

Figure S1 Differentially expressed genes across different LUAD subtypes (AAH, AIS, MIA, IAC). Red dots represent upregulated genes, blue dots represent downregulated genes, and gray dots represent genes with no significant changes. The selection criteria are indicated by dashed lines.

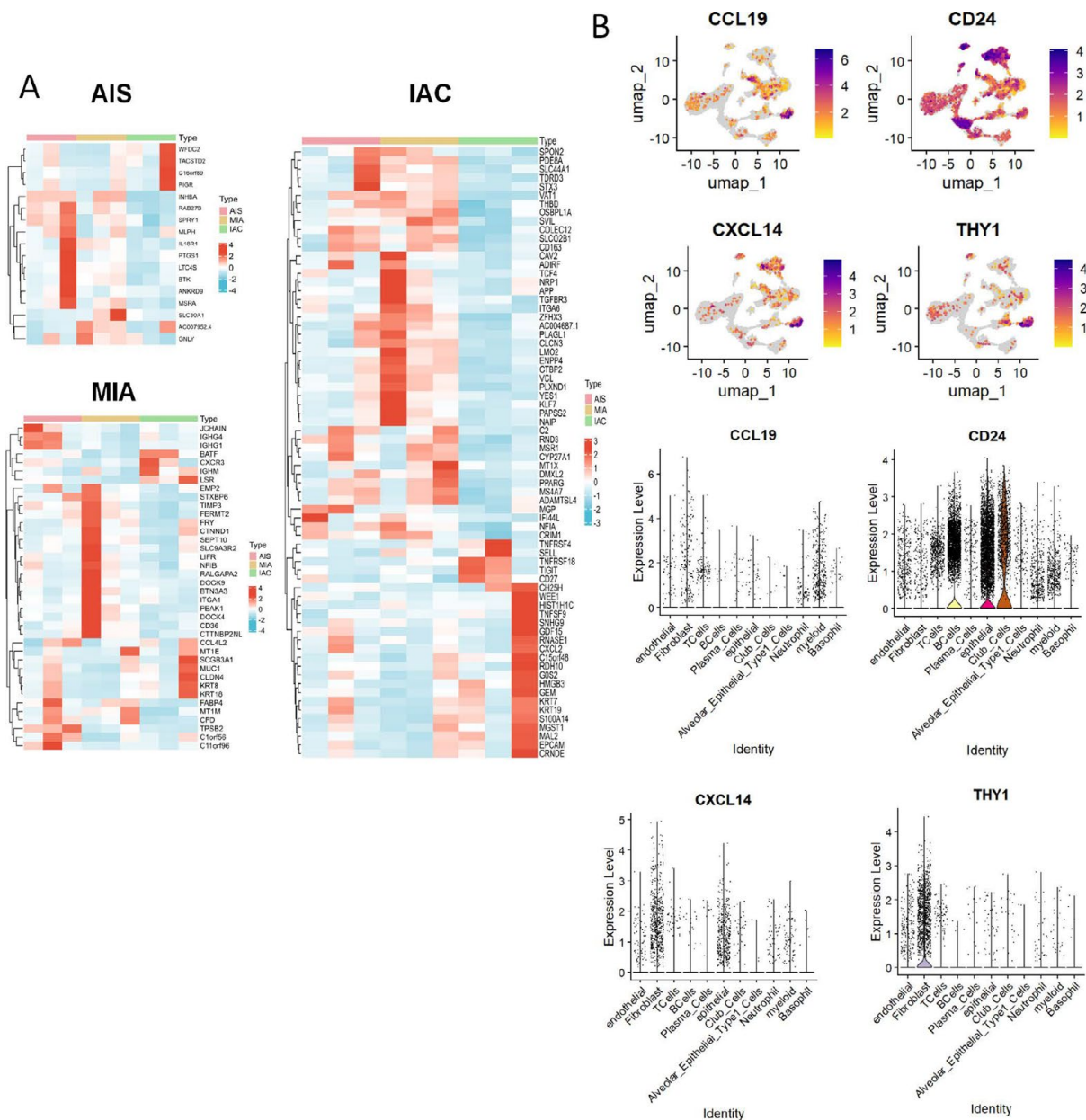


Figure S2 Heatmap of subtype-specific DEGs across LUAD subtypes, with the color bar above annotating the tissue type (A). Expression levels of CCL19, CD24, CXCL14, and THY1 across different cell types. Heatmap and violin plot showing the expression levels of CCL19, CD24, CXCL14, and THY1 in various cell types (B).

