

Expanded View Figures

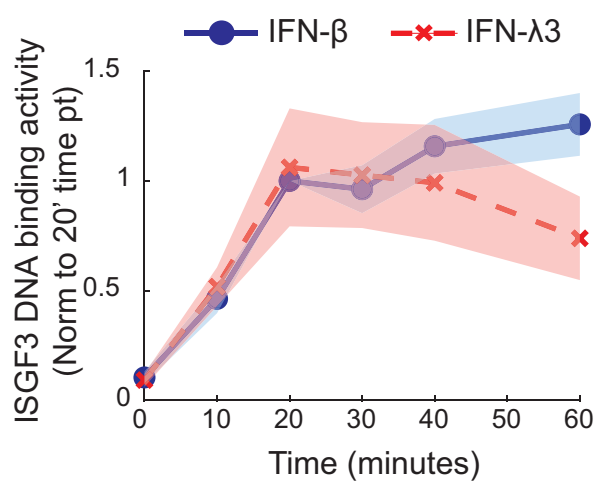


Figure EV1. IFN- β and IFN- λ 3 show comparable ISGF3 activation at the selected concentrations.

Quantified ISGF3 activity upon IFN- β (10 U/ml, blue) and IFN- λ 3 (100 ng/ml, red) stimulation measured by an electrophoretic mobility shift assay (EMSA). Data are a subset of the time course data from Fig 2 indicating the ISGF3 activity in the first hour (i.e., activation phase).

Source data are available online for this figure.

Figure EV2. Applying the adapted IFN signaling dynamical network model to assess STAT2- and IRF9-feedback loop-dependent temporal signaling dynamics.

Using the adapted IFN signaling model (Fig 3), simulations predict ISGF3 binding activity, nuclear and cytoplasmic active and total protein species, and mRNA species when positive feedback loops for STAT2 (yellow line), IRF9 (purple line), and STAT1 (green line) are eliminated or not (thick blue line) during IFN- β stimulation.

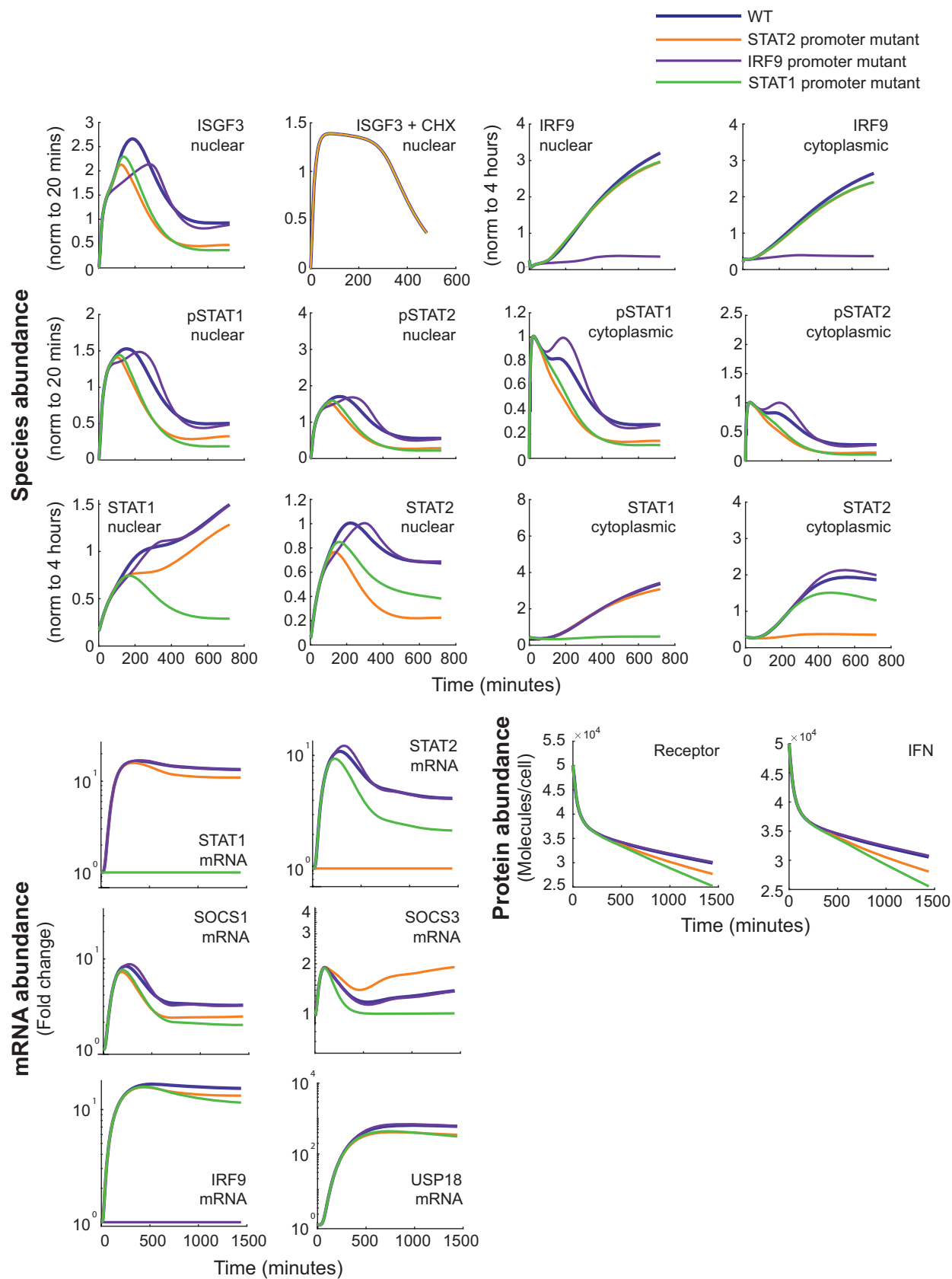


Figure EV2.

