*Supplementary Material*

# Impact of Sustained Transforming Growth Factor-β Receptor Inhibition on Chromatin Accessibility and Gene Expression in Cultured Human Endometrial MSC

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Table S1 Regulation of pathways preventing cellular senescence in A83-01-treated eMSC

| | Category | Term | Genes | Fold Enrichment* |
|---|---|---|---|---|
| **Up-regulated genes** | GOTERM_MF_DIRECT | peroxidase activity | CYGB, GPX3, PTGS2 | 3.74 |
| | GOTERM_BP_DIRECT | response to oxidative stress | CYGB, GPX3, PTGS2, SCARA3, APOE, DUSP1 | 1.46 |
| | GOTERM_BP_DIRECT | cellular oxidant detoxification | CYGB, GPX3, PTGS2, APOE | 1.53 |
| **Down-regulated genes** | KEGG_PATHWAY | p53 signaling pathway | CDK6, CCND2, THBS1, ATM, TP53I3, IGF1, CDKN1A, RPRM, PTEN | 3.82 |
| | BIOCARTA | cyclins and cell cycle regulation | CDK6, CCND2, CDKN2B, CDKN1A | 4.41 |
| | BBID | cyclin-CDK complexes | CDK6, CDKN2B, CDKN1A | 5.97 |
| | GOTERM_CC_DIRECT | cyclin-dependent protein kinase holoenzyme complex | CDK6, CCND2, CDKN1A | 6.04 |
| | BIOCARTA | Cell Cycle: G1/S Check Point | CDK6, ATM, CDKN2B, CDKN1A | 3.67 |
| | KEGG_PATHWAY | cell cycle | CDK6, CCND2, ATM, CDKN2B, CDKN1A | 1.15 |

