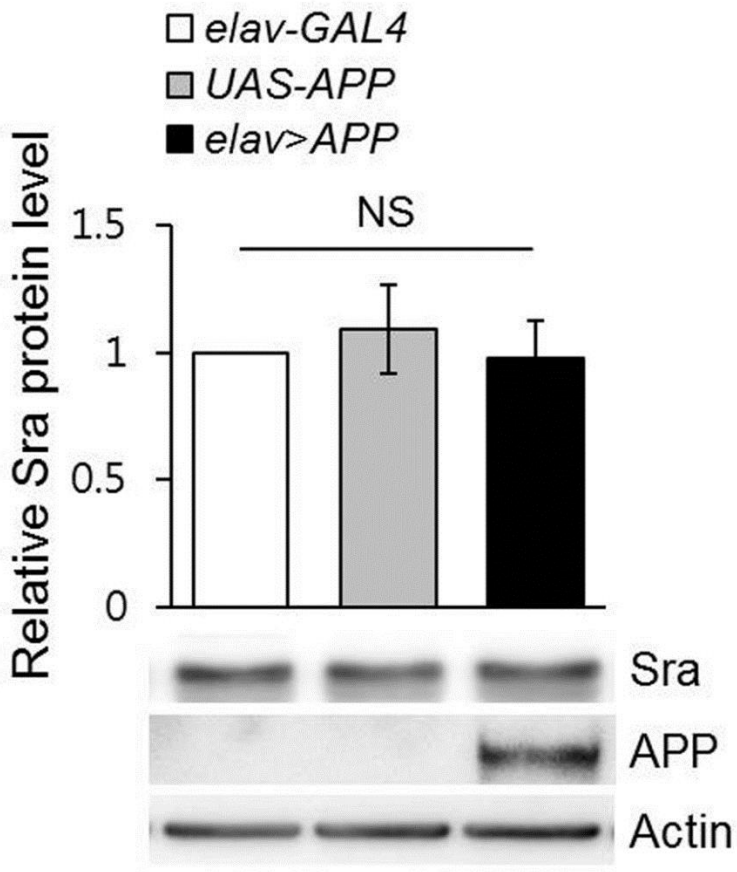

Fig. S1. Western blot analysis of Sra in *APP*-expressing flies. Western blot analysis with an anti-Sra antibody shows that Sra protein is not altered in pan-neuronally *APP*-expressing (*elav>APP*) fly heads compared with that of the control (*elav-GAL4* and *UAS-APP*). Actin was used as an internal loading control. All data are expressed as mean ± s.e. (Tukey-Kramer test, n = 4, NS, not significant).

