

Supplementary Table legend:

Table S1: Clinical information of samples used in the study.

Table S2: Differently expressed genes among epithelial cells.

Table S3: Marker genes of subpopulations of epithelial cells in this study.

Table S4: Gene list of function modules or pathway.

Supplementary Figure legend:

Figure S1: Quality control of single cell sequencing data. Violin plots show number of UMI (nUMI), number of genes (nGene) detected, percent of mitochondrial derived transcripts (percent.mt), and percent of Hematopoietic Blood (percent.HB) derived transcripts per single cell after quality control.

Figure S2: Images of IHC staining of canonical surface markers for T cell (CD3), NK cells (CD56) in NMIBC and MIBC samples.

Figure S3: The epithelial cells sub-population. (A) Dot plot of top 5 marker genes for each epithelial cluster. (B) The result of GO enrichment analysis of clusters. clusters 3, 6, and 16 were enriched in the ribose phosphate metabolic process, while clusters 1, 12, and 17 were enriched in cytoplasmic translation. (C) Heatmap showing the copy number variations (CNVs) evaluated per cell by InferCNV. Two normal-derived epithelial clusters were used as control group.

Figure S4: The relationship between epithelial cells sub-populations and clinical information. (A) The expression of signature markers in each cell type of epithelial cells. (B) Box plots showing the cellular fraction of each T/NK cluster in high grade, low grade, and adjacent normal tissue. (C) Study workflow. Gene expression data of BLCA patients with prognosis information from the GEO and TCGA databases were collected. The TCGA-BLCA cohort includes 436 samples, and GSE13507 cohort includes 165 samples. Subsequently, the marker genes for the epithelial cells subpopulations identified from scRNA-seq data were used to calculate the abundances of these tumor cell sub-populations in bulk cohorts using ssGSEA method. Prognosis and clinical trait analyses were conducted by correlating these cell abundances with the overall survival (OS) of the patients. (D) Box plots showing the epithelial cell sub-populations distribution in cancer and normal in TCGA-BLCA cohorts. (E) Box

plots showing the epithelial cell sub-populations distribution in different pathological T stage in TCGA-BLCA cohort. (F) The survival curves for selected tumor cell sub-populations in TCGA-BLCA.

Figure S5: The relationship between epithelial cells and glycolysis. (A) The expression of glycolysis related genes (HK1, HK2, HIF1A, LDHA) in each cell type of epithelial cells. (B) Violin plot showing the glycolysis signature scores across epithelial cell subpopulations. (C) Correlation between glycolysis signature scores and epithelial cell subpopulations in TCGA-BLCA, alongside Kaplan-Meier survival curves for these subpopulations. Scatter plots display the correlation coefficients (R) and *P*-values, while survival curves indicate overall survival differences between high and low infiltration groups.

Figure S6: T/NK cell remodeling during BC progression. (A) UMAP plots of T/NK cells, colored by cluster, tumor grade, invasive status, and patient origin. (B) Expression patterns of T/NK cell marker genes (related to Figure 4A, B). (C) Dot plot showing the expression levels of signature markers across different T/NK cell subtypes. (D) Box plots comparing the expression scores of T/NK cells between normal and cancerous tissues in the TCGA-BLCA cohort. (E) Diffusion map illustrating the developmental trajectories of CD8⁺ T cells in BC. (F) Kaplan-Meier survival curve showing the overall survival differences between high and low CD8_GZMK infiltration groups in the TCGA-BLCA cohort.

Figure S7: Myeloid cell markers and macrophage signatures. (A) UMAP plots showing the expression of marker genes for myeloid cells (related to Figure 6A, B). (B) Heatmaps illustrating the differential expression patterns of M0, M1, and M2 macrophage signatures across various macrophage subsets in adjacent tissues, NMIBC, and MIBC samples.

Figure S8: Reclustering of mast cells and transcription factor (TF) activity analysis. (A) UMAP plots of mast cells, colored by invasion status (invasive, non-invasive, normal), individual samples, and tumor grade (high, low, normal). (B) UMAP plots displaying TF activity for selected genes (NFKB1, DDIT3, CREM, and JUNB), with density gradients representing activity levels (related to Figure 7G).

