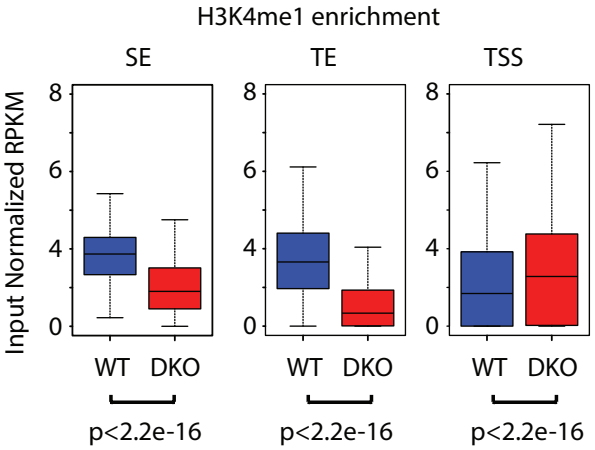
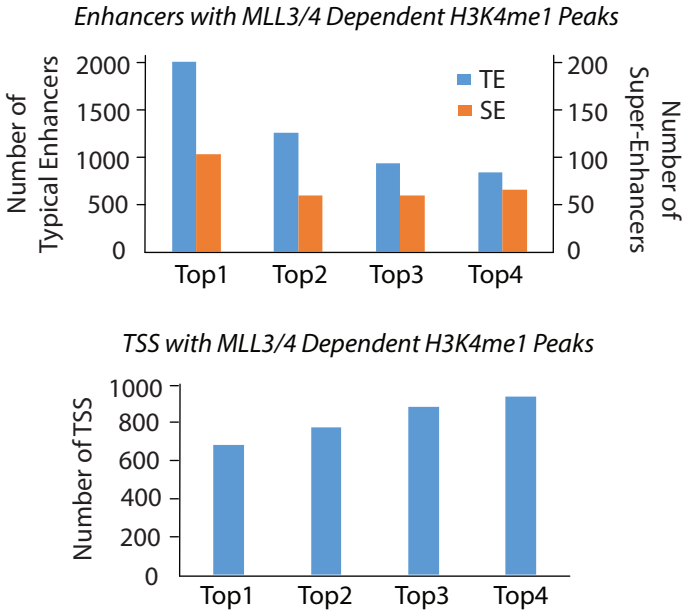
Figure S2

