Supporting Information to the manuscript:

Key aromatic/hydrophobic amino acids controlling a cross-amyloid peptide interaction versus amyloid self-assembly

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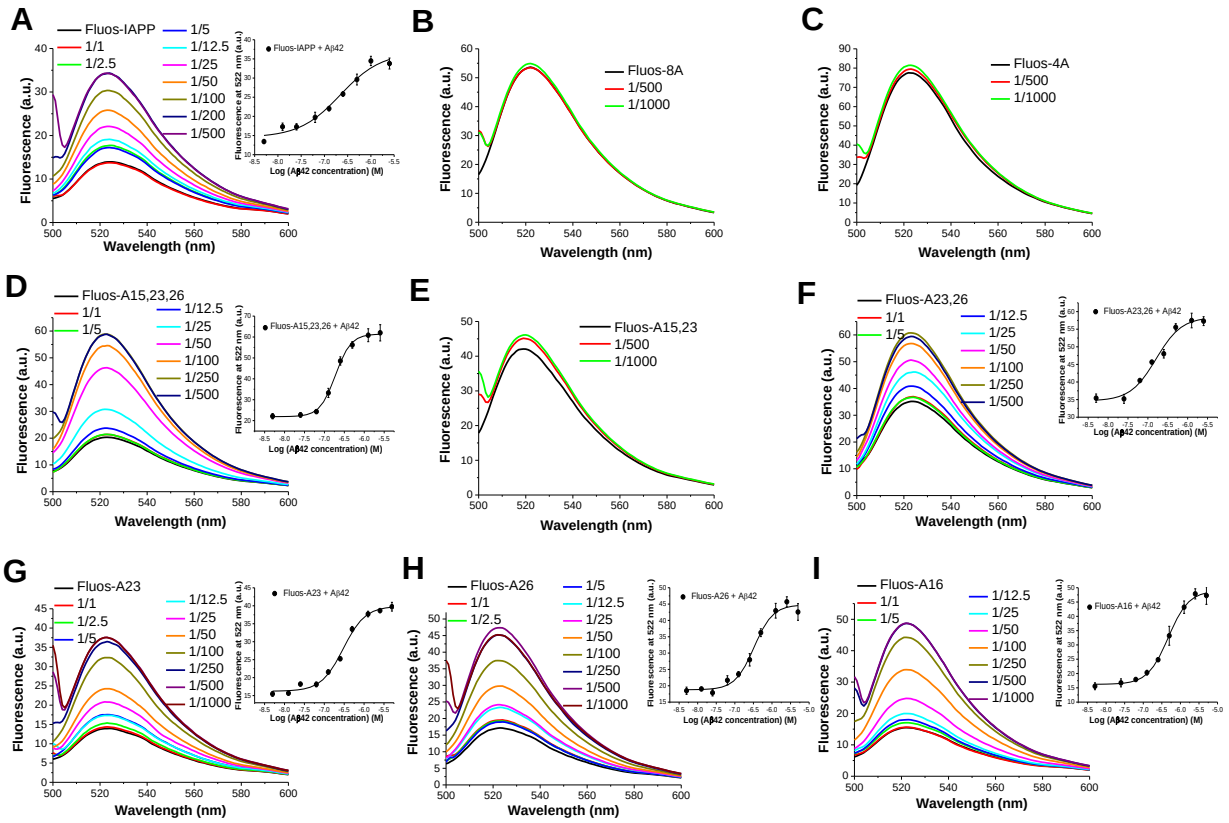
Supporting Tables

