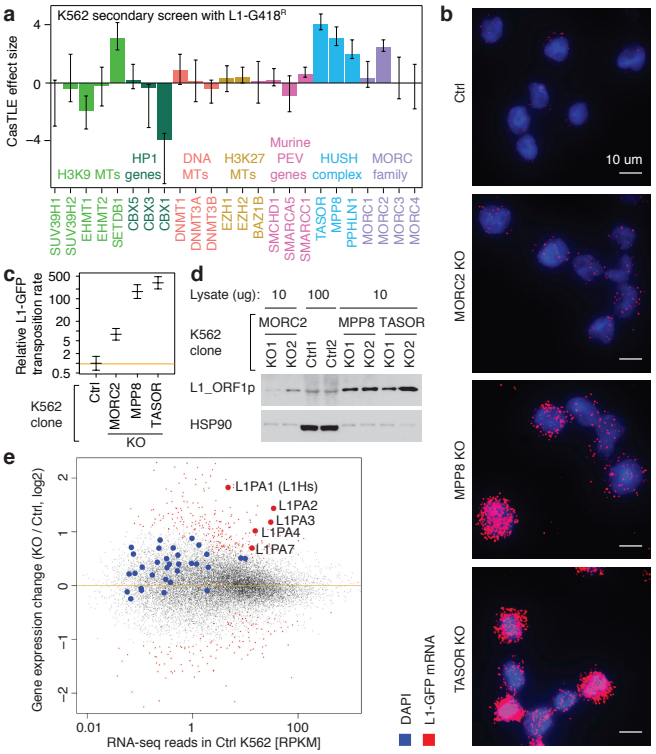

Figure 2 | HUSH and MORC2 silence L1 transcription to inhibit retrotransposition. a. The maximum effect size (center value) of indicated heterochromatin regulators, estimated by CasTLE from two independent K562 secondary screens with 10 independent sgRNAs per gene. Error bars, 95% credible intervals. b. Visualization of L1-GFP mRNAs in dox-induced K562 clones, from single smFISH experiment that was independently repeated twice with similar results. See also Extended Data Fig. 4d,e. c. L1-GFP retrotransposition rate[18] (center value) in K562 clones, from logistic regression fit of the GFP(+) cell counts at 7 time points (0, 5, 10, 15, 20, 25, 30 days post-induction) and two independent clones per gene. Over 200 GFP(+) cells per cell count. Data normalized to Ctrl. Bar, 95% credible interval. d. Endogenous L1_ORF1p level in K562 clones by western blots, HSP90 as loading control. Three experiments repeated independently with similar results. e. RNA-seq read counts from MORC2 KO, MPP8 KO and TASOR KO K562 clones, compared to Ctrl RNA-seq reads. n = 6 + 2 biologically independent RNA-seq experiments). Dots represent transcripts; large dots represent L1 transcripts. Red, significant changes (padj < 0.1, DESeq analysis); blue and gray, insignificant changes.