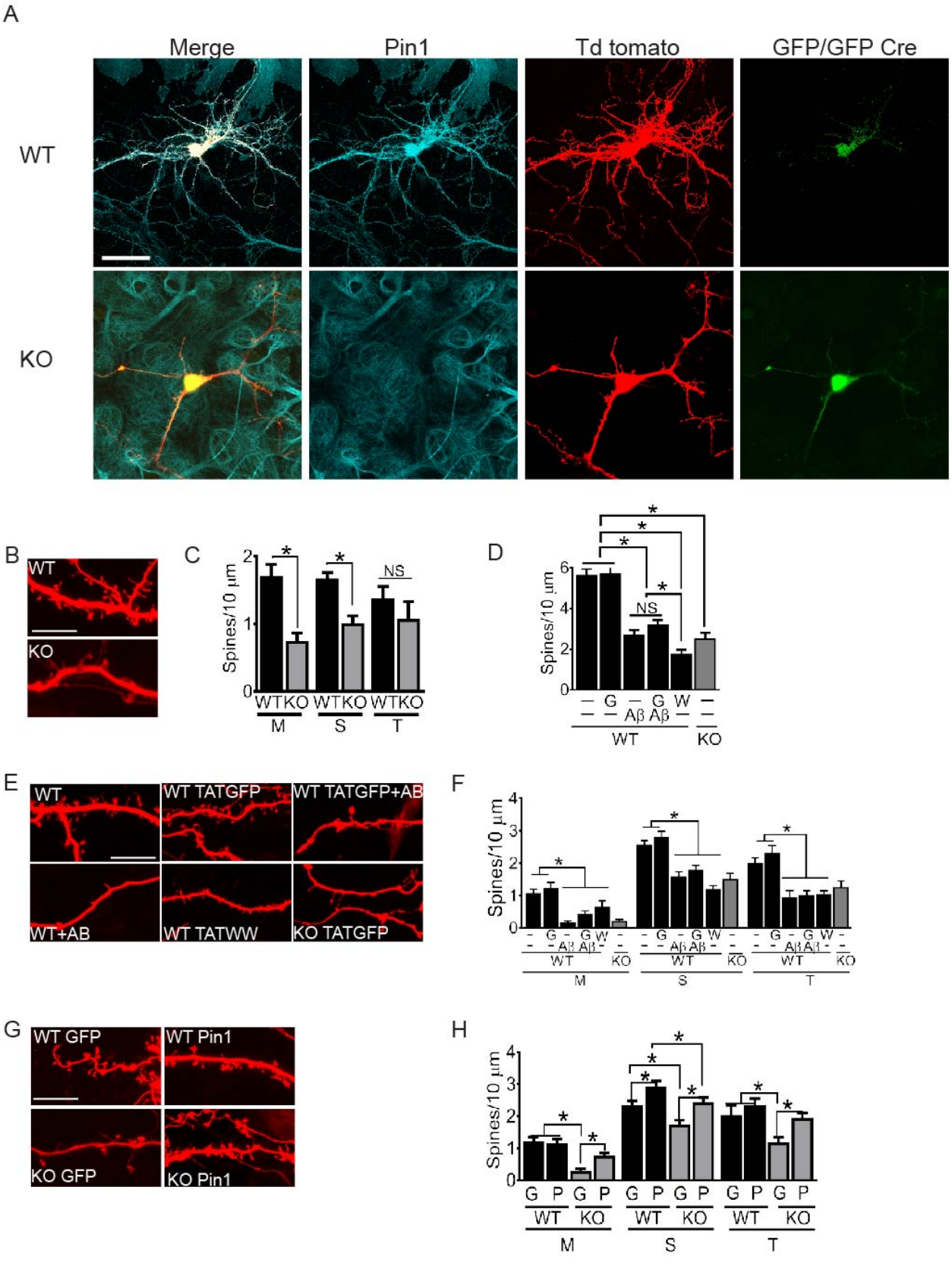
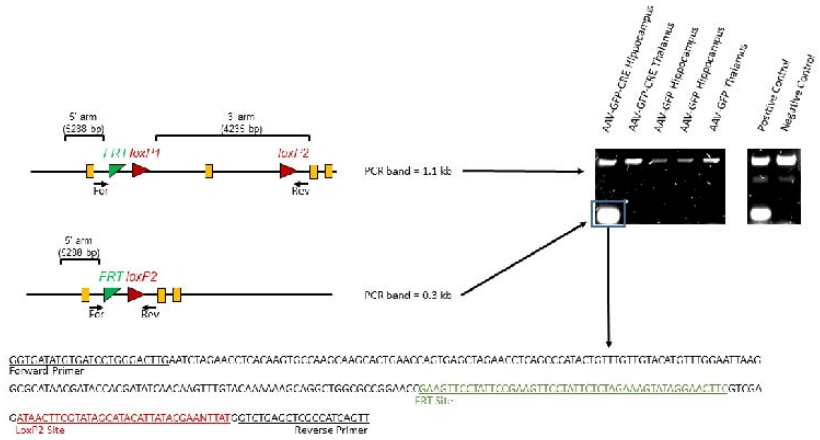
Supplemental Figure Legends



