Supporting Information

Cationic Amphiphilic Peptide Chaperone Rescues $A\beta_{42}$ Aggregation and Cytotoxicity

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Materials and Method:

All reagents and chemicals used were purchased from commercial suppliers with good purity grade and used without any further purification. The flat bottom polystyrene 96- well plates and Human Aggregated Beta Amyloid ELISA Kit were purchased from Invitrogen Bio services. Rink Amide Resin, all N-Fmoc protected amino acids and $A\beta_{42}$ peptide (>95% purity) were purchased from GL Biochem, China. ^{15}N-Labeled $A\beta_{42}$ was procured from r-Peptide (Bogart, GA) and used directly in the NMR experiments. Sodium phosphate buffer was prepared using 10 mM sodium phosphate with 150 mM NaCl and 1 mM EDTA and pH was adjusted to 7.4 by adding either dil. HCl or NaOH. All dry solvents, reagents, Thioflavin T, and antibiotics were obtained from Sigma-Aldrich. The bacterial media were purchased from Becton-Dickinson (Franklin Lakes, USA). RPMI and FBS were purchased from Lonza (Lonza, USA). The bacterial panel including *E. coli* ATCC 25922, *K. pneumoniae* BAA-1705, *S. aureus* ATCC 29213, *P. aeruginosa* ATCC 27853 *A. baumannii* BAA-1605, and *Enterococcus sp* was procured from Biodefense and Emerging Infections.

Solid Phase Peptide Synthesis and HPLC Purification:

Peptides **P1**-**P4** were synthesized through a manual solid phase peptide synthesis on Rink amide resin at 0.2 mmol scale using standard Fmoc- conditions. The combination of HBTU and HOBt was used as coupling reagents, DIPEA was used as an activator base, NMP was used as a coupling solvent and 20% piperidine in DMF was used for the Fmoc- group deprotection. To release the peptides from the solid support, the resin was stirred for about 3 hours in a 10 mL cocktail containing trifluoroacetic acid (TFA)/ triisopropylsilane/water/phenol (90:5:5:5). The resin was filtered. The filtrate containing crude peptides was evaporated under reduced pressure and the gummy residue was triturated with cold diethyl ether (50 mL). The precipitate was separated through centrifugation. The crude peptides were again dissolved in 10 mL of

ACN/H_2O and purified on a C_{18} column using reversed-phase HPLC. Acetonitrile and water gradient system containing 0.1% of TFA at a 2 ml flow rate was used to purify the peptides. The mass of the purified peptides was confirmed by MALDI-TOF/TOF analysis. The lyophilised pure peptides were used for further studies.

Antimicrobial Activity:

The antimicrobial activity of **P1** was performed according to the reported procedure.[1] Briefly, the cultures of bacterial strains were inoculated in TSB and OD_{600} was measured, followed by dilution to ~10^6 cfu/mL. The stock solution of **P1** (10 mg/mL) was prepared in DMSO and tested against the various bacteria from 64 mg/L to 0.5 mg/L in a two-fold serial dilution with 2.5 μL of each concentration added to the well of a 96- well microtiter plate. In continuation, 97.5 μL of bacterial suspension was added to each well containing **P1**. The drug Levofloxacin has used as a positive control and the buffer solution was used as a negative control. The microtiter plates containing bacterial strain and **P1** were incubated at 37 °C for 18-24 hours following which MIC was determined. Experiments were performed in triplicate using duplicate samples.

Preparation of the Amyloid Beta$_{42}$:

The Aβ_{42} (2mg) was dissolved in 2 ml of 1,1,1,3,3,3- hexafluoroisopropanol (HFIP) and then kept for occasional vortex at room temperature for 1 hour to maintain in a monomeric state. After this, it was aliquoted into small fractions (0.5 mg/ample) and HFIP was evaporated from the sample by keeping sample vials overnight in a laminar flow hood. The sample vials containing Aβ_{42} were then lyophilized overnight and stored at -80 °C until further. Before the usage, the lyophilized Aβ_{42} was dissolved in DMSO to make the stock 2 mM stock solutions of monomeric Aβ_{42} in DMSO. The Aβ_{42} aggregates were prepared by the addition of 10 mM sodium phosphate buffer to the stock solution of Aβ_{42} in DMSO. The final volume of the Aβ_{42}

solution was maintained at 100 μL and incubated at 37 °C. The aggregation kinetics of the $A\beta_{42}$ in the presence of appropriate concentrations of peptides were studied in 10 mM sodium phosphate buffer (pH 7.4) and the final volume was maintained at 100 μL. The concentration of $A\beta_{42}$ was kept at a constant 25 μM in all experiments.

Thioflavin T (ThT) Fluorescence-Based Kinetic Assay:

The aggregation kinetics of $A\beta_{42}$ were studied using a ThT-fluorescence assay. The measurements of ThT- fluorescence were carried out on flat bottom black polystyrene nonbinding 96-well plates. The samples were excited at 440 nm and fluorescence emission was monitored at 482 nm. The stock solution of $A\beta_{42}$ (0.55 mM) was prepared in DMSO and it will be appropriately diluted with sodium phosphate buffer before starting the aggregation kinetic experiments. The stock solution of ThT (200 μM) in 10 mM sodium phosphate buffer (pH 7.4) was prepared. The ratio for ThT to $A\beta_{42}$ was maintained at 20:25 μM, respectively. The control assay was performed by the addition of 4.5 μL of $A\beta_{42}$ to the 10 μL of the ThT in sodium phosphate buffer and the volume was adjusted to 100 μL using the buffer. For the inhibition kinetics assay, different concentrations of peptides were added to the wells containing 4.5 μL of $A\beta_{42}$ and 10 μL of the ThT. The final concentration of the peptides in the wells was maintained at 250, 125, 75, 25, 12.5, 7.5, and 2.5 μM. The solution containing $A\beta_{42}$, ThT and peptides was incubated at 37 °C and subjected to the fluorescence measurements for a period of 48 hours with orbital shaking for 120 s prior to each reading. Measurements were performed in three independent experiments. Kinetic graphs were plotted using Origin (version 9.1). Kinetic Parameters t_{50} (h), Lag time (h), k_{app} (h^{-1}) were calculated from the ThT assays[2,3].

Circular Dichroism Spectroscopy:

Circular dichroism spectroscopy analysis was carried out using the Jasco J-815 spectropolarimeter. For CD experiments, the stock solution of $A\beta_{42}$ (0.55 mM in 10mM NaOH)

was diluted to 50 μM in sodium phosphate buffer. The sodium phosphate buffer without peptides and $A\beta_{42}$ was used as a blank. The 50 μM concentrations of both $A\beta_{42}$ and **P1** were used for CD measurements. The CD spectra of **P1** alone, $A\beta_{42}$ alone and the mixture containing both **P1** and $A\beta_{42}$ at 0 hour and 24 hours of incubation at 37 °C were recorded in triplicate.

High Resolution Transmission Electron Microscopy (HR-TEM) Analysis:

$A\beta_{42}$ (100 μM) was incubated (i) alone and (ii) in the presence of peptide with an equimolar ratio for about 48 hours in sodium phosphate buffer. The stock solutions were prepared as mentioned above. Aliquots of all the samples were diluted 10 times with water. From each sample, 1 μL of the aliquots were drop casted onto glow discharged individual carbon coated 200 mesh Cu grids (Ted Pella Inc., Redding, CA). Further, the grids were negatively stained with 2% uranyl acetate (Polysciences, Inc, Warrington, PA) in double distilled water and air dried. Stained grids were examined under Bruker High-Resolution Transmission Electron Microscope to take the final images.

AFM Analysis:

$A\beta_{42}$ (100 μM) was incubated (i) alone and (ii) in the presence of peptide with an equimolar ratio for 48 hours. The stock solutions were prepared as mentioned above. The aliquots of all the samples were diluted 10 times with water. From each sample, 1 μL of the aliquots were drop casted on a cleaned silicon wafer plate (SiO_2/Si substrate), dried at room temperature and finally kept in the desiccator for 10 min before taking the images. Freshly prepared solutions were used in all the experiments. The drop casted samples on silicon wafer plates were examined under Keysight's AFM instrument 5500 to take the final images.

DLS Study:

The solution of $A\beta_{42}$ (100 μM) in 10 mM sodium phosphate buffer (pH 7.4) was prepared as mentioned above and incubated (i) alone and (ii) in the presence of peptide with an equimolar ratio for about 24 hours. The stock solutions were prepared as mentioned above. Aliquots of all the samples were diluted 10 times with water. The size distribution was plotted against the diameter of $A\beta_{42}$ self-assembly.

Laser Scanning Confocal Microscopy study:

$A\beta_{42}$ (100 μM) was incubated (i) alone and (ii) in the presence of peptide with an equimolar ratio for 48 hours. The stock solutions were prepared as mentioned above. The aliquots of all the samples were diluted 10 times with water. 10 μL of the Thioflavin T was added in each sample as a fluorescent indicator. From each sample, 5 μL of the aliquots were drop casted on a cleaned glass slide and covered with a thin cover slip then imaged using OLYMPUS ZX81 laser scanning confocal microscopy by inverting the sample (λex: 440 nm, λem: 482 nm).

Cell culture:

SHSY5Y-human neuroblastoma cells were cultured in DMEM (Dulbecco's modified essential medium)/F12 (Sigma, USA) medium in humidified 5% (v/v) CO_2/air at 37 °C in 10% (v/v) (fetal bovine serum) FBS (Invitrogen, USA) and 100 U/mL penicillin. After reaching ~95% confluence, cells were split by using 0.25% trypsin-EDTA (Sigma) in to fractions to carry out the experiment. We were seeded 10^4 cells in each well in 96-well plates and incubated at 37 °C up to 24 hours.

Cell Viability Assay:

The MTT experiments (3,(4,5-dimethylthiazol-2-yl)2,5- diphenyltetrazolium bromide) were performed on human neuroblastoma cell line SH-SY5Y as reported earlier.[4] Briefly, after 24

hours incubation of cells in a 96-well plate at 37 °C, the medium was replaced with the solution containing 10 μM $A\beta_{42}$ aggregates diluted in DMEM/F12 medium. In order to understand the effect of **P1** on the cytotoxicity of $A\beta_{42}$ aggregates, 10 μM $A\beta_{42}$ of was mixed and 1, 3, 5, 10, and 30 μM concentrations of **P1**, 10 μM **P2** and 10 μM **P3** and incubated over a period of 12 hours at 37 °C prior to treatment of cells. The cells were treated with the mixture of $A\beta_{42}$ containing different concentrations of **P1**, **P2** and **P3** and the plates were incubated at 37 °C in humidified 5% (v/v) CO_2/air. The MTT reduction assay was performed after 24 hours of treatment of the peptides and $A\beta_{42}$. After the addition of MTT (0.5 mg/mL), the cells were incubated at 37 °C for about 4 hours in a CO_2 incubator. Further, the supernatant was removed from the each well and DMSO (200 μL) was added to solubilize the dye formazan. The plates were again incubated in a humidified CO_2 incubator for about 15−20 min. The absorbance was measured at 570 nm using the multi-mode microplate reader. The cell viability was compared to the cells without peptides and $A\beta_{42}$. The $A\beta_{42}$ without peptides was used as a positive control. Similarly, the cytotoxicity of peptides were also examined without $A\beta_{42}$. Each data point represents an average of three independent triplet-well trials.

^{1}H-^{15}N HSQC NMR Spectroscopy:

The experiments of ^{1}H-^{15}N HSQC NMR were performed on an 800 MHz Bruker instrument. The monomeric ^{15}N labelled $A\beta_{42}$ was prepared as described in the above experiments. The NMR experiments were performed by maintaining the solution ratio of 9:1 (H_2O:D_2O) with 20 mM NaPi (pH 7.4). In each experiment, ^{15}N- $A\beta_{42}$ sample was prepared freshly to maintain $A\beta_{42}$ in the monomeric native form to avoid amyloid formation. The stock solution of **P1** (10 mM) was prepared in Mili Q H_2O. ^{1}H-^{15}N HSQC NMR experiments were performed using fresh sample of 40 μM ^{15}N-$A\beta_{42}$ with 20 mM NaPi buffer having pH 7.4 in the absence and presence of 2 equivalents of **P1** at 283 K with a cryoprobe ($A\beta_{42}$:peptide **P1**; 1:2). All cross peaks were identified with the help of previously assigned spectra from the literature.[5,6] The

addition of peptide **P1** to the ^{15}N- $A\beta_{42}$ sample was less than 2% dilution and the dilution factor was corrected while calculating the perturbation in the chemical shifts of ^{1}H-^{15}N resonances. The NMR spectra were processed and analysed by using TOPSIN software. Chemical shift perturbations of all the residues (^{1}H-^{15}N) were determined by using the equation $\Delta_{ppm} = [(5X\Delta^{1}H)^2 + (\Delta^{15}N)^2]^{1/2}$.

