

SUPPLEMENTAL INFORMATION

A β 42-oligomer Interacting Peptide (AIP) neutralizes toxic amyloid- β 42 species and protects synaptic structure and function

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SUPPLEMENTAL FIGURE LEGENDS

Fig. S1: AFM micrographs showed no fibril formation of A β 42 wt and A β 42 G33A when co-incubated with the AIP. Both A β 42 wt and A β 42 G33A co-incubated with AIP were present as oligomeric and globular structures (scale bar = 100 nm). Without AIP (scale bar = 800 nm) A β 42 formed mature fibrils after 24 hours incubation, while there was no difference between A β 42 G33A incubated with or without AIP. Solely oligomeric and globular structures were detected for A β 42 G33A after 24 hours incubation.

Fig. S2: Effects of D-AIP on A β 42 wt aggregation. (A) TEM analyses showed that A β 42 wt aggregation was inhibited by D-AIP. Scale bar = 100 nm. (B) SEC analyses of aggregation behavior of A β 42 wt peptides co-incubated with AIP for 0, 4 or 8 hours. A β 42 wt peptides were mainly present as tetra-/hexamers, which slightly increased in size after 8 hours of incubation. (C) SH-SY5Y cells were treated for 12 hours with 4- or 8-hour preincubated A β 42 wt peptide, in the presence and absence of D-AIP, and the cell viability was determined using MTT assay. Co-incubation with AIP neutralized A β 42 wt-induced neurotoxic effects, while AIP itself was non-toxic. The graph depicts the mean \pm SEM of viability expressed as a %, normalized to vehicle-treated cells. *** $p < 0.001$, One-way ANOVA followed by Dunnett's multiple comparison *post-hoc* test was performed (D-AIP treatment as control). Number of independent experiments: A β 42 4 h, n = 7; A β 42 + AIP 4 h, n = 9; A β 42 8 h, n = 12; A β 42 + AIP 8 h, n = 13; AIP, n = 3.

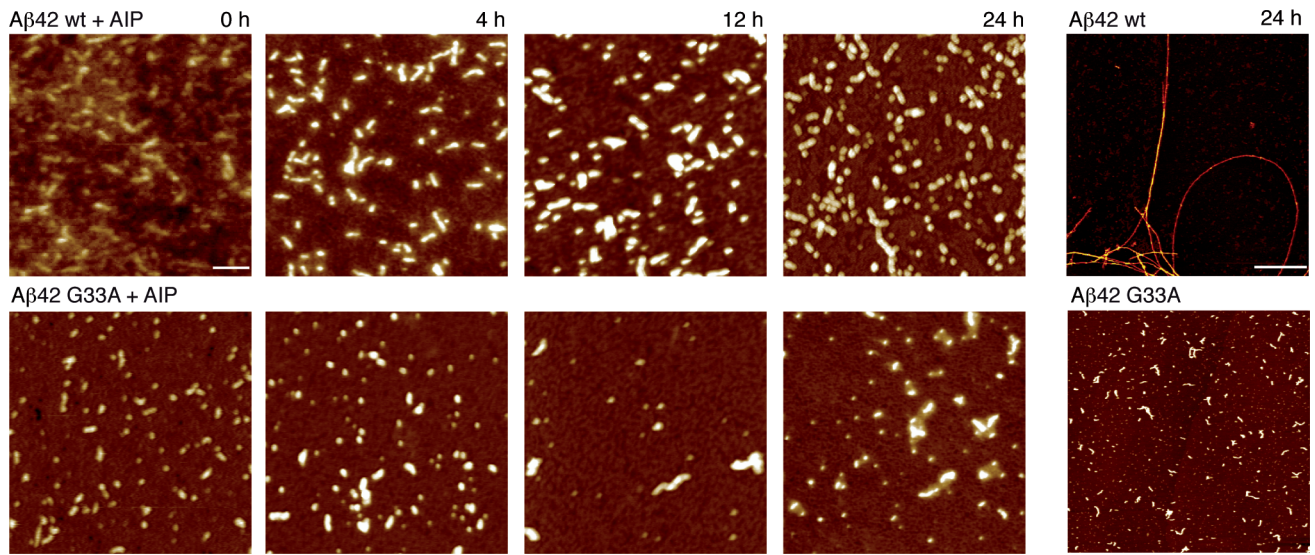
Fig. S3: Possible poses of L-AIP to A β 42 and A β 42 G33A docking. (A) L-AIP-A β 42 complex obtained from flexible docking, top pose #6. L-AIP is in green sticks representation with nitrogen colored in blue, oxygen in red and hydrogens of polar side chains involved in H-bonds (dashed lines) in yellow. Gly33 and Gly37 are in red and marked with arrows, and Asp23 in black. Sulfur of Met35 is colored yellow. Visible N- and C-termini and interacting residue are shown in normal font for A β 42 and in italics for L-AIP. In the inset, A β 42 is