S1: Pin1 loss of Aβ42 causes spine loss.

(**A**) Representative immunofluorescence images of DIV21 $Pin1^{fl/fl}$ neurons after transfection on DIV7 with Td-tomato and NLS-GFP (WT) or NLS-GFP-Cre (KO). Cells were stained and visualized as shown. Scale bar = 50 μm. (**B**) Representative dendritic shaft analyzed for spines in **Fig. 1A**. (**C**) The total spine counts from **Fig. 1A** subtyped as mushroom (M), stubby (S) and thin (T) for DIV21 WT (black) and DIV21 KO (grey) neurons. (**D**) Total spine counts in WT (black) or KO (grey) untransduced neurons or transduced with TAT-GFP (G) or TAT-WW (W) ± Aβ42 (Aβ). (**E**) Representative dendritic shaft analyzed for spines in **fig. S1C**. (**F**) Total spine counts from **fig. S1D** sub-typed as M, S and T spines of WT (black) and KO (grey) neurons transduced with TAT-WW (W) or TAT-GFP (G). (**G**) Representative dendritic shaft analyzed for spines in **Fig. 1B**. (**H**) Total spine counts from **Fig. 1B** subtyped as M, S and T for WT (black) and KO (grey) neurons transduced with TAT-Pin1 (P) or TAT-GFP (G). Scale bar = 10 μm (**S1A**, **S1C**, **S1F**). The data are mean ± SEM. N >100 spines from ≥15 images and ≥ 3 coverslips per condition were counted. * = $P<0.05$ by Fisher's LSD Test following two-way analysis of variance (ANOVA) (**S1B**, **S1C**, **S1E**, **S1G**).

