Figure S1

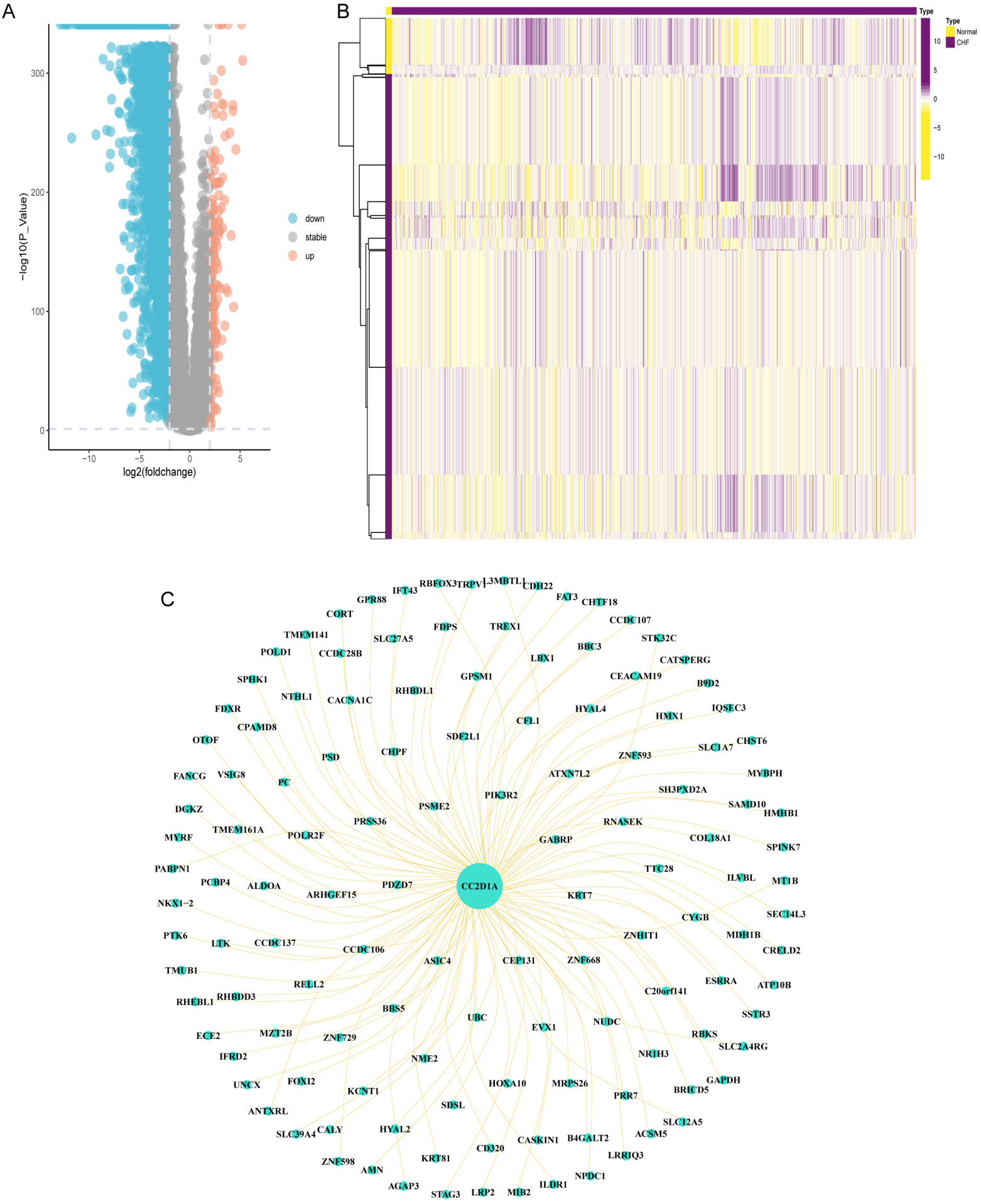


Figure S1. (A–B) Volcano plot and heatmap of DEGs between CHF and normal peripheral blood samples. (C) Gene co-expression network of the turquoise module from WGCNA, showing high-confidence interactions (edge weight > 0.575).

