Supporting Information

**Amyloid Peptides Incorporating a Core Sequence from the Amyloid Beta Peptide and Gamma Amino Acids: Relating Bioactivity to Self-Assembly**

Valeria Castelletto, Ge Cheng, Ian W. Hamley
Dept of Chemistry, University of Reading, Whiteknights, Reading RG6 6AD, UK

**Experimental Methods**

**Materials**
The following materials were used in the preparative examples: Fmoc-Phe-Wang resin (100-200 mesh, 0.66 mmol g\(^{-1}\) substitution), Fmoc-d-Phe-Wang resin (100-200 mesh, 0.66 mmol g\(^{-1}\) substitution), Fmoc-Phe-OH, Fmoc-d-Phe-OH, Fmoc-Val-OH, Fmoc-d-Val-OH, Fmoc-Leu-OH, Fmoc-d-Leu-OH, Fmoc-Lys(Boc)-OH, Fmoc-d-Lys(Boc)-OH, Fmoc-\(\beta\)-Ala-OH, and Fmoc-\(\gamma\)-Abu-OH (Fmoc-GABA) were purchased from Novabiochem (UK). (R)-Fmoc-4-amino-6-methyl-heptanoic acid, (R)-Fmoc-4-amino-5-phenyl-pentanoic acid and (R)-Fmoc-4-amino-5-(4-tert-butoxyphenyl)-pentanoic acid were purchased from PolyPeptide Laboratories France SAS. Trifluoroacetic acid (TFA), piperidine and triisopropylsilane (TIPS) were purchased from Sigma-Aldrich. HOBr/DMF (a mixture of 1-hydroxybenzotriazole and dimethylformamide), DIPEA/NMP (a mixture of diisopropylethylamine and N-methylpyrrolidone), and NMP were obtained from Applied Biosystems(UK). Water (HPLC grade), acetonitrile (HPLC grade), dimethylformamide (DMF), methanol (MeOH) and dichloromethane (DCM) and diethyl ether were purchased from Fisher Scientific (UK).

*General Synthesis Methods*
The peptides shown in Scheme 1 were synthesized by solid phase methods using standard FastMoc chemistry [Fmoc (9-fluorenylmethyloxycarbonyl) protecting group and activation by HBTU/HOBt]. A 0.25 mmol scale synthesis was conducted with a fully automated peptide synthesizer (433A Applied Biosystems), which allowed for direct conductivity monitoring of Fmoc deprotection. Alternatively, a batchwise synthesis (> 0.50 mmol scale) was carried out using a fritted reaction glass vessel
equipped with a positive nitrogen pressure or vacuum, whereby appropriate application of positive nitrogen pressure generated sufficient bubbles for effective mixing for a coupling reaction while washing was achieved by pumping solvent through the resin bed. On the pre-loaded Wang resins the peptides were assembled from the C-terminus toward the N-terminus.

In the standard FastMoc protocol, the first step of the reaction was to remove the Fmoc protecting group from the preloaded amino acid using a solution of piperidine in NMP or DMF, followed by washing the resin bed with NMP or DMF. The next step was activation of the carbonyl group of the new amino acid (dissolved in NMP or DMF) using HBTU (dissolved in HOBt, DIPEA, and NMP or DMF). For a batchwise synthesis, HBTU: 2-4 eq. of the resin loading, HOBt: 2-4 eq. of the resin loading and DIPEA: 4-6 eq. of the resin loading were employed for activation. The activated amino acid was transferred from the activation vessel to the reaction vessel containing the previously deprotected amino terminal group of the peptide chain, and coupling was performed with vortex or sufficient nitrogen bubbling. To obtain the highest coupling efficiency, 2-4 times excess of each amino acid was used in each coupling. In the last step, the Fmoc protecting groups on the N-terminus were removed using a solution of piperidine in NMP or DMF, followed by washing the resin bed with NMP or DMF, MeOH and DCM.

