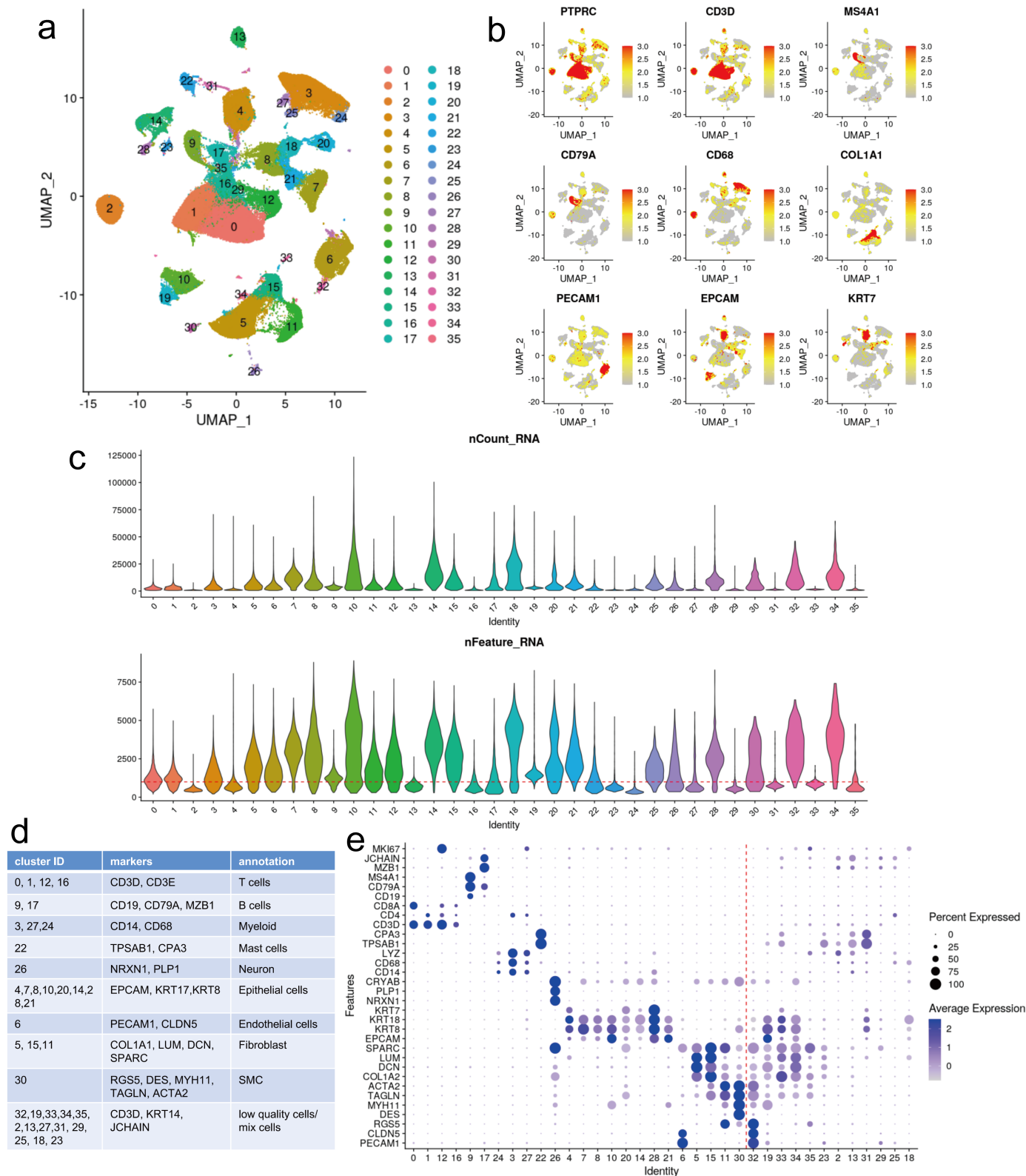
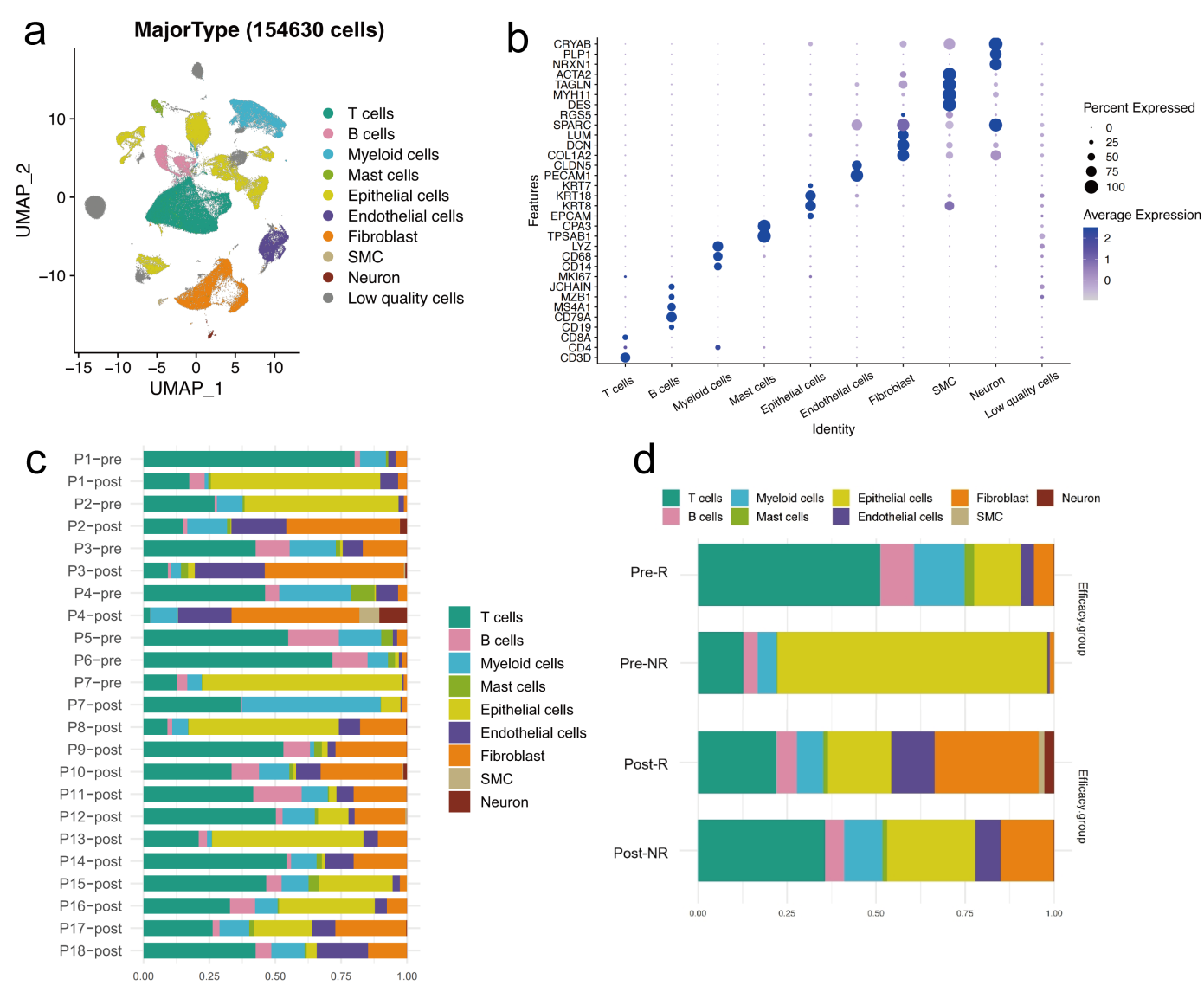


