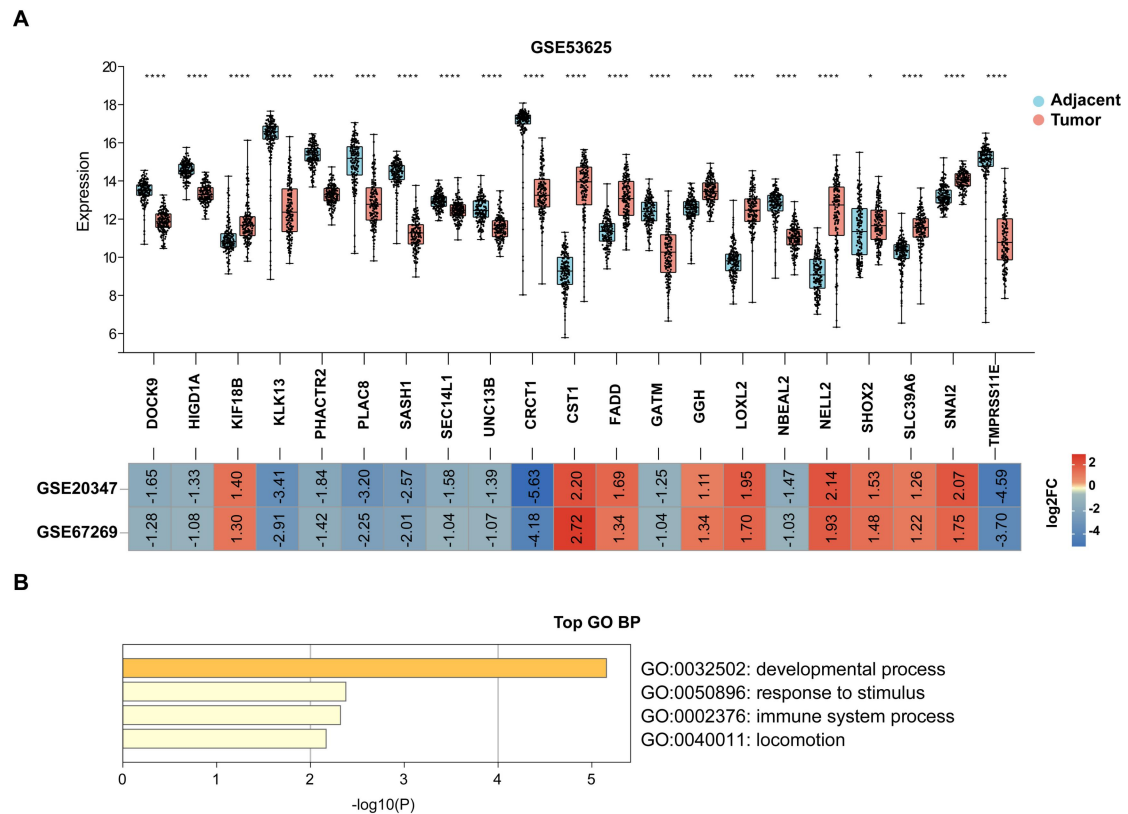
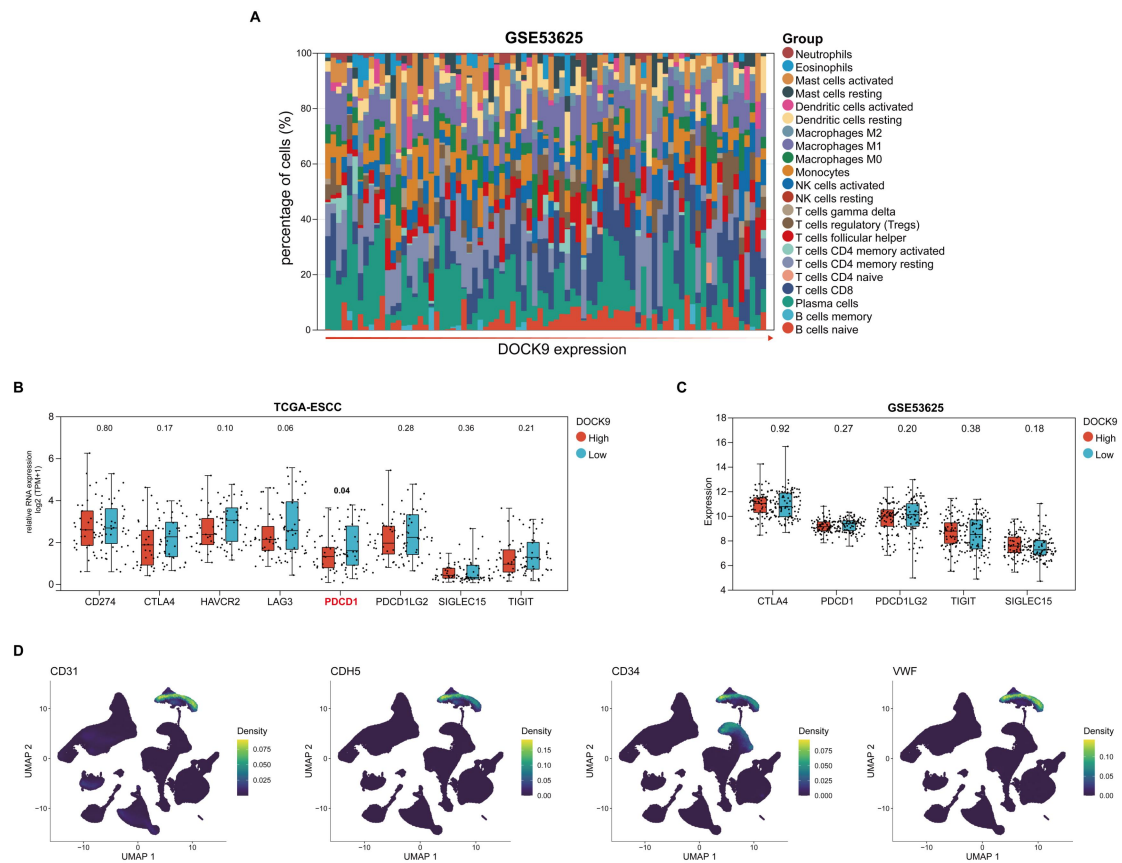