ELISA Assay:

Human Aggregated Beta Amyloid ELISA Kit was procured from Invitrogen Bioservices. The ELISA assay was performed according to the manufacture's protocol. Briefly, to the N-terminus human Aβ-specific monoclonal antibody-coated wells, 100 µL of the $A\beta_{42}$ samples in the absence and presence of **P1** were added and incubated for about 2 hours at room temperature. Each sample was prepared by incubating the 0.60 nM of $A\beta_{42}$ in the absence and presence of peptide **P1** by varying the peptide concentration from 0.5 to 10 equivalent ratio at 37 °C up to 24 hours. The samples were diluted by 1:2 in diluent buffer (contains phosphate buffer saline with bovine protein as a carrier and 0.5% Proclin™ biocide as a preservative) before being added to the 96-well plate. After 2 hours from the addition of the $A\beta_{42}$ samples, the wells were washed four times with Tris-based wash buffer containing 0.05% Tween-20 pH 7.4 (PBST) followed by the addition of 100 µL of Hu Aggregated Aβ Biotin Conjugate solution into each well. The samples were incubated for about 1 hour at room temperature. After washing the wells four times with PBST, the wells were treated with 100 µL of Streptavidin-HRP (horseradish peroxidase-labelled streptavidin) and incubated for 30 min at room temperature. After washing the wells with PBST, the solution of tetramethylbenzidine (TMB) was added and incubated for 30 about min at room temperature in the dark. The reaction was stopped by adding 100 µL of stop solution (0.16 M sulfuric acid) to each well. The absorbance of each well at 450 nm was recorded using multi-mode microplate reader. Experiments were performed in triplicate and averaged.

NMR of Peptide P1:

The NMR experiments of **P1** were performed on 800 MHz spectrometer CD_3OH solvent as reported earlier. The TOCSY was used to assign the residues and ROESY spectrum was used to assign NOEs. The TOPSPIN version 2.1 software was used to analyse the NMR data. High resolution 1D recording was used to measure the Scalar coupling (*J*) values. Amide proton temperature portions (dδ/dT) were measured by recording 1D trial at definite intervals of 10 degrees (K) in the temperature range of 278-318 K.

Modelling: Based on the unambiguous NOEs, the energy minimized structure was calculated using discovery studio version 3.5 software.

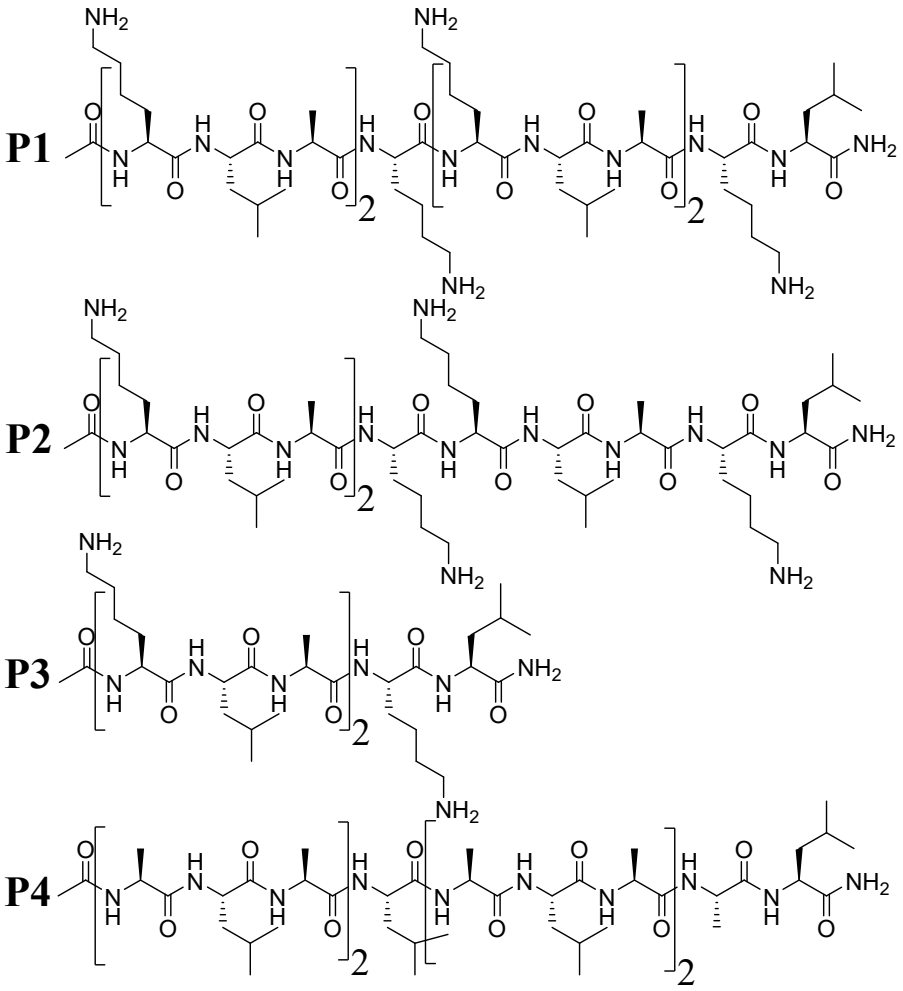


Fig. S1. Peptide Sequences.

Table ST1. Antimicrobial Activity of the peptide **P1**.

Bacteria	*E.coli* ATCC 25922	*S.aureus* ATCC 29213	*K.pneumoniae* BAA 1705	*A.baumannii* BAA 1605	*P.aeruginosa* ATCC 27853
P1	>64	>64	>64	>64	>64
Levofloxacin	0.03	0.125	64	8	0.5

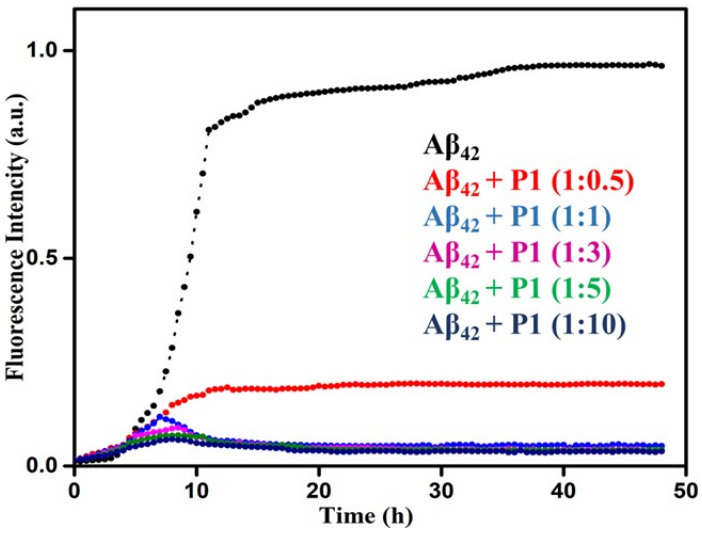


Fig. S2. Kinetic study of the fibrillation of the $A\beta_{42}$ with **P1**. The normalised kinetic profile of the self-assembly of 25 μM of $A\beta_{42}$ in the absence and presence of peptide **P1** by varying the concentration (12.5 μM, 25 μM, 75 μM, 125 μM and 250 μM). Buffer Conditions: 10 mM Sodium Phosphate, 150 mM NaCl, 1mM EDTA and pH 7.4. ThT concentration was 20 μM.

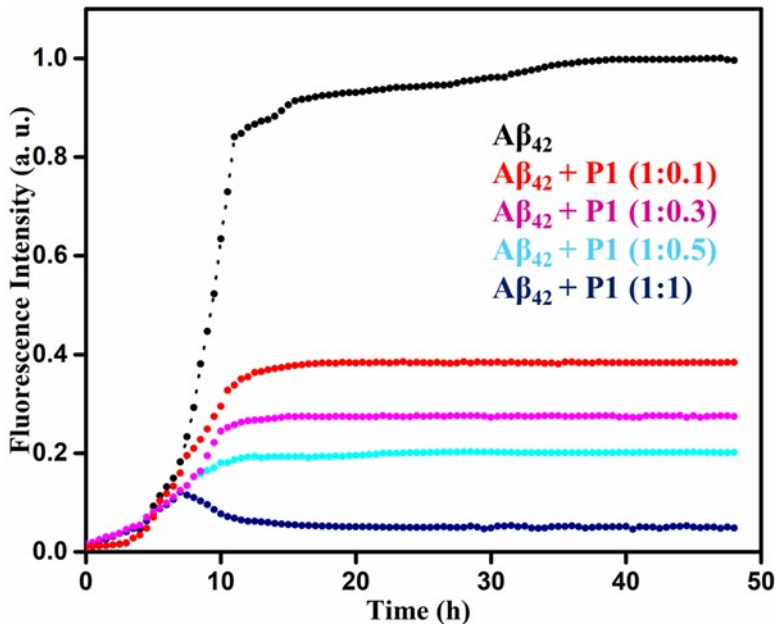


Fig. S3. Kinetic study of the fibrillation of the $A\beta_{42}$ with peptide **P1**. The normalised kinetic profile of the self-assembly of 25 μM of $A\beta_{42}$ in the absence and presence of peptide **P1** with stoichiometric ratios (2.5 μM, 7.5 μM, 12.5 μM, and 25 μM). Buffer Conditions: 10 mM Sodium Phosphate, 150 mM NaCl, 1mM EDTA and pH 7.4. ThT concentration was 20 μM.

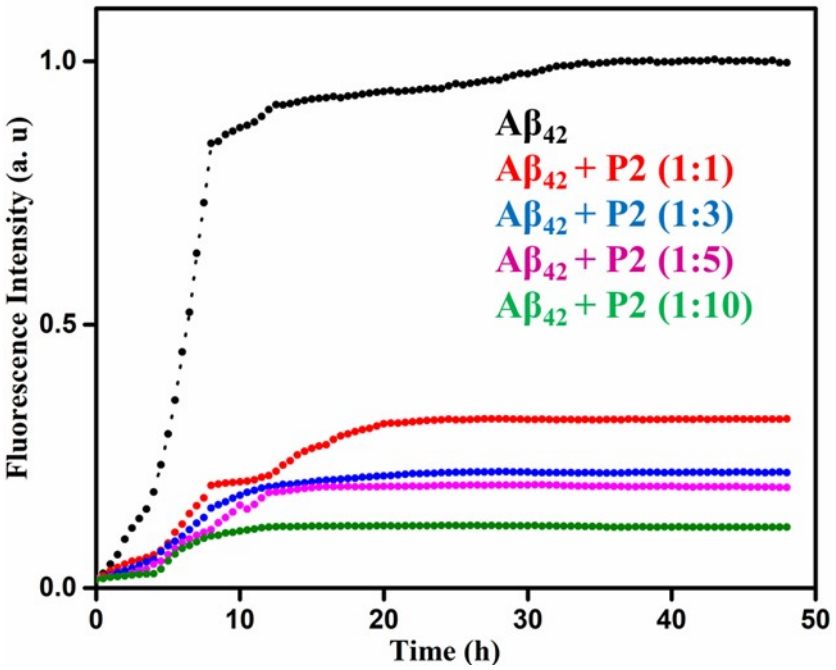


Fig. S4. Kinetic study of the fibrillation of the $A\beta_{42}$ with peptide **P2**. The normalised kinetic profile of the self-assembly of 25 μM of $A\beta_{42}$ in the absence and presence of peptide **P2** with stoichiometric ratios (25 μM, 75 μM, 125 μM, and 250 μM). Buffer Conditions: 10 mM Sodium Phosphate, 150 mM NaCl, 1mM EDTA and pH 7.4. ThT concentration was 20 μM.

