



Supplementary Figure 9. Epigenetic remodeling of CAR T-cells by *EGR2* knockout and effect of type I IFN signaling on the development of memory and exhaustion. **A**, Volcano plots showing differentially accessible chromatin regions within genes between *KLF2*⁺ and *MKI67*⁺ CD8⁺ T-cells. **B**, Volcano plots depicting differentially accessible chromatin regions within genes between *EGR2* and *AAVS1* knockout (KO) CD8⁺ CAR T-cells. **C**, Representative contour plots showing frequencies of TIM3- and LAG3-expressing CD8⁺ CAR-T cells after exposure to IFN β (1ng/mL) following chronic CAR stimulation. **D**, Proportions of CD27⁺ (left) or CD62L⁺ (right) CD8⁺ CAR-T cells after exposure to IFN β . **E**, Representative contour plots showing frequencies of CD45RO⁺CD27⁺ CD8⁺ CAR-T cells after IFNAR blockade (Anifrolumab, 1 μ g/mL) during chronic antigen stimulation. **F**, Frequencies of TIM3⁺LAG3⁺ CD8⁺ CAR-T cells after IFNAR blockade. **G**, Cytolytic capacity of CAR T-cells as measured by normalized cell index kinetics using the xCELLigence real-time cytotoxicity assay following chronic stimulation with target cancer cells in the setting of either IFN β or IFNAR blockade. **H**, Normalized cell index at 75 hours after challenge with target cancer cells. All experiments were conducted using healthy donor T-cells from independent donors (Mann-Whitney test, $n = 4$). * $P < 0.05$, * $P < 0.01$, *** $P < 0.001$, ns.: not significant.