SUPPLEMENTAL MATERIAL

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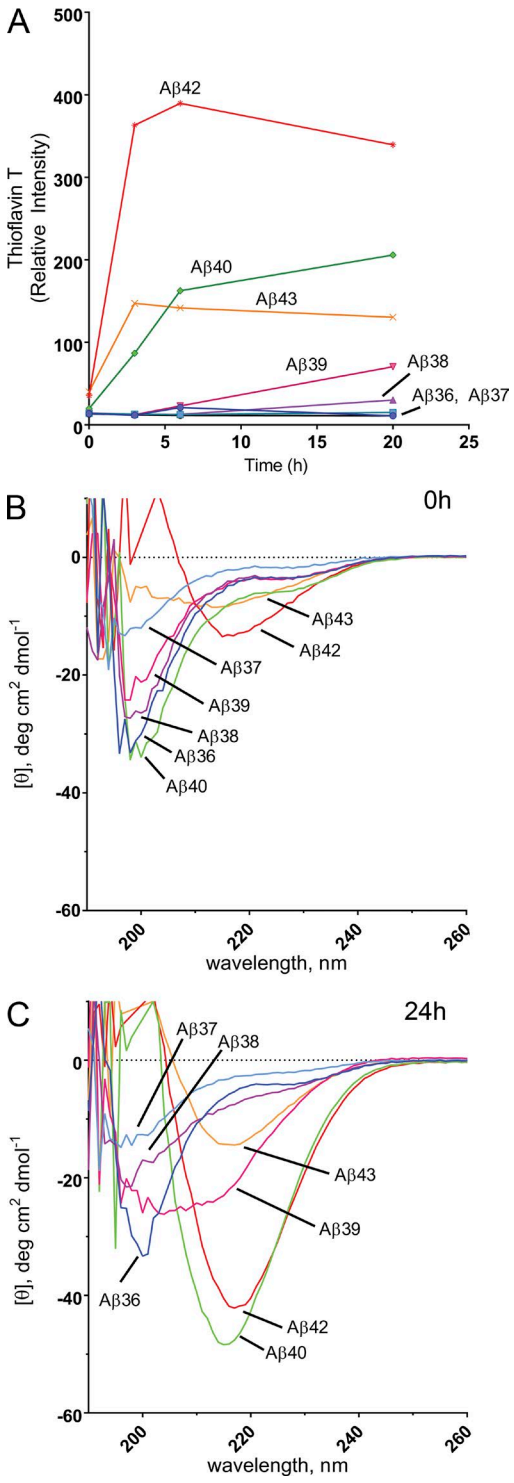

Figure S1. **Under standard aggregation conditions, short Aβ do not form β-sheet structures like Aβ42.** Monomeric Aβ36–40, Aβ42, and Aβ43 (100 µM) were incubated in buffer (20 mM Tris-HCl, 150 mM NaCl, pH 8.0) with shaking at 37°C. **(A)** At the indicated times, aliquots were diluted 15-fold for measurement of Thioflavin T fluorescence. **(B and C)** Secondary structure of Aβ37 and Aβ42 was measured in far-UV circular dichroism (CD) spectra of monomeric peptides (before incubation; B) and aggregated peptides (after 24 h of incubation; C). Of note, an initial peptide lot of Aβ37 from Anaspec did show an increase in Thioflavin T fluorescence and a shift in CD spectra to β-sheet. We were unable to reproduce this with two additional lots of peptide and show the representative data from these two lots of peptide. Lot-to-lot variance in aggregatability of synthetic Aβ is a well-documented phenomenon in the field, and can also be highly dependent on handling of the peptide before the aggregation assays.