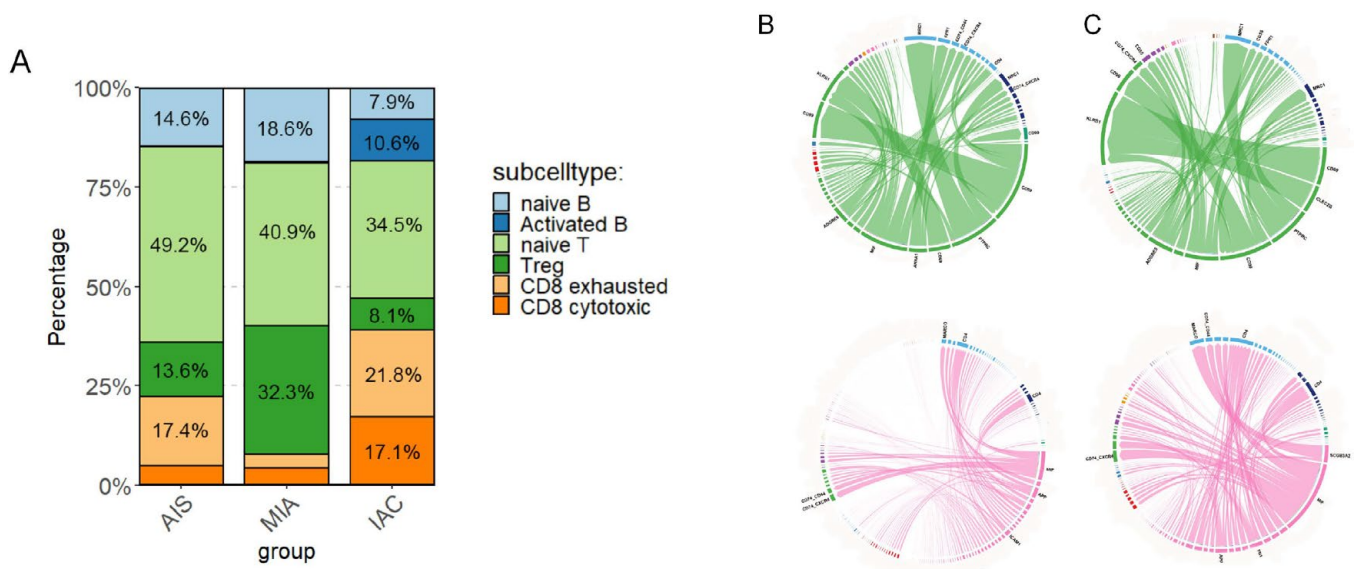


Figure S3 Immune cell heterogeneity, intercellular communication, and functional characteristics across AIS, MIA, and IAC subtypes. (A) Bar chart showing the proportional distribution of T cell and B cell subpopulations across LUAD subtypes. (B,C) Chord diagrams illustrate cell-cell communication between T cells and other cells, as well as between tumor cells and other cells, in the AIS (B) and MIA (C) stages. Edge width indicates interaction strength.