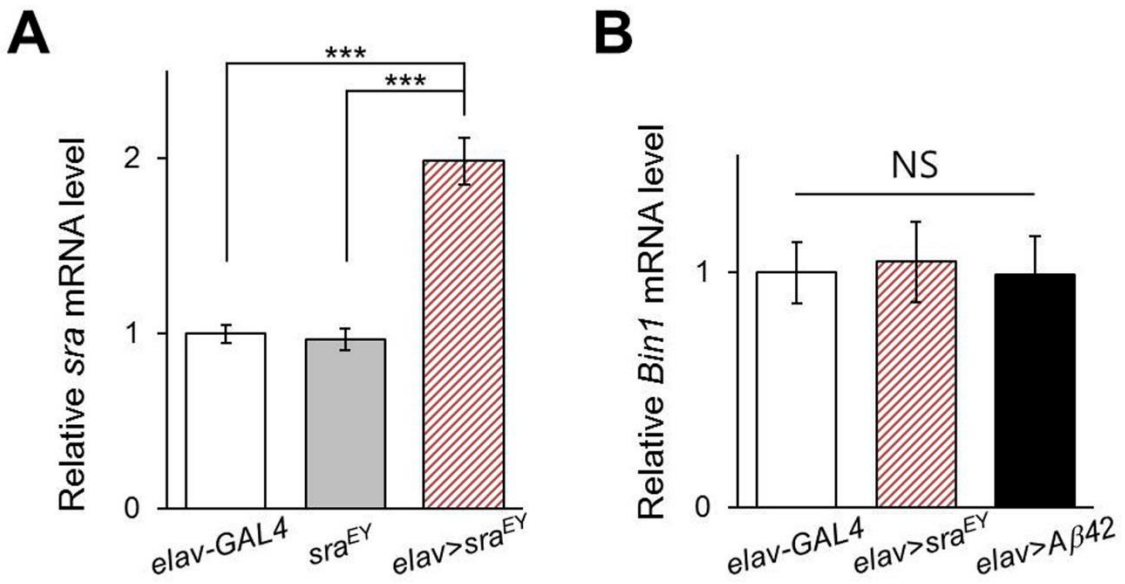

Fig. S2. Analyses of *sra* and *Bin1* gene expression in adult fly heads using real-time quantitative PCR. (A) Real-time quantitative PCR results show relative fold change in *sra* (A) and *Bin1* (B) transcript levels for the indicated fly lines. All data are expressed as mean ± s.e. (A, Tukey-Kramer test, $n \geq 4$, ***$p < 0.001$; B, Tukey-Kramer test, $n \geq 10$; NS, not significant).

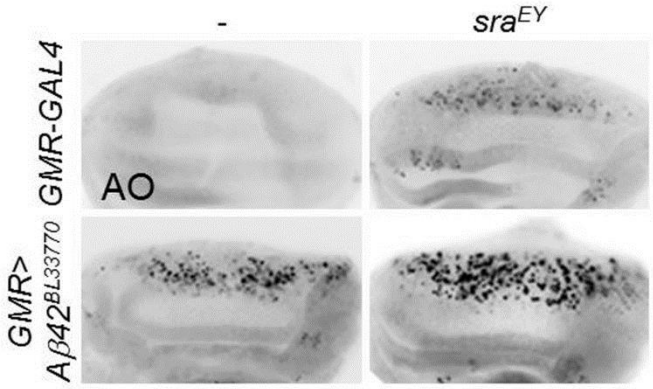

Fig. S3. Overexpression of *sra* aggravates *Aβ42*-induced cell death in the *Drosophila* larval eye disc. Representative images of AO-stained *sra*- and *Aβ42*-expressing larval eye imaginal discs (n = 10). AO, acridine orange.

