Figure S1: Pan-cancer expression of TREM1 in tumor and normal tissues.

Figure S2: Cox regression analysis of TREM in TCGA pan-cancer.

Figure S3: Function enrichment analysis.

Figure S4: GSEA annotated with hallmark gene sets in pan-cancer.

Figure S5: Correlation analysis between TREM1 expression and the infiltration levels of immune cells.

Figure S6: Correlation analysis between TREM1 expression and immunomodulatory genes.

Table S1: Abbreviations of cancers in TCGA.

Table S2: Oligo sequences used in quantitative real-time PCR.

Table S3: Detailed information of TME-related signatures.

A

BLCA * | BRCA *** | CESC ns | CHOL ns | COAD *** | ESCA *** | HNSC *** | KICH * | KIRC *** | KIRP ***

TREM1 expression log2(TPM+1)

normal tumor (repeated across panels)

LIHC ** | LUAD *** | LUSC *** | PAAD ns | PCPG ns | PRAD ns | READ ns | STAD *** | THCA *** | UCEC ns

TREM1 expression log2(TPM+1)

normal tumor (repeated across panels)

B

Expression of TREM1 in BLCA based on individual cancer stages
Transcript per million
Normal (n=19) | Stage1 (n=2) | Stage2 (n=137) | Stage3 (n=129) | Stage4 (n=132)
TCGA samples
** *** **

Expression of TREM1 in COAD based on individual cancer stages
Transcript per million
Normal (n=41) | Stage1 (n=45) | Stage2 (n=110) | Stage3 (n=80) | Stage4 (n=39)
TCGA samples
*** *** *** ***

Expression of TREM1 in ESCA based on individual cancer stages
Transcript per million
Normal (n=11) | Stage1 (n=13) | Stage2 (n=78) | Stage3 (n=55) | Stage4 (n=9)
TCGA samples
* *** *** *

Expression of TREM1 in HNSC based on individual cancer stages
Transcript per million
Normal (n=44) | Stage1 (n=27) | Stage2 (n=71) | Stage3 (n=81) | Stage4 (n=264)
TCGA samples
*** *** *** ***

Expression of TREM1 in KIRC based on individual cancer stages
Transcript per million
Normal (n=72) | Stage1 (n=267) | Stage2 (n=57) | Stage3 (n=123) | Stage4 (n=84)
TCGA samples
*** *** *** **

Expression of TREM1 in KIRP based on individual cancer stages
Transcript per million
Normal (n=32) | Stage1 (n=140) | Stage2 (n=21) | Stage3 (n=29) | Stage4 (n=11)
TCGA samples
*** *

Expression of TREM1 in READ based on individual cancer stages
Transcript per million
Normal (n=10) | Stage1 (n=30) | Stage2 (n=51) | Stage3 (n=51) | Stage4 (n=24)
TCGA samples
*** ***

Expression of TREM1 in STAD based on individual cancer stages
Transcript per million
Normal (n=34) | Stage1 (n=18) | Stage2 (n=123) | Stage3 (n=169) | Stage4 (n=41)
TCGA samples
*** *** ***

Expression of TREM1 in THCA based on individual cancer stages
Transcript per million
Normal (n=59) | Stage1 (n=284) | Stage2 (n=52) | Stage3 (n=112) | Stage4 (n=55)
TCGA samples
*** *** *** *