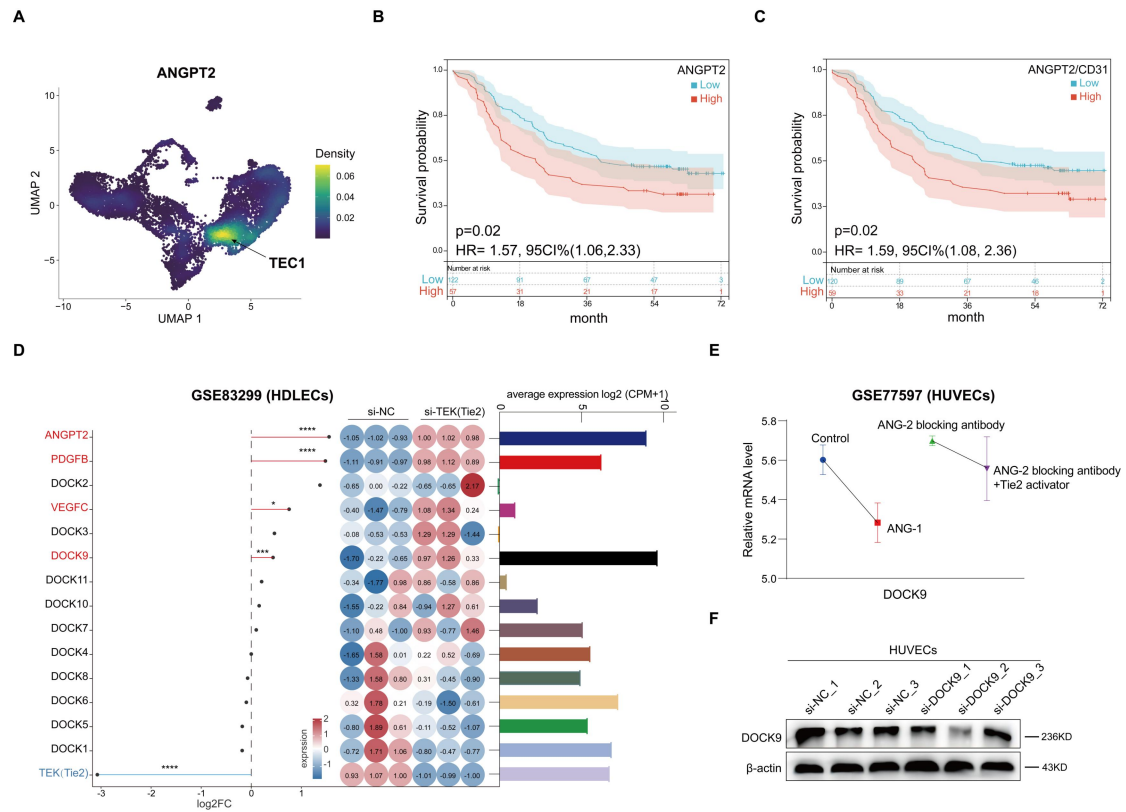


Supplementary Fig. 1 (A) The boxplot visualizes the expression profiles of the 21 signature genes within the GSE53625 dataset. Accompanying the boxplot, a heatmap displays the log2FC values of these 21 genes, contrasting tumor tissue with adjacent non-tumor tissue, as derived from the GSE20347 and GSE67269 datasets. (B) A bar chart represents the top enriched Gene Ontology (GO) Biological Process (BP) terms due to the enrichment analysis of the 21 genes used in risk modeling. (**** $p < 0.0001$, * $p < 0.05$ VS. adjacent)

corresponding to each subcluster's Gene Set Variation Analysis (GSVA) score of Gene Ontology Biological Processes (GO BP) in the combined endothelial cell data from the GSE160269 and GSE188900. A complementary dot plot underscores the top five high-variance genes within each subcluster, the dot size represents the proportion of the gene expressed in the corresponding subclusters of endothelial cells, and the dot colors represent the gene expression level. (C) A 2D UMAP visualization delineates the nuclear density distribution of PDGFB and VEGFC within the endothelial cell subclusters derived from the combined GSE160269 and GSE188900 datasets. (D) Bubble plots demonstrate selected ligand-receptor interactions between high DOCK9 expression endothelial cells and low DOCK9 expression endothelial cells. Ligand-expressing cells are marked in red, receptor-expressing cells (endothelial cells) in blue, the ligand receptors specific to each group are labeled with colors.



