Figure S1. Summary of results in forward Mendelian Randomization using meta-analysis. (A): Result of lung cancer to SS. (B): Result of ovarian cancer to SS. (C): Result of endometrial cancer to SS. (D): Result of breast cancer to SS. (E): Result of colorectal cancer to SS.

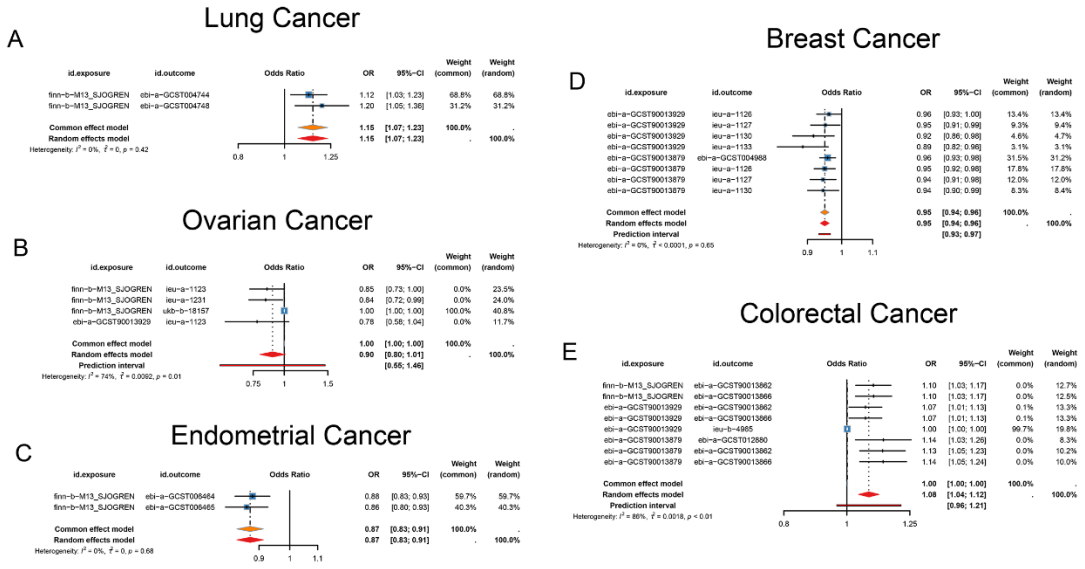


Figure S2. Summary of results in backward Mendelian Randomization using meta-analysis. (A): Result of SS to female genital cancer. (B): Result of SS to lung cancer.

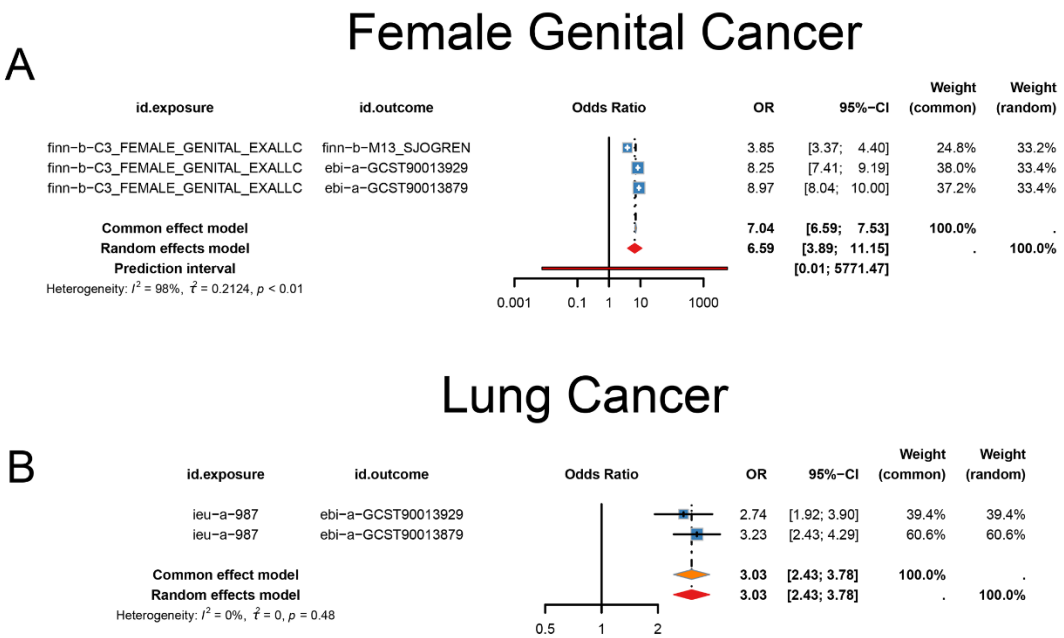


Figure S3. (A)&(B): Correlation between HLA-DPB2 and HLA-DPB1. (A) rooted in TIMER. The expression level of HLA-DPB1 was displayed on the x axis while HLA-DPB2 on the y axis. (B) rooted in TCGA. The expression level of HLA-DPB1 was displayed on the y axis while HLA-DPB2 on the x axis. (C): Correlation between immune cells and genes of DPB1&DPB2 estimated by Cibersort. Cell types were displayed on the y axis while genes on the x axis. For colors, gray means insignificance (P>0.05), in other significant colors (P<0.05), red demonstrates positive correlation while blue demonstrates negative. (D) Colocalisation analysis between the expressions of HLA-DPB2 and HLA-DPB1.

