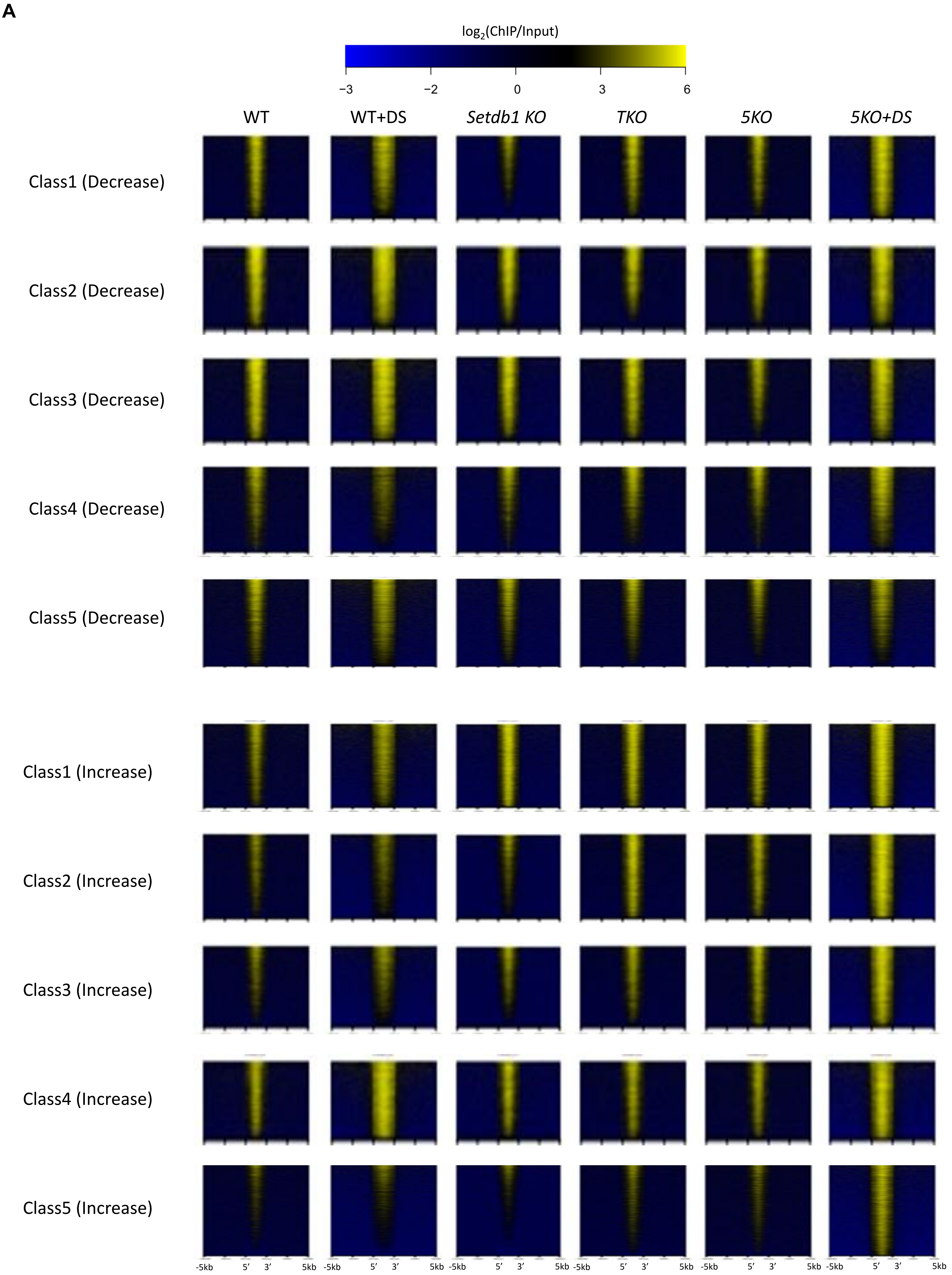
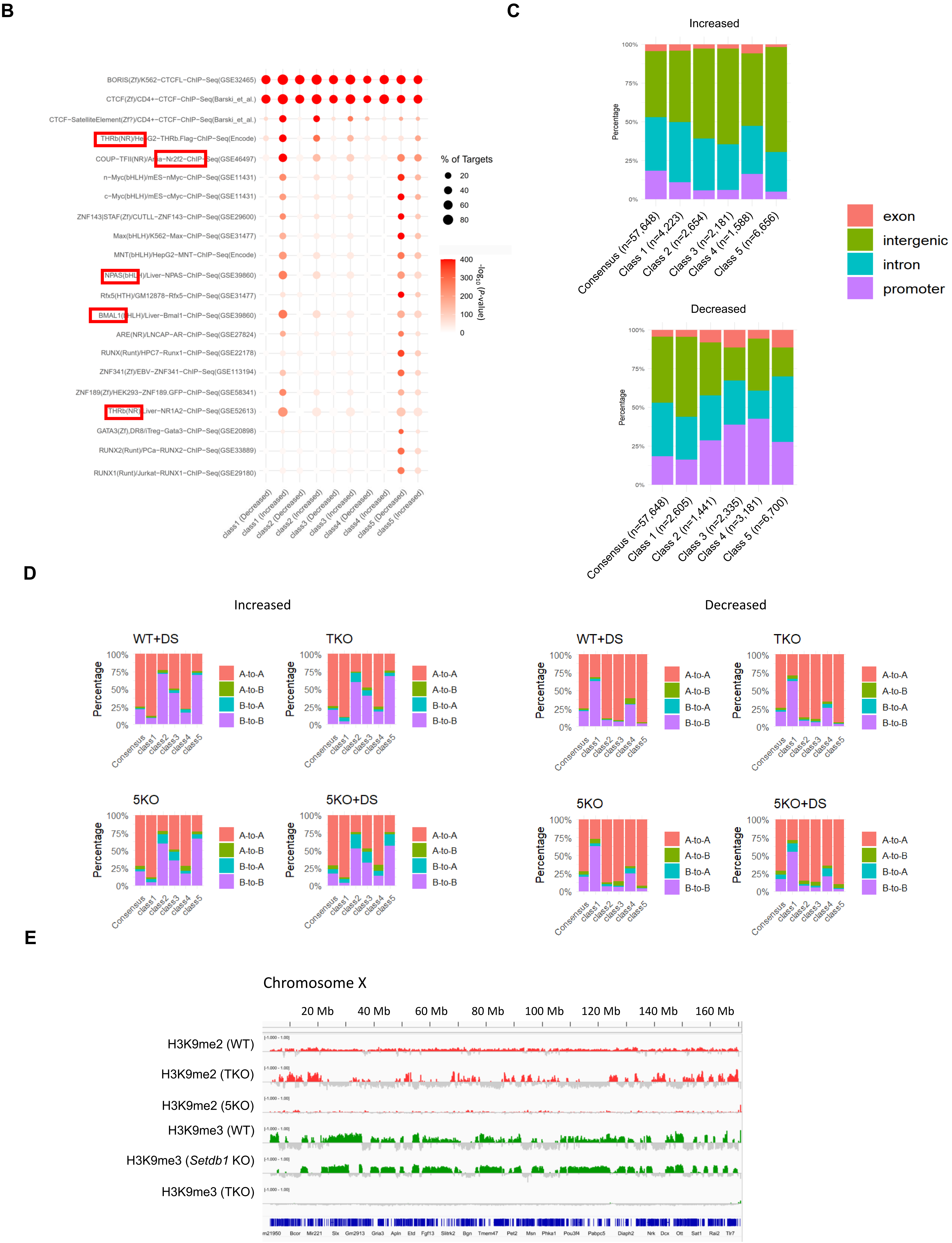
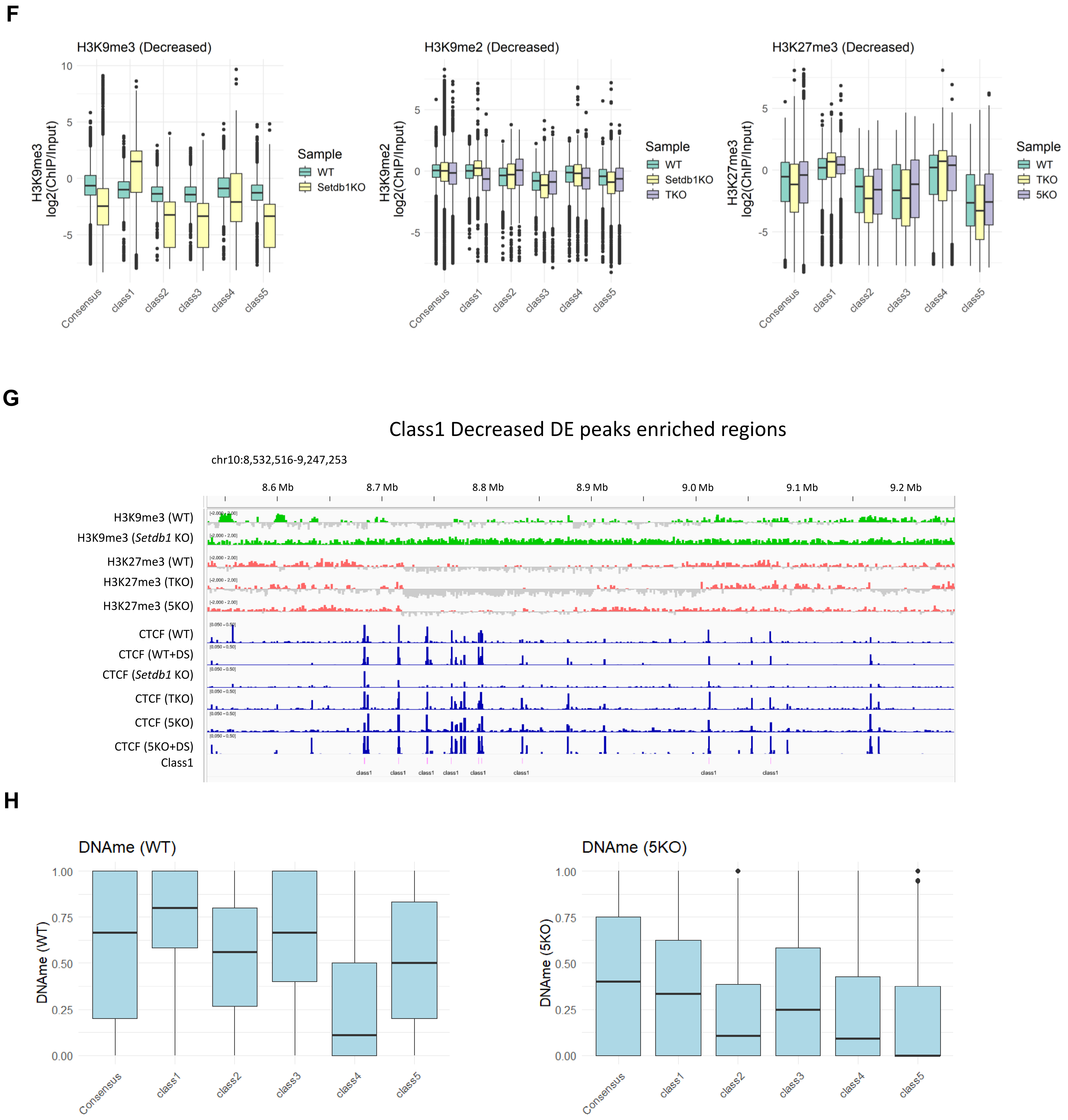
Supplemental Figure S1



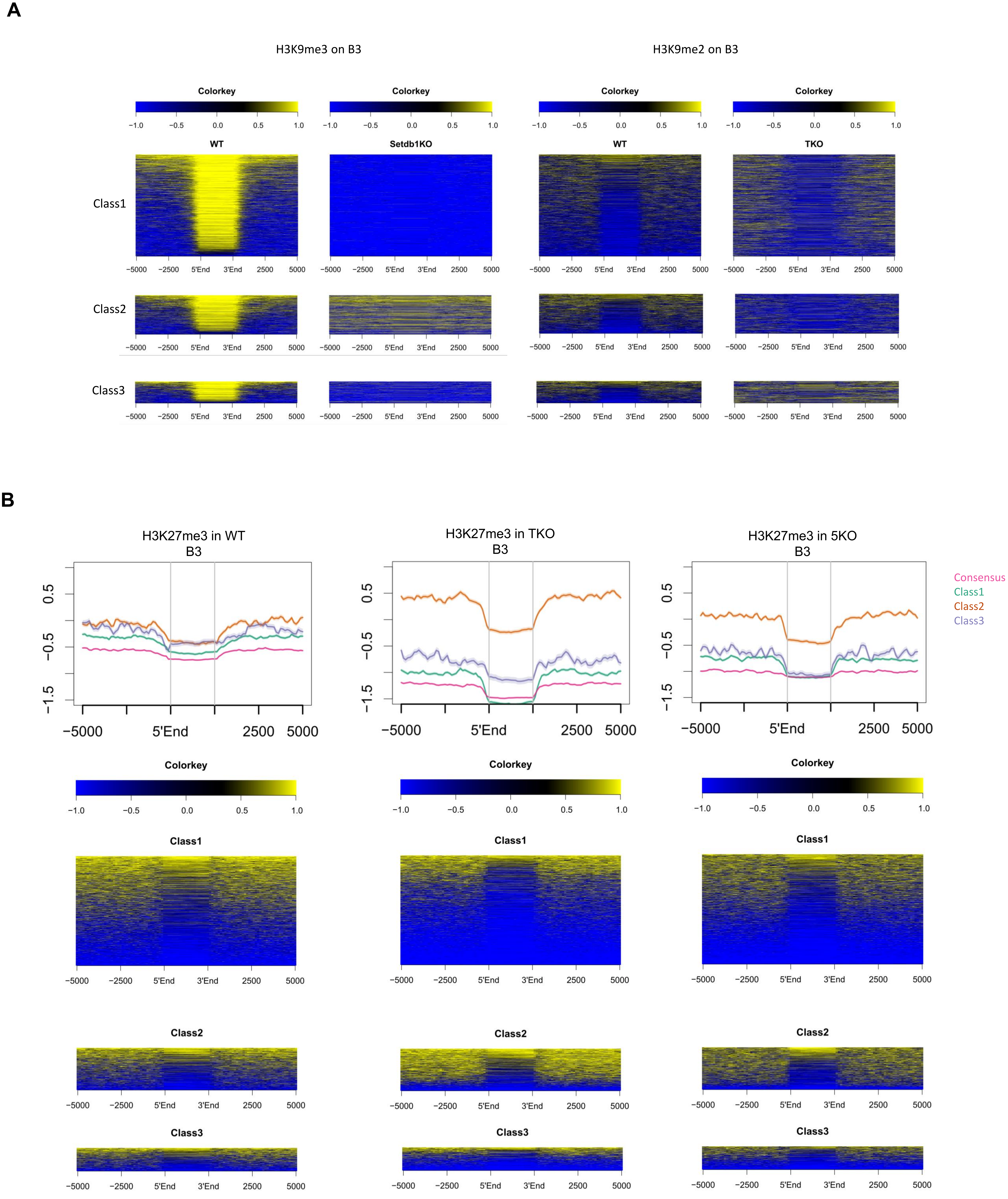
Supplemental Figure S1

