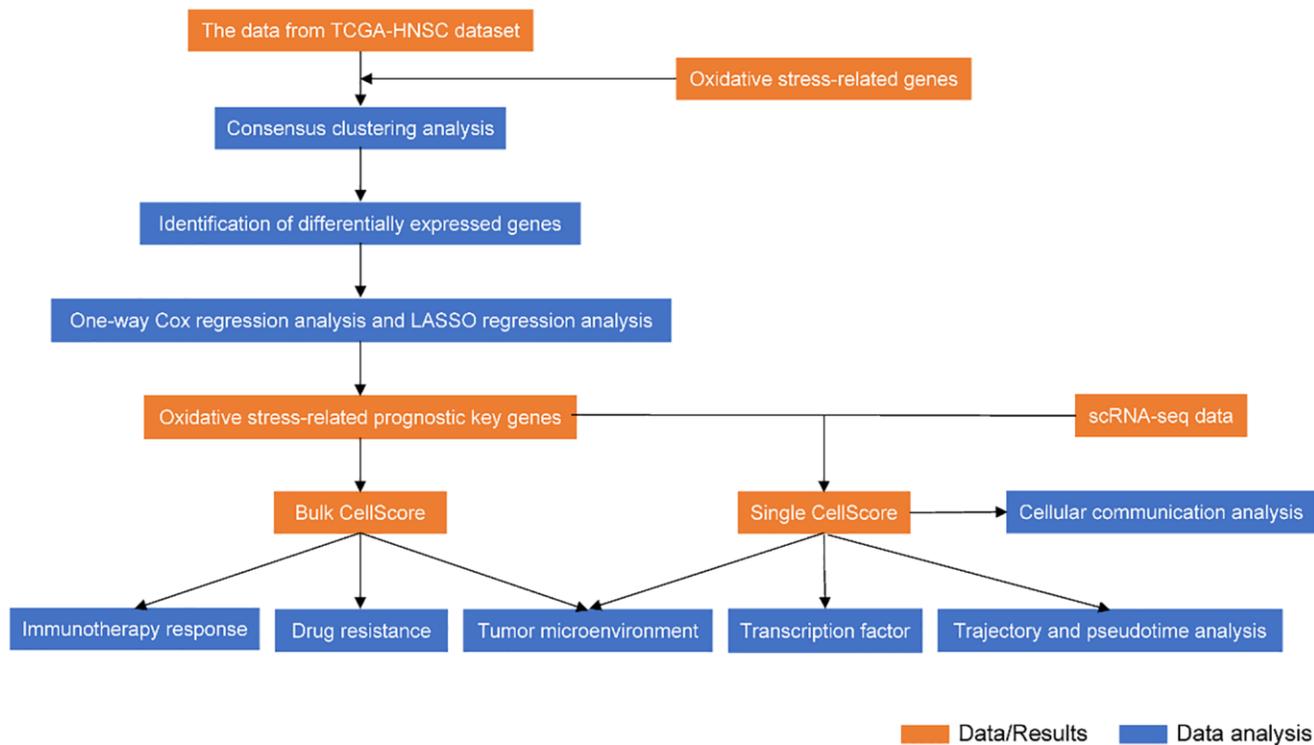
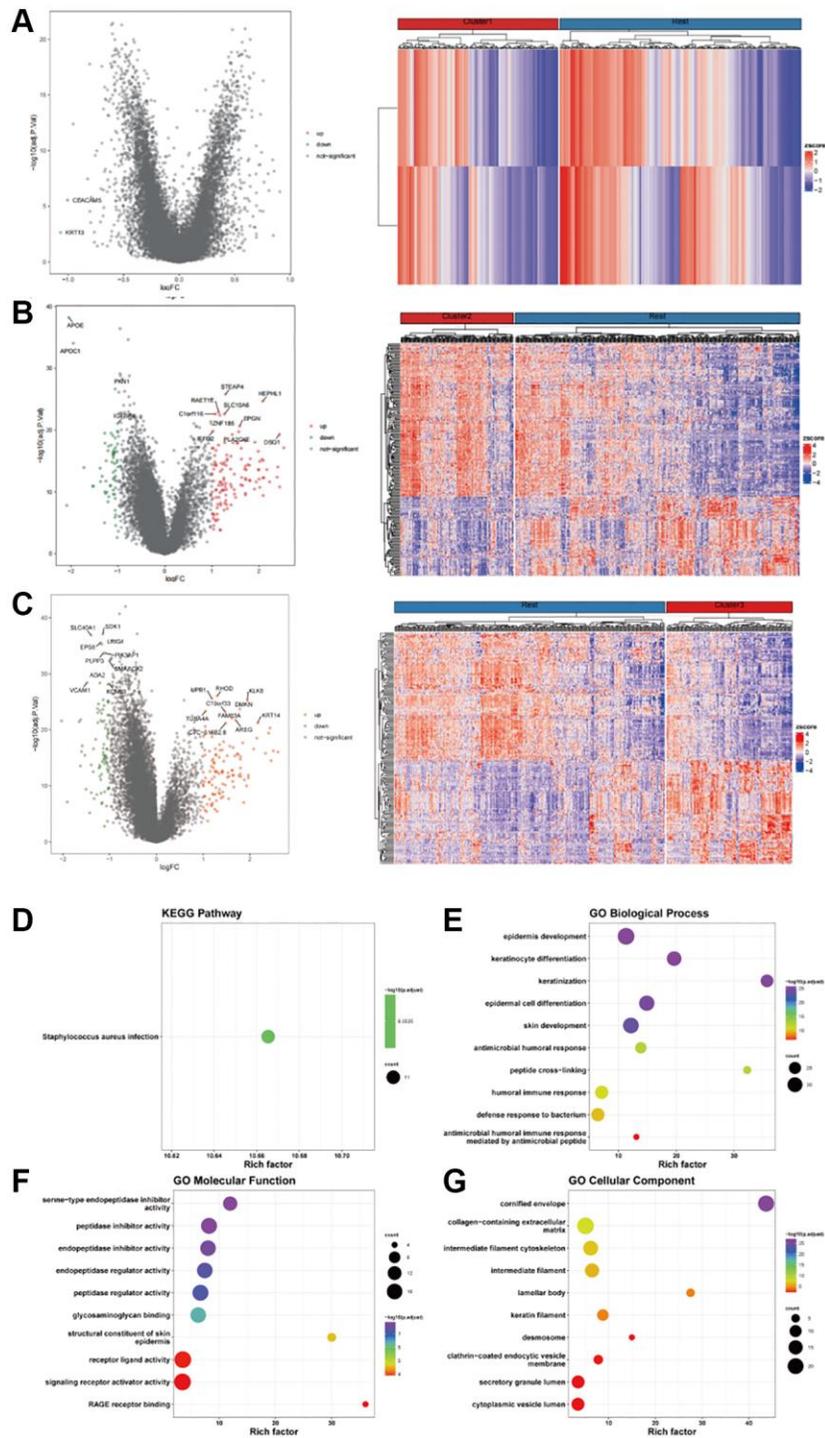


