Supplementary information

Amyloid-β-derived Peptidomimetics inhibits Tau aggregation

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Synthesis of peptidomimetics and purification. The control peptide (LPFFD) and N-methyl glycine (sarcosine: Sr) substituted peptidomimetics, P3 (Thymine-Lys-Leu-Val-Phe-Phe), P4 (Thymine-Sr-Leu-Sr-Phe-Sr-Ala), P5 (Thymine-Lys-Sr-Val-Sr-Phe-Sr) and P6 (Gly-His-Lys-Sr-Val-Sr-Phe-Sr) were synthesized following standard 9-fluorenylmethoxycarbonyl (Fmoc) chemistry on an automated peptide synthesizer from Syro II (MultiSynTech). Rink amide resin (Novabiochem) was used as a solid support for the peptidomimetic synthesis. Fmoc-protected sarcosine (Sr) was prepared and directly used for the synthesis of P4 and P5 in the peptide synthesizer. HBTU was used as coupling reagent for amino acids in presence of DIPEA with DMF as solvent. For deprotection of Fmoc, 40% piperidine in DMF was used. P3 and LPFFD were synthesized with a coupling time of 1 h per amino acid, whereas for P4, P5 and P6 coupling time was increased to 2 h to obtain higher coupling yields. All the peptides and peptidomimetics were purified using a reverse-phase preparative HPLC on the C18 column at 40°C. Product purity was greater than 98% as ascertained by analytical HPLC. The molecular masses of the peptides and their mimetics were verified with HRMS (Q-TOF) (Table 1).

Table 1. HPLC and HRMS traces for P3, **P4, P5, P6 and LPFFD**

Name	Sequence	Actual mass	Obtained mass $[M+H]^+$
P3	**Thymine**- Lys-Leu-Val-Phe-Phe	818.4565	818.4581
P4	**Thymine**-**Sr**-Leu-**Sr**-Phe-**Sr**-Ala	728.3731	728.3716
P5	**Thymine**-Lys-**Sr**-Val-**Sr**-Phe-**Sr**	771.4153	771.4146
P6	Gly-His-Lys-**Sr**-Val-**Sr**-Phe-**Sr**	821.4398	821.4391 $[M+Na]^+$
LPFFD	Lys-Pro-Phe-Phe-Asp	637.3344	637.3348

Sr = Sarcosine (N-methylglycine).

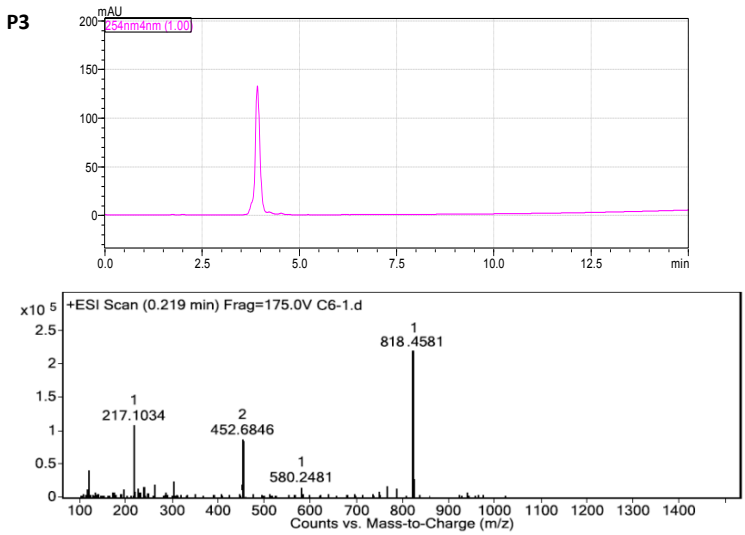

Figure S1. P3 was purified using a reverse-phase preparative HPLC on Shimadzu, using the Phenomenex, RP-C18 (5µm, 4.6 × 250 mm) column. Water and acetonitrile was used as mobile phase at a ratio of 75:25 with 0.1% TFA v/v. The run was conducted by injecting 20 µL peptide, a flow rate of 0.8 mL/min was maintained for 15 minutes run time.

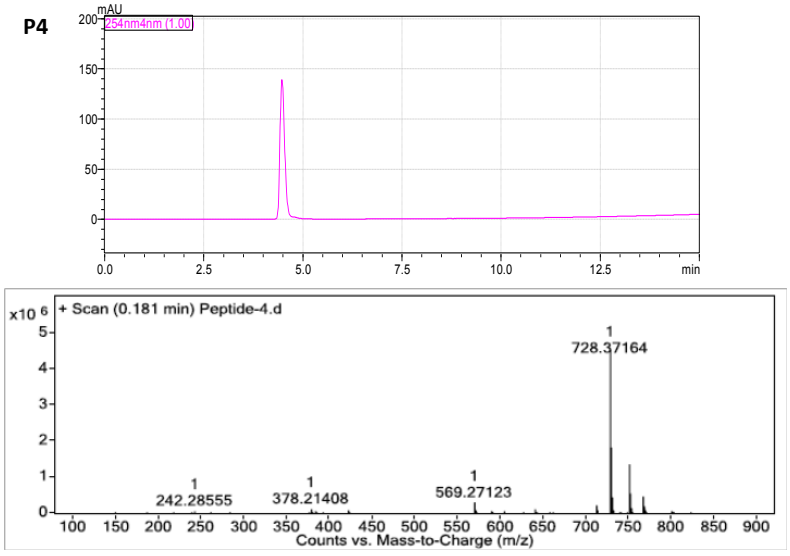

Figure S2. P4 was purified using a reverse-phase preparative HPLC on Shimadzu, using the Phenomenex, RP-C18 (5µm, 4.6 × 250 mm) column. Water and acetonitrile was used as mobile phase at a ratio of 70:30 with 0.1% TFA v/v. The run was conducted by injecting 20 µL peptide, a flow rate of 0.8 mL/min was maintained for 15 minutes run time.