Supplementary Figure 1



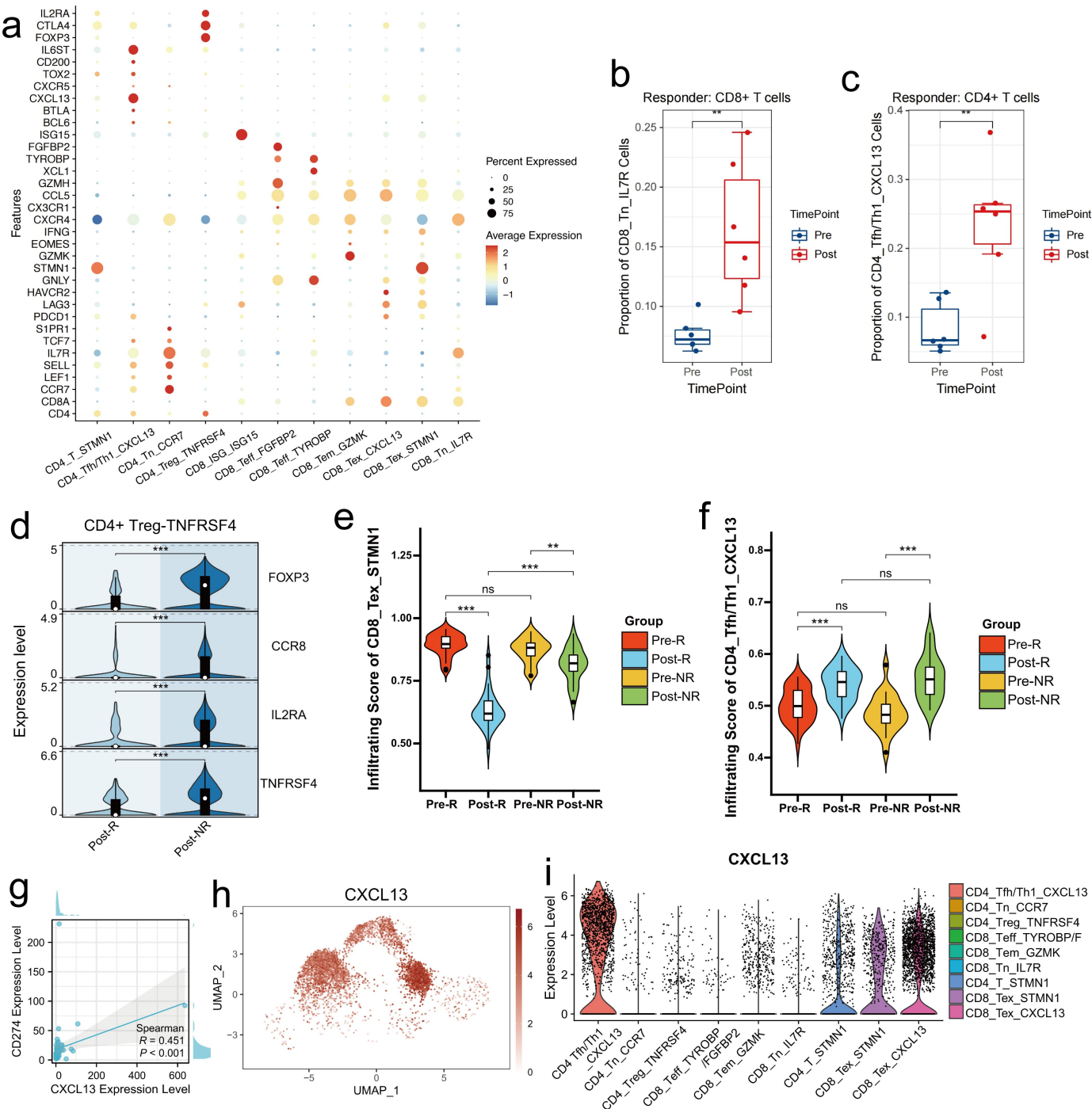
Supplementary Figure 1. Cell type clustering. **a.** UMAP plot of 154,630 cells labeled by cell clusters after removing contamination. $n = 23$. **b.** Expression of marker genes for cell type classification ($n = 23$ for all UMAP plots). **c.** Cell quality visualization. **d.** Marker genes for cell type classification. **e.** Bubble plot showing expression level of marker genes for all cell clusters.

