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

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Figure 1


Figure 2

A AAV mediated human P301Ltau expression AAV injected into left EC: "ITR-CBA- eGFP $\frac{29}{80}$ P301 Lau - WPRE-polyA-ITR" Expressed proteins:


Detection of tau propagation by huTau immunostaining:



B AAV eGFP-2a-P301Ltau expression in mouse cortical primary neurons (7days expression)


8 8 weeks $\downarrow$
horizontal sections, immunostaining

D


Injected ipsilateral hemisphere


E
Non-injected contralateral hemisphere


Figure 3


Figure 4

A Tau in CTX of 9 month-old rTg4510(-Mapto/)



B Whole brain weight



E CA1 volume

$\square W T$ ■rTg4510 $\square \mathrm{rTg} 4510-$ Mapt $^{\omega 0} \square$ Mapt ${ }^{\omega 0}$

Gliosis in CTX of rTg4510(-Maptor)


Figure 5


Figure 6
A Deteregent extraction of $\mathrm{rTg} 4510\left(-\right.$ Mapt $\left.^{2 / 0}\right)$ cortices


B Native PAGE of oligomeric tau in rTg4510(-Mapt ${ }^{2 / 0}$ ) TBS brain extracts


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

no lipofectamine

rTg4510Maptor



+ lipofectamine


HEK293 CFP/YFP-tau treated with rTg4510-(Mapt ${ }^{\circ / 0}$ ) brain extract, no lipofectamine


## Figure EV1

Genotype verification through qPCR

primers targeting $5^{\prime}$-CCC AAT CAC TGC CTA TAC CC-3' primers targeting $5^{\prime}$-CACCAAAATCCGGAGAAGGA-3' human tansgene product $5^{\prime}$-CCA CGA GAA TGC GAA GGA-3' mouse tau exon 7 5'-CTTTGCTCAGGTCCACCGGC-3'
primers targeting 5 '-TGG TGA AGC AGG CAT CTG AG-3' GAPDH $5^{\prime}$-TGC TGT TGA AGT CGC AGG AG-3'

## Figure Ev2

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





Figure EV3
A Propagation of human full-length tau: $N \square C$
N -terminus (Tau13, monoclonal) C-terminal half (DAKO, polyclonal)


B GABA-ergic neurons and glia in the dentate gyrus of ECrTgTau-Mapt ${ }^{2 / 0}$ mice
ECrTgTau-Mapt ${ }^{010}$


C GABA-ergic neurons and glia in the dentate gyrus of ECrTgTau mice
ECrTgTau


Figure EV4

A DAPI count in EC layer II/III


B Synapsin-1 in EC


Figure EV5


Figure EV6


Ubiquitin
CHOP



Figure EV7
A Tangles vs. neuron loss
B Tangles vs. CTX thinning

- Tg4510 OrTg4510-Mapt ${ }^{\circ}$ - Tg4510 OrTg4510-Mappo



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