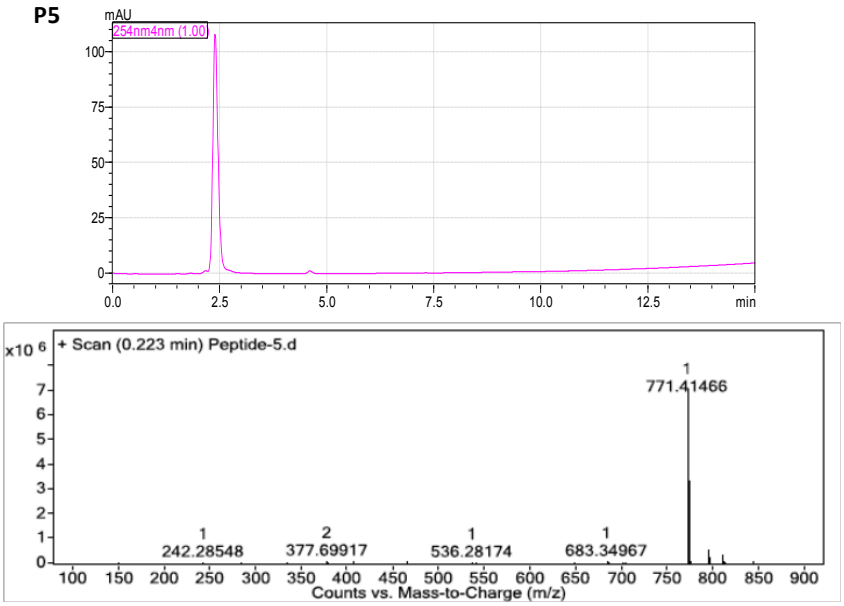

Figure S3. P5 was purified using a reverse-phase preparative HPLC on Shimadzu, using the Phenomenex, RP-C18 (5µm, 4.6 × 250 mm) column. Water and acetonitrile was used as mobile phase at a ratio of 84:16 with 0.1% TFA v/v. The run was conducted by injecting 15 µL peptide, a flow rate of 0.8 mL/min was maintained for 15 minutes run time.

P6

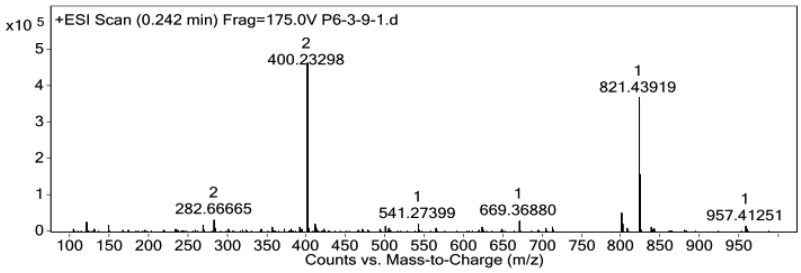

Figure S4. P6 was purified using a reverse-phase preparative HPLC on Shimadzu, using the Phenomenex, RP-C18 (5µm, 10 × 250 mm) column. Water and acetonitrile was used as mobile phase at a ratio of 46:54 with 0.1% TFA v/v. The run was conducted by injecting 200 µL peptide, a flow rate of 4 mL/min was maintained for 15 minutes run time.

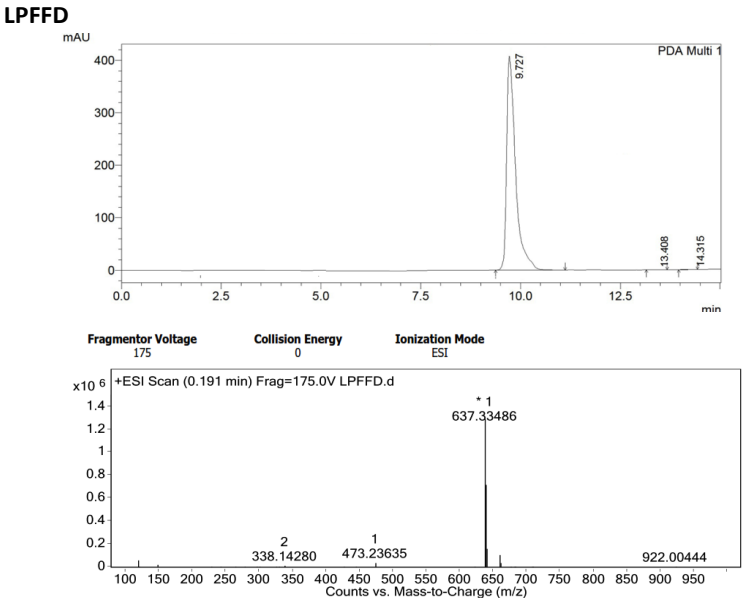

Figure S5. LPFFD was purified using a reverse-phase preparative HPLC on Shimadzu, using the Phenomenex, RP-C18 (5µm, 10 × 250 mm) column. Water and acetonitrile was used as mobile phase at a ratio of 34:66 with 0.1% TFA v/v. The run was conducted by injecting 100 µL peptide, a flow rate of 4 mL/min was maintained for 15 minutes run time.