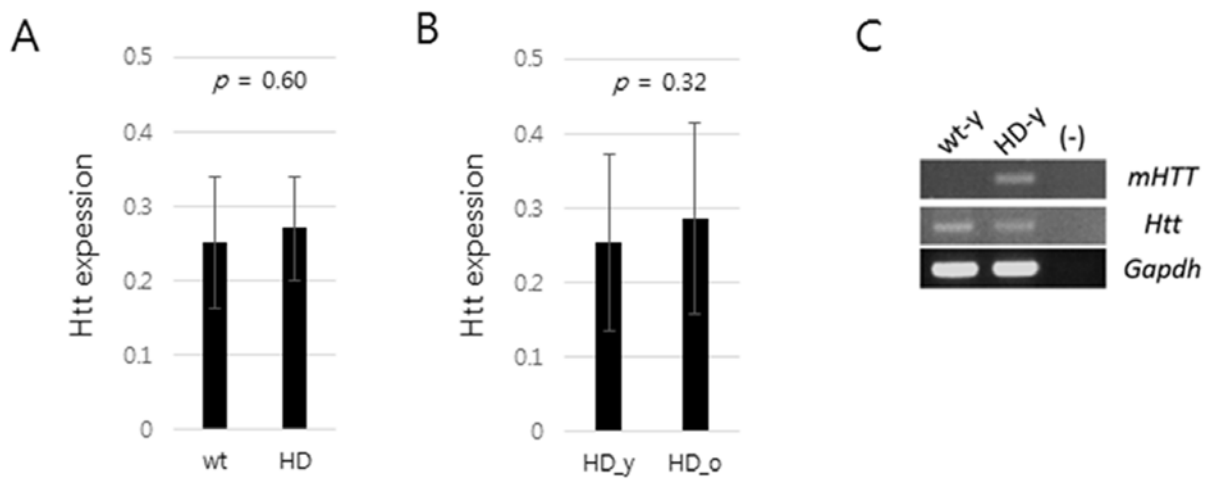
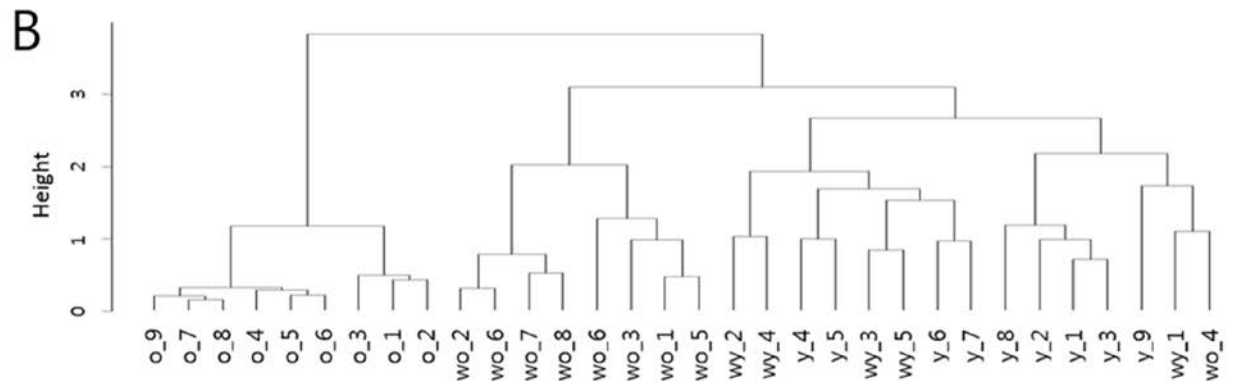
