

Supporting Information

Amyloid- β peptide 37, 38 and 40 individually and cooperatively inhibit amyloid- β 42 aggregation

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		effector peptide			
		A β ₃₇	A β ₃₈	A β ₄₀	A β ₄₂
affected peptide	A β ₃₇		not studied	moderate acceleration, co-aggregation	strong acceleration, independent aggregation
	A β ₃₈	not studied		moderate acceleration, co-aggregation	strong acceleration, independent aggregation
	A β ₄₀	moderate inhibition, co-aggregation	moderate inhibition, co-aggregation		moderate acceleration, independent aggregation ¹
	A β ₄₂	moderate inhibition, independent aggregation	moderate inhibition, independent aggregation	negligible effect, independent aggregation ¹	

strong inhibition no effect strong acceleration

Table S1 Summary of results for unseeded binary mixtures. Each row shows the effect that different alloforms have on the aggregation of that peptide. Acceleration of aggregation is indicated by green, inhibition is indicated by red. Results for A β ₄₀/A β ₄₂ mixture taken from [1].

		seed peptide			
		A β ₃₇	A β ₃₈	A β ₄₀	A β ₄₂
monomer	A β ₃₇	strong acceleration	strong acceleration	moderate acceleration	moderate acceleration
	A β ₃₈	strong acceleration	strong acceleration	moderate acceleration	moderate acceleration
	A β ₄₀	moderate acceleration	moderate acceleration	strong acceleration	no acceleration ¹
	A β ₄₂	no acceleration	no acceleration	no acceleration ¹	strong acceleration

no acceleration moderate acceleration strong acceleration

Table S2 Summary of results for cross-seeding. Rows show the monomer, with columns showing the seed peptide. Acceleration of aggregation is indicated by green. Results for A β ₄₀/A β ₄₂ cross-seeding taken from [1].

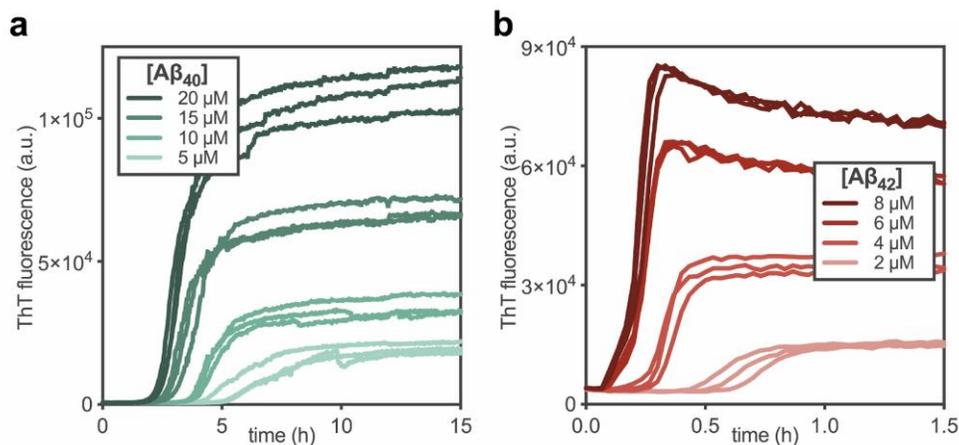


Figure S1 Aggregation kinetics of (a) $A\beta_{40}$ and (b) $A\beta_{42}$ in 20 mM sodium phosphate buffer, pH 7.4, with 200 μ M EDTA, 0.02% NaN_3 , and 20 μ M ThT. The concentrations shown here are identical to those used for each peptide in binary mixtures with $A\beta_{37}$ and $A\beta_{38}$ (Figure 4 for $A\beta_{40}$ and Figure 6 for $A\beta_{42}$).

