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Removing endogenous tau does not prevent tau propagation yet reduces its neurotoxicity

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Figure 1

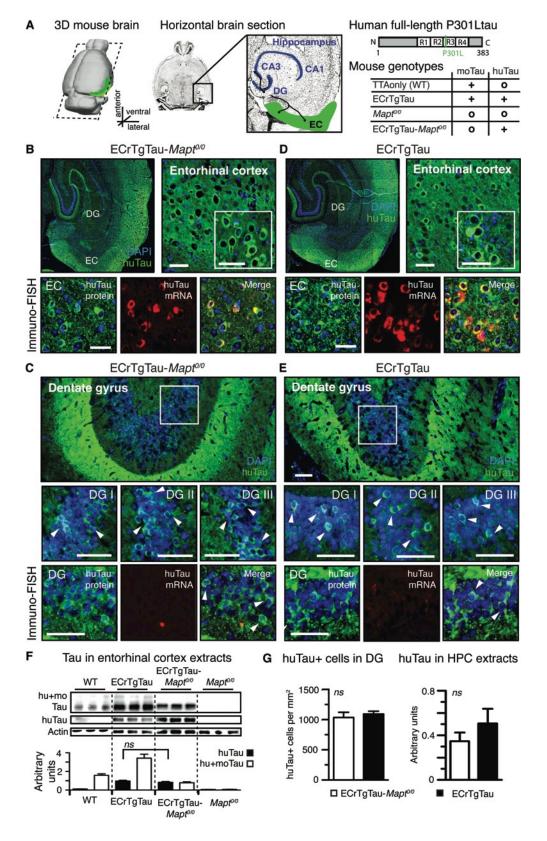


Figure 2

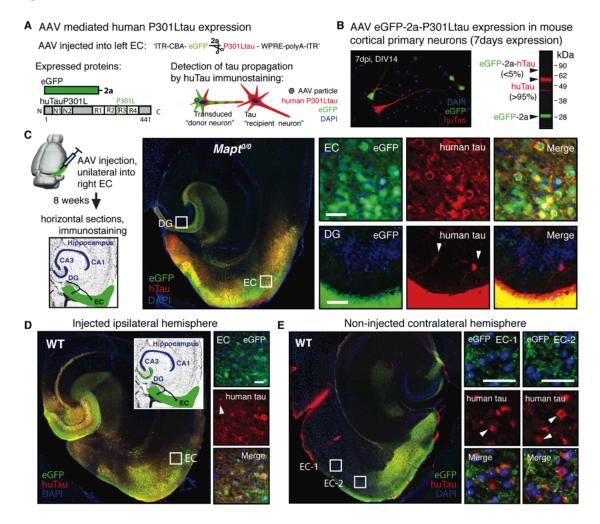


Figure 3

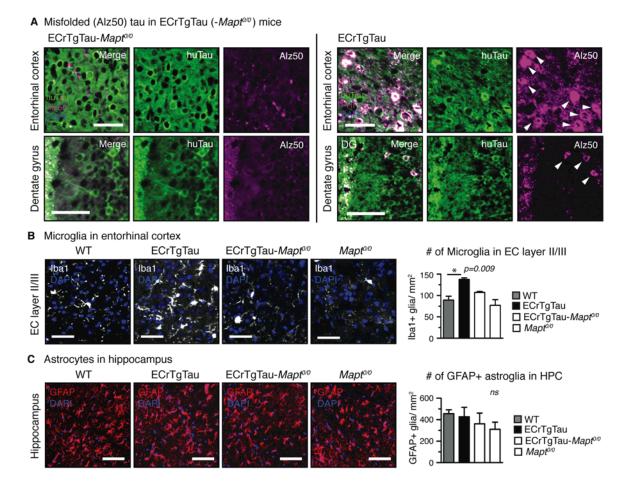


Figure 4

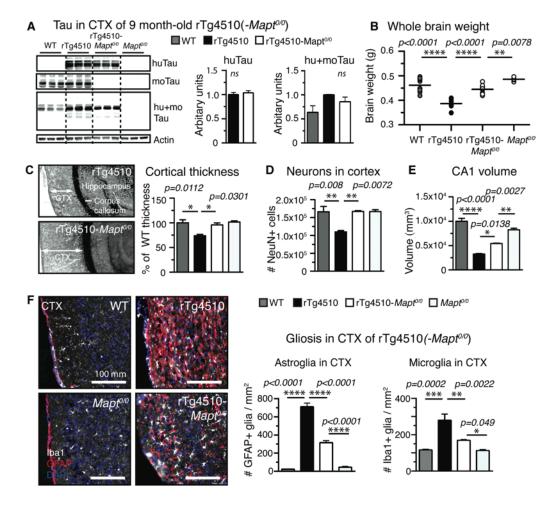


Figure 5

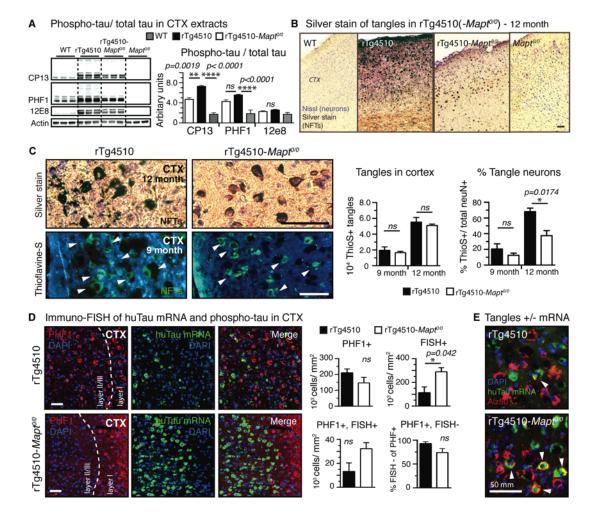
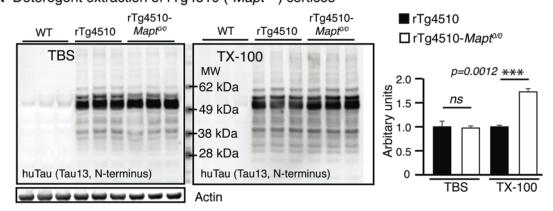
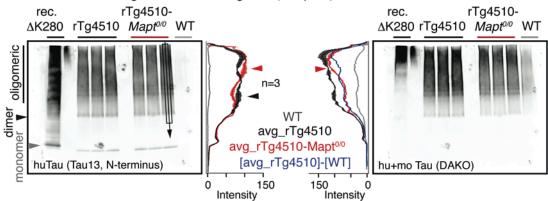


Figure 6 **A** Deteregent extraction of rTg4510 (-*Mapt*^{0/0}) cortices



B Native PAGE of oligomeric tau in rTg4510(-Mapt^{0/0}) TBS brain extracts



C HEK293 CFP/YFP-tau seeding assay of rTg4510(-Mapt^{0/0}) TBS brain extracts

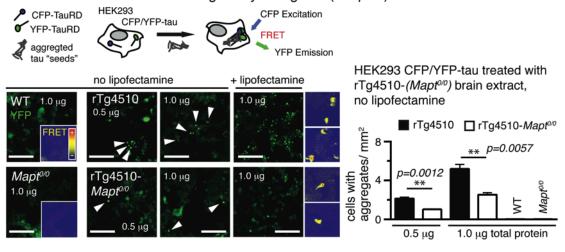
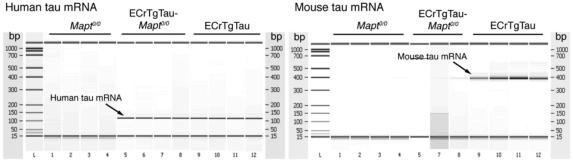


Figure EV1

Genotype verification through qPCR

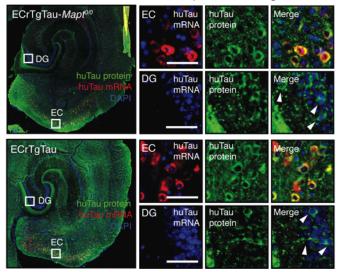


primers targeting 5'-CCC AAT CAC TGC CTA TAC CC-3' primers targeting 5'-CACCAAAATCCGGAGAAGGA-3' mouse tau exon 7 5'-CTTTGCTCAGGTCCACCGGC-3'

primers targeting 5'-TGG TGA AGC AGG CAT CTG AG-3'
GAPDH 5'-TGC TGT TGA AGT CGC AGG AG-3'

Figure Ev2

