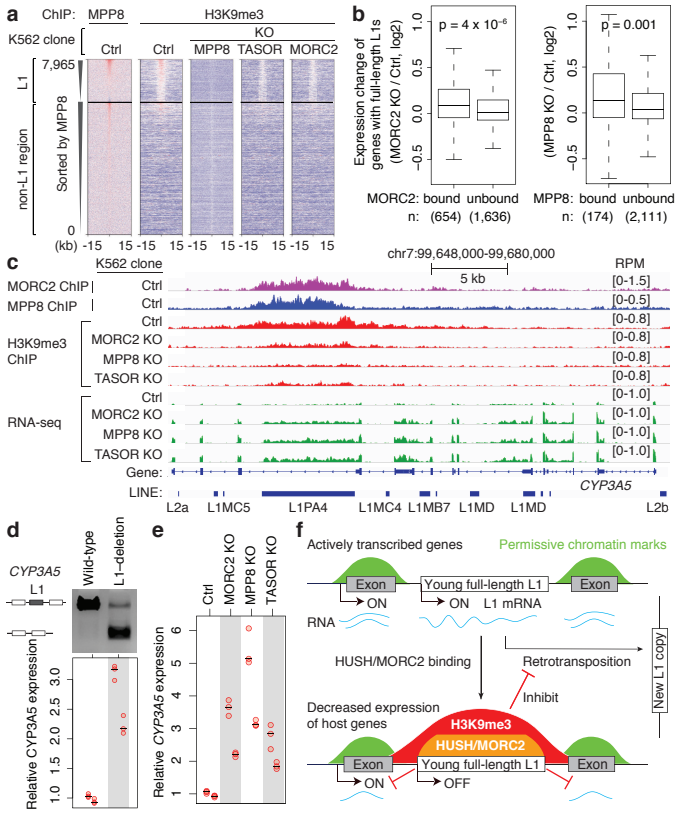

Figure 4 | HUSH/MORC2 binding at L1s decreases active host gene expression. a. Heatmaps showing MPP8 and H3K9me3 ChIP signal enrichment, centered on MPP8 and MORC2 summits and separated by L1 presence or absence. b. Expression change of genes with intronic full-length L1s that are bound or unbound by MORC2 or MPP8 (RNA-seq reads from KO K562 clones compared to Ctrl). Box plots show median and interquartile range (IQR), whiskers are 1.5× IQR. p-value, two-sided Mann-Whitney-Wilcoxon test. c. Genome browser tracks: HUSH/MORC2 loss causing H3K9me3 decrease at the target L1 and expression increase at both the target L1 and its host gene, independently repeated once with similar results. d. Deleting the target intronic L1 from *CYP3A5* in K562 increases *CYP3A5* expression, by RT-qPCR normalized to wild-type sample. n = 2 biological replicates x 3 technical replicates (center value as median). Gel image confirms L1 deletion; two experiments repeated independently with similar results. e. RT-qPCR for *CYP3A5* expression in K562 clones, normalized to Ctrl. n = 2 biological replicates x 3 technical replicates (center value as median). f. Model: HUSH/MORC2 bind young full-length L1s within transcriptionally active genes, and promote H3K9me3 deposition at target L1s to silence L1 transcription. This pathway not only inhibits L1 retrotransposition, but also decreases host gene expression.