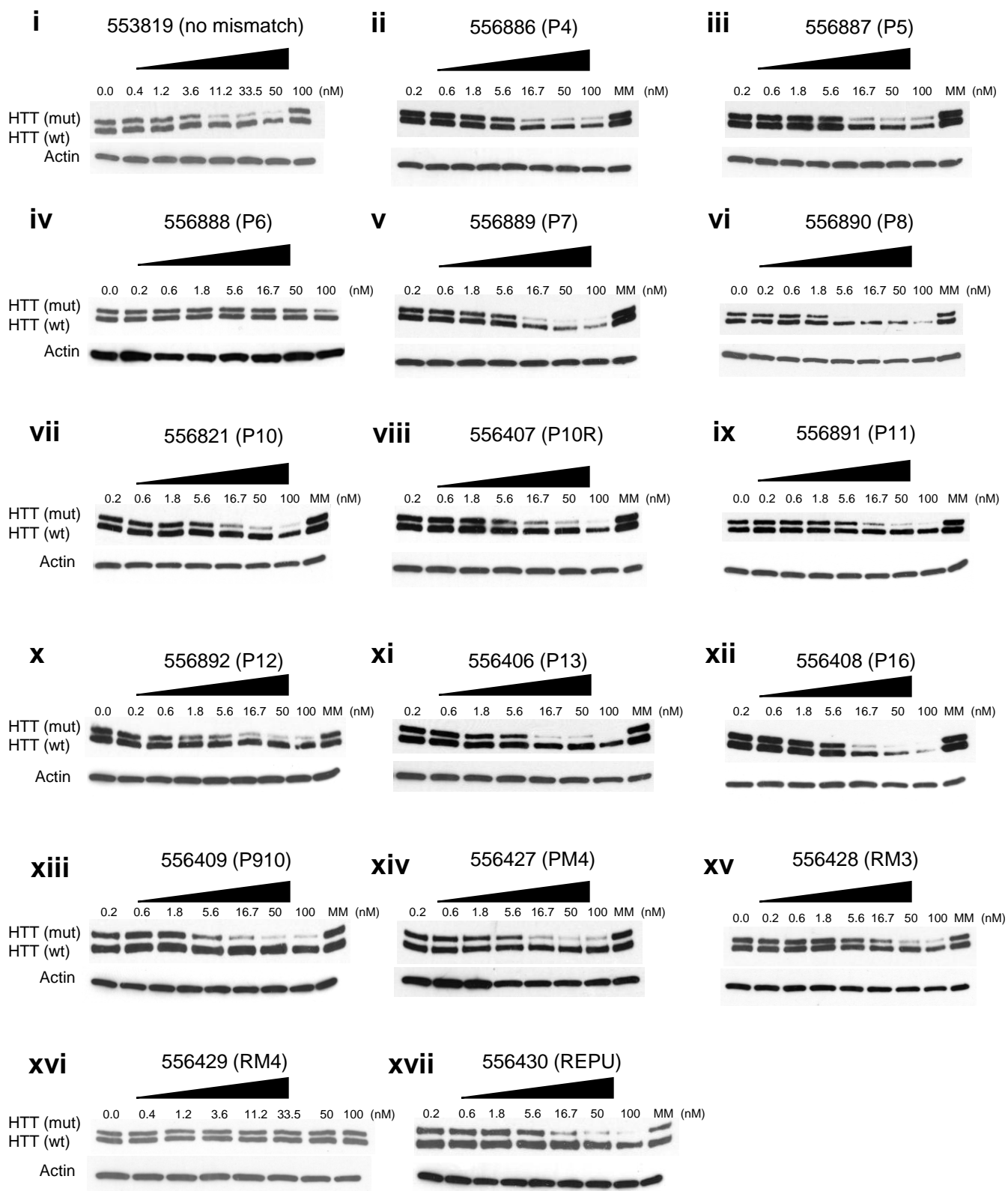


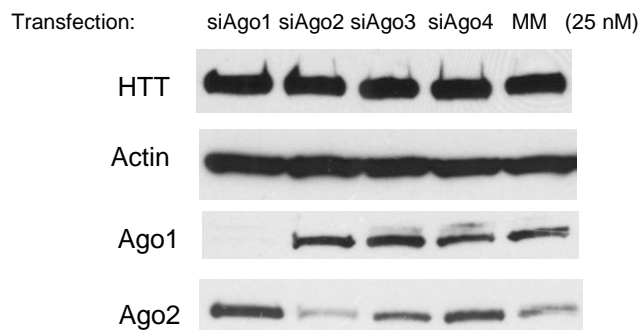
# Supplemental Figure 1



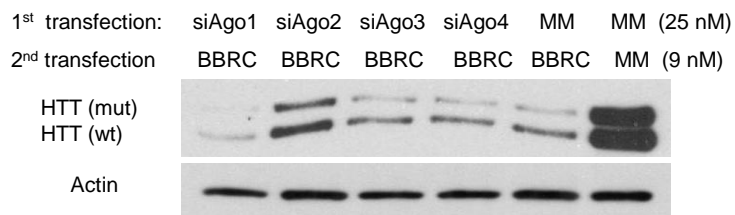
**Supplementary Figure S1. Western analysis of the effects on HTT expression of ss-siRNAs with mismatched bases at different positions, related to Figure 1.** Inhibition of HTT expression by ss-siRNAs with mismatched bases at: (i) none, (ii) P4, (iii) P5, (iv) P6, (v) P7, (vi) P8, (vii) P10, (viii) P10R, (ix) P11, (x) P12, (xi) P13, (xii) P16, (xiii) P9,10, (xiv) P9,10,11, (xv) P4,10,16, (xvi) P3,8,13,17, (xvii) none (different registry). Representative western blot images are presented. MM: an RNA duplex containing multiple mismatches at 50 nM.