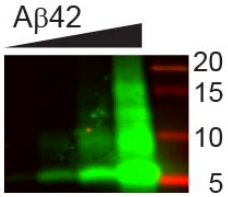
A



B

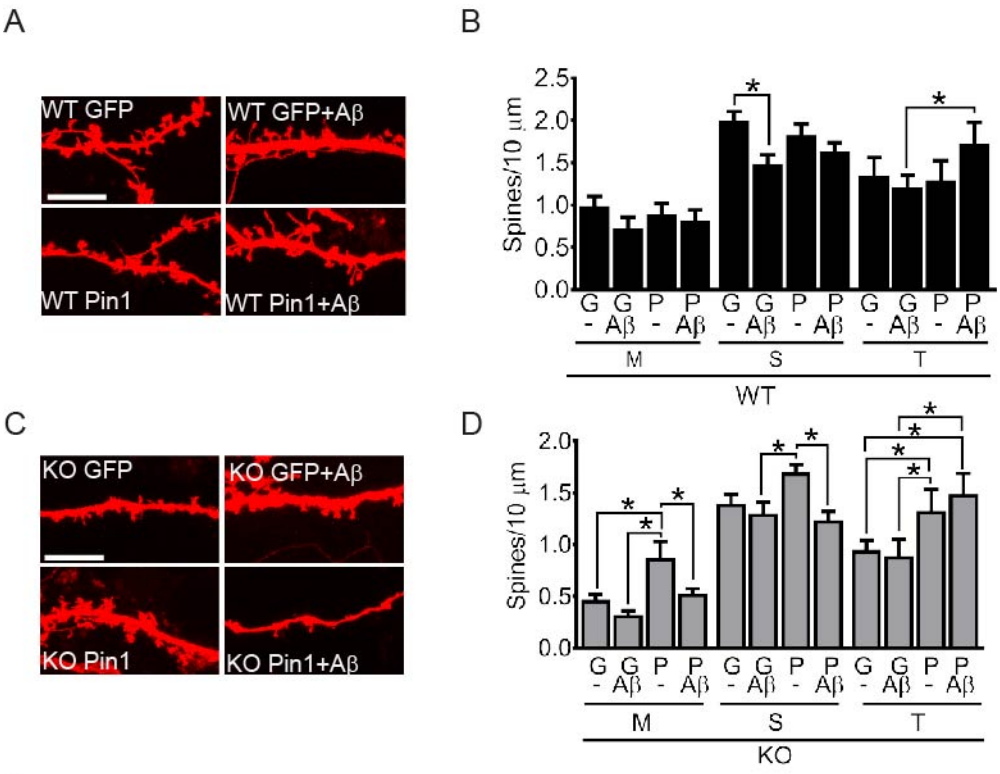
NP Number	Age	Sex	Region	Clinical Diagnosis	Braak Stage	PMI (hr)
16479	60	M	Parietal	Control	n/a	5.0
24385	73	M	Parietal	Control	n/a	4.75
24509	67	M	Frontal	Control	n/a	9.5
35289	71	F	Frontal	AD	VI	12.7
44810	56	F	Parietal	AD	VI	6.2
45408	73	M	Parietal	AD	VI	15.5
46879	76	F	Parietal	AD	VI	36.2
47833	82	M	Parietal	AD	VI	40.8

C



S2: Pin1 successfully recombined in mouse hippocampus after AAV-GFP-CRE

(**A**) Pre- and post-recombination of the conditional locus of Pin1$^{fl/fl}$ mice with PCR products. After laser capture of GFP+ or - cells from the hippocampus of AAV-GFP or AAV-GFP-Cre injected mice, DNA was analyzed for recombination by PCR. (**B**) Demographics of AD or control samples used in **Fig. 2A** and **2B**. (**C**) Multimeric Aβ42 analyzed by western blot.

