



Extended Data Figure 10 | HUSH/MORC2 binding at intronic L1s results in the decreased expression of active host genes. a. Genome browser tracks illustrating loss of HUSH/MORC2 causing decreased H3K9me3 over the intronic L1PA5 element and concomitant increase in the expression of host gene *RABL3*. Experiment was repeated once with similar results. b. Loss of HUSH/MORC2 leads to increased Pol II signals at 5'UTR and decreased Pol II signals within L1 bodies at HUSH-bound L1PA elements (orange bars). Heatmaps show Pol II density change in KO K562 clones compared to Ctrl, centered on the L1 5' end and sorted by MPP8 ChIP signal. c. Deletion of the intronic L1 within *RABL3* causes

increased *RABL3* expression. Upper panel: an agarose gel analysis of the PCR assay with primers flanking the HUSH/MORC2-bound intronic L1; two experiments repeated independently with similar results. Lower panel: RT-qPCR analysis of *RABL3* expression. The *RABL3* expression level was normalized to beta-actin mRNA. All samples were then normalized to wild-type sample. $n = 2$ biological replicates \times 3 technical replicates (center value as median). d. Depletion of MORC2, MPP8, TASOR increases *RABL3* expression. RT-qPCR data normalized as in panel c). $n = 2$ biological replicates \times 3 technical replicates (center value as median).