Supplementary Figure 2



Supplementary Figure 2. Distribution of various cell types. **a.** UMAP plots of 154,630 cells visualizing major cell types. n = 23. **b.** Bubble plot showing expression level of marker genes for major cell types. **c.** Proportions of diverse cell types within each sample. **d.** Cell components of pre-treatment samples from responders (Pre-R, n = 6) and non-responders (Pre-NR, n = 1), and post-treatment specimens from responders (Post-R, n = 6) and non-responders (Post-NR, n = 10).

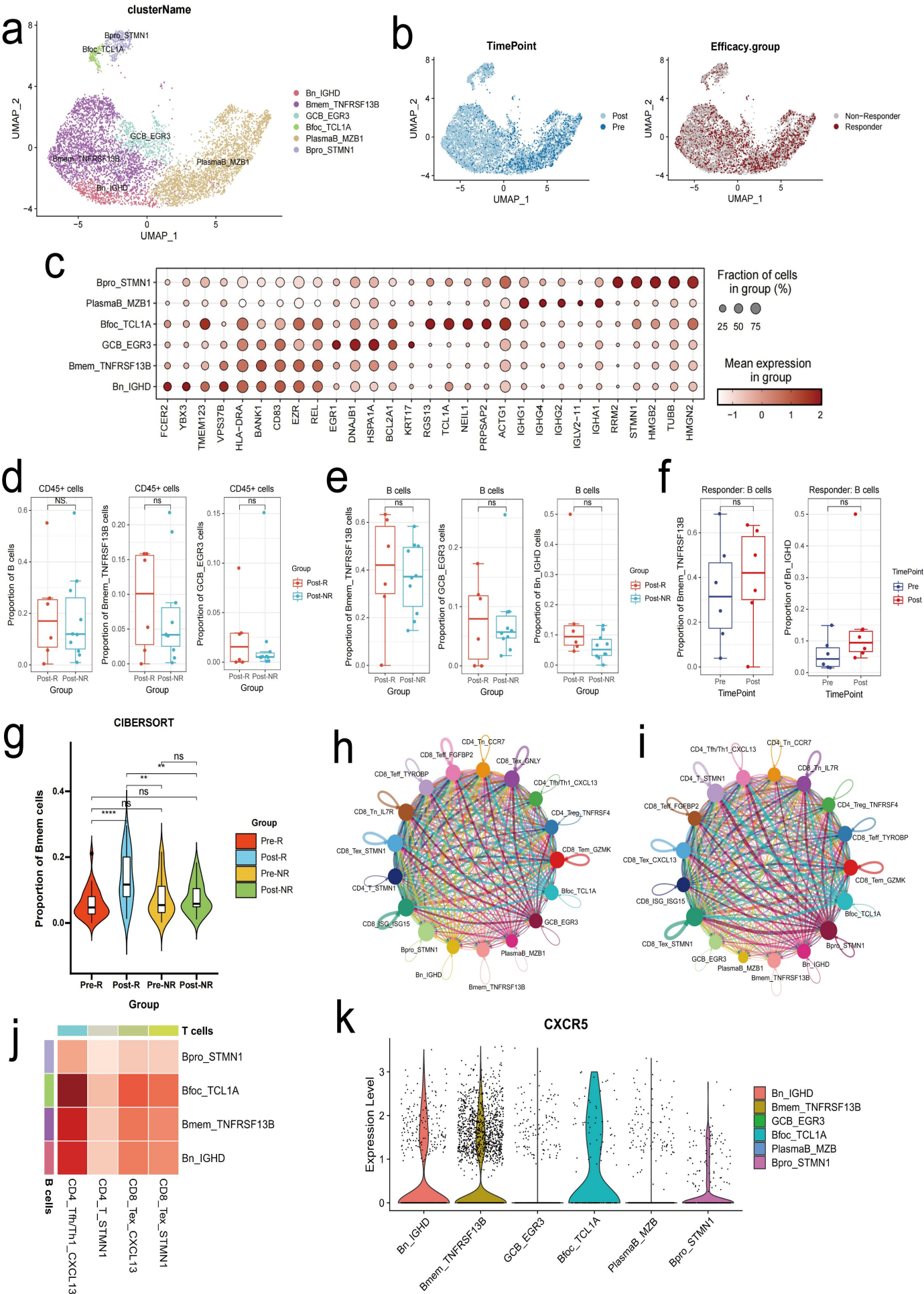
Supplementary Figure 3



Supplementary Figure 3. Detailed characteristics of T cell subsets in ESCC before and after immunochemotherapy.