Expression of TREM1 in UCEC based on individual cancer stages
Transcript per million
Normal (n=35) | Stage1 (n=341) | Stage2 (n=52) | Stage3 (n=124) | Stage4 (n=29)
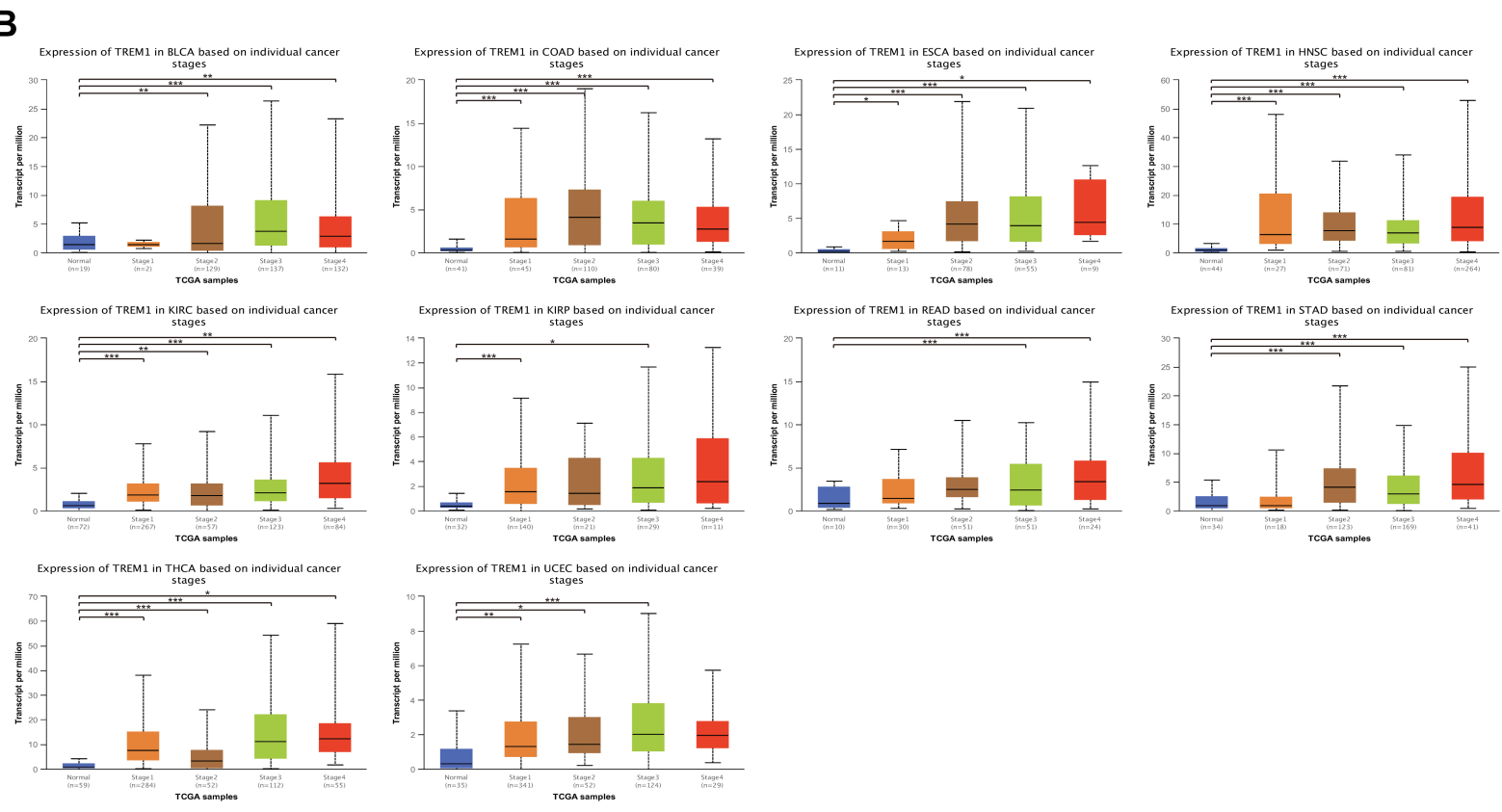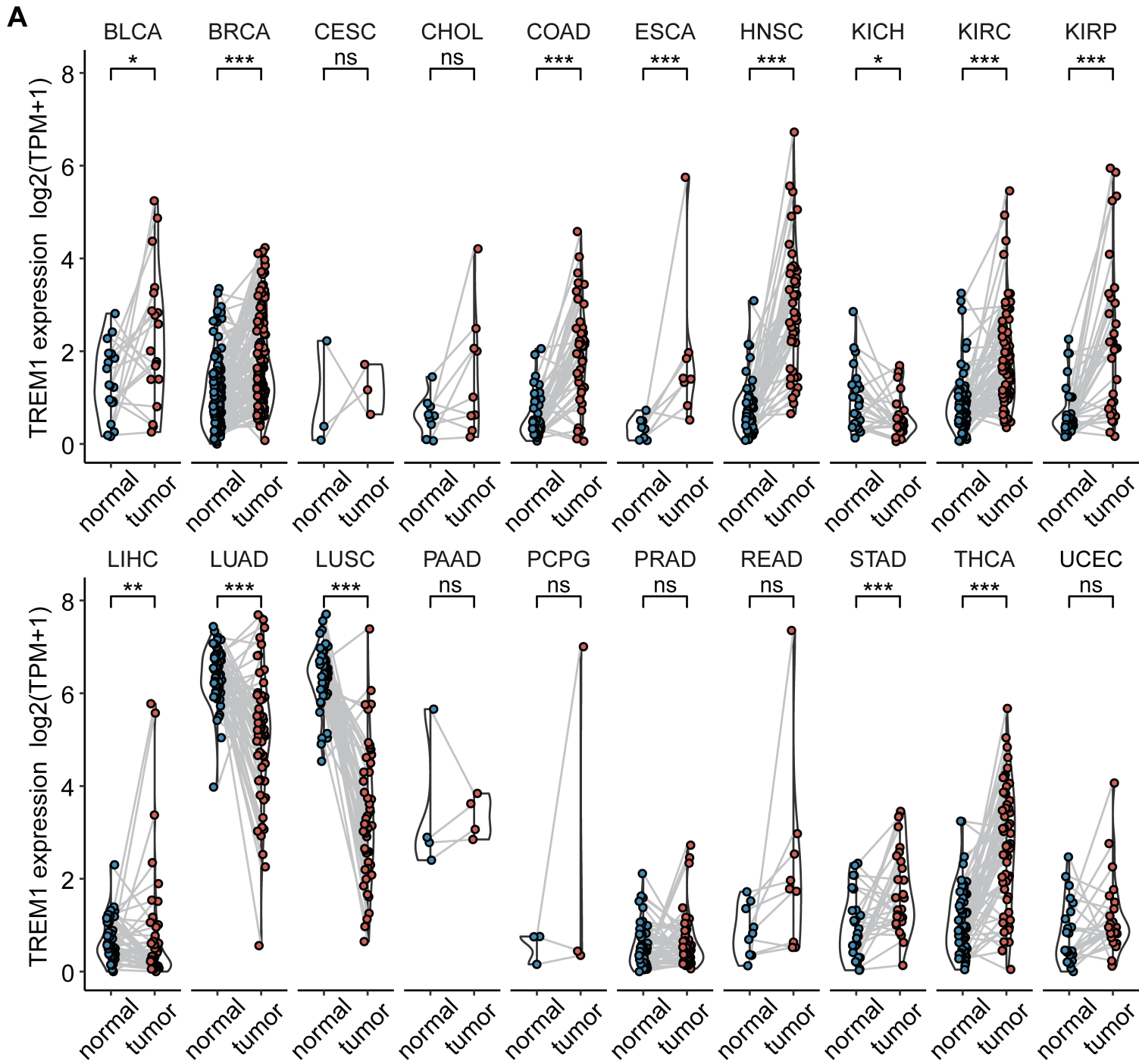TCGA samples
** * ***

