig S10 Storage modulus (G′) and loss modulus (G″) of 2.0 wt% Ag^+-D-**KC** hydrogel (a) at different oscillating strain and (b) at different frequencies under a strain of 3%.

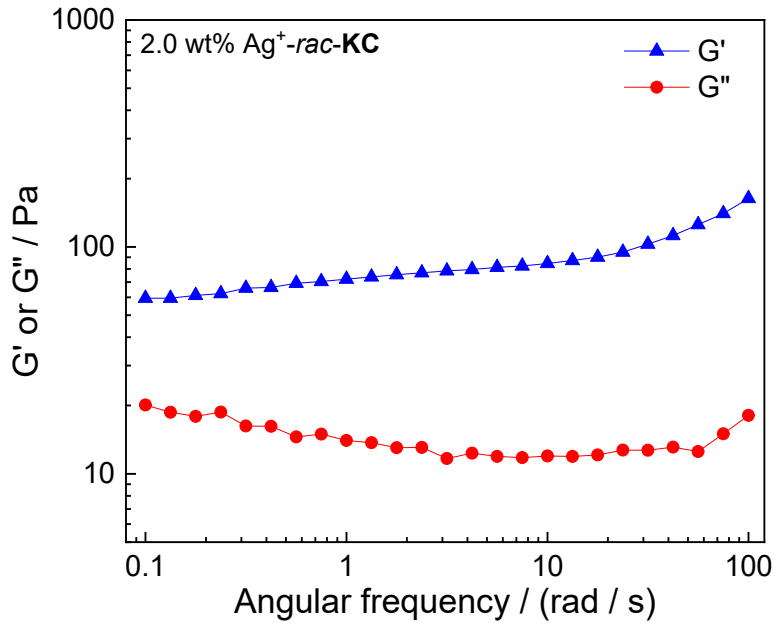

Fig S11 Storage modulus (G′) and loss modulus (G″) of 2.0 wt% Ag^+-*rac*-**KC** hydrogel at different frequencies under a strain of 1%.

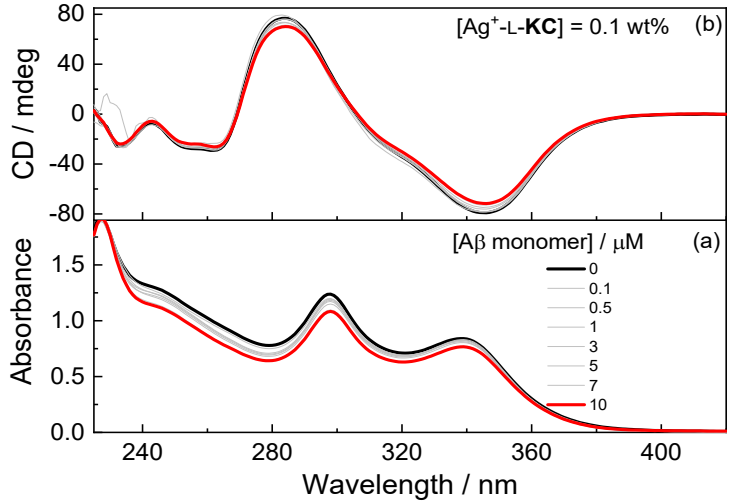

Fig. S12 Absorption (a) and CD (b) spectra of 0.1 wt % Ag^{+}-L-**KC** hydrogel in the presence of Aβ(1-40) monomer of increasing concentration. Spectra were all measured using a 1-mm cuvette. [Aβ(1-40)] = 0.1 - 10 μM.