In the cleavage step, the obtained peptide attached to the solid support was treated with a mixture of 95% TFA, 2.5% triisopropylsilane, and 2.5% water, and the mixture was stirred at room temperature for approximately 4 h, followed by filtration. The cleaved resin was washed three times with TFA. During the cleavage the side chain protecting groups (Boc) were removed by TFA. The obtained peptide solution was collected and concentrated by evaporating TFA under vacuum, followed by precipitating in cold diethyl ether. The crude product was separated by centrifugation and decanting the supernatant. The crude peptide was redissolved in HPLC grade water/acetonitrile co-solvent, then purified by reverse phase HPLC (Perkin Elmer 200). The eluents for the preparative HPLC were 0.1% TFA in HPLC grade water and 0.1% TFA acetonitrile. During HPLC a gradient solvent was used, where the acetonitrile portion increased linearly from 0% to 90% over 20 min and then decreased linearly to 0% over 10 min. A sample injection (injected with Perkin Elmer
Series 200 Autosampler) was run on a C18 preparative column (Vp 250/10 Nucleosil, Macherey-Nagel, 7μm, 250mm× 10 mm) for 30 min with flow rates 4 ml/min at 35 °C (Perkin Elmer Series 200 Peltier Column Oven). A UV/vis detector (Perkin Elmer Series 200 UV/vis Detector) monitored the sample elution at 238 or 254 nm. The fractions of the peptide were collected, followed by lyophilization to give a white solid, which was characterized by ESI-MS and 1H NMR.

Note: Fmoc-Phe-Wang resin, Fmoc-Phe-OH, Fmoc-Val-OH, Fmoc-Leu-OH, Fmoc-Lys(Boc)-OH, Fmoc-γ-Abu-OH (Fmoc-GABA) and Fmoc-β-Ala-OH were employed for peptide CG-54 and CG-56; while Fmoc-d-Phe-Wang resin, Fmoc-d-Phe-OH, Fmoc-d-Val-OH, Fmoc-d-Leu-OH, Fmoc-d-Lys(Boc)-OH, (R)-Fmoc-4-amino-6-methyl-heptanoic acid, (R)-Fmoc-4-amino-5-phenyl-pentanoic acid and (R)-Fmoc-4-amino-5-(4-tert-butoxyphenyl)-pentanoic acid for peptide III, IV and V.

Synthesis of Peptide I

The complete sequence of the peptide was GABA-GABA-Lys-Leu-Val-Phe-Phe. It was assembled from the C-terminus towards the N-terminus, which was performed with a fully automated peptide synthesizer (433A Applied Biosystems). Pre-loaded resin Fmoc-Phe-Wang resin with 0.66 mmol/g substitution of Fmoc-Phe-OH was used as the solid support. The resin (378.80 mg with 0.25 mmol of Fmoc-Phe-OH) was swollen in NMP, followed by removing the Fmoc protecting group from the preloaded amino acid with 20% piperidine in NMP. Four times excess of each amino acid was used in 0.25 mmol coupling cycles. The Fmoc-amino acid was dissolved with 2.1 g NMP, 2.0 g of 0.45 M HBTU/HOBt in DMF, and 2 M DIEA, then transferred to the 41-mL reaction vessel to effect each coupling. After each coupling a solution of 20% piperidine/NMP was introduced and allowed to remove the Fmoc protecting group with the ABI 433A Peptide Synthesizer, monitoring the extent of deprotection. Each coupling and Fmoc deprotection was followed by washing the resin with NMP automatically by the synthesizer. The obtained peptide attached to the solid support was treated with an acidic cleavage cocktail (95% TFA, 2.5% water, and 2.5% TIPS) concomitant with deprotection of lysine’s ε-amino-Boc groups. After the mixture was stirred at room temperature for approximately 4 h, it was filtered. The obtained peptide solution was precipitated in cold diethyl ether and the crude product was separated by centrifugation and decanting the supernatant. The crude peptide was
purified by RP-HPLC (RP-HPLC retention time = 12.37 min), followed by lyophilization to give a white solid.

