Supplementary material

Table S1. Description of cohorts in the study.

		12 mo		9 mo		12 mo, 1:10 dil	18 mo	6 mo
		PrP.APPsi/ Tau-P301L	PrP.APPsi	PrP.APPsi/ Tau-P301L	PrP.APPsi	PrP.APPsi	PrP.APPsi	PrP.APPsi
AD 1	M	2	3	1	1	5	---	4
	F	2	0	3	1	1	---	4
AD 2	M	2	2	3	0	5	---	4
	F	2	2	2	2	4	---	4
PA 1	M	2	3	---	---	---	4	---
	F	2	1	---	---	---	7	---
PA 2	M	1	3	---	---	---	2	---
	F	2	2	---	---	---	4	---
PA 3	M	2	2	---	---	---	2	---
	F	3	3	---	---	---	8	---
PA 4	M	1	3	3	1	6	2	3
	F	1	2	5	2	3	5	1
NDC 1	M	2	2	1	3	---	2	2
	F	1	2	1	1	---	3	4
NDC 2	M	1	4	---	---	---	---	---
	F	4	1	---	---	---	---	---
uninjected	M	1	2	2	1	5	1	3
	F	2	1	3	4	1	6	2

Table S2. Description of cohorts used in the study.

		PrP.APPsi/ M20	PrP.APPsi
AD/CAA 9	**M**	1	3
	F	4	2
AD 10	**M**	3	2
	F	4	3
LBAD/ CAA 11	**M**	3	2
	F	1	2
LBAD 12	**M**	2	3
	F	4	1
NDC/PA 13	**M**	4	2
	F	1	3
NDC 14	**M**	3	2
	F	3	3
uninjected	**M**	4	5
	F	3	3