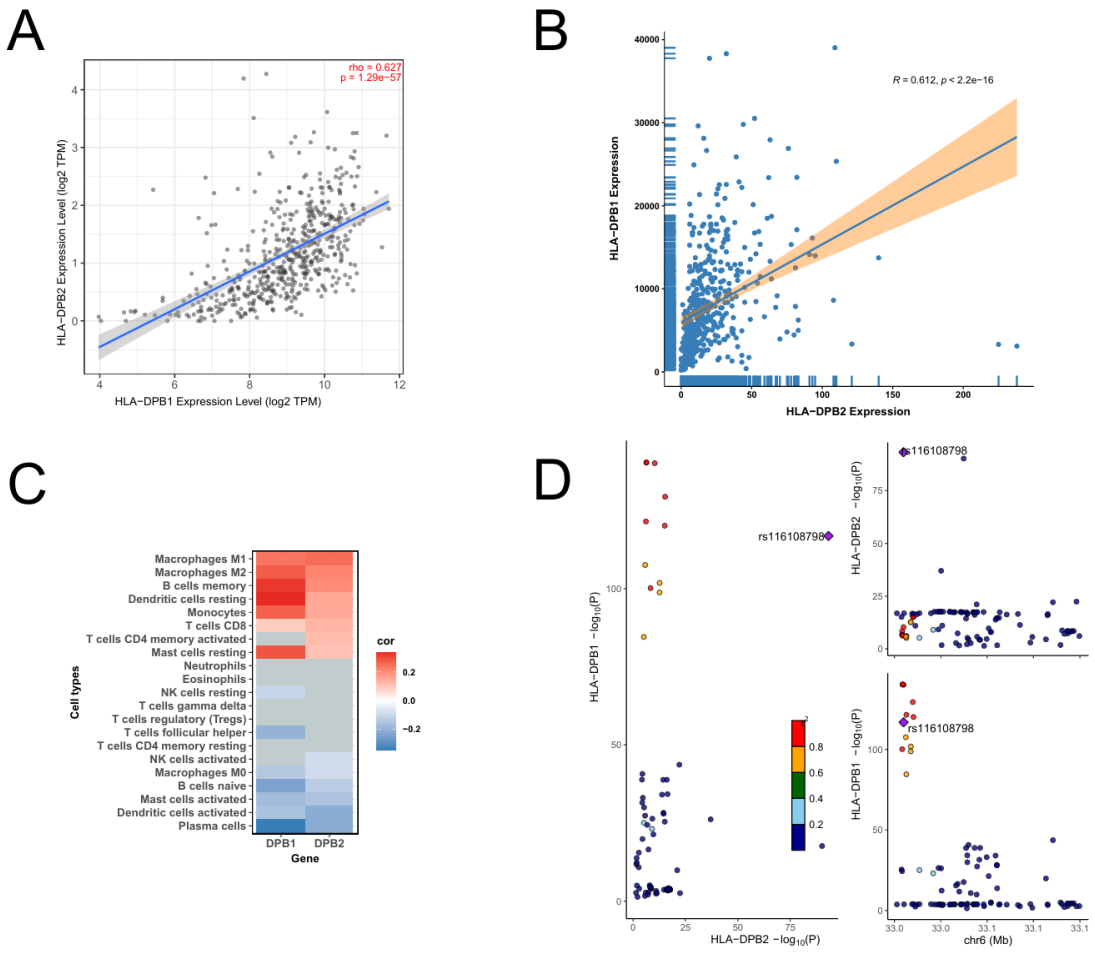


Figure S4. PPI networks between HLA-DPB1 and green module genes. The PPI enrichment p-value < 10 e-16 and avg.local clustering coeffident is 0.429.

