Figure S1 The H&E staining image of a GBC patient in our single-cell experiment. Scale bar represents 100 μm.
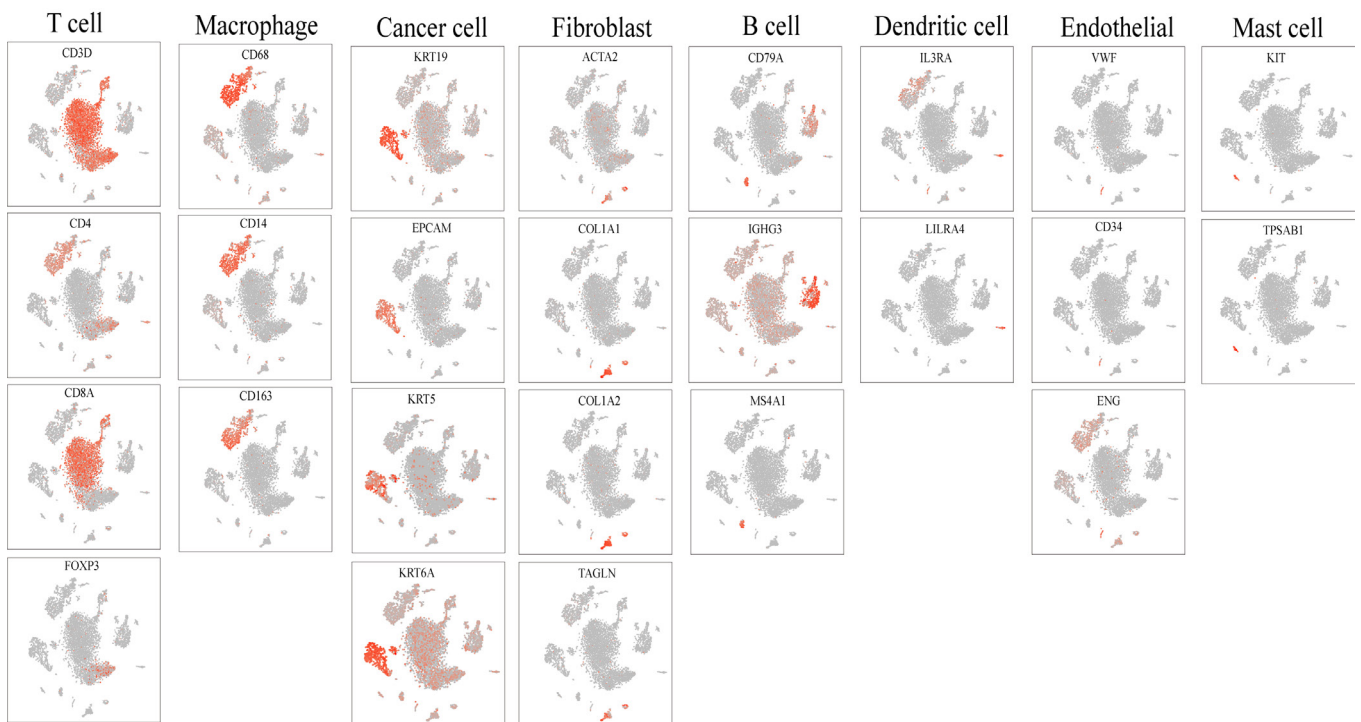

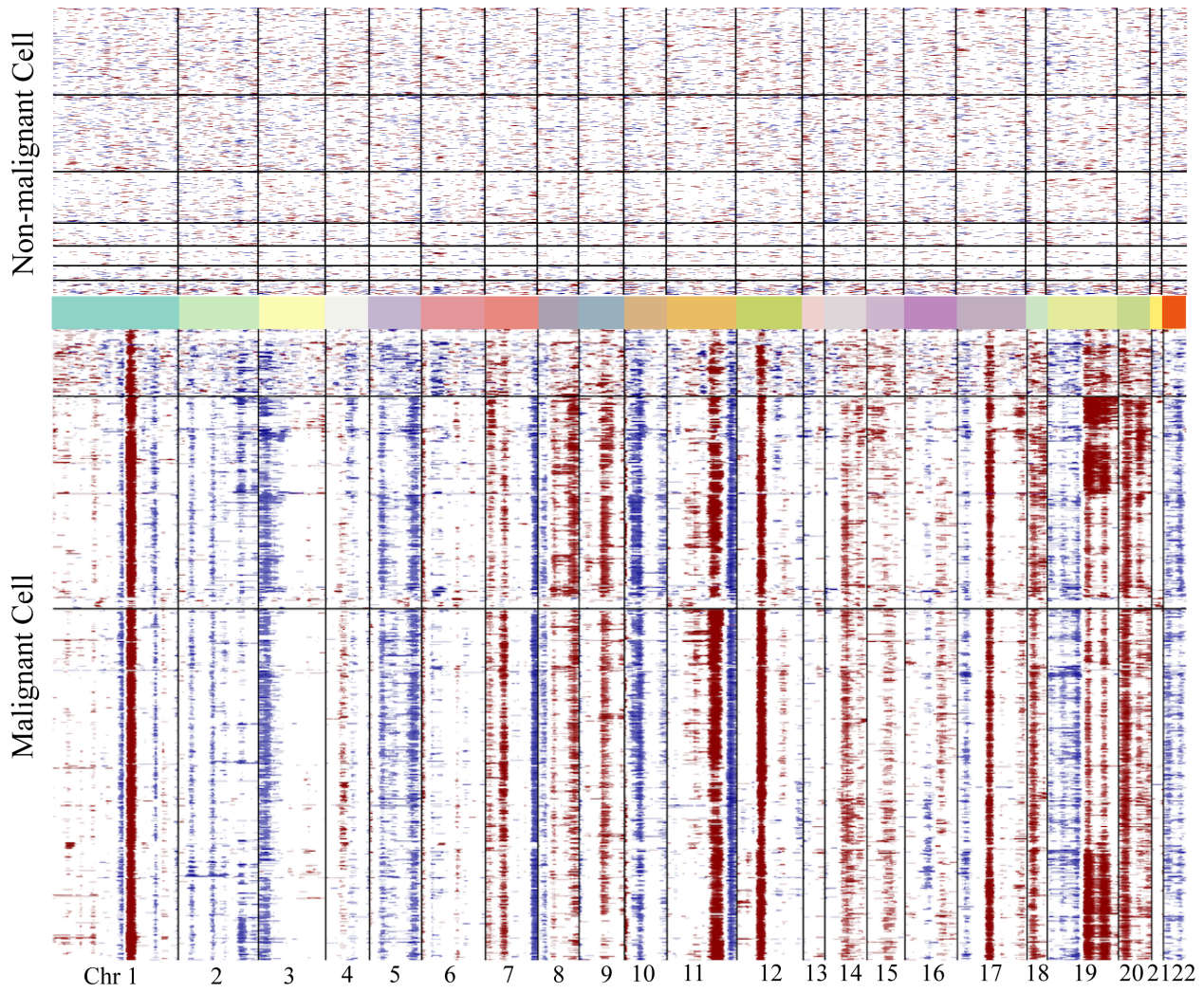**Figure S2** Marker genes of major cell types were visualized into tSNE plot.

Figure S3 A heatmap showing CNVs for malignant and nonmalignant cells. Red: amplification; blue: deletion.