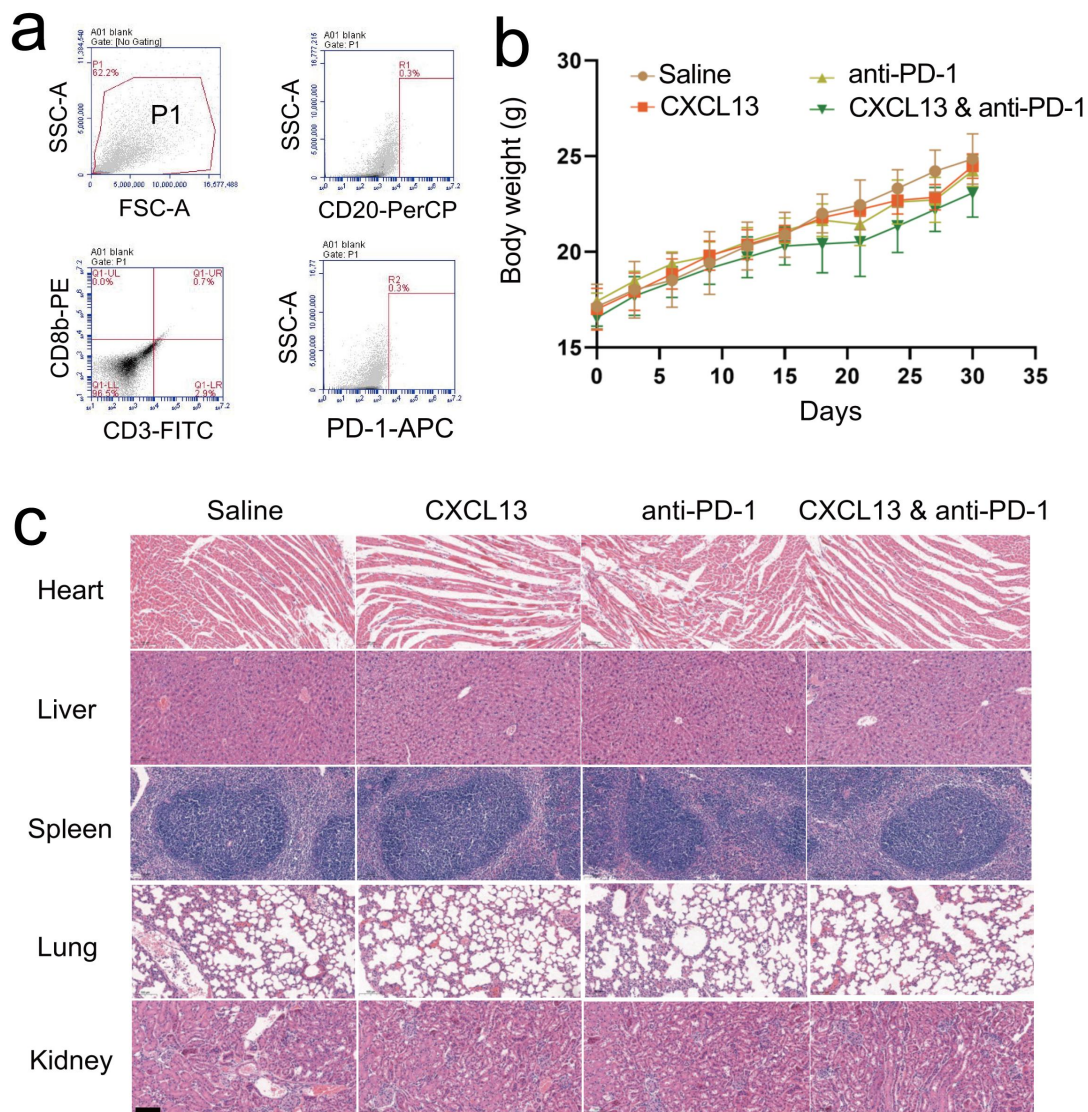
a. Bubble plot showing differential expression of marker genes for various T cell clusters. **b.** Proportion of CD8⁺ Tn-IL7R in all CD8⁺ T cells before (Pre, n = 7) and after (Post, n = 16) immunotherapy. **p-value < 0.01 of Wilcoxon test. The box indicates median +/- interquartile range; whiskers represent minima and maxima. Detailed information of each sample is provided in the Source Data. **c.** Proportion of CD4⁺ Tn-CCR7 in all CD4⁺ T cells before and after immunotherapy. **p-value < 0.01 of Wilcoxon test. Pre, n = 7; Post, n = 16. The box indicates median +/- interquartile range; whiskers represent minima and maxima. Source data are provided as a Source Data file. **d.** Expression of marker genes for activation of immunosuppressive CD4⁺ Tregs in CD4⁺ Treg-TNFRSF4. ***p-value < 0.001 of two-sided Wilcoxon rank-sum test. Post-R, n = 6; Post-NR, n = 10. Boxes indicate median +/- interquartile range; whiskers represent 1.5-fold of the interquartile range. **e.** The difference in infiltration score of CD8⁺ Tn-STMN1 among distinct treatment timepoints and efficacy groups in external validation cohort. **p-value < 0.01, ***p-value < 0.001 of Mann Whitney U test. Pre-treatment samples of responders (Pre-R, n = 32) and non-responders (Pre-NR, n = 22); Post-R (matched with Pre-R, n = 32) and Post-NR (matched with Pre-NR, n = 22). Boxes indicate median +/- interquartile range; whiskers represent 1.5-fold of the interquartile range. Detailed information of each sample is provided in the Source Data. **f.** The infiltration score of CD4⁺ Tfh/Th1-CXCL13 among distinct treatment timepoints and efficacy groups in external validation cohort. ***p-value < 0.001 of Mann Whitney U test. Pre-R, n = 32; Pre-NR, n = 22; Post-R, n = 32; Post-NR, n = 22. Boxes indicate median +/- interquartile range; whiskers represent 1.5-fold of the interquartile range. Source data are provided as a Source Data file. **g.** Scatterplots showing significant correlations between pre-treatment mRNA expression level of CXCL13 with that of CD274. Spearman-correlation test. Pre-treatment samples, n = 54. **h.** UMAP plot showing the distribution of CXCL13 in 27,594 T cells. n = 23. **i.** The expression level of CXCL13 in various T cell clusters.