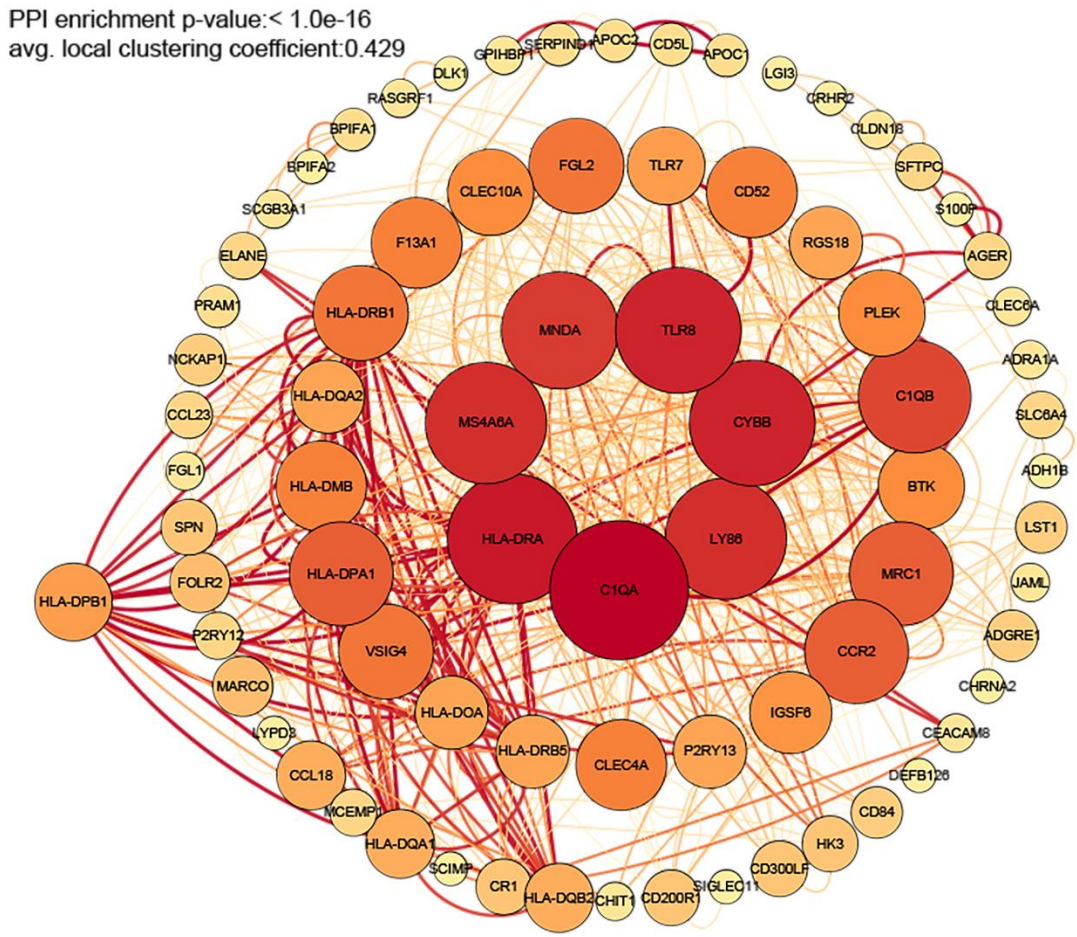


Figure S5. UMAP plot of immune cells in early and advanced stage of lung cancer. Red: early stage; Blue: advanced stage.

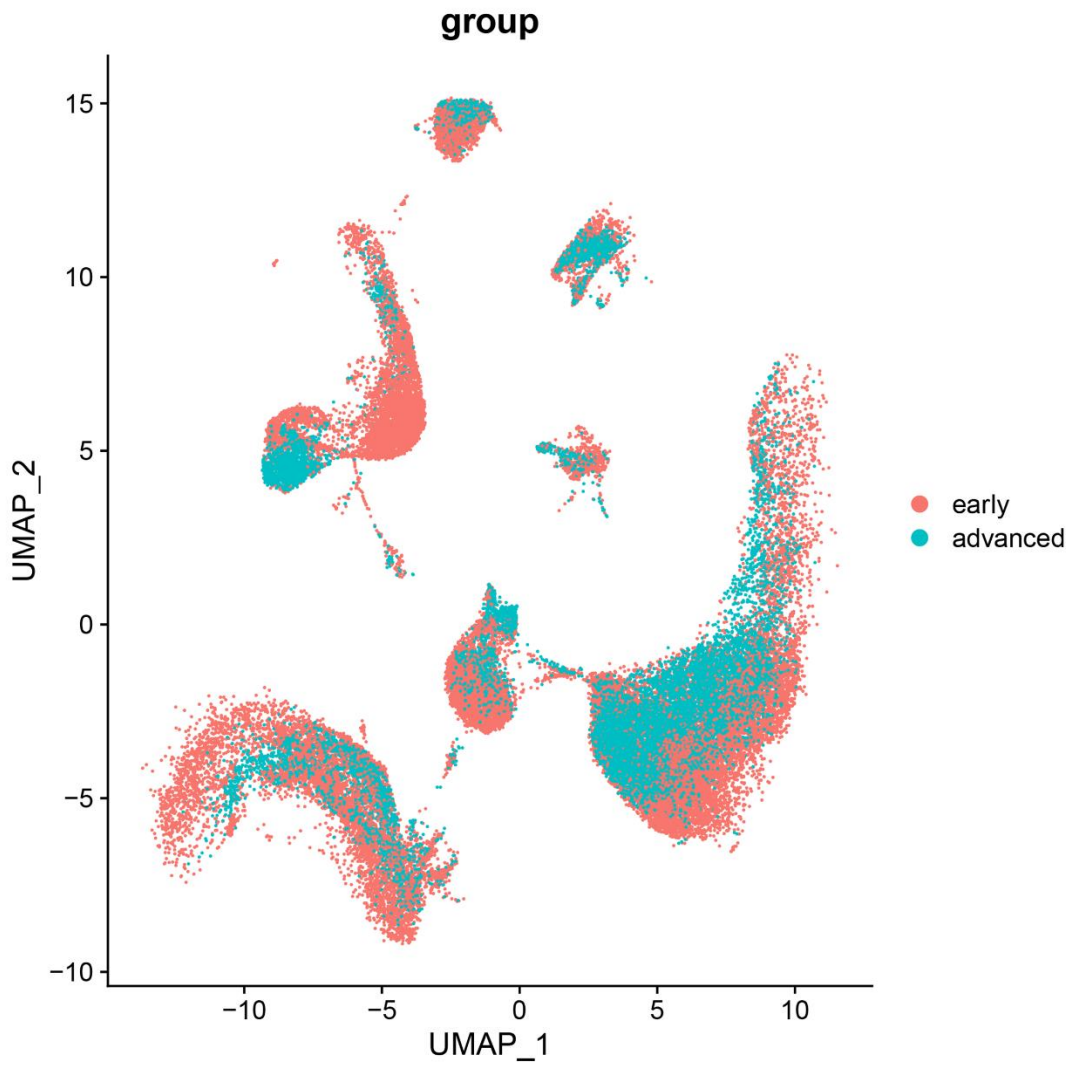


Figure S6. UMAP plot of the scRNA-seq dataset GSE131907 of lung cancer immune cells. 25 clusters were identified. Downscaling was performed by The "RunUMAP" function and visualized using UMAP plots.