Figure S1

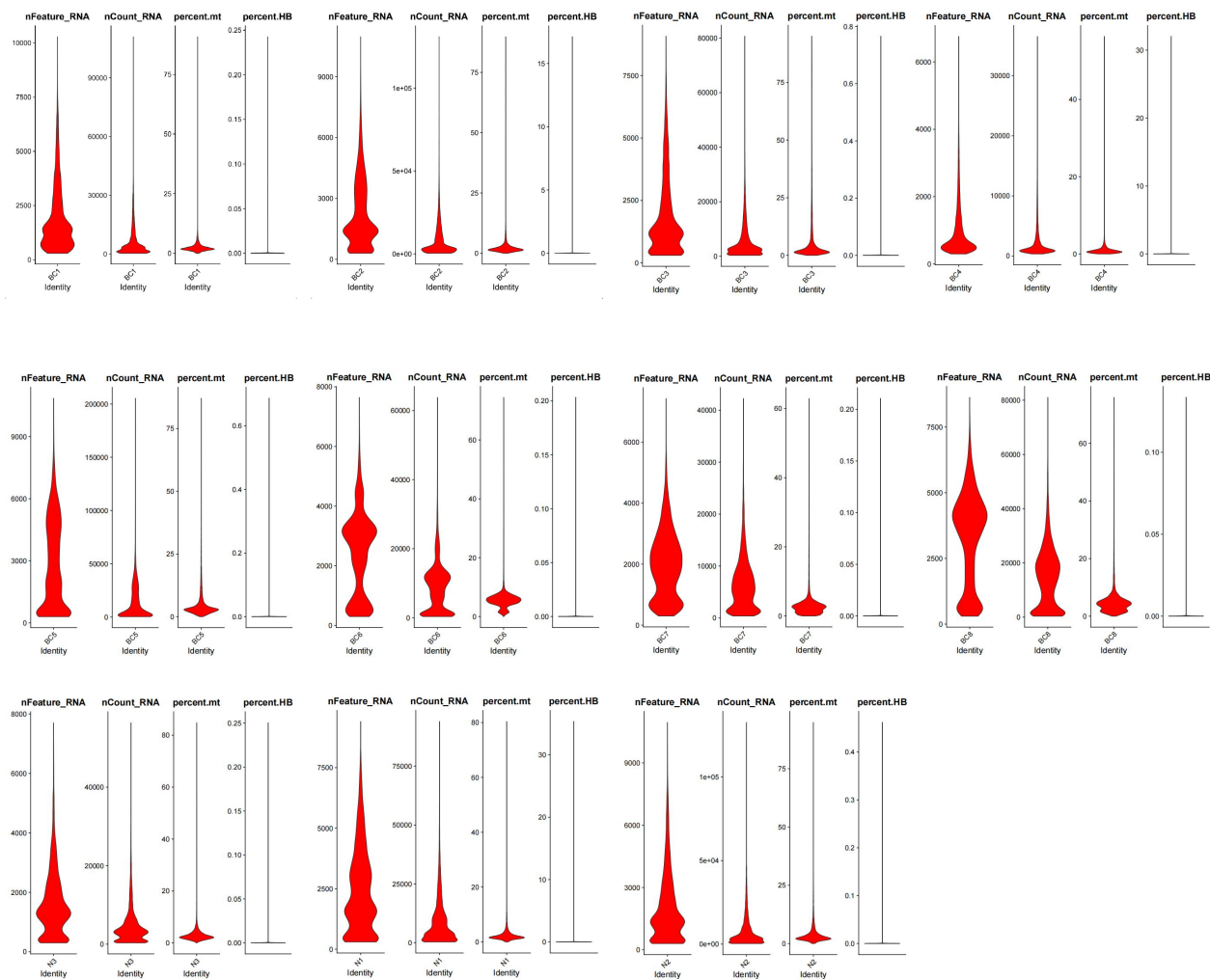


Figure S2