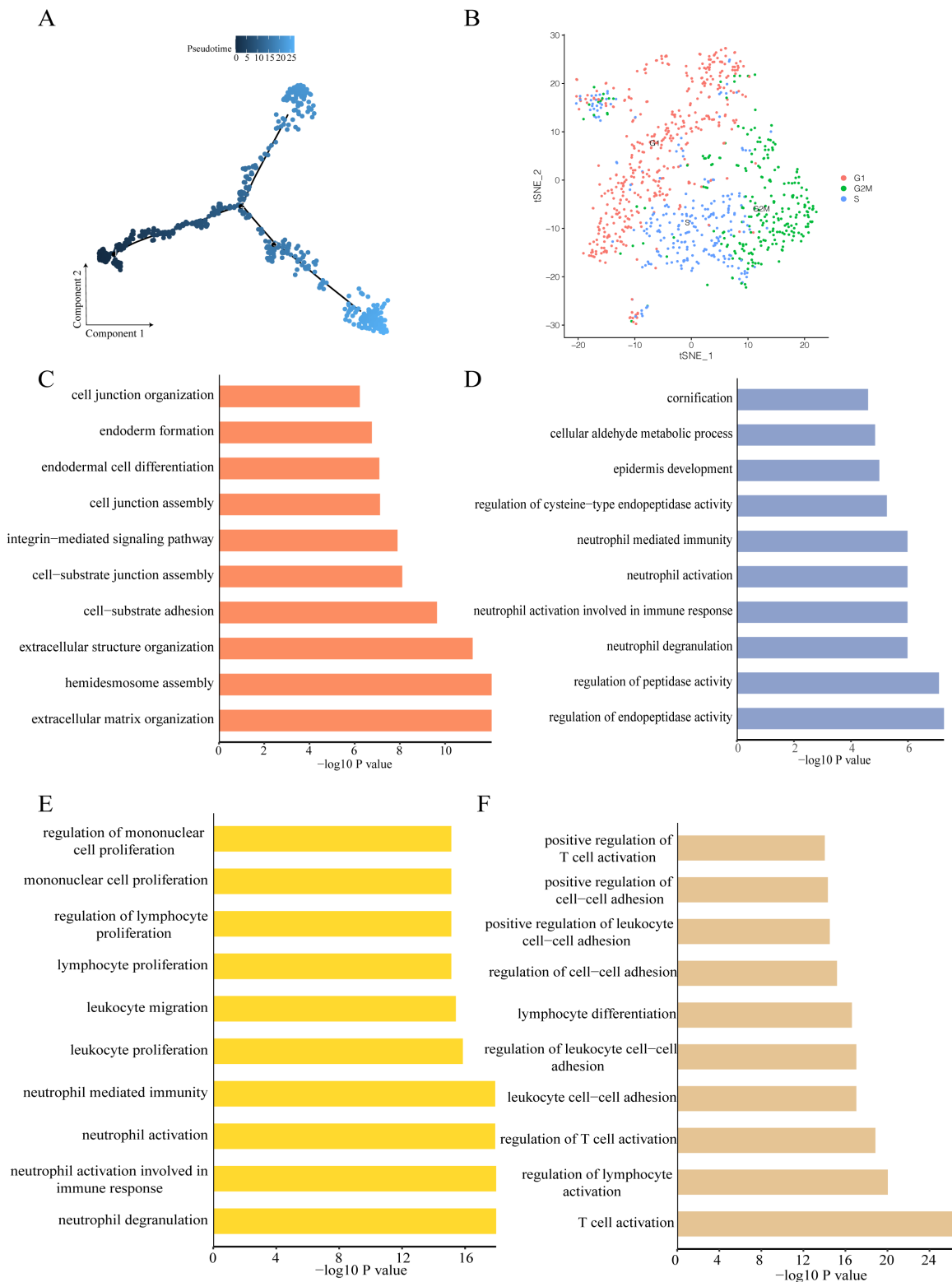
Figure S4 The heterogeneity of malignant cells. (A) Differentiation trajectory of malignant cells color coded for pseudotime. (B) tSNE plot colored by cell cycle status. (C,D,E,F) The top 10 enriched biological process GO terms in cancer cell subcluster 1 (C), subcluster 2 (D), subcluster 5 (E), and subcluster 6 (F).