Figure S2

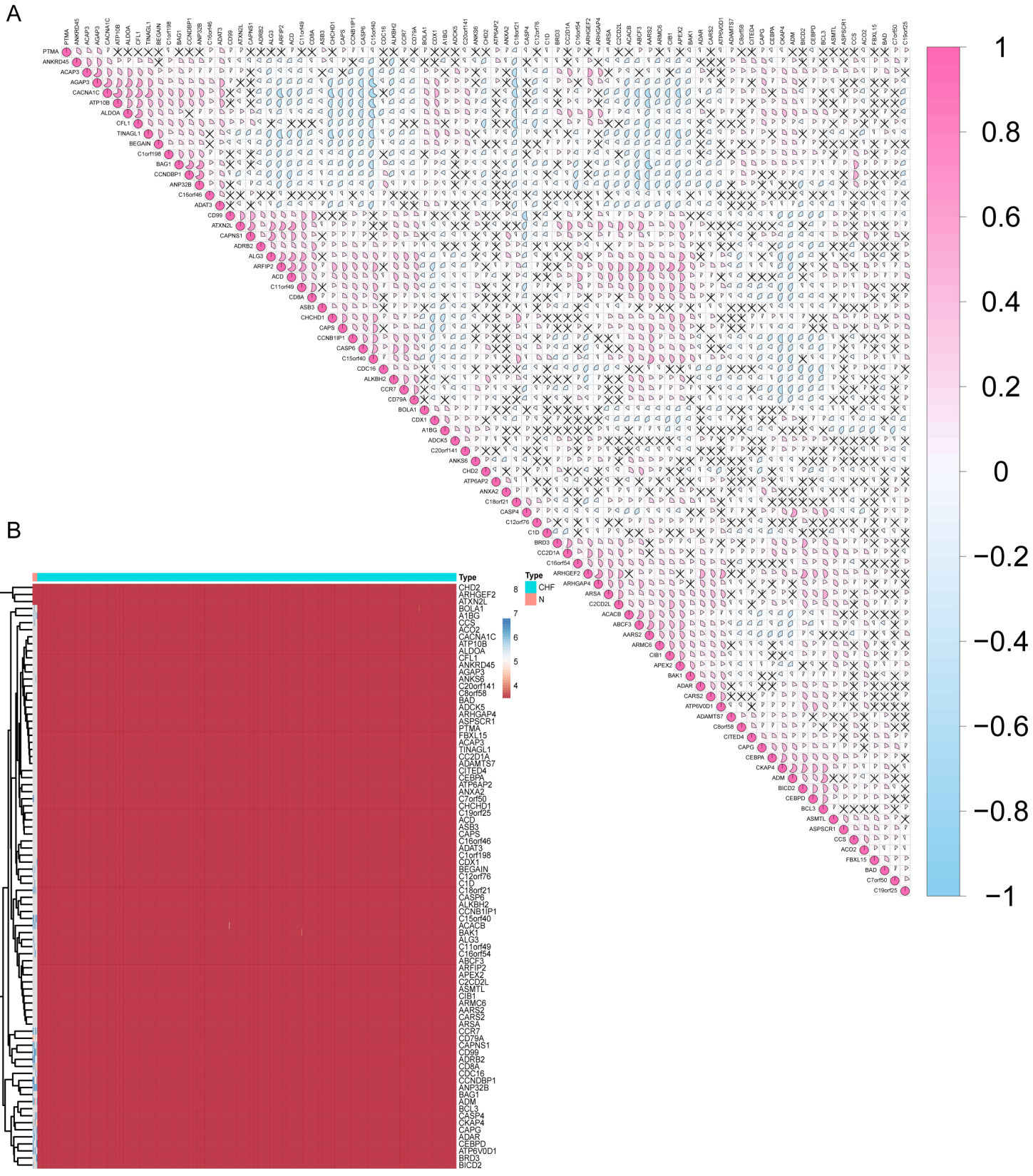


Figure S2. (A) Correlation matrix of the 83 candidate genes. The sector area in each cell represents the magnitude of the Pearson correlation coefficient. (B) Hierarchical clustering heatmap of the 83 overlapping candidate genes from LASSO, RF, and SVM-RFE models.

