Expanded View Figures

Figure EV1. Transcriptional changes of human EC genes in response to TNF-α-stimuli.

A, B Gene ontology (GO) analysis of TNF-α-up-regulated genes in class 1 (A) and class 2 (B), as determined in Fig 1A. The *P*-values of each category analyzed by DAVID (https://david.ncifcrf.gov/) are shown in the bar graphs.

C Heat map representation of the TNF-α-down-regulated genes. Genes were classified based on the TNF-α-treated time points, using the algorithm "HOPACH".

D GO analysis of TNF-α-down-regulated genes, as determined in (C). The *P*-values of each category analyzed from DAVID are shown in the bar graphs.

Source data are available online for this figure.

Figure EV1.

A

p65 (with TNF-α)

20.1%
32.6%
47.3%

promoter (+5kb TSS)
intragenic
intergenic

B

De novo motif	Database Name (JASPAR)	-log10 P value
	MA0061.1_NF-kappaB (NFkB)	4.38E+02
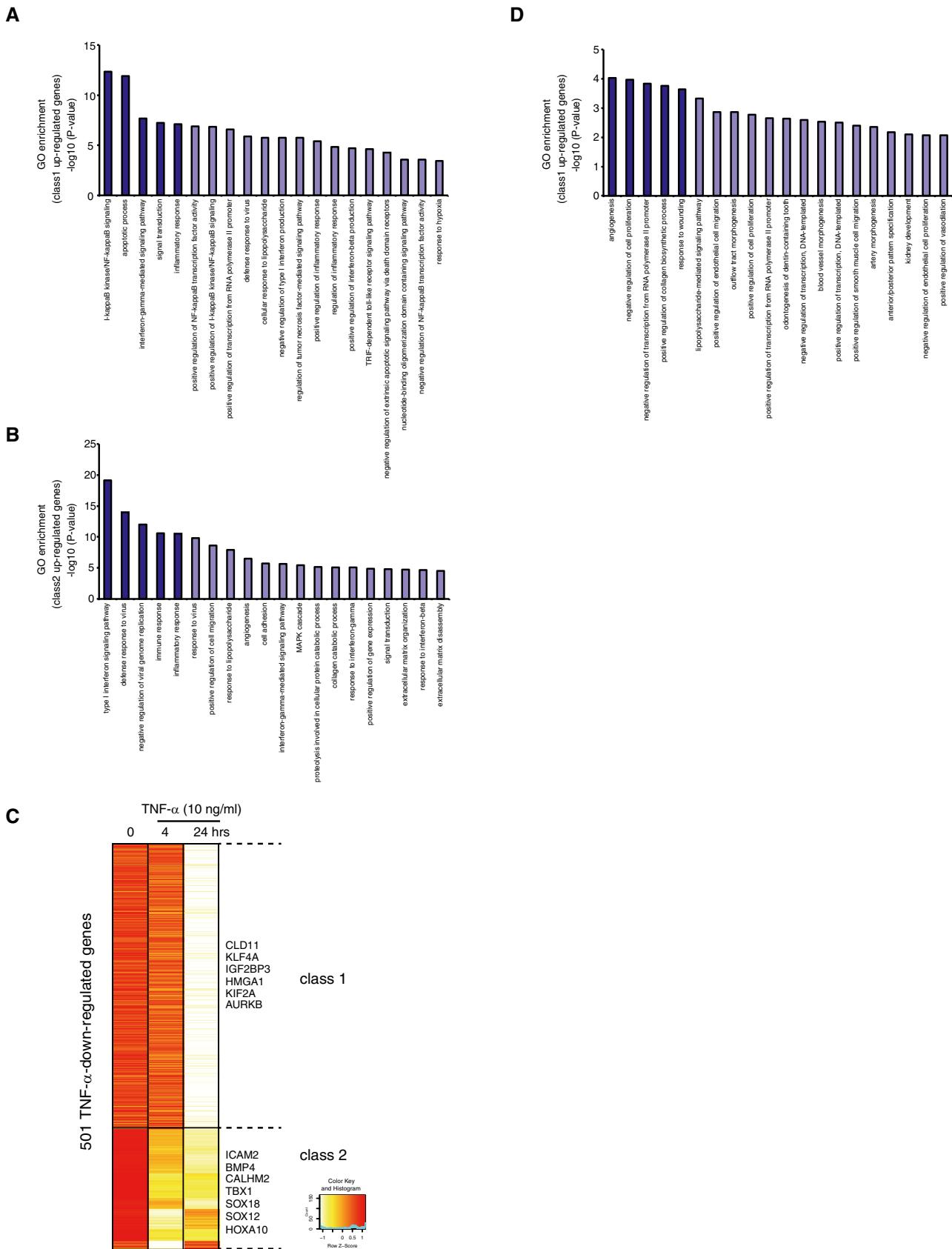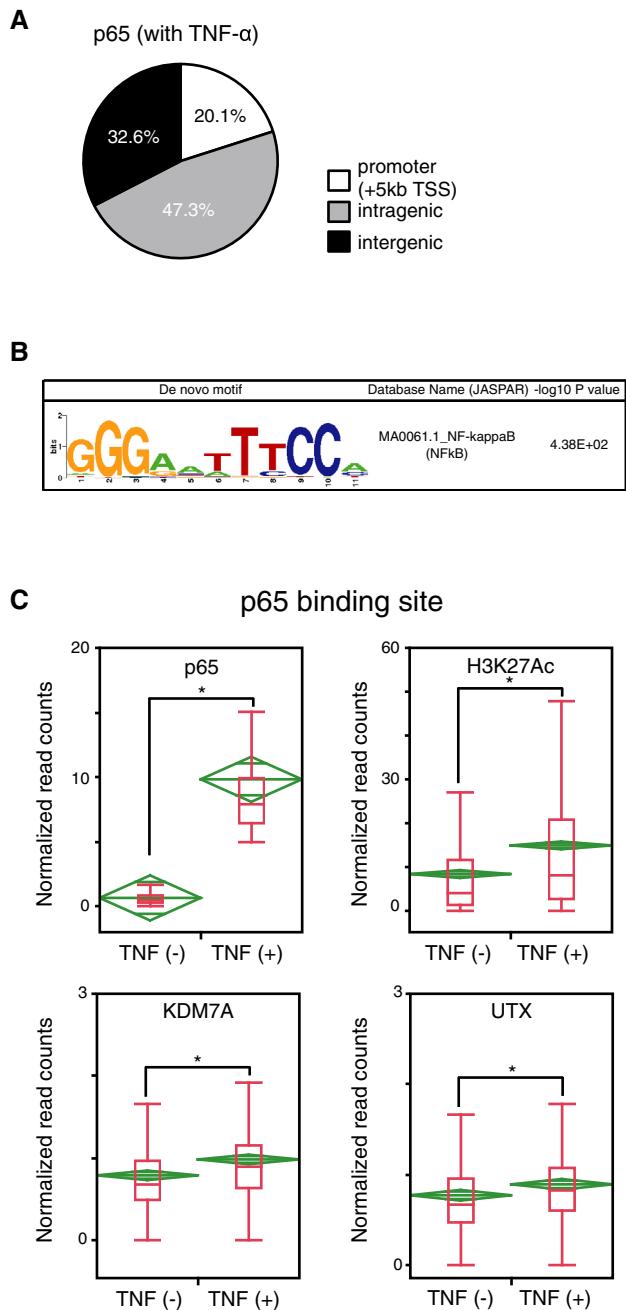
Figure EV2. Gain of KDM7A and UTX recruitment at the p65-related elements during TNF-α-signaling in human ECs.

A   Pie chart of p65 binding site distribution in ECs with TNF-α (+).

B   *De novo* motif analysis of p65 binding sequences in TNF-α-stimulated ECs. The *P*-value indicates significant enrichment of the transcription factor binding motif in p65 binding sites in comparison to a size-matched random background.

C   Boxplots of p65, H3K27ac, KDM7A, and UTX signals at all p65 binding sites in ECs before and after TNF-α stimulation. The *Y*-axis indicates normalized read counts. The horizontal line within the box represents the median sample value. The ends of the box represent the 3rd and 1st quantiles. The whiskers extend from the ends of the box to the outermost data point that falls within the distances computed as follows: 3rd quartile +1.5* (interquartile range) and 1st quartile −1.5* (interquartile range). Mean diamonds representing confidence intervals appear. The vertical span of each diamond represents the 95% confidence interval for the mean of each group. Graphs are representative of two independent experiments.
*$P < 0.05$ compared to TNF-α (−). Statistical differences were analyzed by the Student's *t*-test.

