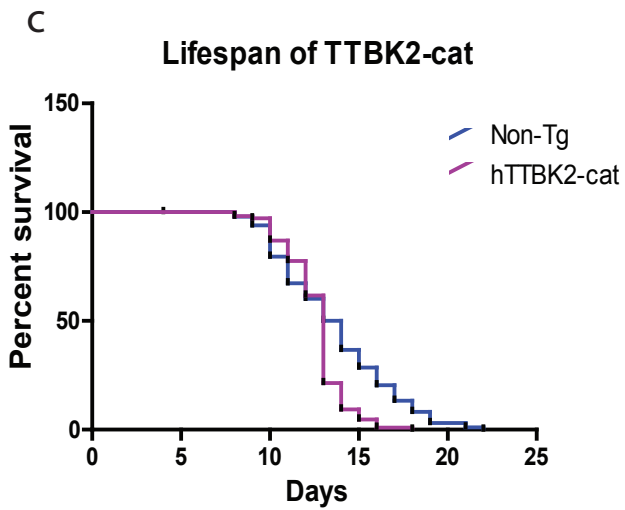
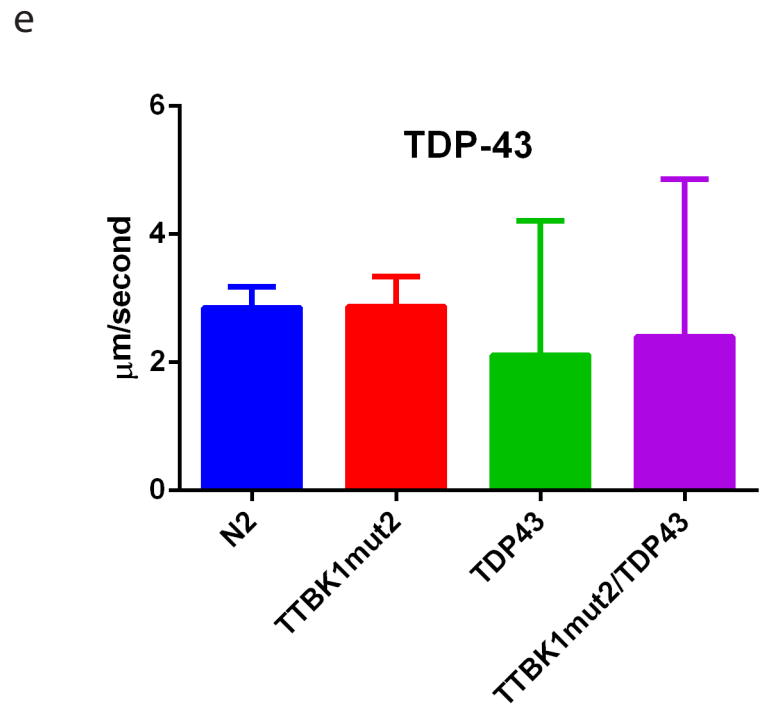
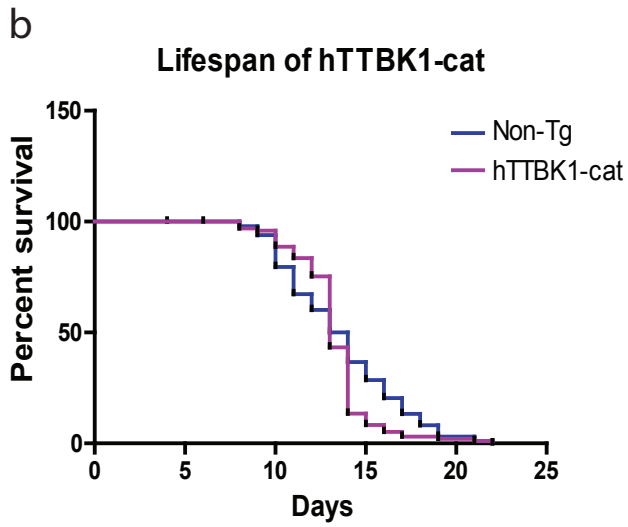