Figure S3

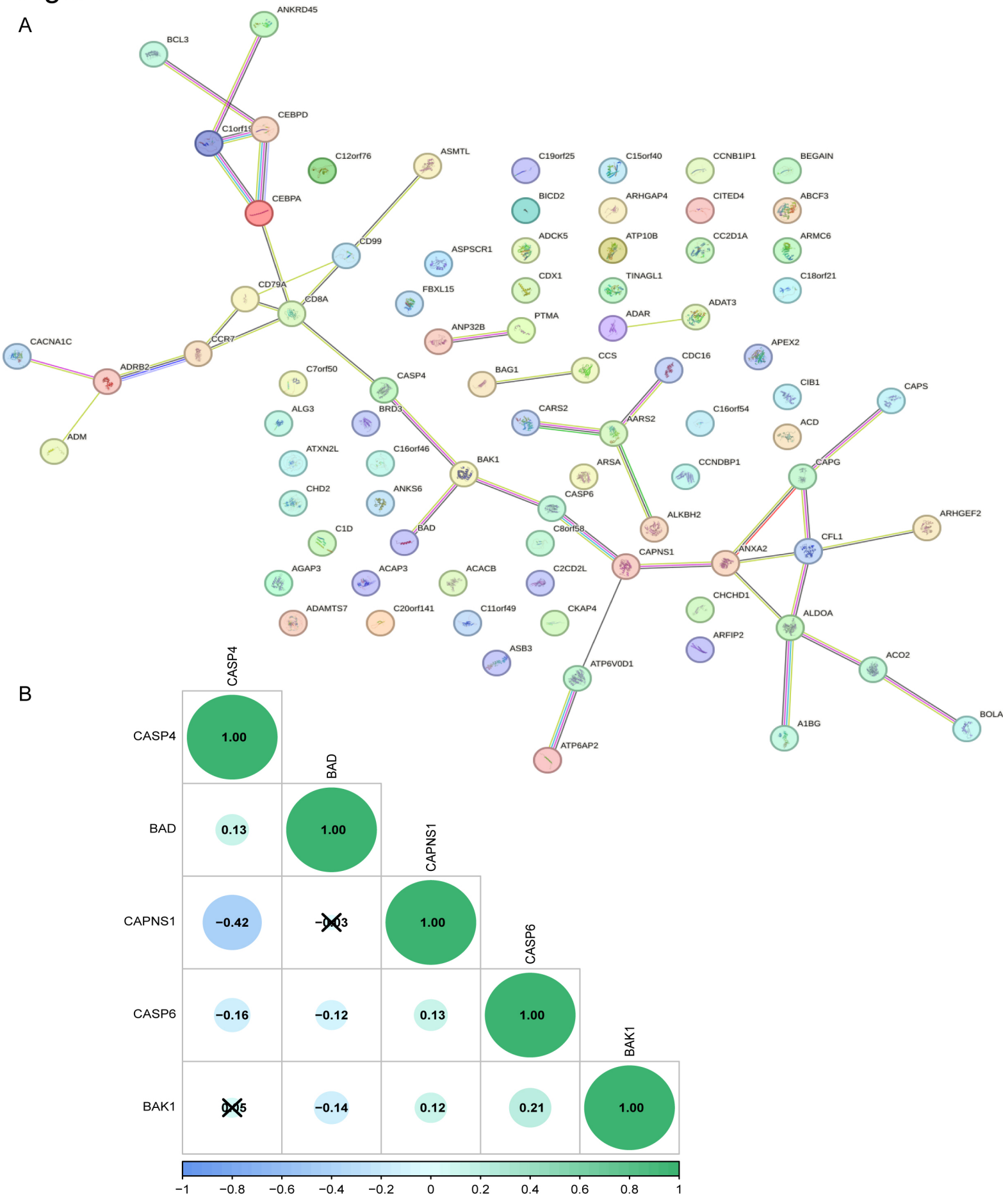


Figure S3. (A) PPI network of overlapping genes identified by machine learning algorithms. (B) Pearson correlation of the five key genes from the MCL module, with values inside the circles indicating correlation coefficients.