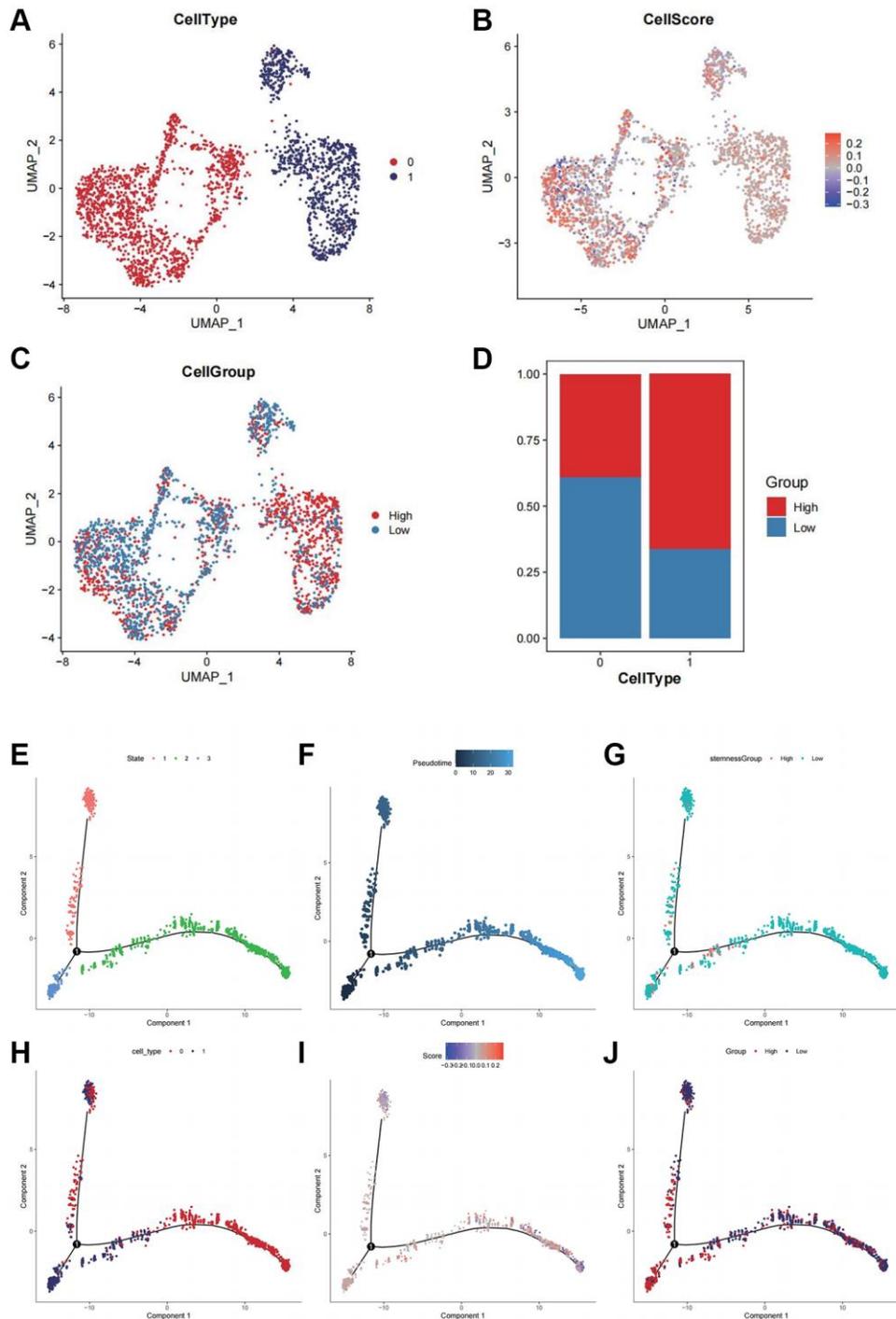
## SUPPLEMENTARY FIGURES