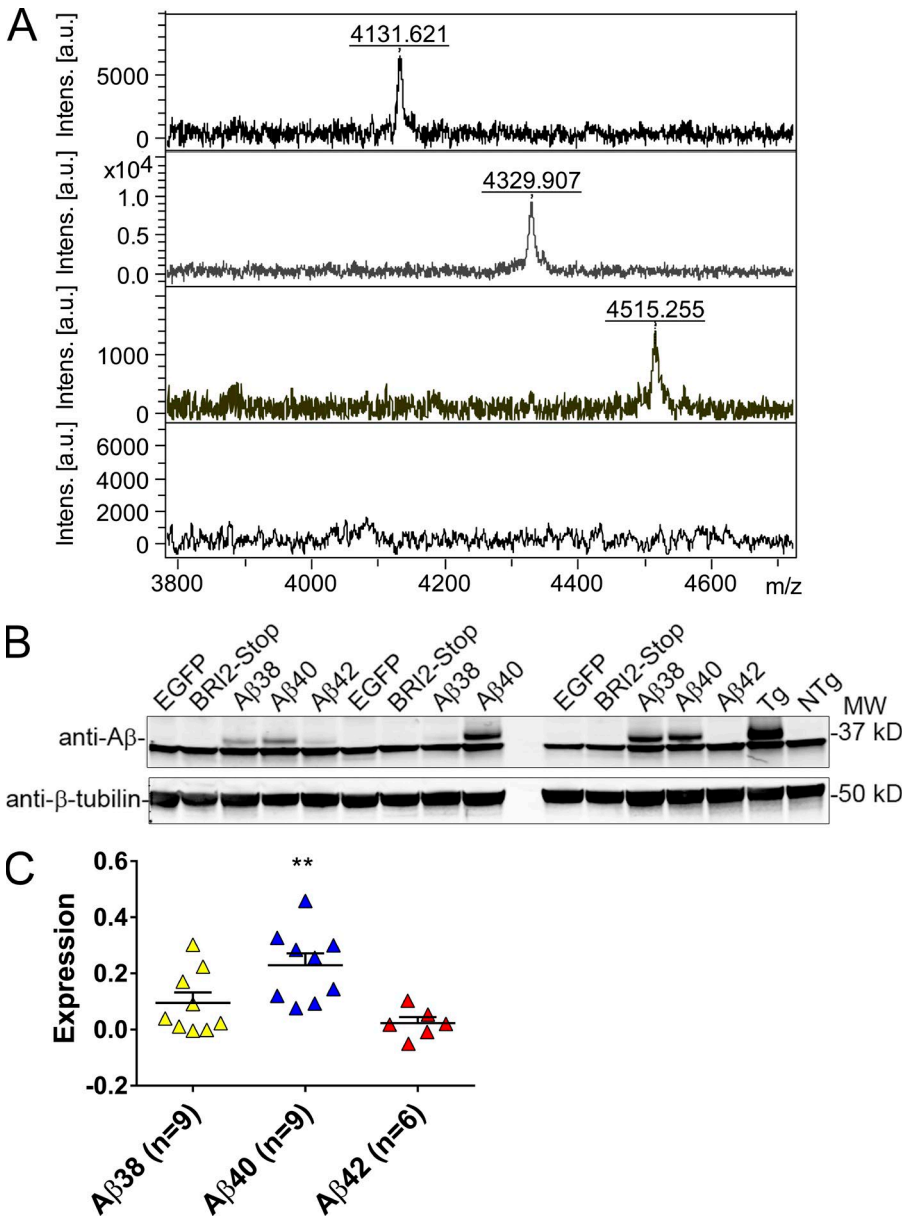

Figure S2. **Aβ38, Aβ40, and Aβ42 expression in NTgCRND8 mice. (A)** Immunoprecipitation/mass spectrometry spectra from 1 ml of conditioned media from transiently transfected HEK 293T cells expressing BRI2-Aβ38, BRI2-Aβ40, or BRI2-Aβ42. The *m*/*z* value of peaks representing Aβ38, Aβ40, and Aβ42 are labeled. **(B)** Representative anti-Aβ immunoblots of the sequentially extracted SDS lysate from 9-mo-old NTgCRND8 mice expressing Aβ38, Aβ40, BRI2-Stop, and EGFP and 6-mo-old NTgCRND8 mice expressing Aβ42. Molecular weight markers are indicated on the right. The lower panel represents blots probed with anti–β-tubulin antibody to depict loading amount. **(C)** Densitometric analysis of Aβ levels (37-kD band) normalized to β-tubulin. Data represents mean ± standard error of the mean; $n = 6–9$ (**, $P \leq 0.01$, one-way ANOVA with Dunnett's multiple comparison test).