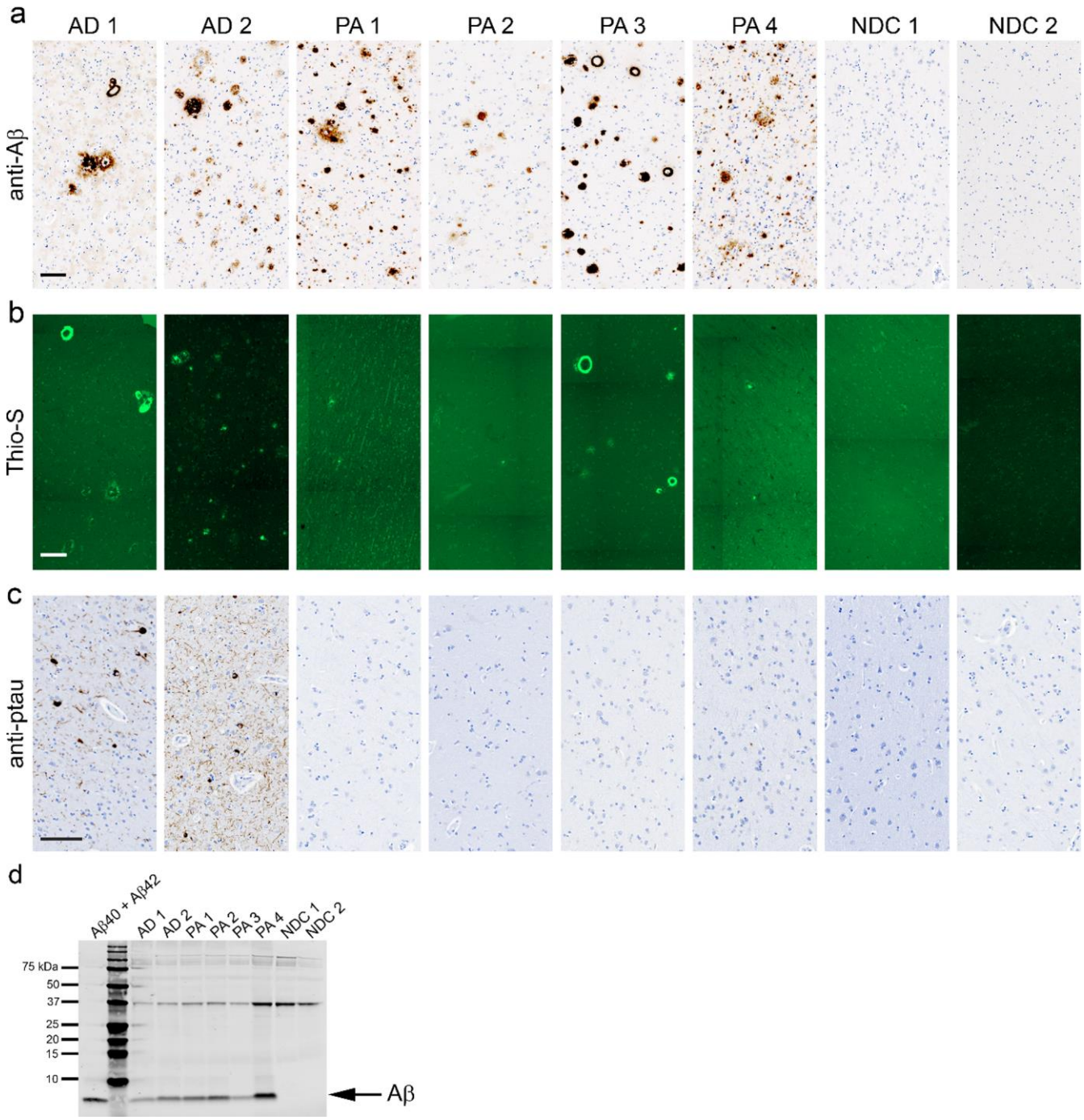
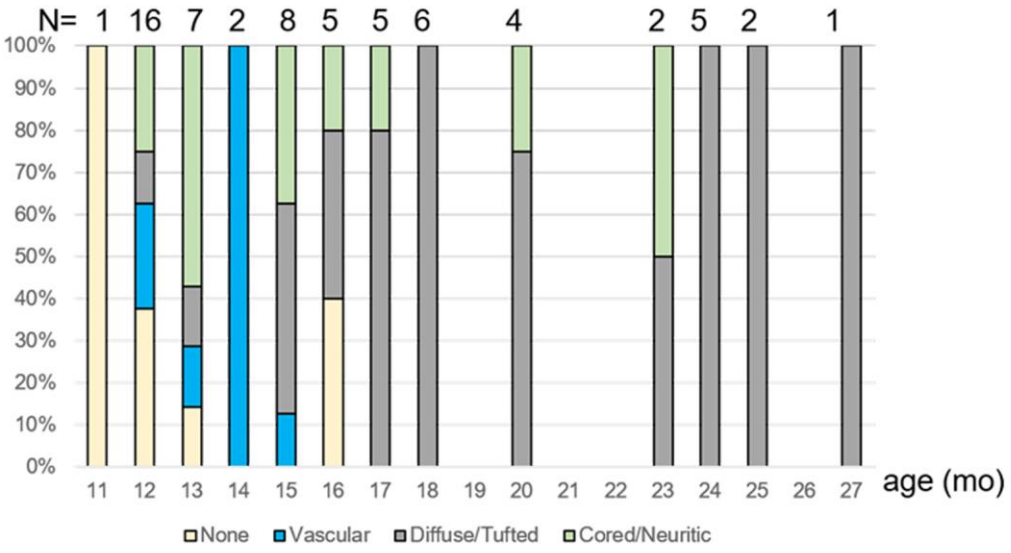
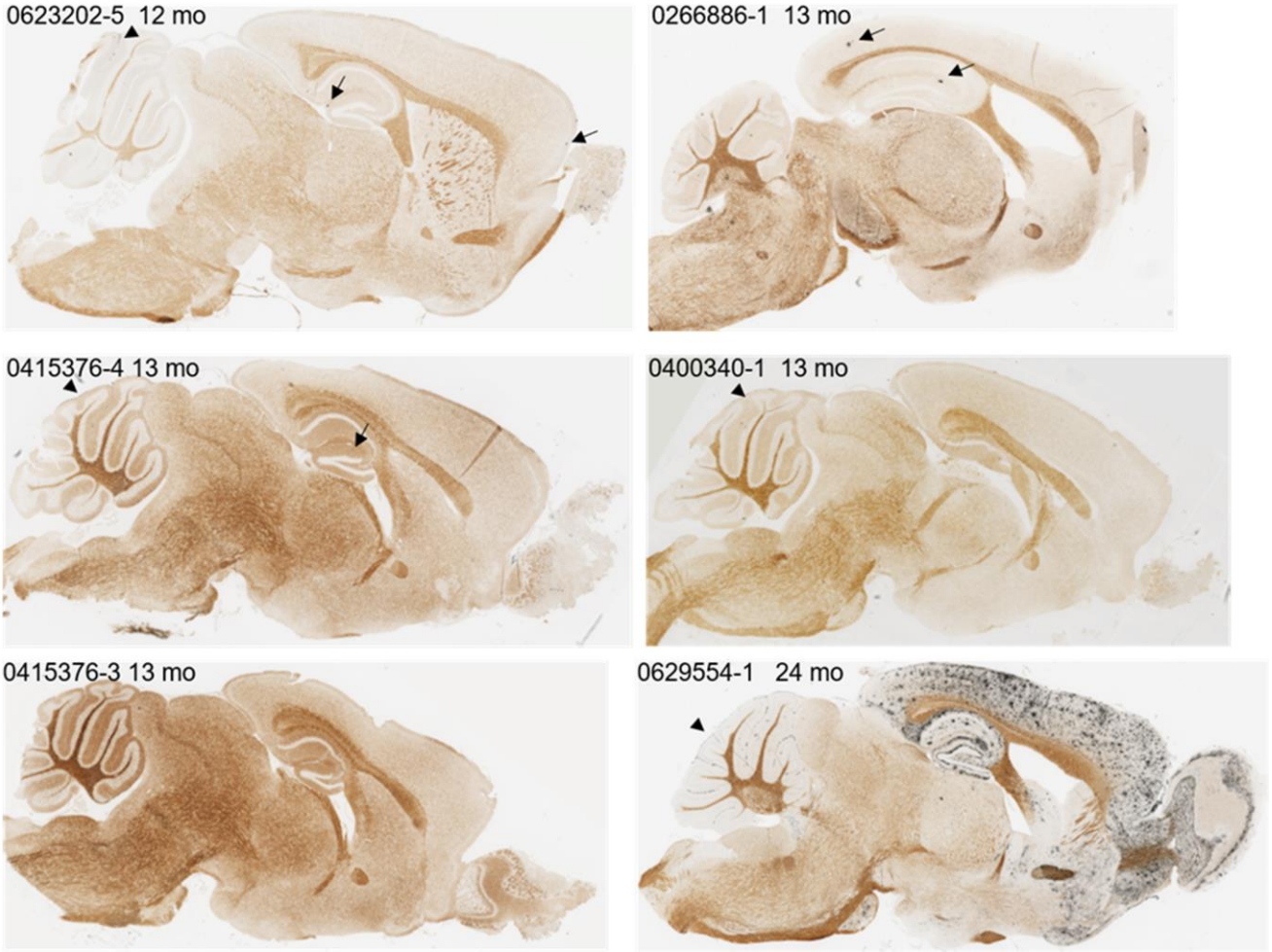


Fig. S1 Characterization of human brain samples. Representative images from the cortex of 2 AD cases, 4 PA cases, or 2 NDC cases stained with (a) biotinylated anti-Aβ mAb Ab5 (anti-Aβ 1-16), counterstained with hematoxylin, (b) Thio-S, and (c) anti-tau mAb 7F2 (anti-tau pThr205), counterstained with hematoxylin. Scale bar: 100 µm. (d) Human brain lysates were subjected to SDS-PAGE and immunoblotted with anti-Aβ mAb Ab5 (Aβ1-16) to detect Aβ levels in samples. Aβ40 and Aβ42 were control. The band at 37 kDa is a non-specific reactant.