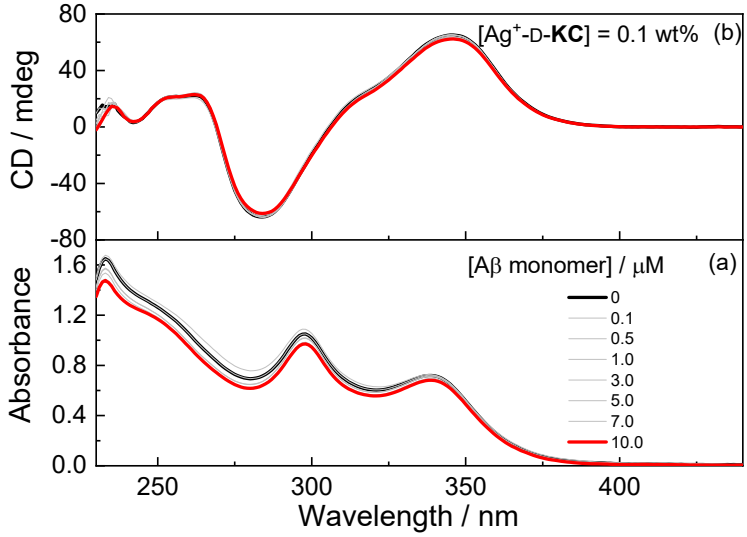

Fig. S13 Absorption (a) and CD (b) spectra of 0.1 wt % Ag^{+}-D-**KC** hydrogels in the presence of Aβ (1-40) monomer of increasing concentration. Spectra were all measured using a 1-mm cuvette. [Aβ(1-40)] = 0.1 - 10 μM.

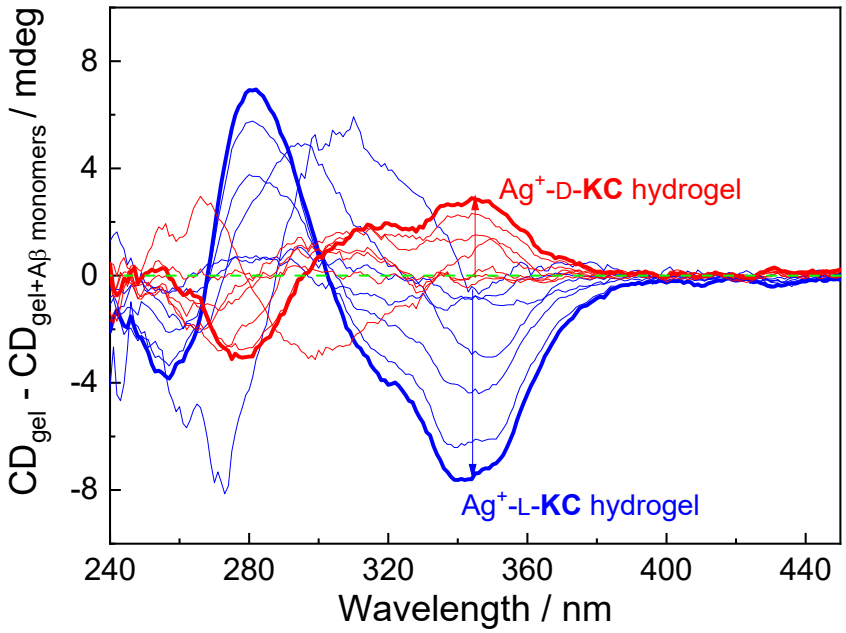

Fig. S14 CD spectra of 0.1 wt % Ag$^+$-L-**KC** or Ag$^+$-D-**KC** hydrogel in the presence of Aβ(1-40) monomer of increasing concentration. [Aβ(1-40)] = 0.1 - 10 μM.

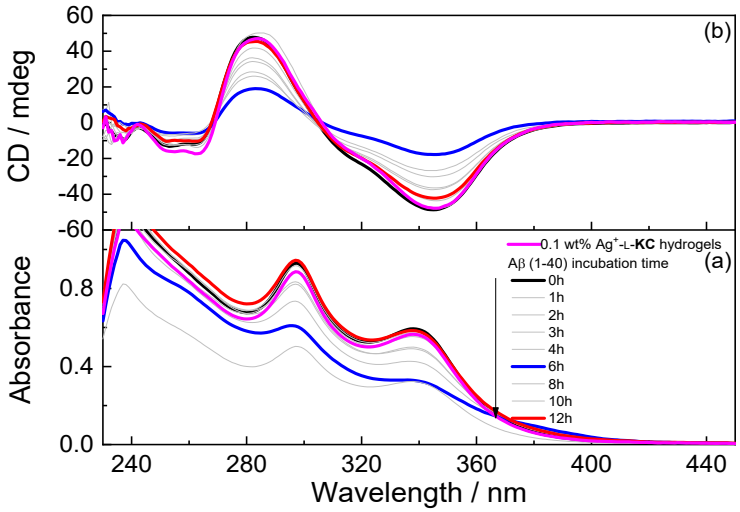

Fig. S15 Absorption (a) and CD (b) spectra of 0.1 wt % Ag$^+$-L-**KC** hydrogel in the presence of 1 μM Aβ(1-40) after different duration of incubation. Spectra were all measured using a 1-mm cuvette.

