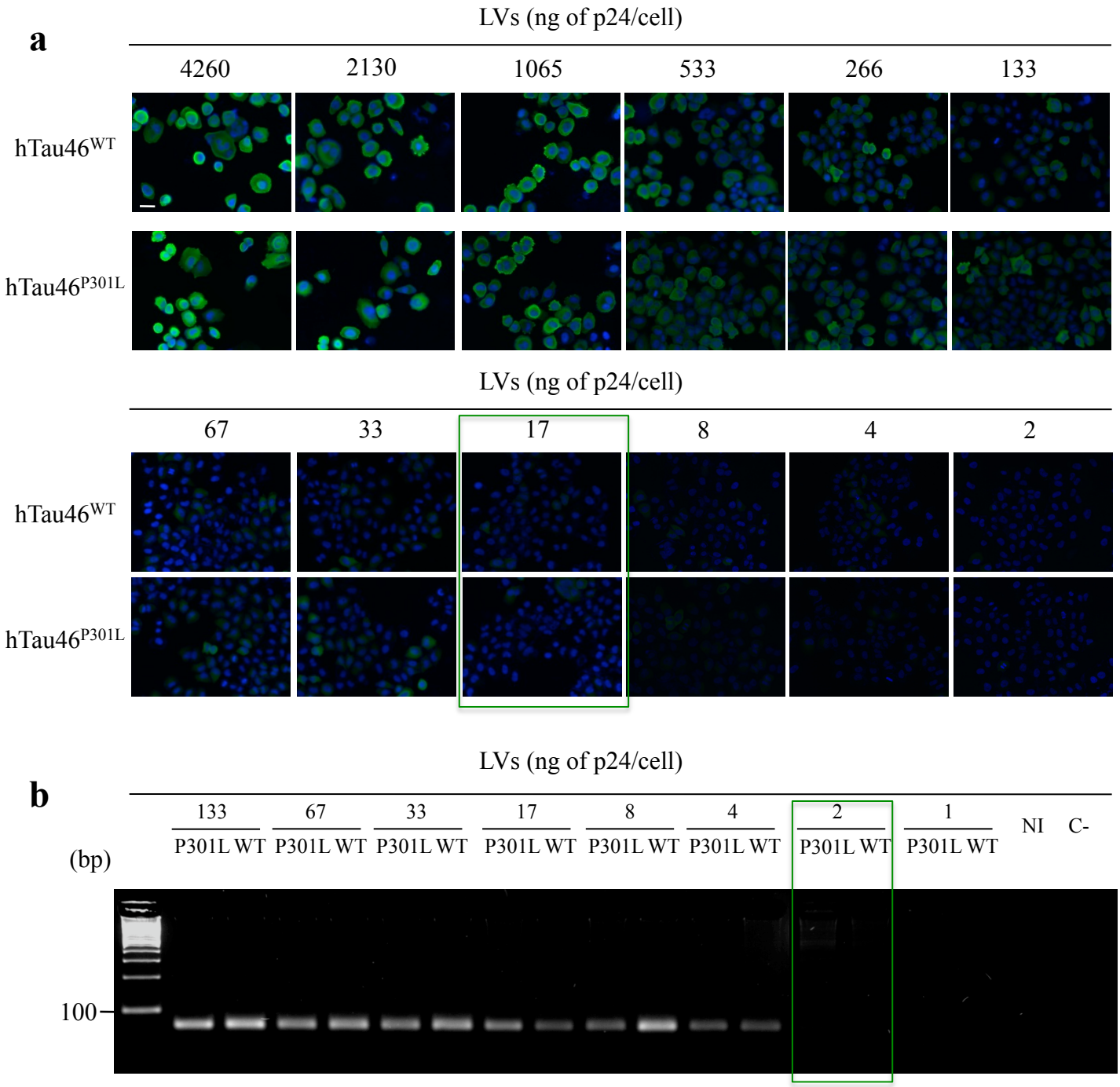
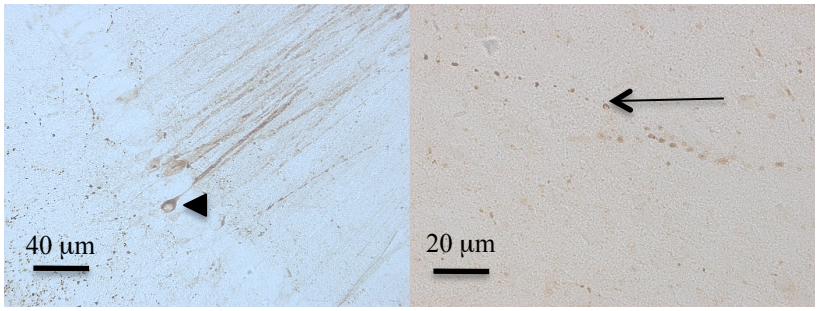