A





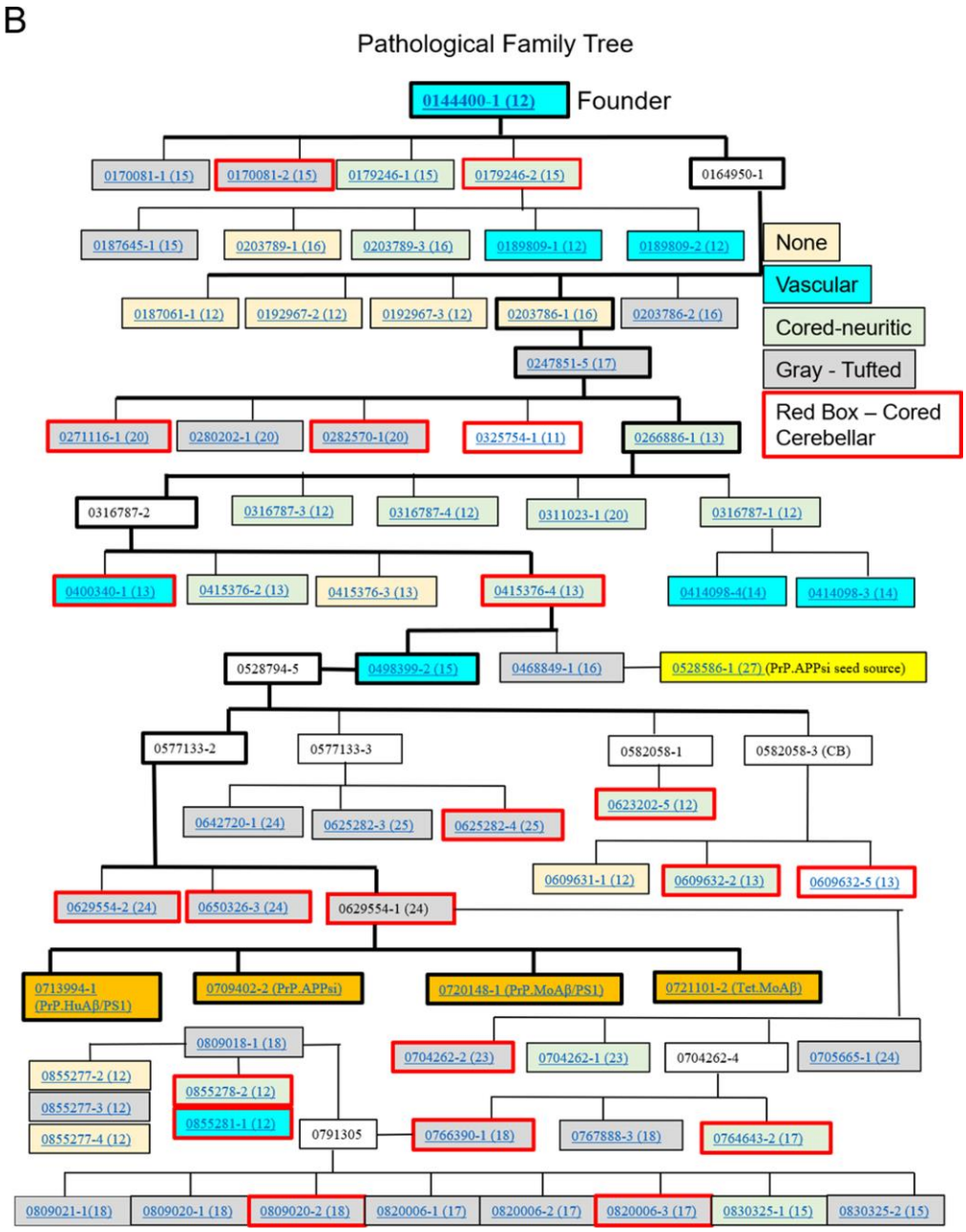


Fig. S2 Summary of pathological findings across generations of PrP.APPsi mice. (a) The percentage of animals exhibiting each morphology of amyloid deposit, grouped by age. For mice aged 11 to 15 months, the percentage indicated in blue indicates animals that had only meningeal deposits. Examples of the types of amyloid pathology visible in PrP.APPsi mice after CS-silver stain are shown in the bottom of panel (a). Across all ages, if the animal exhibited diffuse or cored deposits in the cortex or hippocampus, there was also vascular deposition in the meninges. Light gold = no amyloid deposition. Blue = only vascular deposition. Light green = cored or neuritic plaques more abundant than diffuse deposits. Gray = predominantly diffuse deposition. (b) Each rectangle represents a single animal with each animal identified by an identification number. The ages of the mice are indicated in the parentheses to the right of the animal identification number. For example, 0767888-3 (18) indicates animal number 0767888-3 that was 18 months old at harvest. The bright yellow rectangle indicates the mice used as source of PrP.HuAPPsi inoculum seeds. The orange rectangles indicate mice that were breeders to produce the newborn animals injected with inoculum (which is indicted in the brackets in each rectangle). The color code is the same as in (a) with the following additions. Red box = cored plaques in cerebellum. White = no paraffin embedded tissue available.