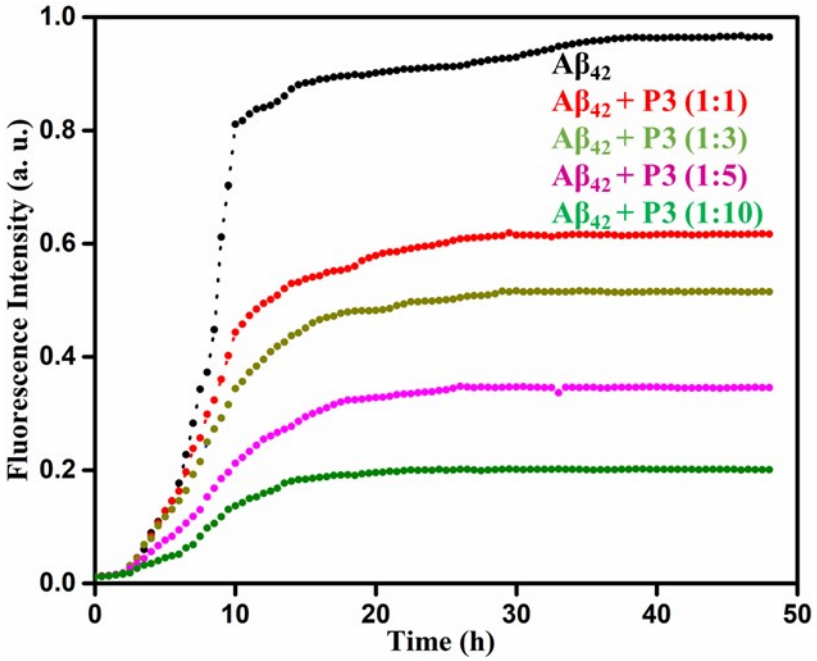


Fig. S5. Kinetic study of the fibrillation of the $A\beta_{42}$ with peptide **P3**. The normalised kinetic profile of the self-assembly of 25 μM of $A\beta_{42}$ in the absence and presence of peptide **P3** with stoichiometric ratios (25 μM, 75 μM, 125 μM, and 250 μM). Buffer Conditions: 10 mM Sodium Phosphate, 150 mM NaCl, 1mM EDTA and pH 7.4. ThT concentration was 20 μM.

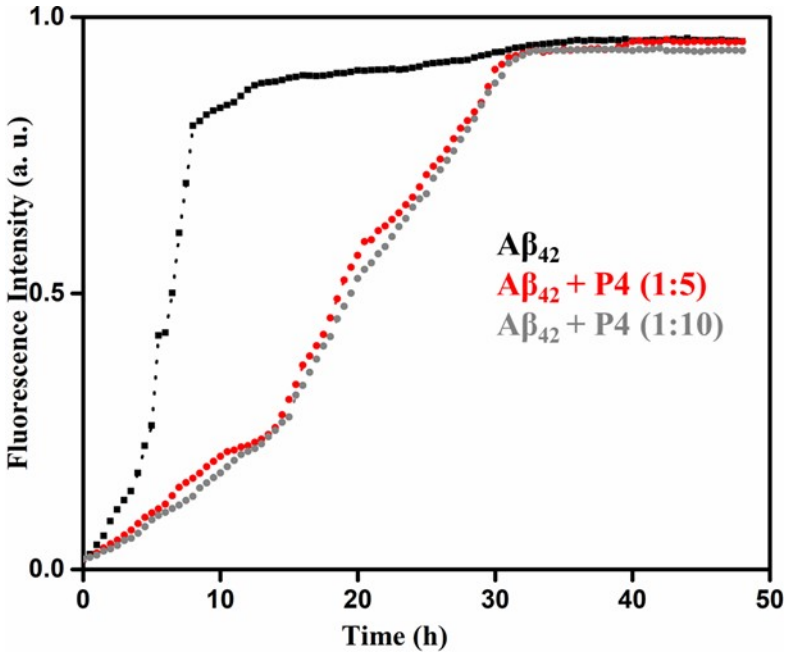


Fig. S6. Kinetic study of the fibrillation of the $A\beta_{42}$ with peptide **P4**. The normalised kinetic profile of the self-assembly of 25 μM of $A\beta_{42}$ in the absence and presence of peptide **P4** with stoichiometric ratios (125 μM, and 250 μM). Buffer Conditions: 10 mM Sodium Phosphate, 150 mM NaCl, 1mM EDTA and pH 7.4. ThT concentration was 20 μM.

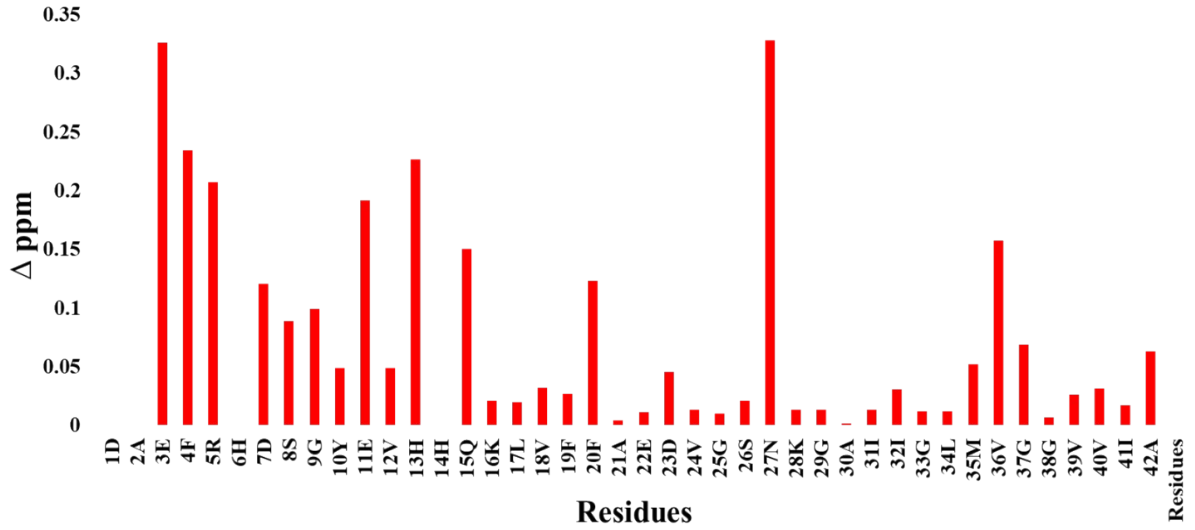


Fig. S7. Chemical Shift Perturbation study by ^{1}H-^{15}N HSQC NMR spectra. A plot of change in peak position of all residues in ^{15}N-isotopically labelled $A\beta_{42}$ (40 μM) after addition of peptide **P1** (80 μM). HSQC NMR experiments were conducted at 283 K in 10 mM sodium phosphate buffer, pH 7.4.

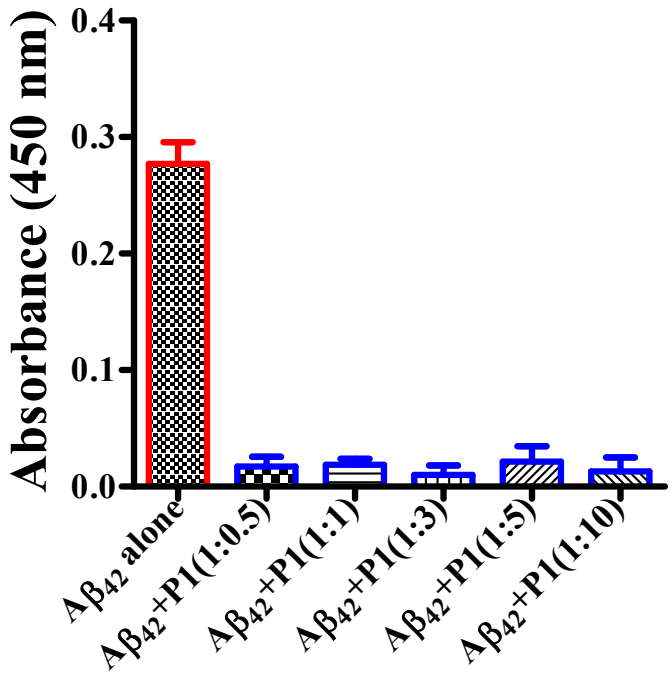


Fig. S8. Detection of aggregated $A\beta_{42}$ fibrils using ELISA in the absence and presence of P1. A substantial decrease in the absorbance was observed in the presence of the peptide at the concentration of 0.5 equivalent and above. The peptide also showed a weak absorbance at under identical conditions. $A\beta_{42}$ samples were incubated at 37 °C up to 24 hours in the absence and presence of peptide **P1** with different concentrations. Data was plotted after subtracting from the chromogen blank and the peptide **P1**. Error bars shown here represents an average of three independent triplicate values.

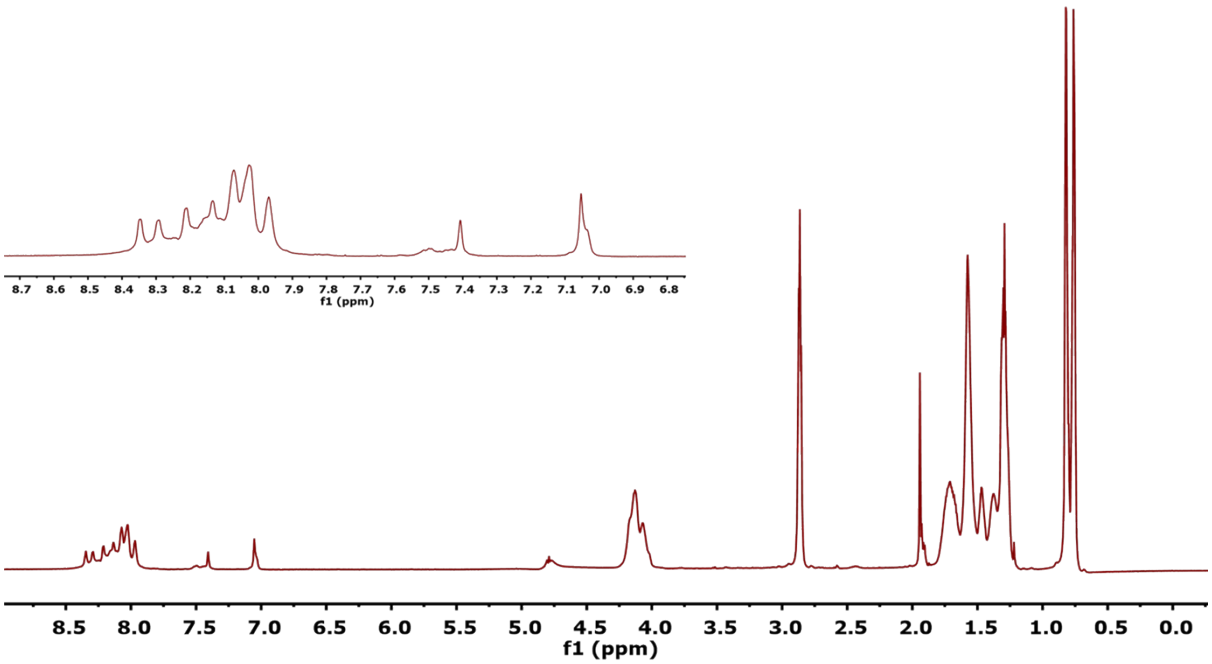


Fig. S9. 800 MHz ^{1}H NMR of peptide **P1** in PBS (pH 7.4) at 288 K.