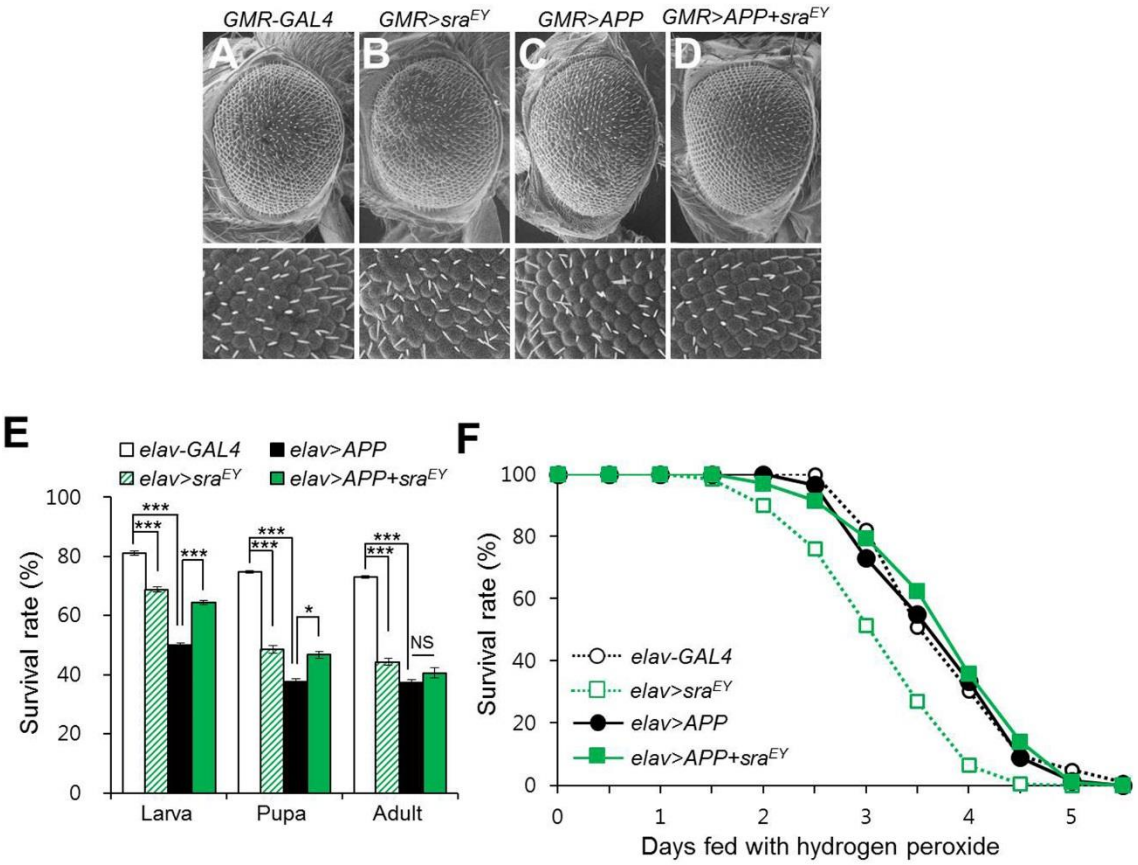

Fig. S4. Overexpression of *sra* partially rescues *APP*-expressing fly phenotypes. (A-D) Eye phenotypes induced by ectopic expression of *APP* in the developing eye were partially rescued by *sra* overexpression. The *APP*-expressing adults exhibit a mild rough eye phenotype (C) relative to that of the control eye (A). Overexpression of *sra* alone resulted in a marginally rough eye phenotype (B) when compared to that of the control (A). Overexpression of *sra* in *APP*-expressing flies rescued the rough eye phenotype (D) relative to that of *APP*-expressing flies (C). The lower pictures are the magnified images of the each genotype in the upper pictures. (E) Survival rates of pan-neuronal *APP*-expressing flies with *sra* overexpression (*elav>APP+sra*^{EY}). The effects of overexpressed *sra* (*elav>sra*^{EY}) in the

control (*elav-GAL4*) are also shown (Tukey-Kramer test, n ≥ 400, *p < 0.05, ***p < 0.001, NS, not significant). (F) Survival rates of *APP*-expressing flies overexpressing *sra* under oxidative stress conditions (n = 200). The Kaplan-Meier estimator and log-rank test was used to determined significant differences in survival rates of samples. *elav-GAL4* vs *elav>sra*^{EY}: p < 0.0001; *elav-GAL4* vs *elav>APP*: p = 0.5813; *elav>sra*^{EY} vs *elav>APP+sra*^{EY}: p < 0.0001; *elav>APP* vs *elav>APP+sra*^{EY}: p = 0.2268.