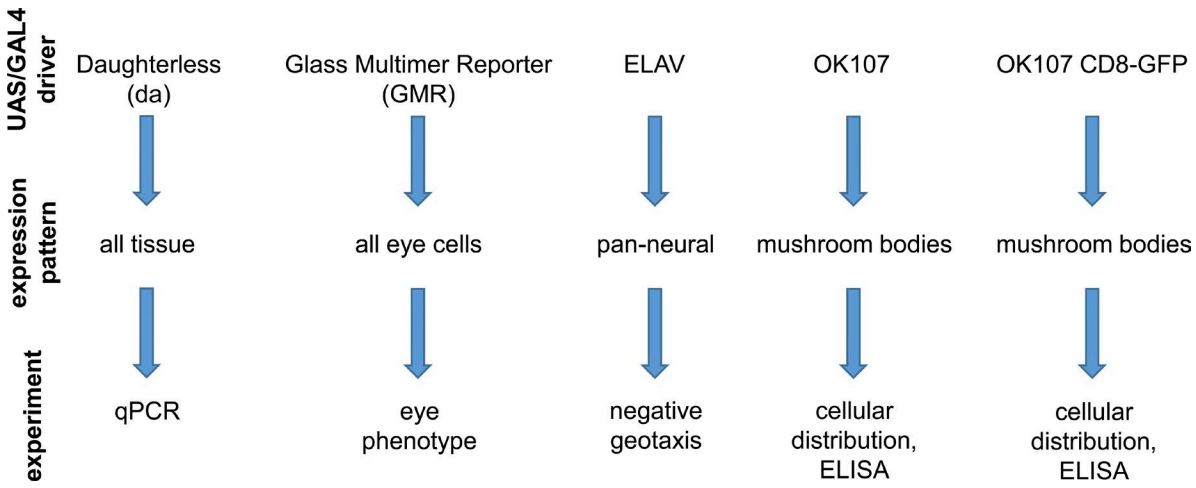

Figure S3. ***Drosophila* drivers used in this study.** Experimental design was based on expression pattern of Aβ transgenes, which were driven by the Gal4/UAS system. The Gal4 drivers, resulting expression patterns, and experimental applications used in this study are depicted.

Table S1. **Statistical analysis of Aβ levels from Aβ solubilized with RIPA, 2% SDS, and guanidine from 1- and 30-d-old flies expressing Aβ peptides**