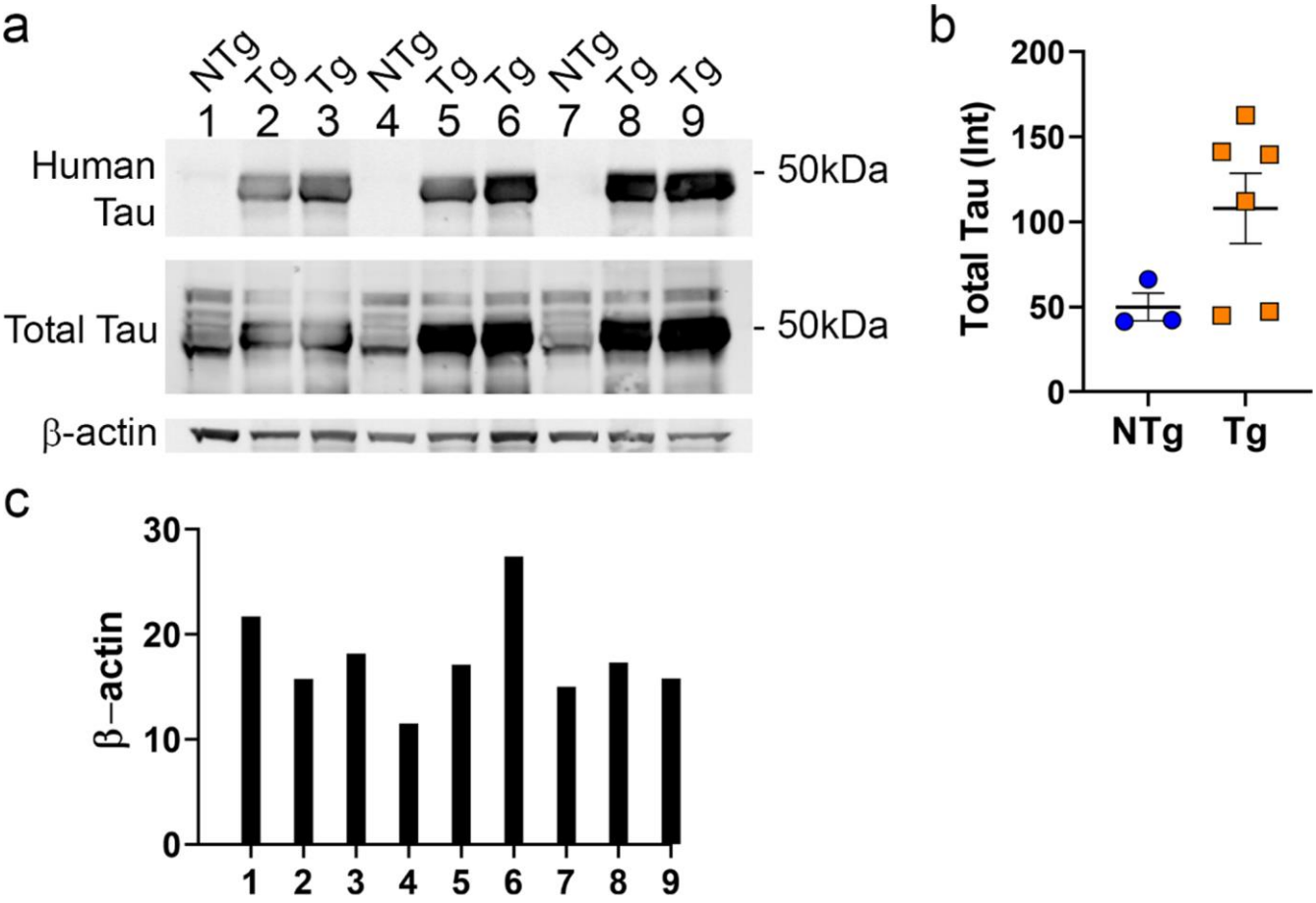


Fig. S3 Expression levels of tau in iTau-P301L mice. (a) PBS brain lysates of 2.5-6 month old iTau-P301L mice (n=6) and nontransgenic littermates (n=3) were subjected to SDS-PAGE and immunoblotted with anti-tau (Tau-13 [human tau] and 3026 [human and mouse tau]) and anti-β-actin as loading control. (b) The intensity of tau bands was quantified and graphed. (c) The intensity of β-actin bands compared across samples is graphed.

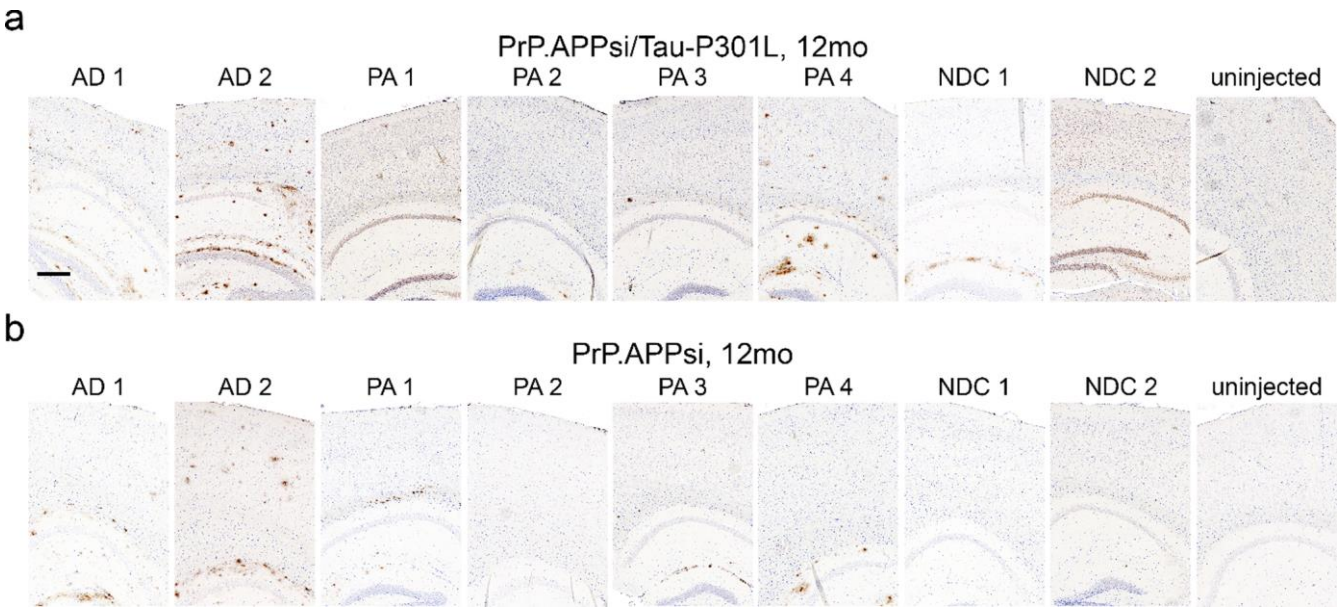


Fig. S4 Variation in Aβ seeding. Representative images of (a) PrP.APPsi/Tau-P301L and (b) PrP.APPsi mice injected with AD, PA, or NDC lysate at neonatal day P0. Brain sections (hemibrain) stained with biotinylated anti-Aβ mAb Ab5 (anti-Aβ 1-16) and counterstained with hematoxylin. Images show cases with the least (+) abundant amyloid pathology. Scale bar: 100 µm.

