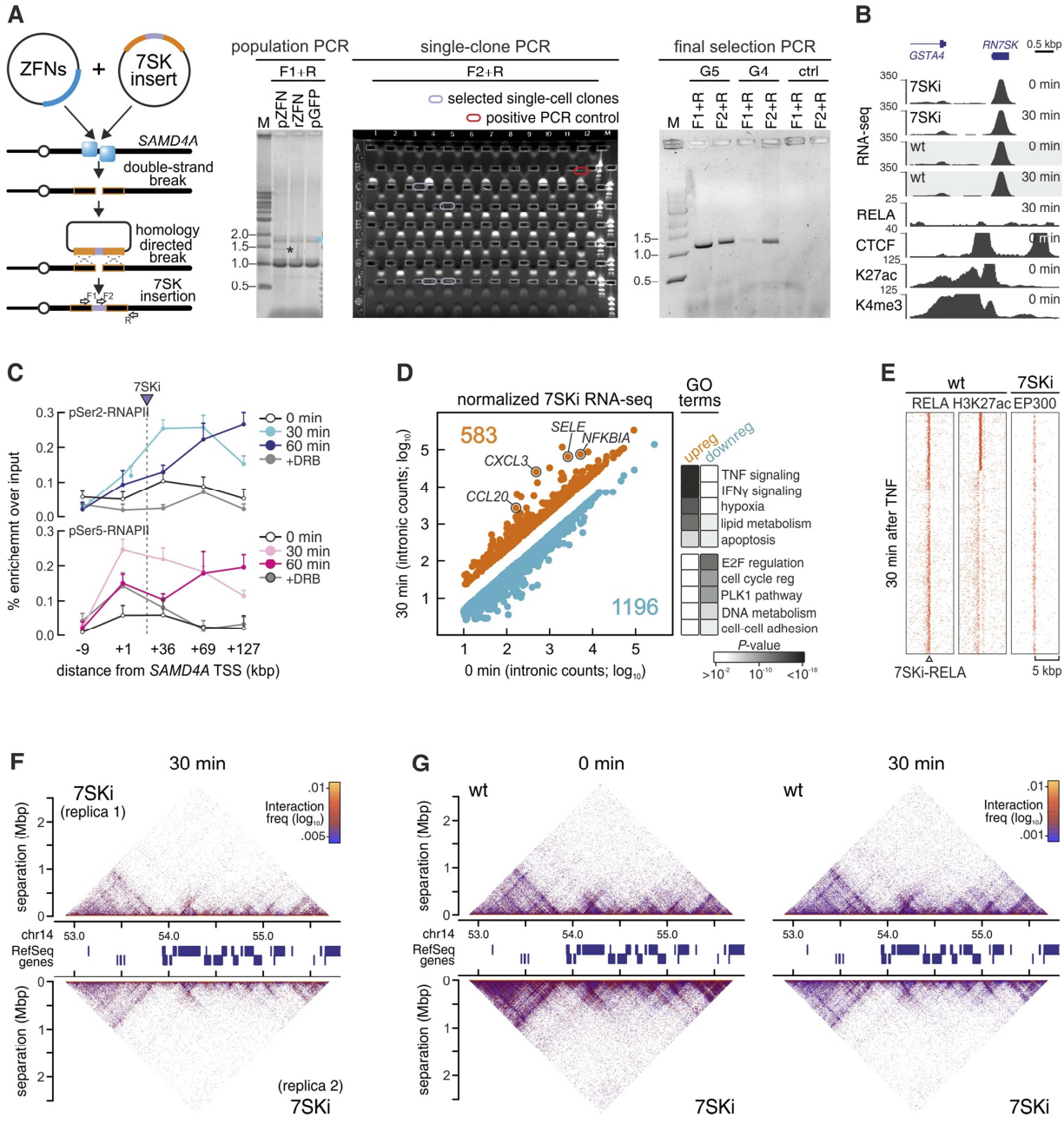

Supplemental Fig. S9. Isolation and properties of clone 7SKi carrying the inserted *RN7SK* promoter. (***A***) Isolation of the 7SKi HUVEC clone. *Left panel*: Genome editing strategy. Cells were co-transfected with ZFN-encoding plasmids plus a vector carrying the *RN7SK* promoter inserted between two 750-bp regions homologous to the *SAMD4A* target region. Following homologous recombination, the *RN7SK* promoter is inserted in one *SAMD4A* allele. A similar event at the second allele generates a homozygous line. *Middle panel*: A PCR screen (using primers F1 and R) is now performed on a fraction of the population to assess modification efficiency; the black star marks the amplimer expected from the correct insertion, the blue star marks a spurious band. *Right panel*: The remaining co-transfected population was dispersed in 96-well plates, individual clones screened by PCR (using primers F2 and R), and amplimers

resolved by electrophoresis in 96-well E-Gels (Invitrogen); red ovals mark bands given by positive PCR controls, and light-purple ovals desired amplimers; selected single-cell clones were grown and analyzed. *Fourth panel*: Two clones (G4 and G5) were subjected to a final PCR-screen (using the primers indicated; "ctrl" indicates a no-template test); G5 was heterozygous and G4 homozygous for the insertion. All downstream experiments were conducted using clone G4 ("7SKi"). (***B***) Browser view showing total RNA-seq profiles (in reads per million) along the endogenous *RN7SK* gene at 0 and 30 min post-stimulation in both wild-type (wt) and 7SKi HUVECs; ChIP-seq data are also shown. (***C***) Binding of RNA polymerase II to the wild-type locus assessed using ChIP-qPCR and antibodies targeting RNAPII isoforms phosphorylated at either the Ser2 (*top*) or Ser5 (*bottom*) residues in the C-terminal domain of its largest catalytic subunit. Results are displayed as per cent enrichment over input for 0, 30, and 60 min post-stimulation in the presence of absence of DRB (±SD; n=2). The position of the *RN7SK* insertion in modified cells is also indicated (*dashed line*). (***D***) *Left*: Intronic RNA levels ($\log_{10}$ counts; 30- versus 0-min levels) in 7SKi HUVECs after normalization. Only up- (*orange*) and downregulated (*blue*) genes are shown, and typical TNF-responsive genes indicated. *Right*: The most significantly enriched GO terms for up-/down-regulated genes are listed. (***E***) Heat maps showing that RELA binding to active *cis*-elements (marked by EP300) in 7SKi HUVECs coincides with active and RELA-bound sites in wild-type HUVECs (marked by H3K27ac and RELA signal). (***F***) T2C (*Apo*I) contact maps from two replicates in the 2.8 Mbp around *SAMD4A* obtained at 30 min. (***G***) Merged T2C (*Apo*I) contact maps in the 2.8 Mbp around *SAMD4A* obtained in wild-type (wt) and 7SKi HUVECs at 0 and 30 min post-stimulation.