Comparison	RIPA-solubilized Aβ		2% SDS–solubilized Aβ		Guanidinium-solubilized Aβ	
	Day 1	Day 30	Day 1	Day 30	Day 1	Day 30
Aβ36 vs. GFP	ns	ns	na	na	ns	ns
Aβ36 vs. Aβ37	ns	ns	na	na	ns	****
Aβ36 vs. Aβ38	ns	ns	na	na	ns	ns
Aβ36 vs. Aβ39	***	ns	na	na	ns	ns
Aβ36 vs. Aβ40	***	ns	na	na	ns	ns
Aβ36 vs. Aβ42	ns	ns	na	na	****	****
Aβ36 vs. Aβ43	ns	ns	na	na	ns	ns
Aβ37 vs. GFP	*	ns	****	****	ns	****
Aβ37 vs. Aβ36	ns	ns	na	na	ns	****
Aβ37 vs. Aβ38	ns	ns	****	****	ns	***
Aβ37 vs. Aβ39	**	ns	****	****	ns	***
Aβ37 vs. Aβ40	*	ns	****	****	ns	***
Aβ37 vs. Aβ42	*	ns	***	****	****	****
Aβ37 vs. Aβ43	**	ns	na	****	ns	***
Aβ38 vs. GFP	ns	ns	ns	ns	ns	ns
Aβ38 vs. Aβ36	ns	ns	na	na	ns	ns
Aβ38 vs. Aβ37	ns	ns	****	****	ns	***
Aβ38 vs. Aβ39	***	ns	***	ns	ns	ns
Aβ38 vs. Aβ40	***	ns	**	ns	ns	ns
Aβ38 vs. Aβ42	ns	ns	****	*	****	****
Aβ38 vs. Aβ43	ns	ns	na	ns	ns	ns
Aβ39 vs. GFP	****	ns	****	ns	ns	ns
Aβ39 vs. Aβ36	***	ns	na	na	ns	ns
Aβ39 vs. Aβ37	**	ns	****	****	ns	***
Aβ39 vs. Aβ38	***	ns	***	ns	ns	ns
Aβ39 vs. Aβ40	ns	ns	ns	ns	ns	ns
Aβ39 vs. Aβ42	****	ns	*	ns	****	****
Aβ39 vs. Aβ43	****	ns	na	ns	ns	ns
Aβ40 vs. GFP	****	ns	****	ns	ns	ns
Aβ40 vs. Aβ36	***	ns	na	ns	ns	ns
Aβ40 vs. Aβ37	*	ns	****	****	ns	***
Aβ40 vs. Aβ38	***	ns	**	ns	ns	ns
Aβ40 vs. Aβ39	ns	ns	ns	ns	ns	ns
Aβ40 vs. Aβ42	****	ns	***	ns	****	****
Aβ40 vs. Aβ43	****	ns	na	ns	ns	ns
Aβ42 vs. GFP	ns	ns	****	**	****	****
Aβ42 vs. Aβ36	ns	ns	na	na	****	****
Aβ42 vs. Aβ37	*	ns	***	****	****	****
Aβ42 vs. Aβ38	ns	ns	****	*	****	****
Aβ42 vs. Aβ39	****	ns	*	ns	****	****
Aβ42 vs. Aβ40	****	ns	***	ns	****	****
Aβ42 vs. Aβ43	ns	ns	na	ns	****	****
Aβ43 vs. GFP	ns	ns	na	ns	ns	ns
Aβ43 vs. Aβ36	ns	ns	na	na	ns	ns
Aβ43 vs. Aβ37	**	ns	na	****	ns	***
Aβ43 vs. Aβ38	ns	ns	na	ns	ns	ns
Aβ43 vs. Aβ39	****	ns	na	ns	ns	ns
Aβ43 vs. Aβ40	****	ns	na	ns	ns	ns
Aβ43 vs. Aβ42	ns	ns	na	ns	****	****

na, not applicable; ns, not significant ($P > 0.05$); *, $P \leq 0.05$; **, $P \leq 0.01$; ***, $P \leq 0.001$; ****, $P \leq 0.0001$, one-way ANOVA with Tukey's multiple comparison test.

Table S2. **Details of Q-RT-PCR primers and probes used in study**

Gene	Reference ID	Primers	Probe (5′FAM/3′quencher)	Amplicon length
Argos		Forward: 5′-CCATGACAGCGGTTACGAG-3′ Reverse: 5′-TGTTGGATCCCACGTCTTC-3′	probe #131	68 nt
β-tubulin	S60740.1	Forward: 5′-CACTTCCTAACCTTTTGCTTTCC-3' Reverse: 5′-ATGCCATTGCTGTCGATG-3′	probe #14	75 nt
L32	NM_001144655	Forward: 5′-TGCATTAGTGGGACACCTTCT-3′ Reverse: 5′-GTGCGCTTCTTCACGATCT-3′	probe #107	73 nt