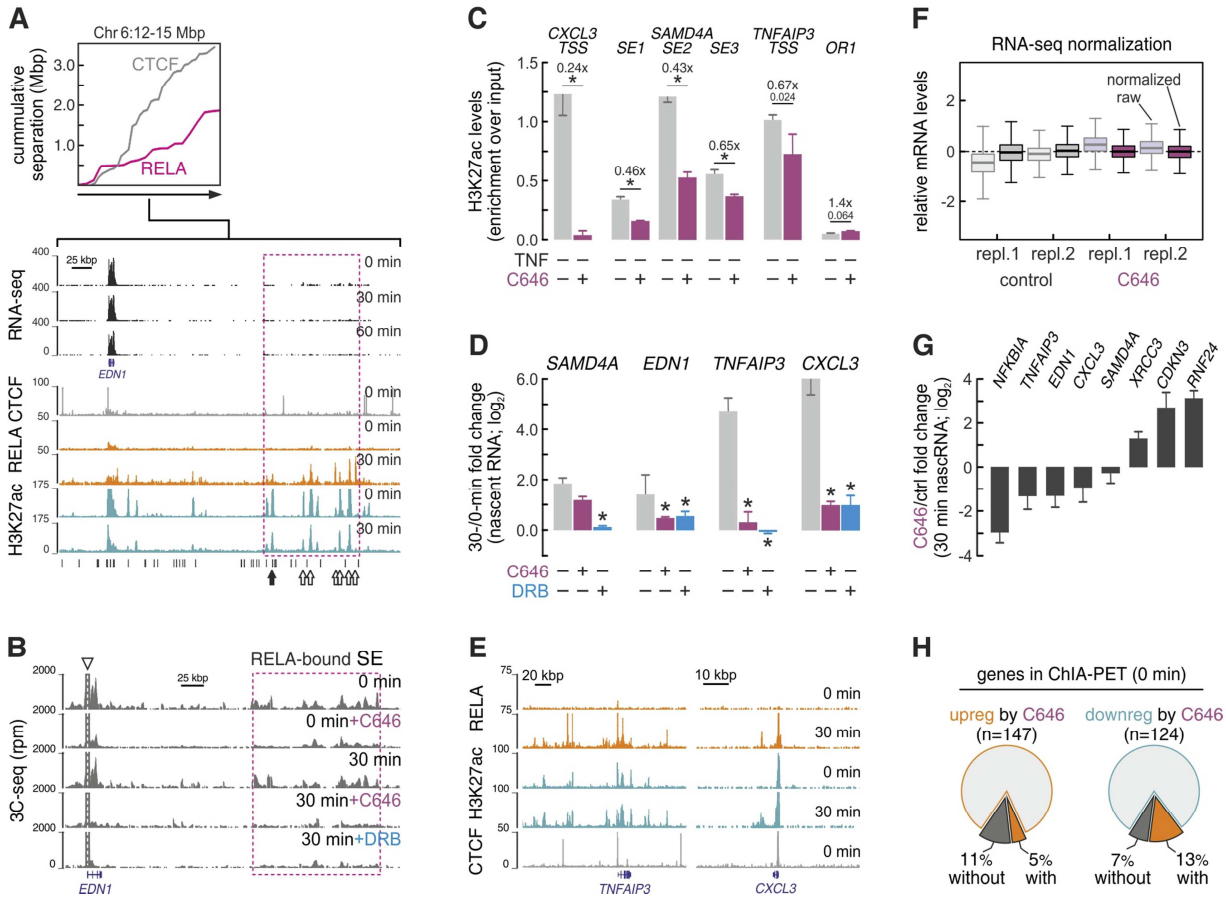

Supplemental Fig. S7. The effect of C646 treatment on TNF-responsive genes. (***A***) *Top*: cumulative separation of RELA (30 min) and CTCF peaks (0 min) in the 3 Mbp around *EDN1*. *Bottom*: Browser view of RNA- and ChIP-seq data (in reads per million) around *EDN1*. The RELA-bound super-enhancer (*magenta box*) and peaks "with" (*black arrows*) or "without" NF-κB motif (*white arrows*) are demarcated. (***B***) Browser view of 3C-seq data (in rpm) around *EDN1* using its TSS as viewpoint (*yellow triangle*) in the presence/absence of inhibitors. *Magenta rectangle*: enhancer cluster interacting with *END1*. (***C***) H3K27ac enrichments (±SD; n=2) at RELA-bound enhancers in *CXCL3*, *SAMD4A*, and *TNFAIP3* assessed using ChIP-qPCR in the presence/absence of C646; *: significantly different; $P<0.01$, two-tailed Student's unpaired *t*-test. The inactive *OR1* locus serves as a negative control. (***D***) Log_2-fold changes in nascent RNA levels (±SD; n=3) induced by TNF at 30 min post-stimulation in the presence or absence of inhibitors (assessed using RT-qPCR). *: significantly different to untreated levels; $P<0.01$, two-tailed Student's unpaired *t*-test. Note that for *CXCL3* primers targeting exonic RNA were used due to its rather short introns. (***E***) Browser views of RELA, H3K27ac, and CTCF ChIP-seq data (in reads per million) along the TNF-induced *TNFAIP3* and *CXCL3* loci on Chromosomes 6 and 4, respectively. (***F***) Box plots showing the relative mRNA expression levels in two "spiked" RNA-seq replicas generated in the presence (*purple*) or absence (*dark grey*) of C646 before ("raw") or after sample normalization ("normalized"). (***G***) Log_2-fold changes in intronic RNA levels (±SEM; n=2) between C646-treated and untreated cells at 30 min. (***H***) Pie charts showing the fraction of genes up- (*left*) or downregulated by c646 (*right*) that are present in 0-min ChIA-PET data and connected to "with" (orange) or "without" RELA-bound peaks.