depicted in surface representation (in gray) and Gly33 and Gly37 in red, Asp23 in black and Met35-sulfur in yellow. (B) AIP-A β 42 G33A complex obtained from flexible docking, top two poses. L-AIP is in green sticks representation with nitrogen colored in blue, oxygen in red and hydrogens of polar side chains involved in H-bonds (dashed lines) in yellow. Ala33 is in magenta and Gly37 in red and marked with arrows, and Asp23 in black. Sulfur of Met35 is colored yellow. Visible N- and C-termini and interacting residues are in normal font for A β 42 G33A and in italics for L-AIP. In the inset A β 42 G33A is depicted in surface representation (in gray) and Ala33 in magenta, Gly37 in red, Asp23 in black and Met35-sulfur in yellow.

Fig. S4: Preferred poses of L-AIP to A β 42 and A β 42 G33A docking. (A-F) L-AIP-A β 42 complexes obtained from flexible docking, top six poses. L-AIP is in green sticks representation with nitrogen colored in blue, oxygen in red and hydrogens of polar side chains in white. A β 42 is depicted in surface representation (in gray) and Gly33 and Gly37 in red, Asp23 in black and Met35 sulfur in yellow. N- and C-termini of A β 42 are marked with N or C. (G-I) L-AIP-A β 42 G33A complexes obtained from flexible docking, top three poses. L-AIP is in green sticks representation with nitrogen colored in blue, oxygen in red and hydrogens of polar side chains in white. A β 42G33A is depicted in surface representation (in gray) and Ala33 in magenta, Gly37 in red, Asp23 in black and Met35 sulfur in yellow. N- and C-termini of A β 42G33A are marked with N or C.

Fig. S5: Preferred poses of D-AIP to A β 42 docking. (A-G) D-AIP-A β 42 complexes obtained from flexible docking, top seven poses. D-AIP is in green sticks representation with nitrogen colored in blue, oxygen in red and hydrogens of polar side chains in white. A β 42 is depicted in surface representation (in gray) and Gly33 and Gly37 in red, Asp23 in black and Met35-sulfur in yellow. N- and C-termini of A β 42 are marked with N or C.