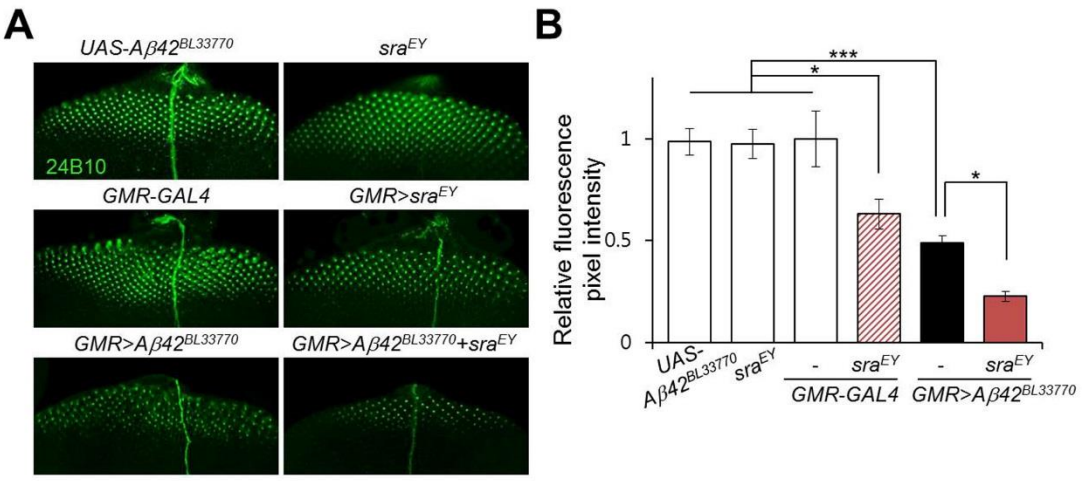

Fig. S5. Overexpression of *sra* aggravates *Aβ42*-induced phenotypes in *Aβ42*-expressing flies. (A) Representative immunohistochemistry images of photoreceptor neurons in larval eye discs. Each indicated fly was stained with an anti-Chaoptin antibody (24B10) to show photoreceptor neurons. Magnification of the pictures, ×200. (B) The graph shows the relative fluorescence pixel intensity in photoreceptor neurons (Tukey-Kramer test, $n \geq 10$, $^{*}p < 0.05$, $^{***}p < 0.001$, NS, not significant).