Figure S1. Pan-cancer expression of TREM1 in tumor and normal tissues. **(A)** Expression level of TREM1 in tumor and paired normal tissues in TCGA pan-cancer. **(B)** TREM1 expression in various AJCC stages in indicated tumor types. *P < 0.05, **P < 0.01, ***P < 0.001. AJCC, American Joint Committee on Cancer; TCGA, The Cancer Genome Atlas. Abbreviation list of tumor cohorts from TCGA is given in **Table S1**.
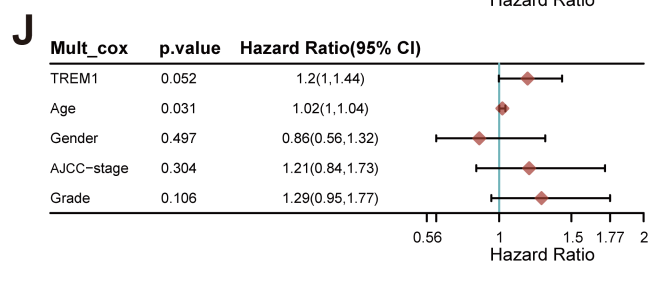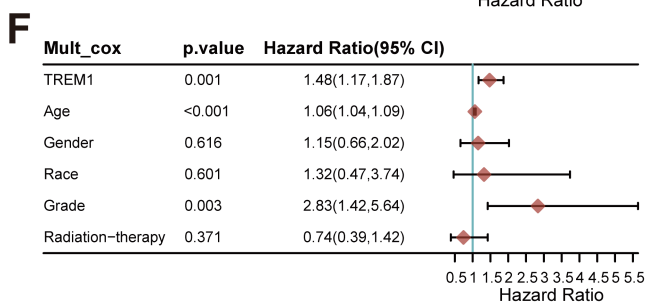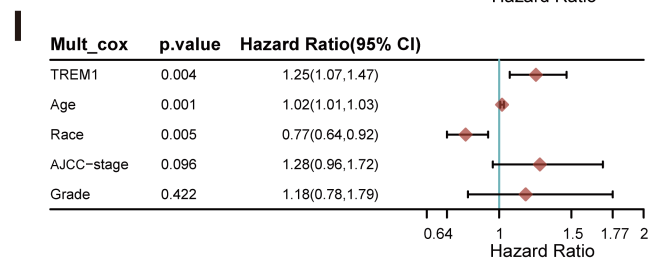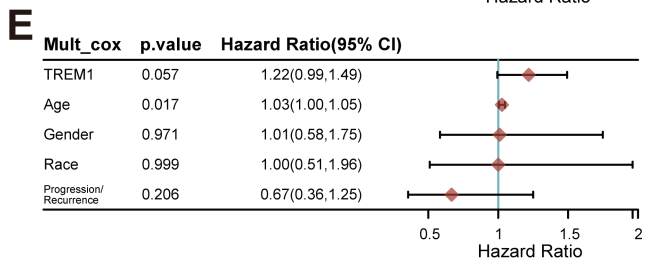
A