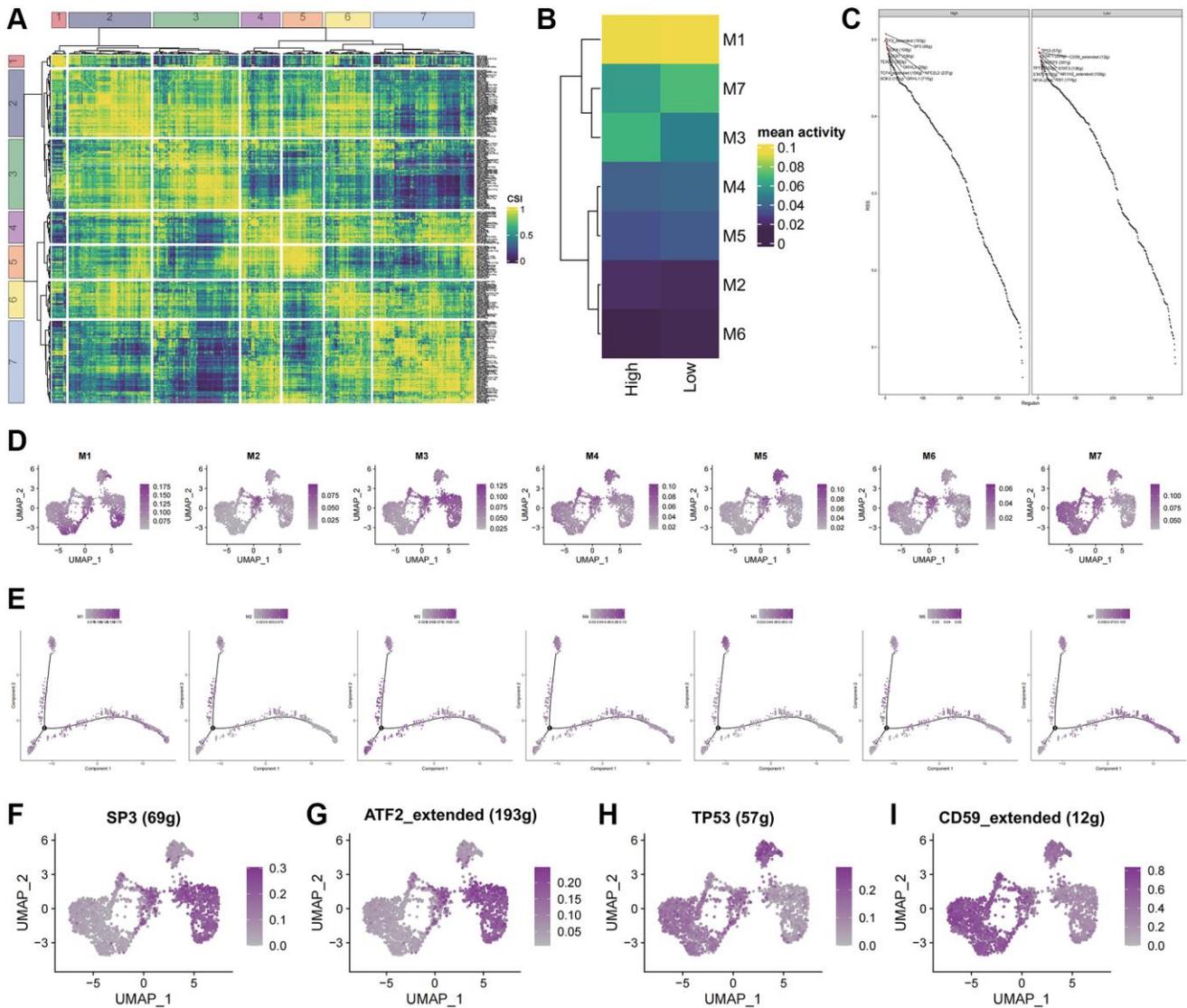
Supplementary Figure 1. The analysis flow chart of the study.