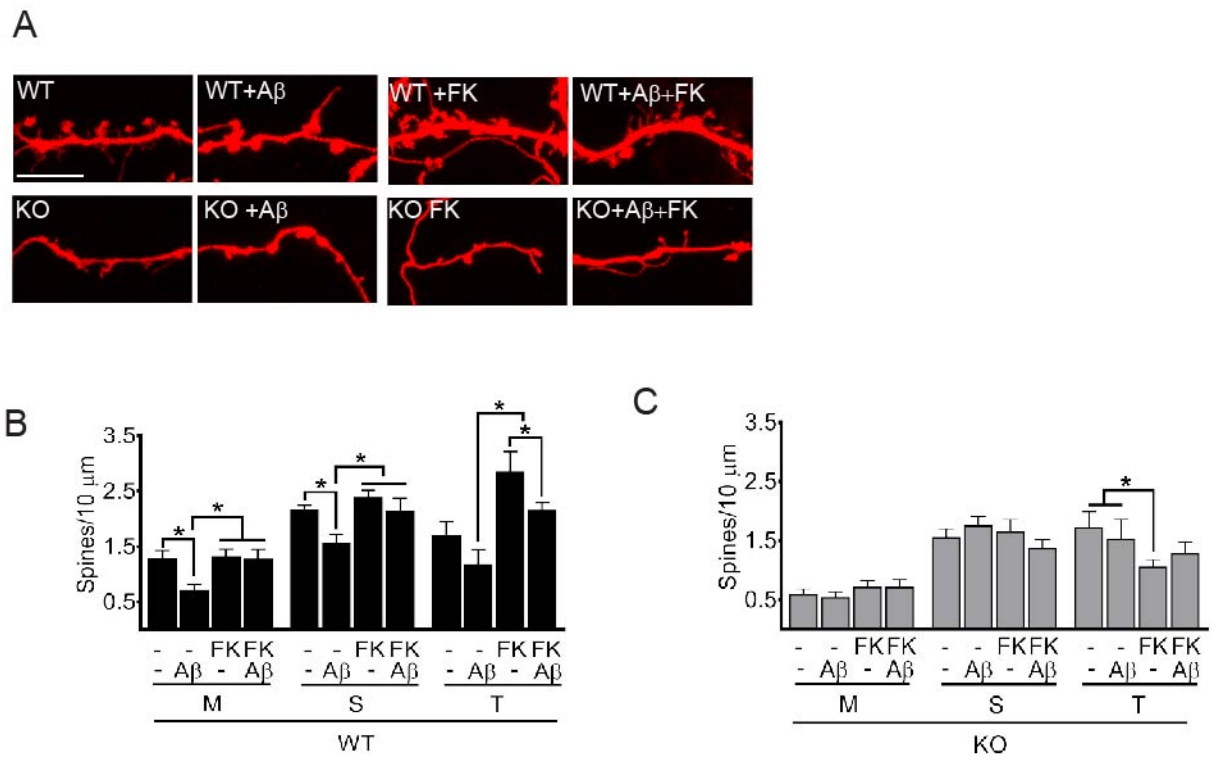


E

Gene	CN Subunit	kD	Peptides	% Coverage
Pin1	--	18.4	163	92
Ppp3ca	catalytic	58.8	41	55
Ppp3cb	catalytic	59.0	26	47
Ppp3r1	regulatory	18.2	17	78

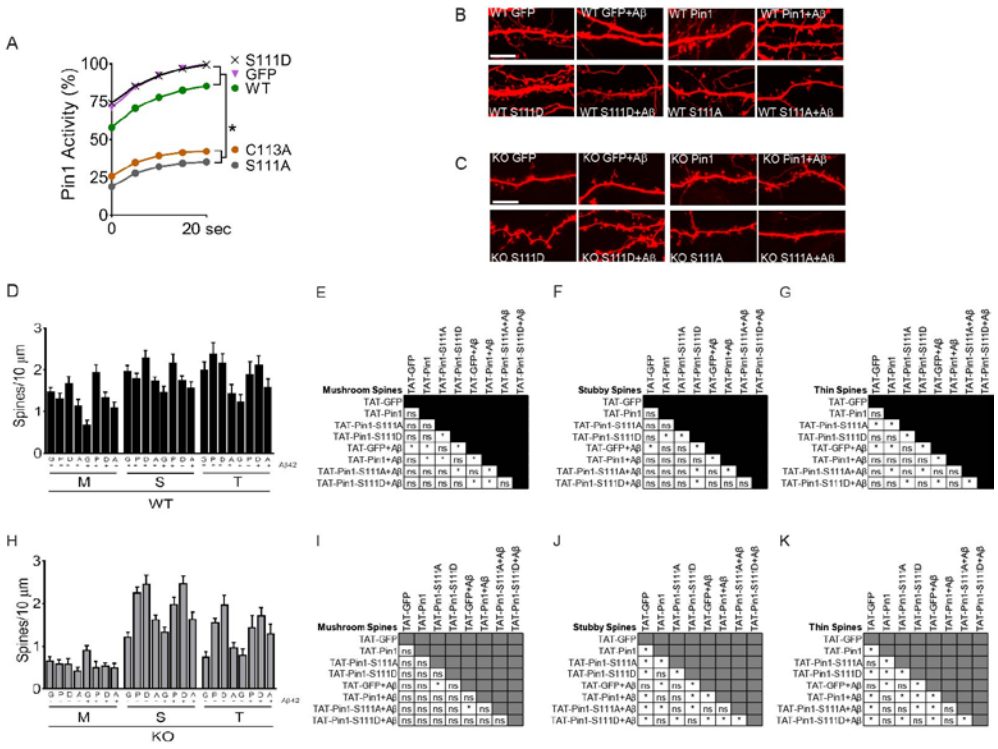
S3: Pin1 reconstitution restores mature spine counts after Aβ42.