	Hazard Ratio	OS	P value
PRAD	2.67 [0.88, 8.09]		0.084
TGCT	1.81 [0.92, 3.58]		0.086
UVM	1.66 [0.34, 8.06]		0.531
THYM	1.65 [0.53, 5.09]		0.387
KICH	1.62 [0.84, 3.14]		0.153
LIHC	1.39 [1.21, 1.60]		<0.001
THCA	1.39 [0.95, 2.04]		0.091
LGG	1.36 [1.17, 1.58]		<0.001
CESC	1.33 [1.13, 1.57]		0.001
KIRC	1.32 [1.18, 1.47]		<0.001
KIRP	1.24 [0.94, 1.64]		0.131
PAAD	1.24 [1.05, 1.45]		0.010
OV	1.19 [1.03, 1.38]		0.017
LUSC	1.16 [1.05, 1.28]		0.003
MESO	1.16 [0.98, 1.37]		0.078
UCEC	1.15 [0.91, 1.46]		0.238
GBM	1.14 [1.01, 1.28]		0.036
STAD	1.14 [0.99, 1.30]		0.064
CHOL	1.12 [0.73, 1.71]		0.613
ESCA	1.12 [0.91, 1.39]		0.278
DLBC	1.11 [0.73, 1.68]		0.638
UCS	1.11 [0.78, 1.58]		0.559
HNSC	1.10 [1.00, 1.22]		0.059
PCPG	1.10 [0.54, 2.26]		0.785
ACC	1.09 [0.82, 1.47]		0.547
READ	1.09 [0.77, 1.55]		0.632
BLCA	1.07 [0.97, 1.19]		0.167
SKCM	1.07 [0.78, 1.49]		0.666
BRCA	1.06 [0.90, 1.25]		0.469
SARC	1.04 [0.91, 1.18]		0.598
COAD	1.00 [0.85, 1.18]		0.955
LUAD	0.93 [0.85, 1.02]		0.110