Supplementary Figure 4



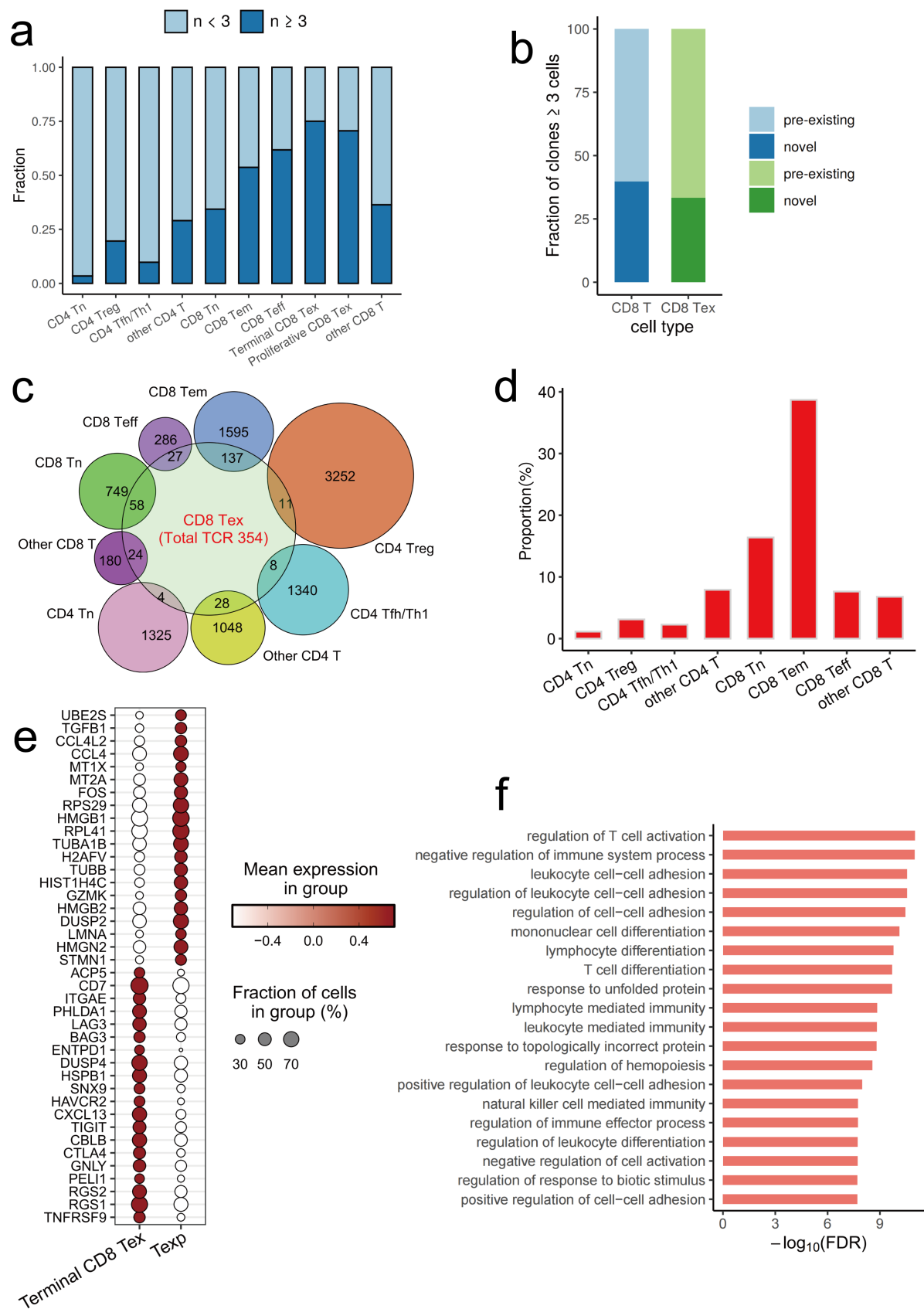
Supplementary Figure 4. Dynamics of B cell subsets during nICT treatment in ESCC. **a.** Clustering of 7,516 B cells, colored and labeled by distinct cluster names. n = 23. **b.** UMAP plot showing B cells annotated by timepoints (left) and efficacy groups (right). n = 23. **c.** Bubble plot showing differential expression of marker genes for various B cell clusters. **d.** Proportion of B cells, Bmem-TNFRSF13B and GCB-EGR3 cells in all CD45⁺ cells after immunotherapy. Wilcoxon test. Post-treatment samples from responder (Post-R), n = 6; Post-treatment samples from non-responder (Post-NR), n = 10. For each boxplot, the center line represents the median, the box indicates the upper and lower quartiles, and the whiskers show minima and maxima. Detailed information of each sample is provided in the Source Data. **e.** Fraction of Bmem-TNFRSF13B, GCB-EGR3 and Bn-IGHD cells in all B cells after immunotherapy. Wilcoxon test. Post-R, n = 6; Post-NR, n = 10. Boxes indicate median +/- interquartile range; whiskers show minima and maxima. Source data are provided as a Source Data file. **f.** Fraction of Bmem-TNFRSF13B and Bn-IGHD cells in all B cells from responders before and after immunotherapy. Wilcoxon test. Pre, n = 7; Post, n = 16. Boxes indicate median +/- interquartile range; whiskers represent minima and maxima. Source data are provided as a Source Data file. **g.** The difference in infiltration score of Bmem-TNFRSF13B cells among distinct treatment timepoints and efficacy groups in external validation cohort. **p-value < 0.01, ****p-value < 0.0001 of t-test. Pre-treatment samples of responders (Pre-R, n = 32) and non-responders (Pre-NR, n = 22); Post-R (matched with Pre-R, n = 32) and Post-NR (matched with Pre-NR, n = 22). Boxes indicate median +/- interquartile range; whiskers represent 1.5-fold of the interquartile range. **h.** Cell-cell interaction network among various B cell and T cell clusters in post-treatment responders. **i.** Cell-cell interaction network among various B cell and T cell clusters in post-treatment non-responders. **j.** Ligand-receptor interaction potential mediated by CXCL13-CXCR5 signaling between B cell and T cell clusters. **k.** The expression level of CXCR5 in various B cell clusters.

