

Supplementary Material

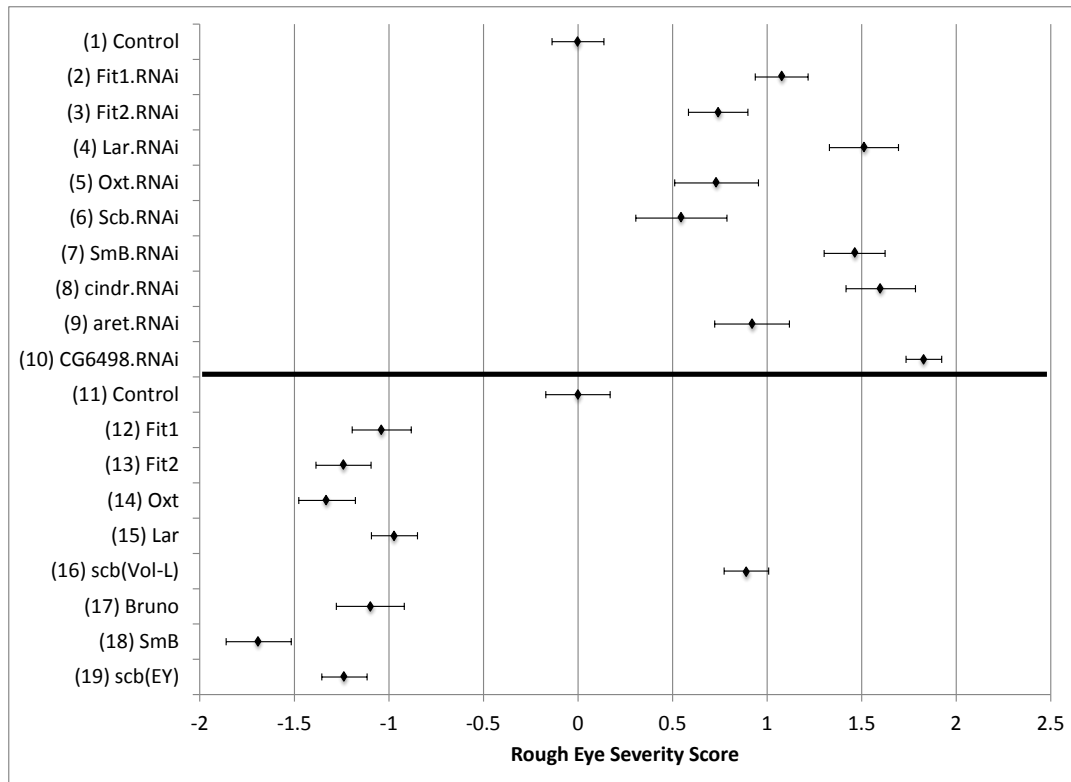
Functional screening in *Drosophila* identifies Alzheimer's disease susceptibility genes and implicates Tau-mediated mechanisms

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Supplementary Figure 1. Quantitative Scoring of Tau modifier effects.