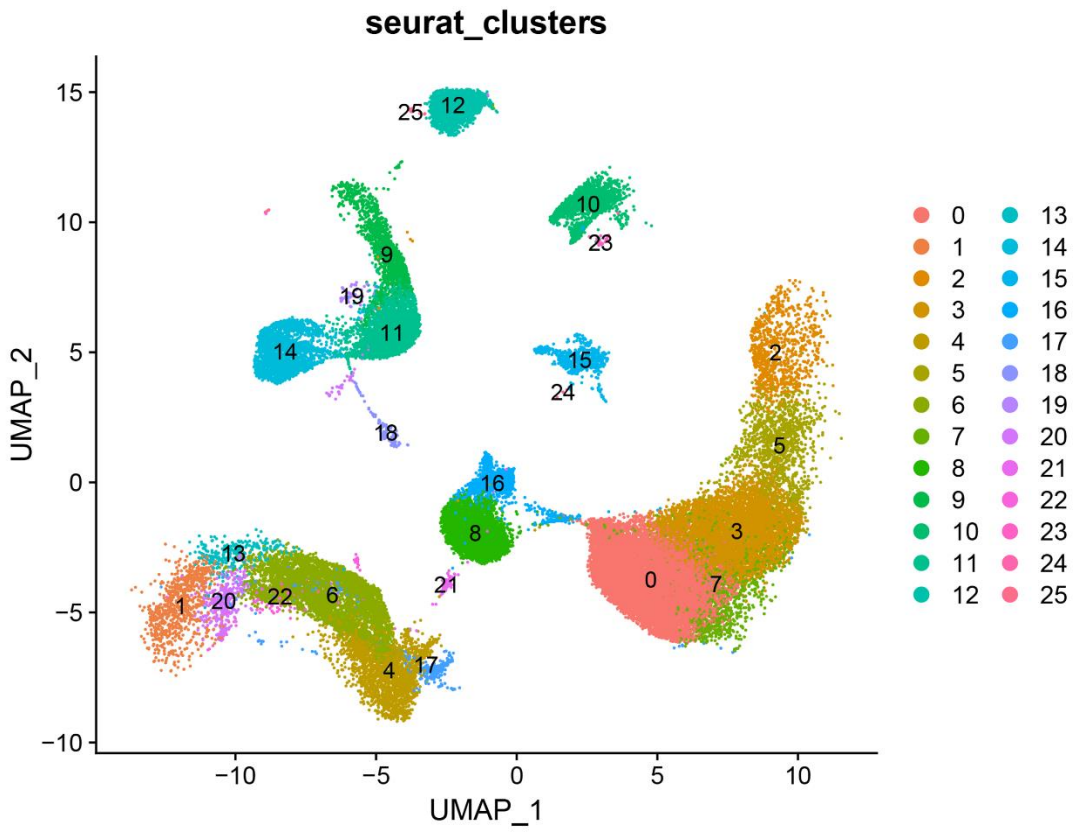


Figure S7. Heatmap of the expression of different cell clusters TOP genes. In the heat map, each column represents one group of cell and each row represents one gene, and the gradual color ranging from blue to red represents the changing process from low to high expression.