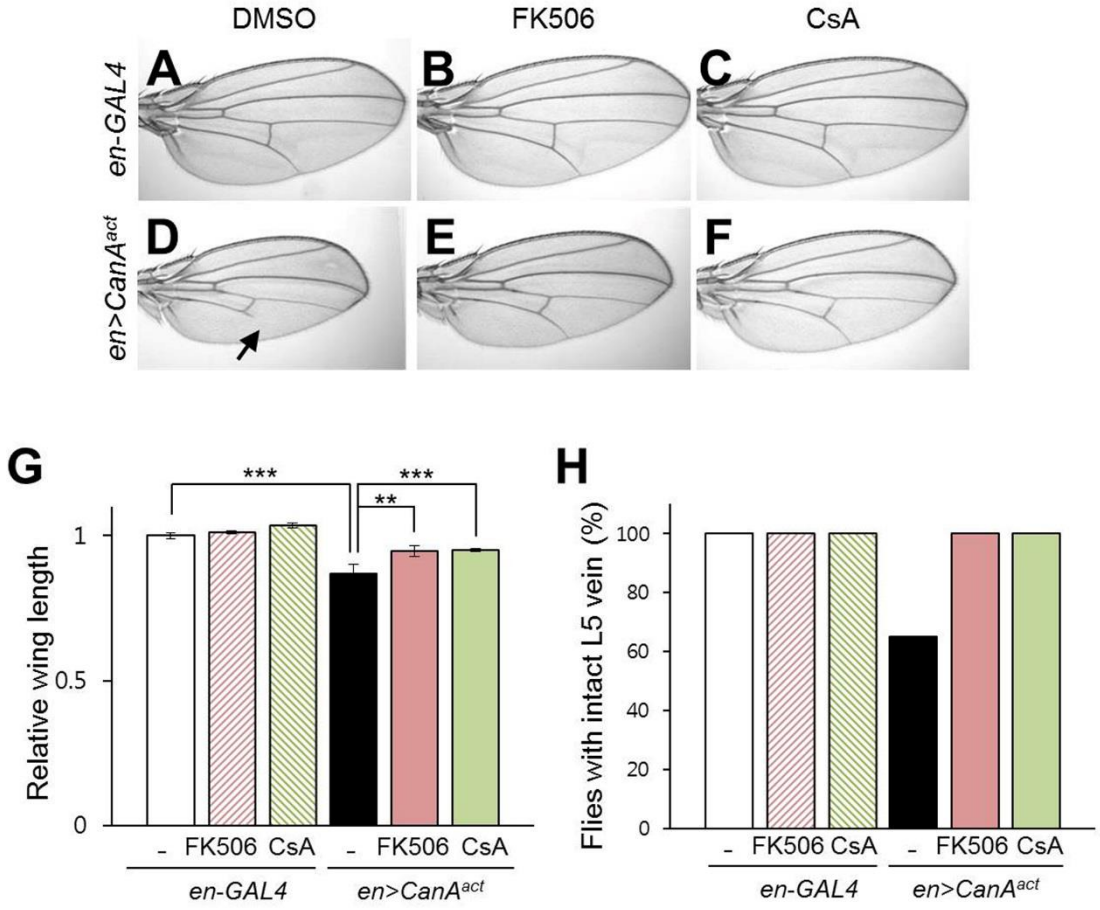

Fig. S6. Chemical calcineurin inhibitors inhibit calcineurin signaling. FK506 and CsA, chemical calcineurin inhibitors, suppress the phenotypes induced by a constitutively active form of calcineurin (*CanA*^{act}). (A-F) Representative images of developing wing phenotypes in DMSO-fed (A, D), 50 μM FK506-fed (B, E), and 20 μM CsA-fed (C, F) flies with (D-F; *en>CanA*^{act}) or without (A-C; *en-GAL4*) *CanA*^{act} expression. The reduced wing size and loss of wing veins (arrow) resulting from *CanA*^{act} expression were suppressed by the inhibitors. (G, H) The graph shows the relative size (G, all data are expressed as mean ± s.e., Tukey-Kramer test, n = 20, **p < 0.01, ***p < 0.001) and intact L5 vein (H, n = 20) in the developing wing in each experimental group. CsA, cyclosporin A.

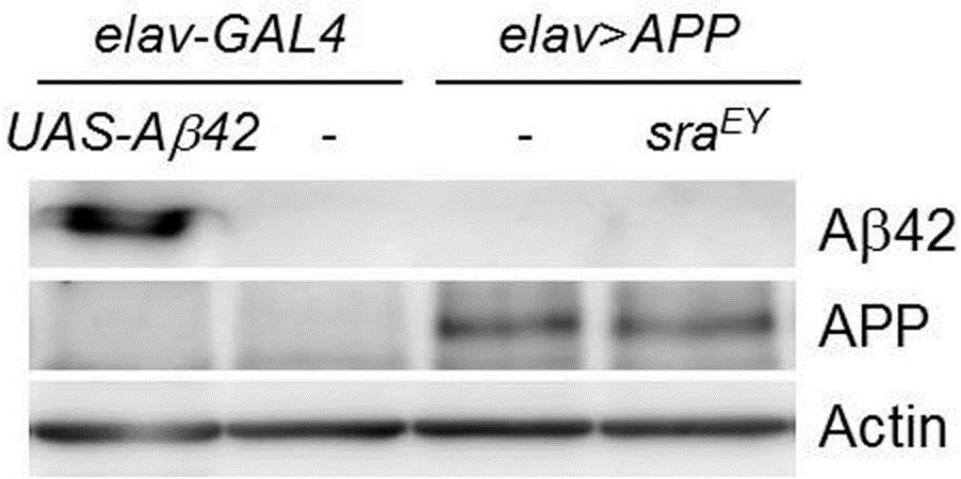

Fig. S7. Western blot analysis of Aβ42 levels in the head region of *Aβ42*- or *APP*-expressing flies. Aβ42 protein is not produced in *APP*-expressing (*elav>APP*) fly heads. The head extract of *Aβ42*-expressing flies (*elav>Aβ42*) was used as a positive control. Actin was used as an internal loading control.

Table S1. The genotypes of samples in figures.