Figure S4

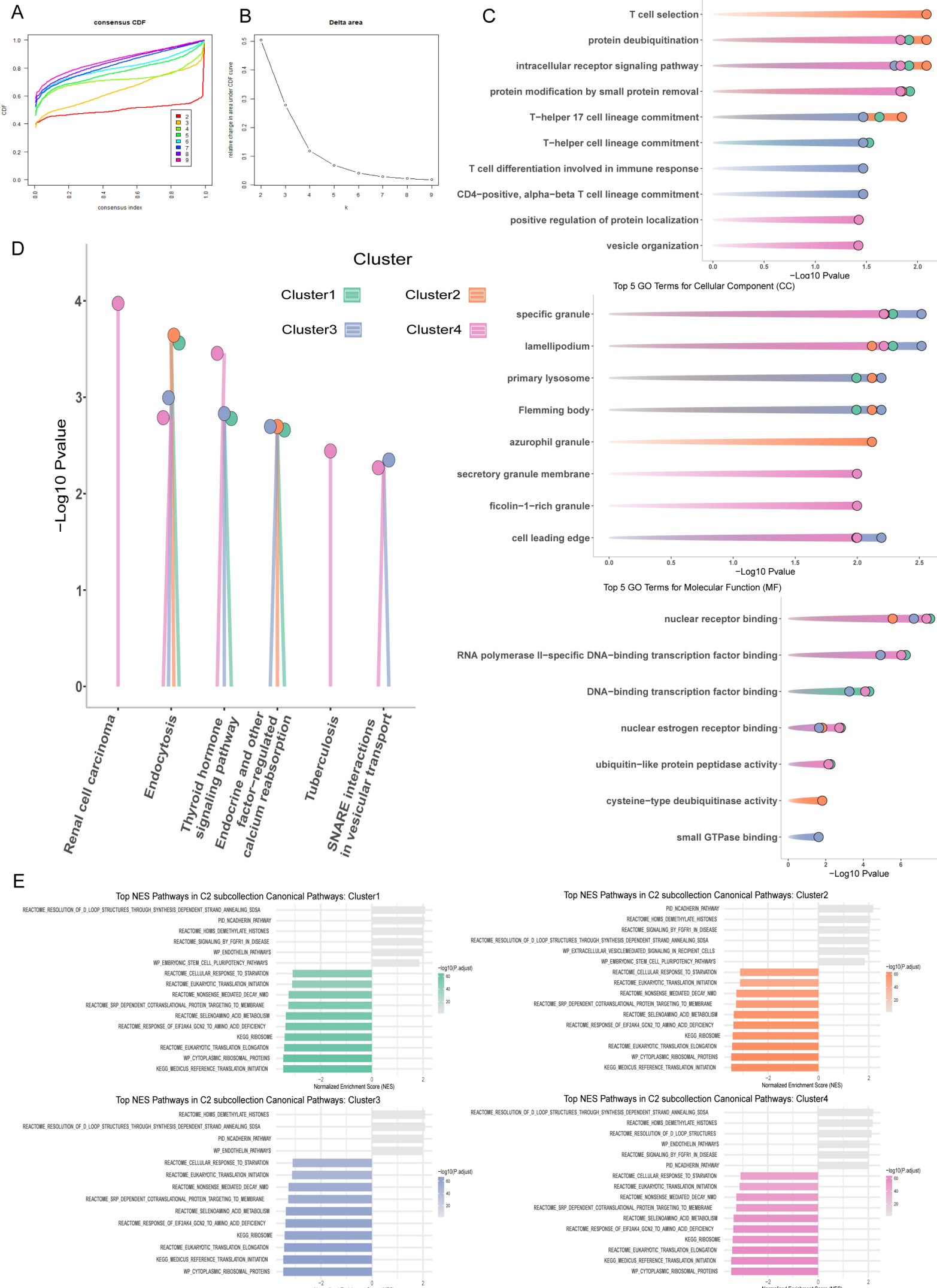

A
consensus CDF
CDF
consensus index
B
Delta area
relative change in area under CDF curve
k
C
Top 5 GO Terms for Biological Process (BP)
T cell selection
protein deubiquitination
intracellular receptor signaling pathway
protein modification by small protein removal
T−helper 17 cell lineage commitment
T−helper cell lineage commitment
T cell differentiation involved in immune response
CD4−positive, alpha−beta T cell lineage commitment
positive regulation of protein localization
vesicle organization
−Log10 Pvalue
D
Cluster
Cluster1
Cluster2
Cluster3
Cluster4
−Log10 Pvalue
Renal cell carcinoma
Endocytosis
Thyroid hormone signaling pathway
Endocrine and other factor−regulated calcium reabsorption
Tuberculosis
SNARE interactions in vesicular transport
Top 5 GO Terms for Cellular Component (CC)
specific granule
lamellipodium
primary lysosome
Flemming body
azurophil granule
secretory granule membrane
ficolin−1−rich granule
cell leading edge
−Log10 Pvalue
Top 5 GO Terms for Molecular Function (MF)
nuclear receptor binding
RNA polymerase II−specific DNA−binding transcription factor binding
DNA−binding transcription factor binding
nuclear estrogen receptor binding
ubiquitin−like protein peptidase activity
cysteine−type deubiquitinase activity
small GTPase binding
−Log10 Pvalue
E
Top NES Pathways in C2 subcollection Canonical Pathways: Cluster1
REACTOME_RESOLUTION_OF_D_LOOP_STRUCTURES_THROUGH_SYNTHESIS_DEPENDENT_STRAND_ANNEALING_SDSA