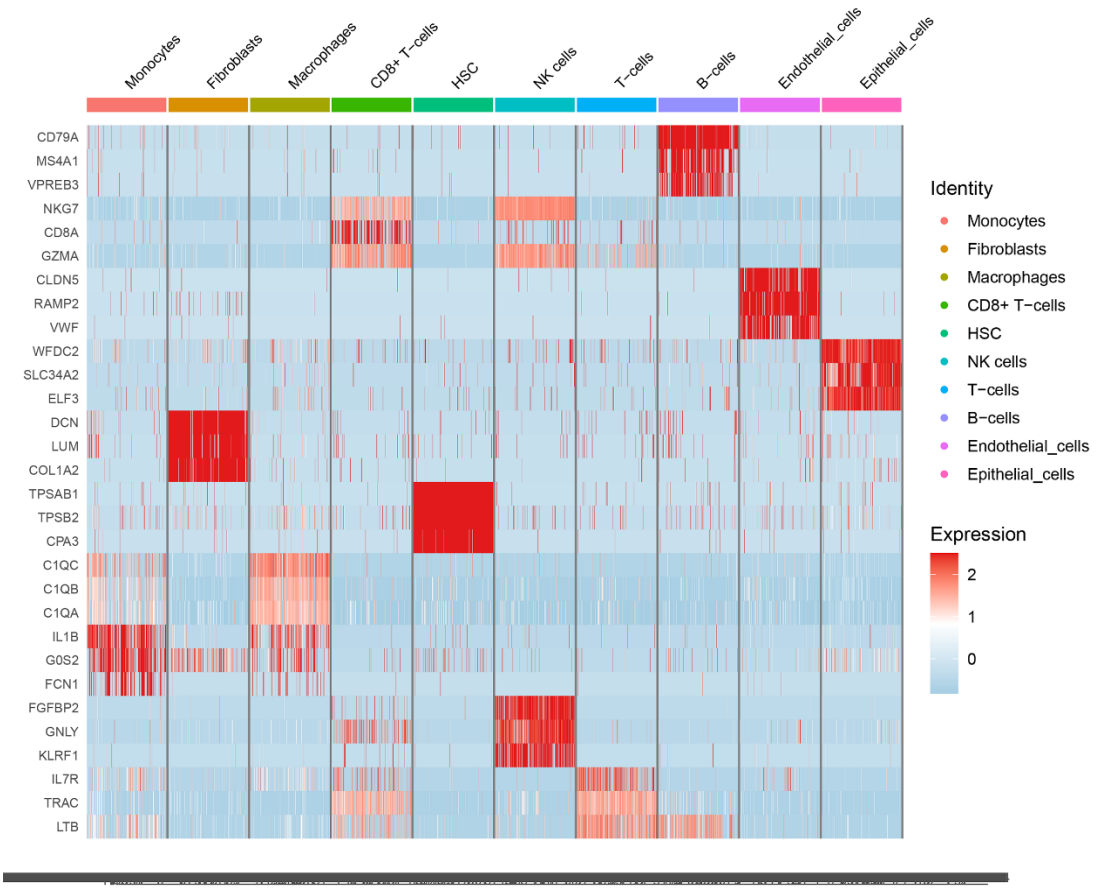


Figure S8. Graphical representation of HLA-DPB1 gene expression in various immune cells. This figure displays the log2-fold change in gene expression levels across different immune cell types. The color coding for the bars represents the percentage difference in gene expression, with darker shades indicating a greater fold change. When the percentage difference of immune cell is above 0, it represents a significantly high expression of HLA-DPB1 (red marker). Otherwise, it shows a low expression (blue marker).

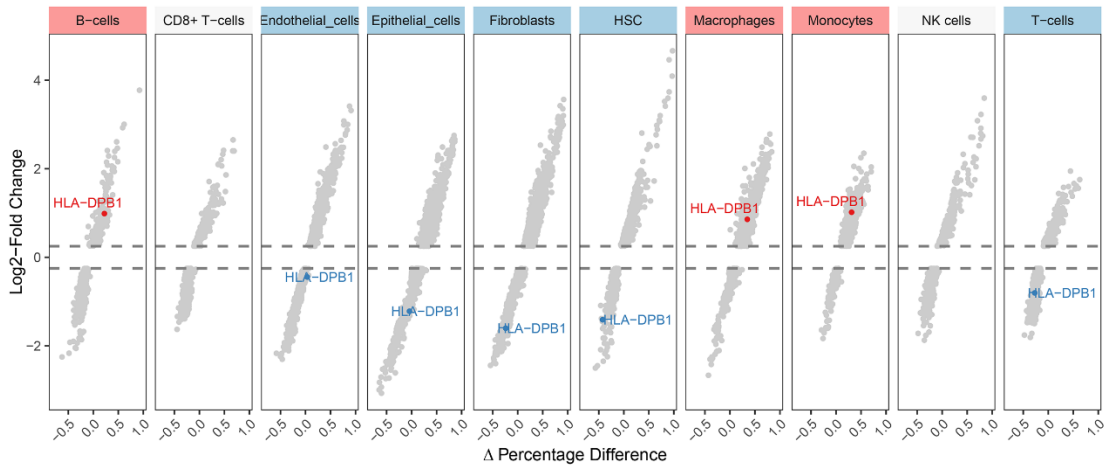


Figure S9. Marker genes of B memory cell and B GC cell for cell annotation in UMAP.

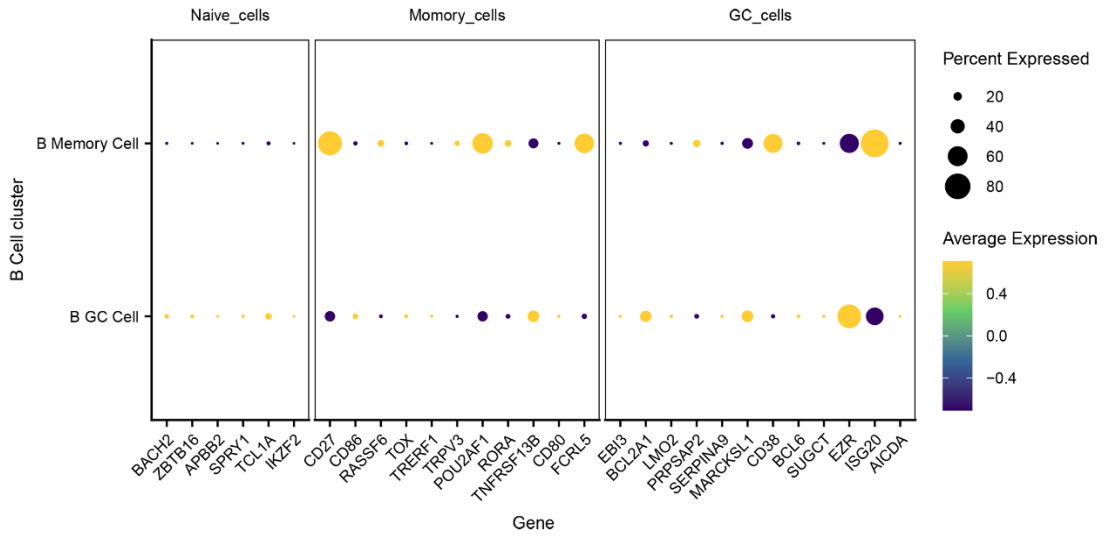


Figure S10. GSEA of three HLA-DPB1 related function. Rank in ordered dataset is displayed on the x axis. On the y axis, from bottom to the top, distribution of Ranked List Metric, positions of each gene, and enrichment score line chart are displayed. Different colors match different functions. All the ESs are above 0.