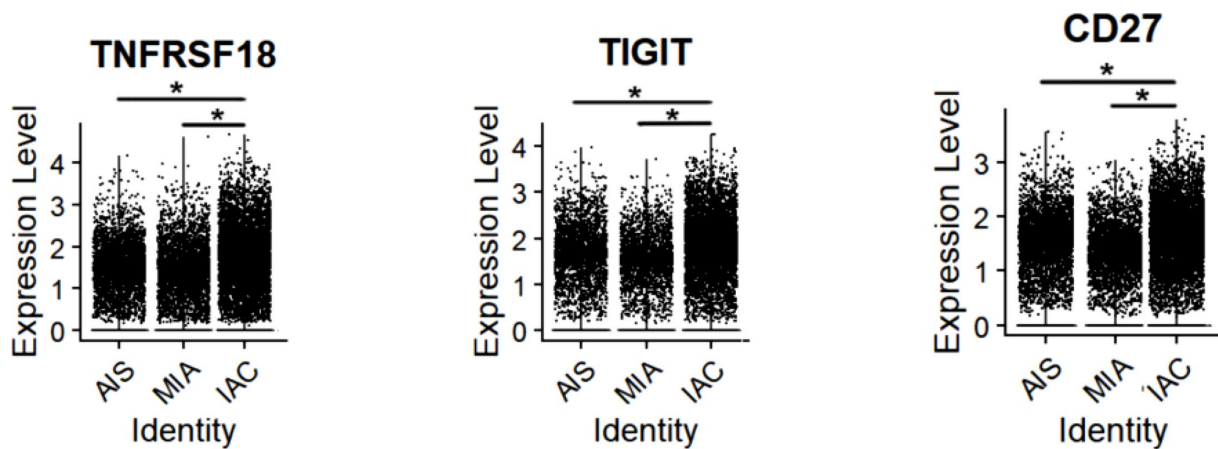
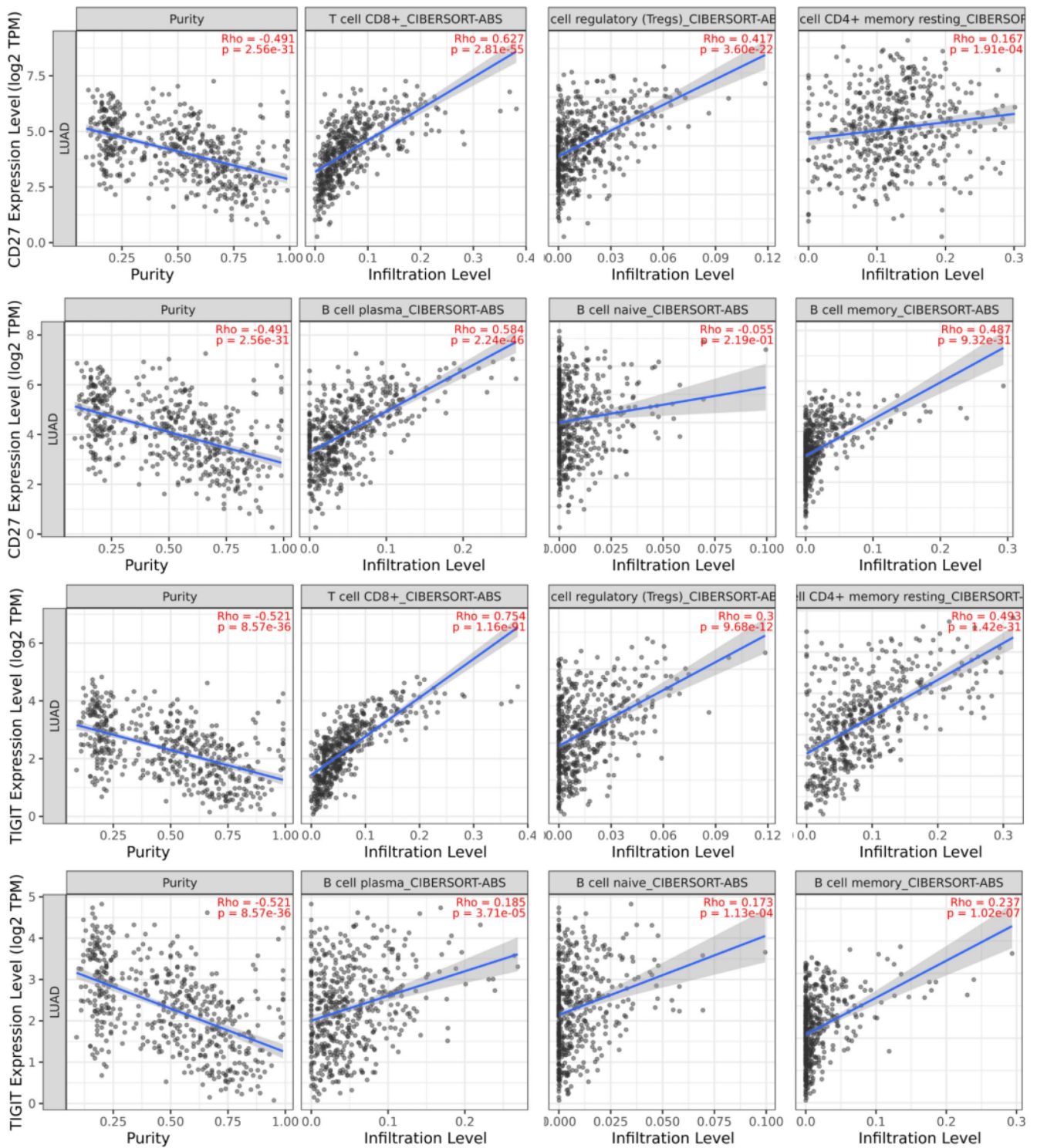