Figure S1



Suppl. Fig. 2

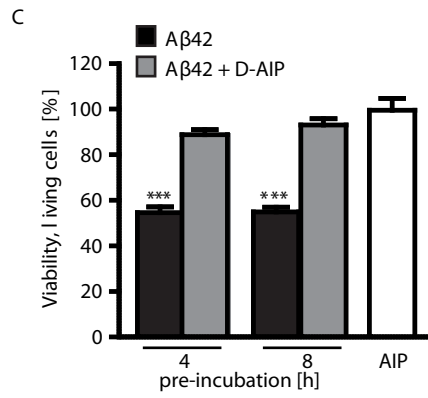
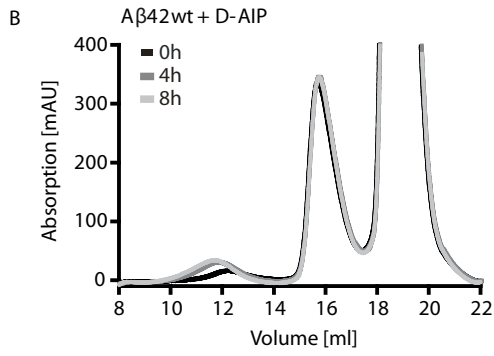
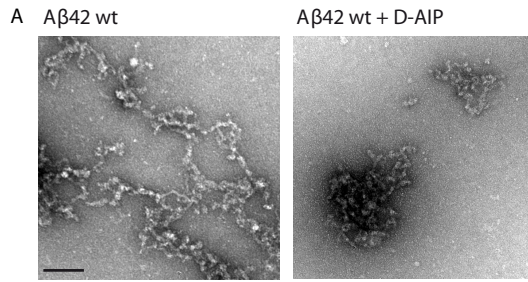
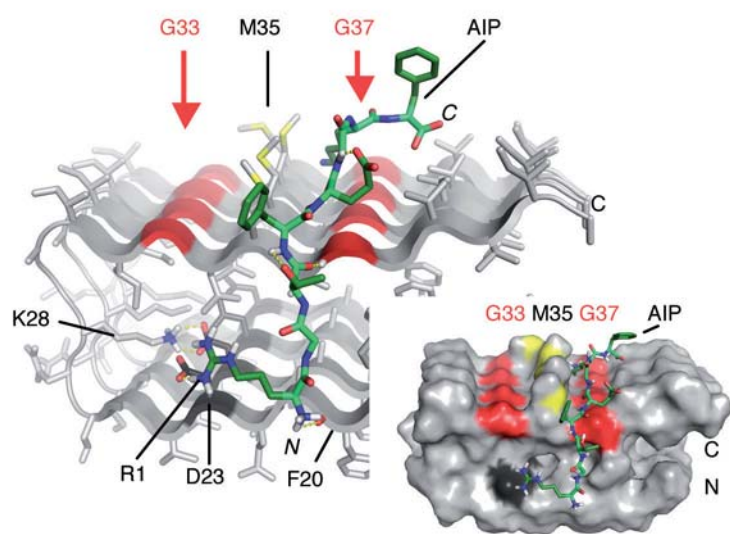


Figure S3

A L-AIP to A β 42 Pose #6



B L-AIP to A β 42G33A Poses #1-2

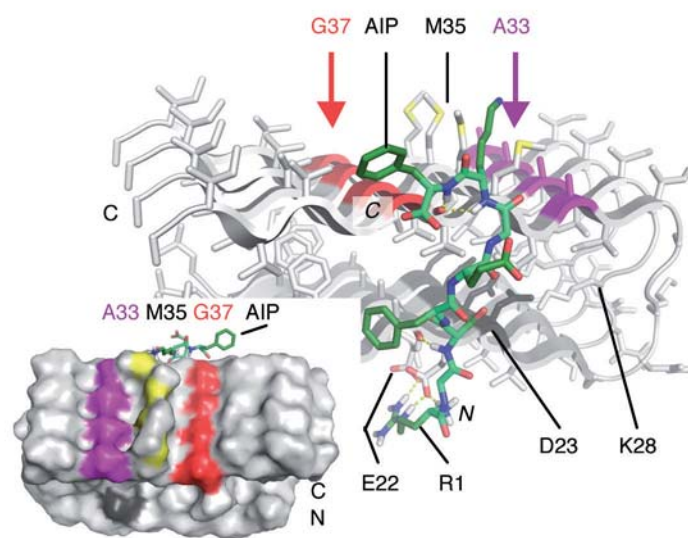
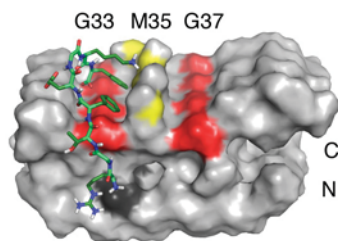
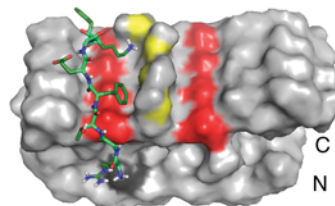