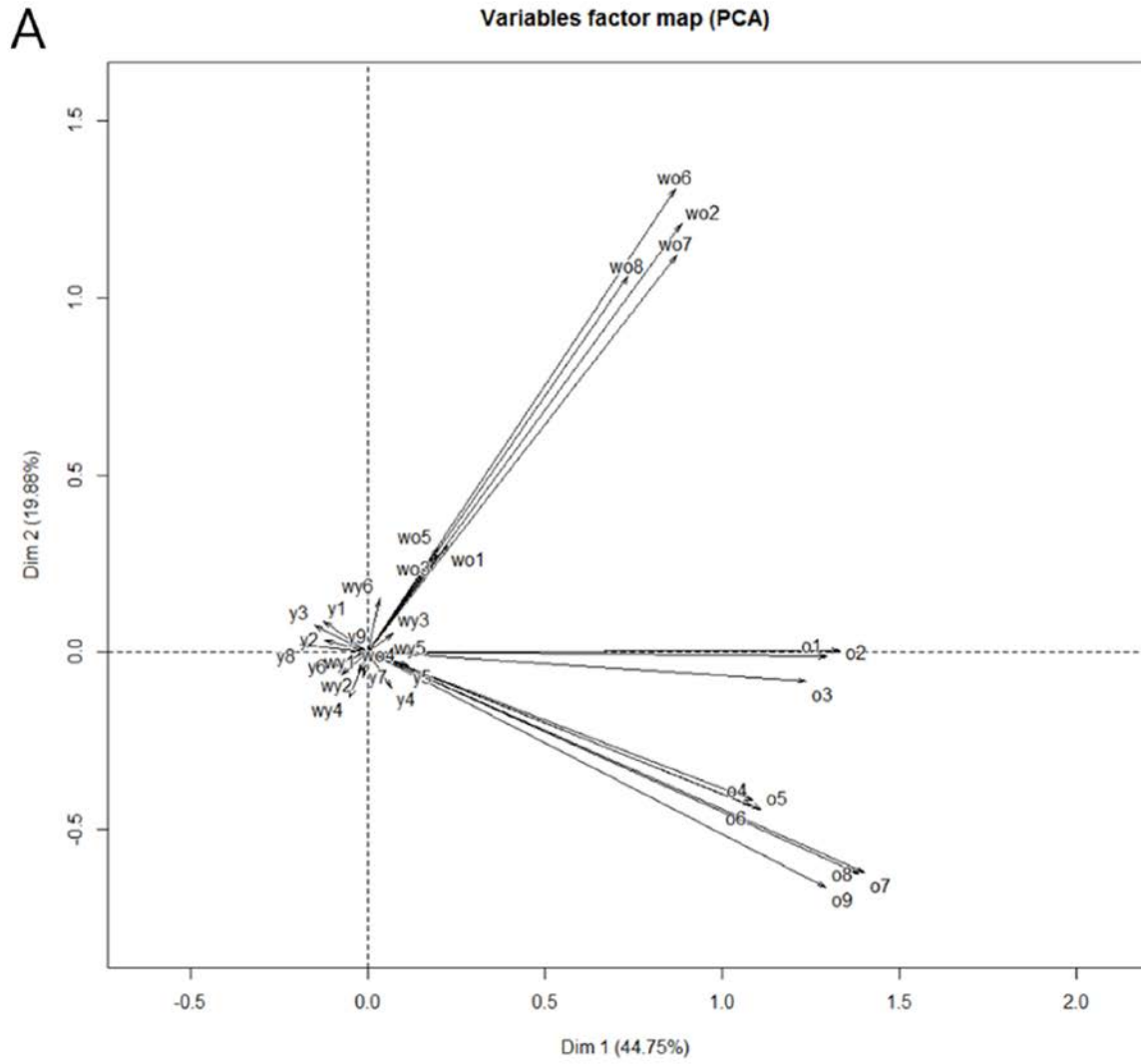


