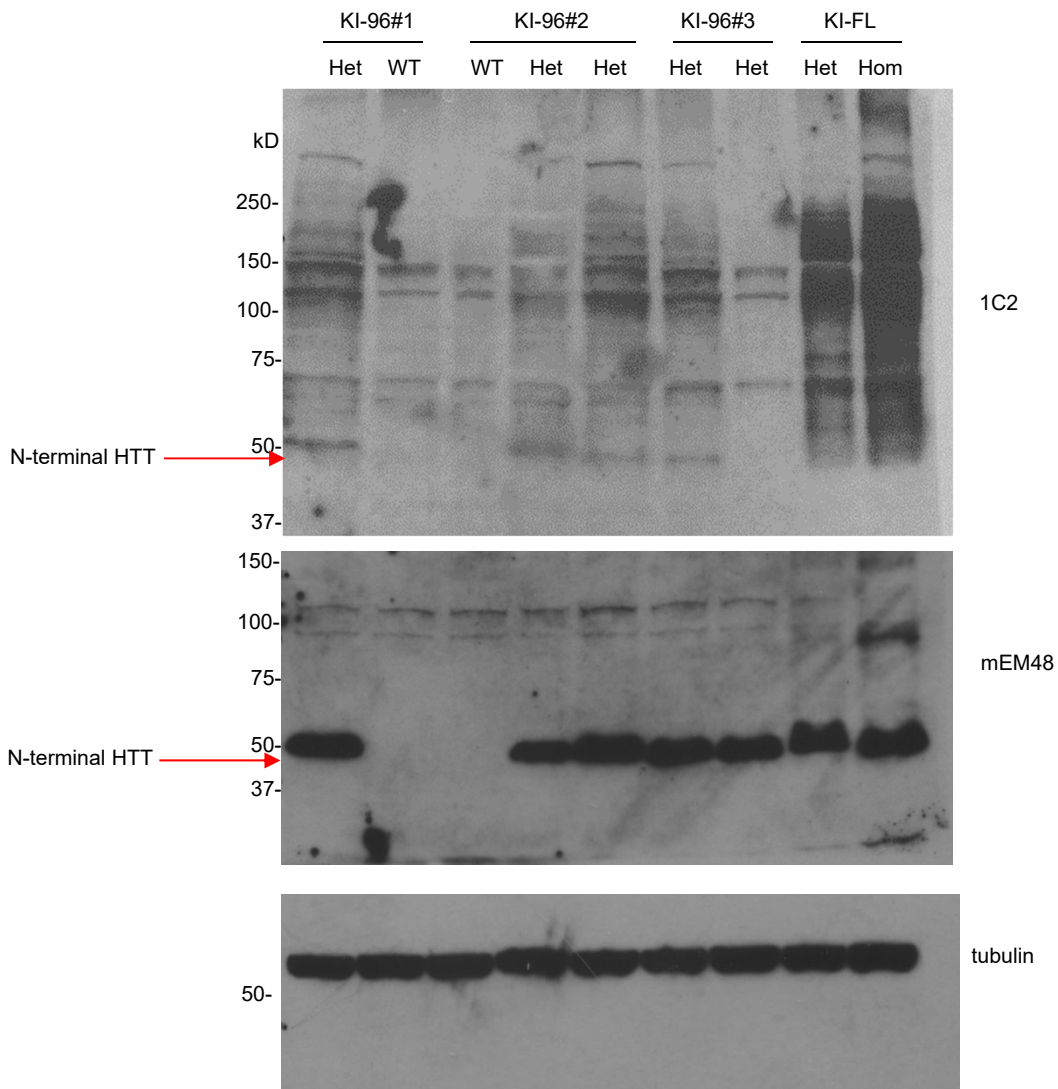
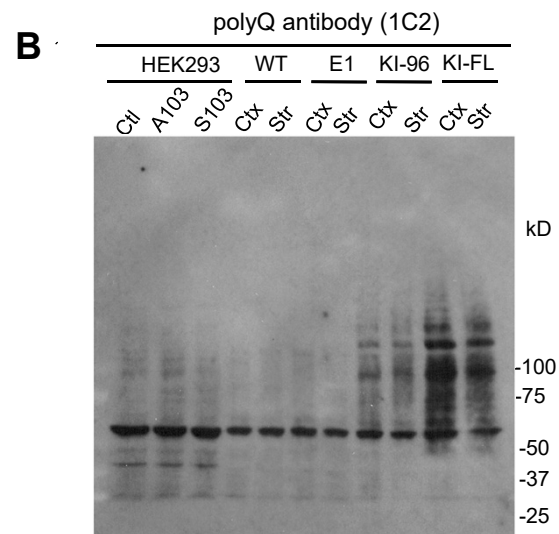
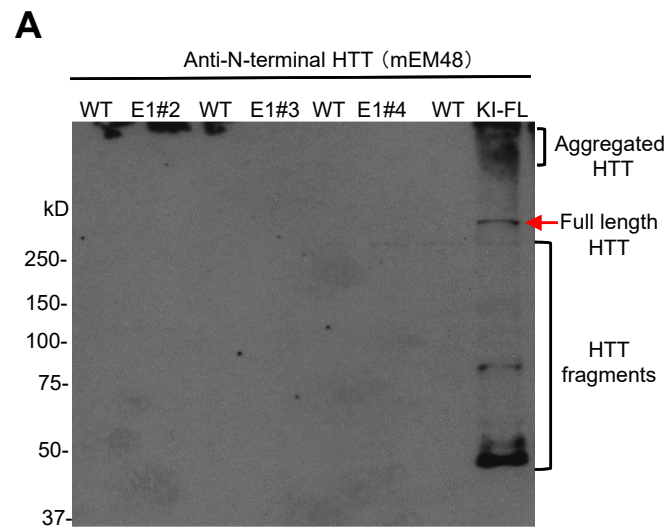