PID_NCADHERIN_PATHWAY
REACTOME_HDMS_DEMETHYLATE_HISTONES
REACTOME_SIGNALING_BY_FGFR1_IN_DISEASE
WP_ENDOTHELIN_PATHWAYS
WP_EMBRYONIC_STEM_CELL_PLURIPOTENCY_PATHWAYS
REACTOME_CELLULAR_RESPONSE_TO_STARVATION
REACTOME_EUKARYOTIC_TRANSLATION_INITIATION
REACTOME_NONSENSE_MEDIATED_DECAY_NMD
REACTOME_SRP_DEPENDENT_COTRANSLATIONAL_PROTEIN_TARGETING_TO_MEMBRANE
REACTOME_SELENOAMINO_ACID_METABOLISM
REACTOME_RESPONSE_OF_EIF2AK4_GCN2_TO_AMINO_ACID_DEFICIENCY
KEGG_RIBOSOME
REACTOME_EUKARYOTIC_TRANSLATION_ELONGATION
WP_CYTOPLASMIC_RIBOSOMAL_PROTEINS
KEGG_MEDICUS_REFERENCE_TRANSLATION_INITIATION
−log10(P.adjust)
Normalized Enrichment Score (NES)
Top NES Pathways in C2 subcollection Canonical Pathways: Cluster2
PID_NCADHERIN_PATHWAY
REACTOME_HDMS_DEMETHYLATE_HISTONES
REACTOME_SIGNALING_BY_FGFR1_IN_DISEASE
REACTOME_RESOLUTION_OF_D_LOOP_STRUCTURES_THROUGH_SYNTHESIS_DEPENDENT_STRAND_ANNEALING_SDSA
WP_EXTRACELLULAR_VESICLEMEDIATED_SIGNALING_IN_RECIPIENT_CELLS
WP_EMBRYONIC_STEM_CELL_PLURIPOTENCY_PATHWAYS
REACTOME_CELLULAR_RESPONSE_TO_STARVATION
REACTOME_EUKARYOTIC_TRANSLATION_INITIATION
REACTOME_NONSENSE_MEDIATED_DECAY_NMD
REACTOME_SRP_DEPENDENT_COTRANSLATIONAL_PROTEIN_TARGETING_TO_MEMBRANE
REACTOME_SELENOAMINO_ACID_METABOLISM
REACTOME_RESPONSE_OF_EIF2AK4_GCN2_TO_AMINO_ACID_DEFICIENCY
KEGG_RIBOSOME
REACTOME_EUKARYOTIC_TRANSLATION_ELONGATION
WP_CYTOPLASMIC_RIBOSOMAL_PROTEINS
KEGG_MEDICUS_REFERENCE_TRANSLATION_INITIATION
−log10(P.adjust)
Normalized Enrichment Score (NES)
