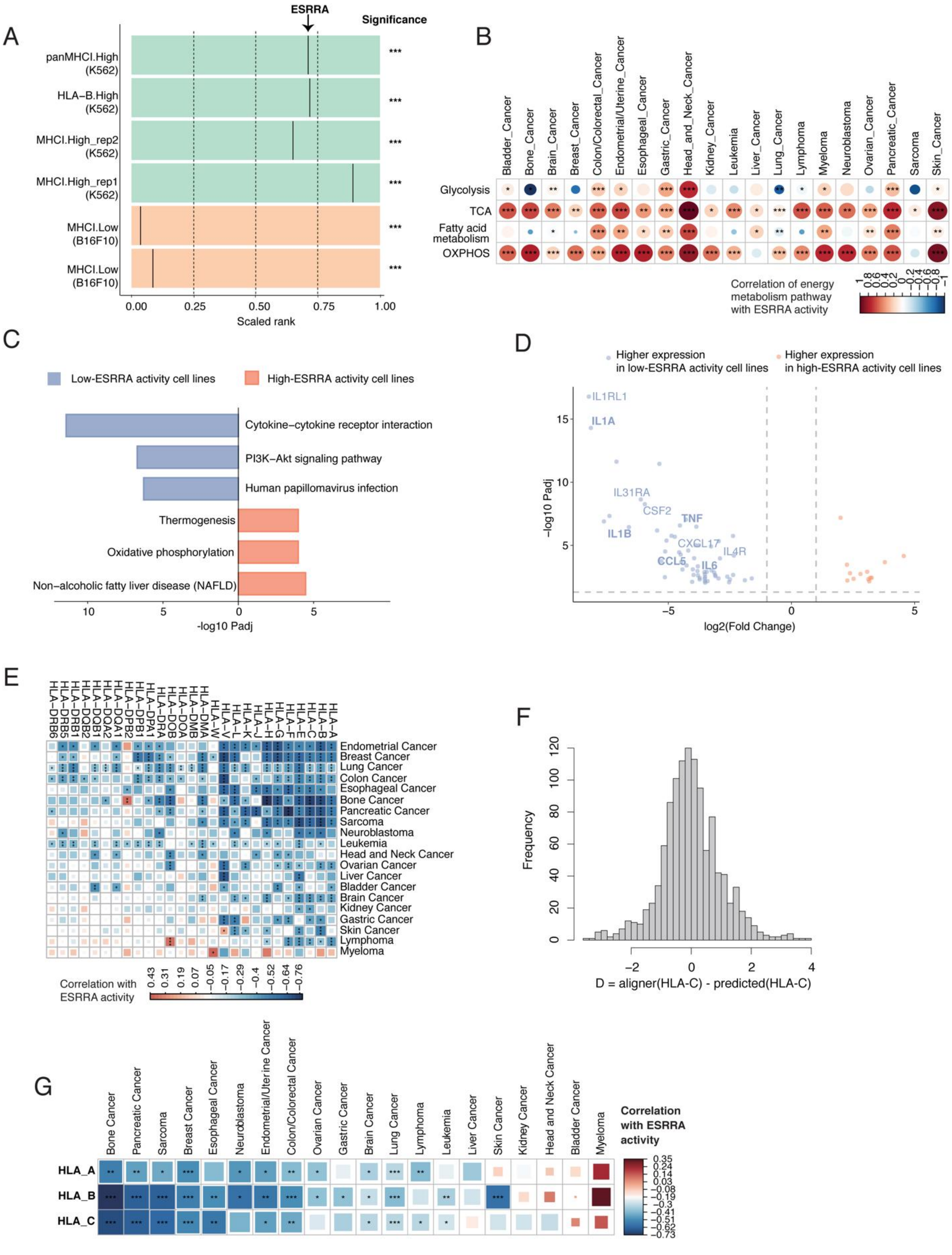

Fig. S7. Energy metabolism and immune signaling by targeting ESRRA *in vitro.*

p-value <0.05 *; <0.01 **;<0.001 ***

(**A**) ESRRA knockout in cancer cells enhances MHC-I expression. Rows correspond to CRISPR screens followed by cell sorting by either high (green rows) or low (orange rows) levels of MHC-I protein expression in a cancer cell line (shown in brackets). The black line represents the relative position of ESRRA knockout among all gene knockouts ranked from most depleted to least depleted. The depletion significance of ESRRA knockout was calculated by CRISPhieRmix. (**B**) The correlations of ESRRA activity with activation levels (estimated using ssGSEA score) of energy metabolism pathway across CCLE cancer types. (**C**) Pathways enrichment of upregulated genes in high (red) or low(blue) ESRRA activity cell lines in Cancer Cell Line Encyclopedia (CCLE). (**D**) Fold change and significance of differential expressed genes between high vs. low ESRRA activity cell lines. Macrophage-polarizing cytokines are labeled. (**E**) Correlations between the ESRRA activity and expression of antigen presentation genes in CCLE cancer types. (**F,G**) Analysis of ESRRA activity correlation with antigen presentation genes in CCLE cell lines: (**F**) Distribution of the HLA-C expression difference between the aligner and predicted. (**G**) Spearman correlations between ESRRA activity and expression of MHC-I genes across different cancer types in CCLE data.