



**Supplemental Fig. S6.** Identification of RELA-bound super-enhancers. HUVECs were TNF-stimulated for 0 or 30 min. **(A)** Cumulative separations of RELA "with" and "without" peaks along Chromosomes 1, 6, 14, and 17. **(B)** The distribution of H3K27ac ChIP-seq signal (0 min) for "stitched" peaks that lie <12.5 kbp apart (as in Hnisz et al. 2013). SEs are contained within the part of the curve with slope >1 (highlighted grey) and include those associated with *CLEC9A*, *SOX17*, *FOS*, and *SAMD4A*. Inset: A Venn diagram showing that 468 out of the 608 SEs defined using H3K27ac are also bound by RELA at 30 min. **(C)** Diagrams illustrating the distribution of 30-min RELA ChIP-seq signal for "stitched" peaks that lie <12.5 kbp apart (as in panel B). SEs are contained within the part of the curve highlighted grey, and include those associated with *CXCL2*, *HIVEP2*, *IRF1*, *FOS*, and *SAMD4A* (but not *CLEC9A* or *SOX17*). Inset: A Venn diagram showing that 98 out of the 212 RELA-SEs can also be identified using H3K27ac signal. **(D)** Browser view illustrating ChIP-seq and ChIA-PET profiles around a typical SE (rectangle) associated with the TNF-responsive *FOS* gene. **(E)** Log<sub>2</sub>-fold change in intronic RNA levels of genes associated (within the same TAD) with RELA-, H3K27ac- or RELA+H3K27ac- ("both") SEs. \*: significantly different mean;  $P < 0.01$ , two-tailed Student's unpaired *t*-test. **(F)** The most significantly enriched GO terms assigned to genes associated with RELA, all, or RELA+H3K27ac-bound SEs that lie in the same TAD. **(G)** Bar graphs show the fraction of SEs that encode the canonical motif, associate with TNF-responsive genes in the same TAD, are intragenic, or lie in genes that are >50 kbp in length.