Figure S4

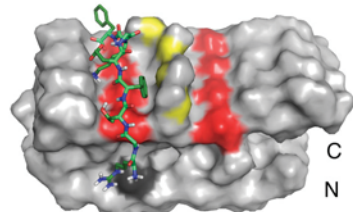
A #1 L-AIP to A β 42



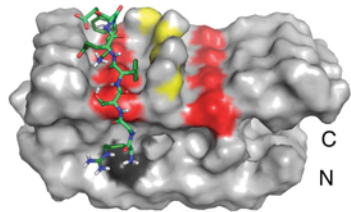
B #2



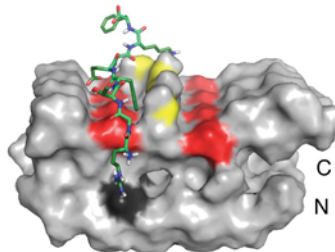
C #3



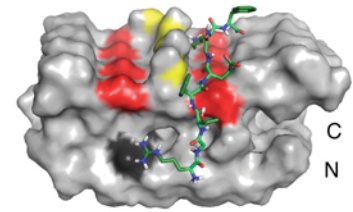
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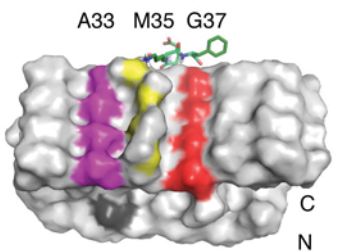
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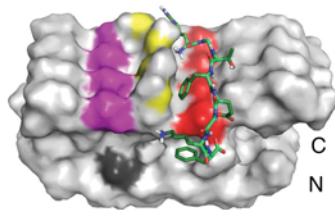
F #6



G #1 L-AIP to A β 42 G33A



H #2



I #3

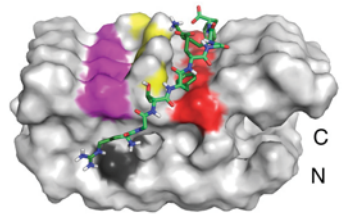
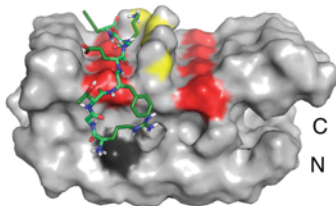


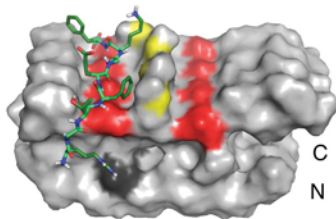
Figure S5

A #1 D-AIP to A β 42

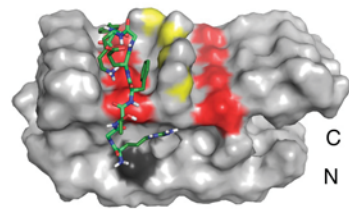
G33 M35 G37



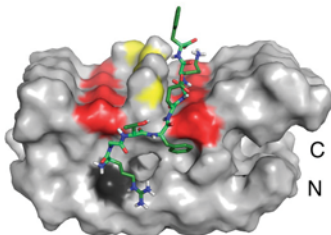
B #2



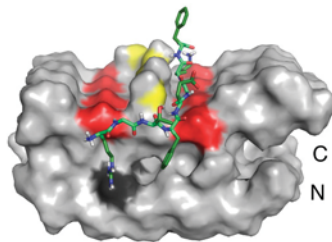
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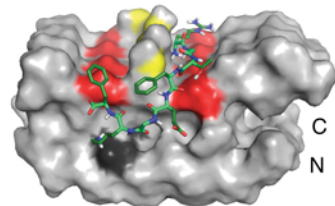
D #4



E #5



F #6



G #7