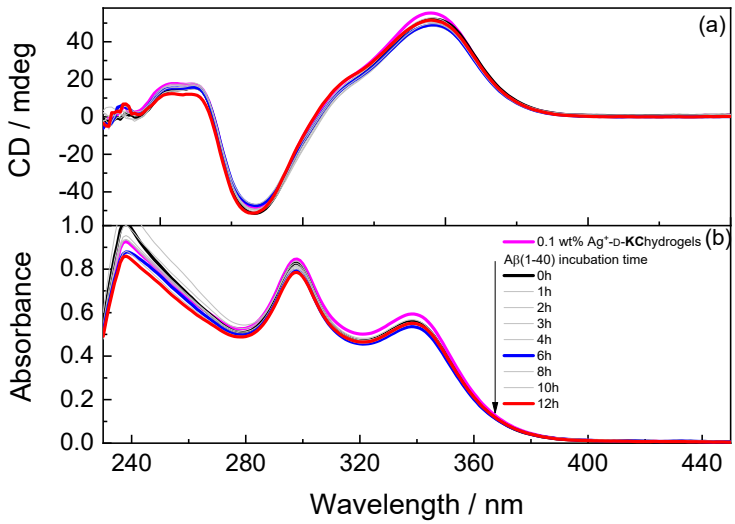

Fig. S16 Absorption (a) and CD (b) spectra of 0.1 wt % Ag^{+}-D-**KC** hydrogel in the presence of 1 μM Aβ(1-40) after different duration of incubation. Spectra were all measured using a 1-mm cuvette.

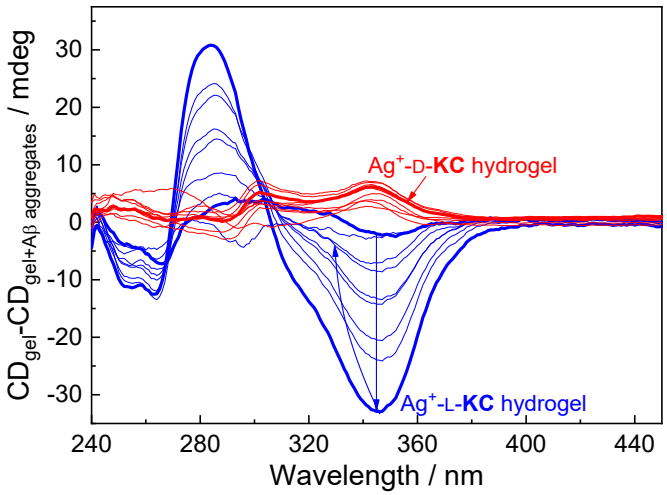

Fig. S17 CD spectra of 0.1 wt % Ag^{+}-L-**KC** or Ag^{+}-D-**KC** hydrogel with 1 μM Aβ(1-40) aggregates after different duration of incubation ranging from 0 to 12 h.

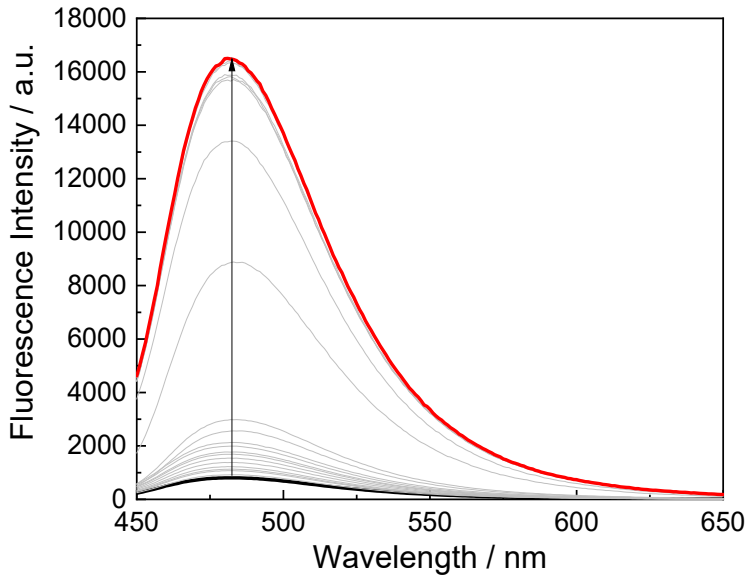

Fig. S18 Fluorescence spectra of ThT after incubation with Aβ(1-40) for different duration. λ_{ex} = 430 nm, excitation and emission slits were set at 5 nm and 10 nm, respectively. [ThT] = 25 μM, [Aβ(1-40)] = 50 μM.