Supplementary Fig. 3 (A) A stacked bar chart represents the proportion of 22 distinct immune cell types, as determined by the CIBERSORT algorithm, in the GSE53625 dataset, arranged based on the high or low expression of DOCK9. (B) A box plot illustrates the differential expression of immune checkpoints between the high (top 50%) and low (bottom 50%) DOCK9 expression groups in ESCC patients from the TCGA database. (C) A box plot exhibits the differential expression of immune checkpoints between the high (top 50%) and low (bottom 50%) DOCK9 expression groups in ESCC patients within the GSE53625 dataset. (D) A UMAP density plot showcases the expression distribution of four endothelial cell markers (CD31, CDH5, CD34, and VWF) within the GSE160269 dataset.



Supplementary Fig. 4 (A) A UMAP density plot illustrates the distribution of ANGPT2 expression within the consolidated single-cell RNA-seq data of endothelial cells from ESCC patients. (B) Kaplan-Meier survival analysis demonstrates the relationship between ANGPT2 expression and overall patient survival in the GSE53625 dataset. The p-value is determined via the log-rank test. (C) Kaplan-Meier survival analysis depicts the association between ANGPT2/CD31 expression and overall patient survival in the GSE53625 dataset, with the p-value calculated using the log-rank test. (D) A heatmap represents the expression of DOCK family genes (DOCK1-11), ANGPT2, PDGFB, VEGFC and TEK following TEK knockdown in HDLEC cells. Accompanying dot plots depict the log2FC value of the differential analyses between si-TEK and si-NC and the p-value (<0.05). Bar graphs display the mean expression abundance of each gene within the cells. (E) Dot line chart show the relative RNA expression of DOCK9 in control, ANG-1,

ANG-2 blocking antibody, and ANG-2 blocking antibody+ Tie2 activator. (F) Western blot reveals the DOCK9 expression in both si-NC and three si-DOCK9 (sequences 1,2,3) groups. (**** $p<0.0001$, *** $p<0.001$, * $p<0.05$)