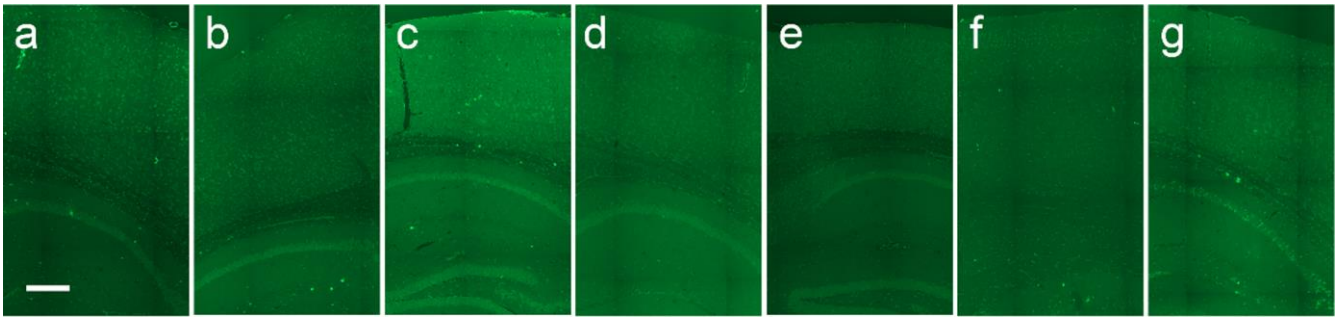


Fig. S5 Seeded Thio-S positive deposits are sparse in hippocampus and cortex. (a-g) Images of hippocampus and cortex of 7 different PrP.APPsi mice injected with PA 3 at neonatal day 0, aged 12 months, and stained with Thio-S. Scale bar: 100 µm. n=7.

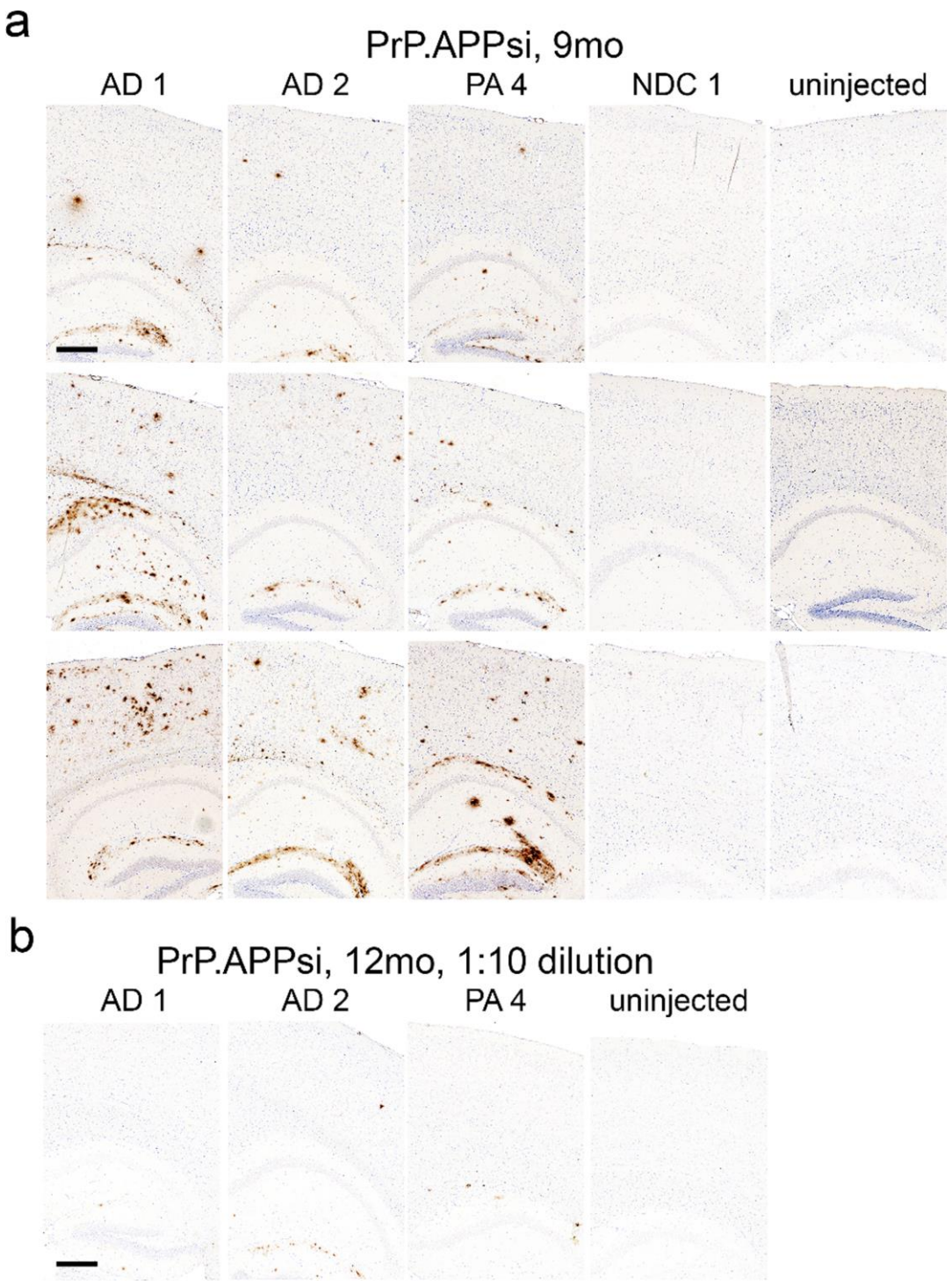


Fig. S6 Seeded amyloid pathology at 9 months is variable. (a) PrP.APPsi mice were injected at P0 with lysates from AD 1 and 2, PA 4, and NDC 1 and aged 12 months. Uninjected mice served as the control. Representative brain sections were stained with biotinylated anti-Aβ mAb Ab5 (anti-Aβ 1-16) and counterstained with hematoxylin. Scale bar: 100 µm. AD 1: n=6; AD 2: n=7; PA 4: n=9; NDC 1: n=6; uninjected: n=10. Three panels for each group are shown, depicting the least, moderate and most pathology in each group. (b) Lysates from AD 1 and 2, and PA 4 were diluted by a factor of ten, and were injected into PrP.APPsi mice at neonatal day 0 and aged 12 months. Representative brain sections were stained with biotinylated anti-Aβ mAb Ab5 (anti-Aβ 1-16) and counterstained with hematoxylin. Scale bar: 100 µm. AD 1: n=5; AD 2: n=8; PA 4: n=8; uninjected: n=6.