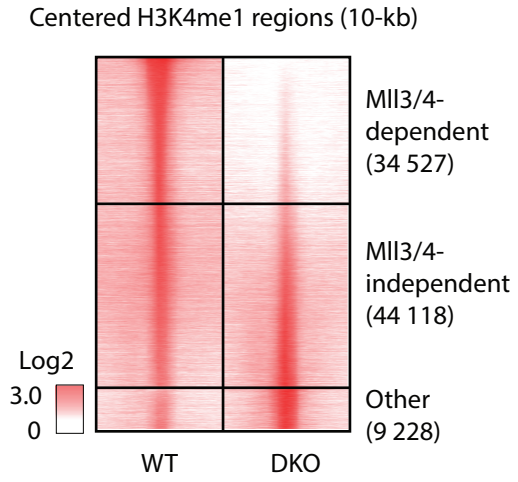
A



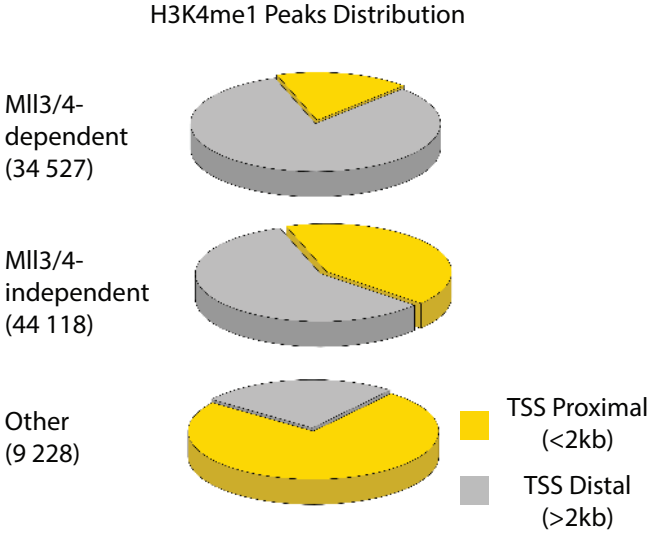

B



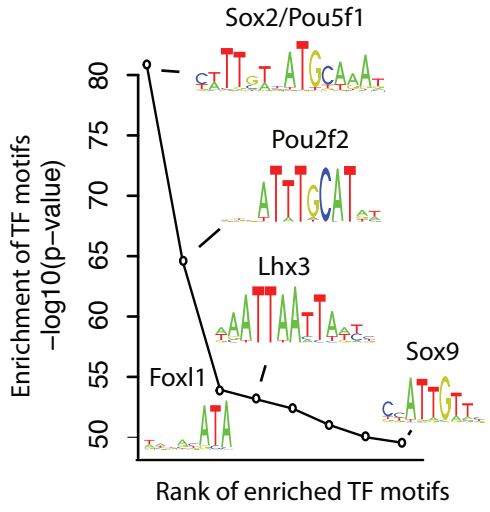

C




D




E




F

| Category | GO term | p value |
|---|---|---|
| Mll3/4-dependent | Somatic Stem Cell Maintenance | 2.98e-43 |
| | Maintenance of Location in Cell | 1.12e-42 |
| | Maintenance of Protein Location in Cell | 3.75e-38 |
| | Regulation of Notch Signaling Pathway | 6.96e-34 |
| | Nagetive Regulation of MAPK activity | 3.27e-30 |
| Mll3/4-independent | Peptidyl-lysine Modification | 1.41e-85 |
| | Protein Acylation | 5.85e-77 |
| | Protein Acetylation | 8.16e-73 |
| | Regulation of Gene Expression, Epigenetic | 9.47e-73 |
| | Peptidyl-lysine Acetylation | 1.12e-65 |

**Figure S2. Mll3/4 Are Required for Genome-wide Deposition of H3K4me1 at promoter-distal Enhancers, Related to Figure 1**

**(A)** Comparison of H3K4me1 ChIP-seq signals between WT and DKO cells at cis-regulatory elements (TE and SE, defined by (Whyte et al., 2013) and within 2 kb of TSS. SE, super-enhancer. TE, typical enhancer. TSS, transcription starting site. Median values were shown as vertical lines in the box plots, the upper edge and lower edge show the 25th and 75th quantile, and error bars indicate 10th and 90th quantile. p value was computed with two-tail Student t-test.

**(B)** MLL3/4-dependent H3K4me1 peaks are subcategorized into four quantiles based on the level of H3K4me1 variation upon MLL3/4 depletion (Top1 represents the top 25% peaks with most dramatic change of H3K4me1 signal). Top panel: y-axis shows number of typical enhancers (blue) or super-enhancers (orange) that are intersected with the indicated H3K4me4 peaks; Bottom panel: y-axis shows the number of TSS that is intersected with the indicated H3K4me1 peaks.

**(C)** Heatmap (right) showing the distribution of H3K4me1 ChIP-seq signal within 10 kb of peak summits in WT and DKO cells respectively. Each row represents the same 10-kb window surrounding the peak summit in E14 and DKO cells. Color key shows the log2 transformed RPKM.

**(D)** Distribution of H3K4me1 regions in different genomic positions relative to TSS.

**(E)** Result of motif enrichment analysis performed with the top 500 Mll3/4-dependent H3K4m1 peaks as foreground and the bottom 500 Mll3/4-independent H3K4m1 peaks as background. Note that motif for Sox2, a master regulator of embryonic stem cell pluoripotency, has the lowest p value.

**(F)** Shown is the result of Gene Ontology analysis using all Mll3/4-dependent H3K4me1 regions as foreground and all H3K4me1 regions as background.