***** Fold enrichment represents enrichment of the indicated GO term in A83-01 treated versus untreated samples.

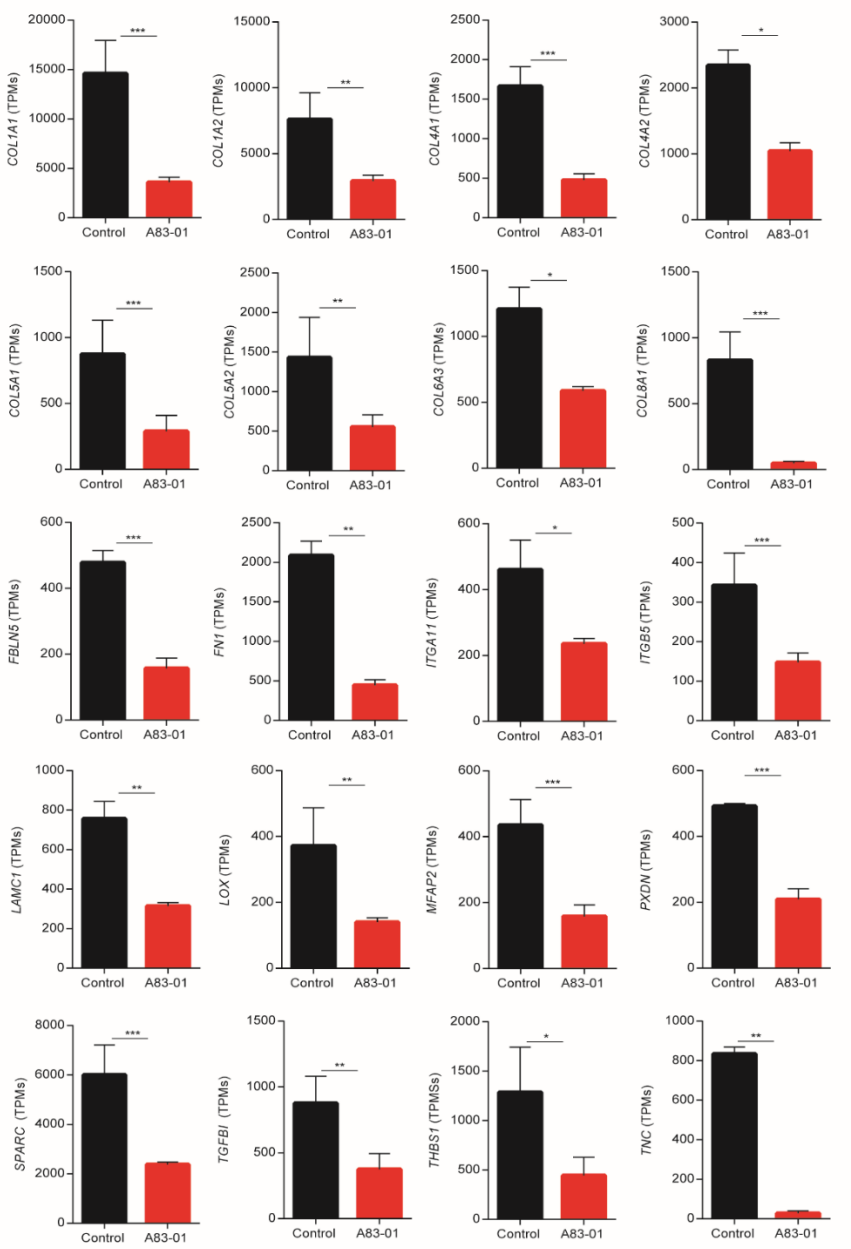


**Figure S1. ECM genes down-regulated in response to A83-01 treatment.** Graphs showings changes in level of gene expression of the top 16 most abundant ECM genes negatively regulated by TGFβ-R inhibition, represented as changes in TPMs. Data represent mean ± SEM; Y-axis shows TPMs; *indicates $q < 0.05$, ** $q < 0.01$ and *** $q < 0.001$.