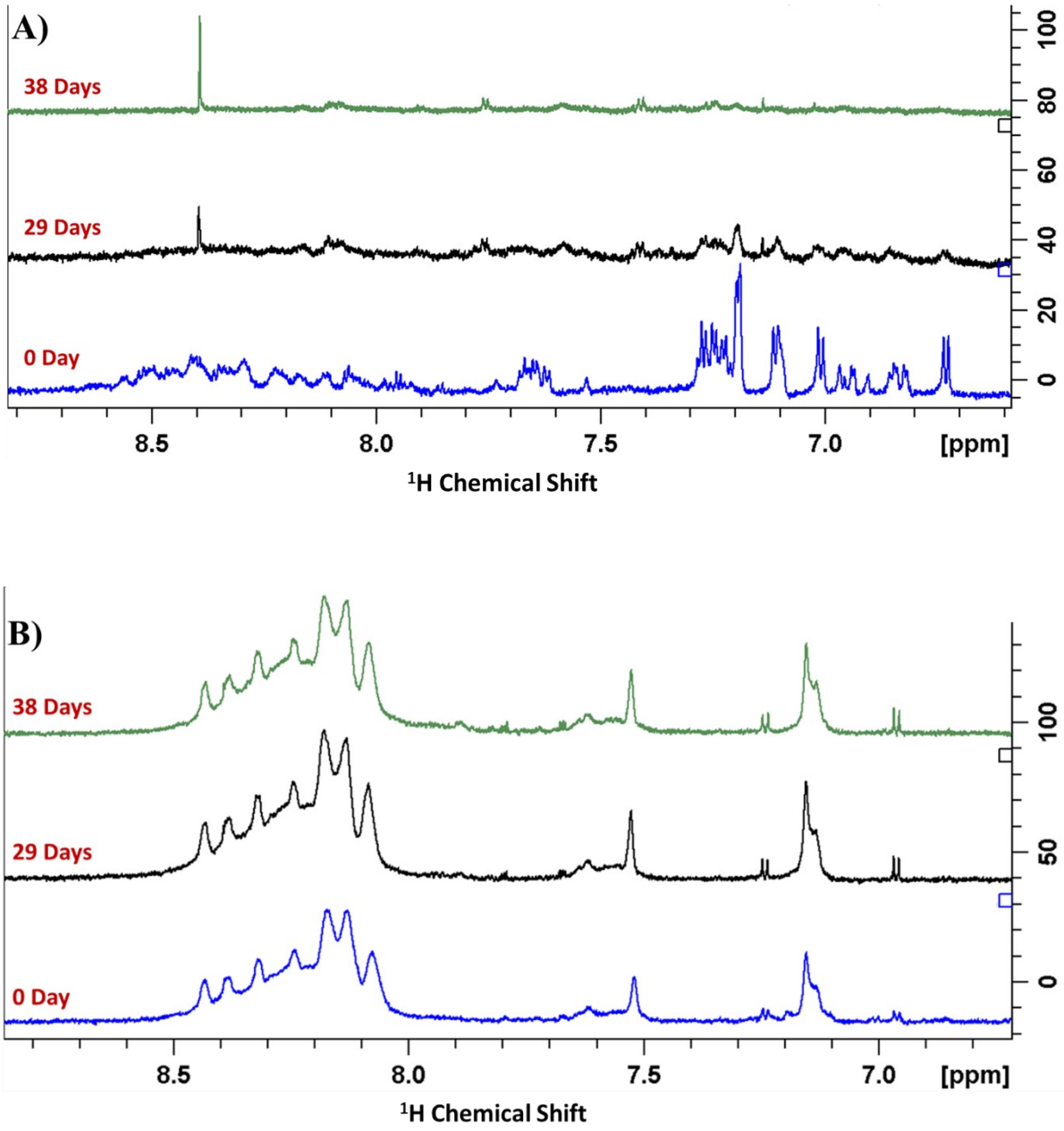


Fig. S10. ^{1}H NMR of the Amide region of A) $A\beta_{42}$ alone and B) $A\beta_{42}$ with peptide **P1** in the ratio of 1:2. Both experiment were performed by maintaining the solution ratio of 9:1

(H_2O:D_2O) with 20 mM NaPi (pH 7.4) on 800 MHz Bruker instrument at 283 K with a cryoprobe.

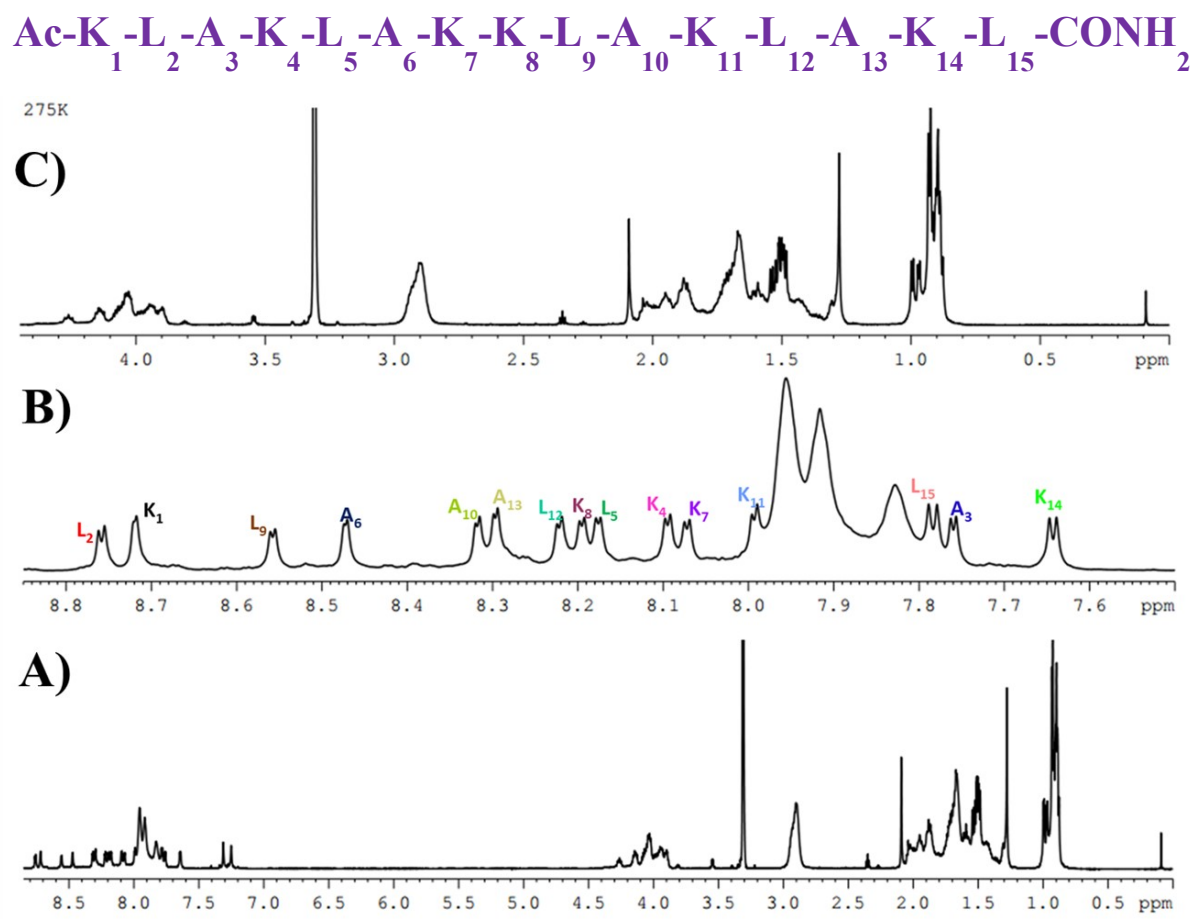


Fig. S11. 800 MHz ^{1}H NMR of peptide **P1** in CD_3OH at 275 K. A) Bottom trace shows the full spectrum of the ^{1}H NMR of peptide **P1**. B) Middle trace shows the amide expanded region of the peptide **P1**. C) Top trace shows the aliphatic region of the peptide **P1**.

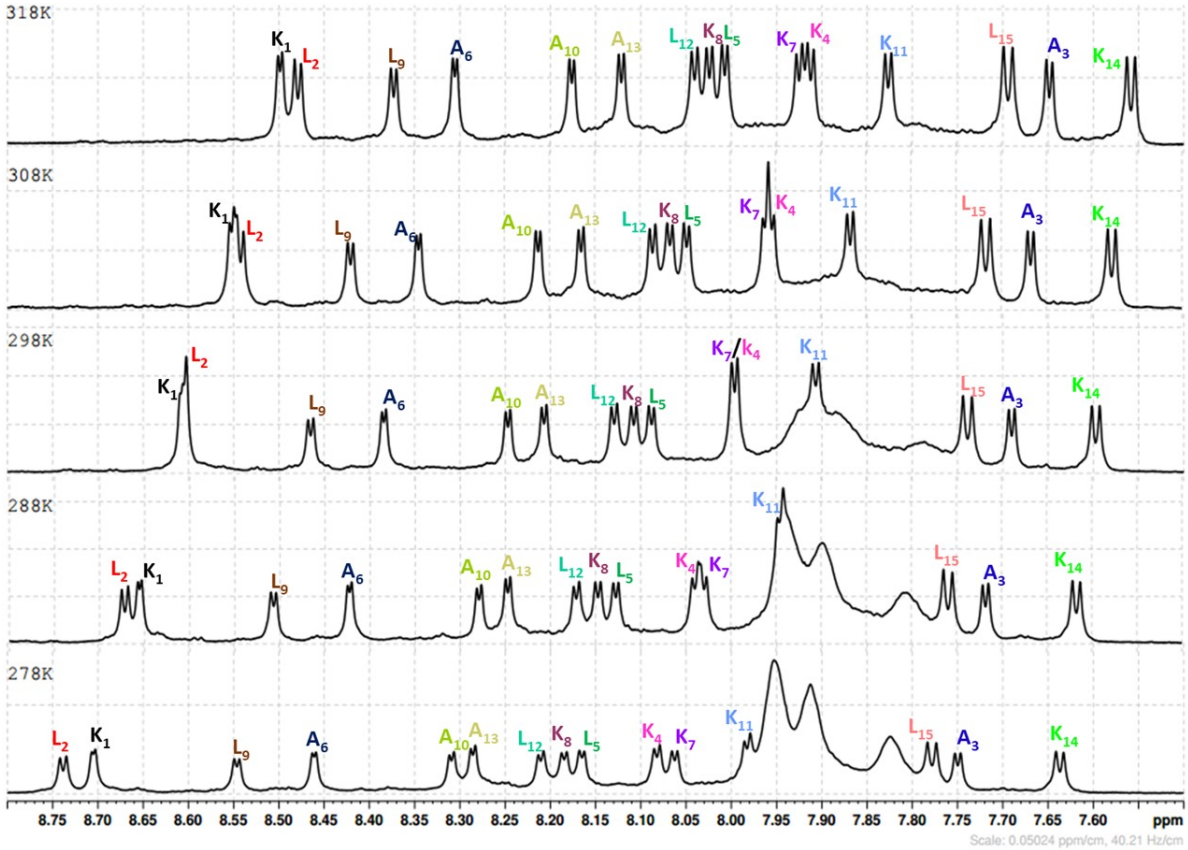


Fig. S12. Temperature dependent ^{1}H NMR spectra of peptide **P1**. Change in chemical shifts of all amide protons with increasing temperature from 278K to 318 K. Spectra were recorded in 800 MHz spectrometer in CD_3OH.