\[ \text{MS(ESI)m/z for } C_{43}H_{66}N_{8}O_{8} \text{ [M+H]}^+ \text{calcld 824.5116, found [M+H]}^+, \]
824.5132; [M+2H]^{2+} calcd 412.5264, found 412.7599. \^{1} \text{H NMR (400 MHz methanol-d}_{4}, \text{ppm): 0.79 (d, } J = 6.8 \text{ Hz, 3H), 0.84 (d, } J = 6.4 \text{ Hz, 3H), 0.92 (d, } J = 6.4 \text{ Hz, 3H),}
0.97 (d, } J = 6.4 \text{ Hz, 3H), 1.42-1.56(m, 3H), 1.59-1.73(m, 5H), 1.80 (m, 3H), 1.93(m, 3H), 2.30(m, 2H), 2.36 (t, } J = 7.2 \text{ Hz, 2H), 2.83-3.06(m, 6H), 3.10-3.22(m, 4H), 4.10 (m, 1H), 4.32(dd, } J = 10 \text{ Hz, 4.8 Hz, 1H), 4.39(q, } J = 4.8 \text{ Hz, 1H), 4.62 (m, 2H), 7.19-7.29(m, 10H), 7.85, 8.07, 8.19, 8.25[\text{amide-H}].

**Synthesis of Peptide II**

The complete sequence of the peptide was β-Ala-β-Ala-Lys-Leu-Val-Phe-Phe. It was assembled from the C-terminus towards the N-terminus, which was performed with a fully automated peptide synthesizer (433A Applied Biosystems). Pre-loaded resin Fmoc-Phe-Wang resin with 0.66 mmol/g substitution of Fmoc-Phe-OH was used as the solid support. The resin (378.80 mg, with 0.25 mmol of Fmoc-Phe-OH) was swollen in NMP, followed by removing the Fmoc protecting group from the preloaded amino acid with 20% piperidine in NMP. Four times excess of each amino acid was used in 0.25 mmol coupling cycles. The Fmoc-amino acid was dissolved with 2.1 g NMP, 2.0 g of 0.45 M HBTU/HOBt in DMF, and 2 M DIEA, then transferred to the 41-mL reaction vessel to effect each coupling. After each coupling a solution of 20% piperidine/NMP was introduced and allowed to remove the Fmoc protecting group with the ABI 433A Peptide Synthesizer monitoring the extent of deprotection. Each coupling and Fmoc deprotection was followed by washing the resin with NMP automatically by the synthesizer. The obtained peptide attached to the solid support was treated with an acidic cleavage cocktail (95% TFA, 2.5% water, and 2.5% TIPS) concomitant with deprotection of lysine’s ε-amino-Boc groups. After the mixture was stirred at room temperature for approximately 4 h, it was filtered. The obtained peptide solution was precipitated in cold diethyl ether and the crude product was separated by centrifugation and decanting the supernatant. The crude peptide was purified by RP-HPLC (RP-HPLC retention time = 12.46 min), followed by lyophilization to give a white solid.
MS(ESI)m/z for C_{41}H_{62}N_{8}O_{8} [M+H]^{+} calcd 795.4670, found [M+H]^{+}, 795.4763; [M+2H]^{2+} calcd 398.2375, found 398.2417. $^1$H NMR (400 MHz methanol-d$_4$, ppm): 0.81 (d, J = 6.4 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.4 Hz, 3H), 0.98 (d, J = 6.4 Hz, 3H), 1.42-1.56(m, 3H), 1.59-1.72(m, 5H), 1.84 (m, 1H), 1.95(sxt, J =6.8 Hz,1H), 2.47(m, 2H), 2.59 (t, J = 6.4 Hz, 2H), 2.85-2.95(m, 3H), 3.03 (m, 1H), 3.09-3.23(m, 4H), 3.41-3.56(m, 2H), 4.11 (m, 1H),4.33(dd, J = 8.0 Hz, 5.6 Hz, 1H), 4.42(q, J = 5.2 Hz, 1H), 4.64 (m, 2H), 7.19-7.29(m, 10H),7.90, 8.01, 8.19[amide-H].