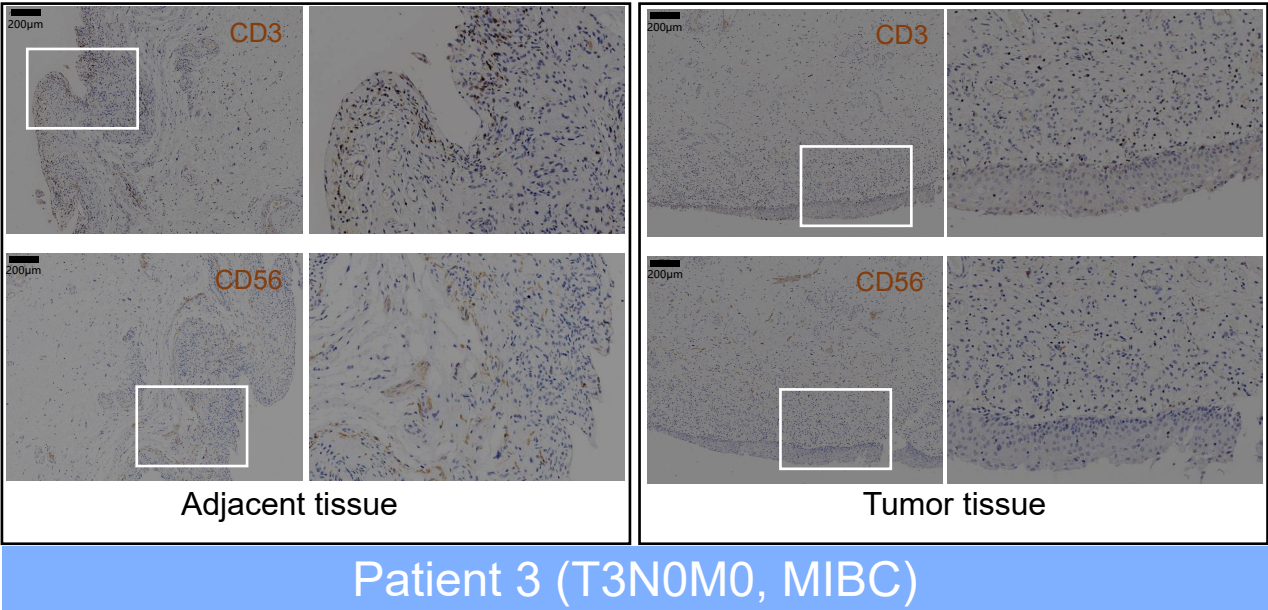
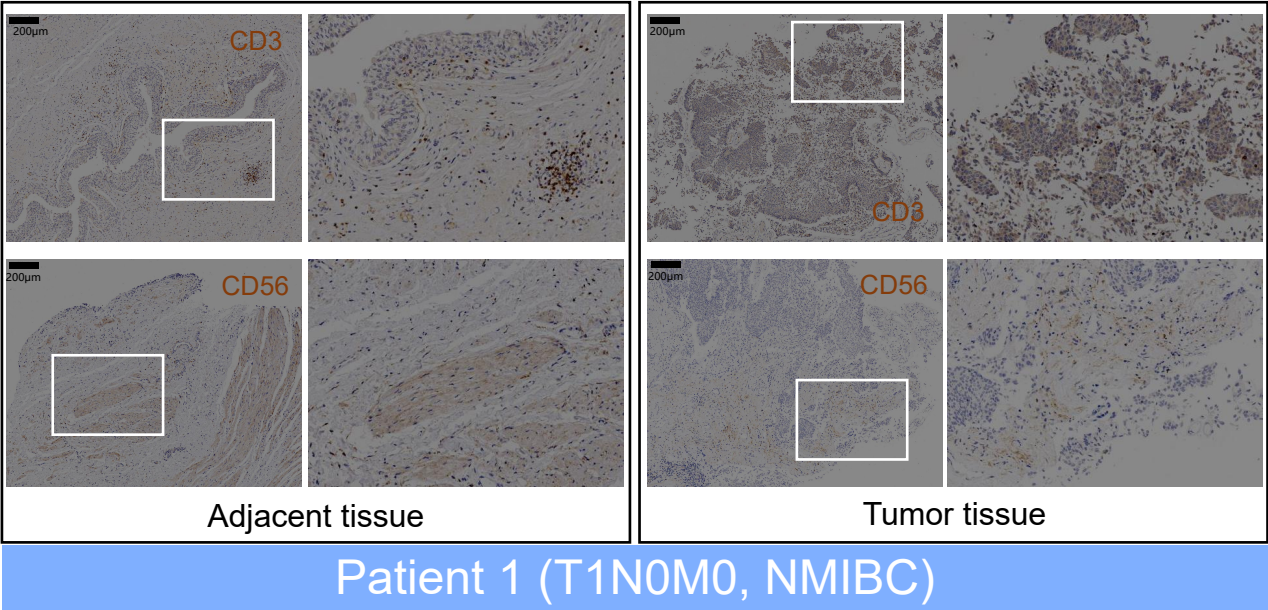