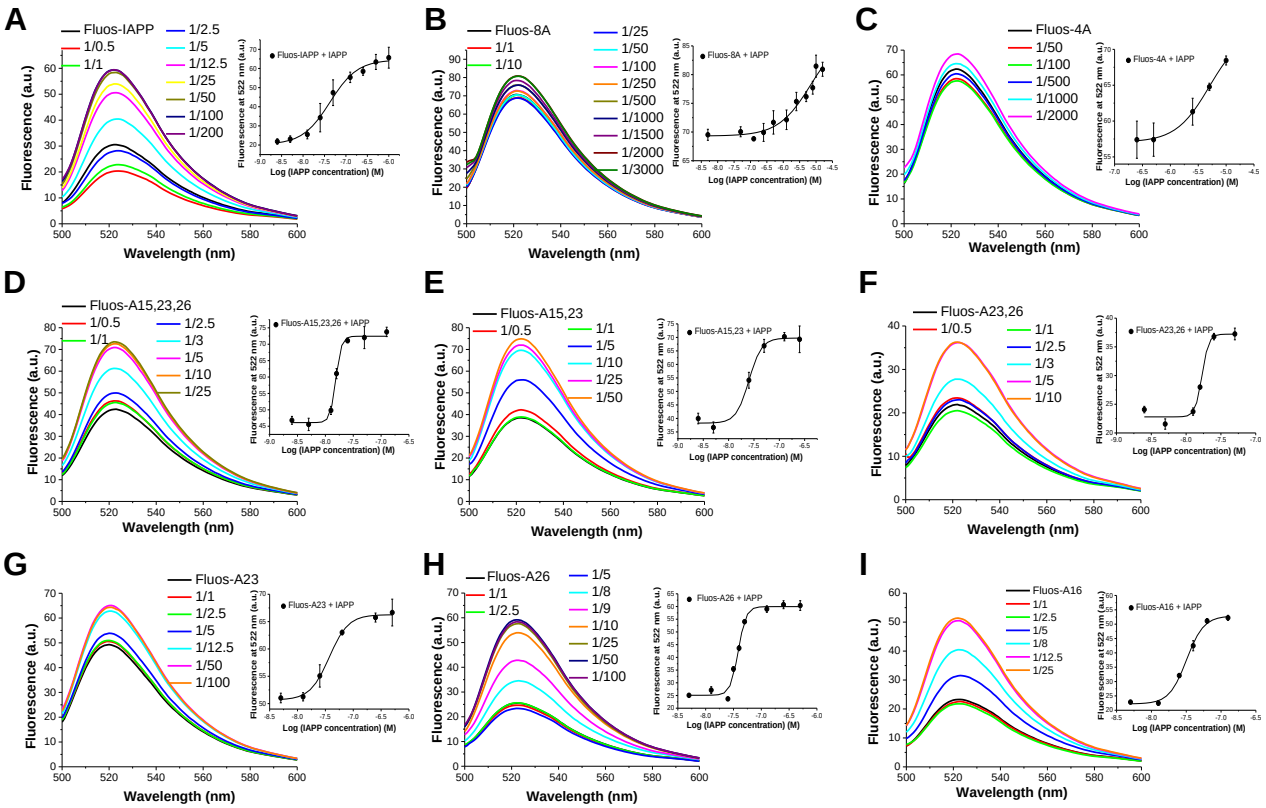
Supporting Table 1. Mean value (±SD) of Cα-atom root-mean-square deviation (RMSD) and solvent-accessible surface area (SASA) calculated from MD simulation (3 μs).

IAPP & mutants	**Cα-RMSD (Å)**	**SASA (Å^2)**
IAPP	1.31 (±0.1)	205 (±57)
A23	1.13 (±0.1)	318 (±103)
A26	1.44 (±0.2)	159 (±73)
A15,23	1.15 (±0.1)	282 (±87)
4A	2.68 (±0.2)	568 (±145)