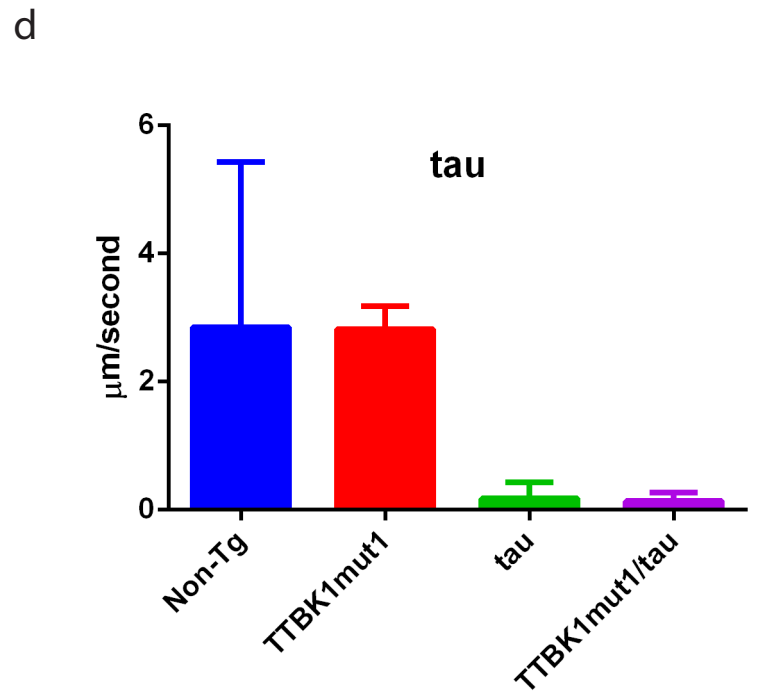
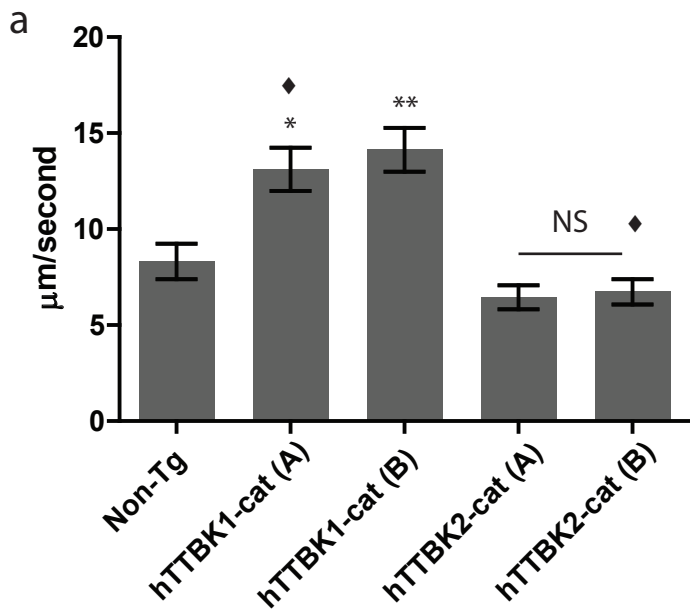