**Synthesis of Peptide III**

The complete sequence of the peptide was [(R)-(4-amino-5-phenyl]pentanoyl-[(R)-4-amino-5-phenyl]pentanoyl-(R)-Lys-(R)-Leu-(R)-Val-(R)-Phe-(R)-Phe. It was assembled from the C-terminus towards the N-terminus, which was performed with a fully automated peptide synthesizer (433A Applied Biosystems). Pre-loaded resin Fmoc-D-Phe-Wang resin with 0.66 mmol/g substitution of Fmoc-D-Phe-OH was used as the solid support. The resin (378.80 mg, with 0.25 mmol of Fmoc-D-Phe-OH) was swollen in NMP, followed by removing the Fmoc protecting group from the preloaded amino acid with 20% piperidine in NMP. Four times excess of each amino acid was used in 0.25 mmol coupling cycles. The Fmoc-amino acid was dissolved with 2.1 g NMP, 2.0 g of 0.45 M HBTU/HOBt in DMF, and 2 M DIEA, then transferred to the 41-mL reaction vessel to effect each coupling. After each coupling a solution of 20% piperidine/NMP was introduced and allowed to remove the Fmoc protecting group with the ABI 433A Peptide Synthesizer monitoring the extent of deprotection. Each coupling and Fmoc deprotection was followed by washing the resin with NMP automatically by the synthesizer. The obtained peptide attached to the solid support was treated with an acidic cleavage cocktail (95% TFA, 2.5% water, and 2.5% TIPS) concomitant with deprotection of lysine’s ε-amino-Boc groups. After the mixture was stirred at room temperature for approximately 4 h, it was filtered. The obtained peptide solution was precipitated in cold diethyl ether and the crude product was separated by centrifugation and decanting the supernatant. The crude peptide was purified by RP-HPLC (RP-HPLC retention time = 15.19 min), followed by lyophilization to give a white solid.

MS(ESI)m/z for C_{57}H_{78}N_{8}O_{8} [M+H]^{+} calcd 1003.6022, found [M+H]^{+}, 1003.6026; [M+2H]^{2+} calcd 502.3051, found 502.3043. $^1$H NMR (400 MHz methanol-d$_4$, ppm):
0.69 (d, J = 6.8 Hz, 3H), 0.73 (d, J = 6.8 Hz, 3H), 0.79 (d, J = 6.8 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H), 1.28-1.88 (m, 15H), 2.10-2.28 (m, 4H), 2.58 (m, 1H), 2.70-2.81 (m, 6H), 2.90 (dd, J = 14.0 Hz, 8.0 Hz, 1H), 3.01 (dd, J = 14.0 Hz, 5.2 Hz, 1H), 3.08 (dd, J = 14.0 Hz, 5.2 Hz, 1H), 3.95-4.01 (m, 2H), 4.18-4.32 (m, 2H), 4.53 (m, 2H), 7.05-7.27 (m, 20H), 7.76, 7.90, 7.98, 8.07 [amide-H].

**Synthesis of Peptide IV**

The complete sequence of the peptide was [(R)-4-amino-5-(4-hydroxyphenyl)pentanoyl-[(R)-4-amino-5-(4-hydroxyphenyl)pentanoyl-(R)-Lys-(R)-Leu-(R)-Val-(R)-Phe-(R)-Phe. It was assembled from the C-terminus towards the N-terminus, which was performed with a fully automated peptide synthesizer (433A Applied Biosystems). Pre-loaded resin Fmoc-D-Phe-Wang resin with 0.66 mmol/g substitution of Fmoc-D-Phe-OH was used as the solid support. The resin (378.80 mg, with 0.25 mmol of Fmoc-D-Phe-OH) was swollen in NMP, followed by removing the Fmoc protecting group from the preloaded amino acid with 20% piperidine in NMP. Four times excess of each amino acid was used in 0.25 mmol coupling cycles. The Fmoc-amino acid was dissolved with 2.1 g NMP, 2.0 g of 0.45 M HBTU/HOBt in DMF, and 2 M DIEA, then transferred to the 41-mL reaction vessel to effect each coupling. After each coupling a solution of 20% piperidine/NMP was introduced and allowed to remove the Fmoc protecting group with the ABI 433A Peptide Synthesizer monitoring the extent of deprotection. Each coupling and Fmoc deprotection was followed by washing the resin with NMP automatically by the synthesizer. The obtained peptide attached to the solid support was treated with an acidic cleavage cocktail (95% TFA, 2.5% water, and 2.5% TIPS) concomitant with deprotection of lysine’s ε-amino-Boc groups and tert-butyl groups. After the mixture was stirred at room temperature for approximately 4 h, it was filtered. The obtained peptide solution was precipitated in cold diethyl ether and the crude product was separated by centrifugation and decanting the supernatant. The crude peptide was purified by RP-HPLC (RP-HPLC retention time = 13.96 min), followed by lyophilization to give a white solid.