Supplementary Figure 5



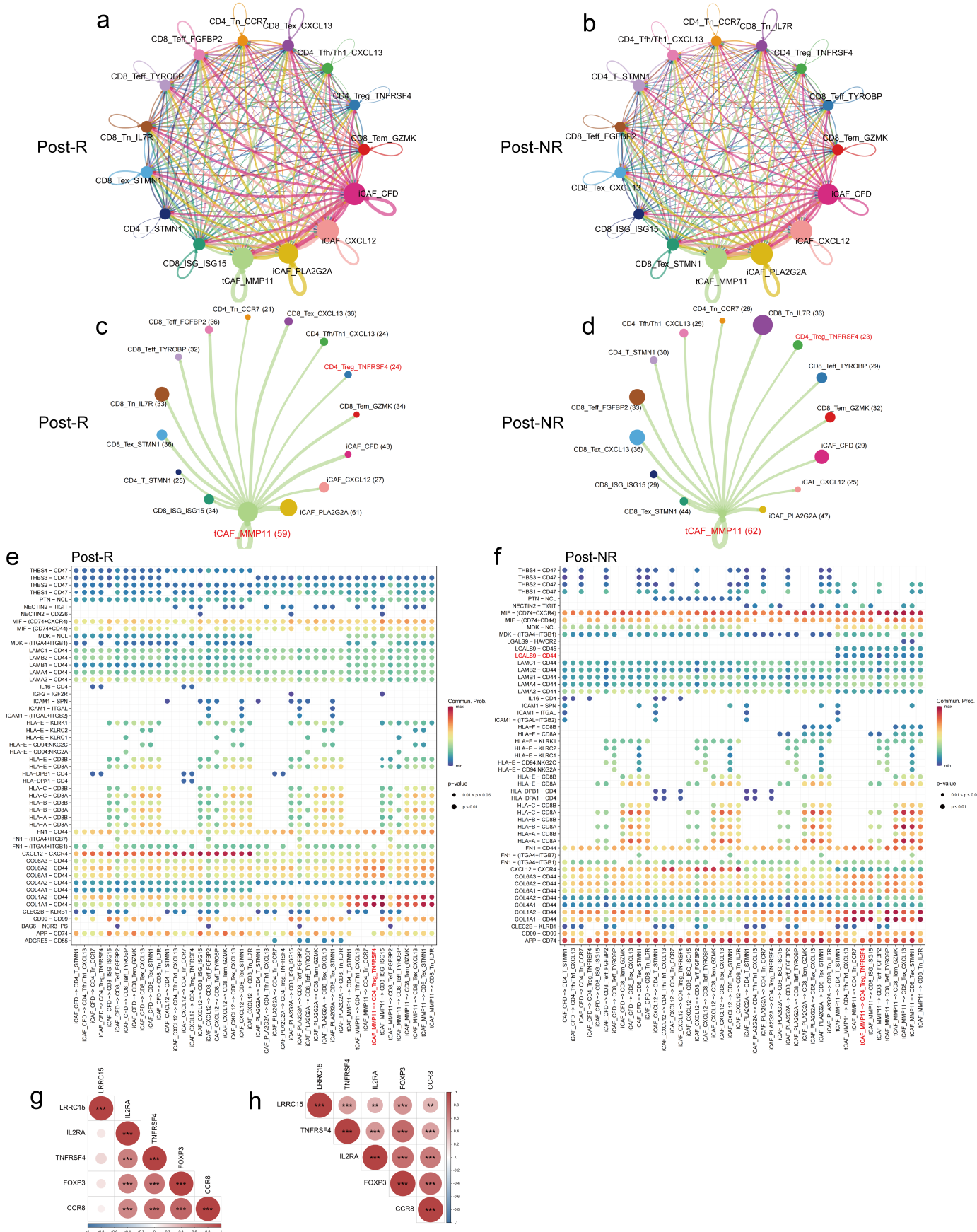
Supplementary Figure 5. The safety of in vivo experiments. **a.** Representative flow cytometry gating strategy for CD20⁺ B cells, CD8⁺ T cells, and PD-1⁺ cells (n = 5 per group). **b.** The body weight change of the mice during the experiment. Short horizontal lines indicate mean $\pm$ SD (n = 5 per group). **c.** Representative HE staining images of major organs of the mice after treatment (n = 5 per group). Scale bar: 100 μ m.