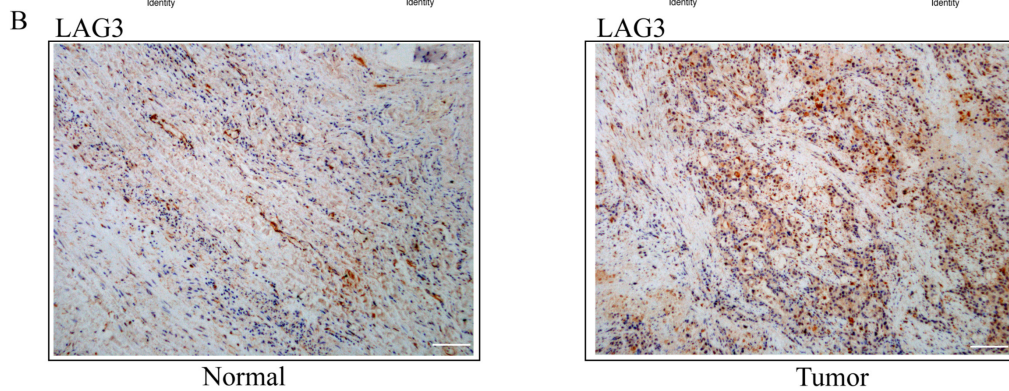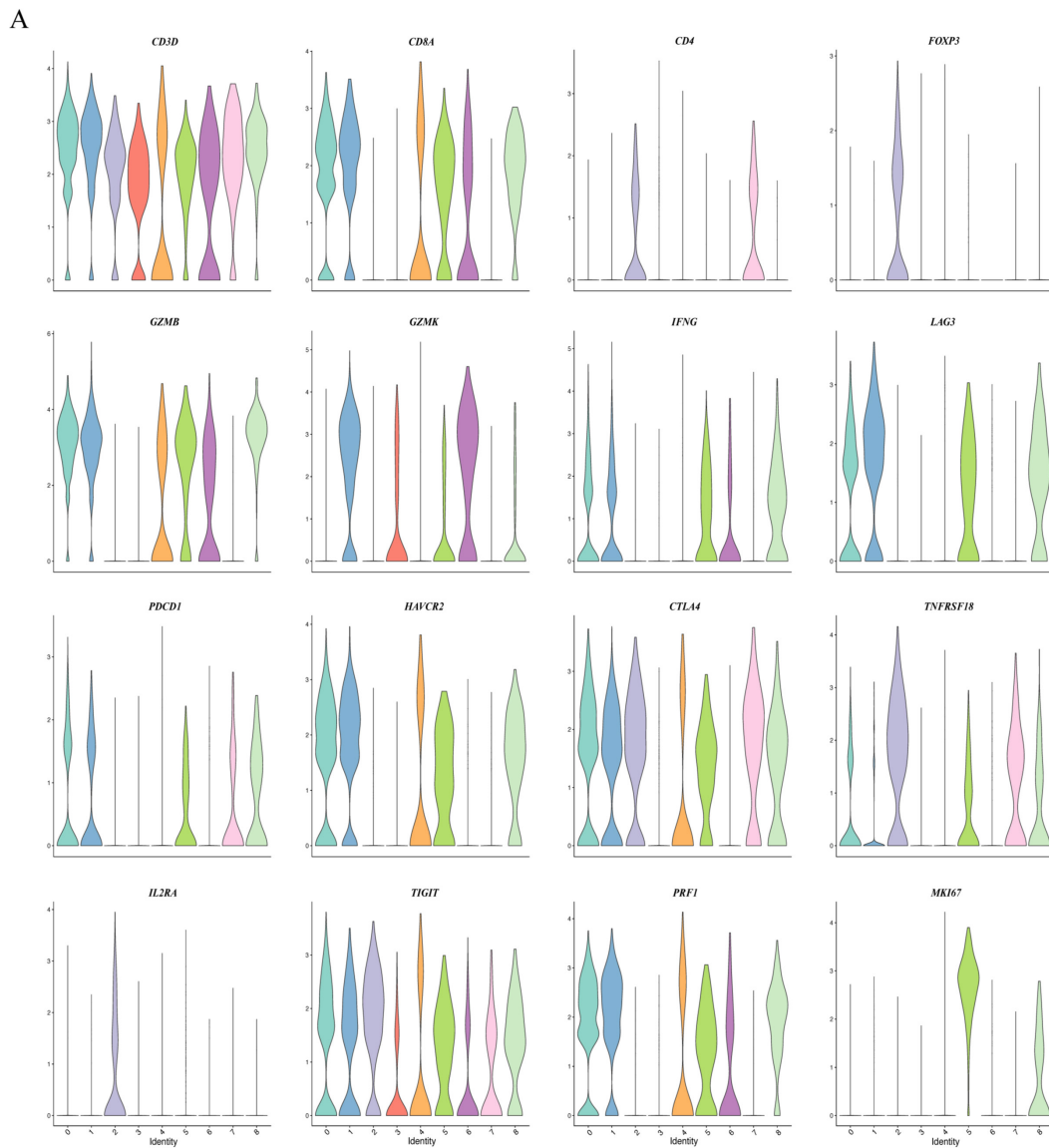
Figure S5 The expression of T cell markers. (A) Violin plots showing the expression of T cell function-associated markers in 9 T cell clusters. (B) LAG3 immunohistochemical staining in tumor and adjacent tissues. Scale bars represent 100 μm. N=5 samples/group.