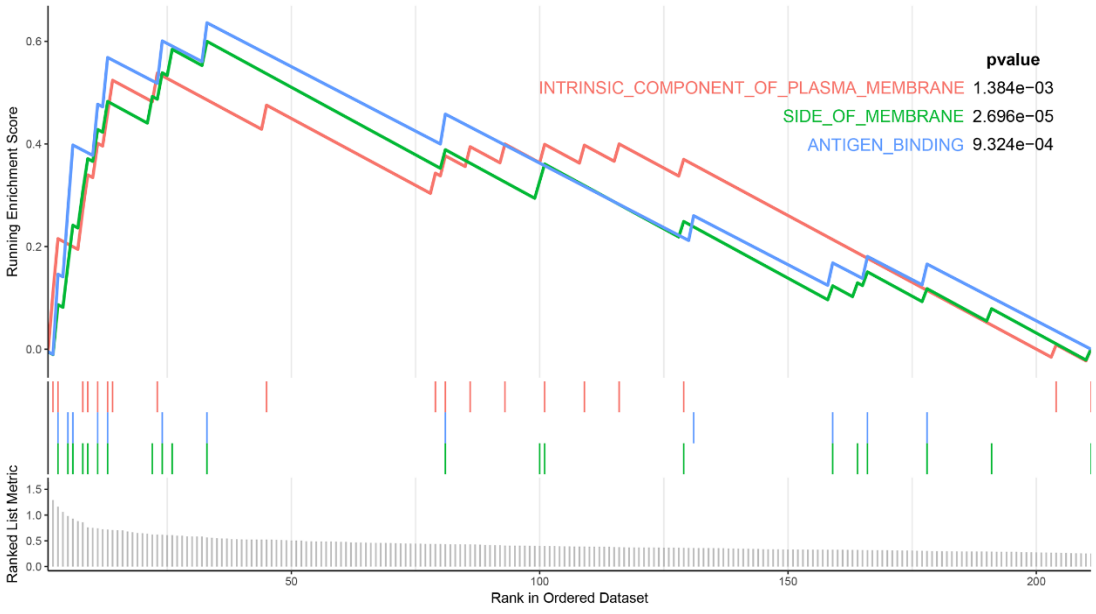


Figure S11. UMAP plots for further downscaling of T cells.

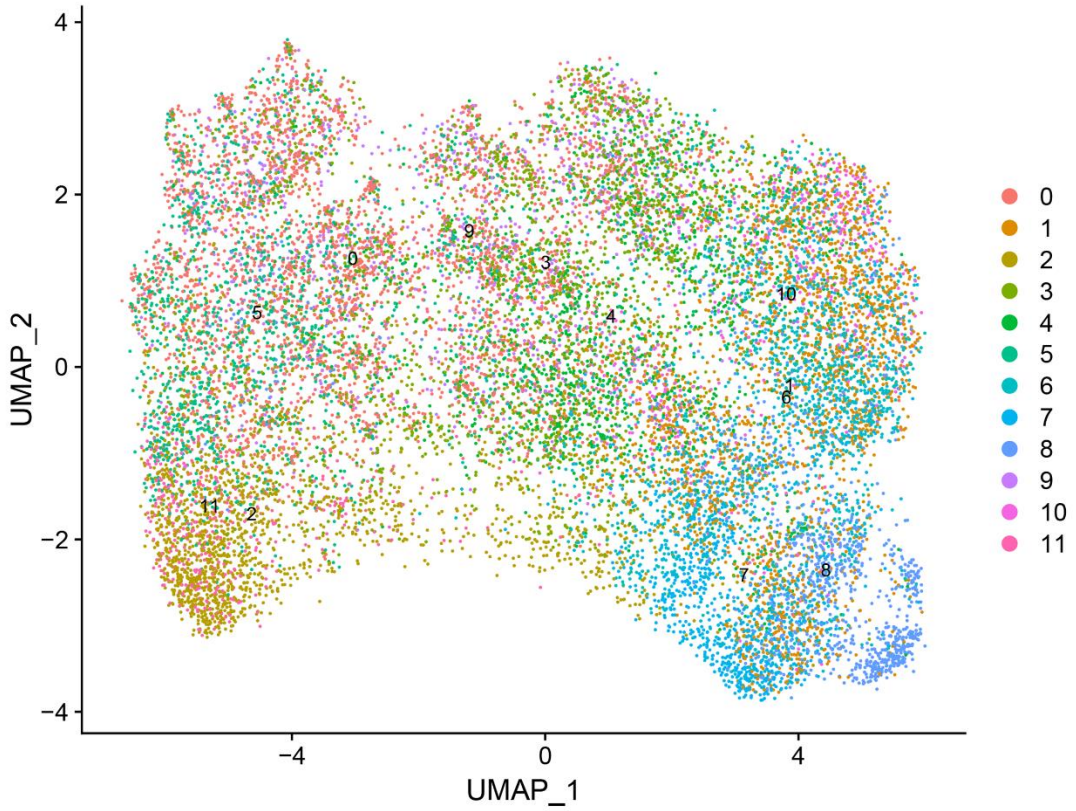


Figure S12. The UMAP plots of T cells re-annotated. The single-cell data were downscaled by UMAPd, and 3 clusters were identified.