No. figure	Symbol	Genotype
Fig. 1		
A-D	*sra>EGFP*	*UAS-2×EGFP/+; sra-GAL4/+*
	sra^{KO}	sra^{KO}/sra^{KO}
E, F	*elav-GAL4*	*elav-GAL4/elav-GAL4*
	UAS-Aβ42	*UAS-Aβ42/UAS-Aβ42*
	elav>Aβ42	*UAS-Aβ42/UAS-Aβ42; elav-GAL4/elav-GAL4*
Fig. 2		
A-P	sra^{EY}	$sra^{EY07182}/+$
	UAS-sra	*UAS-sra/+*
	GMR>sra^{EY}	*GMR-GAL4/+;* $sra^{EY07182}/+$
	GMR>sra	*GMR-GAL4/UAS-sra*
	GMR; $sra^{KO}/+$	*GMR-GAL4/+;* $sra^{KO}/+$
	GMR>DIAP1	*GMR-GAL4/+; UAS-DIAP1/+*
	GMR-GAL4	*GMR-GAL4/+*
	GMR>$Aβ42^{BL33770}$	*GMR-GAL4, UAS-*$Aβ42^{BL33770}/+$
	GMR>$Aβ42^{BL33770}$*+*sra^{EY}	*GMR-GAL4, UAS-*$Aβ42^{BL33770}/+;$ $sra^{EY07182}/+$
	GMR>$Aβ42^{BL33770}$*+sra*	*GMR-GAL4, UAS-*$Aβ42^{BL33770}$*/UAS-sra*
	GMR>$Aβ42^{BL33770}$*;* $sra^{KO}/+$	*GMR-GAL4, UAS-*$Aβ42^{BL33770}/+;$ $sra^{KO}/+$
	GMR>sra^{EY}*+DIAP1*	*GMR-GAL4/+;* $sra^{EY07182}$*/UAS-DIAP1*
Q, S, T	*elav-GAL4*	*elav-GAL4/elav-GAL4*
	elav>Aβ42	*UAS-Aβ42/UAS-Aβ42; elav-GAL4/elav-GAL4*
	elav>sra^{EY}	*elav-GAL4,* $sra^{EY07182}$*/elav-GAL4,* $sra^{EY07182}$
	elav>Aβ42+sra^{EY}	*UAS-Aβ42/UAS-Aβ42; elav-GAL4,* $sra^{EY07182}$*/elav-GAL4,* $sra^{EY07182}$
R	*elav-GAL4*	*elav-GAL4/+*
	sra^{EY}	$sra^{EY07182}/+$
	UAS-Aβ42	*UAS-Aβ42/+*
	elav>Aβ42	*UAS-Aβ42/+; elav-GAL4/+*
	elav>sra^{EY}	*elav-GAL4/*$sra^{EY07182}$

	elav>Aβ42+sra^{EY}	*UAS-Aβ42/+; elav-GAL4/sra^{EY07182}*
Fig. 3		
A-B	*UAS-Aβ42*	*UAS-Aβ42/UAS-Aβ42*
	sra^{EY}	*sra^{EY07182}/sra^{EY07182}*
	elav-GAL4	*elav-GAL4/elav-GAL4*
	elav>sra^{EY}	*elav-GAL4, sra^{EY07182}/elav-GAL4, sra^{EY07182}*
	elav>Aβ42	*UAS-Aβ42/UAS-Aβ42; elav-GAL4/elav-GAL4*
	elav>Aβ42+sra^{EY}	*UAS-Aβ42/UAS-Aβ42; elav-GAL4, sra^{EY07182}/elav-GAL4, sra^{EY07182}*
C	*GMR-GAL4*	*GMR-GAL4/GMR-GAL4*
	GMR>sra^{EY}	*GMR-GAL4/GMR-GAL4; sra^{EY07182}/sra^{EY07182}*
	GMR>Aβ42^{BL33770}	*GMR-GAL4, UAS-Aβ42^{BL33770}/GMR-GAL4, UAS-Aβ42^{BL33770}*
	GMR>Aβ42^{BL33770} +sra^{EY}	*GMR-GAL4, UAS-Aβ42^{BL33770}/GMR-GAL4, UAS-Aβ42^{BL33770}; sra^{EY07182}/sra^{EY07182}*
Fig. 4		
	sra^{EY}	*sra^{EY07182}/+*
	UAS-Aβ42	*UAS-Aβ42/+*
	sra^{EY}	*sra^{EY07182}/+*
	elav-GAL4	*elav-GAL4/+*
	sra^{EY}	*sra^{EY07182}/+*
	elav>Aβ42+sra^{EY}	*UAS-Aβ42/+; elav-GAL4/sra^{EY07182}*
Fig. 5		
	elav-GAL4	*elav-GAL4/+*
	elav>sra^{EY}	*elav-GAL4/sra^{EY07182}*
	elav>Aβ42	*UAS-Aβ42/+; elav-GAL4/+*
	elav>Aβ42+sra^{EY}	*UAS-Aβ42/+; elav-GAL4/sra^{EY07182}*
Fig. 6		
A-K	*GMR-GAL4*	*GMR-GAL4/+*
	GMR>CanA1i	*GMR-GAL4/+; UAS-CanA1 RNAi/+*
	GMR>CanBi	*GMR-GAL4/+; UAS-CanB RNAi/+*
	GMR>Aβ42^{BL33770}	*GMR-GAL4, UAS-Aβ42^{BL33770}/+*
	GMR>Aβ42^{BL33770}+CanA1i	*GMR-GAL4, UAS-Aβ42^{BL33770}/+; UAS-CanA1 RNAi/+*
	GMR>Aβ42^{BL33770}+CanBi	*GMR-GAL4, UAS-Aβ42^{BL33770}/+; UAS-CanB RNAi/+*
	CanA1i	*UAS-CanA1 RNAi/+*