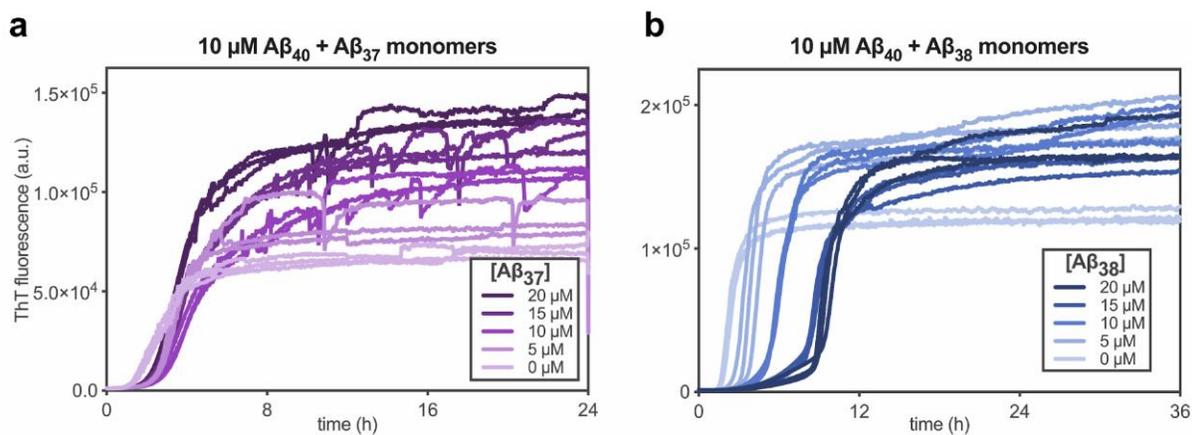


Figure S2 Extended time-course for data shown in Figure 4a-b, showing the effect of $A\beta_{40}$ at varying concentrations on the aggregation of (a) $A\beta_{37}$ or (b) $A\beta_{38}$. Experiments were performed in 20 mM sodium phosphate buffer, pH 7.4, with 200 μ M EDTA, 0.02% NaN_3 , and 20 μ M ThT.

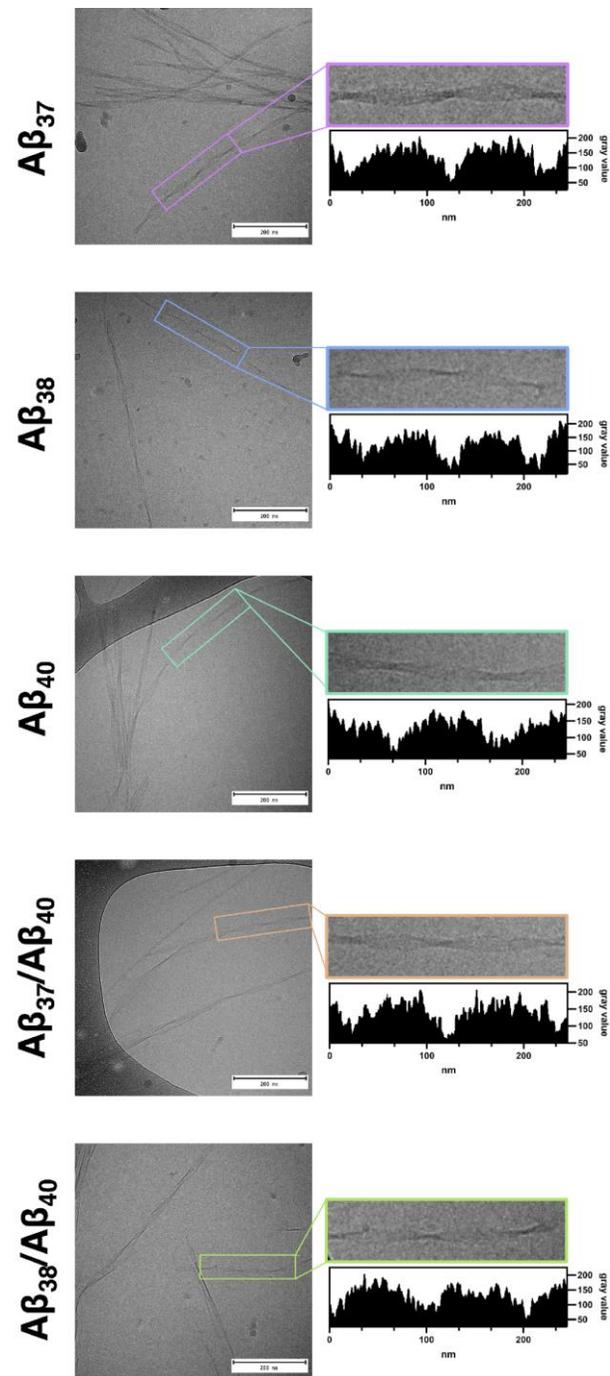


Figure S3 Fibril grey scale profiles, used for the helical half-pitch period measurements shown in Figure 5b. A representative micrograph, fibril segment, and grey scale profile is shown for A β_{37} , A β_{38} , A β_{40} , and binary A β_{37} /A β_{40} and A β_{38} /A β_{40} mixtures. Grey scale profiles were generated using ImageJ.