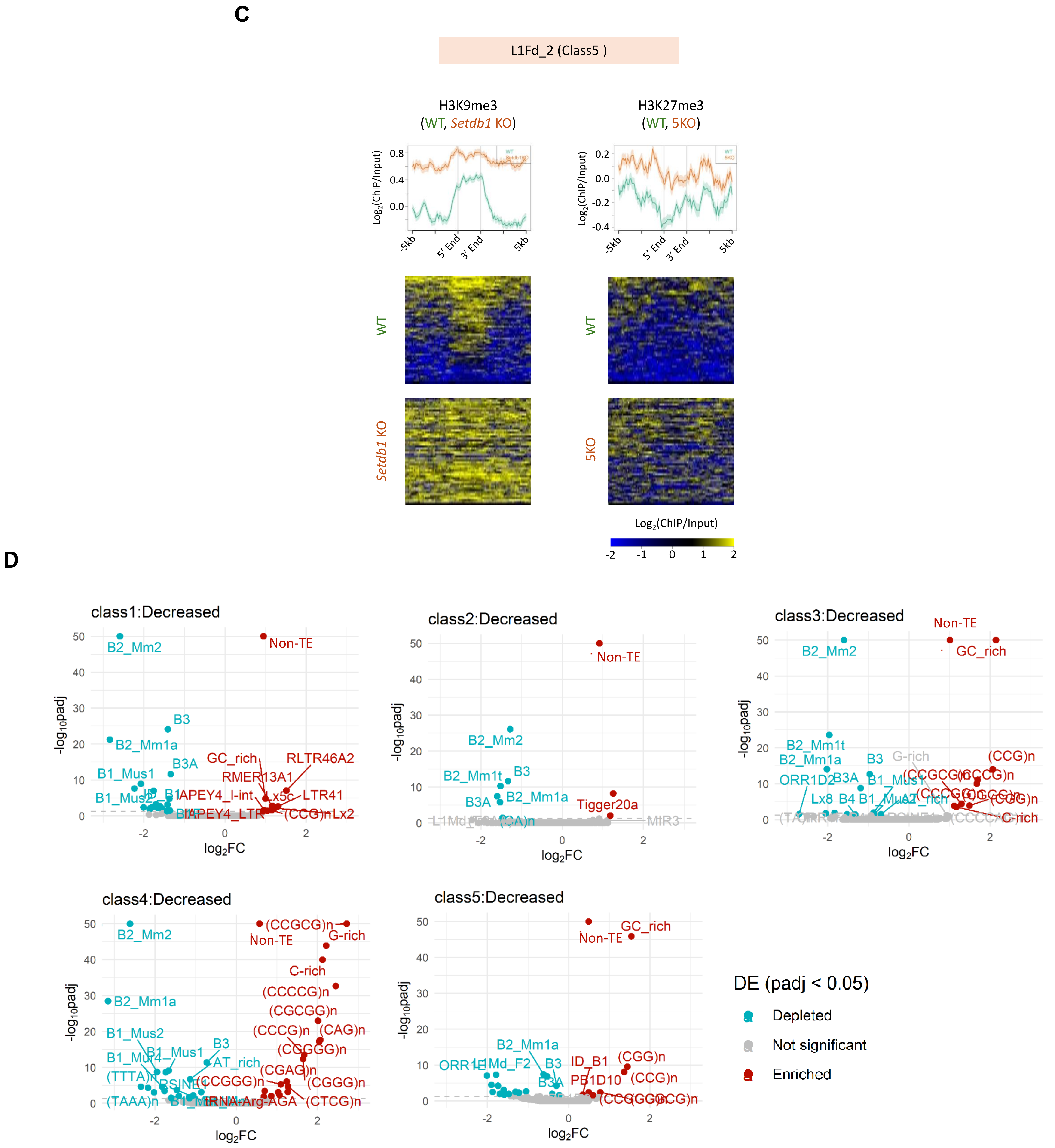




Supplemental Figure 1. Dysregulation of CTCF binding profiles by H3K9/K27 methylation deficiency. (A) Heatmaps of CTCF enrichment around DE peaks. (B) Motif enrichment in DE peaks. (C) The distribution of DE peaks across genomic regions, including promoters, exons, introns, and intergenic regions. (D) A bar graph showing the frequency of compartment changes in DE peaks. (E) Chromosomal view of H3K9me3 profiles in TKO iMEFs. H3K9me3 enrichment is broadly lost across chromosomes in TKO iMEFs. (F) Epigenomic profiles at “Decreased” DE peaks. H3K9me3 enrichment in WT and *Setdb1* KO iMEFs (Top), H3K9me2 enrichment in WT, *Setdb1* KO and TKO iMEFs (Middle), and H3K27me3 enrichment in WT, TKO, and 5KO iMEFs (Bottom). (G) Representative region of “Decreased” Class1 enriched regions. (H) Boxplots of DNA methylation levels of “Increased” DE peaks in WT (left) and 5KO (right).