A Immuno-FISH of huTau mRNA and protein in ECrTgTau mice



B Tau in hippocampal extracts

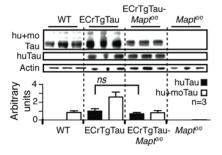
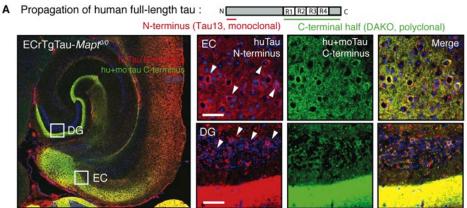


Figure EV3



B GABA-ergic neurons and glia in the dentate gyrus of ECrTgTau-Mapt[®] mice ECrTgTau-Mapt^{0/0} ECrTgTau-Mapt^{0/0} GAD67 Astrocytes huTau Merge Parv Parvalbumin Microglia С GABA-ergic neurons and glia in the dentate gyrus of ECrTgTau mice **ECrTgTau ECrTgTau** GAD67 GAD67 Merge huTau Parv Parvalbumin Microglia

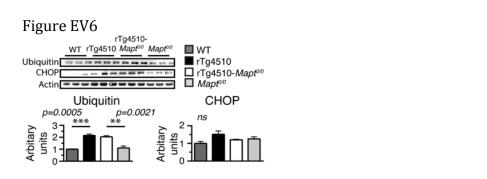
Figure EV4 A DAPI count in EC layer II/III В Synapsin-1 in EC DAPI+ cells / mm2 3000 -ECrTgTau-Arbitary units WT ECrTgTau Mapton Mapton 2000 ■ WT ECrTgTau Actin 1000 ☐ ECrTgTau-Mapt^{0/0} ■ Mapt^{0/0} Figure EV5 Whole brain weight **B** Cortical thickness C Neurons in cortex 12 month 12 month 12 month thickness 100 p=0.0001 n *** p=0.0029 p=0.0006 p=0.0182 Brain weight (g) 8.0 8.0 8.0 0.6 p=0.0035 p=0.08 p=0.0225 cells 2.0x10⁵ ns p=0.08 1.5x10⁵ NeuN+ ⋈ 1.0x10⁵ 50

0.5x10⁵ ð

#

■WT ■rTg4510 □rTg4510-Mapt[∞] □ Mapt[∞]

0 -

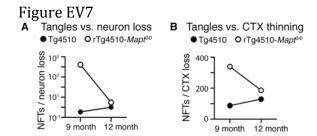


ф

%

WT rTg4510 rTg4510- Mapton

Mapt^{0/0}



C Immuno-FISH of huTau mRNA and protein in rTg4510(-Mapt^{0/0}) - 9 month