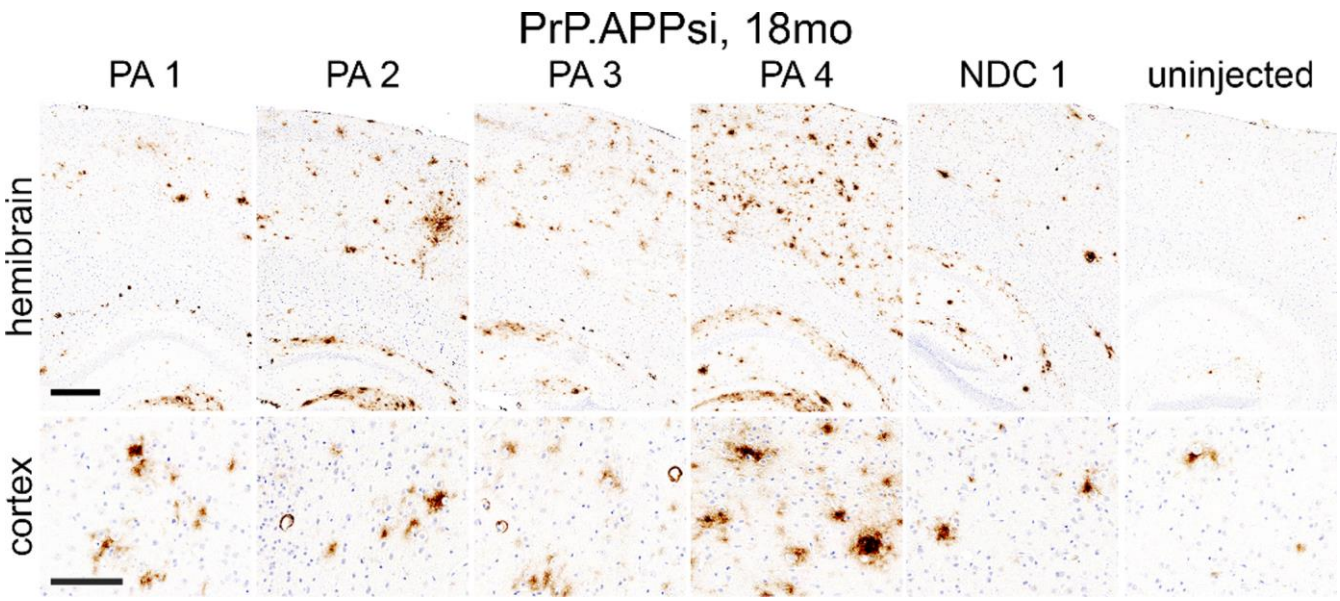


Fig. S7 Robust Aβ deposition at 18 months of age. Representative images of hemi-brain and cortex of PrP.APPsi mice seeded with PA 1-4, and NDC 1 at neonatal day 0, and control, uninjected PrP.APPsi mice, aged 18 months and stained with biotinylated anti-Aβ mAb Ab5 (anti-Aβ 1-16). Scale bar: 100 µm. PA 1: n=11; PA 2: n=6; PA 3: n=10; PA 4: n=7; NDC 1: n=5; uninjected: n=7.