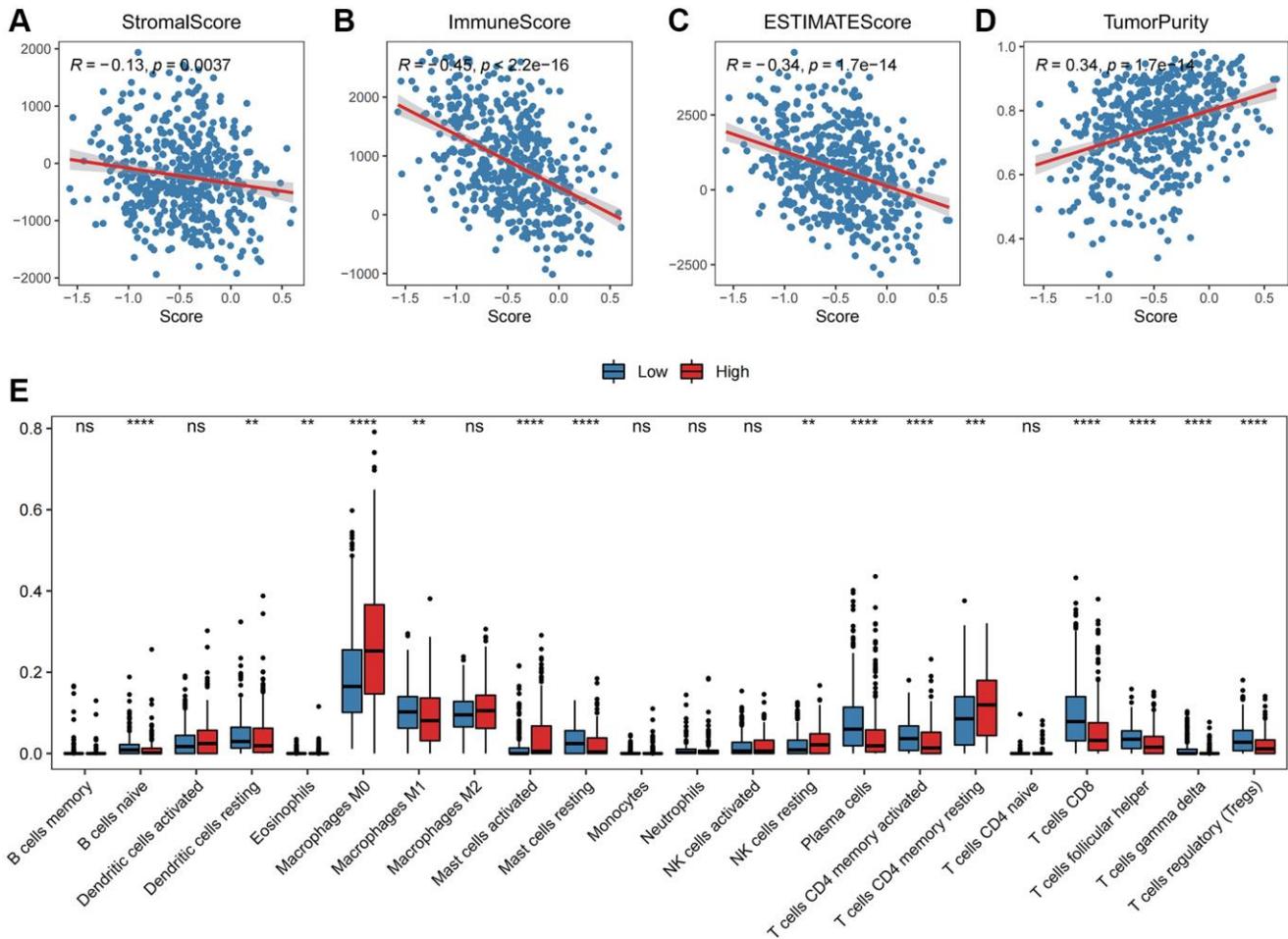
**Supplementary Figure 2. Molecular differences between oxidative stress expression patterns.** (A–C) The volcano plots and heat maps for the DEGs. (D) KEGG functional enrichment analysis for the DEGs. (E) GOBP functional enrichment analysis for the DEGs. (F) GOMF functional enrichment analysis for the DEGs. (G) GOCC functional enrichment analysis for the DEGs.