MS(ESI)m/z for C_{57}H_{78}N_{8}O_{10} [M+2H]^{2+} calcd 518.7999, found 518.2996. \textsuperscript{1}H NMR (400 MHz methanol-d\textsubscript{4}, ppm): 0.79 (d, J = 6.4 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.4 Hz, 3H), 0.95 (d, J = 6.4 Hz, 3H), 1.40-2.01 (m, 15H), 2.24-2.39 (m, 4H),
2.61 (m, 1H), 2.71-2.93(m, 6H), 3.01(dd, J = 14.0 Hz, 8.0 Hz, 1H), 3.09(dd, J = 14.0 Hz, 5.2 Hz, 1H), 3.18(dd, J = 14.0 Hz, 5.2 Hz, 1H), 4.03(m, 1H), 4.11 (m, 1H), 4.33(m, 1H), 4.40(m, 1H), 4.65(m, 2H), 6.72(d, J = 8.4Hz, 2H), 6.81(d, J = 8.8Hz, 2H), 7.04(dd, J =18.4 Hz, 8.4 Hz, 4H), 7.18-7.29(m, 12H), 7.87, 8.04, 8.09, 8.19[amide-H].

**Synthesis of Peptide V**

The complete sequence of the peptide was [(R)-4-amino-6-methyl]heptanoyl-[(R)-4-amino-6-methyl]heptanoyl-(R)-Lys-(R)-Leu-(R)-Val-(R)-Phe-(R)-Phe. It was assembled from the C-terminus towards the N-terminus, which was performed with a fully automated peptide synthesizer (433A Applied Biosystems). Pre-loaded resin Fmoc-D-Phe-Wang resin with 0.66 mmol/g substitution of Fmoc-D-Phe-OH was used as the solid support. The resin (378.80 mg, with 0.25 mmol of Fmoc-D-Phe-OH) was swollen in NMP, followed by removing the Fmoc protecting group from the preloaded amino acid with 20% piperidine in NMP. Four times excess of each amino acid was used in 0.25 mmol coupling cycles. The Fmoc-amino acid was dissolved with 2.1 g NMP, 2.0 g of 0.45 M HBTU/HOBt in DMF, and 2 M DIEA, then transferred to the 41-mL reaction vessel to effect each coupling. After each coupling a solution of 20% piperidine/NMP was introduced and allowed to remove the Fmoc protecting group from the ABI 433A Peptide Synthesizer monitoring the extent of deprotection. Each coupling and Fmoc deprotection was followed by washing the resin with NMP automatically by the synthesizer. The obtained peptide attached to the solid support was treated with an acidic cleavage cocktail (95% TFA, 2.5% water, and 2.5% TIPS) concomitant with deprotection of lysine’s ε-amino-Boc groups. After the mixture was stirred at room temperature for approximately 4 h, it was filtered. The obtained peptide solution was precipitated in cold diethyl ether and the crude product was separated by centrifugation and decanting the supernatant. The crude peptide was purified by RP-HPLC (RP-HPLC retention time = 14.40 min), followed by lyophilization to give a white solid.