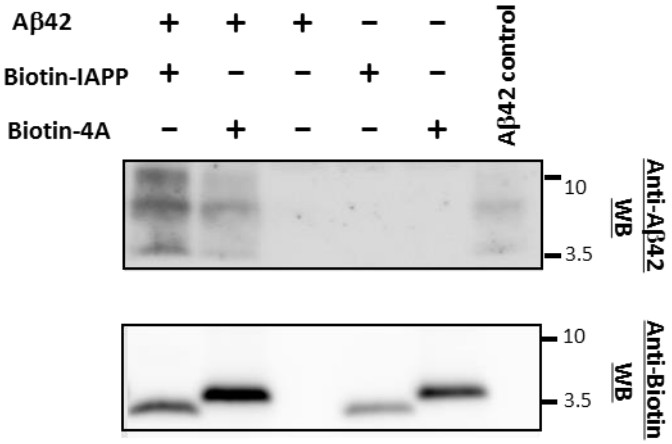
Supporting Figures



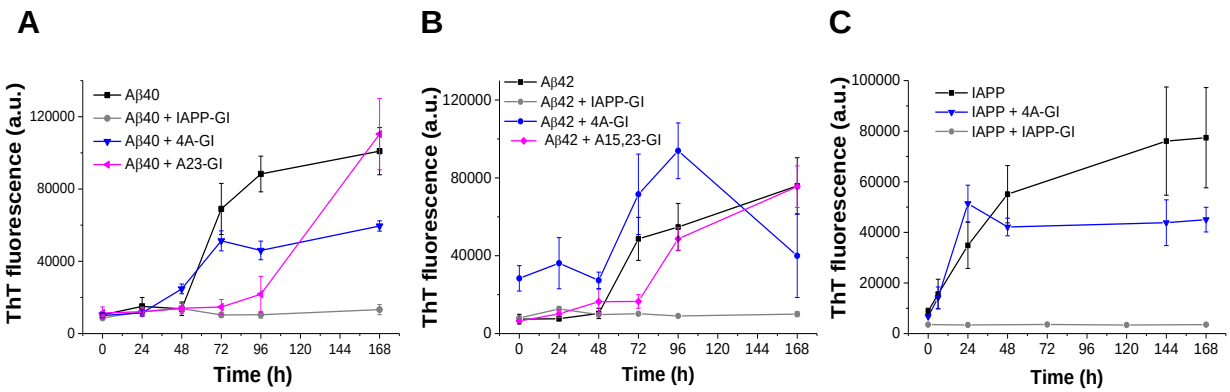
Supporting Figure S1. Determination of app. K_ds of interactions of IAPP and selected Ala mutants (5 nM) with Aβ42 by fluorescence spectroscopic titrations. Fluorescence emission spectra of N^{α}-terminal fluorescein-labeled IAPP or mutants (Fluos-peptide) alone and after titration with Aβ42 (Fluos-peptide/Aβ42 as indicated) are shown for the following peptides: (**A**) IAPP; (**B**) 8A; (**C**) 4A; (**D**) A15,23,26; (**E**) A15,23; (**F**) A23,26; (**G**) A23; (**H**) A26; (**I**) A16. In the insets, the binding curves are shown; data are means (±SD) from three binding curves. Calculated app. K_ds are in Table 2.



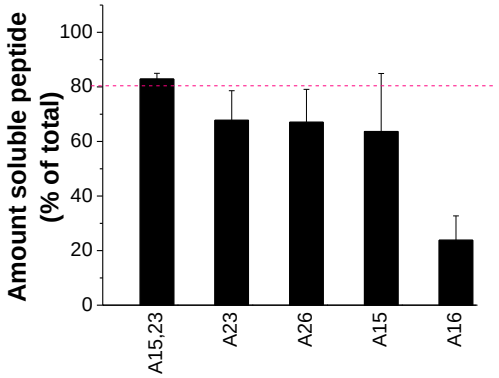
Supporting Figure S2. Determination of app. K_ds of interactions of IAPP and selected Ala mutants (5 nM) with IAPP by fluorescence spectroscopic titrations. Fluorescence emission spectra of N^{α}-terminal fluorescein-labeled IAPP or mutants (Fluos-peptide) alone and after titration with IAPP ((molar ratios Fluos-peptide/IAPP as indicated)) are shown for the following peptides: (**A**) IAPP; (**B**) 8A; (**C**) 4A; (**D**) A15,23,26; (**E**) A15,23; (**F**) A23,26; (**G**) A23; (**H**) A26; (**I**) A16. In the insets, the binding curves are shown; data are means (±SD) from three binding curves. Calculated app. K_ds are in Table 2.