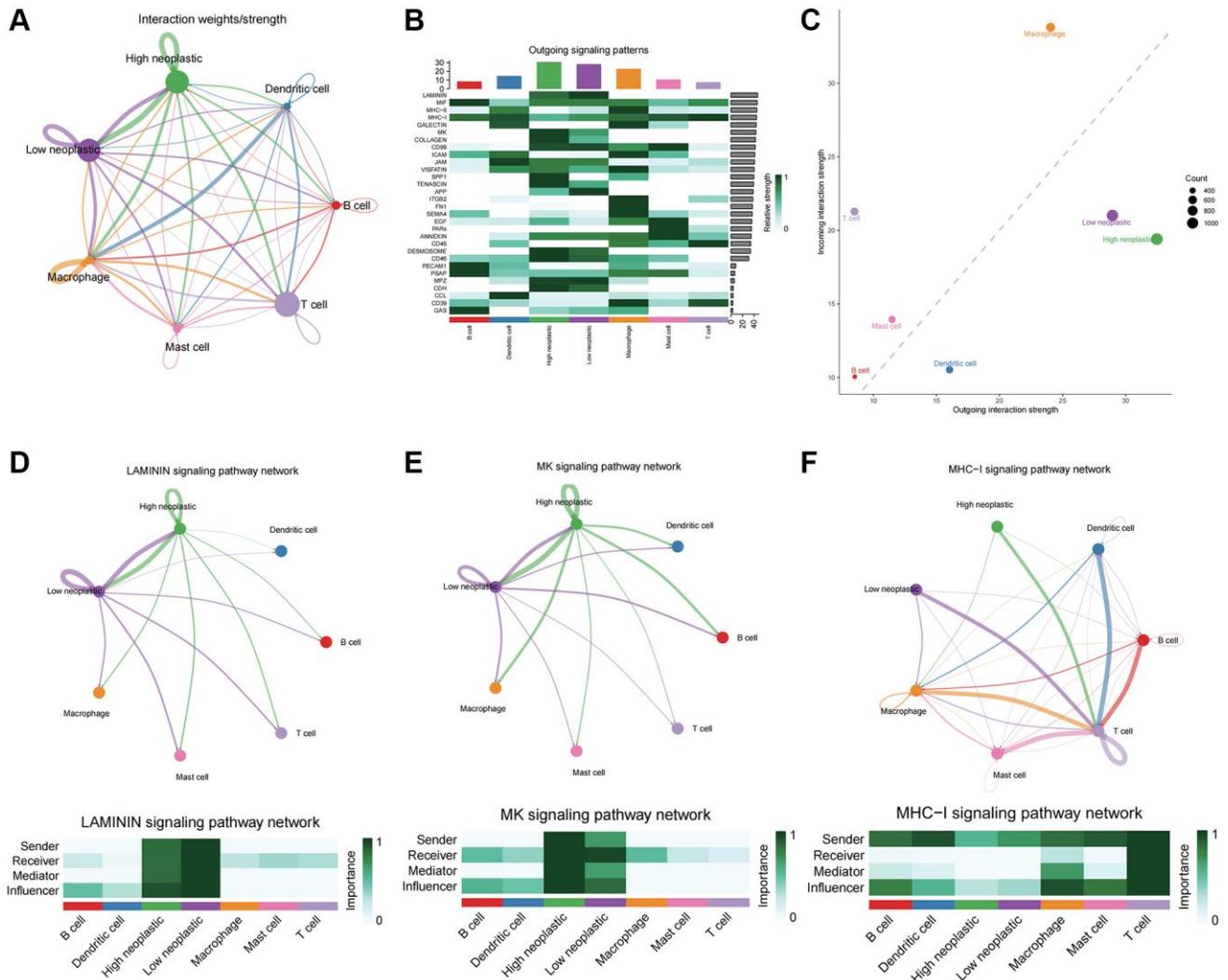
**Supplementary Figure 3. Identification of malignant epithelial cell subgroups.** (A) Distribution of malignant cell subgroups constructed by Uniform Manifold Approximation and Projection (UMAP); Different colors represent different cell types. A point within each group represents a cell. (B) CellScore distribution of malignant epithelial cells constructed by UMAP; Different colors represent different CellScores. (C) CellGroup distribution of malignant epithelial cells constructed by UMAP; Different colors represent different CellGroups. (D) The ratios of cells with high and low CellScores in different CellTypes. (E) The results of trajectory analysis for the tumor malignant cells based on different cell states; Different colors represent different states. (F) The results of trajectory analysis for the tumor malignant cells based on different pseudotime; Different colors represent different pseudotime. (G) The results of trajectory analysis for the tumor malignant cells based on different cell stemness groups; Different colors represent different cell stemness groups. (H) The results of trajectory analysis for the tumor malignant cells based on different cell types; Different colors represent different cell types. (I) CellScore; The results of trajectory analysis for the tumor malignant cells based on different cell scores; Different colors represent different cell scores. (J) The results of trajectory analysis for the tumor malignant cells based on different cell groups; Different colors represent different cell groups.



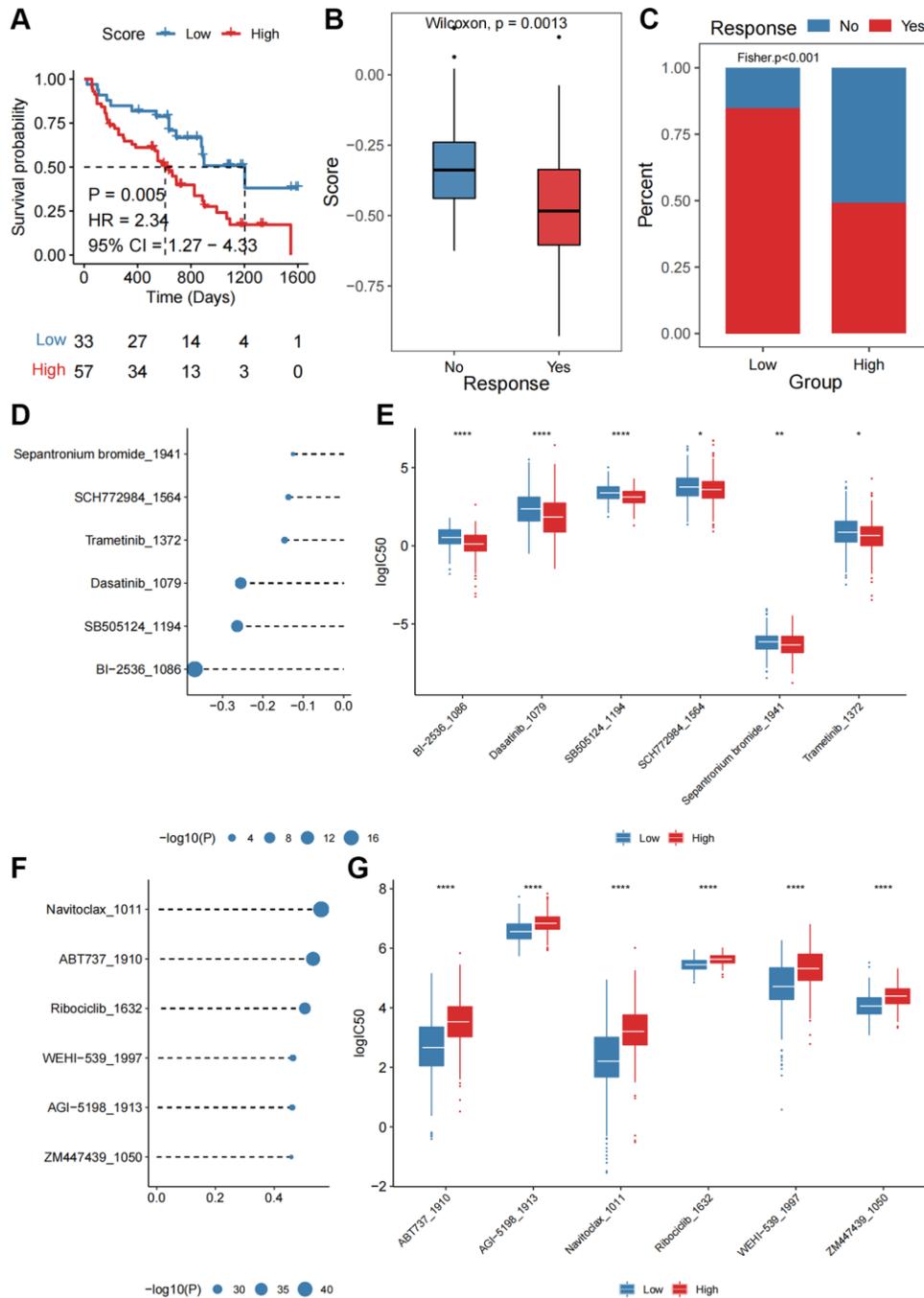