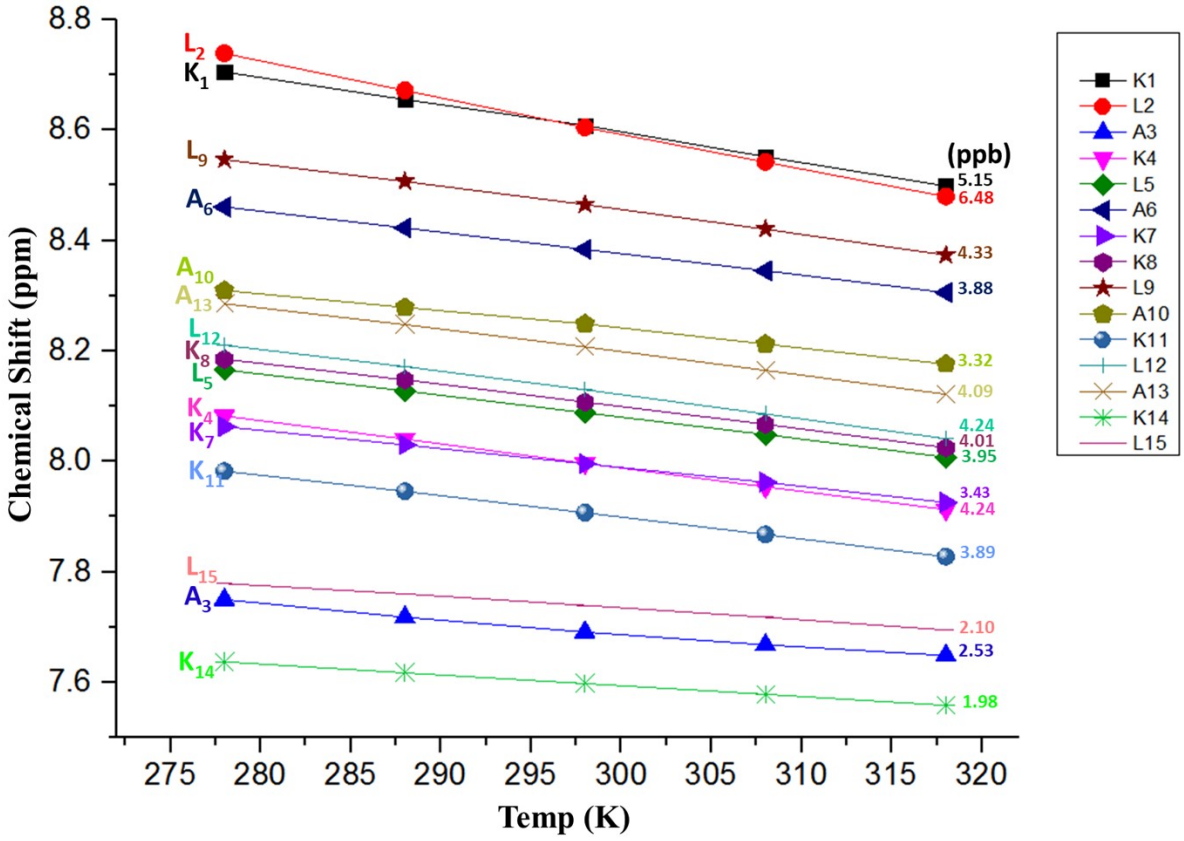
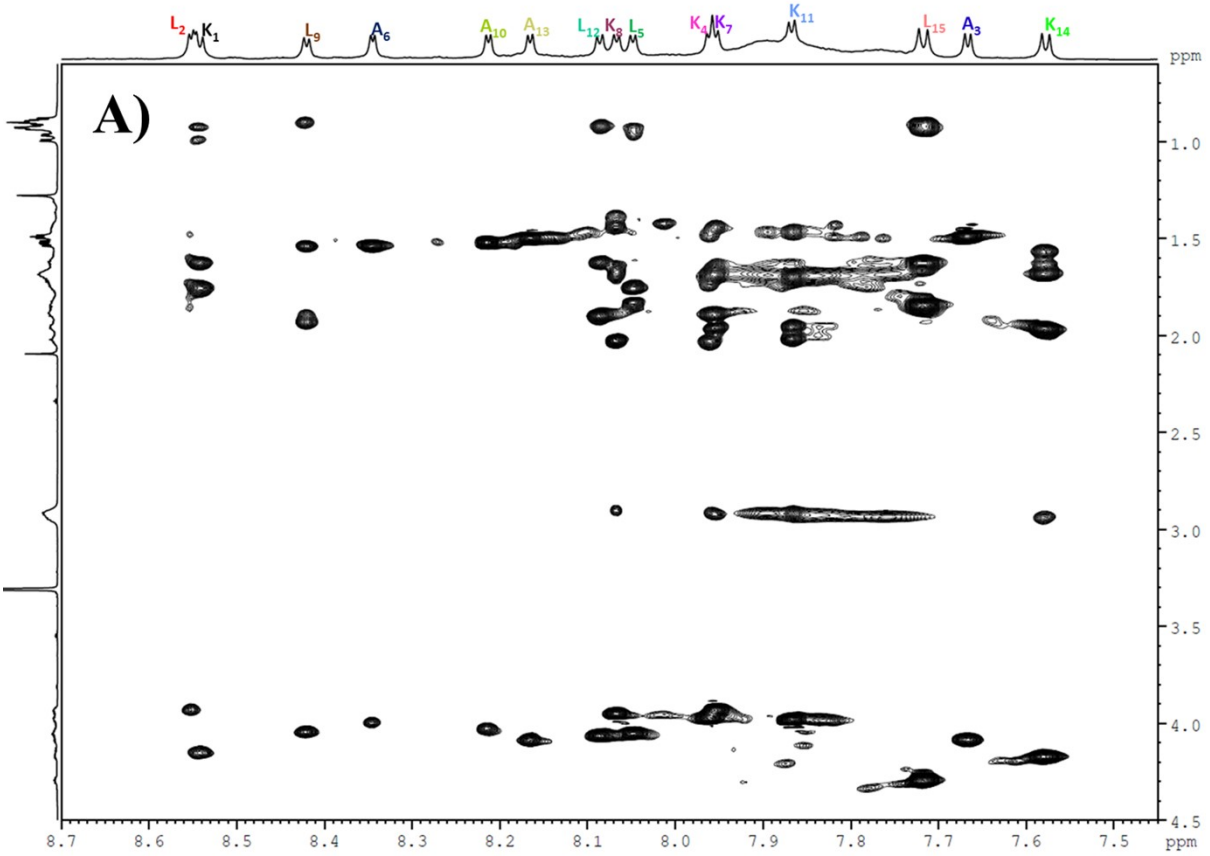


Fig. S13. Temperature dependence of NH chemical shifts of the peptide **P1** with increasing temperature from 278 K to 318 K. Spectra were recorded in 800 MHz spectrometer in CD_3OH.

Table ST2. Tabulation of chemical shifts along with $J_{NH(Hz)}$ scalar couplings and amide temperature coefficients (dδ/dT) for peptide **P1**.

Residue	NH	Hα	H_β	Hγ	Hδ	Hε	NH_3^+	$J_{NH(Hz)}$	Δδ/ΔT(ppb)
K_1	8.72	3.90	1.46	1.58	1.71	1.86/1.81	2.94	2.92	5.15
L_2	8.76	4.15	1.61	1.75	0.99/0.92			5.50	6.48
A_3	7.76	4.07	1.49					5.01	2.53
K_4	8.09	3.91	1.41	1.66	1.89	1.96	2.91	4.90	4.24
L_5	8.18	4.06	1.73/1.42	1.87	0.97/0.93			4.30	3.95
A_6	8.47	3.98	1.54					3.30	3.88
K_7	8.07	3.97	1.47	1.68	1.79/1.89	2.03	2.91	4.64	3.43
K_8	8.19	3.93	1.42	1.48	1.71/1.67	2.03	2.91	4.53	4.01
L_9	8.56	4.04	1.89/1.51	1.96	0.89			4.52	4.33
A_{10}	8.32	4.02	1.52					3.95	3.32
K_{11}	7.99	3.95	1.43	1.69	1.95	2.02	2.90	5.10	3.89
L_{12}	8.22	4.03	1.59	1.90	0.98			4.45	4.24
A_{13}	8.31	4.06	1.51					3.95	4.09
K_{14}	7.64	4.14	1.56	1.67	1.96	1.99	2.92	6.59	1.98
L_{15}	7.78	4.27	1.60	1.88	0.93/0.89			7.60	2.10



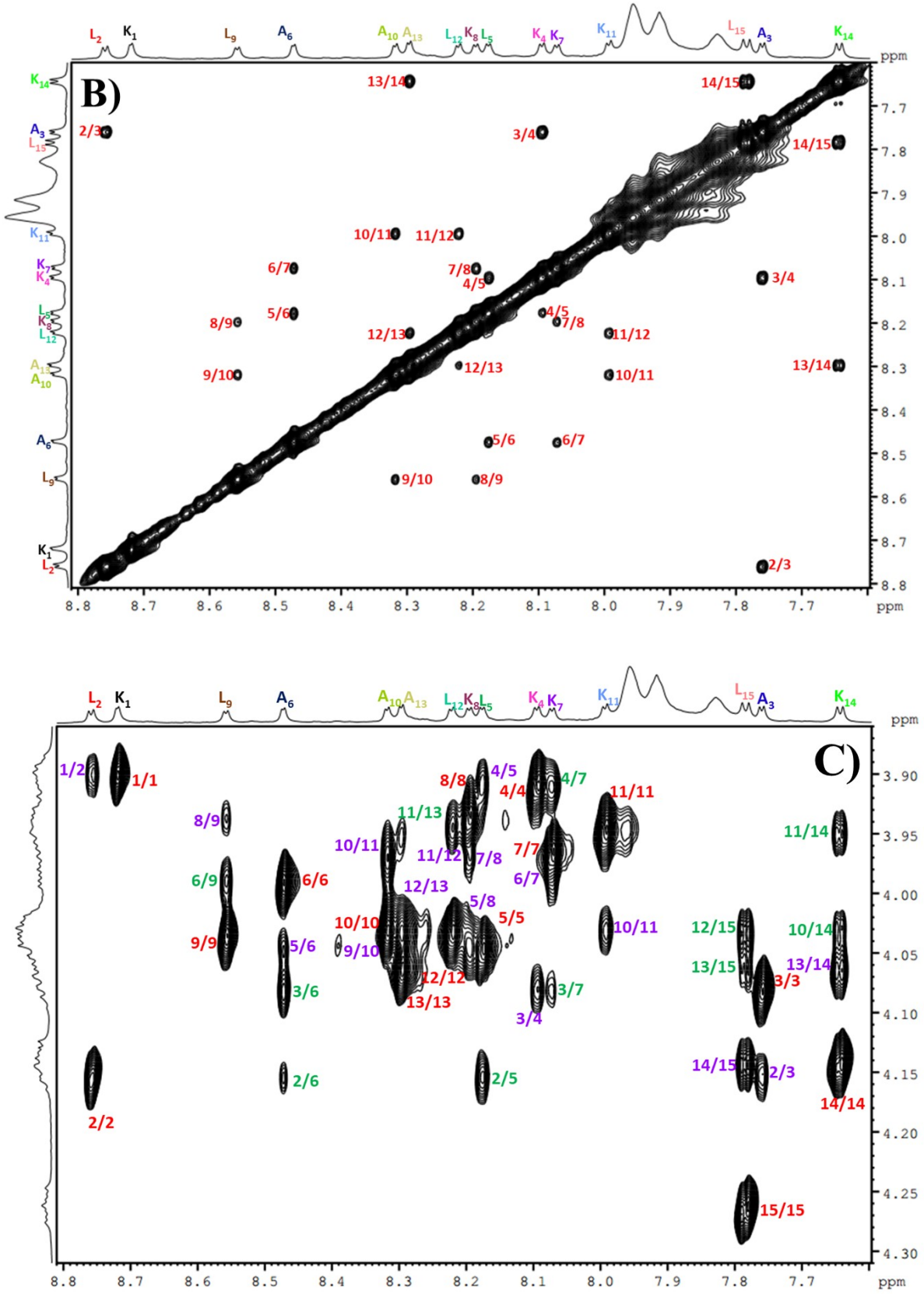


Fig. S14. TOCSY and ROESY spectra of peptide **P1**. A) TOCSY spectra of peptide **P1** at 275 K. ROESY spectra of peptide **P1** B) Amide region, C) Amide-Aliphatic region. Most of these

NOEs were considered in making energy minimized model of the peptide **P1** molecule. Spectra were recorded in 800 MHz spectrometer in CD_3OH.

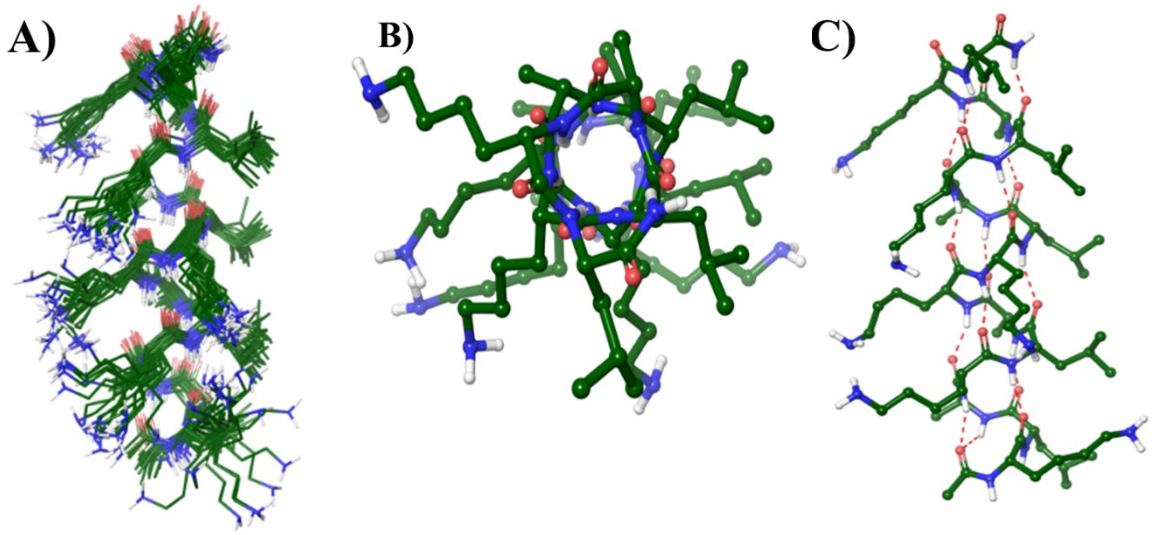


Fig. S15. NMR 3D model of the peptide **P1** deduced from the NOEs in 2D NMR. A) 20-structure superposed. B) C-terminal facing. C) Energy minimized structure.