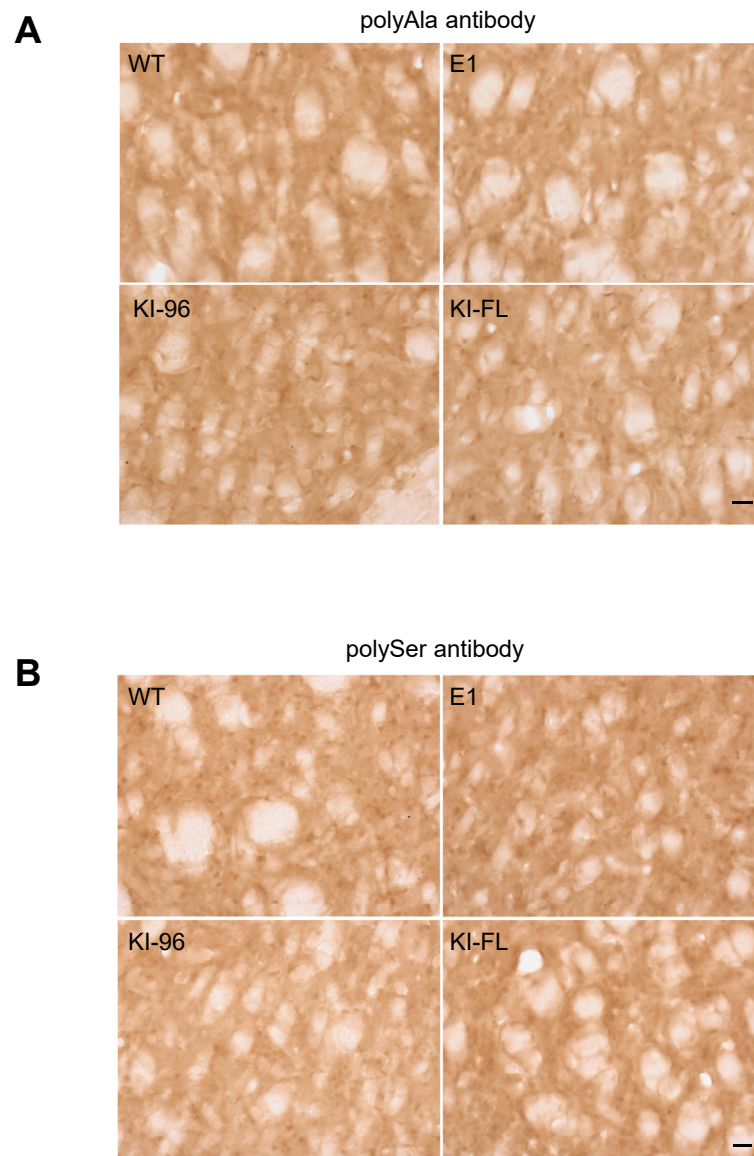
Supplemental Figure 1. (A) Sequencing results showing genomic mutations in different lines of E1 mice. (B) Sequencing results showing genomic mutations in different lines of KI-96 mice. Red arrows are used to indicate the locations of mutations.



