Supplementary Online Information

Aβ42-binding Peptoids as Amyloid Aggregation Inhibitors and Detection Ligands

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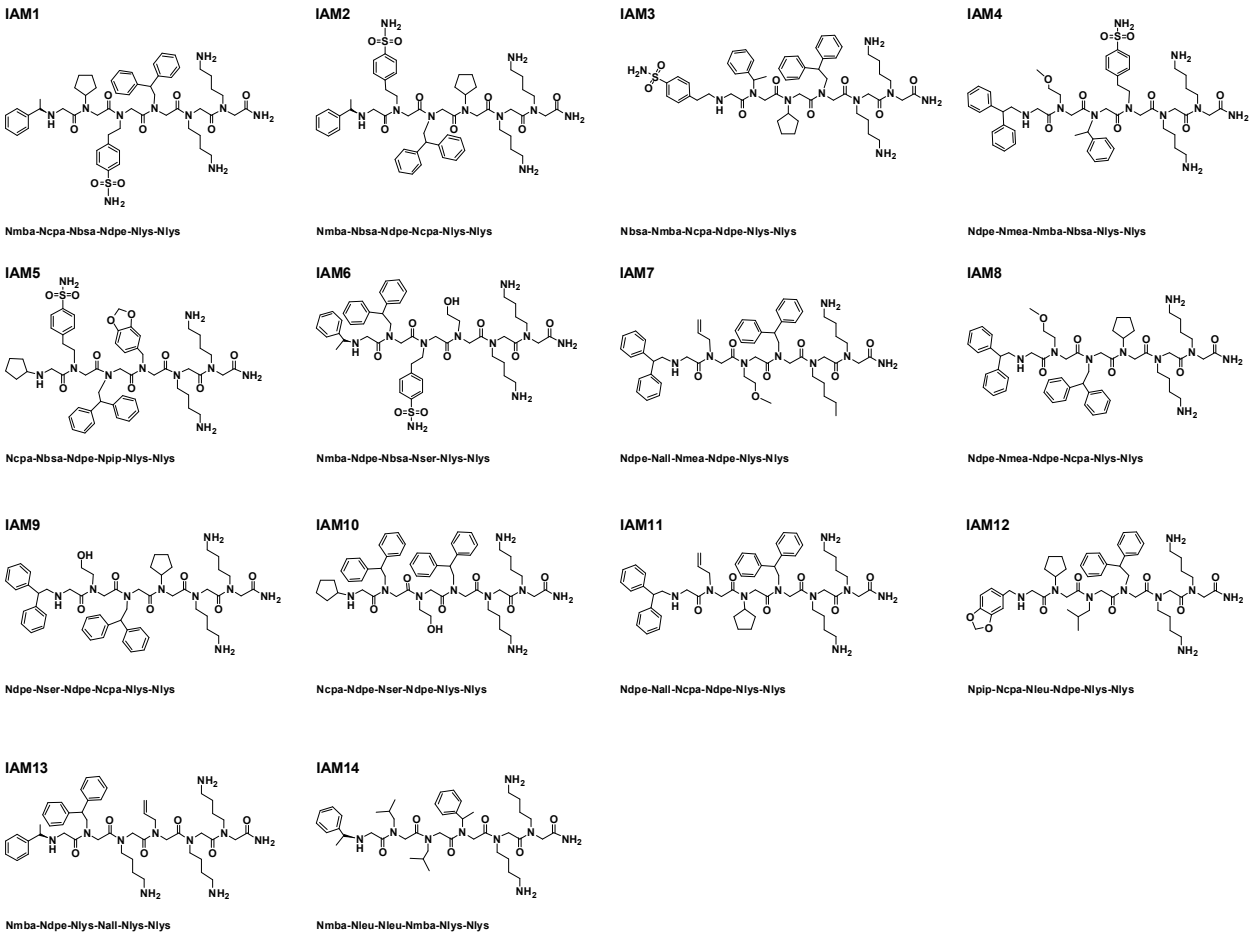
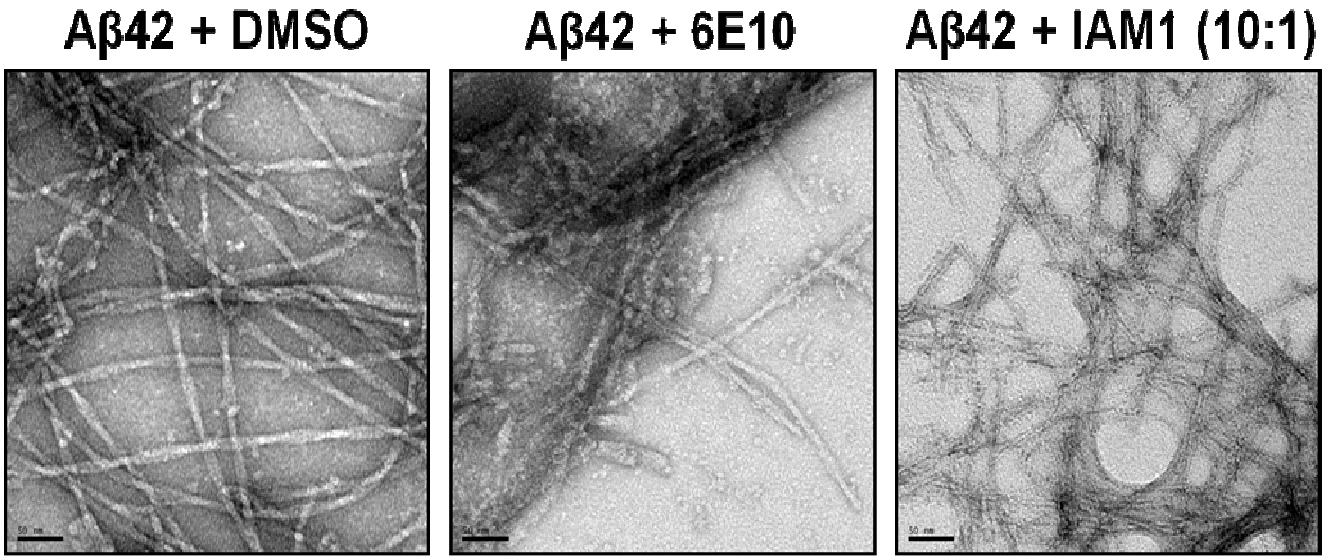