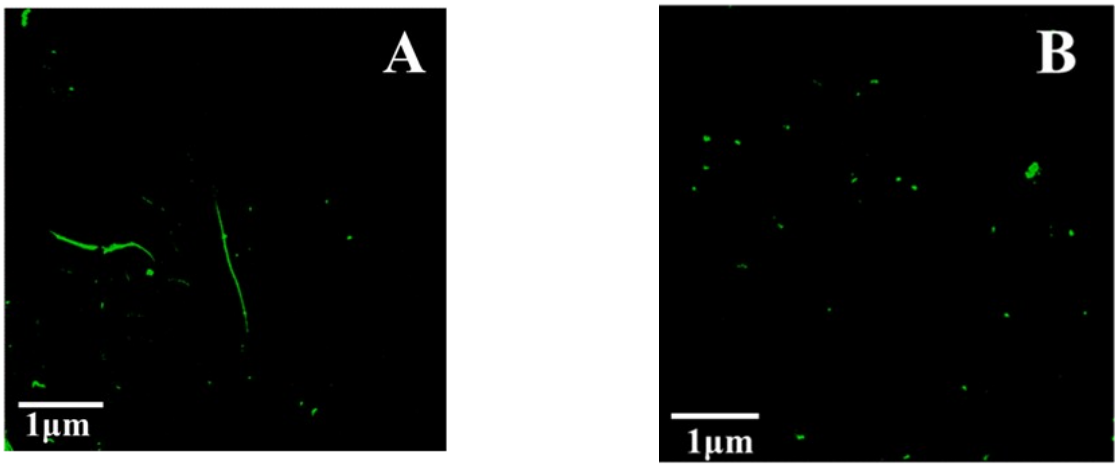
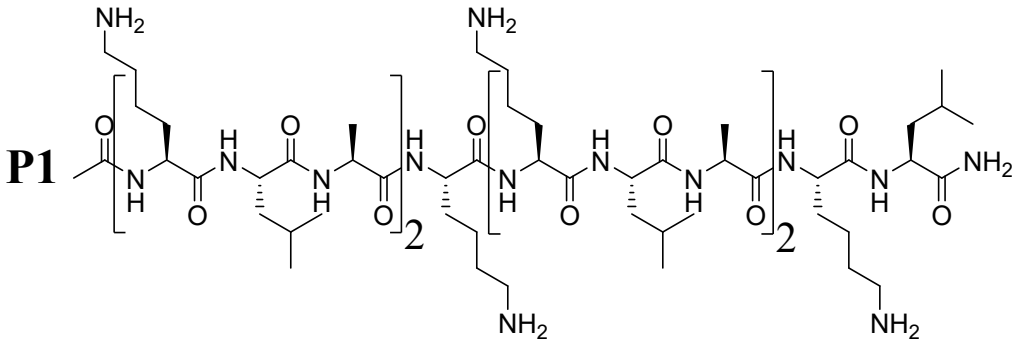
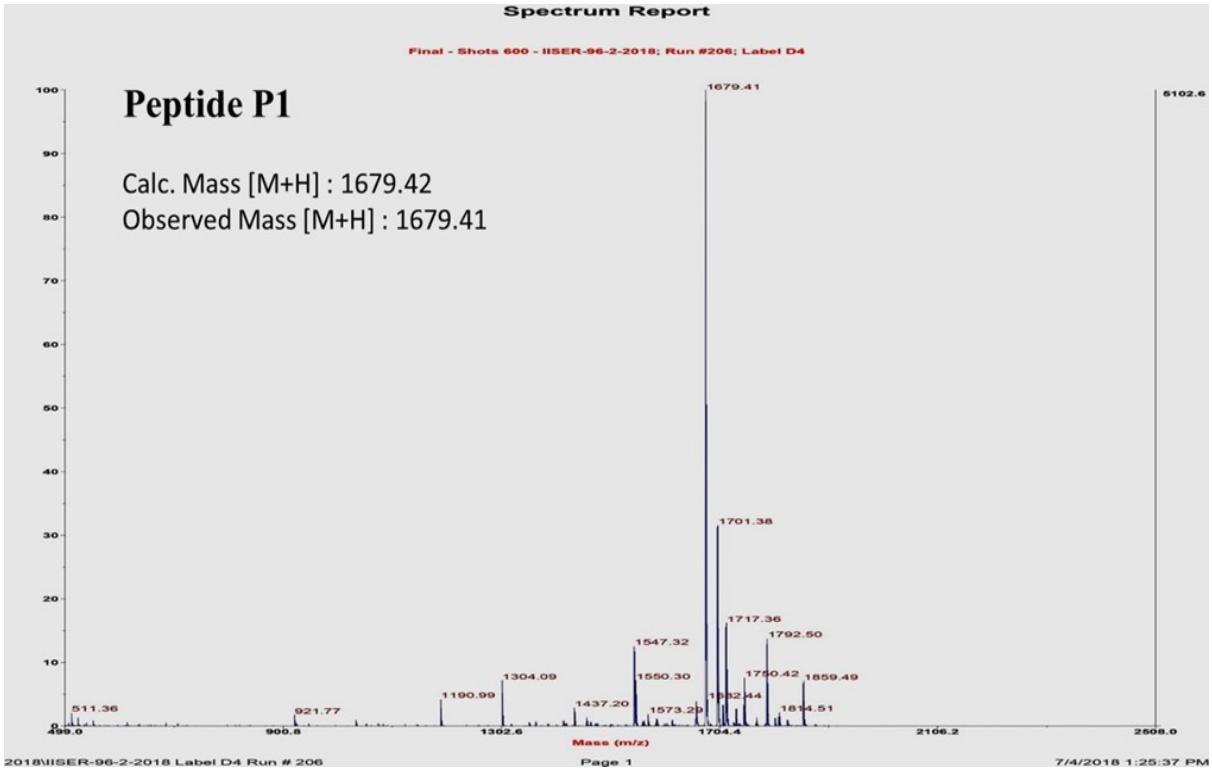
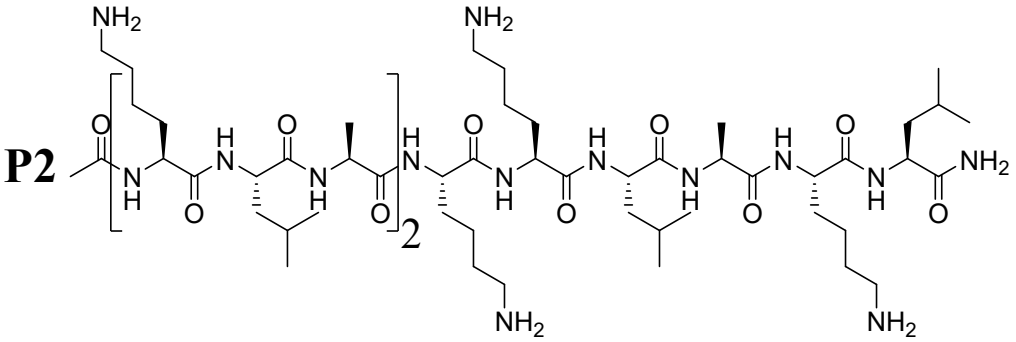


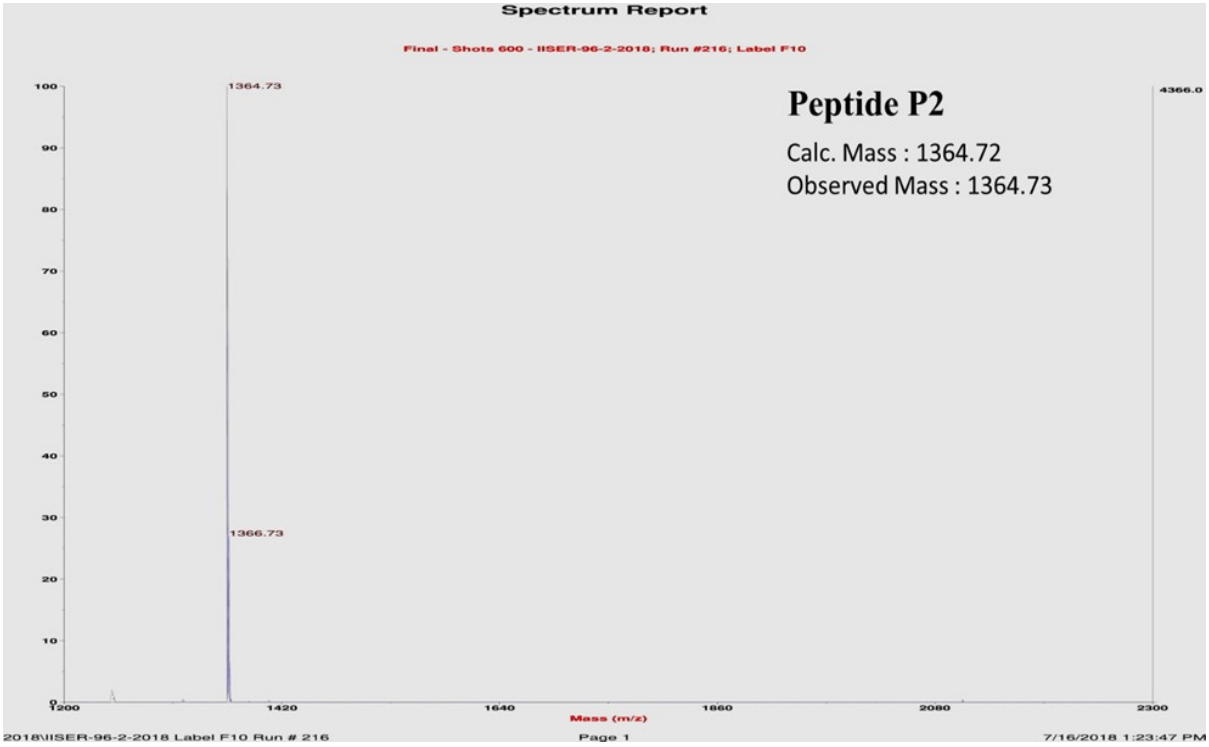
Fig. S16. Effect of peptide **P1** on the kinetics of the self-assembly of $A\beta_{42}$ with confocal images. Self-assembly of the 10 µM $A\beta_{42}$ was incubated at 37 °C up to 48 hours **A)** In the absence of peptide **P1**. **B)** in the presence of peptide **P1**. Buffer Conditions: 10 mM Sodium Phosphate, 150 mM NaCl, 1mM EDTA and pH 7.4.