B

	Hazard Ratio	DSS	P value
PRAD	4.12 [1.02, 16.64]		0.047
THYM	3.11 [0.85, 11.34]		0.086
UVM	1.92 [0.41, 9.02]		0.411
KICH	1.84 [0.96, 3.54]		0.066
TGCT	1.58 [0.71, 3.53]		0.266
KIRC	1.44 [1.27, 1.63]		<0.001
LIHC	1.39 [1.15, 1.67]		0.001
LGG	1.38 [1.18, 1.62]		<0.001
UCEC	1.33 [1.01, 1.75]		0.040
PAAD	1.30 [1.08, 1.56]		0.004
CESC	1.26 [1.02, 1.54]		0.032
KIRP	1.22 [0.87, 1.70]		0.253
THCA	1.20 [0.68, 2.12]		0.536
OV	1.18 [1.00, 1.39]		0.046
BRCA	1.16 [0.94, 1.43]		0.164
GBM	1.15 [1.01, 1.30]		0.033
CHOL	1.14 [0.73, 1.80]		0.559
LUSC	1.13 [0.97, 1.33]		0.126
HNSC	1.11 [0.98, 1.26]		0.109
MESO	1.11 [0.91, 1.36]		0.297
SKCM	1.11 [0.76, 1.60]		0.597
READ	1.10 [0.69, 1.75]		0.692
UCS	1.10 [0.76, 1.59]		0.602
COAD	1.08 [0.88, 1.31]		0.467
BLCA	1.05 [0.92, 1.19]		0.473
ESCA	1.05 [0.81, 1.37]		0.693
STAD	1.04 [0.86, 1.25]		0.685
ACC	1.03 [0.74, 1.45]		0.855
SARC	1.02 [0.89, 1.18]		0.752
DLBC	0.97 [0.52, 1.81]		0.924
LUAD	0.86 [0.77, 0.97]		0.012
PCPG	0.10 [0.00, 7.29]		0.293

C

Mult_cox	p.value	Hazard Ratio(95% CI)
TREM1	0.004	1.41(1.12,1.78)
Age	0.115	1.02(1.00,1.04)
Race	0.926	0.99(0.74,1.31)
AJCC-stage	0.003	1.51(1.14,1.99)
Grade	0.678	0.90(0.55,1.47)
Smoking	0.442	1.25(0.71,2.21)

D

Mult_cox	p.value	Hazard Ratio(95% CI)
TREM1	0.022	1.16(1.02,1.32)
Age	<0.001	1.03(1.02,1.05)
Gender	0.841	0.97(0.71,1.33)
pT-stage	0.058	0.74(0.55,1.01)
AJCC-stage	<0.001	1.97(1.55,2.51)
Grade	<0.001	1.52(1.21,1.90)

E

Mult_cox	p.value	Hazard Ratio(95% CI)
TREM1	0.057	1.22(0.99,1.49)
Age	0.017	1.03(1.00,1.05)
Gender	0.971	1.01(0.58,1.75)
Race	0.999	1.00(0.51,1.96)
Progression/Recurrence	0.206	0.67(0.36,1.25)

F

Mult_cox	p.value	Hazard Ratio(95% CI)
TREM1	0.001	1.48(1.17,1.87)
Age	<0.001	1.06(1.04,1.09)
Gender	0.616	1.15(0.66,2.02)
Race	0.601	1.32(0.47,3.74)
Grade	0.003	2.83(1.42,5.64)
Radiation-therapy	0.371	0.74(0.39,1.42)

G

Mult_cox	p.value	Hazard Ratio(95% CI)
TREM1	<0.001	1.37(1.15,1.62)
Age	0.162	1.01(1.00,1.03)
Gender	0.746	0.94(0.63,1.39)
Race	0.979	1.00(0.80,1.25)
AJCC-stage	0.004	1.33(1.1,1.61)
Grade	0.604	1.07(0.82,1.4)

H

Mult_cox	p.value	Hazard Ratio(95% CI)
TREM1	0.005	1.16(1.05,1.29)
Age	0.011	1.02(1.01,1.04)
Gender	0.194	1.24(0.9,1.72)
pT-stage	0.238	1.15(0.91,1.44)
AJCC-stage	0.061	1.21(0.99,1.48)
Smoking	0.079	0.47(0.21,1.09)