## SUPPLEMENTARY MATERIALS

### Supplemental Figures.



**Figure S1. Huntingtin (*Htt*) expression in wild-type (wt) and mouse models of Huntington's disease (HD).** (A) *Htt* expression levels in splenic T cells from wt and HD mice. Average expression levels of young and aged mice were calculated. (B) *Htt* levels in young (HD\_y) and aged (HD\_o) HD mice. (C) Detection of human mutant *HTT* (*mHTT*) and endogenous *Htt* gene expression in HD mice. (-), no template control.

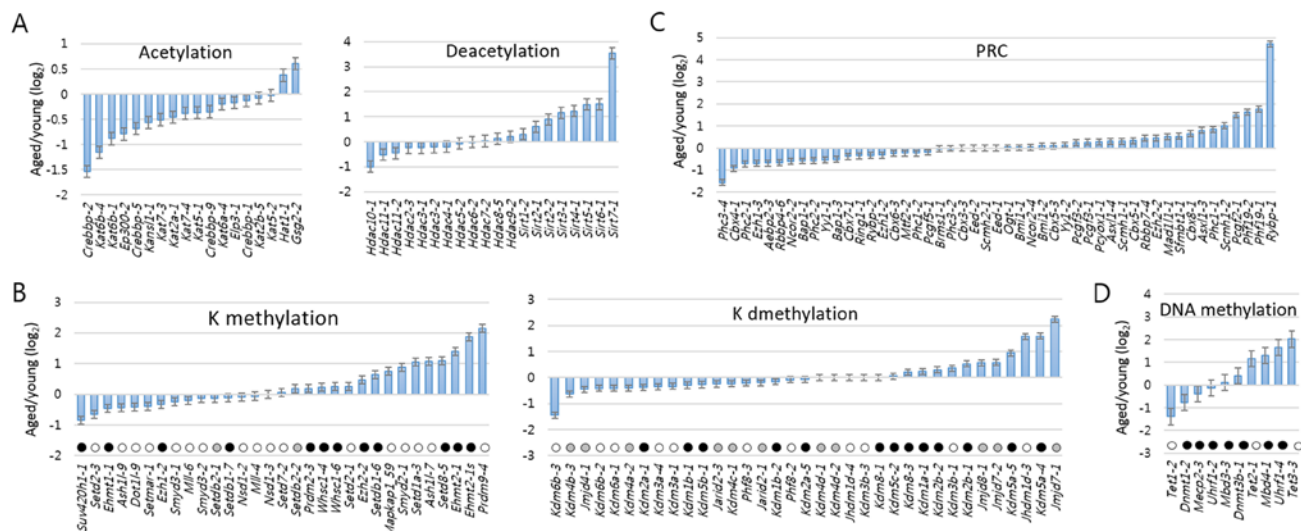


**Figure S2. Correlation analysis.** (A) Principal component analysis (PCA). Four groups are included: wild-type young (wy), wild-type old (wo), Huntington's disease (HD) young (y), and HD old (o). (B) Unsupervised cluster analysis.