**Supplementary Figure 4. Transcription factor regulatory network.** (A) Transcription factors were divided into 7 regulon modules according to the synergistic effect of different transcription factors. (B) The association between CellGroup and regulon modules. (C) The distribution of each regulon's rank and RSS in CellScore high and low groups. (D) The distribution of mean activity of the regulon modules (M1-M7) constructed by UMAP. (E) The distribution of mean activity of the regulon modules (M1-M7) constructed by trajectory analysis. (F) The RSS distribution of the top 2 regulons (SP3) in CellScore high group constructed by UMAP. (G) The RSS distribution of the top 2 regulons (ATF2) in CellScore high group constructed by UMAP. (H) The RSS distribution of the top 2 regulons (TP53) in CellScore low group constructed by UMAP. (I) The RSS distribution of the top 2 regulons (CD59) in CellScore low group constructed by UMAP.



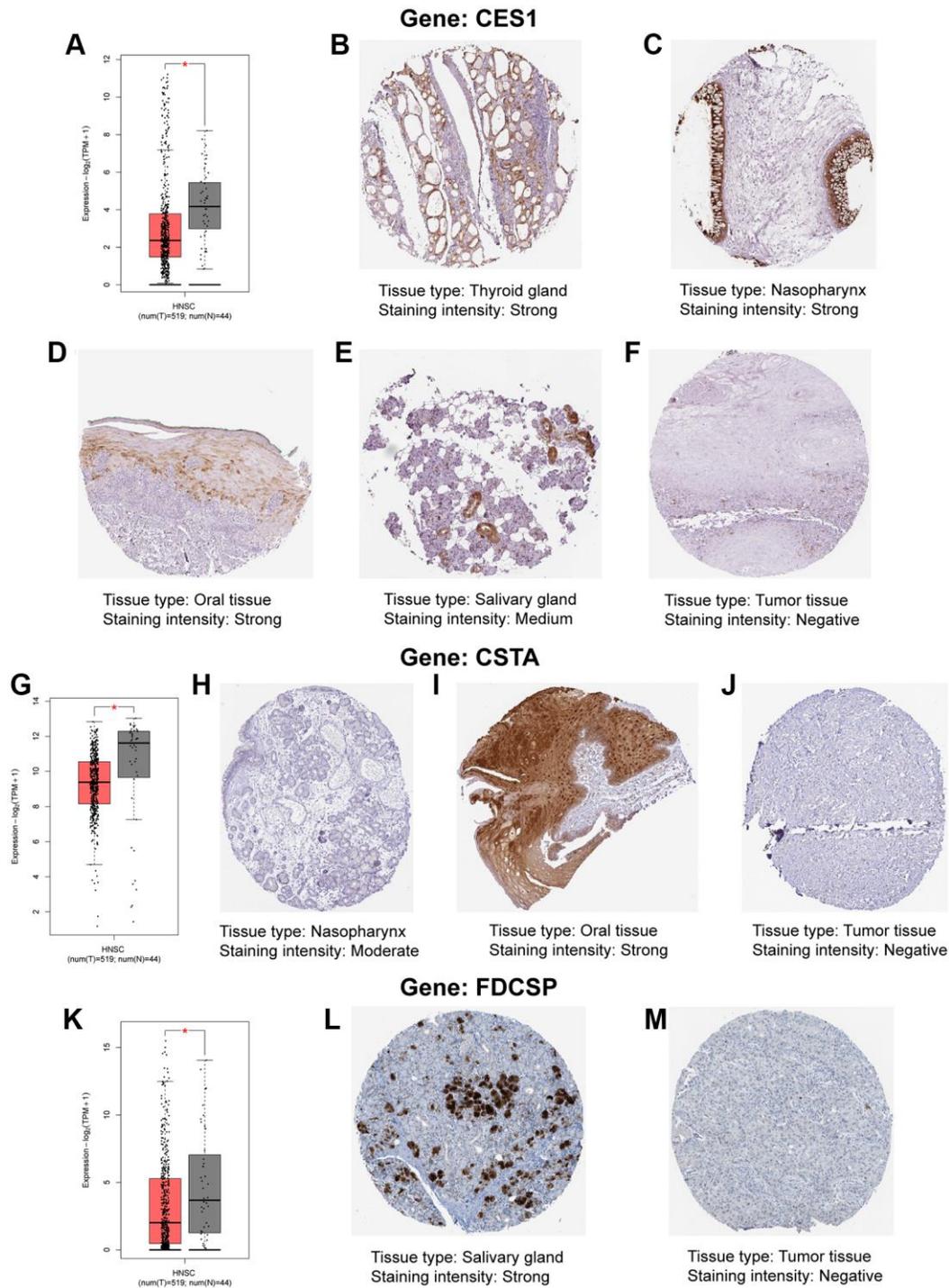
**Supplementary Figure 5. Immune landscape of different subgroups based on bulk data.** (A) Correlation analysis results between the proportion of immune infiltration and stromal score. (B) Correlation analysis results between the proportion of immune infiltration and ImmuneScore. (C) Correlation analysis results between the proportion of immune infiltration and ESTIMATEScore. (D) Correlation analysis results between the proportion of immune infiltration and tumor purity. (E) The fraction of various immune cell infiltration in high and low OSRS. The abscissa axis represents different immune cell names; The vertical axis represents the infiltration ratio; Different colors represent different subgroups.