C   p65 binding site
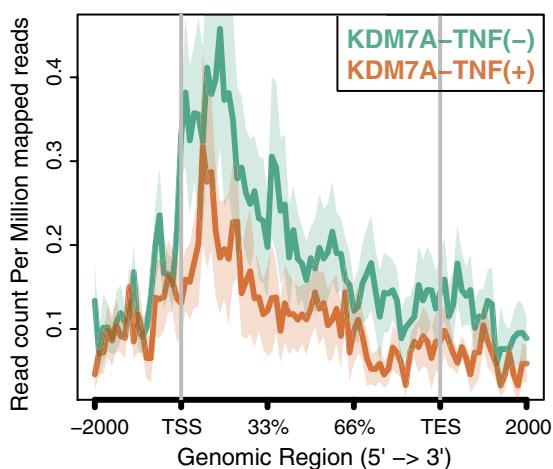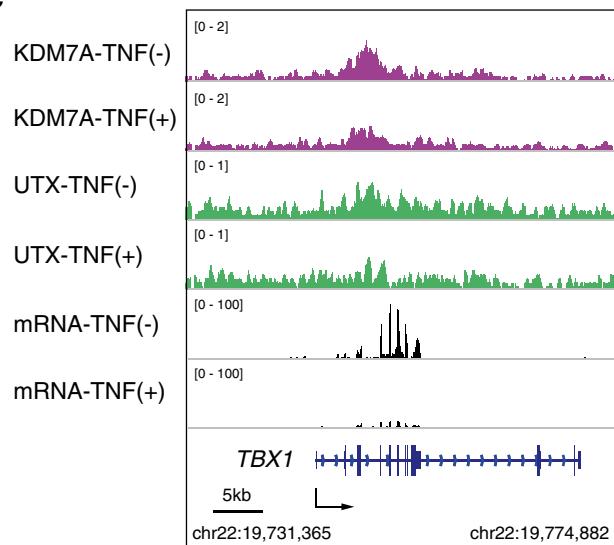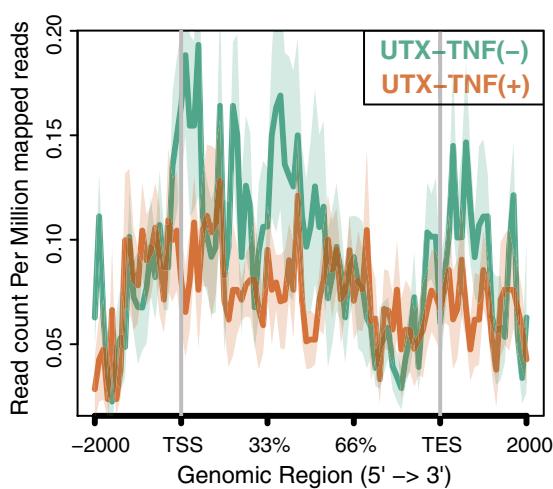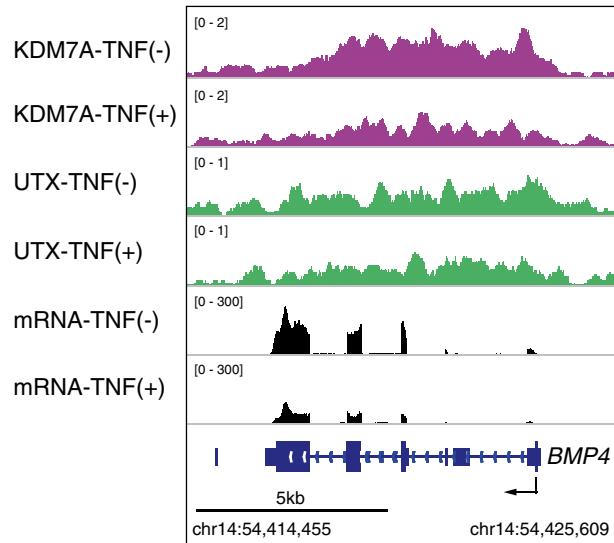
Figure EV3. Loss of KDM7A and UTX recruitment at the developmental gene loci during TNF-α signaling in human ECs.

