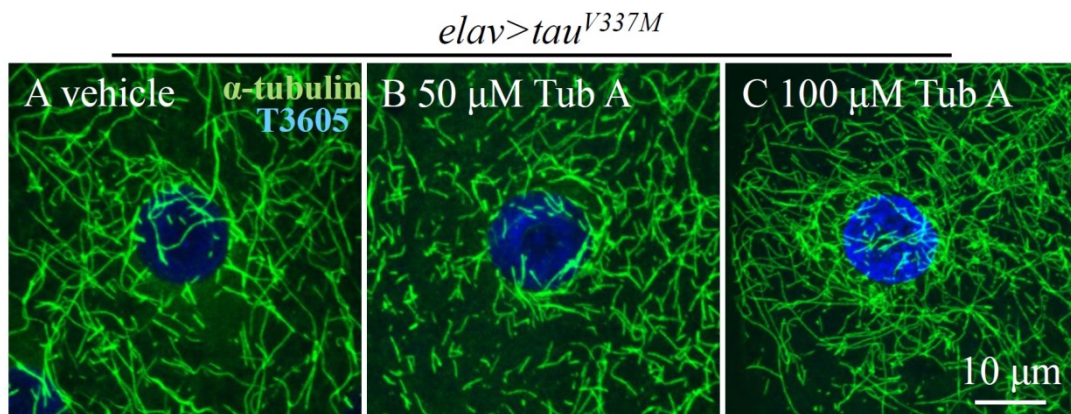
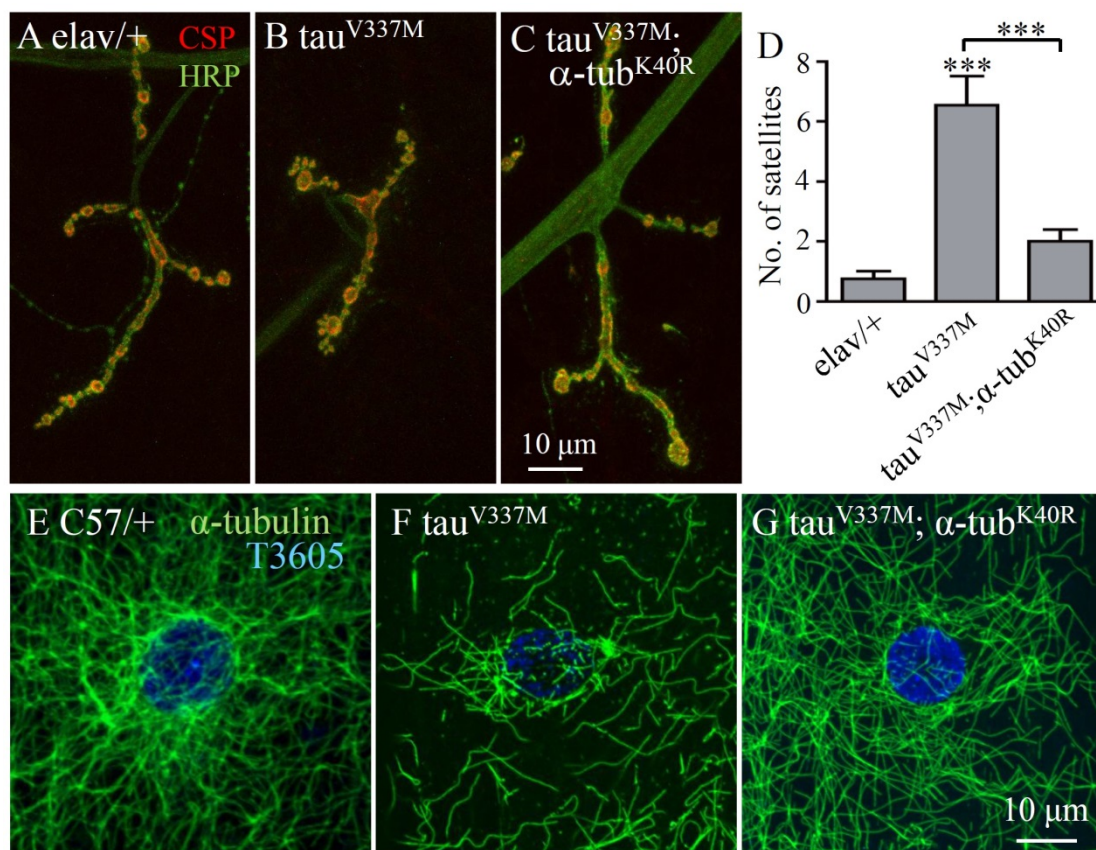


**Fig. S1. Inhibition of HDAC6 by ACY-1215 or tubastatin A does not affect MT network or density.** (A-C) Wild-type 3<sup>rd</sup> instar larval muscles co-stained with anti- $\alpha$ -tubulin (green) to show MT network and T3605 (blue) to show the nucleus. The 2<sup>nd</sup> instar larvae were fed cornmeal medium containing vehicle DMSO (A), 100  $\mu$ M ACY-1215 (B) or 100  $\mu$ M tubastatin A (C) until analysis at the 3<sup>rd</sup> instar larval stage. (D) Quantification of MT densities in 20  $\mu$ m perinuclear area of 3<sup>rd</sup> instar larvae in wild type.



**Fig. S2. Inhibition of HDAC6 rescues MT defects caused by tau<sup>V337M</sup> overexpression in a dose-dependent manner.** (A-C) Third instar larval muscles double-labeled with anti-tubulin to reveal MT network (green) and T3605 to reveal nucleus (blue). The larvae overexpressing tau<sup>V337M</sup> were fed cornmeal medium containing vehicle DMSO (A), 50 μM tubastatin A (B) or 100 μM tubastatin A (C) from 2<sup>nd</sup> instar larval stage. Higher dose of tubastatin A at 100 μM showed a better rescue of MT defects than that at 50 μM.



**Fig. S3.  $\alpha$ -tub<sup>K40R</sup> antagonizes tau toxicity in regulating MT network formation in muscle cells and NMJ growth.** (A-C) Representative NMJ4 from wandering 3<sup>rd</sup> instar larvae double-stained with anti-CSP (red) and anti-HRP (green) to reveal synaptic vesicles and neuronal membrane, respectively. (A) Genetic control *elav-Gal4/+*. (B) Neuronal overexpression of *tau*<sup>V337M</sup> (*elav-Gal4/tau*<sup>V337M</sup>). (C)  $\alpha$ -tub<sup>K40R</sup> mutation rescued the increased number of satellite boutons caused by neuronal *tau*<sup>V337M</sup> overexpression (*elav-Gal4/tau*<sup>V337M</sup>;  $\alpha$ -tub<sup>K40R</sup>). (D) Quantification of the number of satellite boutons in different genotypes.  $n=12$  NMJs for each genotype. \*\*\* $P < 0.001$  (one-way ANOVA). Error bars indicate s.e.m. (E-G) Third instar larval muscles double-stained with anti-tubulin to reveal MT network (green) and T3605 to reveal nucleus (blue). (E) Genetic control *C57-Gal4/+*. (F) Overexpression of *tau*<sup>V337M</sup> in muscles (*C57-Gal4/tau*<sup>V337M</sup>). (G)  $\alpha$ -tub<sup>K40R</sup> mutation rescued MT defects caused by *tau*<sup>V337M</sup> overexpression (*C57-Gal4/tau*<sup>V337M</sup>;  $\alpha$ -tub<sup>K40R</sup>).