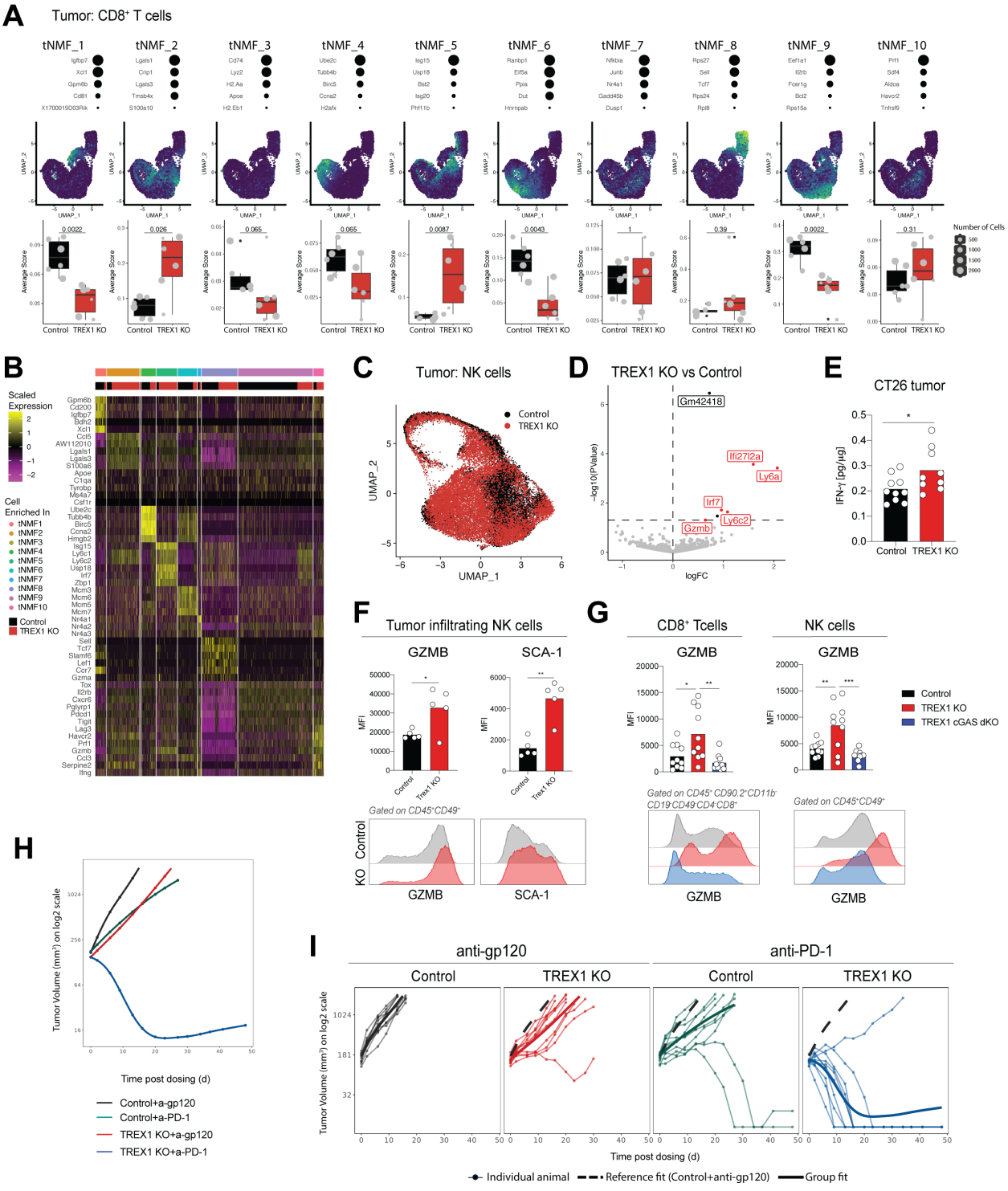

Supplementary Figure 6. TREX1 loss increases CD8 T cell and NK cell activation, limits CD8 T cell exhaustion and enhances the potency of immune checkpoint blockade therapy

A. NMF programs from CD8 T cells (tNMF, Supplementary Table 2). The top five genes contributing to the program are listed with dots sized according to their relative contribution to the NMF program. UMAPs show scaled program scores for the given NMF program from low (blue) to high (yellow). Box plots display the NMF scores averaged by animal (grey points). Size of the points represents the number of cells for each animal. Wilcox rank-sum test. **B.** Heatmap of selected genes related to the CD8 T cell NMF programs. Cells are ordered according to the NMF program with the highest score for the cell, then by tumor genotype. **C.** UMAP of NK cells isolated from control and TREX1 KO CT26 tumors. **D.** Volcano plot of genes differentially expressed between pseudobulk of TREX1 KO and control tumor-infiltrating NK cells. ISGs are labelled in red. The five genes with the lowest p-value (if significant) in each direction are labelled in addition to *Gzmb*. Dashed horizontal line represents a p-value cutoff of 0.05. Only animals with more than 200 cells were included for comparison. **E**. IFN gamma protein levels in CT26 tumors tissue. Circles represent individual animals. Bars represent the mean. Unpaired *t*-test with Welch's correction (Control: n=10, TREX1 KO: n=9). *P < 0.05. **F-G.** Bar graphs and representative flow cytometry histograms showing expression of GZMB and SCA-1 on NK cells and CD8 T cells in tumors of the indicated genotype. Circles represent individual animals. Bars represent the mean. Unpaired t-test with Welch's correction (E, n=5 per group) and one-way ANOVA (F, n=10). *P < 0.05, **P < 0.01, *** P < 0.001. **H.** Extended tumor growth curve shown in Fig. 4E (n=10). **I.** Spider plots showing tumor growth curves of individual animals (n=10).