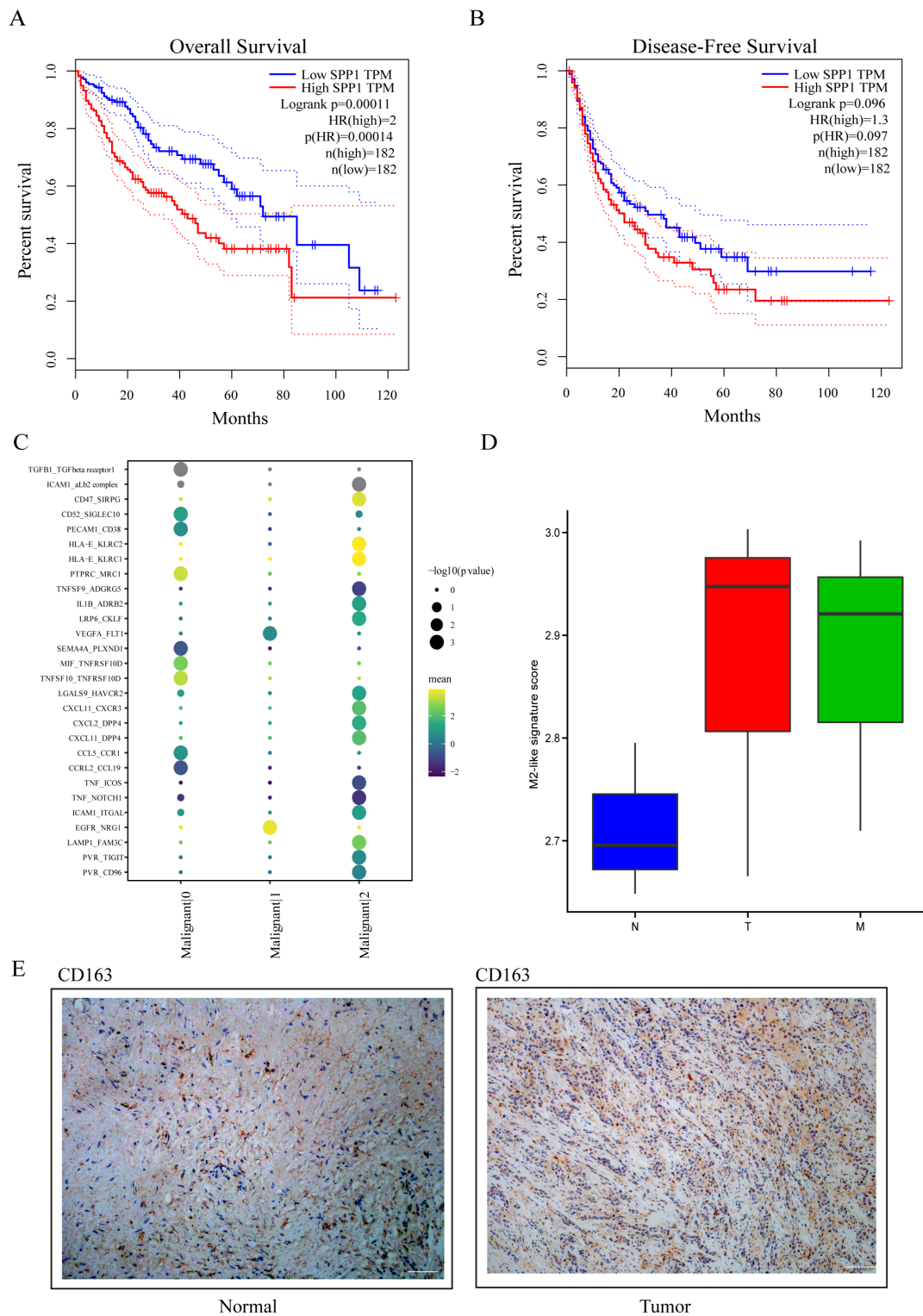
Figure S6 Kaplan-Meier analysis of the relationship of SPP1 with overall survival in TCGA LIHC (A) and disease-free survival in CHOL (B) using the GEPIA website. (C) The significant ligand–receptor pairs between malignant cells and macrophage subclusters. (D) The box plot showing the signature score of M2-like macrophages