Supplemental Figure 1: Characterization of hTTBK-cat *C. elegans* lines

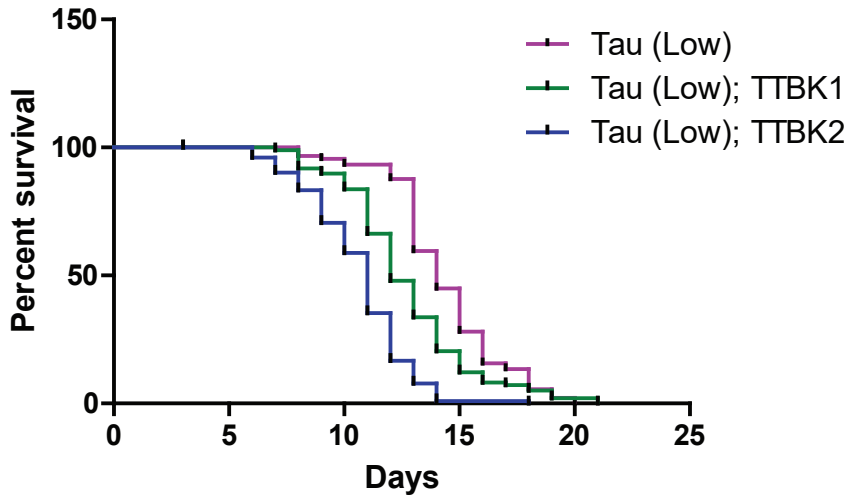
(a) Synchronized TTBK-cat transgenic L4 larvae behavior was measured by radial velocity relative to non-transgenic (non-Tg) animals. Animals were measured for the linear distance traveled from a central reference point over one hour, $N > 75$ for each genotype. Significance was determined using an unpaired T-test. $P = 0.04$ for Non-TG vs. hTTBK1-cat and $P = 0.007$ for Non-Tg vs. hTTBK1-cat. Lines that were selected for further analysis are indicated by black diamonds. (b) Lifespan analysis for hTTBK1-cat. (c) Lifespan analysis for hTTBK2-cat. (d) Extrachromosomal array transgenic TTBK1 kinase dead mutants crossed with Tau transgenic animals. Note that TTBK1 kinase dead mutants have normal locomotion relative to non-tg and do not significantly change tau mediated locomotion defects. (e) Kinase Dead TTBK1 transgenes crossed with TDP-43 transgenic lines. Note that TTBK1 kinase dead mutants do not significantly change TDP-43 mediated locomotion defects.



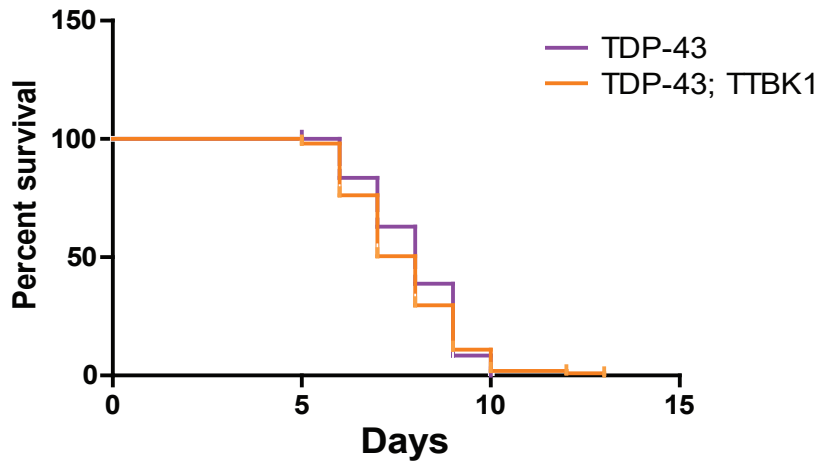
Supplemental Figure 2: Lifespan analyses

Lifespans of each transgenic line was assessed at 25°C. (a) Lifespan analysis of tau versus tau;TTBK1 or tau;TTBK2. Tau median lifespan = 14 days, tau; TTBK1 median lifespan = 13 days, tau; TTBK2 median lifespan = 12 days. Significance was analyzed using a Chi-squared analysis with a Mantel-Cox test. $P=0.04$ for tau vs. tau; TTBK1 and $P<0.001$ for tau vs. tau; TTBK2. (b) Lifespan analysis of TDP-43 versus TDP-43; TTBK1. TDP-43 median lifespan = 8 days, TDP-43; TTBK1 median lifespan = 7.5 days. No significance.