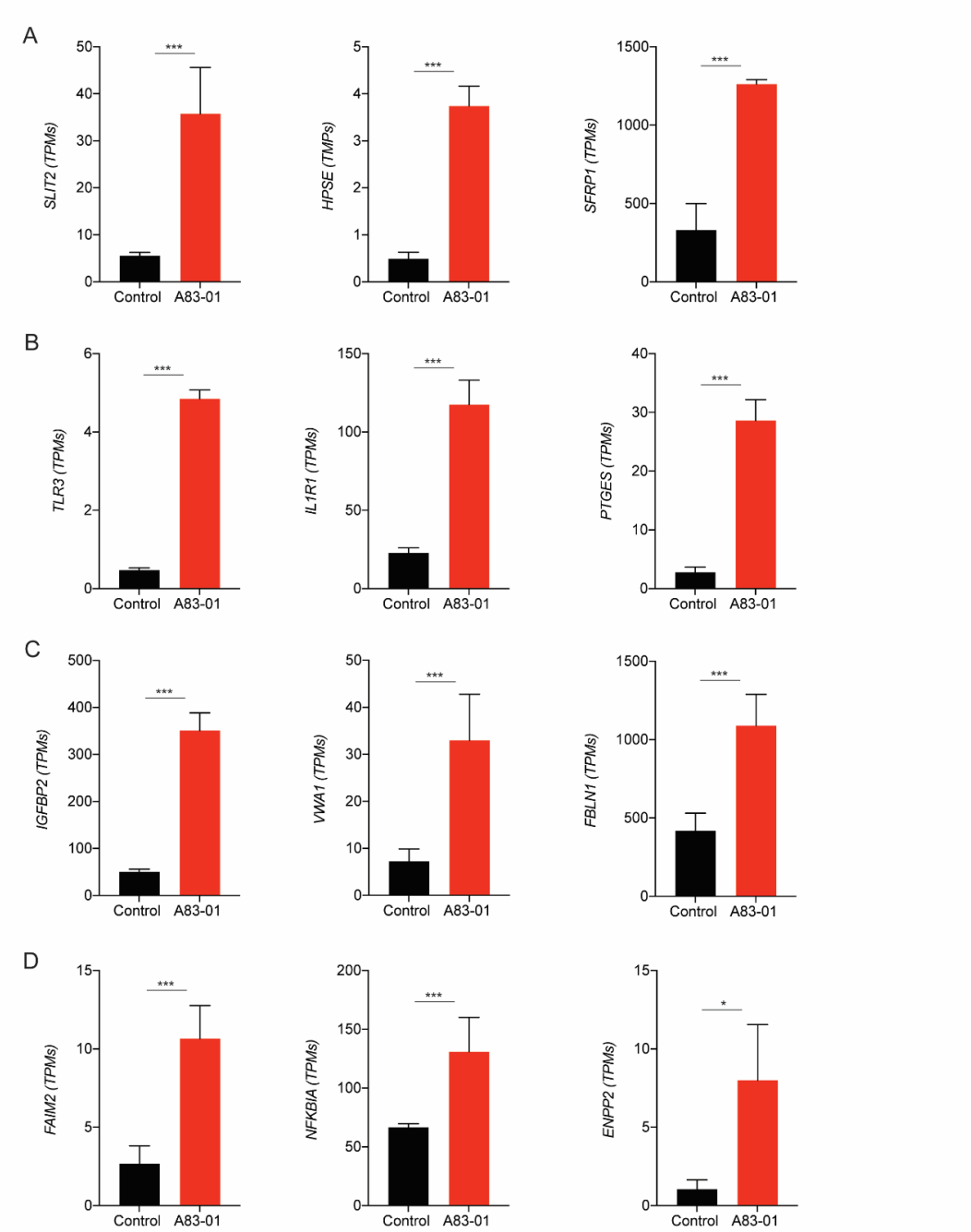


**Figure S2. Examples of angiogenic (A) anti-inflammatory, (B) immunomodulatory (C) antifibrotic and (D) antiapoptotic genes up-regulated in response to A83-01 treatment.** Graph show changes in gene expression level (TPMs) of positively regulated genes by TGFβ-R inhibition. Data represent mean ± SEM; Y-axis shows TPMs; * indicates $q < 0.05$, ** $q < 0.01$ and *** $q < 0.001$.

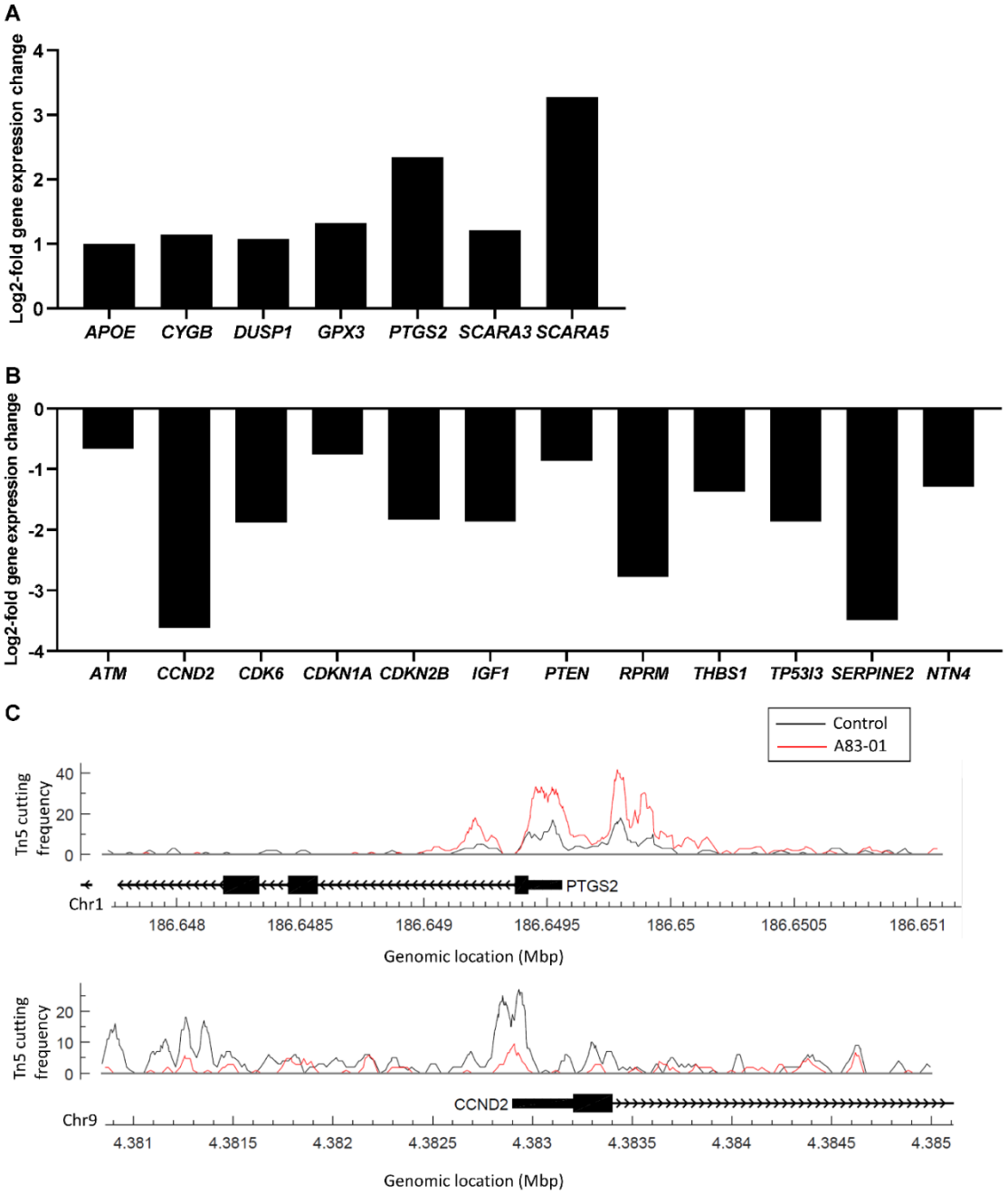


**Figure S3. Regulation of senescence related genes.** A83-01 prevents eMSC senescence through **A)** induction of genes implicated in preventing oxidative damage and **B)** inhibition of cellular senescence-related genes. **C)** ATAC peak showing opening and closing of the chromatin accessibility downstream of the promoter region of *PTGS2* and *CCND2*, respectively. Black and red traces represent untreated and A83-01-treated eMSC. The X-axis shows the genomic location of the ATAC-seq peaks and genes.