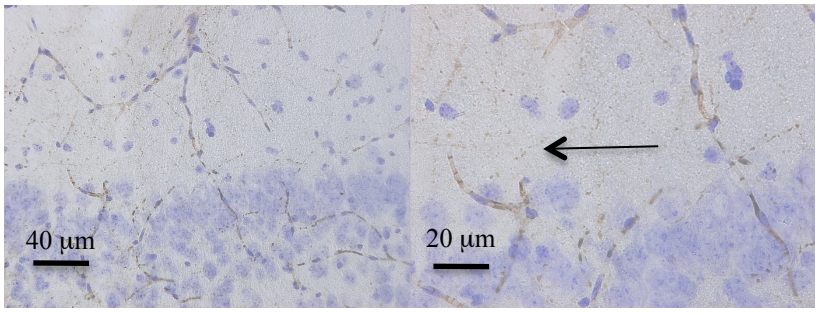
Supplementary figure 1: Equivalent viral titers of LVs-hTau46^{WT} and LVs-hTau46^{P301L}

(a)- HEK293 cells were transduced with increasing amounts of LVs (hTau46^{WT} or hTau46^{P301L}), and transgene expression was detected 48 h post-transduction by immunofluorescence using a rabbit antibody against the C-terminal portion of Tau (Tau C-Ter). hTau46^{WT} (upper panels) and hTau46^{P301L} (lower panels) were labeled using the corresponding Alexa Fluor 488-labeled secondary antibody. Scale bar: 10 µm. **(b)-** HEK293 cells were transduced with increasing amounts of LVs (hTau46^{WT} or hTau46^{P301L}), and total RNA was extracted from cells 48 h post-infection. The presence of the viral RNA was detected using primers specific to a lentiviral sequence, namely, the WPRE ('Woodchuck hepatitis Post-transcriptional Regulatory Element'). In (a) and (b), the green box indicates the viral doses from which the signal was no longer detected.