Supplementary Figure 1: Chemical structures of the fourteen hits peptoids (IAM1-14) isolated from the library screening and sequenced by Edman degradation.



Supplementary Figure 2: Transmission electron microscopic (TEM) analysis of the Aβ42 samples collected at the conclusion of the kinetic ThT assays in the presence of DMSO, 6E10 antibodies and IAM1 peptoid (10:1).

Supplementary Table 1: The MALDI-TOF mass spectrometry data for the peptoids.

Compound	Calculated mass	Mass found $(M+H)^+$)
IAM1	1036.56	1037.32
IAM1-biotin	1390.73	1392.35
(IAM1)2	2368.30	2370.84
(IAM1)2-biotin	2722.48	2725.53
RP	779.57	781.00
RP-biotin	1133.75	1034.87
ASRI	823.54	824.68
ASRI-biotin	1177.72	1178.80

SUPPLEMENTARY METHODS

MATERIALS AND EQUIPMENTS. TentaGel macrobeads were purchased from Rapp Polymere. Rink Amide AM resin was purchased from Novabiochem. Preparative HPLC was performed on a Waters system with a C18 reversed-phase Peptide HPLC column. MALDI-TOF MS was performed on a Voyager-DE PRO biospectrometry Workstation (Applied Biosystems) using α-hydroxyl cinnamic acid as the matrix. A Brunswick Scientific Innova 4400 incubator shaker was used to perform the peptoid syntheses. Edman sequencing of peptoids was performed on an ABI 476A Protein Sequencer (Applied Biosystems). On-bead fluorescence assays were visualized with an Olympus IX70 fluorescence microscope equipped with a DAPI filter set (410 nm excitation and 650 to 700 nm for emission) and a CCD camera. All the other chemical reagents were purchased from commercial sources and used without further purification.