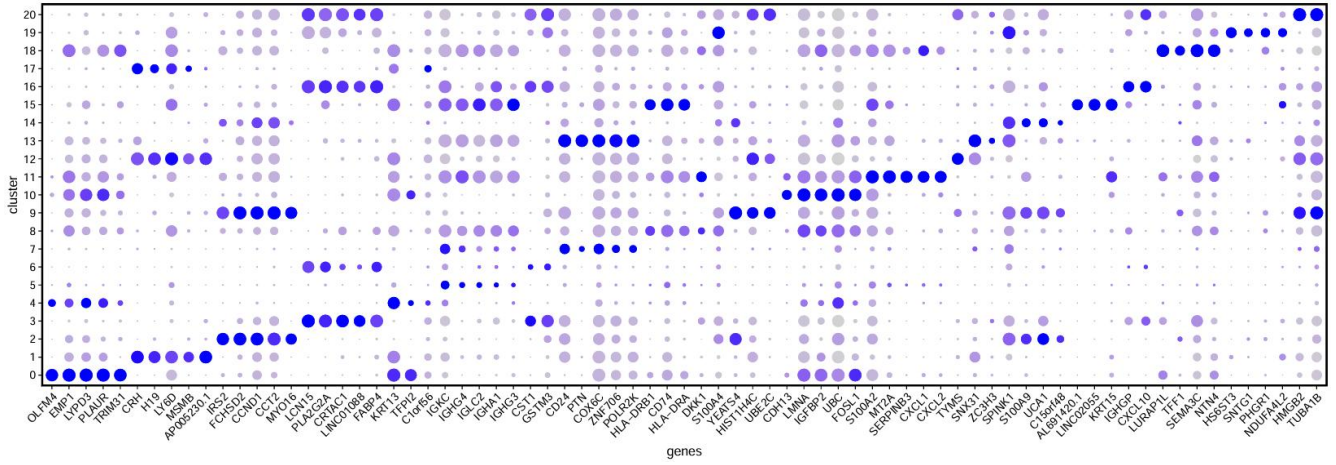
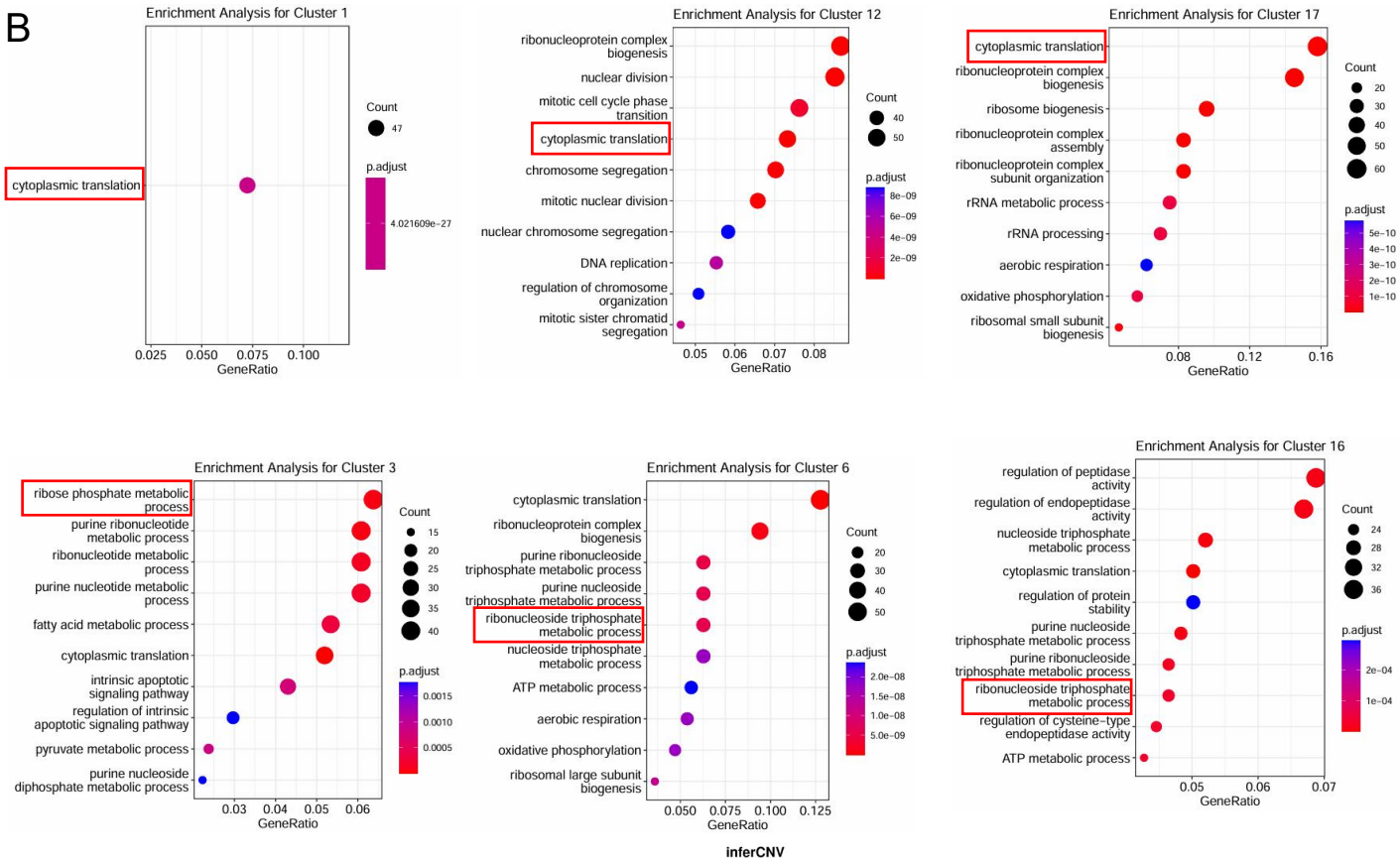