Supplemental Figure 2. Western blotting analysis of the cortex tissues of KI-96 mice and full-length HD KI (KI-FL) mice. Anti-polyQ antibody (1C2) revealed full-length mutant HTT and a number of polyQ containing HTT fragments in KI-FL mouse brain. Only the smallest N-terminal HTT fragment is present in KI-96 mouse brains (upper panel). Mouse antibody to N-terminal HTT (mEM48) could clearly detect the smallest N-terminal HTT fragment in KI-96 and KI-FL mouse brains, but not in wild type (WT) mouse brain (middle panel).

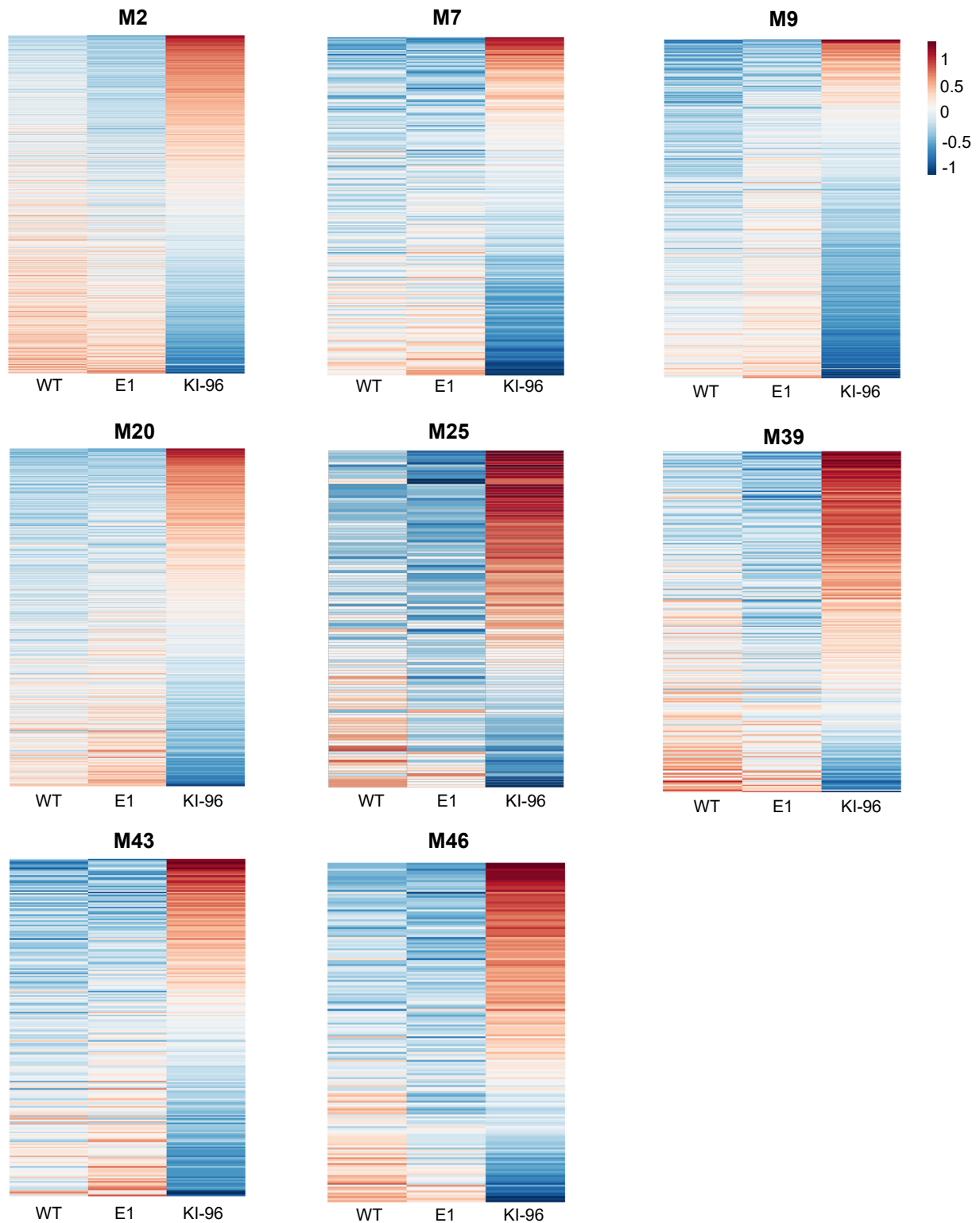


Supplemental Figure 3. (A) Western blotting analysis of HTT with polyQ expansion using mEM48 antibody in WT, E1 and KI-FL mice. **(B)** Western blotting analysis of HTT with polyQ expansion using 1C2 antibody in WT, E1, KI-96 and KI-FL mice.