**MS(ESI)m/z** for C_{57}H_{82}N_{8}O_{8} [M+H]^+ calcld 935.6335, found [M+H]^+, 935.6315; [M+2H]^2+ calcld 468.3207, found 468.3193. **^1H NMR** (400 MHz methanol-d₄, ppm): 0.79 (d, J = 6.8 Hz, 3H), 0.84 (d, J = 6.8 Hz, 3H), 0.90-1.01 (m, 18H),1.25-2.01(m, 21H), 2.27 (t, J = 8.0 Hz, 2H), 2.43 (m, 2H), 2.90(m, 3H), 3.04(dd, J = 14.0 Hz, 8.0 Hz, 1H), 3.18(dd, J = 14.0 Hz, 5.2 Hz, 1H), 4.03(m, 1H), 4.11 (m, 1H), 4.33(m, 1H), 4.40(m, 1H), 4.65(m, 2H), 6.72(d, J = 8.4Hz, 2H), 6.81(d, J = 8.8Hz, 2H), 7.04(dd, J =18.4 Hz, 8.4 Hz, 4H), 7.18-7.29(m, 12H), 7.87, 8.04, 8.09, 8.19[amide-H].
Hz, 1H), 3.11(dd, J = 14.0 Hz, 5.2 Hz, 1H), 3.22(dd, J = 14.0 Hz, 5.2 Hz, 1H), 3.95(m, 1H), 4.11(m, 1H), 4.33-4.42(m, 2H), 4.65(m, 2H), 7.18-7.30(m, 10H), 7.87, 8.04, 8.11, 8.19[amide-H].

*Amyloid β(1-42) binding Studies*

Amyloid Aβ(1-42) (H-Asp-Ala-Glu-Phe-Arg-His-Asp-Ser-Gly-Tyr-Glu-Val-His-His-Gln-Lys-Leu-Val-Phe-Asp-Ala-Glu-Val-Gly-Ser-Asn-Lys-Gly-Ala-Ile-Ile-Gly-Leu-Met-Val-Gly-Gly-Val-Val-Ile-Ala-OH) was purchased from American Peptide Inc. (Sunnyvale, USA). Purity was 95.8% based on RP-HPLC chromatography, M w found 4514.1 by electrospray MS.

In order to prevent any pre-aggregation, Aβ was first dissolved in hexafluoroisopropanol (HFIP) at a final concentration of 1 mg ml⁻¹. HFIP was then evaporated under a slow stream of N₂. Aβ was re-suspended in Tris buffer. When necessary, Aβ was re-suspended in Tris buffer with peptides I, III, IV or V. Aβ/γ-amino acid peptide solutions and samples containing pure Aβ were then incubated at 20°C without agitation. We studied samples containing 50 μM Aβ or mixtures of 50μM Aβ with γ-amino acid peptides in different molar ratios= 1:1, [X] = 1:0.5, 1:1 and 1:2 ([ ] = molar concentration; X= I, III, IV or V). The samples were therefore labelled Aβ:X 1:0, Aβ:X 1:0.5, Aβ:X 1:1 and Aβ:X 1:2.

*Cell Viability Assay*

The activity of the peptides in protecting SH-SY5Y cells from a toxic insult of 10 μM Aβ was assessed using the MTT (where MTT=(3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay. An amount 3 μL of each test compound [five concentrations] and 3 μL of Aβ1-42 [2 mM], both in dimethylsulfoxide (DMSO),
were added to 294 µL of cell media (consisting of Opti-MEM supplemented with 2% FBS, 1% Pen/Strep, 1% L-Gln) and mixed thoroughly. For each sample, 50 µL of the mixture was then aspirated and dispensed into wells containing SH-SY5Y cells (cells were plated 15 hours beforehand at ~30,000 cells/well/50 µl cell media). Final concentrations of compounds tested ranged from 50 µM to 3.7 µM with a final Aβ concentration of 10 µM. Cells were incubated in 5% CO₂ at 37°C for 24 hours and then the MTT assay performed. Briefly, 15 µL of MTT dye was added to each well and incubated for 4 hours. 100 µL of stop/solubilisation solution was added to each well and the plates left overnight in a humidified box at room temperature. The plate was shaken and the absorbance recorded at 570 nm with a reference at 650 nm. The percentage cell viability was determined by normalizing the Δ(OD) values with the live and dead cell controls, 1% DMSO and 0.1% TritonX-100 respectively.

**Thioflavin T Fluorescence Spectroscopy.**

Spectra were recorded at 20 °C on a Perkin Elementar Luminescence spectrometer LS50B with samples in a 0.5 cm thick quartz cell. A solution containing 150 µM ThT in Tris buffer was prepared and used as a solvent to prepare solutions in Table 1. These samples were then incubated for four days. After the period of incubation, the concentration of solutions containing ThT, was reduced by a factor 4 through dilution in Tris buffer. The fluorescence of these samples was then measured using λ<sub>ex</sub>= 440 nm. The fluorescence data were corrected for Tris buffer background.