in GSE132223. N: normal tissue, T: primary tumor, M: metastatic tumor. (E) CD163 immunohistochemical staining in tumor and adjacent tissues. Scale bars represent 100 µm. N=5 samples/group.
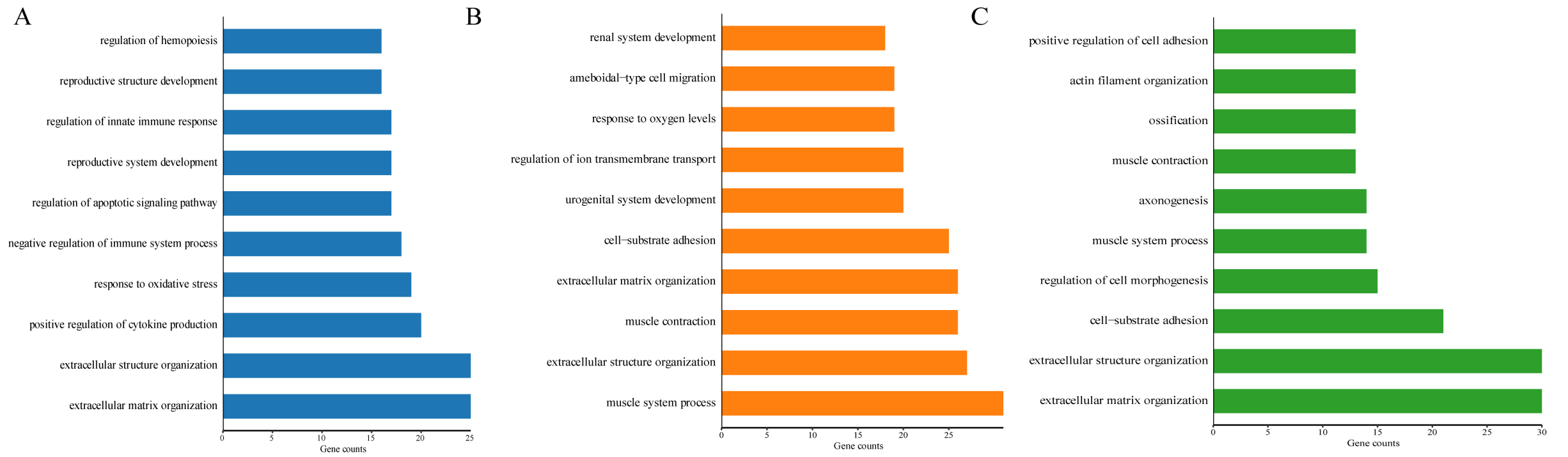
Figure S7 The top 10 enriched biological process GO terms in the CAF subcluster 0 (A), subcluster 1 (B), and subcluster 2 (C).