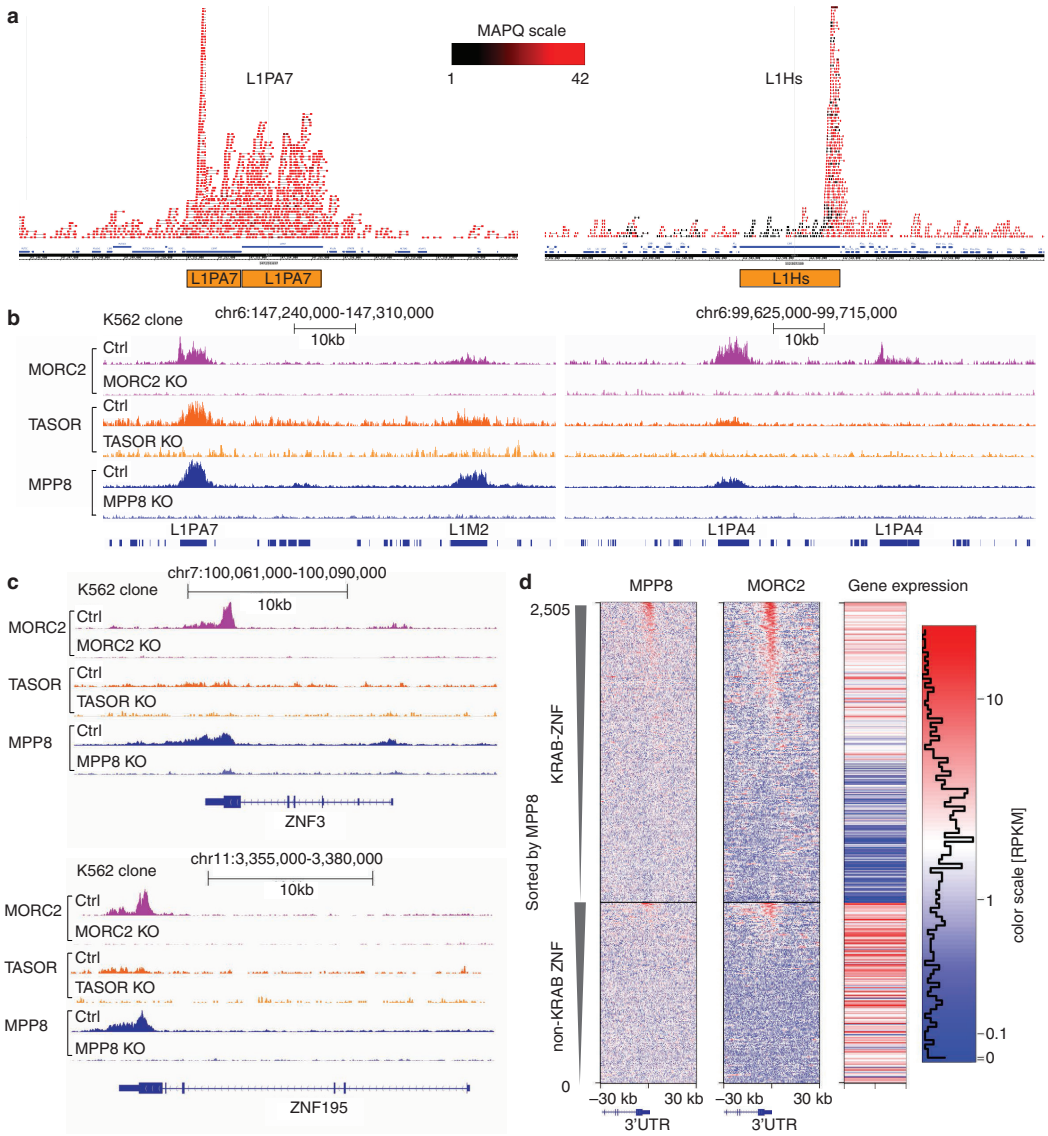

Extended Data Figure 5 | The binding profiles of MORC2, MPP8 and TASOR revealed by ChIP-seq in K562 cells. a. Using a paired-end sequencing strategy for the ChIP-seq, together with the sequence divergence within native L1 elements, we could map ChIP-seq reads to individual L1 instances in the genome. Genome browser snapshots of MORC2 ChIP-seq reads alignment over L1PA7 (left) and L1Hs (right). Experiment was repeated once with similar results. Color scale indicates mapping quality score (MAPQ) for each read pair. MAPQ = 10 log10 p, where p is the probability that true alignment belongs elsewhere. With the exception of L1Hs, which is the youngest and least sequence divergent family, the bodies of L1 repeats are uniquely mappable. In case of L1Hs, the 5'UTR is still mappable to determine the level of L1Hs in Ctrl and KO clones. b. Genome browser snapshots for MPP8 (blue), TASOR (orange) and MORC2 (purple) ChIP-seq read densities from Ctrl and corresponding KO K562 clones at two representative example genomic loci. Experiment was repeated once with similar results. LINE element occurrences are indicated by blue rectangles at the bottom of the plot. Four instances of long L1 elements are named indicating L1 families they belong to. Note complete absence of ChIP-seq signal from KO lines and selectivity toward some but not other L1 instances. Of note, while MPP8 and MORC2 ChIP signals were robust, TASOR ChIPs showed relatively weak enrichments (either due to poor antibody quality or genuine biological properties); for this reason, a subset of our downstream analyses is focused on MORC2 and MPP8. c. In addition to full length L1, HUSH complex and MORC2 bind 3'UTRs of KRAB Zinc Finger (ZNF) genes. Genome browser snapshots of ChIP-seq read densities over representative examples, from both Ctrl and corresponding KO K562 clones. Experiment was repeated once with similar results. d. HUSH complex and MORC2 preferentially bind expressed KRAB-ZNF genes over other ZNF genes. Heatmaps of MPP8 (left) and MORC2 (center) signals over 2,600 ZNF genes, centered in the 3' end of the genes and sorted first by the presence of KRAB domain and then by MPP8 ChIP signal. Upper 1,600 genes are KRAB-ZNF, lower 1,000 non-KRAB ZNF genes. Right heatmaps codes absolute expression level of each gene in RPKM scale from the K562 RNA-seq data (rightmost panel).

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