A, B   Metagene representations of KDM7A (A) and UTX (B) ChIP-seq signals in units of read count per million mapped reads at a meta composite of the genomic regions around TNF-α-down-regulated genes.

C, D   Gene tracks of ChIP-seq signals for KDM7A and UTX, and RNA-seq signals around the *TBX1* (C) and *BMP4* (D) loci in TNF-α (−) and TNF-α (+) ECs. ChIP-seq and RNA-seq signals are visualized by the Integrated Genome Viewer (http://software.broadinstitute.org/software/igv/).

A

Total SE = 311
KDM7A overlap =42
UTX overlap = 19
Both overlap= 176
Non overlap SE = 74

SOX18 rank 144
PECAM rank 123
NR2F2 rank 193
ESAM rank 158
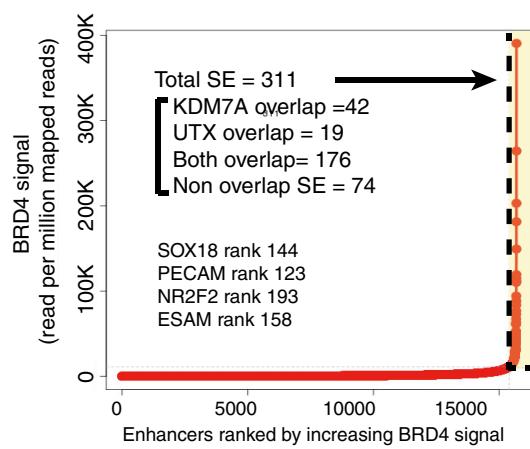
B
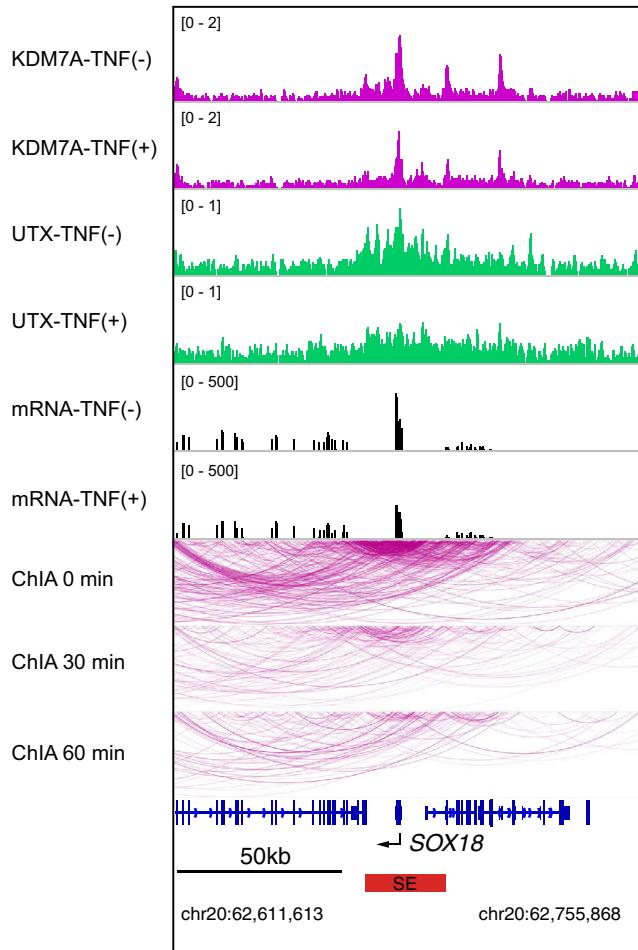
C
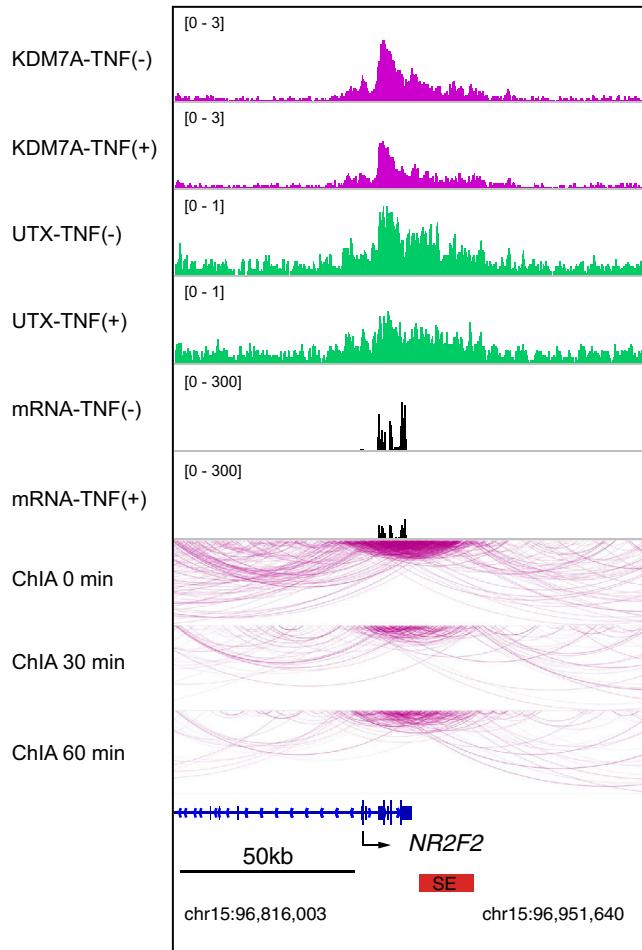
Figure EV4.