I

Mult_cox	p.value	Hazard Ratio(95% CI)
TREM1	0.004	1.25(1.07,1.47)
Age	0.001	1.02(1.01,1.03)
Race	0.005	0.77(0.64,0.92)
AJCC-stage	0.096	1.28(0.96,1.72)
Grade	0.422	1.18(0.78,1.79)

J

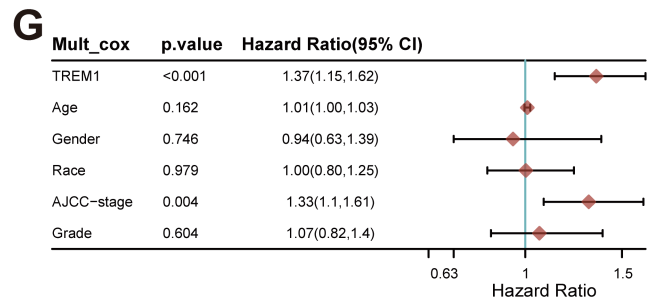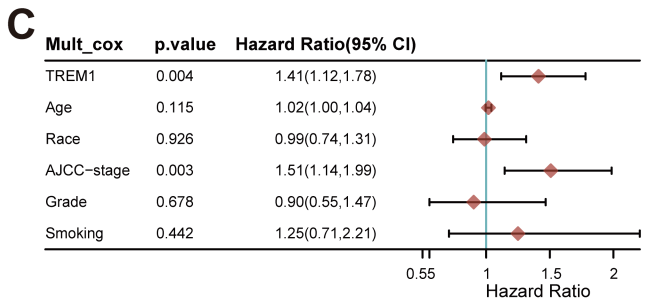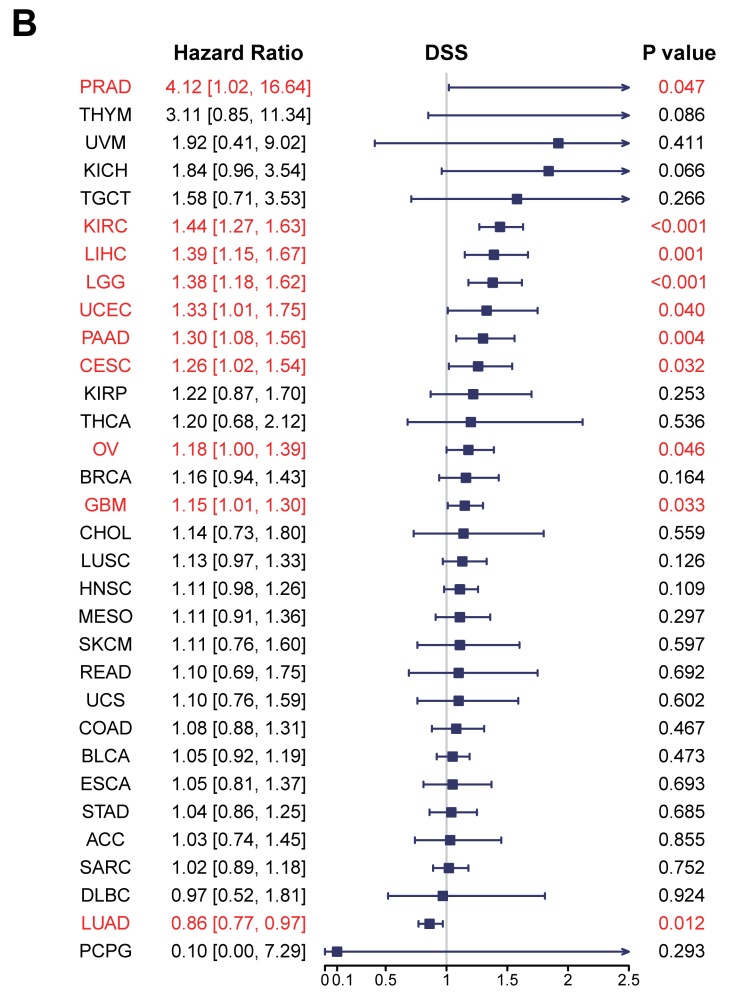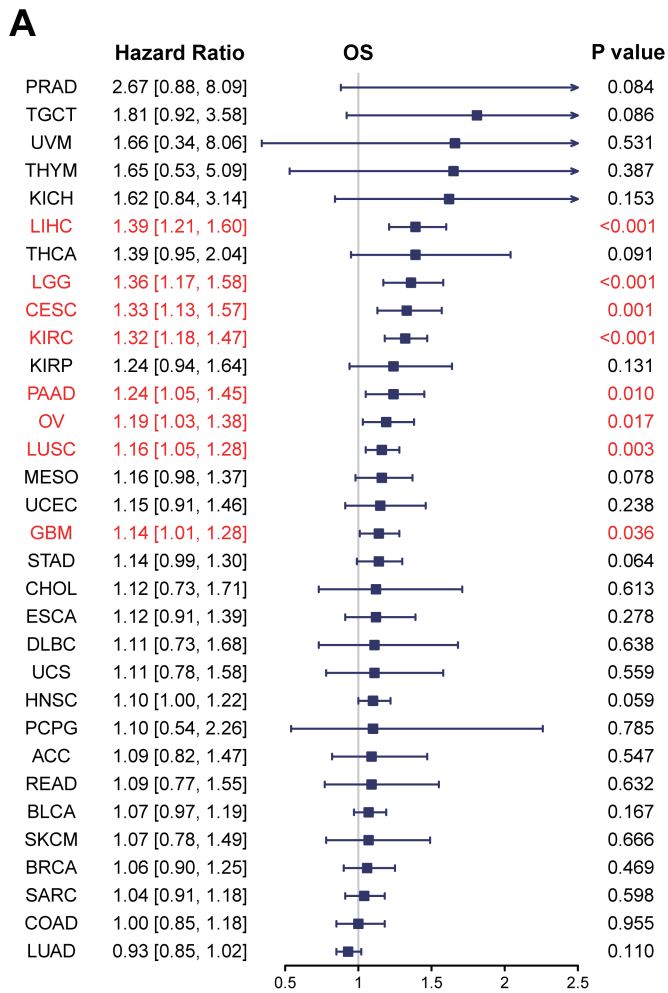| Mult_cox	p.value	Hazard Ratio(95% CI)
TREM1	0.052	1.2(1,1.44)
Age	0.031	1.02(1,1.04)
Gender	0.497	0.86(0.56,1.32)
AJCC-stage	0.304	1.21(0.84,1.73)
Grade	0.106	1.29(0.95,1.77)