Supplementary Figure 6



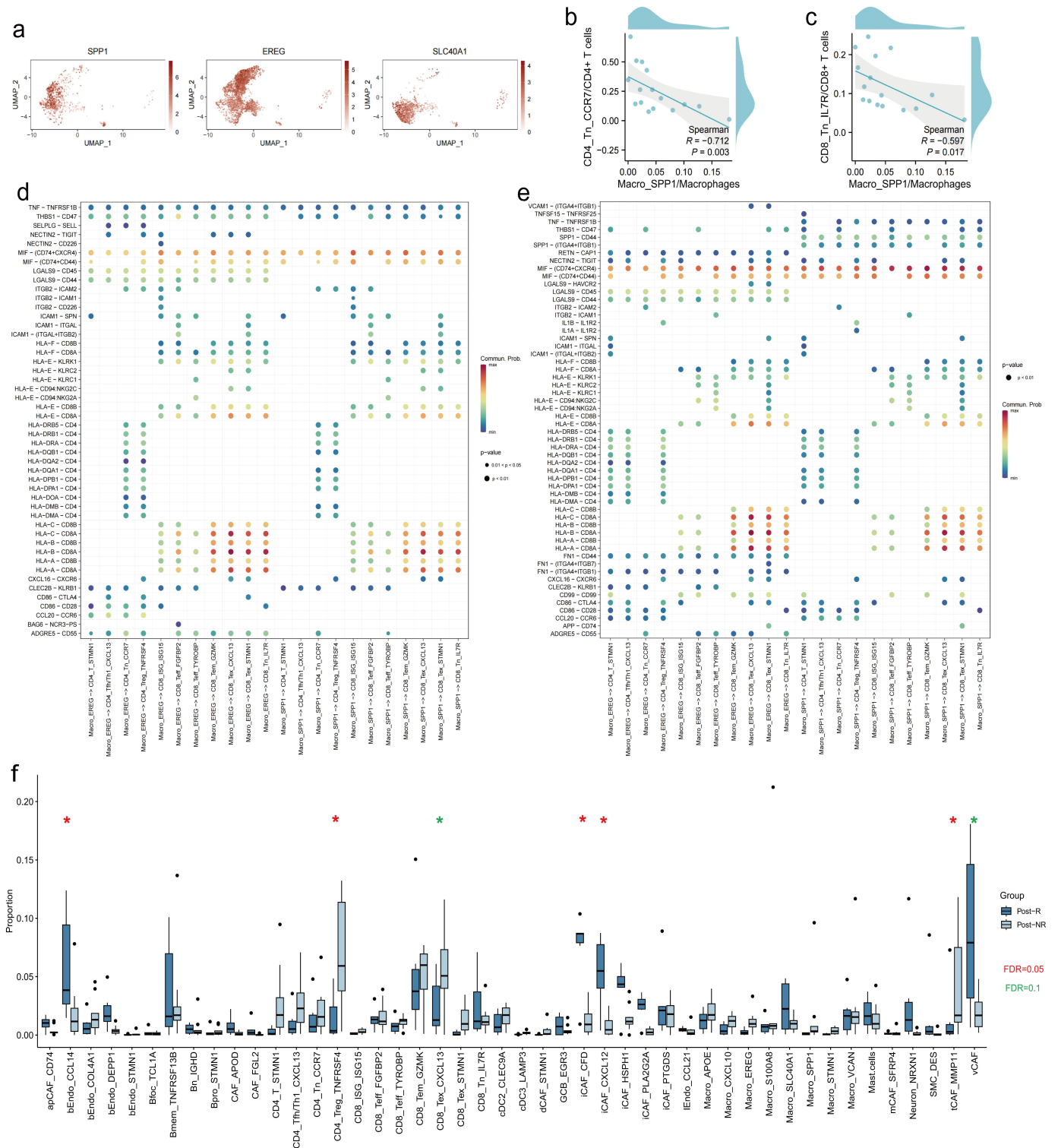
Supplementary Figure 6. Clonality features and dynamics of T cell receptors. **a.** Fractions of TRB clones with different sizes ($n < 3$ and $n \geq 3$) for different T cell clusters in all samples enrolled in scTCR-seq. **b.** Fractions of pre-existing and novel TRB clones ($n \geq 3$) in CD8⁺ T and CD8⁺ Tex cells. **c.** Venn diagram showing the shared TRB clones between CD8⁺ Tex and other T cell subtypes. The numbers of shared TRB clones are annotated. **d.** Proportion of shared TRB clones in various T cell subtypes. **e.** Bubble plot showing differential expressed genes (DEGs) between CD8⁺ terminal Tex and Texp cells. **f.** GO analysis of upregulated DEGs in CD8⁺ terminal Tex compared to Texp.