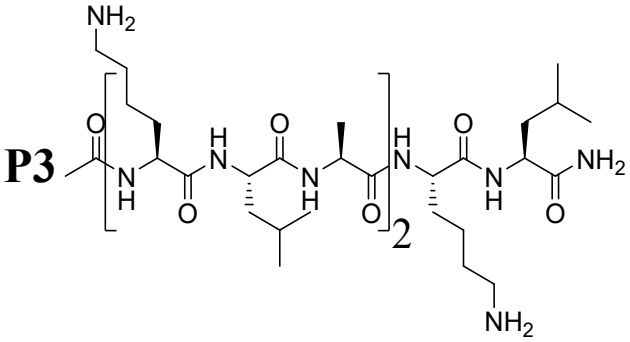
Mass Spectra of Peptides:

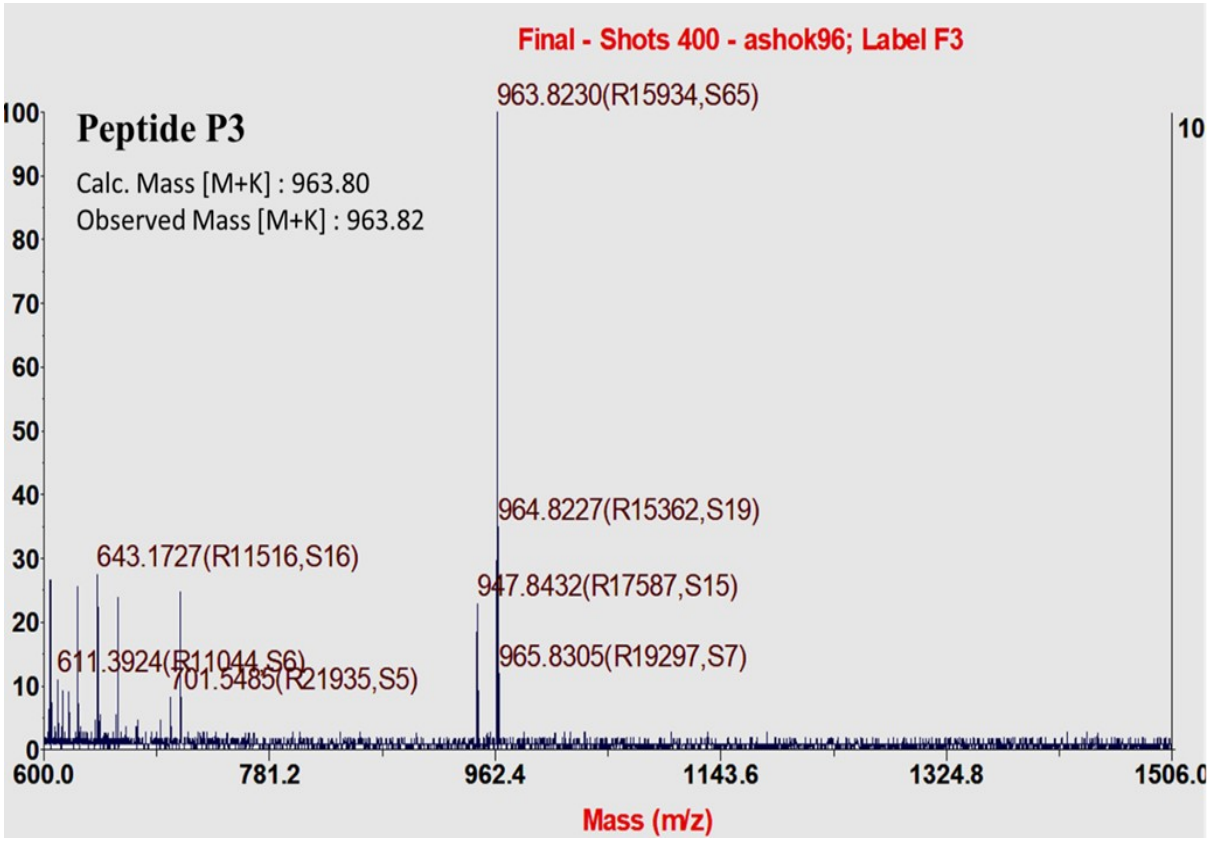


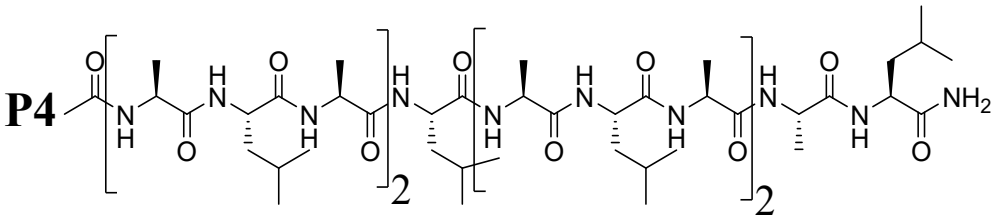



P2
NH2
NH2
NH2
NH2
NH2
2


Spectrum Report
Final - Shots 600 - IISER-96-2-2018; Run #216; Label F10
Peptide P2
Calc. Mass : 1364.72
Observed Mass : 1364.73
1364.73
1366.73
Mass (m/z)
2018\IISER-96-2-2018 Label F10 Run # 216
Page 1
7/16/2018 1:23:47 PM


P3
NH2
NH2
NH2
2


Final - Shots 400 - ashok96; Label F3
Peptide P3
Calc. Mass [M+K] : 963.80
Observed Mass [M+K] : 963.82
963.8230(R15934,S65)
964.8227(R15362,S19)
947.8432(R17587,S15)
965.8305(R19297,S7)
643.1727(R11516,S16)
611.3924(R11044,S6)
701.5485(R21935,S5)
100
90
80
70
60
50
40
30
20
10
0
600.0
781.2
962.4
1143.6
1324.8
1506.0
Mass (m/z)



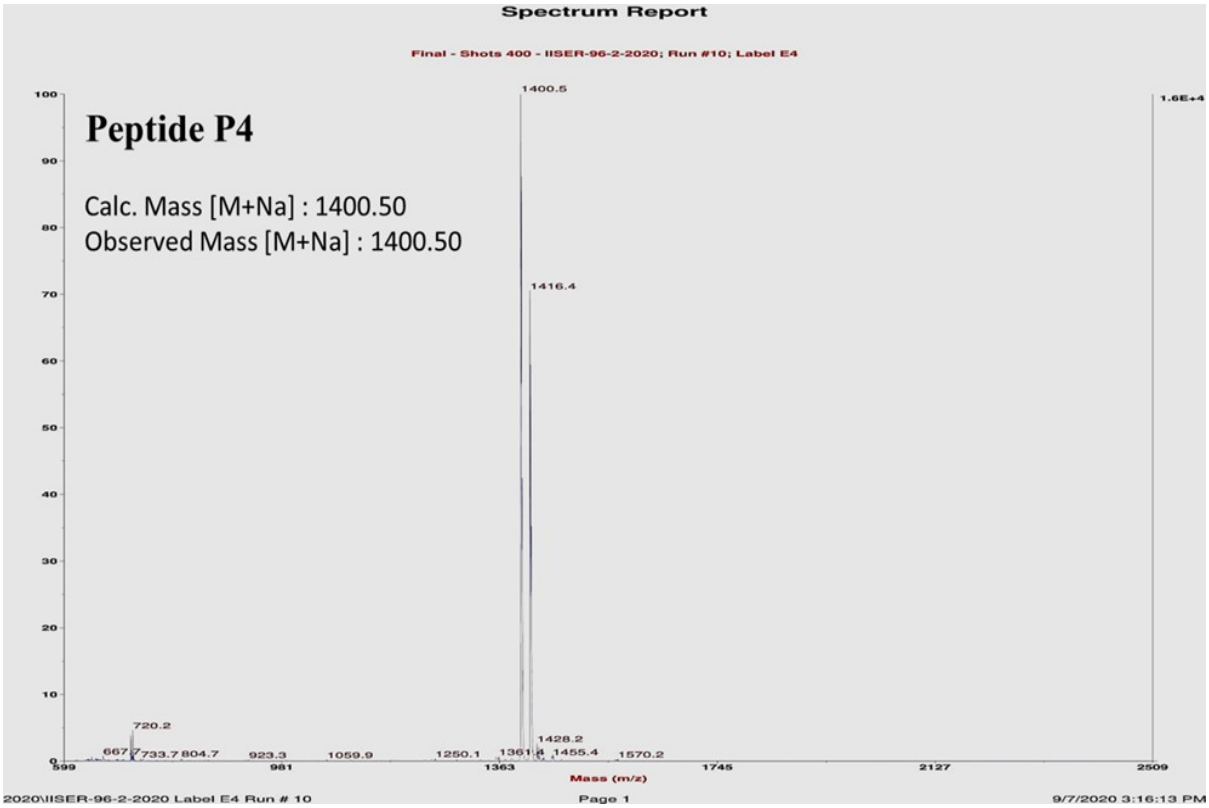
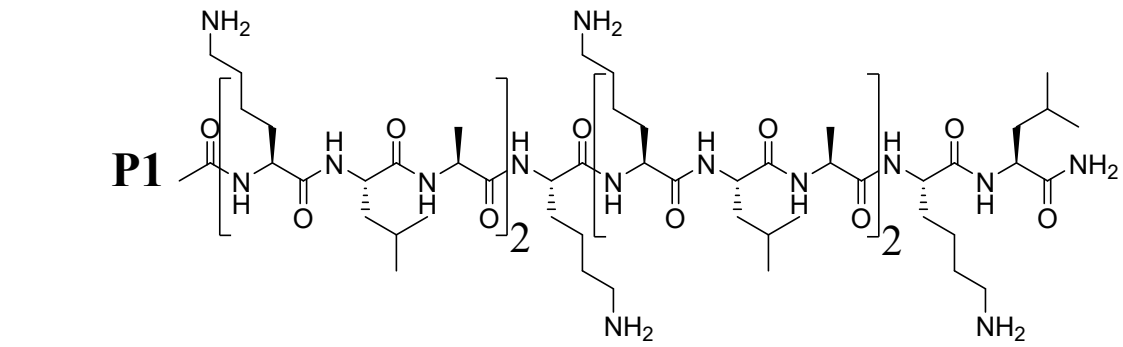


Fig. S17. Mass spectra of peptides.

HPLC profiles of peptides:



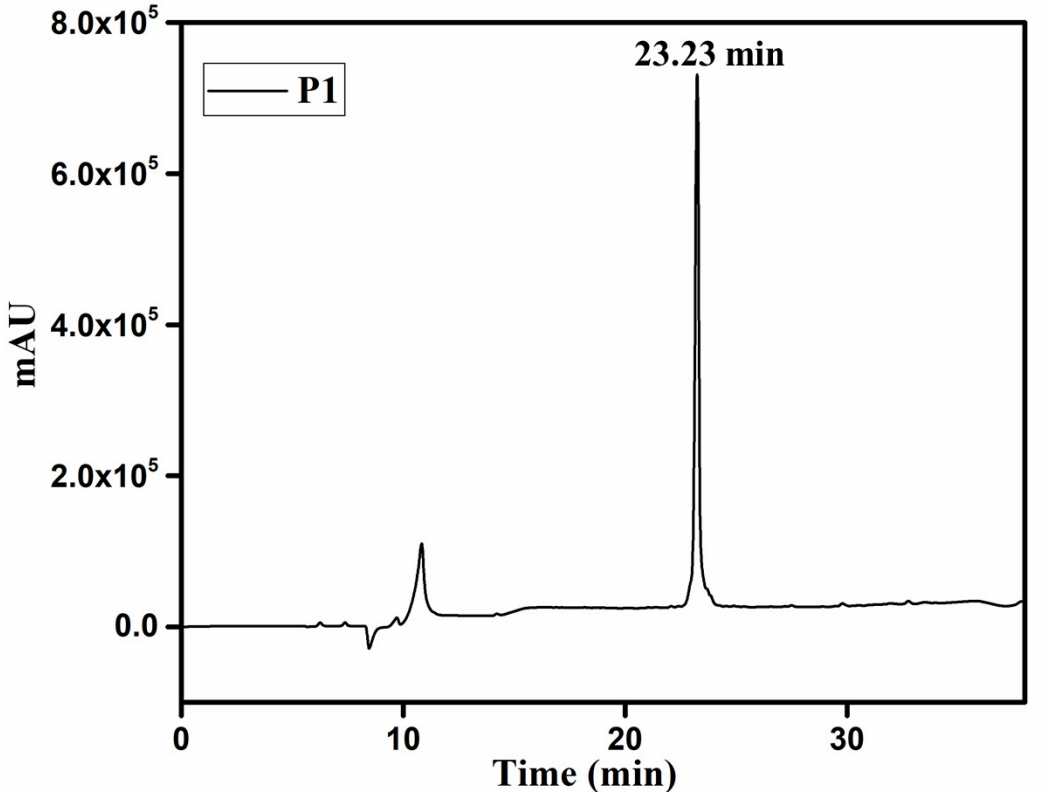
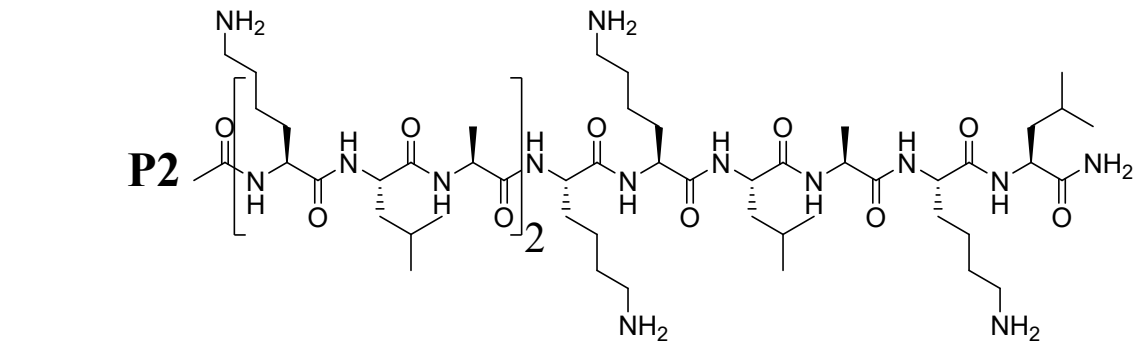


Fig. S18: Reverse phase HPLC profile of 15-mer peptide **P1** recorded on analytical C_{18} column (5µm, 4.6 x 250 mm column) at 220 nm using ACN/H_2O gradient system at a flow rate of 2 mL/Min.



