

TDP-43 Induced Mouse Model

C57BL/6 mice were injected into the motor cortex with adeno-associated viral (AAV) particles with serotype 9 that express human TDP-43 (AAV9-GFP-hTDP-43). Animals were 3 months of age at start and analyzed for 6 months. Control animals were injected with AAV9-GFP. AAV9-GFP-hTDP-43 injected animals show:

- Increased anxiety
- Learning deficits
- Early motor impairments
- Increased neuroinflammation
- Increased ubiquitination
- Neuronal loss

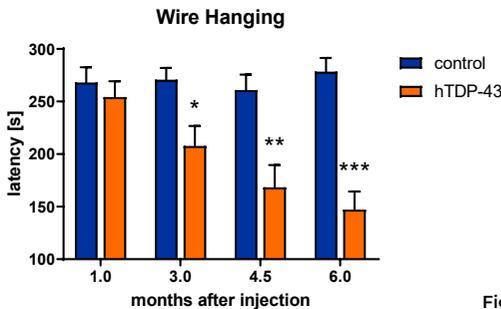


Figure 1: Wire hanging in AAV9-GFP-hTDP-43 and control mice. Latency to fall off the wire was measured. Two-Way-ANOVA with Bonferroni *post hoc* test. Mean + SEM. Control: n = 16, hTDP-43: n = 20. * p < 0.05, ** p < 0.01, *** p < 0.001.

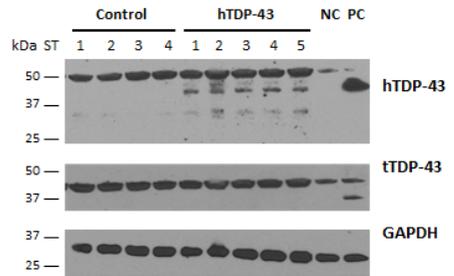


Figure 2: Western blot analysis of human and total TDP-43 expression in the cortex of AAV9-GFP-hTDP-43 and control mice 6 months after injection. Samples were homogenized in RIPA buffer. GAPDH as loading control. PC: positive control = hippocampal RIPA sample of transgenic TDP-43 mouse. NC: negative control = untreated wild type mouse.

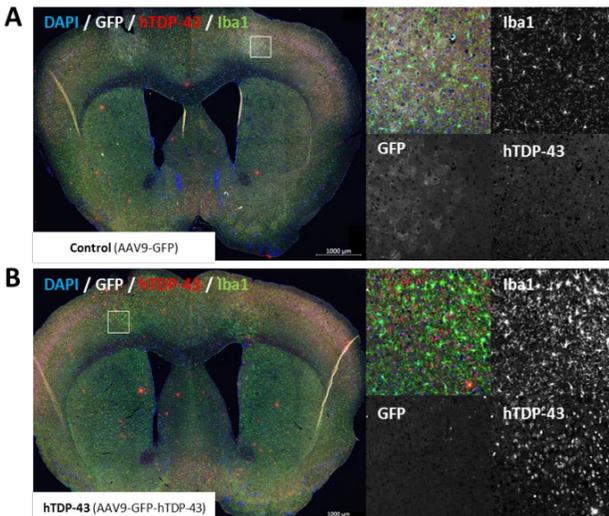


Figure 3: Immunolabeling of GFP (white), human TDP-43 (red), Iba1 (microglia marker, green) and nuclei (DAPI, blue) in the brain of AAV9-GFP-hTDP-43 injected and control mice. Coronal cut brain samples at 0.62 mm. White box: Area of injection magnified at the right. Virus was injected bilaterally into the motor cortex region M1 of 3 months old mice. Mice were sampled 6 months after injection.