Figure S3

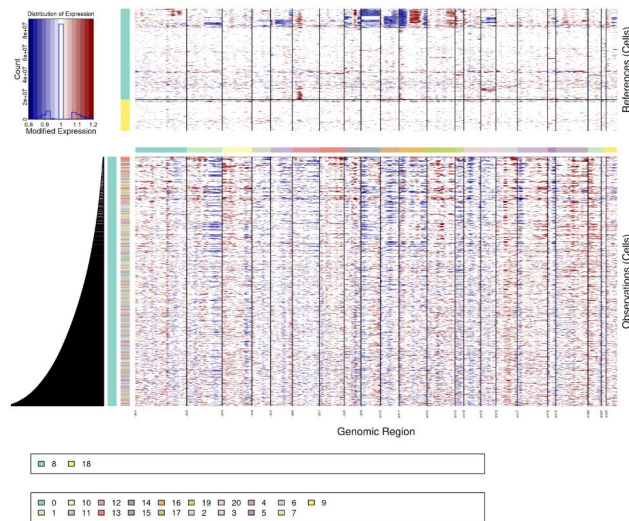
A



B



C



A

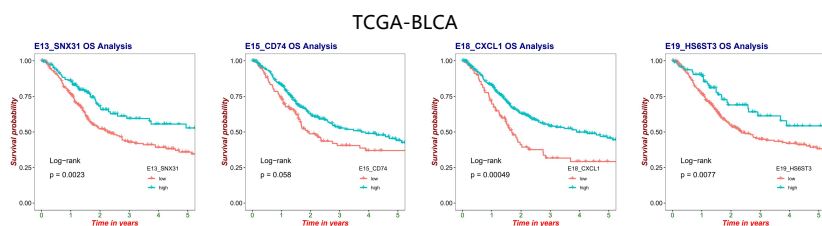
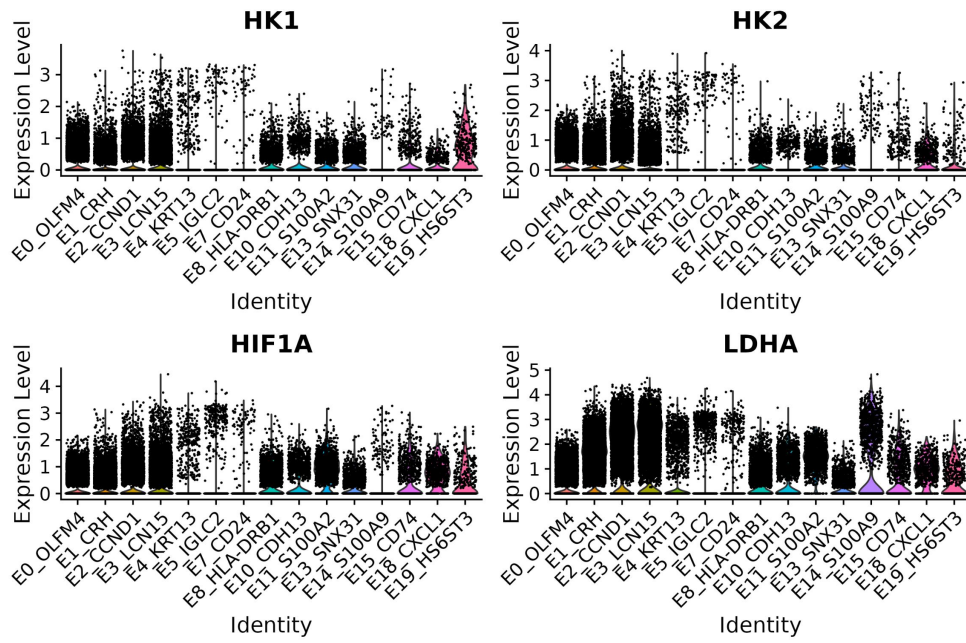
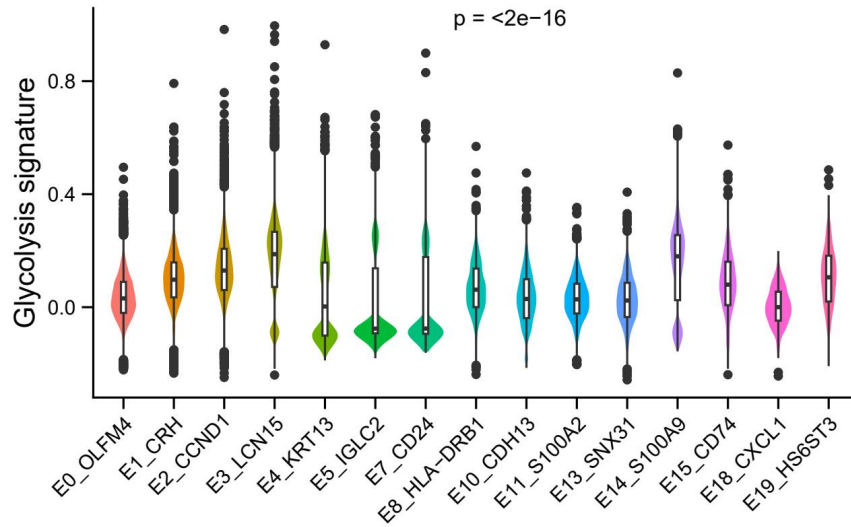