L, M	*elav-GAL4*	*elav-GAL4/+*
	elav>CanA1i	*elav-GAL4/UAS-CanA1 RNAi*
	elav>Aβ42	*UAS-Aβ42/+; elav-GAL4/+*
	elav>Aβ42+CanA1i	*UAS-Aβ42/+; elav-GAL4/UAS-CanA1 RNAi*
Fig. S1		
	elav-GAL4	*elav-GAL4/+*
	UAS-APP	*UAS-APP-N-myc/+*
	elav>APP	*UAS-APP-N-myc/+; elav-GAL4/+*
Fig. S2		
	elav-GAL4	*elav-GAL4/+*
	sra^{EY}	$sra^{EY07182}/+$
	elav>sra^{EY}	*elav-GAL4/*$sra^{EY07182}$
	elav>Aβ42	*UAS-Aβ42/+; elav-GAL4/+*
Fig. S3		
	GMR-GAL4	*GMR-GAL4/GMR-GAL4*
	GMR>sra^{EY}	*GMR-GAL4/GMR-GAL4;* $sra^{EY07182}/sra^{EY07182}$
	GMR>$Aβ42^{BL33770}$	*GMR-GAL4, UAS-*$Aβ42^{BL33770}$*/GMR-GAL4, UAS-*$Aβ42^{BL33770}$
	GMR>$Aβ42^{BL33770}$*+*sra^{EY}	*GMR-GAL4, UAS-*$Aβ42^{BL33770}$*/GMR-GAL4, UAS-*$Aβ42^{BL33770}$*;* $sra^{EY07182}/sra^{EY07182}$
Fig. S4		
A-D	*GMR-GAL4*	*GMR-GAL4/+*
	GMR>sra^{EY}	*GMR-GAL4/+;* $sra^{EY07182}/+$
	GMR>APP	*GMR-GAL4/UAS-APP-N-myc*
	GMR>APP+sra^{EY}	*GMR-GAL4/UAS-APP-N-myc;* $sra^{EY07182}/+$
E, F	*elav-GAL4*	*elav-GAL4/+*
	elav>sra^{EY}	*elav-GAL4/*$sra^{EY07182}$
	elav>APP	*UAS-APP-N-myc/+; elav-GAL4/+*
	elav>APP+sra^{EY}	*UAS-APP-N-myc/+; elav-GAL4/* $sra^{EY07182}$
Fig. S5		
	UAS-$Aβ42^{BL33770}$	*UAS-*$Aβ42^{BL33770}$*/UAS-*$Aβ42^{BL33770}$
	sra^{EY}	$sra^{EY07182}/sra^{EY07182}$
	GMR-GAL4	*GMR-GAL4/GMR-GAL4*
	GMR>sra^{EY}	*GMR-GAL4/GMR-GAL4;* $sra^{EY07182}/sra^{EY07182}$

	GMR>Aβ42^{BL33770}	*GMR-GAL4, UAS-Aβ42^{BL33770}/GMR-GAL4, UAS-Aβ42^{BL33770}*
	GMR>Aβ42^{BL33770}+sra^{EY}	*GMR-GAL4, UAS-Aβ42^{BL33770}/GMR-GAL4, UAS-Aβ42^{BL33770}; sra^{EY07182}/sra^{EY07182}*
Fig. S6		
	en-GAL4	*en2.4-GAL4/+*
	en>CanA^{act}	*en2.4-GAL4/UAS-CanA^{act}*
Fig. S7		
	elav>Aβ42	*UAS-Aβ42/+; elav-GAL4/+*
	elav-GAL4	*elav-GAL4/+*
	elav>APP	*UAS-APP-N-myc/+; elav-GAL4/+*
	elav>APP+sra^{EY}	*UAS-APP-N-myc/+; elav-GAL4/sra^{EY07182}*