Figure S4 Expression levels of TNFRSF18, TIGIT, and CD27 across different LUAD subtypes. Violin plots displaying the expression levels of TNFRSF18, TIGIT, and CD27 in different LUAD subtypes. *, $P < 0.05$.



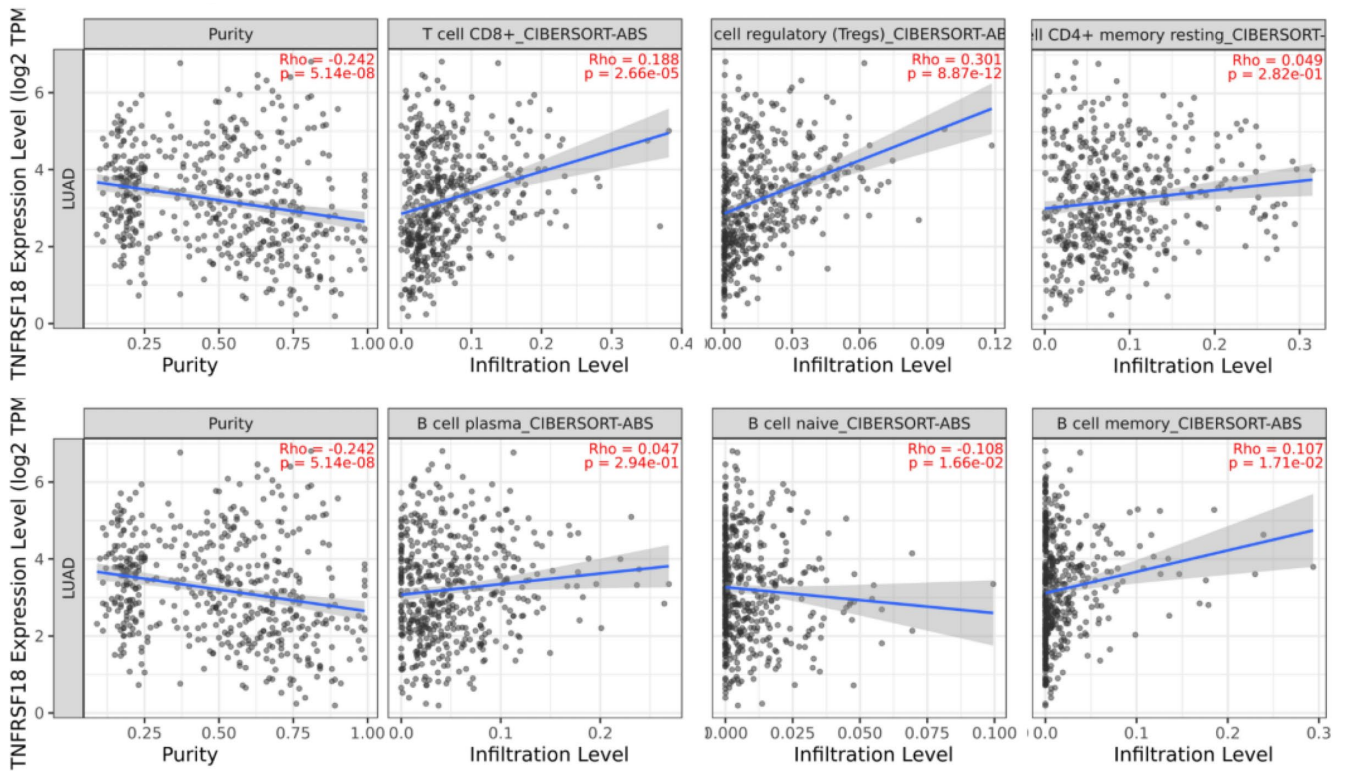
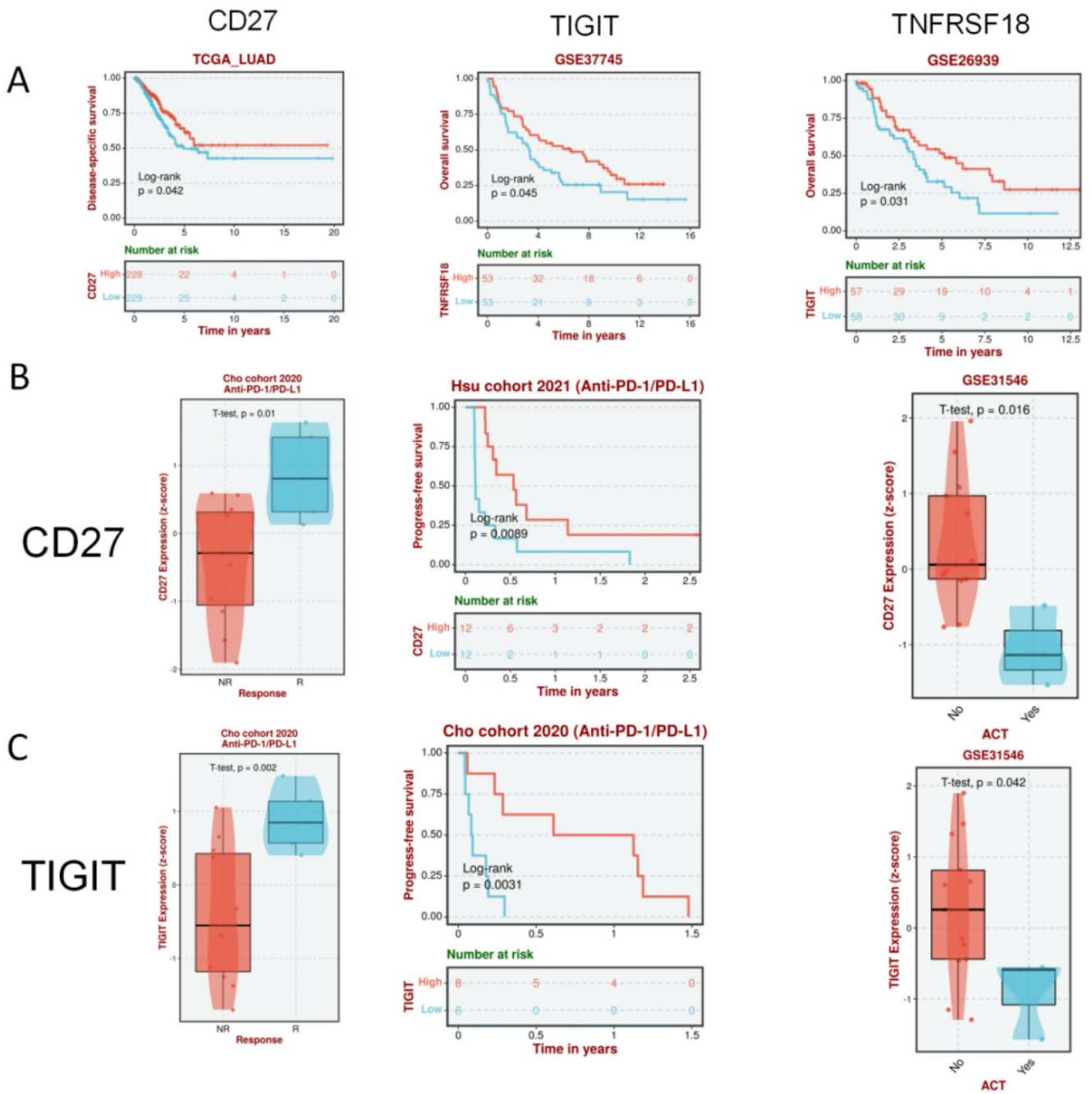


Figure S5 Correlation between CD27, TIGIT, and TNFRSF18 and tumor immune infiltration levels. Scatter plots show the relationship between gene expression levels and the infiltration levels of T cells (CD8+ T cells, Tregs, CD4+ memory resting) and B cells (plasma B cells, naive B cells, memory B cells).