**Supplementary Figure 6. Results of the cellular communication analysis.** (A) The graph of all the cell–cell communications and cell–cell interaction network. (B) The statistical heat map of the signaling dominant of top 30 significant pathways. (C) The statistical point map of the signaling dominant. The abscissa axis represents outgoing interaction strength; The vertical axis represents incoming interaction strength; Different colors represent different immune cells. (D) The graph of the cell–cell communications and cell–cell interaction network of LAMININ signaling pathway. (E) The graph of the cell–cell communications and cell–cell interaction network of MK signaling pathway. (F) The graph of the cell–cell communications and cell–cell interaction network of MHC-I signaling pathway.



**Supplementary Figure 7. The oxidative stress-related prognostic signature predicts the therapeutic outcomes of patients with HNSCC.** (A) KM survival curves of high and low Score groups in PRJEB23709 cohort. The abscissa axis represents the survival time; The vertical axis represents the survival probability; Different colors represent different risk subgroups. (B) The OSRS distribution of different response groups in PRJEB23709 cohort. The abscissa axis represents different treatment responses; The vertical axis represents the risk score; Different colors represent different subgroups. (C) The percent of patients with response or no response to immunotherapy in the low Score and high Score groups. The abscissa axis represents different score groupings (low or high); The vertical axis represents the percentage; Different colors represent different subgroups of immunotherapy responses. (D) The