Figure EV3. CRISPR-Cas9 gene editing effectively mutates ISGF3 binding motifs in STAT2 and IRF9 gene promoters.

- A Nucleotide sequences of the promoter regions of murine IRF9 (ENSMUSG00000002325) and STAT2 (ENSMUSG000000040033) genes containing an ISGF3 binding motif. Distance from TSS was selected based on the locus of the IRF9 transcript (ENSMUST00000138037.2) and STAT2 transcript (ENSMUST00000085708.3). Data of the IRF9 promoter and STAT2 promoter regions from cDNA of IRF9 promoter and STAT2 promoter mutant MLE-12 lung epithelial cells measured using Sanger sequencing. Alterations near the targeted ISGF3 binding motif are indicated in red text. Data are from two biological replicates.
- B Pie charts of unique DNA sequences of the promoter regions of IRF9 and STAT2 genes, indicating the percentage of DNA sequences of the promoter region of IRF9 and STAT2 from IRF9 promoter and STAT2 promoter mutant cells, respectively, measured using amplicon sequencing. The WT variant comprised 21% of the total IRF9 DNA and 9% of the STAT2 DNA, with mutant variants found in the remaining 79 and 91%, respectively.

Source data are available online for this figure.

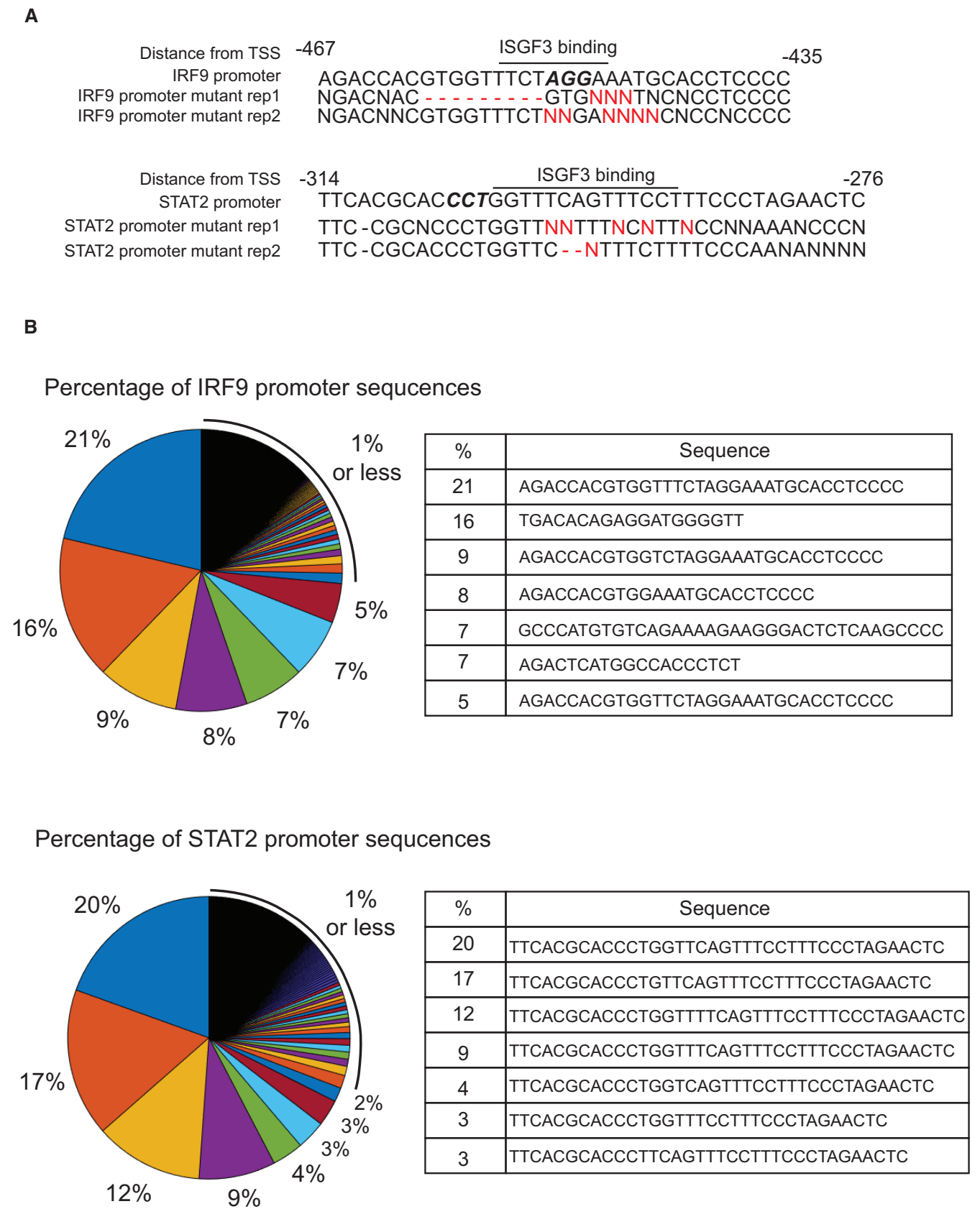


Figure EV3.