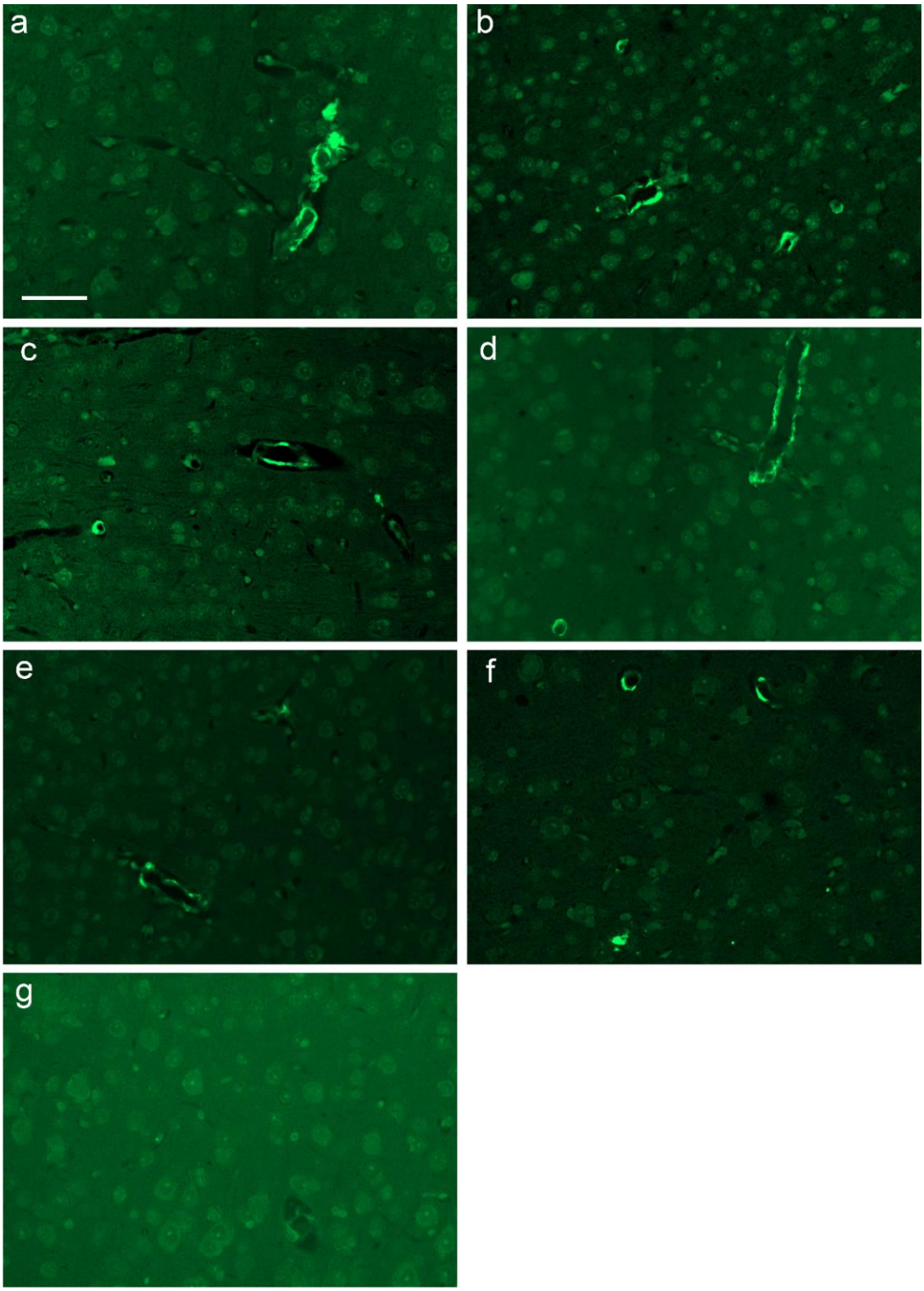


Fig. S8 Injection of PA 3 induced modest cerebral amyloid angiopathy. PrP.APPsi/Tau-P301L and PrP.APPsi were seeded by PA 3 at neonatal day 0 and aged 12 months. (a-g) Thio-S staining of representative sections (hemi-brain) from seven different mice seeded by PA 3. Scale bar: 50 µm.

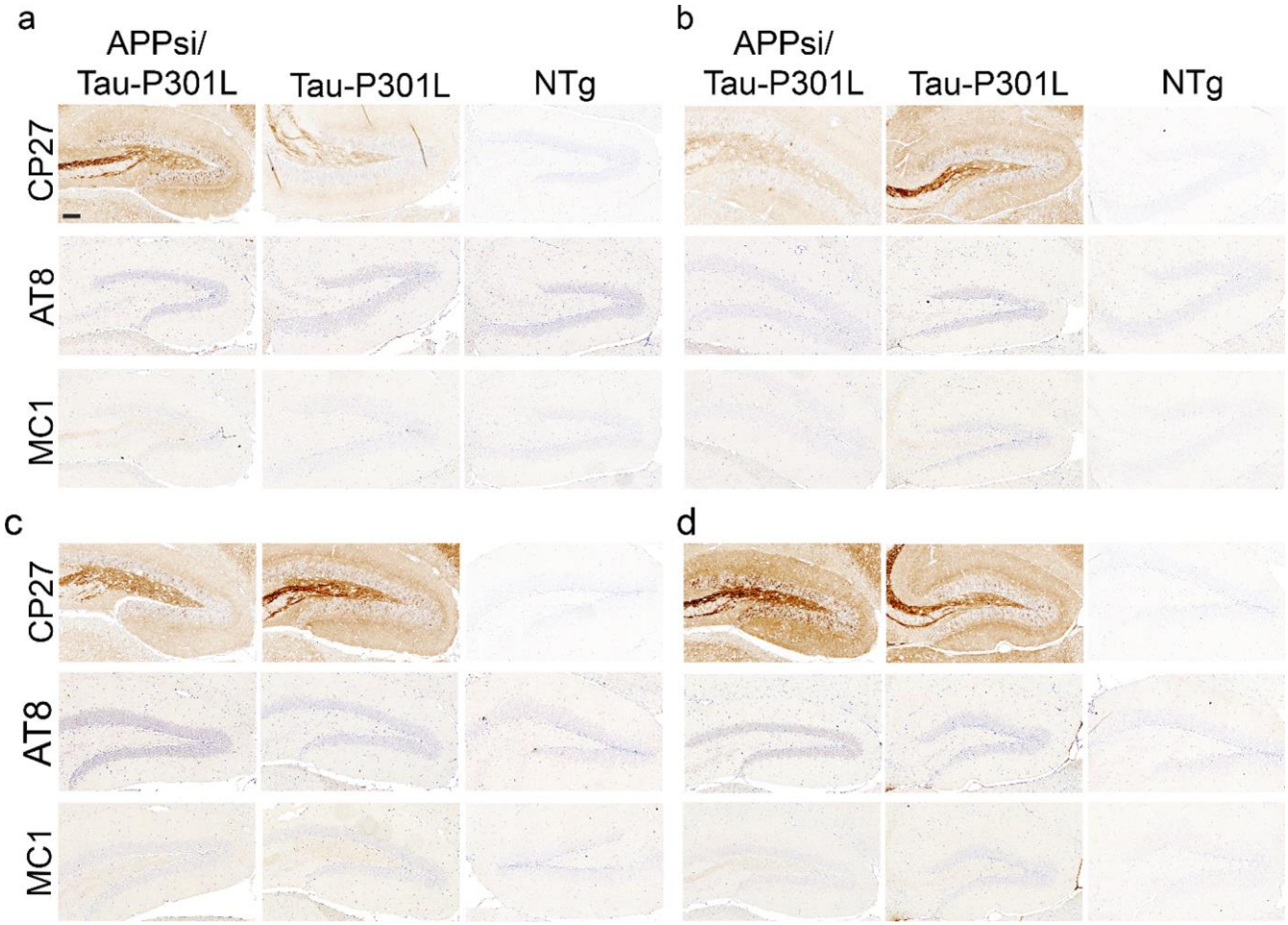


Fig. S9 Amyloid seeding did not induce tau pathology. Representative images of hippocampus of PrP.APPsi/Tau-P301L, Tau-P301L, and non-transgenic (NTg) mice injected with (a) AD 1, (b) AD 2, (c) NDC 1, and (d) NDC 2, aged 12 months. Brain sections were stained with tau antibodies, CP27 (anti-htau130-150), AT8 (anti-pSer202/pThr205), and MC1 (anti-tau313-322. Scale bar: 100 µm. The number of PrP.APPsi/Tau-P301L, Tau-P301L, or NTg mice injected with each lysate, respectively, were as follows: AD 1: n=3, n=3, n=3; AD 2: n=2, n=4, n=3; NDC 1: n=3, n=2, n=3; NDC 2: n=4, n=3, n=3.