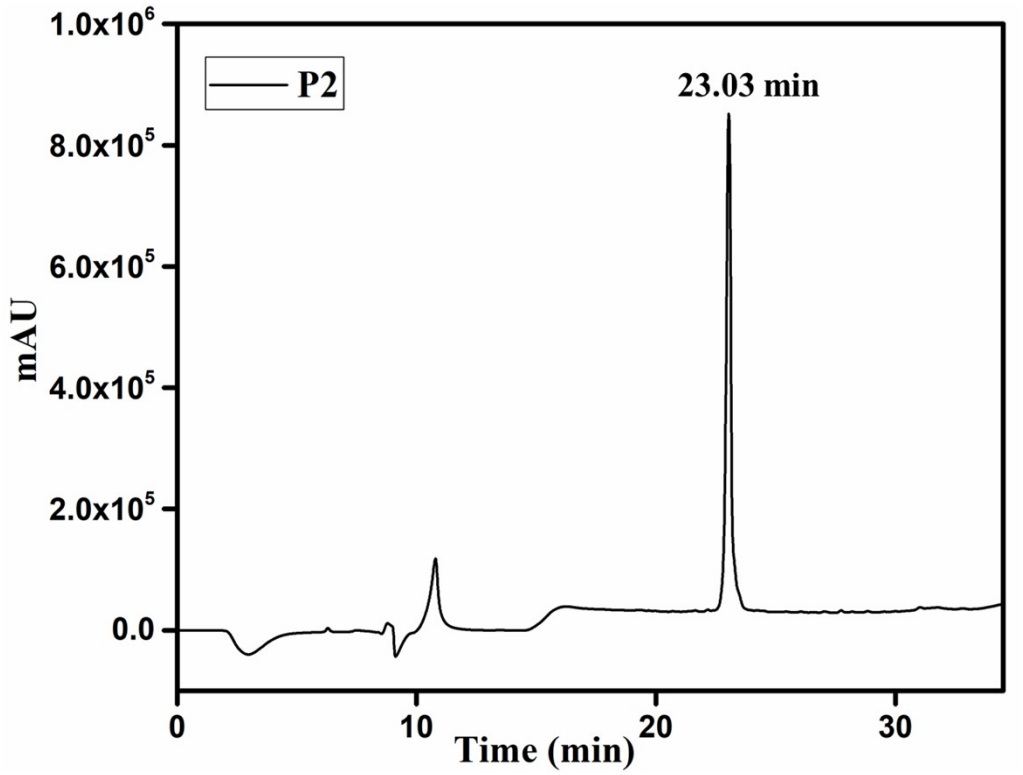


Fig. S19: Reverse phase HPLC profile of 12-mer peptide **P2** recorded on analytical C_{18} column (5µm, 4.6 x 250 mm column) at 220 nm using ACN/H_2O gradient system at a flow rate of 2 mL/Min.

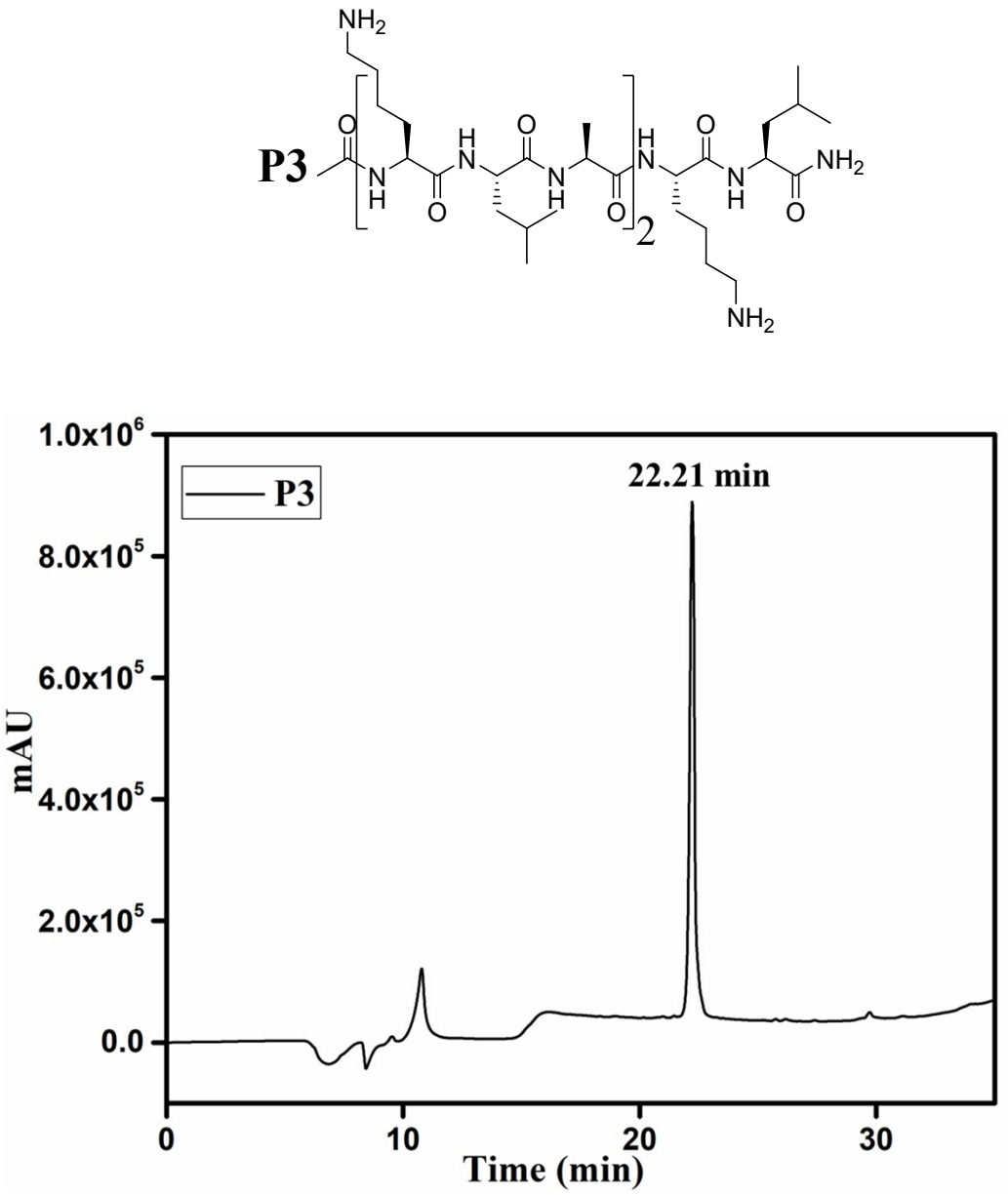
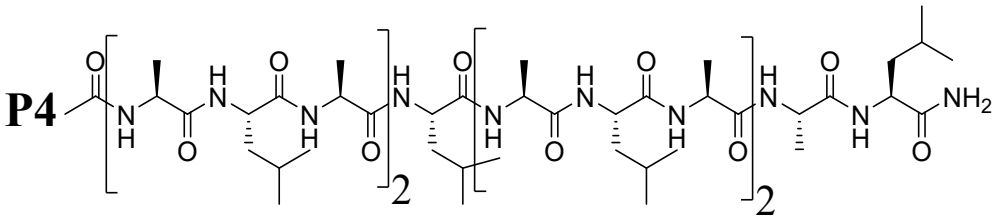


Fig. S20: Reverse phase HPLC profile of 8-mer peptide **P3** recorded on analytical C_{18} column (5µm, 4.6 x 250 mm column) at 220 nm using ACN/H_2O gradient system at a flow rate of 2 mL/Min.



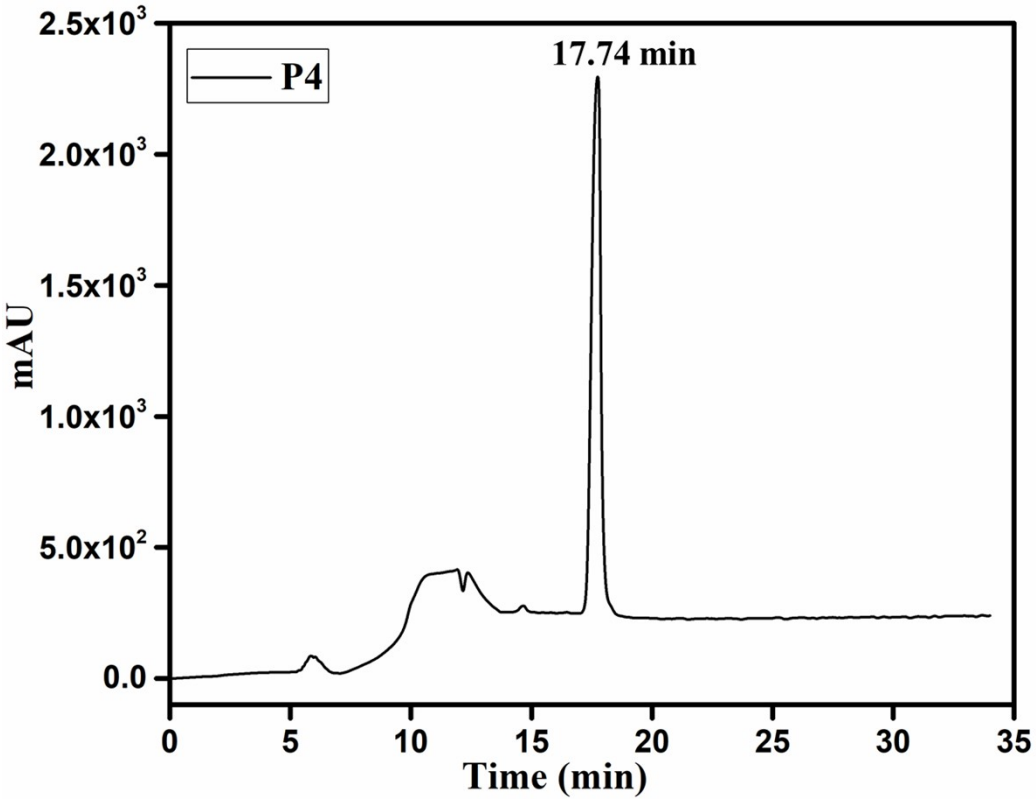


Fig. S21: Reverse phase HPLC profile of 15-mer peptide **P4** recorded on analytical C_{18} column (5µm, 4.6 x 250 mm column) at 220 nm using MeOH/H_2O gradient system at a flow rate of 2 mL/Min.

Table ST3 : ThT assay Kinetic Parameters [t_{50} (h), Lag time (h), k_{app} (h^{-1})] for the aggregation effect on $A\beta_{42}$ in the presence of Peptides.

Sample	t_{50} (h)	Lag time (h)	k_{app} (h^{-1})
$A\beta_{42}$ alone (25 µM)	9.34533 ± 0.25	6.3586 ± 0.32	0.66991 ± 0.016
$A\beta_{42}$ + P1 (1:0.5)	6.09333 ± 0.39	1.86553 ± 0.69	0.47505 ± 0.036
$A\beta_{42}$ + P2 (1:1)	9.59 ± 0.37	0.75207 ± 0.46	0.22631 ± 0.002
$A\beta_{42}$ + P3 (1:1)	8.22667 ± 0.30	2.141 ± 0.36	0.32866 ± 0.003
$A\beta_{42}$ + P4 (1:5)	18.32 ± 0.40	7.5234 ± 0.54	0.18527 ± 0.002

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