Synthesis of IAM1 attached to TentaGel macrobeads. TentaGel macrobeads (50 mg, 24 μmol) were incubated in N, N-dimethyl formamide (DMF, anhydrous) at room temperature for 1 h and then incubated with diisopropylcarbodiimide (DIC, 189 mg, 1.5 mmol, 1 M in 1.5 ml in DMF) and chloroacetic acid (CAA, 142 mg, 1.5 mmol, 1 M in 1.5 ml DMF) at 37^{o}C for 1 h. After the reaction, beads were washed with DMF. Then N-(tert-butoxycarbonyl)-1,4-diaminobutane (282 mg, 1.5 mmol, 0.5 M in 3 ml NMP) was added to the beads and the reaction mixture was shaken at 37^{o}C for 2 h. The beads were again washed with DMF. The above two steps were repeated once. Then the above two reaction steps were repeated four times in which N-(tert-butoxycarbonyl)-1,4-diaminobutane was replaced with 2,2-diphenylethylamine (296 mg, 1.5 mmol, 0.5 M in 3 ml NMP), 4-(2-aminoethyl)benzenesulfonamide (300 mg, 1.5 mmol, 0.5 M in 3 ml NMP), cyclopentylamine (128 mg, 1.5 mmol, 0.5 M in 3 ml NMP) and (R)-(+)-α-methyl-benzylamine (182 mg, 1.5 mmol, 0.5 M in 3 ml NMP), respectively. After the

completion of synthesis, beads were washed sequentially with DMF and methanol. Side chain protective groups were cleaved and the beads were again washed sequentially with DMF and dichloromethane and stored at 4 °C until further use.

Synthesis of (IAM1)2. Rink Amide AM resin (100 mg, 0.071 mmol; 200-400 mesh, capacity: 0.71 mmol/g) was incubated in DMF at room temperature for 1 h. The resin was then incubated with 4 ml 20 % piperidine in DMF with shaking at room temperature for 20 min. This reaction step was repeated once and the resin was washed with DMF. Then the resin was mixed with Fmoc-Lys(Dde)-OH (0.355 mmol, 189 mg), HBTU (0.355 mmol, 135 mg), HOBt (0.355 mmol, 48 mg) and N-methylmorpholine (0.71 mmol, 72 mg) in 4 ml DMF at room temperature for 3h. The resin was washed with DMF and then incubated with 4 ml 20 % piperidine in DMF with shaking at room temperature for 20 min. This reaction step was repeated once and the resin was washed with DMF. Then the resin was mixed with Fmoc-β-Ala-OH (0.355 mmol, 111 mg; AnaSpec), HBTU (0.355 mmol, 135 mg), HOBt (0.355 mmol, 48 mg) and N-methylmorpholine (0.71 mmol, 72 mg) in 4 ml DMF at room temperature overnight. The resin was washed with DMF and then incubated with 4 ml 20 % piperidine in DMF at room temperature for 20 min. This reaction step was repeated once and the resin was washed with DMF. Then the resin was mixed with Fmoc-6-Ahx-OH (0.355 mmol, 125 mg; Fluka), HBTU (0.355 mmol, 135 mg), HOBt (0.355 mmol, 48 mg) and N-methylmorpholine (0.71 mmol, 72 mg) in 4 ml DMF at room temperature for 3 h. After this point, the synthesis procedure was similar to that in the synthesis of IAM1.

Synthesis of biotin-IAM1, biotin-RP, biotin-ASR1 and biotin-(IAM1)2 attached to TentaGel macrobeads. Rink Amide AM resin (100 mg, 0.071 mmol; 200-400 mesh, capacity: 0.71 mmol/g) was incubated in DMF at room temperature for 1 h. Then the resin

was incubated with 4 ml 20 % piperidine in DMF with shaking at room temperature for 20 min. This reaction step was repeated once and the resin was washed with DMF. The resin was mixed with Fmoc-Lys(Biotin)-OH (0.355 mmol, 211 mg), HBTU (0.355 mmol, 135 mg), HOBt (0.355 mmol, 48 mg) and N-methylmorpholine (0.71 mmol, 72 mg) in 4 ml DMF at room temperature overnight. The resin was washed with DMF and then incubated with 4 ml 20 % piperidine in DMF with shaking at room temperature for 20 min. This reaction step was repeated once and the resin was washed with DMF. After this point, the synthesis procedure was similar to the respective peptoid synthesis without biotin.