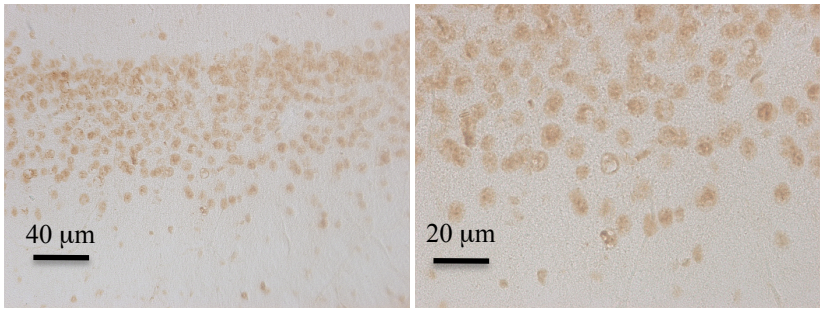
AT8, 8 months post-LV-injection



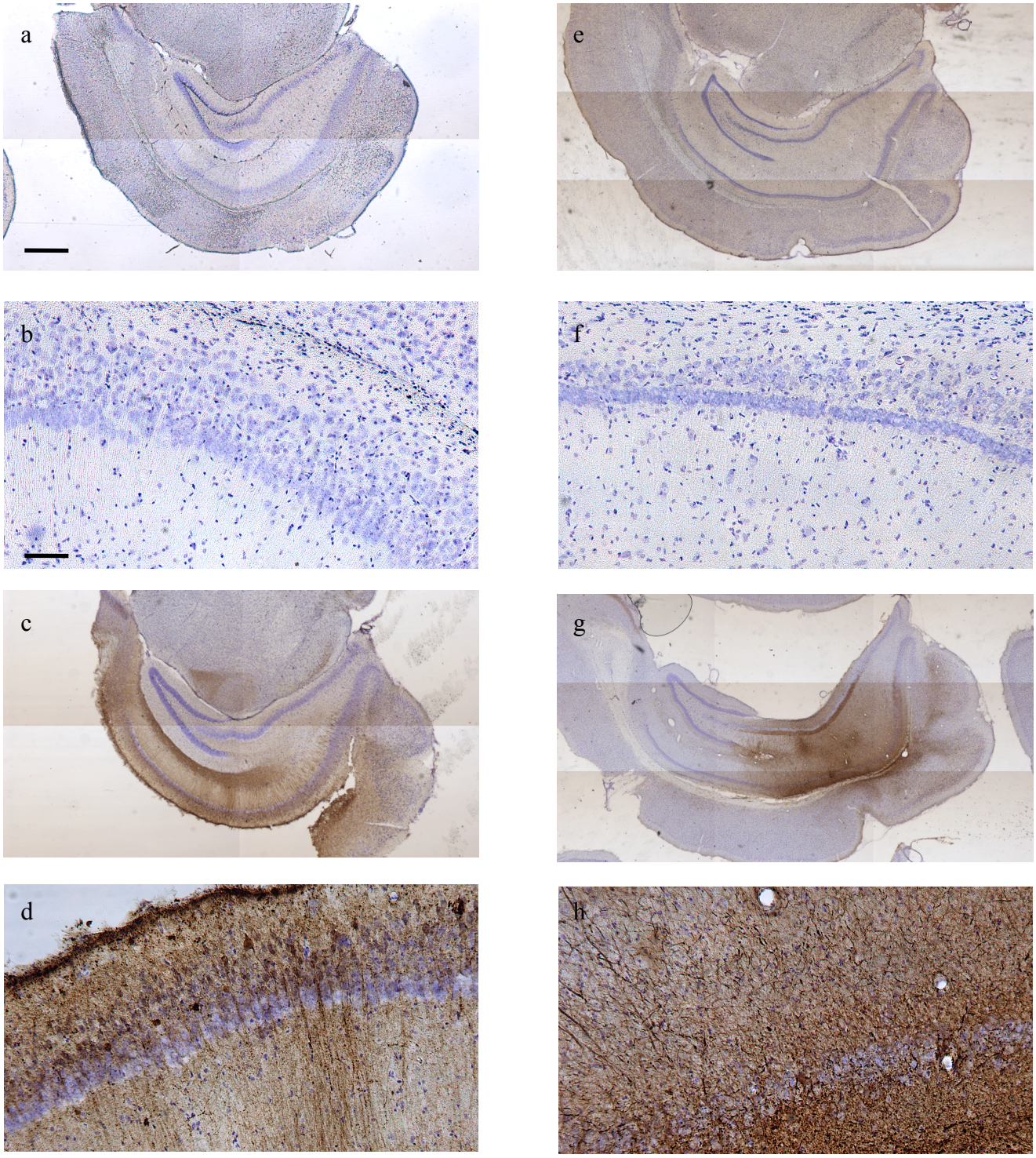
MC1, 8 months post-LV-injection



AT100, 8 months post-LV-injection



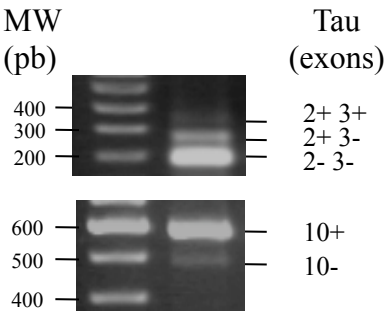
Supplementary figure 2: hTau46^{WT} does not drive Tau aggregation in mouse brains
LVs encoding hTau46^{46WT} were bilaterally injected into the CA1 layer of C57Bl/6 mouse brains. Eight months later, the animals were sacrificed, and their brains were processed for immunohistochemistry. Mouse brain sections through the hippocampus were incubated with the primary antibodies AT8, MC1 and AT100, which label hTau46^{WT}, and immunolabeling was completed using a biotinylated anti-mouse IgG. Cresyl violet staining was performed to localize neurons. Scale bars are indicated on the photomicrographs. Note the sparse neuritic labeling seen with AT8 and MC1 and the absence of labeling by AT100, indicating a lack of Tau aggregation.



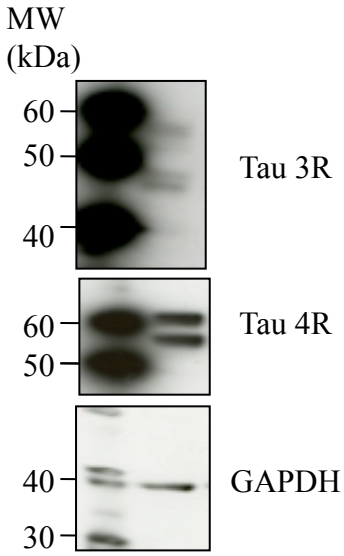
Supplementary figure 3: Tau is expressed at similar level in rat and mouse brains after lentiviral delivery

PBS, LVs encoding hTau46^{46WT} or eGFP was bilaterally injected into the CA1 layer of rat brains. Eight months later, the animals were sacrificed, and their brains were processed for immunohistochemistry. Mouse brain sections through the hippocampus were incubated with the primary antibody ADx215, which labels total Tau, and immunolabeling was completed using a biotinylated anti-mouse IgG. Cresyl violet staining was performed to localize neurons. Scale bars represent 250 µm for a, e, c and g and 80 µm for b, f, d and h.

a



b



Supplementary figure 4: The Wistar rat brain hippocampus expresses six Tau isoforms as seen in the human brain

(a)- PCR detection of Tau mRNA exon splicing in the hippocampus. Transcripts were detected using specific primers for exons 2+3+ (362 bp), 2+3- (275 bp), 2-3- (188 bp), 10+ (580 bp) and 10- (487 bp). **(b)-** Western blotting for 3- and 4-repeat (3R and 4R) Tau isoforms in hippocampal lysates was performed using specific antibodies.

In **(a)** and **(b)**, analyses were performed in 2-month-old, non-injected rats.