Top NES Pathways in C2 subcollection Canonical Pathways: Cluster3
REACTOME_HDMS_DEMETHYLATE_HISTONES
REACTOME_RESOLUTION_OF_D_LOOP_STRUCTURES_THROUGH_SYNTHESIS_DEPENDENT_STRAND_ANNEALING_SDSA
PID_NCADHERIN_PATHWAY
WP_ENDOTHELIN_PATHWAYS
REACTOME_CELLULAR_RESPONSE_TO_STARVATION
REACTOME_EUKARYOTIC_TRANSLATION_INITIATION
REACTOME_NONSENSE_MEDIATED_DECAY_NMD
REACTOME_SRP_DEPENDENT_COTRANSLATIONAL_PROTEIN_TARGETING_TO_MEMBRANE
REACTOME_SELENOAMINO_ACID_METABOLISM
REACTOME_RESPONSE_OF_EIF2AK4_GCN2_TO_AMINO_ACID_DEFICIENCY
KEGG_RIBOSOME
REACTOME_EUKARYOTIC_TRANSLATION_ELONGATION
KEGG_MEDICUS_REFERENCE_TRANSLATION_INITIATION
WP_CYTOPLASMIC_RIBOSOMAL_PROTEINS
−log10(P.adjust)
Normalized Enrichment Score (NES)
Top NES Pathways in C2 subcollection Canonical Pathways: Cluster4
REACTOME_RESOLUTION_OF_D_LOOP_STRUCTURES_THROUGH_SYNTHESIS_DEPENDENT_STRAND_ANNEALING_SDSA
REACTOME_HDMS_DEMETHYLATE_HISTONES
REACTOME_RESOLUTION_OF_D_LOOP_STRUCTURES
WP_ENDOTHELIN_PATHWAYS
REACTOME_SIGNALING_BY_FGFR1_IN_DISEASE
PID_NCADHERIN_PATHWAY
REACTOME_CELLULAR_RESPONSE_TO_STARVATION
REACTOME_EUKARYOTIC_TRANSLATION_INITIATION
REACTOME_NONSENSE_MEDIATED_DECAY_NMD
REACTOME_SRP_DEPENDENT_COTRANSLATIONAL_PROTEIN_TARGETING_TO_MEMBRANE
REACTOME_SELENOAMINO_ACID_METABOLISM
REACTOME_RESPONSE_OF_EIF2AK4_GCN2_TO_AMINO_ACID_DEFICIENCY
KEGG_RIBOSOME
REACTOME_EUKARYOTIC_TRANSLATION_ELONGATION
KEGG_MEDICUS_REFERENCE_TRANSLATION_INITIATION
WP_CYTOPLASMIC_RIBOSOMAL_PROTEINS
−log10(P.adjust)
Normalized Enrichment Score (NES)