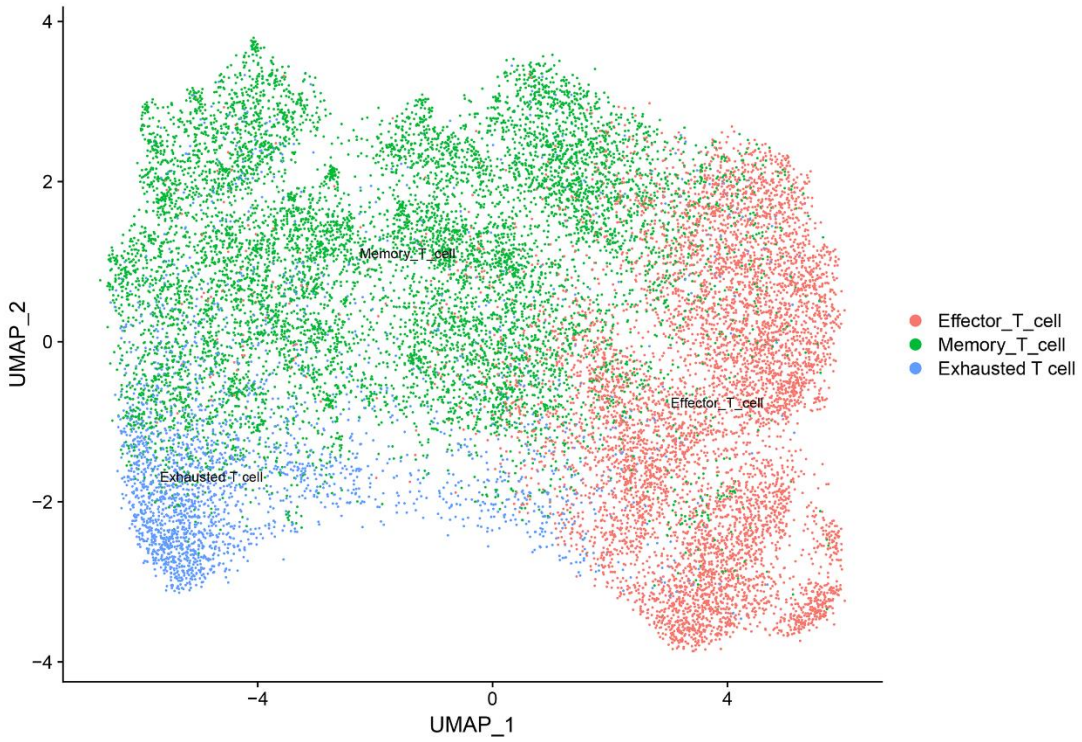


Figure S13. The heatmap of marker genes for re-annotation of T cells.

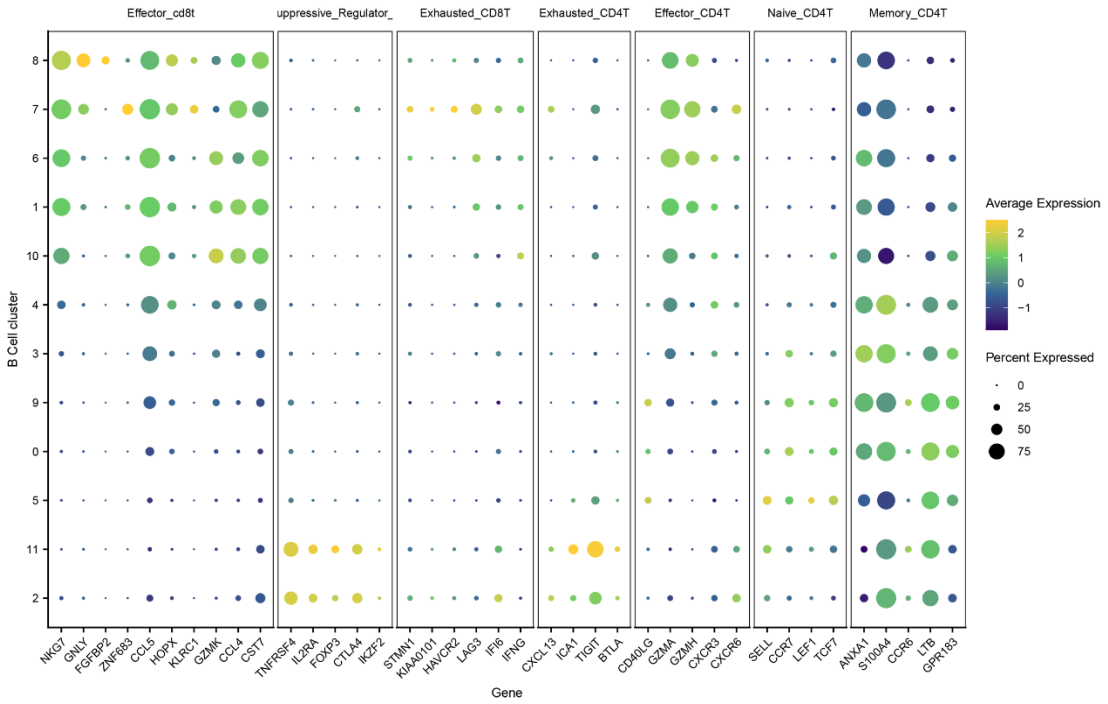


Figure S14. Diffusion maps for the T cells. (A): Color is based on the T cells clusters. Red: Effect T cells; Green: Exhausted T cells; Blue: Memory T cells. (B): Color is based on the pseudotime using Monocle2.