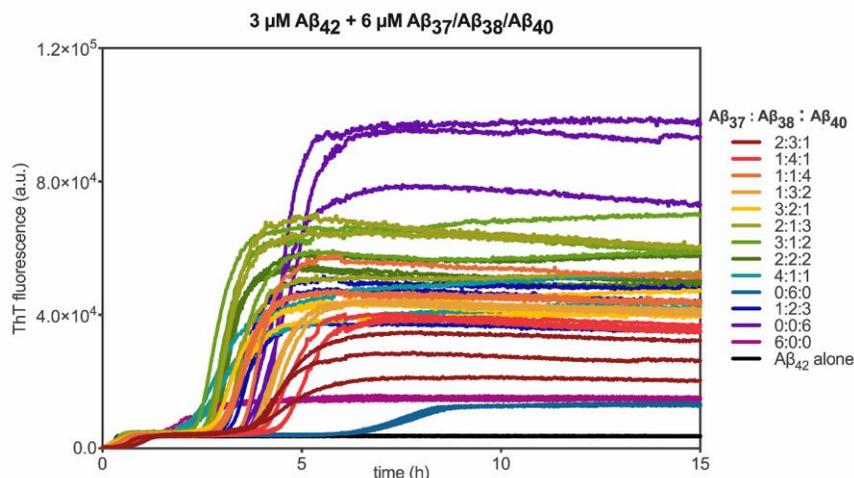


Figure S4 Full aggregation profile for 3 μM $\text{A}\beta_{42}$ with 6 μM of $\text{A}\beta_{37}/\text{A}\beta_{38}/\text{A}\beta_{40}$ mixtures in varying molar ratios (close-up of first fluorescence transition shown in Figure 11). The coloring of each sample corresponds to that in Figure 11. Experiments were performed in 20 mM sodium phosphate buffer, pH 7.4, with 200 μM EDTA, 0.02% NaN_3 , and 20 μM ThT.

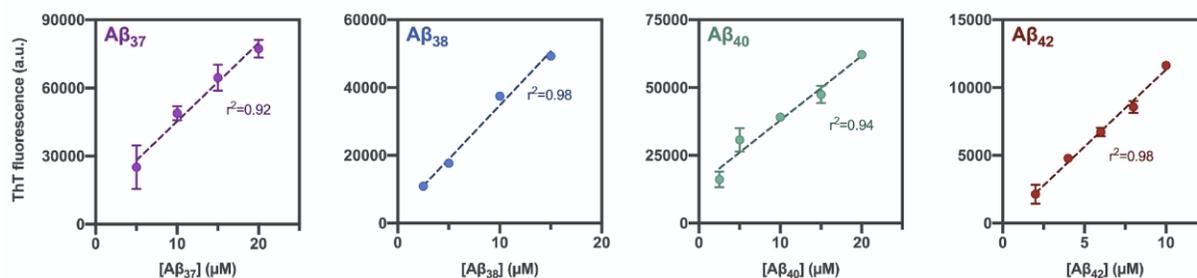


Figure S5 ThT fluorescence scales linearly with aggregate concentration for each of $\text{A}\beta_{37}$ (pink), $\text{A}\beta_{38}$ (blue), $\text{A}\beta_{40}$ (green), and $\text{A}\beta_{42}$ (red). Readings were taken at the final fluorescence plateau for each sample; points represent the triplicate mean, with error bars showing standard deviation. Experiments were performed in 20 mM sodium phosphate buffer, pH 7.4, with 200 μM EDTA, 0.02% NaN_3 , and 20 μM ThT.

Supporting References

- (1) Cukalevski, R.; Yang, X.; Meisl, G.; Weininger, U.; Bernfur, K.; Frohm, B.; Knowles, T. P. J.; Linse, S. The $\text{A}\beta_{40}$ and $\text{A}\beta_{42}$ Peptides Self-Assemble into Separate Homomolecular Fibrils in Binary Mixtures but Cross-React during Primary Nucleation. *Chem. Sci.* **2015**, 6 (7), 4215–4233. <https://doi.org/10.1039/C4SC02517B>.