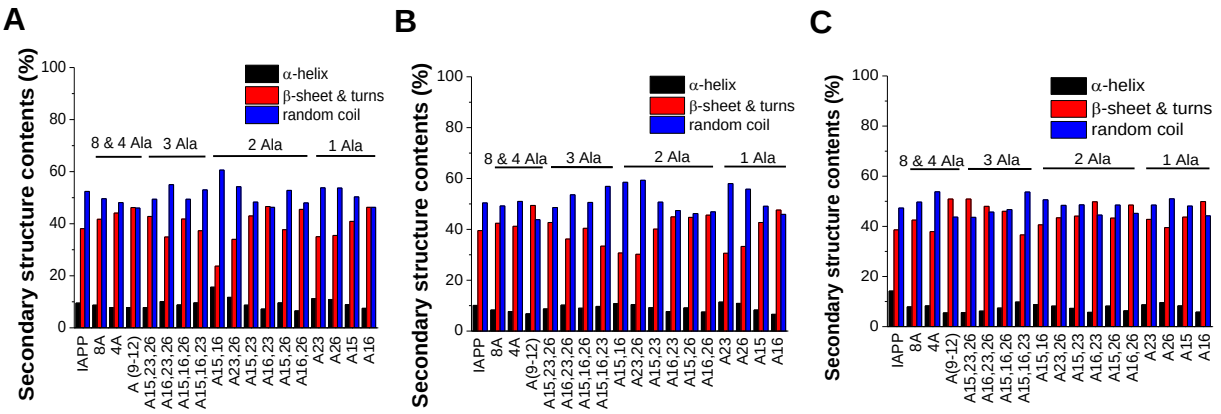
Supporting Figure S3. Pull-down assay of Biotin-4A- and Biotin-IAPP-Aβ42 hetero-assemblies. Top: Anti-Aβ42 Western blot (WB) analysis of a mixture of Aβ42 (5 μM) + Biotin-IAPP (2.5 μM), a mixture of Aβ42 (5 μM) + Biotin-4A (2.5 μM), Aβ42 (5 μM) alone, and Biotin-IAPP or Biotin-4A (2.5 μM) alone as indicated following biotin pull-down and peptide dissociation from beads. Lane "Aβ42 control", Aβ42 not incubated with beads. Bottom: Anti-Biotin WB of same incubations as in upper panel. Results shown are representative of 3 assays.



Supporting Figure S4. Effects of IAPP-GI and its Ala mutants on amyloidogenesis of Aβ40, Aβ42 and IAPP. (**A**) Effects on Aβ40 fibrillogenesis. Fibrillogenesis of Aβ40 (16.5 μM) alone or with IAPP-GI, 4A-GI or A23-GI (1/1) were determined by the ThT binding assay. (**B**) Effects on Aβ42 fibrillogenesis. Fibrillogenesis of Aβ42 (16.5 μM) alone or with IAPP-GI, 4A-GI or A15,23-GI (1/1) were determined by the ThT binding assay. (**C**) Effects on amyloidogenesis of IAPP. Fibrillogenesis of IAPP (12 μM) alone or with IAPP-GI or 4A-GI (1/1) was followed by the ThT binding assay. All data shown in (**A**-**C**) are means (±SD) from 3 assays.



Supporting Figure S5. Solubilities of A15,23 and single Ala mutants at 50 and 20 μM, respectively (aq. buffer, pH 7.4). Mutants were incubated for 7 days and solubilities were determined by a sedimentation assay (means (±SD), 3 assays). Peptide amounts (% of total) in supernatants at 7 days of incubation are shown; a mutant is judged as soluble when $\geq$ 80% is found in supernatant (indicated by a dotted red line).



Supporting Figure S6. Calculated secondary structure contents of IAPP and mutants via deconvolutions of CD spectra at peptide concentrations of 5 μM (**A**), 10 μM (**B**) and 50 μM (**C**).