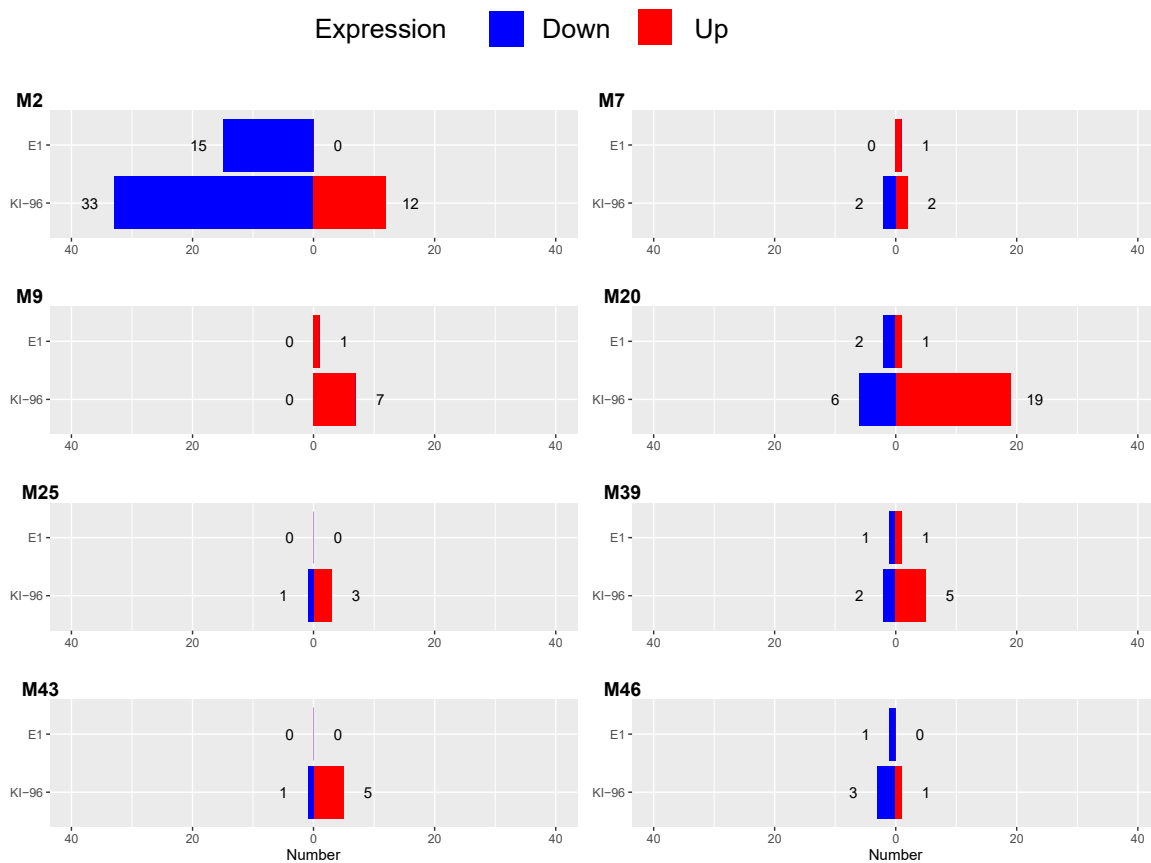


Supplemental Figure 4. (A) Immunohistochemistry of the striatum of WT, E1, KI-96 and KI-FL mice using polyAla antibody. **(B)** Immunohistochemistry of the striatum of WT, E1, KI-96 and KI-FL mice using polySer antibody. Scale bar: 50 μ m.

Supplemental Figure 5



Supplemental Figure 5. Heatmap view of gene expression in different striatum modules (M2: repeat-associated HD signaling; M7: cell death signaling; M9: mitochondria and transport; M20: UBI conjugation; M25: glutamate receptor signaling; M39: DNA repair; M43: fatty acid catabolic process; M46: glucocorticoid signaling).



Supplemental Figure 6. Overview of significantly changed genes in different striatum modules when comparing E1 or KI-96 mice to WT mice, respectively (M2: repeat-associated HD signaling; M7: cell death signaling; M9: mitochondria and transport; M20: UBI conjugation; M25: glutamate receptor signaling; M39: DNA repair; M43: fatty acid catabolic process; M46: glucocorticoid signaling).