(**A**) Representative dendritic shaft analyzed in **Fig. 3A**. Scale bar = 10 µm. (**B**) Total spine counts from **Fig. 3A** subtyped as M, S and T for DIV21 WT (black) neurons transduced with TAT-GFP (G) or TAT-Pin1 (P) ± Aβ42 (Aβ). (**C**) Representative dendritic shaft analyzed in **Fig. 3B**. Scale bar = 10 µm. (**D**) Total spine counts from **Fig. 3B** subtyped as M, S and T for DIV21 KO (grey) neurons transduced with TAT-GFP (G) or TAT-Pin1 (P) ± Aβ42 (Aβ). (**E**) SN proteins, number of independent peptides and percent coverage identified by mass spectrometry associated with Pin1. The data are mean ± SEM. N >100 spines from ≥15 images and ≥ 3 coverslips per condition were counted. * = P<0.05 by Fisher's LSD Test following two-way analysis of variance (ANOVA) (**S2B**, **S2D**).



S4: FK506 restoration of spines requires Pin1.

(**A**) Representative dendritic shaft analyzed in **Fig. 4A**. Scale bar = 10 µm. (**B)** Total spine counts from **Fig. 4A** subtyped as M, S and T for DIV21 WT (black) or (**C**) DIV21 KO (grey) neurons ± FK506 (FK) ± Aβ42 (Aβ). The data are mean ± SEM. N >100 spines from ≥15 images and ≥ 3 coverslips per condition were counted. * = $P<0.05$ by Fisher's LSD Test following two-way analysis of variance (ANOVA) (**S3B**, **S3C**).



S5: Pin1-S111D restores spine counts in WT or KO cells treated with Aβ42.

(**A**) SN were transduced with 100 nM TAT-GFP, TAT-Pin1-S111D, TAT-Pin1 (WT), TAT-Pin1-S111A or TAT-Pin1-C113A prior to lysis and isomerase activity determination. The means are N ≥ 8 replicates per treatment, * = $P < 0.05$ by Fisher's LSD Test following two-way analysis of variance (ANOVA). (**B**) Representative dendritic shaft analyzed in **Fig. 4C**. Scale bar = 10 µm. (**C**) Representative dendritic shaft analyzed in **Fig. 4D**. Scale bar = 10 µm. (**D**) Total spine counts from **Fig. 4C** subtyped into M, S and T spine densities of WT (black) neurons that were treated with TAT-GFP (G), TAT-Pin1 (P), TAT-Pin1-S111A (A) or TAT-Pin1-S111D (D) for 3 hr prior to vehicle (-) or 100 nM Aβ42 (Aβ) for 1 additional hour. (**E-G**) Statistical significance of (**E**) mushroom, (**F**) stubby and (**G**) thin WT (black) spines presented in **S4D**. (**H**) Same as in (**D**) except KO (grey) neurons from **Fig. 4D**. (**I-K**) Statistical significance of (**I**) mushroom, (**J**) stubby and (**K**) thin KO (grey) spines presented in **S4H**. The data are mean ± SEM. N >100 spines from ≥15 images and ≥ 3 coverslips per condition were counted (**S5D**, **S5H**). * = $P<0.05$ by Fisher's LSD Test following two-way analysis of variance (ANOVA) (**S5E** thru **G** and **S5I** thru **K**).