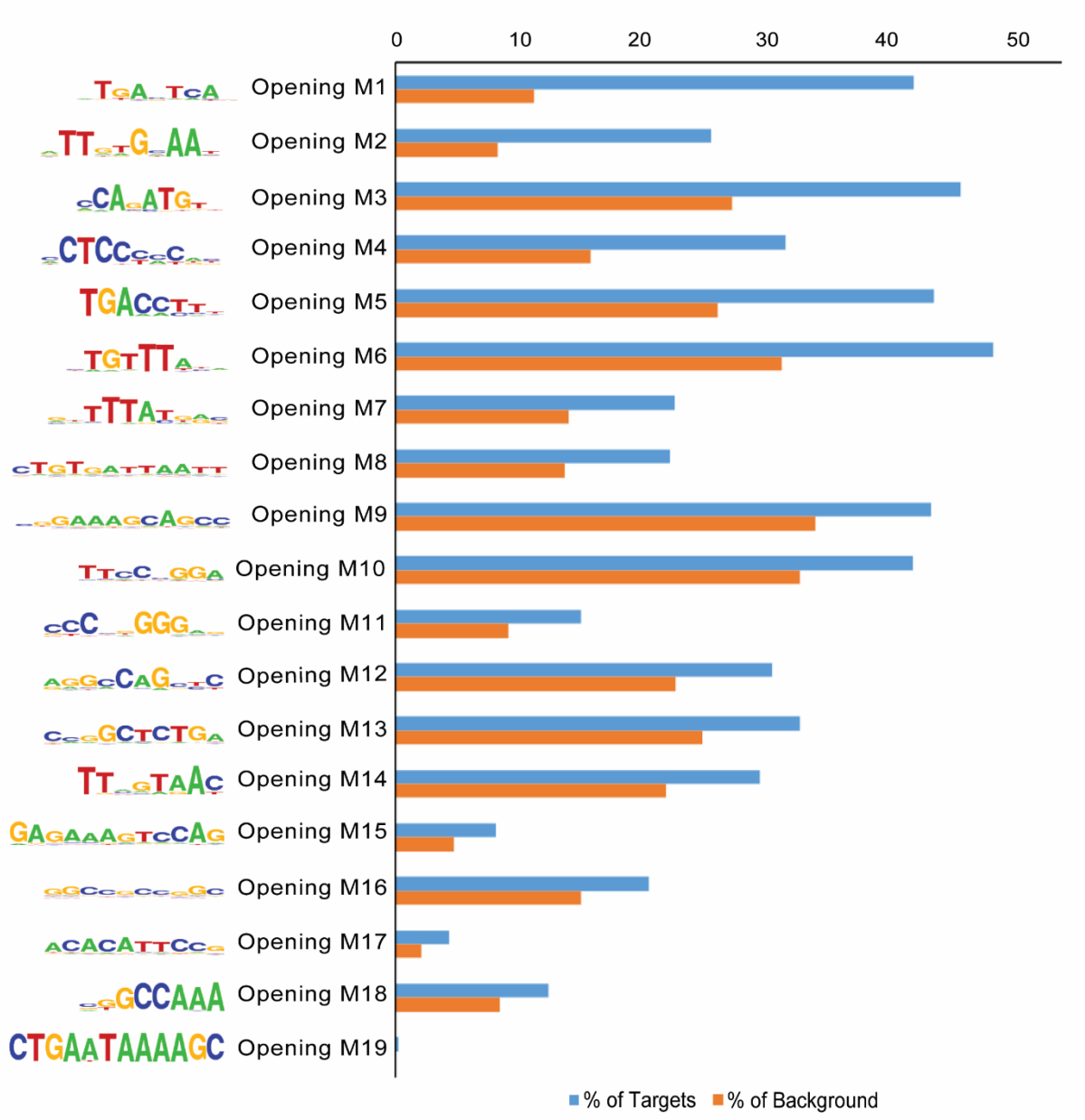


**Figure S4. Enrichment of TF binding motifs in opening genomic regions.** Total of 19 TF binding motifs enriched in the opening ATAC-seq peaks. The frequency (%) of peaks (blue bars) containing a given motif is shown relative to genomic regions randomly selected from the genome (orange bars) (±50 kb from TSS, matching size, and GC/CpG content.