Supplementary Figure 7



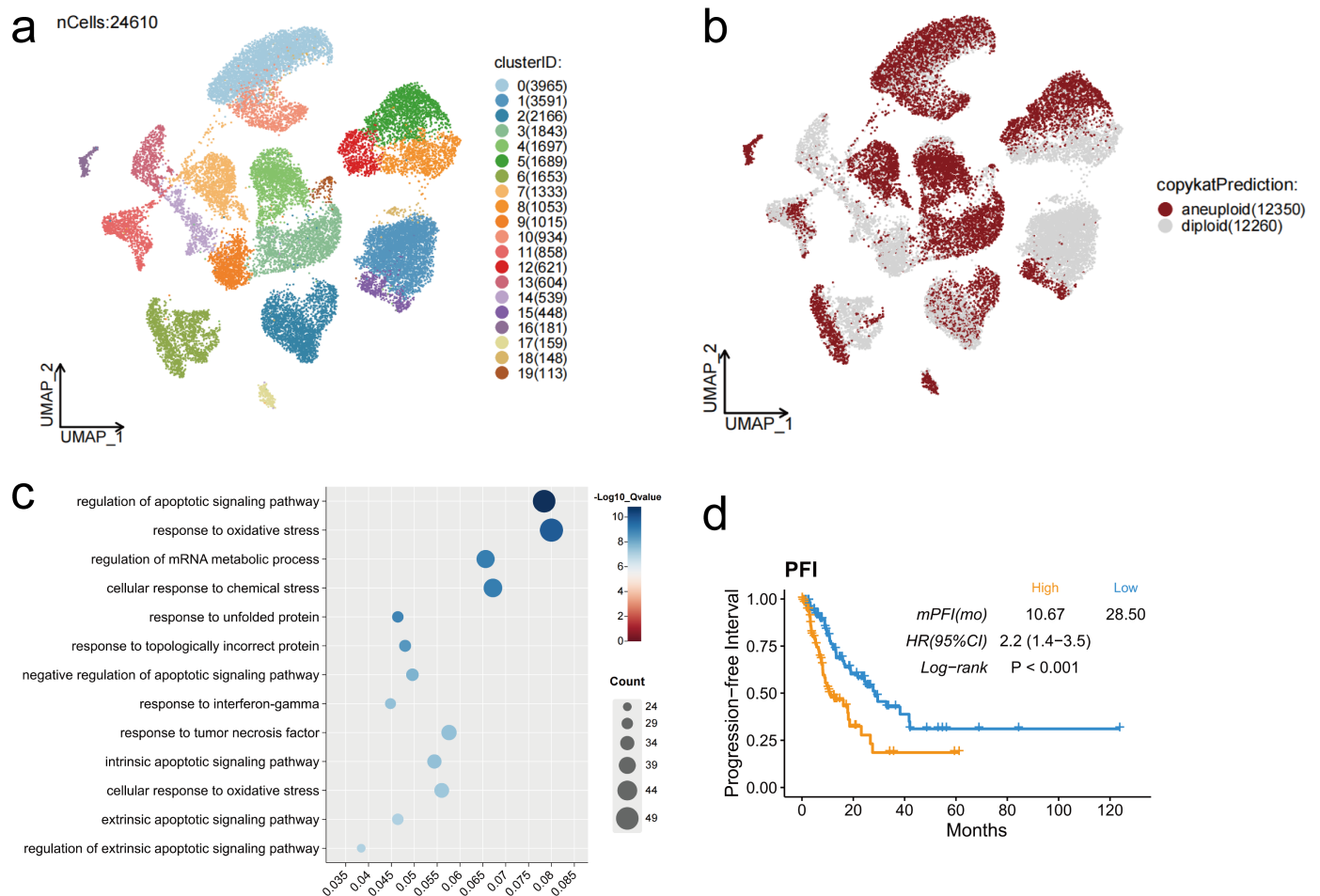
Supplementary Figure 7. Cell-cell interaction network between CAFs and T cells. **a.** CellChat analysis showing cell-cell communication among various CAF and T cell clusters in post-treatment responders. **b.** CellChat analysis showing cell-cell communication among various CAF and T cell clusters in post-treatment non-responders. **c.** Number of significant ligand-receptor pairs from tCAF-MMP11 cells to T cell subsets in post-treatment responsive tumors. **d.** Number of significant ligand-receptor pairs from tCAF-MMP11 cells to T cell subsets in post-treatment non-responsive tumors. **e.** Heatmap displaying the activity and regulatory potential of the prioritized ligands in CAFs driving corresponding receptors of T cells in post-treatment responders. **f.** Heatmap displaying the activity and regulatory potential of the prioritized ligands in CAFs driving corresponding receptors of T cells in post-treatment non-responders. **g.** Correlation between LRRC15 and marker genes of immunosuppressive CD4⁺ Tregs in pre-treatment tumors of the external validation cohort. Spearman-correlation test. **h.** Correlation between LRRC15 and marker genes of immunosuppressive CD4⁺ Tregs in post-treatment tumors from validation cohort. Spearman-correlation test.

Supplementary Figure 8



Supplementary Figure 8. Features and dynamics of macrophages. **a.** UMAP plot showing the distribution of SPP1, EREG and SLC40A1 in 9,703 myeloid cells. $n = 23$. **b.** Scatterplot of a significant correlation between post-treatment cell proportion of CD4⁺ Tn-CCR7 in CD4⁺ T cells with that of Macro-SPP1 in macrophages. Spearman-correlation test. **c.** Scatterplot showing a significant correlation between post-treatment cell proportion of CD8⁺ Tn-IL7R in CD8⁺ T cells with that of Macro-SPP1 in macrophages. Spearman-correlation test. Post-treatment samples, $n = 16$ for both **b** and **c**. **d.** Heatmap displaying the activity and regulatory potential of the prioritized ligands in Macro-SPP1 and Macro-EREK driving corresponding receptors of T cells in post-treatment responders. **e.** Heatmap displaying the activity and regulatory potential of the prioritized ligands in Macro-SPP1 and Macro-EREK driving corresponding receptors of T cells in post-treatment non-responders. **f.** Boxplots of compositional changes from post-treatment surgical samples of non-responders (Post-NR, light blue, $n = 10$) to responders (Post-R, dark blue, $n = 6$). Single-cell compositional data analysis (scCODA) for detecting statistical significance of compositional differences between two groups. Reference for scCODA: bEndo-NEAT1. FDR at 0.05 (red) or 0.1 (green). For each boxplot, the center line represents the median, the box indicates the upper and lower quartiles, and the whiskers show 1.5-fold of the interquartile range.

Supplementary Figure 9



Supplementary Figure 9. Difference in malignant epithelial cells between distinct efficacy groups.

a. UMAPs of 24,610 epithelial cells, annotated by cell clusters. $n = 23$. **b.** UMAP plot showing epithelial cells colored by aneuploid and diploid variations. $n = 23$. **c.** Significant enrichment of upregulated DEGs of malignant epithelial cells in Gene Ontology terms. **d.** Progression-free survival analysis of SPP1 expression in TCGA esophageal carcinoma (ESCA) cohort ($n = 182$). Cox regression hazard ratios (HR) and 95% confidence intervals (CI) are shown with log-rank p-values.