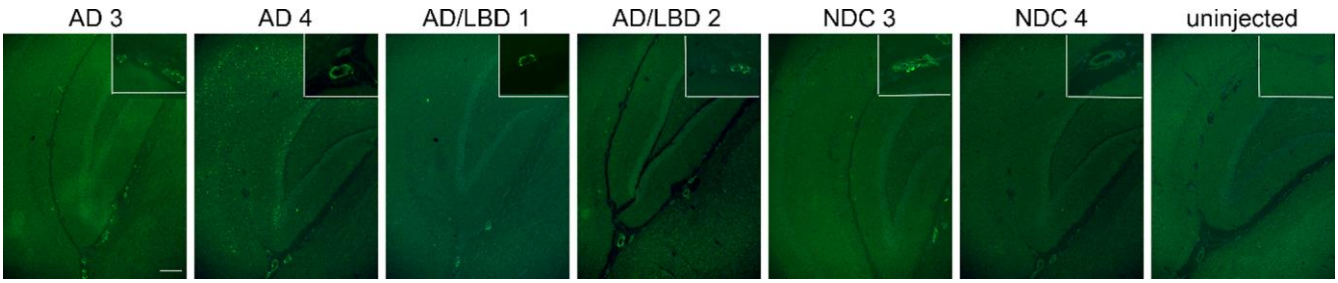


Fig. S10 Cerebral injection of AD and AD/LBD brain lysates with abundant CAA results in sparse Thio-S positive staining in blood vessels of PrP.APPsi/M20 mice. Newborn mice were injected with AD, AD/LBD, and NDC brain lysates and aged to 12 months. Representative brain sections stained with Thio-S. n=4-8. Scale bar: 100 µm, inset 40 µm.

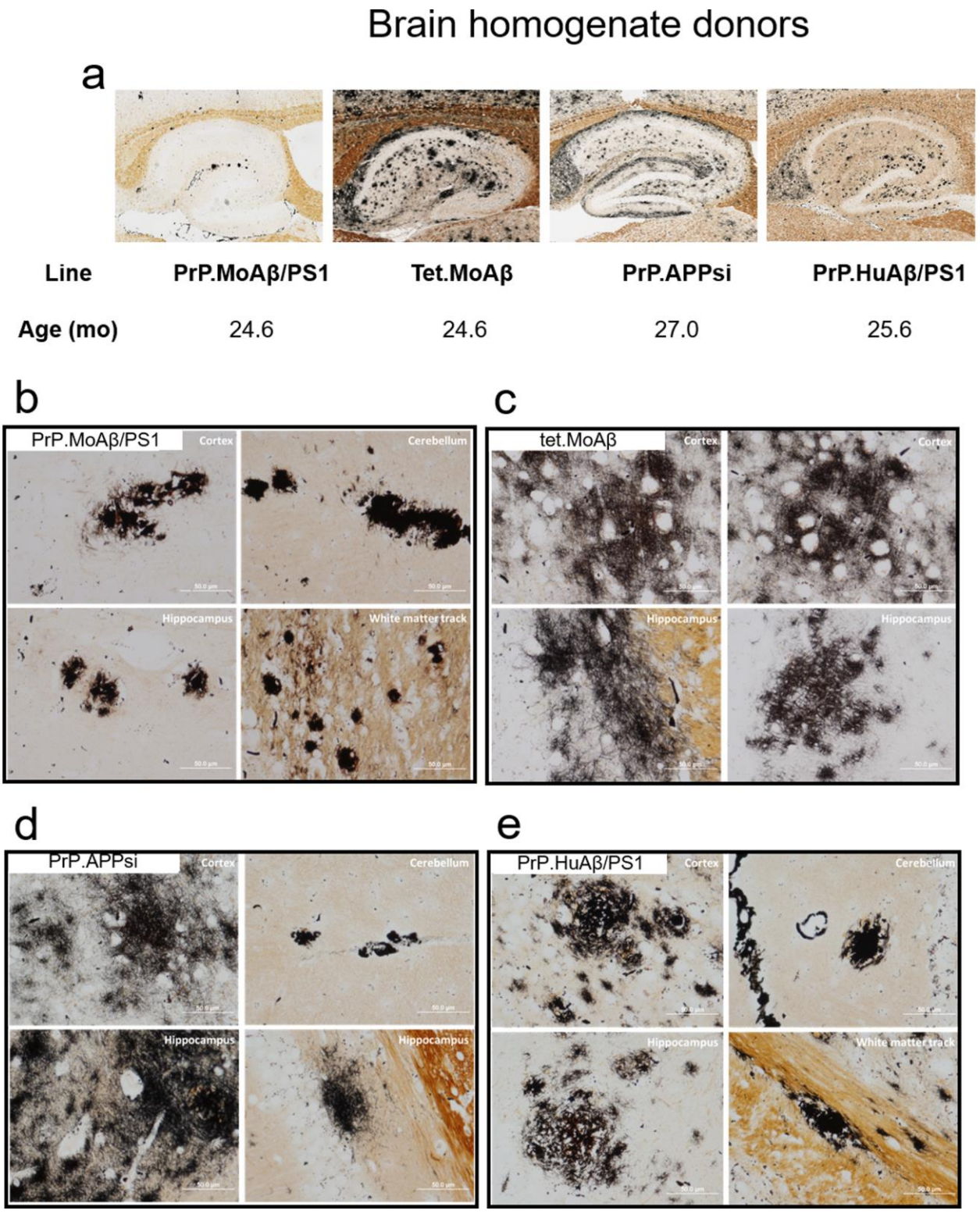


Fig. S11 Examples of Aβ pathology in the donor animals used to generate Aβ seeding inoculum. Each image in the figure was generated by Campbell-Switzer-silver staining as described in Methods. a) Low power images of hippocampal sections from each of the donor animals used to prepare inoculum. (b-e) High power images of pathology in cortex, hippocampus, cerebellum and white matter in PrP.MoAβ/PS1 mice (b) Tet.MoAβ mice (e) PrP.APPsi mice (d), and PrP.HuAβ/PS1 mice (e).