Figure S5

A



B



C

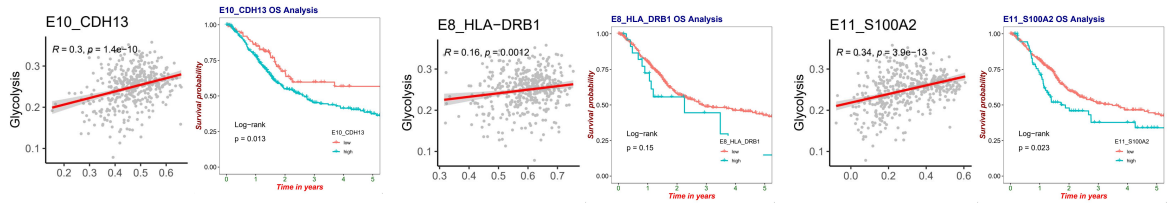


Figure S6

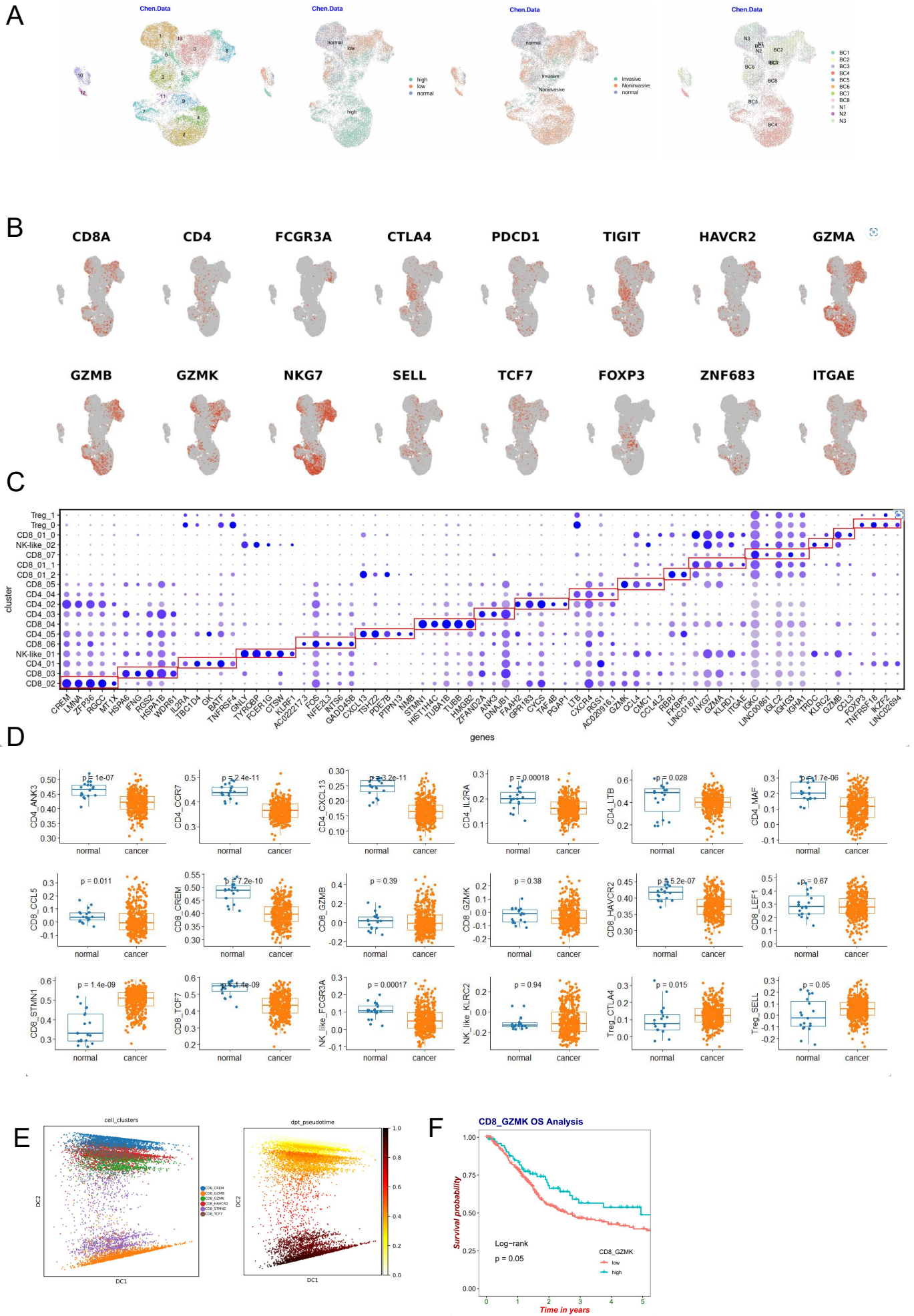
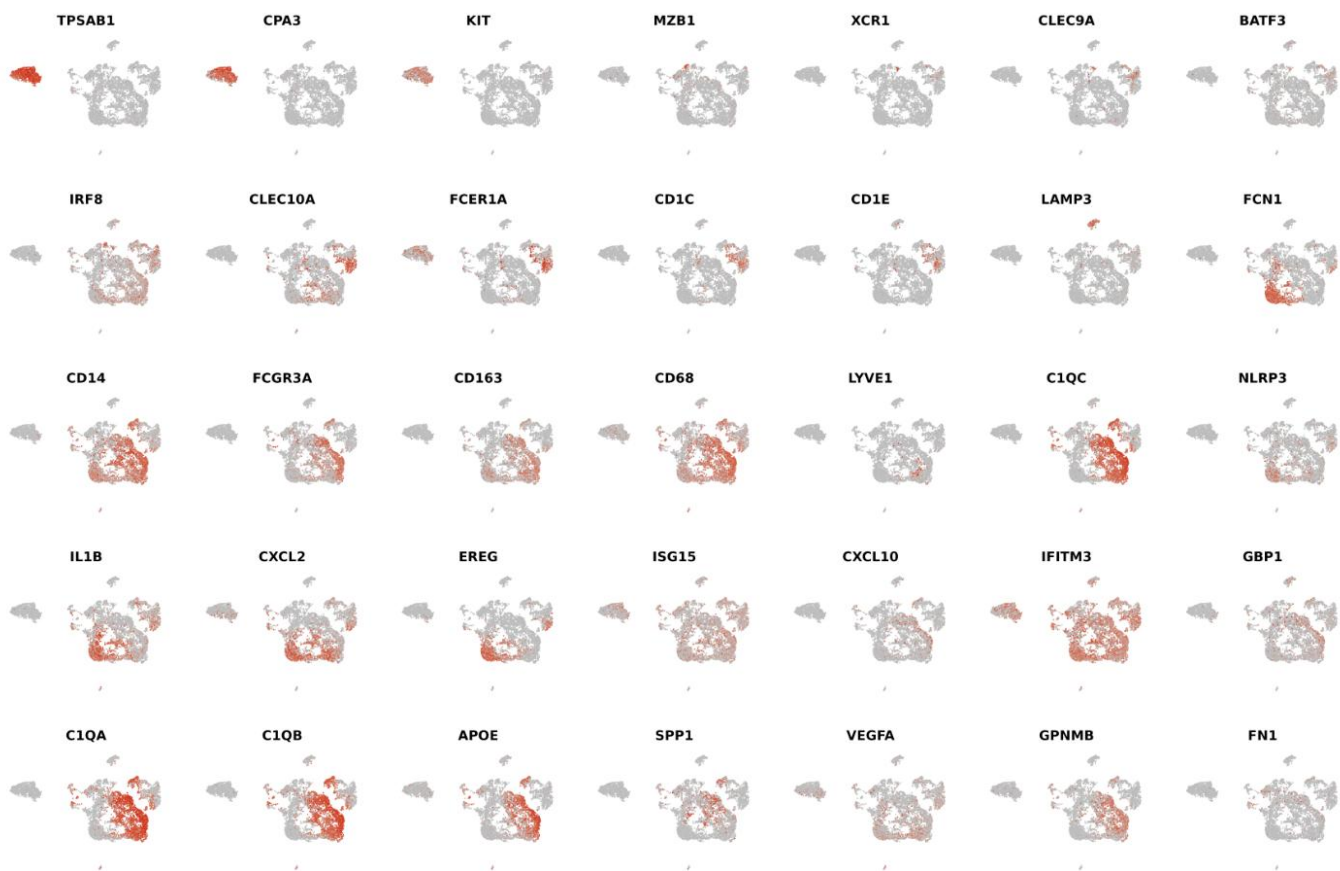