a Lifespan of tau X TTBK1 and TTBK2

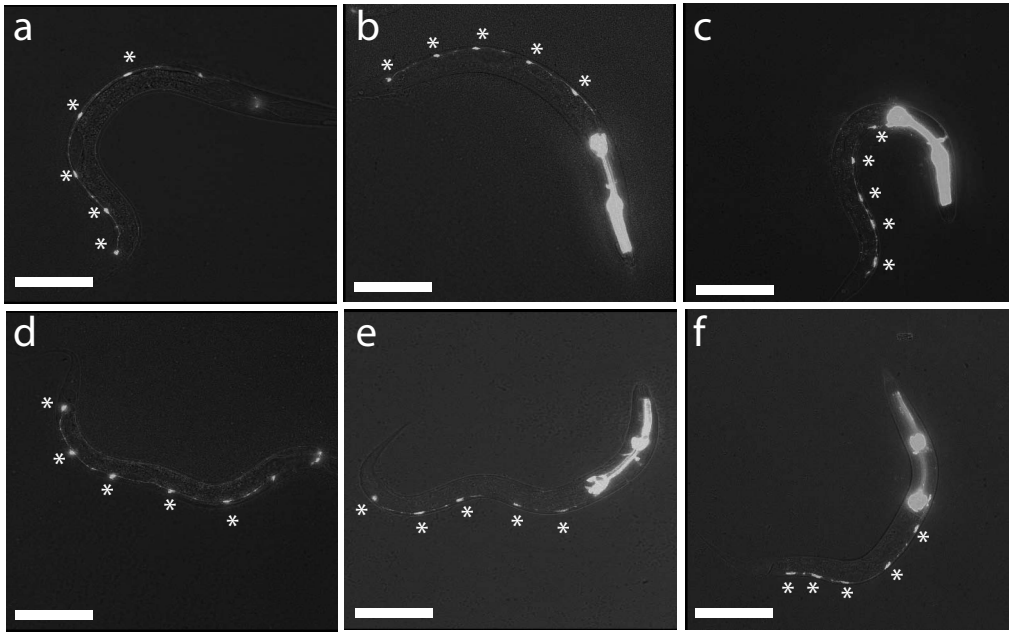


b Lifespan of TDP-43 X TTBK1

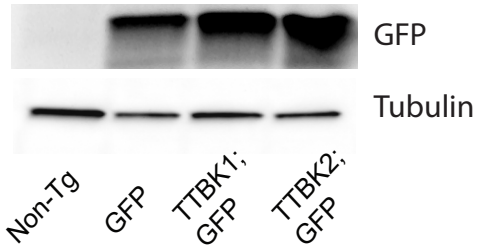


Supplemental Figure 3: L1 transgenic *C. elegans* are developmentally normal and GFP levels are unaffected by hTTBK1 or hTTBK2 expression

GFP-labeled D-type GABAergic motor neurons were observed in L1 larval transgenic animals *in vivo* living worms. (a) TTBK1 (b) tau (high) (c) tau (high); TTBK1 (d) TTBK2 (e) tau (low) (f) tau (low); TTBK2. Asterisks indicate live neurons. Scale bar=50um. (g) GFP expression levels are not influenced by the presence of hTTBK1-cat or hTTBK2-cat.



g



Supplemental Figure 4: TTBK2 does not affect TDP-43 phenotypes

(a) Staged hTTBK2-cat; TDP-43 transgenic L4 larvae do not exhibit significantly decreased radial velocity relative to TDP-43 transgenic animals. Animals were measured for the linear distance traveled from a central reference point over one hour, $N > 100$ for each genotype. Significance was determined using an unpaired T-test. $P = 0.13$ versus TDP-43. (b) hTTBK2-cat; TDP-43 transgenic animals have slightly increased but not statistically significant total TDP-43 and pTDP-43 relative to TDP-43 animals. Bar graphs represent six independent replicate immunoblots of (c) Total TDP-43 and (d) pTDP. Graphs are plotted in relative intensity. Significance was determined using an unpaired T-test. $P = 0.059$ for total TDP and $p = 0.13$ for pTDP.