Figure EV4. KDM7A and UTX- recruitment correlated with SEs in resting human ECs.

A   Plot of enhancers defined in TNF-α-untreated ECs, ranked by increasing BRD4 signal. Super enhancers (SEs) were defined by ROSE (Loven *et al*, 2013; Whyte *et al*, 2013), based on the ChIP-Seq signals for BRD4 (Brown *et al*, 2014b). SEs are indicated by dashed lines and yellow boxes. The numbers denote the total SEs and their classification based on the binding of KDM7A and UTX. Representative SE-related genes are indicated in the graph.

B, C ChIA-PET interactions of active RNA pol II around the *SOX18* (B) and *NR2F2* (C) loci integrated with the ChIP-seq profiles of KDM7A and UTX, and the RNA-seq profiles in TNF-α (−) and TNF-α (+) ECs. ChIA-PET interactions were visualized by the WashU Epigenome Browser (http://epigenomegateway.wustl.edu/browser/). Interactions detected by ChIA-PET are depicted with purple lines. Red bars show control-specific SEs.

Figure EV5. TNF-α treatment rapidly induced chromosomal conformation changes in human ECs.

A, B Hi-C contact matrices from chromosome 1 (A) and chromosome 4 (B): the whole chromosome, at 1-Mb resolution (top); 50-kb resolution (middle); 3-kb resolution (bottom). Left: TNF-α 0 min; Right TNF-α 60 min. Green boxes indicate regions used for zoom in. The highest resolution maps show 500-kb regions including the *VCAM1* (A) and *IL8* (B) loci, respectively. The color intensity of each pixel represents the normalized number of contacts between a pair of loci.

C, D Virtual 4C views and heat map of Hi-C data around the *VCAM1* (C) and *IL8* (D) loci. Virtual 4C is calculated from Hi-C datasets, using bins covering the indicated viewpoints. The *Y*-axis in the virtual 4C view indicates the number of reads that interact to the viewpoint bin. Control reads are raw counts, and TNF-α reads were normalized to control reads. Valid chromatin loops were calculated by HiCCUPS (https://github.com/theaidenlab/juicer/wiki/Download) and are shown with black lines. Topologically associating domains (TADs) were calculated by TADtool (https://github.com/vaquerizaslab/tadtool) and are shown as blue bars. The number denotes the Aggregate Peak Analysis (APA) score at the indicated areas (Rao *et al*, 2014). Red lines indicate TNF-α-specific SEs.

Figure EV5.