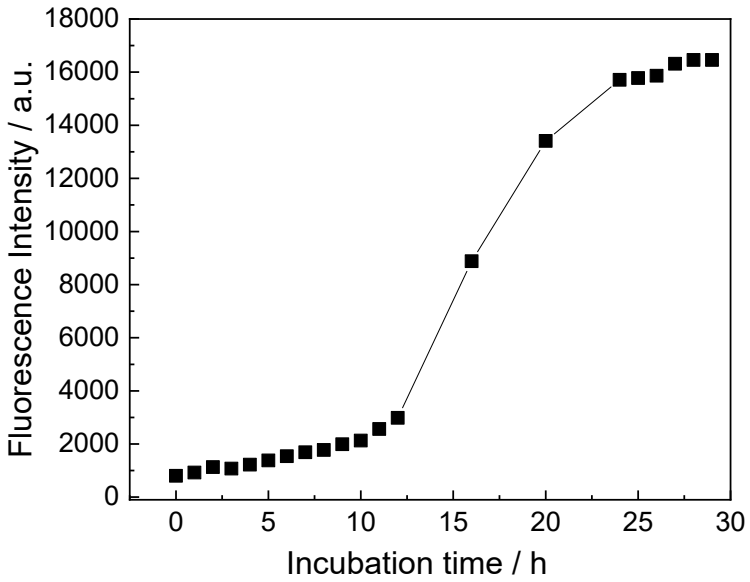

Fig. S19 Plots of fluorescence intensity of ThT at 483 nm versus incubation time with Aβ(1-40). [ThT] = 25 μM, [Aβ(1-40)] = 50 μM.

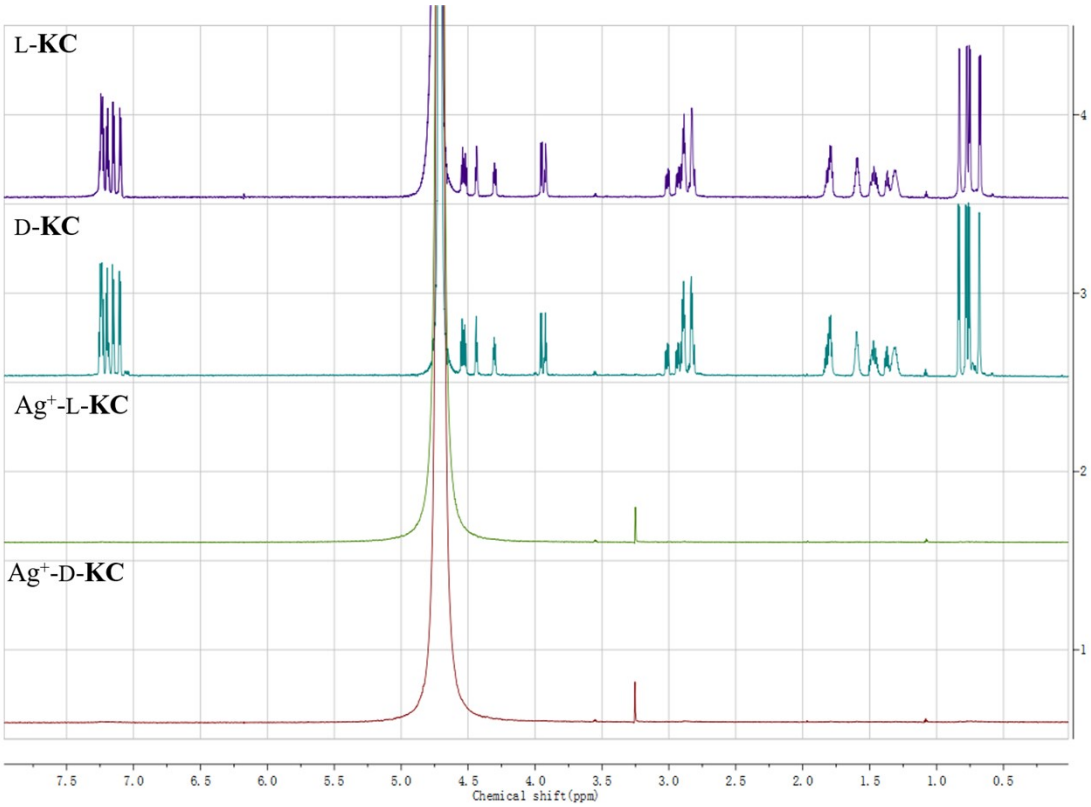

Fig. S20 850 MHz ^{1}H NMR spectra of L-**KC**, D-**KC**, Ag^{+}-L-**KC** and Ag^{+}-D-**KC** in D_2O, at 0.66 mM.