Figure S4. (A) Cumulative distribution function (CDF) plot for evaluating clustering stability. (B) Delta area plot showing the relative change in CDF for different cluster numbers. (C) Top 5 enriched GO terms in BP, CC, and MF categories of each cluster based on upregulated DEGs. (D) KEGG pathways enriched in each cluster based on upregulated DEGs. (E) GSEA results of C2CP gene set for each cluster. Enriched terms were ranked by the absolute value of NES, and the top 10 terms from each direction were selected. For clusters with fewer than 10 positively enriched terms, all available terms are shown.

Figure S5


A
100%
80%
60%
40%
20%
0%
Relative Percent
Cluster1
Cluster2
Cluster3
Cluster4
B cells naive
B cells memory
Plasma cells
T cells CD8
T cells CD4 naive
T cells CD4 memory resting
T cells CD4 memory activated
T cells follicular helper
T cells regulatory (Tregs)
T cells gamma delta
NK cells resting
NK cells activated
Monocytes
Macrophages M0
Macrophages M1
Macrophages M2
Dendritic cells resting
Dendritic cells activated
Mast cells resting
Mast cells activated
Eosinophils
Neutrophils
B
Immune Composition Heatmap (CIBERSORTx)
Group
Cluster1
Cluster2
Cluster3
Cluster4
4
2
0
−2
−4
Group
Neutrophils
T cells CD4 naive
B cells memory
T cells CD8
NK cells resting
Eosinophils
B cells naive
Mast cells activated
Macrophages M0
T cells gamma delta
Macrophages M2
Dendritic cells activated
Dendritic cells resting
Plasma cells
Macrophages M1
T cells follicular helper
T cells regulatory (Tregs)
NK cells activated
T cells CD4 memory activated
Mast cells resting
T cells CD4 memory resting
Monocytes
C
Cluster
Cluster1
Cluster2
Cluster3
Cluster4
Fraction of Mast cells resting
Fraction of Mast cells activated
Fraction of NK cells resting
Fraction of B cells memory
Fraction of T cells CD8
Fraction of T cells gamma delta
Fraction of T cells CD4 memory resting
Fraction of Dendritic cells activated
Fraction of Monocytes
Fraction of Macrophages M1
Fraction of Macrophages M2
Fraction of Eosinophils
Fraction of Neutrophils
Fraction of Plasma cells
Fraction of T cells CD4 naive
Fraction of T cells regulatory (Tregs)

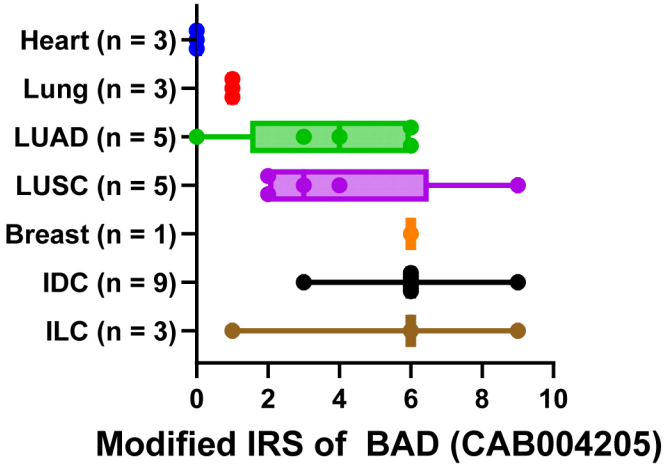
Figure S5. (A) Stacked bar plot showing the relative proportions of 22 immune cell types in each cluster based on CIBERSORTx. (B) Heatmap of immune cell composition across the clusters. (C) Pairwise comparisons of immune cell types among clusters. (***p < 0.001, **p < 0.01, *p < 0.05, ns: not significant)

