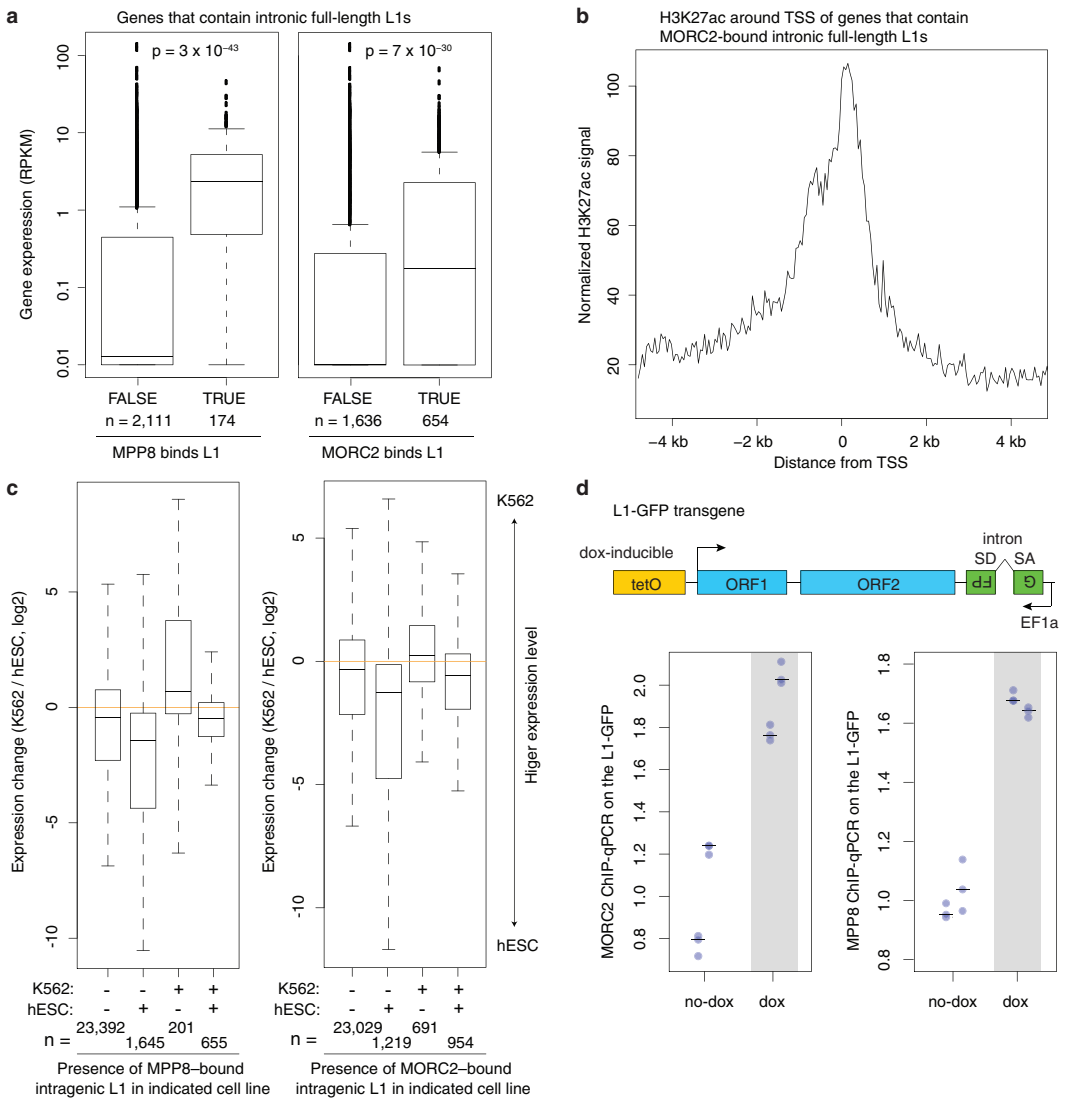

Extended Data Figure 8 | HUSH/MORC2 preferentially bind intronic L1s within actively transcribed genes. a. Genes that contain MPP8 or MORC2 bound intronic L1s are expressed at significantly higher levels in Ctrl K562 cells, compared to genes that contain intronic full-length L1s unbound by MPP8 or MORC2. p-value, two-sided Mann-Whitney-Wilcoxon test. Box plots show median and interquartile range (IQR), whiskers are 1.5× IQR. b. The promoters of genes that contain MPP8 or MORC2 bound intronic full-length L1s are marked by transcriptionally permissive H3K27ac in wild-type K562 cells. H3K27ac ChIP-seq data are taken from K562 epigenome pilot study, accession number PRJEB8620. TSS, transcription start site. c. Genes selectively occupied by MORC2/MPP8 either in K562 or in hESC cells exhibit higher gene expression in the corresponding cell line (p-values = 4.3×10^{-107} for MPP8 binding; p-values = 5.0×10^{-92} for MORC2 binding, Kruskal-Wallis test). Boxplots defined as in panel a. RNA-seq datasets for hESC are from SRA entries SRR2043329 and SRR2043330. d. ChIP-qPCR assays quantifying HUSH/MORC2 binding to an inducible L1 transgene in K562 cells before or after its transcriptional induction via Dox. Transcriptional induction increases binding of MORC2 and MPP8 to the L1 transgene. n = 2 biological replicates x 3 technical replicates (center value as median).