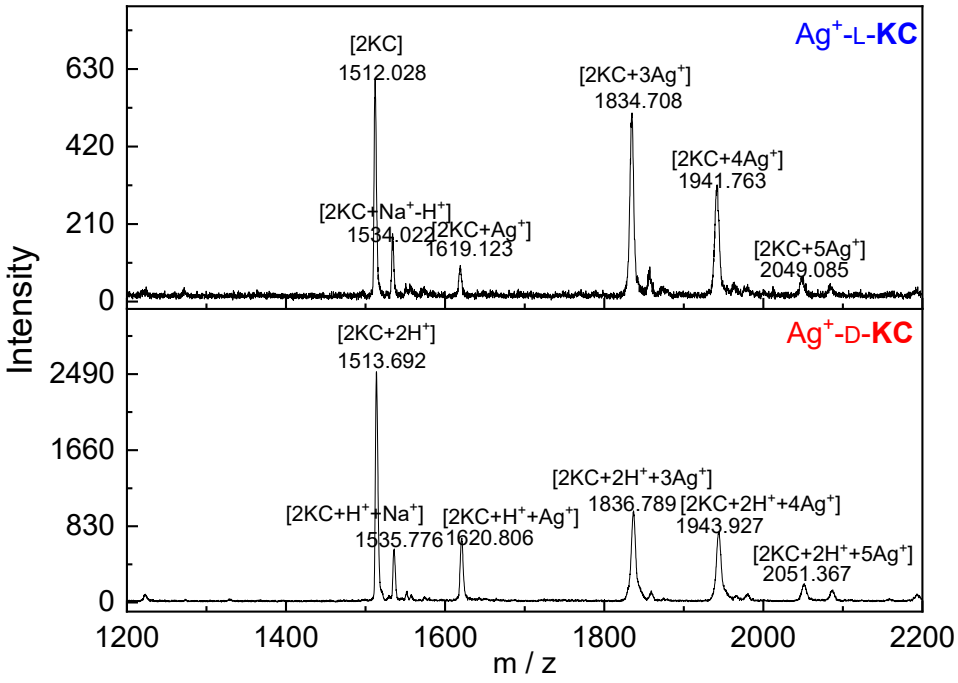

Fig. S21 MALDI-TOF mass spectra of Ag^{+}-L-**KC** and Ag^{+}-D-**KC** hydrogels.

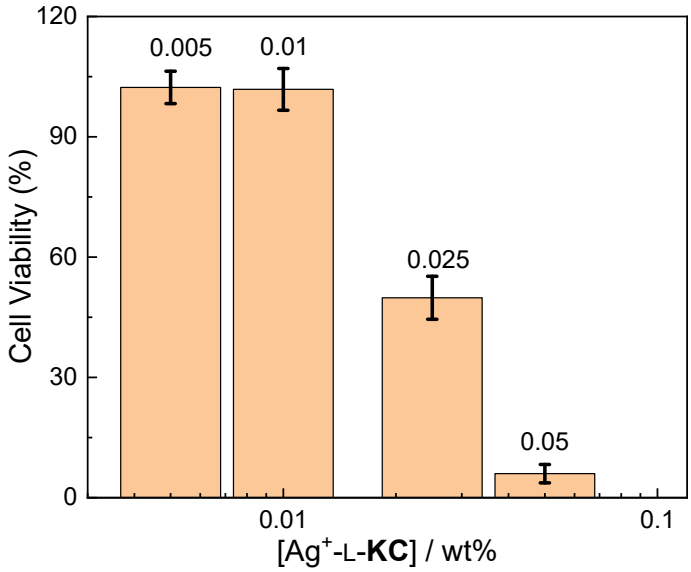

Fig. S22 Cytotoxicity of Ag^{+}-L-**KC** at concentrations of 0.005 wt%, 0.01 wt%, 0.025 wt% and 0.05 wt%, respectively.