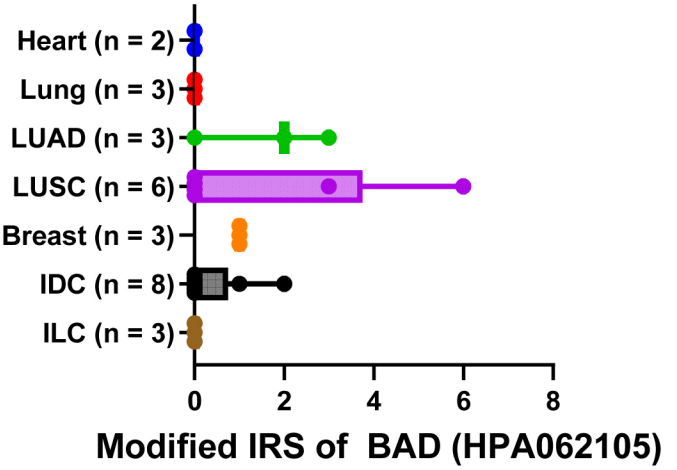
Figure S6

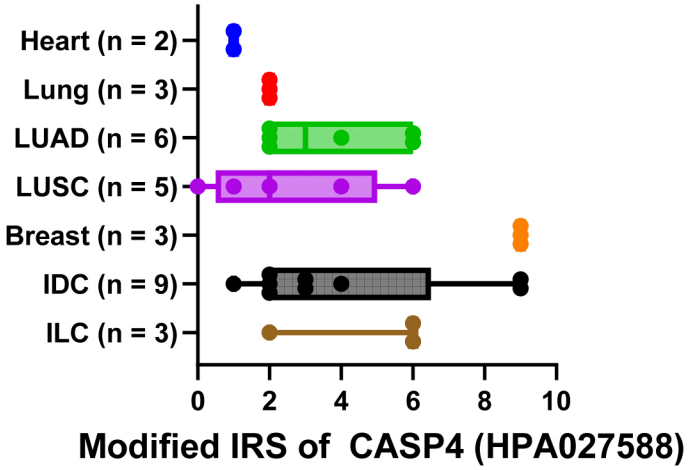

Score of Cytolytic_activity
Score of B_cells
Score of APC_co_inhibition
Score of Inflammation−promoting
Score of Type_I_IFN_Response
Score of TIL
Score of Th2_cells
Score of HLA
Score of Tfh
Score of T_helper_cells
Score of Parainflammation
Score of CD8+_T_cells
Score of NK_cells
Score of Th1_cells
Score of aDCs
Score of Check−point
Score of CCR
Score of Macrophages
Score of T_cell_co−inhibition
Score of Type_II_IFN_Response
Score of DCs
Score of Treg
Score of pDCs
Score of Neutrophils
Score of APC_co_stimulation
Score of T_cell_co−stimulation
Cluster
Cluster1
Cluster2
Cluster3
Cluster4

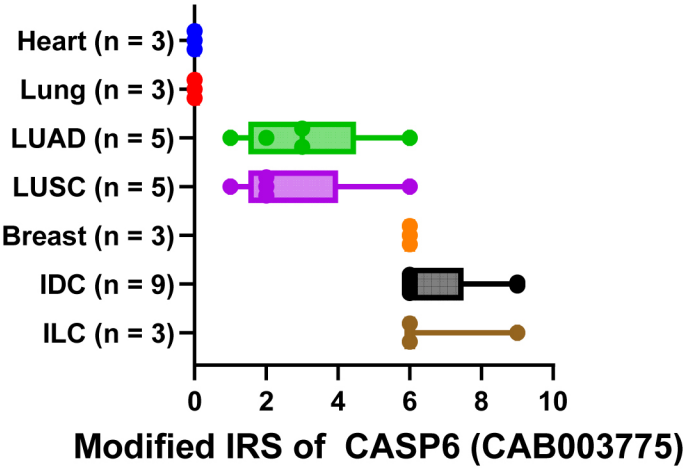
Figure S6. Pairwise comparisons of immune functions among clusters. (***p < 0.001, **p < 0.01, *p < 0.05, ns: not significant)

Figure S7









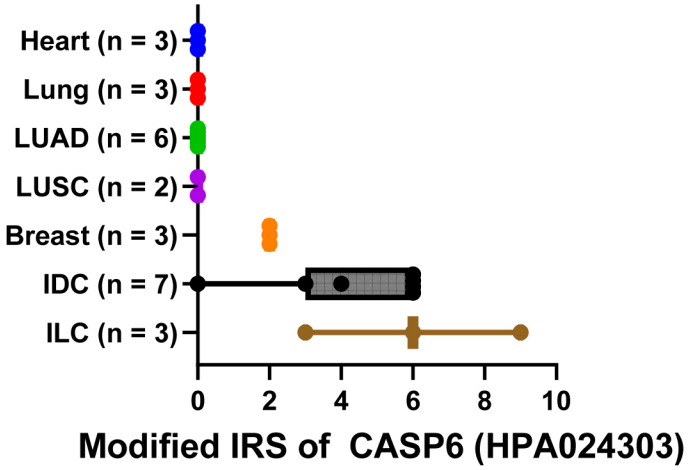


Figure S7. Supplementary Modified IRS distributions of the cluster-driven key genes, based on staining intensity and positive cell fraction in normal heart, lung, and breast tissues, as well as LUAD, LUSC,IDC, and ILC. Only genes with multiple validated antibodies in the HPA are included.