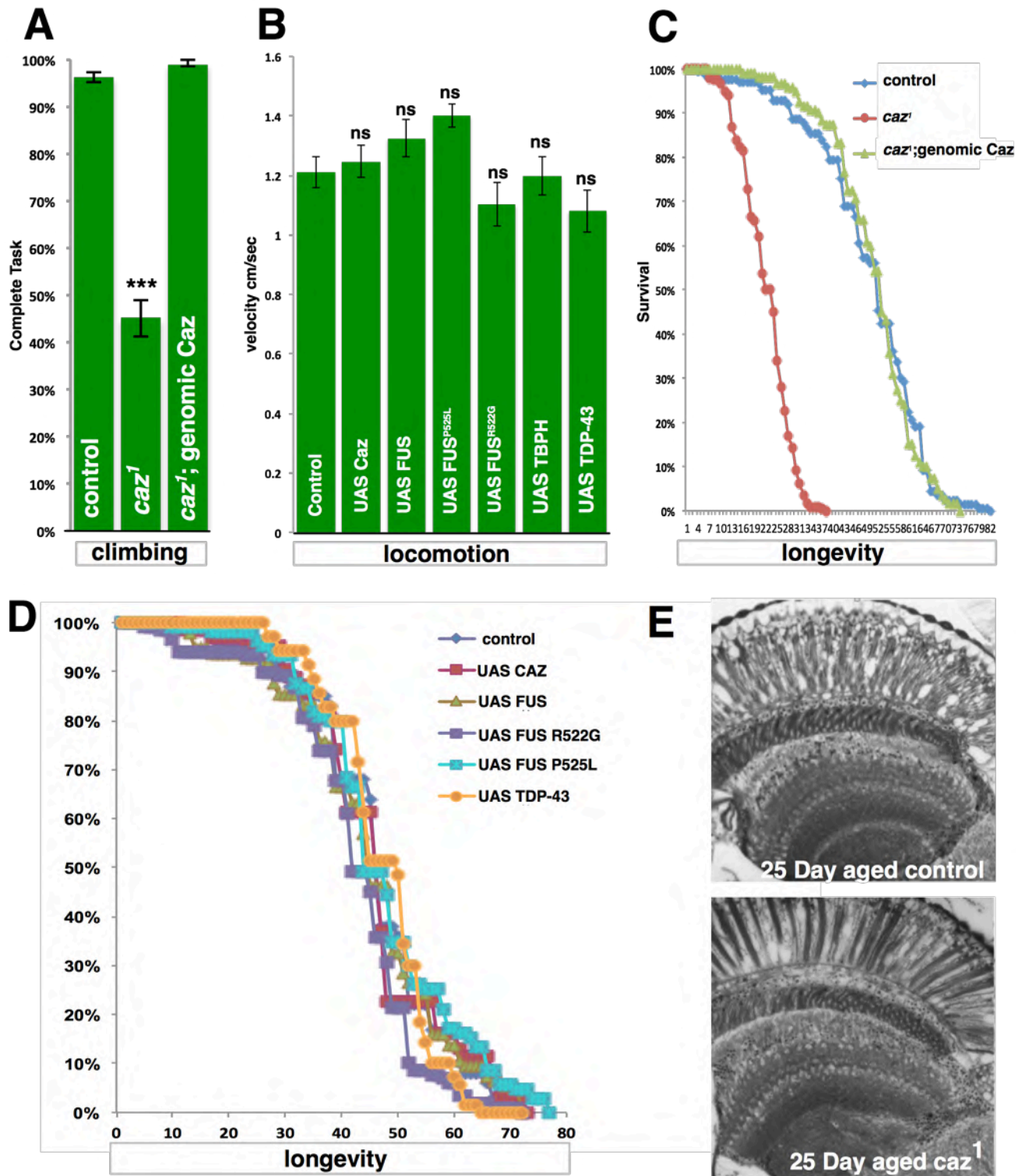


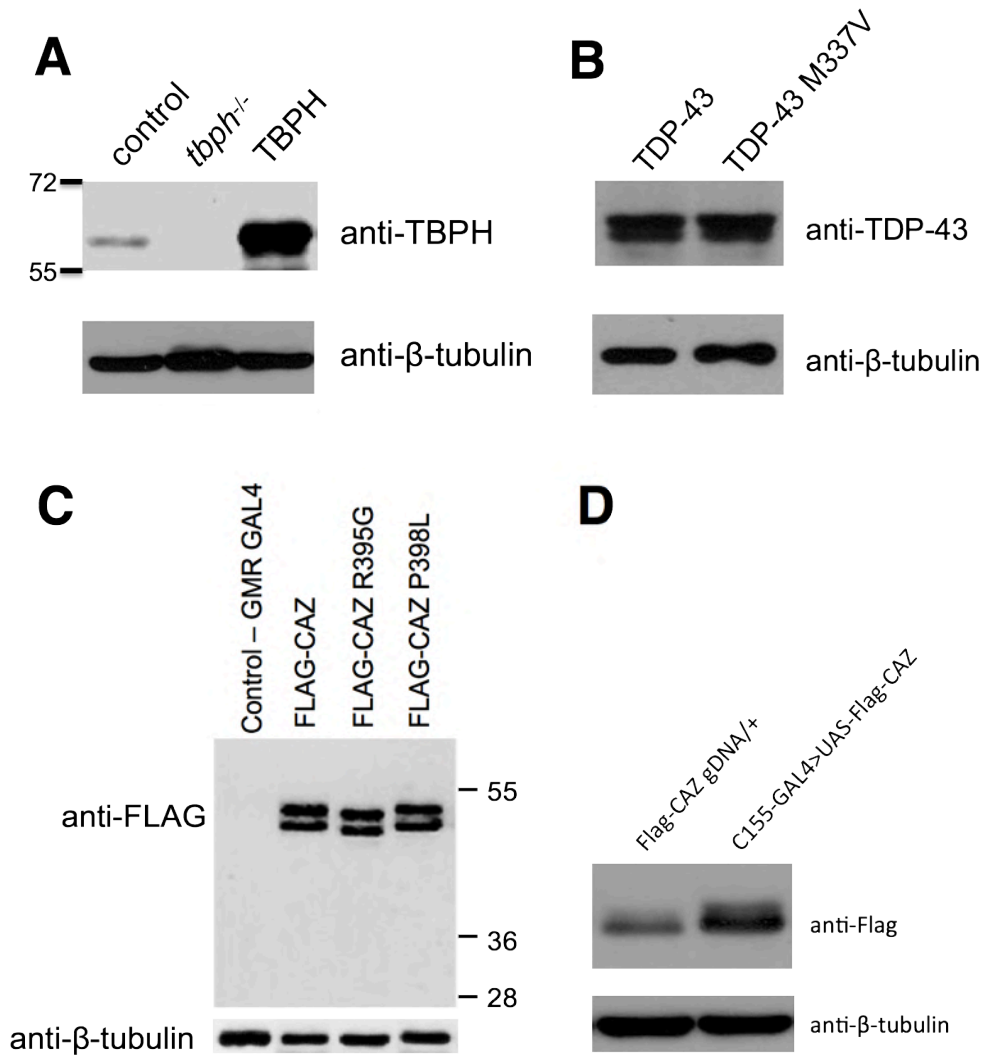
**Supplementary Figure 1: Drosophila Caz and Human FUS are similar and located in the nucleus.**

(A) Alignment of Human FUS/TLS (NP004591) and *Drosophila* Caz. Identity is indicated by green boxes, double and similarity by yellow boxes (B) Caz, FUS and FUS mutants are found in the nucleus. [Left] *Drosophila* motor neuron cell bodies expressing UAS-Caz, UAS-FUS, UAS-FUS<sup>R522G</sup> and UAS-FUS<sup>P525L</sup> (green), Histone-YFP (red), and cytoplasmic β-galactosidase (blue) driven by the motor neuron driver OK319Gal4. Single channel images of UAS-Caz, UAS-FUS, UAS-FUS<sup>R522G</sup> and UAS-FUS<sup>P525L</sup>. All transgenic proteins localize to the nucleus of motor neurons. (C) Western blot analysis of Flag-tagged FUS, FUS<sup>R522G</sup> and FUS<sup>P525L</sup> driven by GMR-GAL4 indicate protein expression levels are identical.



**Supplementary Figure S2: Caz genomic rescue, transgene overexpression controls and brain sections.**

(A) Climbing ability of 1 day old male flies of control (precise excision), *caz*<sup>1</sup> and *caz*<sup>1</sup> mutants with a *caz* genomic rescue transgene. Task was scored as percentage if animals able to climb 15 cm up a 30 cm tall cylinder in 5 minutes. (n>50). *caz* mutant climbing defects are fully rescued by the *Caz* genomic transgene. \*\*\*=p< 0.001. (B) Walking speed of adult male flies expressing transgenic *Caz*, *FUS*, *FUS*<sup>P525L</sup>, *FUS*<sup>R522G</sup>, *TBPH* and *TDP-43* using the pan-neuronal driver *C155-GAL4* (n>10). No defects were produced by overexpression on any transgene. (C) Percent survival of adult male flies of control (precise excision), *caz*<sup>1</sup> and *caz*<sup>1</sup> mutants with a *caz* genomic rescue transgene (n>100). *caz* mutant lifespan is completely rescued by the *Caz* genomic transgene. (D) Longevity of adult male flies expressing transgenic *Caz*, *FUS*, *FUS*<sup>P525L</sup>, *FUS*<sup>R522G</sup> and *TBPH* using the pan-neuronal driver *C155-GAL4* (n>100). (E) Eye and brain optic lobe sections from 25 day old precise excision control and *caz*<sup>1</sup> mutant adult males. *caz* mutants do not have signs of extensive neuron loss.



### Supplementary Figure S3: Mutant and transgene expression levels

(A) anti-TBPH antibody specifically detects a predicted 58 kD TBPH band in control, but not in *tbph*<sup>-/-</sup> (*tbph*<sup>Δ23</sup>/Df(2R)BSC660) adult 1 day old mutants. This band is more pronounced when UAS-TBPH is overexpressed in heads with GMR-GAL4. (B) The protein levels detected by anti-human TDP-43 of TDP-43 and TDP-43<sup>M337V</sup> driven by elav-GAL4 are similar. (C) Western blot analysis of Flag-tagged Caz, Caz<sup>R395G</sup> and Caz<sup>P398L</sup> driven by GMR-GAL4 indicate protein expression levels are identical. (D) The protein levels detected of C155-Gal4 driven Caz in adult brain is approximately twice the level produced by the genomic Caz transgene.