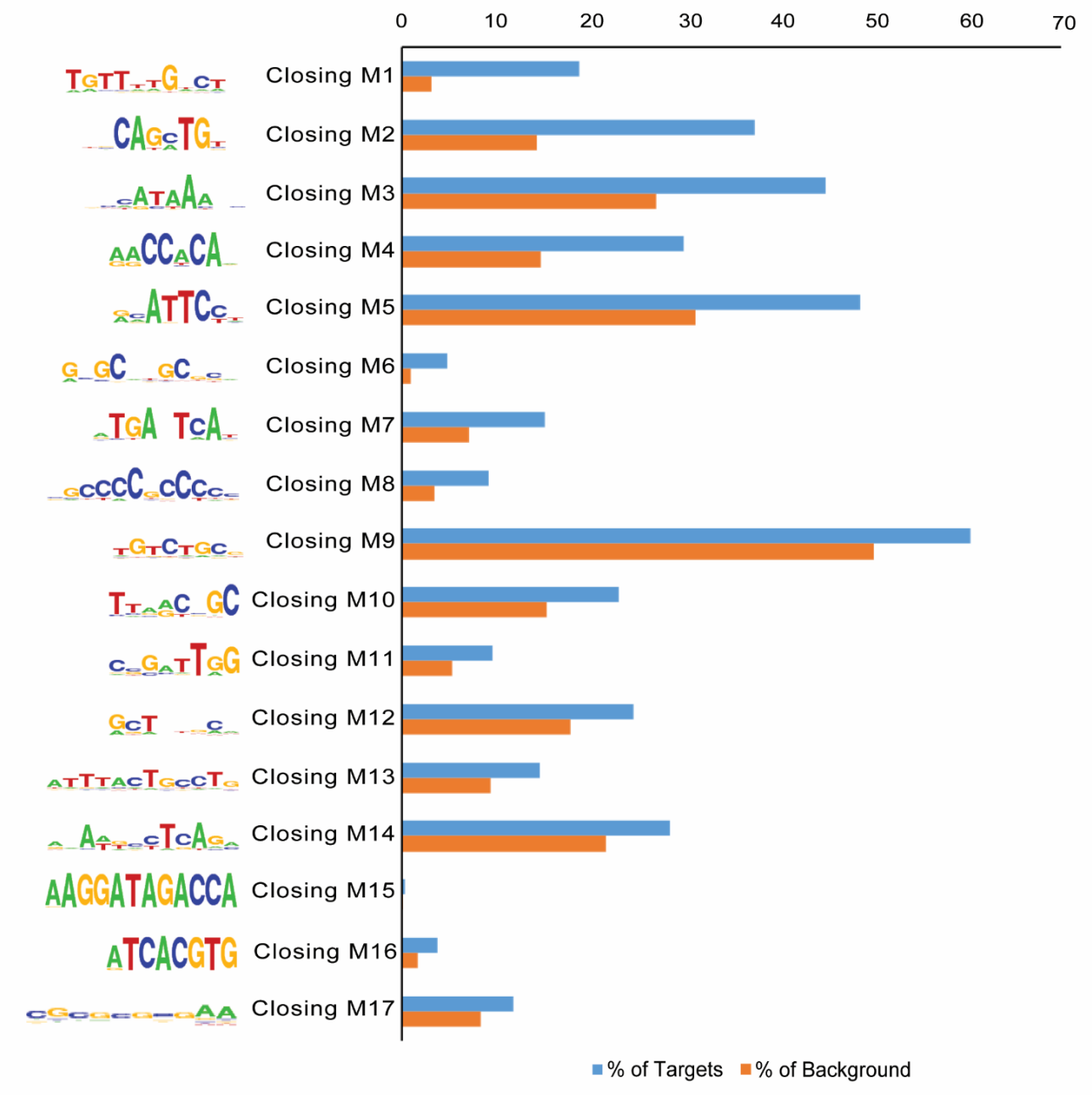


**Figure S5. Depletion of TF binding motifs in closing genomic regions.** Total of 17 TF binding motifs enriched in the closing ATAC-seq peaks. The frequency (%) of peaks (blue bars) containing a given motif is shown relative to genomic regions randomly selected from the genome (orange bars) (±50 Kb from TSS, matching size, and GC/CpG content).