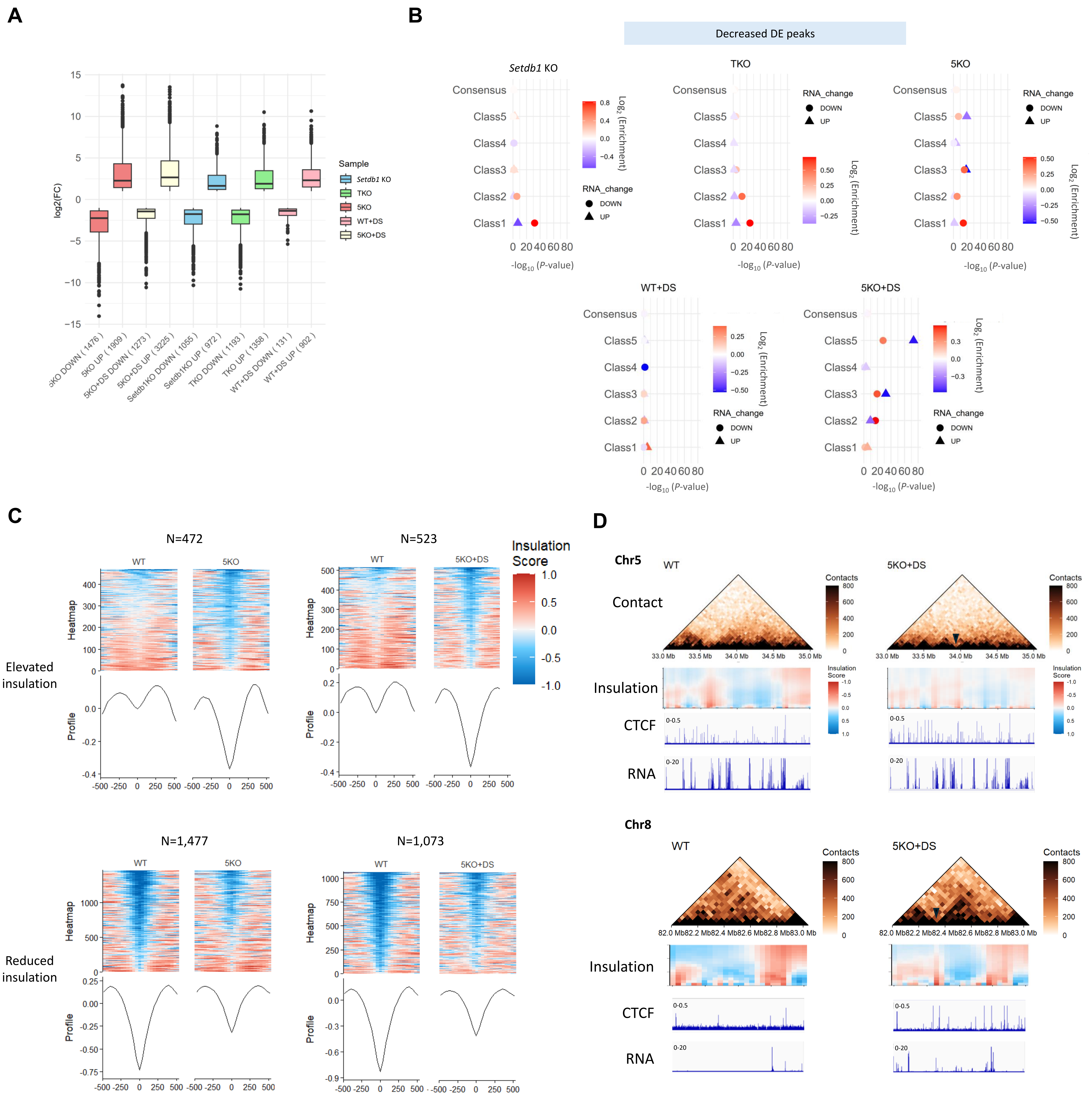
Supplemental Figure S2





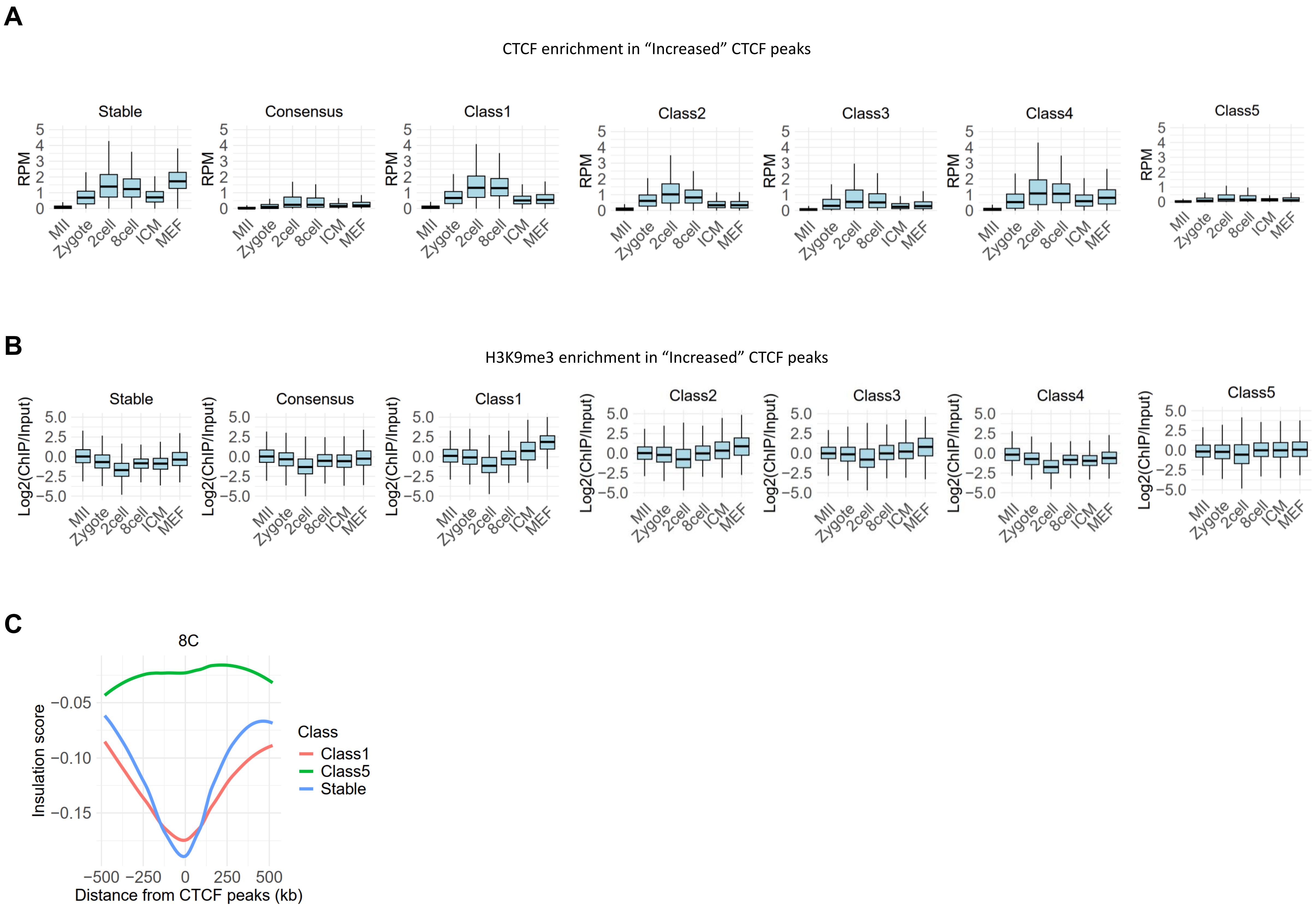
Supplemental Figure 2. Prevention of abnormal CTCF bindings at repetitive elements by H3K9/K27 methylation. (A, B) CTCF enrichment of H3K9me3 (A, left), H3K9me2 (A, right), and H3K27me3 (B) at SINE B3 copies overlapping with Class 1, 2, or 3. (C) Epigenome profiles around L1Fd_2 elements overlapping with Class 5 increased DE peaks. In WT iMEFs, H3K9me3, regulated by SETDB1, is enriched. However, when H3K9 methylation is lost, H3K27me3 becomes enriched instead. (D) Enrichment of repeat type in “Decreased” DE peaks. The volcano plots represent the enrichment of each repeat type in DE peaks, with the x-axis showing Log_2(FC) and the y-axis showing $-log_{10}$(adjusted P-value). Repeat types that are significantly enriched or depleted (adj. P-value < 0.01) are highlighted in red and blue, respectively.

Supplemental Figure S3



Supplemental Figure 3. Association of DE peaks with changes in gene expression and 3D genome structure. (A) Violin plot showing the expression changes of differentially expressed genes. (B) A dot plot showing the enrichment of differentially expressed genes around "Decreased "DE peaks. The x-axis represents -log10(adj. P-value). The enrichment results for upregulated and downregulated genes are represented by circles and triangles, respectively. (C) Tornado plot showing insulation score around differentially insulated regions in 5KO and 5KO+DS. (D) A representative region showing concurrent increases in CTCF binding, insulation, and gene expression changes in 5KO+DS.

Supplemental Figure S4



Supplemental Figure 4. Association of DE peaks with 3D genome structures in mouse early embryos. (A) Dynamics of CTCF enrichment in Increased DE peaks during early mouse development. (B) Dynamics of H3K9me3 enrichment in Increased DE peaks during early mouse development. (C) Average insulation score in 8-cell stage around Increased DE peaks.