correlation between the top six negatively correlated drugs and the Score. The abscissa axis represents the value of the correlation coefficient; The vertical represents six different drugs. (E) The logIC50 value of the top six negatively correlated drugs in low and high Score groups. The abscissa axis represents six different drug names; The vertical axis represents the logIC50 value; Different colors represent different risk score subgroups. (F) The correlation between the top six positively correlated drugs and the Score; The abscissa axis represents the value of the correlation coefficient; The vertical represents six different drugs. (G) The logIC50 value of the top six positively correlated drugs in low and high Score groups. The abscissa axis represents six different drug names; The vertical axis represents the logIC50 value; Different colors represent different risk score subgroups.



**Supplementary Figure 8. IHC staining images of the genes involved in the prognostic signature.** (A) The RNA expression level of CES1 in normal head and neck and HNSCC tumor tissues. (B–F) The IHC images showing the protein expression levels of CES1 in thyroid gland (B), nasopharynx (C), oral tissue (D), salivary gland (E) and HNSCC tumor tissue (F). (G) The RNA expression level of CSTA in normal head and neck and HNSCC tumor tissues. (H–J) The IHC images showing the protein expression levels of CSTA in nasopharynx (H), oral tissue (I) and HNSCC tumor tissue (J). (K) The RNA expression level of FDCSP in normal head and neck and HNSCC tumor tissues. (L, M) The IHC images showing the protein expression levels of FDCSP in salivary gland (L) and HNSCC tumor tissue (M).