## Supplemental Figure 2

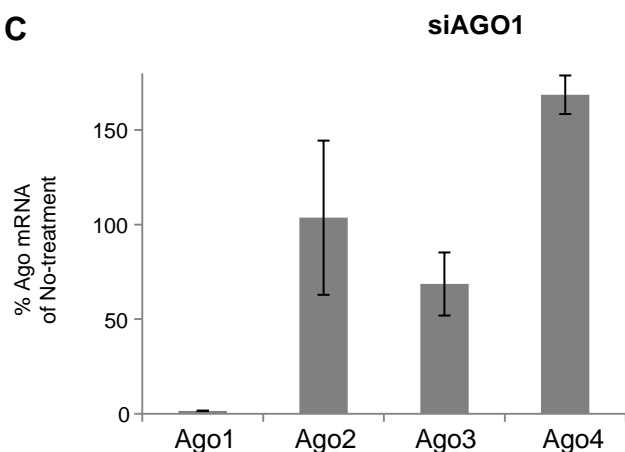
**A**



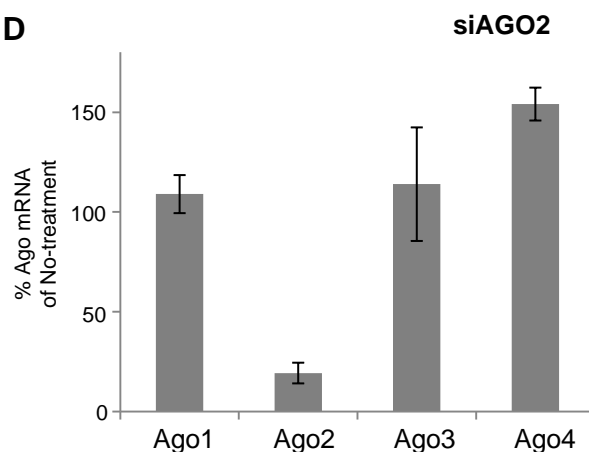
**B**



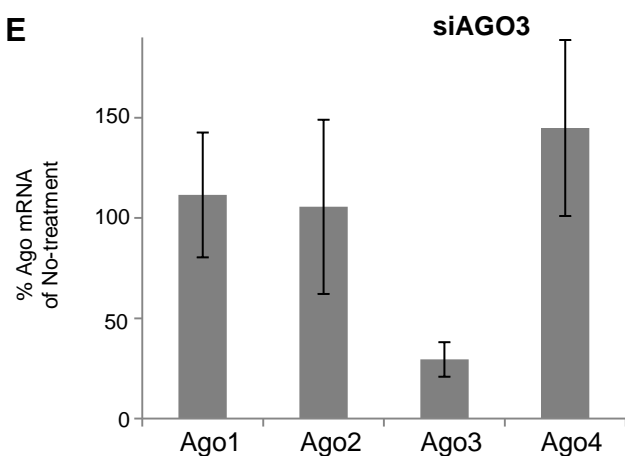
**C**



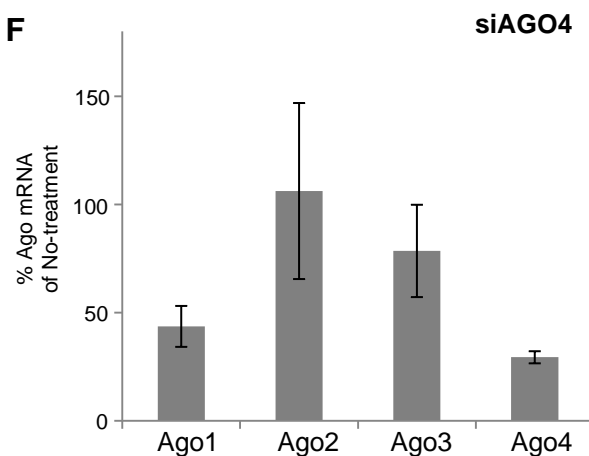
**D**



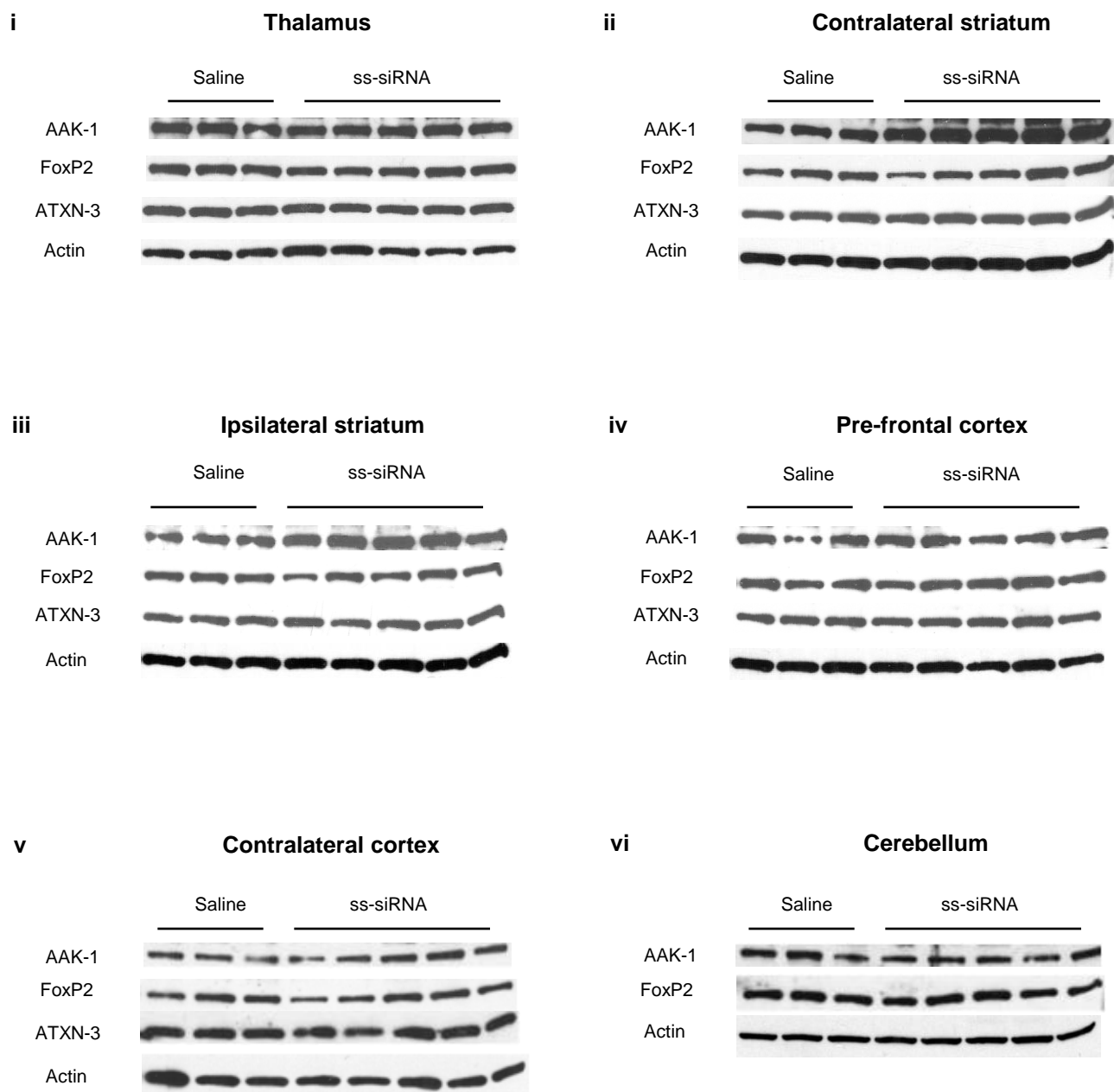
**E**



**F**



**Figure S2, knockdown efficiencies of AGO1-4 by siRNAs, related to Figure 2.** (A) AGO1 and AGO2 knockdowns by siRNA shown by western blot. (B) AGO2 reversal was sufficient to reverse HTT knockdown by BBRC, a canonical siRNA duplex targeting HTT outside of CAG-repeat region. (C-F) AGO1-4 knockdowns by siRNAs (25nM) shown by Q-PCR with relative Ago mRNA levels normalized to no treatment samples. Error bars represent standard error of the mean (SEM) from three independent experiments.



**Figure S3. Protein levels of several CAG-repeat-containing genes after ss-siRNA treatments in various mouse brain tissues, related Figure 5.** No significant changes are observed in the several poly-Q peptides after *in vivo* administration of ssRNA 537775 in: (i) thalamus; (ii) contralateral striatum; (iii) ipsilateral striatum; (iv) pre-frontal cortex; (v) contralateral cortex; (vi) cerebellum.