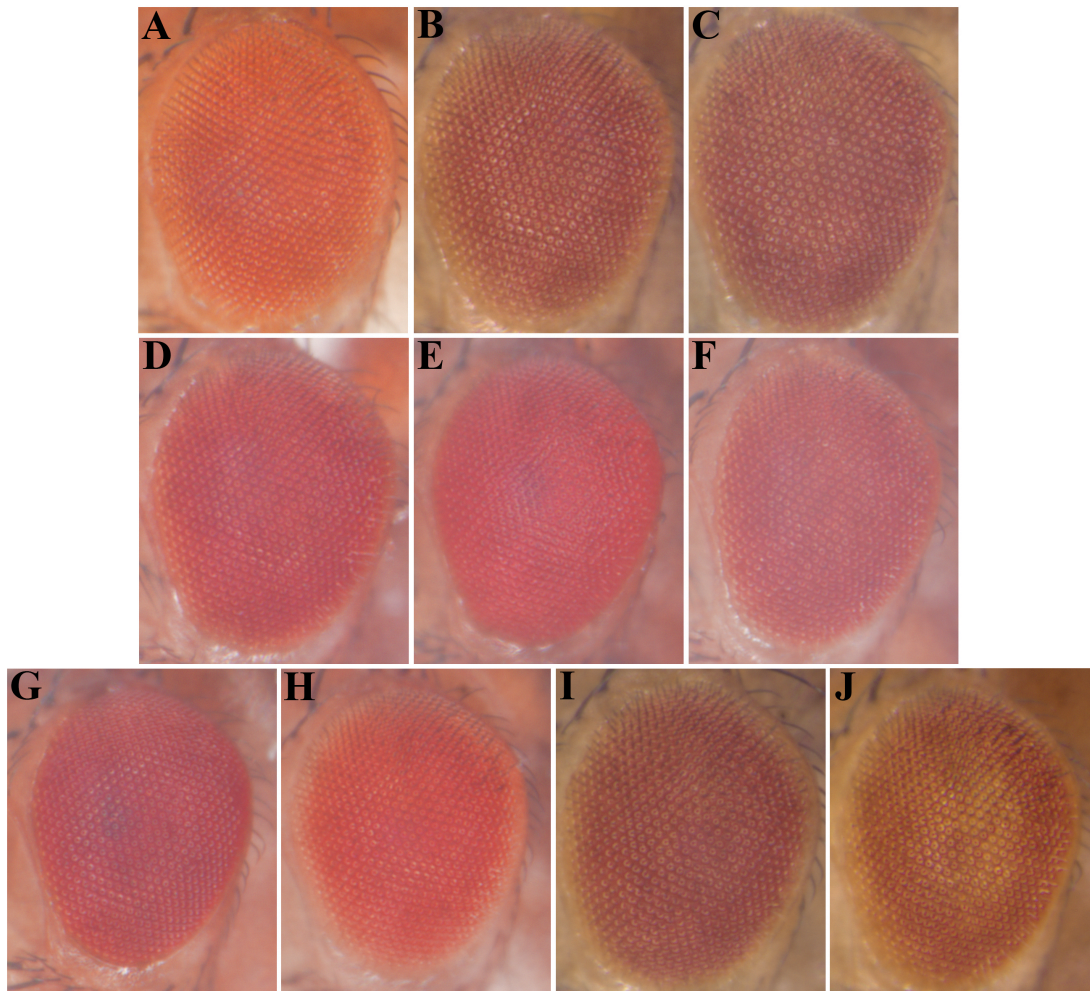
Modifier effects were scored using a 6-level, semi-quantitative rating scale of rough eye severity: 0 (*wildtype* eye), 1 (*very mild rough*, <50% facet disruption), 2 (*mild rough*, 50-100% facet disruption, 0-25% reduction in eye size), 3 (*moderate rough*, 100% facet disruption, 25-50% reduction in eye size), 4 (*severe rough*, additionally with one of the following features--ommatidial fusions, darkened/discolored areas, or >50% reduction in eye size), 5 (*very severe rough*, two or more of the characteristic severe features are present). RNAi modifiers (top) were tested in the presence of *UAS-Dcr2*. Enhancement or suppression of Tau toxicity was quantified as the average deviation in the rough eye severity score relative to control Tau transgenic flies, *UAS-Tau^{V337M}/+*; *GMR-Gal4,UAS-Dcr2/+* (top) or *UAS-Tau^{V337M}/+*; *GMR-Gal4/+* (bottom), respectively. Using pair-wise independent sample t-tests, all modifiers effects were found to be highly significant ($p < 0.001$). In order to facilitate comparisons of modifier effects relative to the two control conditions, the results were centered at 0, based on the mean control score. Mean and 95% confidence intervals are shown. At least 20 animals were scored for each experimental genotype.



Supplementary Figure 2. Enhancers are not significantly toxic independent of Tau.

Control crosses were performed to evaluate the effect of lines discovered to enhance Tau toxicity, when expressed in the absence of the *tau*^{V337M} transgene.

- (A) *GMR-Gal4,UAS-Dcr2* / +
- (B) *GMR-Gal4,UAS-Dcr2* / +; *UAS-doxl.RNAi* / +
- (C) *GMR-Gal4,UAS-Dcr2* / +; *UAS-cindr.RNAi* / +
- (D) *GMR-Gal4,UAS-Dcr2* / *UAS-Fit1.IR.v46495*
- (E) *GMR-Gal4,UAS-Dcr2* / *scb.IR.JF02696*
- (F) *UAS-Lar.IR.v36270* / +; *GMR-Gal4, UAS-Dcr2* / +
- (E) *GMR-Gal4,UAS-Dcr2* / *SmB.IR.HMS05097*
- (F) *GMR-Gal4,UAS-Dcr2* / +; *UAS-aret.IR.v41567* / +
- (F) *GMR-Gal4,UAS-Dcr2* / *UAS-CG6498.IR.v35100*
- (G) *GMR-Gal4* / *UAS-Scb(VolL)*



Supplementary Table 1. *Drosophila* orthologs of AD Susceptibility Loci.

HUMAN GENE	FLY GENE	DIOPT SCORE	PREDICTION ALGORITHMS
<i>Conserved</i>			
PICALM	lap	9	Compara, Homologene, Inparanoid, Isobase, OrthoDB, orthoMCL, Phylome, RoundUp, TreeFam
BIN1	Amph	7	Compara, Homologene, Inparanoid, orthoMCL, Phylome, RoundUp, TreeFam
ABCA7	CG1718	2	Compara, orthoMCL
ABCA7	CG6052	2	Compara, orthoMCL
CD2AP	cindr	4	Compara, Isobase, RoundUp, TreeFam
EPHA1	Eph	5	Compara, OrthoDB, orthoMCL, Phylome, TreeFam
<i>No or Low conservation</i>			
CR1	fw	1	Phylome
CD33	hbs	1	Phylome
APOE		0	
CLU		0	