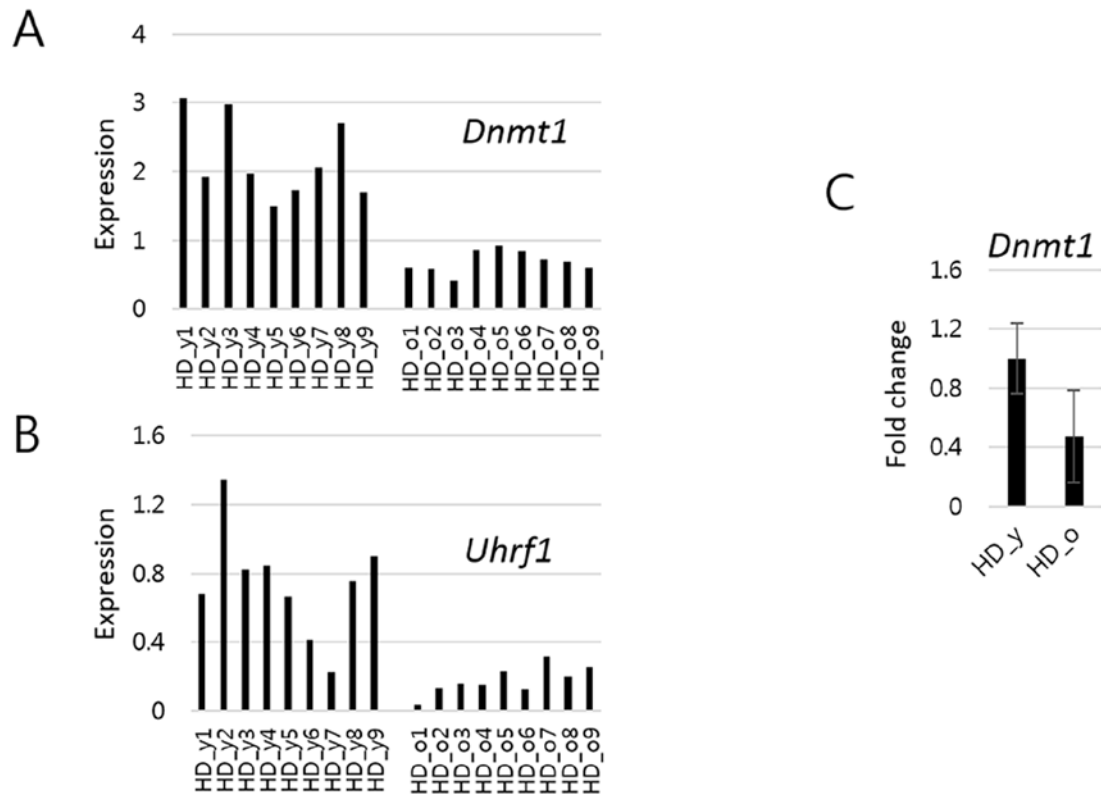
Gene id	Category	No. Count	M/R ratio* in young	M/R ratio* in aged	log <sub>2</sub> FC	P-val	FDR
Ig1_55	Ageing	510	0.004	0.392	6.515	1.39E-16	4.41E-14
Clu_2	Ageing	13224	0.046	1.457	4.980	1.4E-12	2.23E-10
PADI4_1	Arg_meth	3139	0.002	0.205	6.530	4.02E-12	4.26E-10
Clu_1	Ageing	1268	0.041	0.636	3.951	5.89E-08	0.0000468
PRMT6_1	Arg_meth	919	0.041	0.591	3.847	0.00000116	0.0000739
Cd44_1	Ageing	2140	0.010	0.195	4.248	0.00000057	0.0000302
Casp1_2	Ageing	5674	0.353	2.104	2.577	0.000000977	0.0000444
RPRD1A_2	etc	5537	0.066	0.821	3.644	0.00000123	0.000049
Casp1_1	Ageing	14597	0.870	5.325	2.613	0.00000431	0.000152169
RNF38_5	Ubiq	2148	0.109	1.130	3.378	0.0000193	0.000612567
Il6_1	Ageing	1428	0.007	0.131	4.138	0.0000591	0.001708404
JMJD7_1	Lys_demeth	3779	0.323	1.534	2.246	0.000338713	0.008975895
Rel_26	Ageing	1733	0.145	0.944	2.704	0.000437244	0.009931695
Ier3_1	Ageing	463	0.129	0.855	2.724	0.000426953	0.009931695

\* M/R ratio, the ratio of the mouse sequence counts relative to the rat's counts

**Figure S3. Differentially expressed target sequences between wild-type young and aged mice.** Gene id, gene symbol\_amplicon number. Expression level of each amplicon was measured by calculating the ratio (M/R) of cDNA counts relative to rat spike-in counts. No Count, the number of read count of each amplicon. FC, fold change. FDR, false discovery rate.



**Figure S4. Fold changes in the amount of amplicons in aged wild type mice compared to young mice.** Fold changes were measured for the epi-driver gene amplicons in the categories of acetylation and deacetylation (A), lysine (K) methylation and K demethylation (B), Polycomb-repressive complex (PRC) (C), and DNA methylation (D). In B and D, amplicons are differentially marked according to the modification effects of their proteins on chromatin accessibility: open circles indicate increased accessibility; solid circles indicate reduced accessibility; and grey circles for cases involving either increased or reduced accessibility.



**Figure S5.** Amplicon levels of *Dnmt1* (A) and *Uhrf1* (B) in young and aged mouse models of Huntington's disease (HD\_y and HD\_o, respectively). (C) quantitative real-time PCR analysis of *Dnmt1* gene expression.