**Cryogenic Transmission Electron Microscopy**

Experiments were performed at Unilever Research, Colworth, Bedford, UK. Sample preparation was carried out using a CryoPlunge 3 unit (Gatan Instruments) employing
a double blot technique. Approximately 3 µl of sample was pipetted onto a plasma etched (15 s) 400 mesh holey carbon grid (Agar Scientific) held in the plunge chamber at approx 90% humidity. The samples were blotted, from both sides for 0.5, 0.8 or 1.0 s dependant on sample viscosity. The samples were then plunged into liquid ethane at a temperature of -170 °C. The grids were blotted to remove excess ethane then transferred, under liquid nitrogen to the cryo TEM specimen holder (Gatan 626 cryo holder) at -170 °C. Samples were examined using a Jeol 2100 TEM operated at 200 kV and imaged using a Gatan Ultrascan 4000 camera and images captured using DigitalMicrograph software (Gatan).

*X-ray Diffraction*

X-ray diffraction was performed on stalks prepared from 2 wt% solutions in water. The stalks were mounted (vertically) onto the four axis goniometer of a RAXIS IV++ X-ray diffractometer (Rigaku) equipped with a rotating anode generator. The XRD data was collected using a Saturn 992 CCD camera.

*Fourier Transform Infra-Red (FTIR) Spectroscopy*

Peptides were dissolved in D₂O. Spectra were measured on a Nicolet Nexus spectrometer with DTGS detector. Solutions of peptide were sandwiched between two CaF₂ plate windows (spacer 0.025 mm). Spectra were scanned 128 times over the range of 4000-900 cm⁻¹.

*Circular Dichroism Spectroscopy*

CD spectra were measured at 20 °C for each solution using a Chiroscan spectropolarimeter (Applied Photophysics, UK). Peptide solutions were loaded into
0.1 or 0.01 mm quartz cells. Spectra were obtained from 200 to 260 nm with a 0.5 nm step and 1 second collection time per step, taking five averages.

For the binding studies, CD spectra were calculated for each molar ratio of Aβ(1-42) to peptide I, III, IV or V. The CD spectra were calculated based on addition of spectra of the components (Aβ(1-42) and peptides) on a molar ellipticity basis using the molar concentrations for the mixtures for which CD spectra were measured.

The post-acquisition smoothing tool from Chirascan software was used to remove random noise elements from the averaged spectra. A residual plot was generated for each curve in order to verify whether or not the spectrum has been distorted during the smoothing process. The CD signal from the solvent was subtracted from the CD data of the peptide solutions. Following background correction, the CD data were normalized to molar mean residue ellipticity.
SI Table 1. Spacings (in Å) from fibre XRD patterns (Fig.2)

<table>
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<th>Assignment</th>
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<th>IV</th>
<th>V</th>
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<td>24.9(1)</td>
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<td>Stacking of β-sheets</td>
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a) As it was prepared from a more concentrated solution (since stalks could not be prepared from more dilute solution), this sample exhibits many more reflections.
Figures

SI Fig.1. CD spectra for peptides I, III, IV and V (o) along with 50 μm Aβ (Δ) and mixtures (lines) at the molar ratios indicated.
SI Fig. 2. CD spectra for mixtures of peptides I, III, IV and V with Aβ (…) along with calculated spectra (——), based on addition of spectra of components (SI Fig. 1).
SI Fig.3. Thioflavin T binding study of III to Aβ(1-42).
SI Fig.4. Fibre x-ray diffraction patterns. (a) I, prepared from a 6.7 wt% solution, (b) III, prepared from a 1 wt% solution, (c) IV, prepared from a 1.8 wt% solution, (d) V, prepared from a 1.8 wt% solution.
SI Fig.5. FTIR spectra for peptides at higher concentration (2-3 wt%).
**SI Fig.6.** Hydrogel formation by (a) peptide I (2 wt%) and (b) peptide III (1 wt%).
References

