**Supplementary Figure 1**. Comparison of expression of genes in proximity of CREAM-specific COREs were significantly higher than genes in proximity of ROSE-specific COREs in both GM12878 and K562 cell lines.

**Supplementary Figure 2**. Comparing the percentage of COREs which overlap with promoters, exons, introns, and intergenic regions for COREs identified by CREAM or ROSE in GM12878 and K562 cell lines.

**Supplementary Figure 3**. Difference between enrichment of transcription factor binding intensity within CREAM-identified COREs and ROSE-identified COREs excluding the CRE-free gaps.