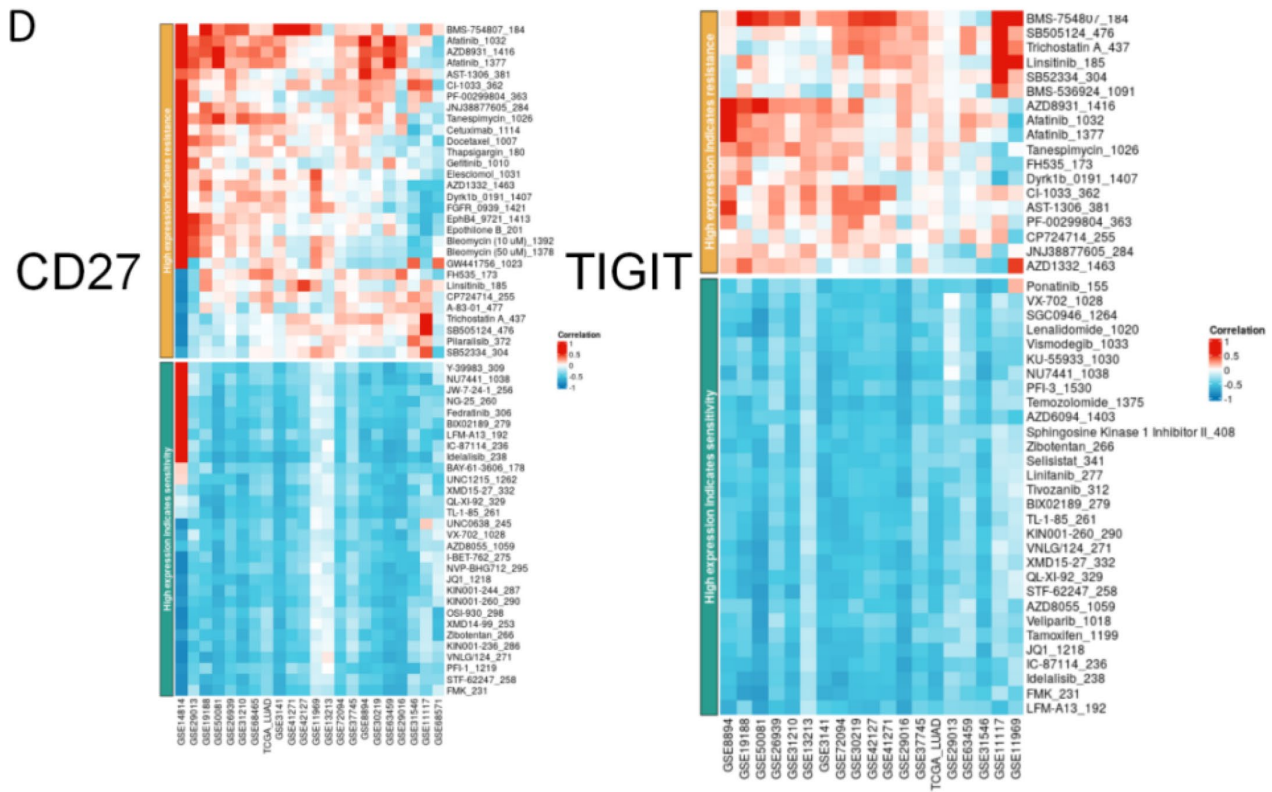


Figure S6 Prognostic value, immunotherapy relevance, and drug association analyses of CD27, TIGIT, and TNFRSF18 in LUAD. (A) Kaplan-Meier survival curves of CD27, TIGIT, and TNFRSF18 expression in the TCGA-LUAD, GSE37745, and GSE26939 cohorts. (B) Expression differences and survival analyses of CD27 in anti-PD-1/PD-L1-treated cohorts (Cho cohort 2020 and 2021), as well as comparison of CD27 expression between immune-active (ACT) and immune-non-active (ND) subtypes in the GSE13516 dataset. (C) Expression differences and survival analyses of TIGIT in the anti-PD-1/PD-L1-treated cohort (Cho cohort 2020), and comparison of TIGIT expression between ACT and ND subtypes in the GSE13516 dataset. (D) Heatmaps showing the correlations between CD27 and TIGIT expression levels and multiple anti-cancer drugs.