Figure S7

A



B

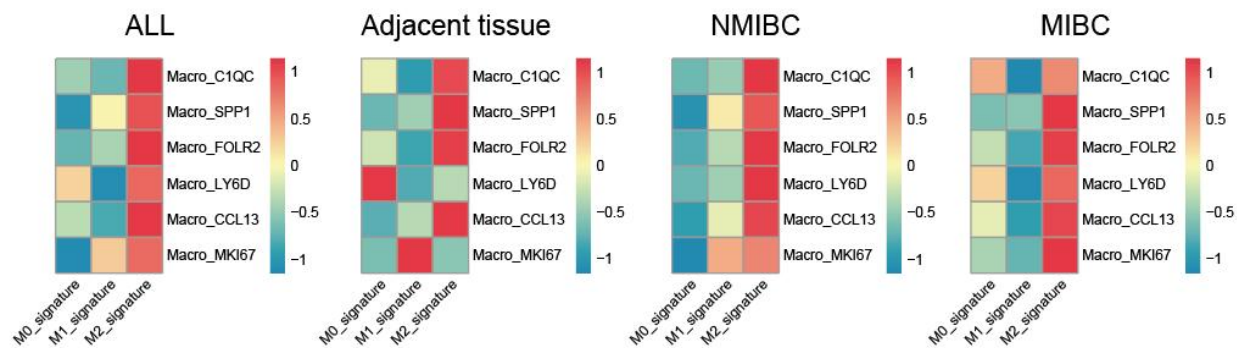


Figure S8