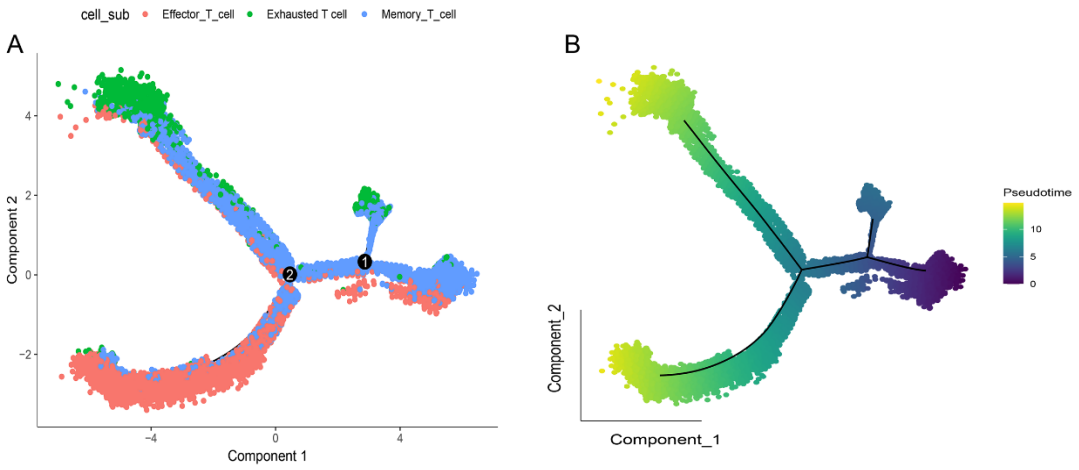
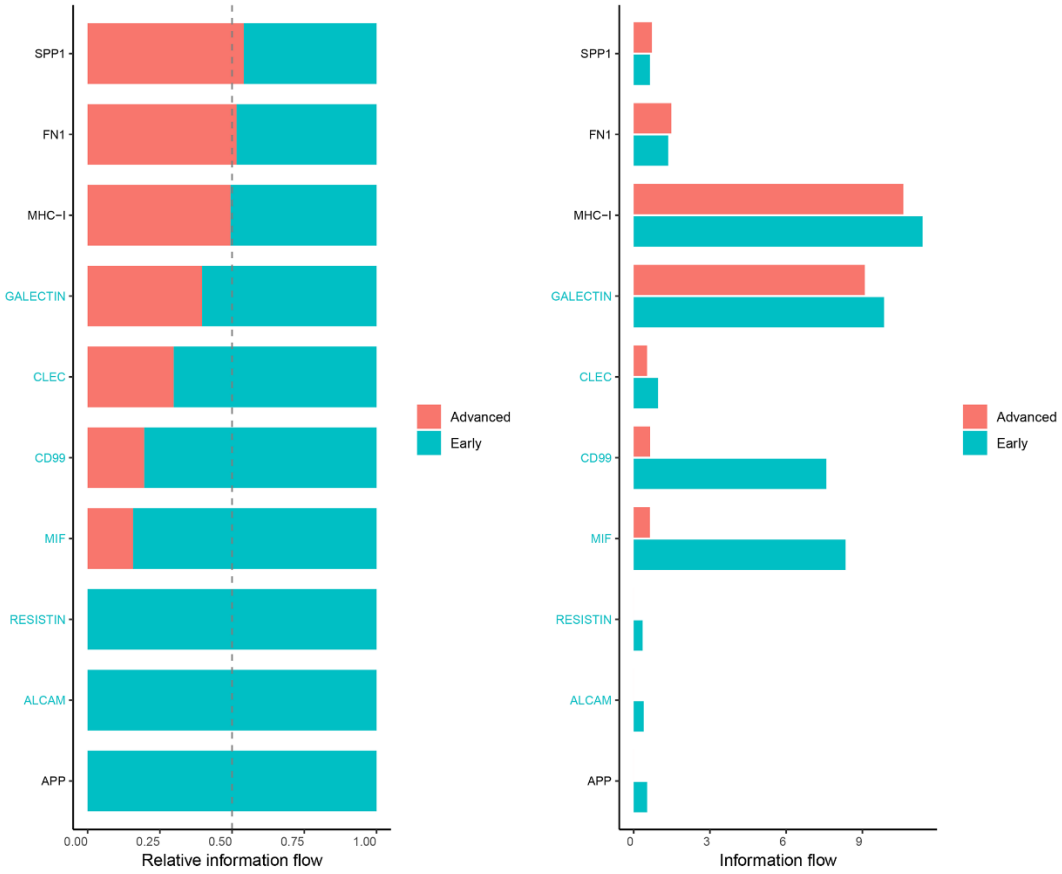


Figure S15. Variations of Effector T Cell to Macrophages and Monocytes of different ligand-receptor pairs by contrasting the strength in early and advanced stages. (A): Processed information by calculating the relative ratio of each pair in early and advanced stage. (B): The real information of each pair in early and advanced stage. The pairs in blue are statistically significant. Red: Advanced stage; Blue: Early stage.


SPP1
FN1
MHC−I
GALECTIN
CLEC
CD99
MIF
RESISTIN
ALCAM
APP
0.00
0.25
0.50
0.75
1.00
Relative information flow
Advanced
Early
SPP1
FN1
MHC−I
GALECTIN
CLEC
CD99
MIF
RESISTIN
ALCAM
APP
0
3
6
9
Information flow
Advanced
Early