Figure S2. Cox regression analysis of TREM in TCGA pan-cancer. **(A, B)** Forest plots showing the relation between TREM1 expression and OS **(A)** or DSS **(B)** of different tumors. Red represents the significant results (P < 0.05). **(C-J)** Forrest plots displaying the result of multivariable Cox regression analysis for OS in CESC **(C)**, KIRC **(D)**, GBM **(E)**, LGG **(F)**, LIHC **(G)**, LUSC **(H)**, OV **(I)** and PAAD **(J).** DSS, disease-specific survival; OS, overall survival; TCGA, The Cancer Genome Atlas. Abbreviation list of tumor cohorts from TCGA is given in **Table S1**.
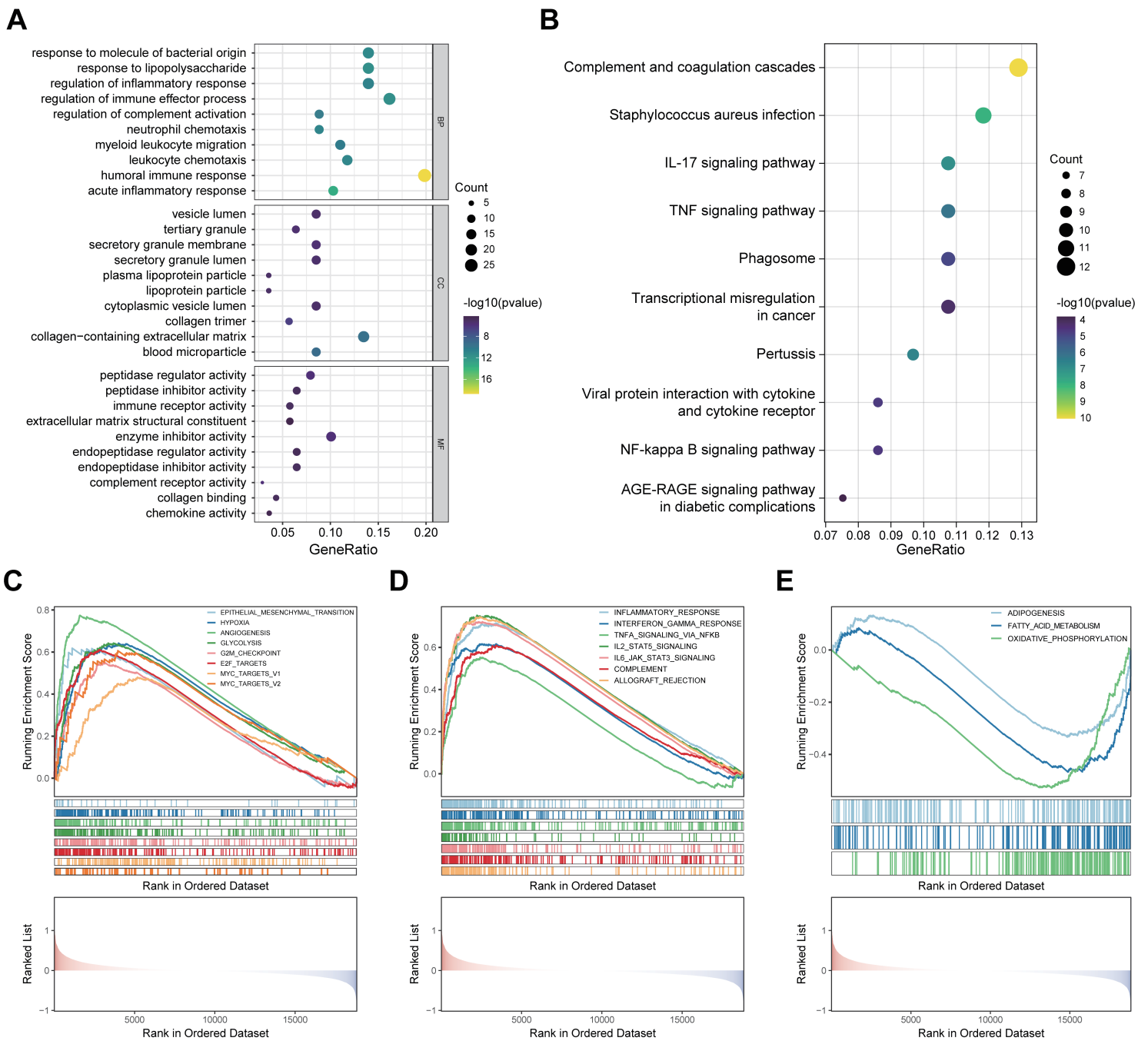
Figure S3. Function enrichment analysis. **(A, B)** Functional annotation of the DEGs between high- and low-TREM1 groups with GO **(A)** and KEGG **(B)** terms in KIRC **(C-E)** GSEA plot for significantly enriched Hallmark gene sets associated with TRME1 in KRIC. DEGs, differentially expressed genes; GO, Gene Ontology; GSEA, Gene Set Enrichment Analysis; KEGG, Kyoto Encyclopedia of Genes and Genomes; KIRC, Kidney renal clear cell carcinoma.

Gene Set Enrichment Analysis of 50 Hallmark Gene Sets

Figure S4. GSEA annotated with hallmark gene sets in pan-cancer. Bubble plot exhibiting the result of GSEA between high- and low-TREM1 subgroups in indicated tumor types. The size and color of the circle represent FDR and NES, respectively. FDR, false discovery rate; GSEA, Gene set enrichment analysis; NES, normalized enrichment score. Abbreviation list of tumor cohorts from TCGA is given in Table S1.
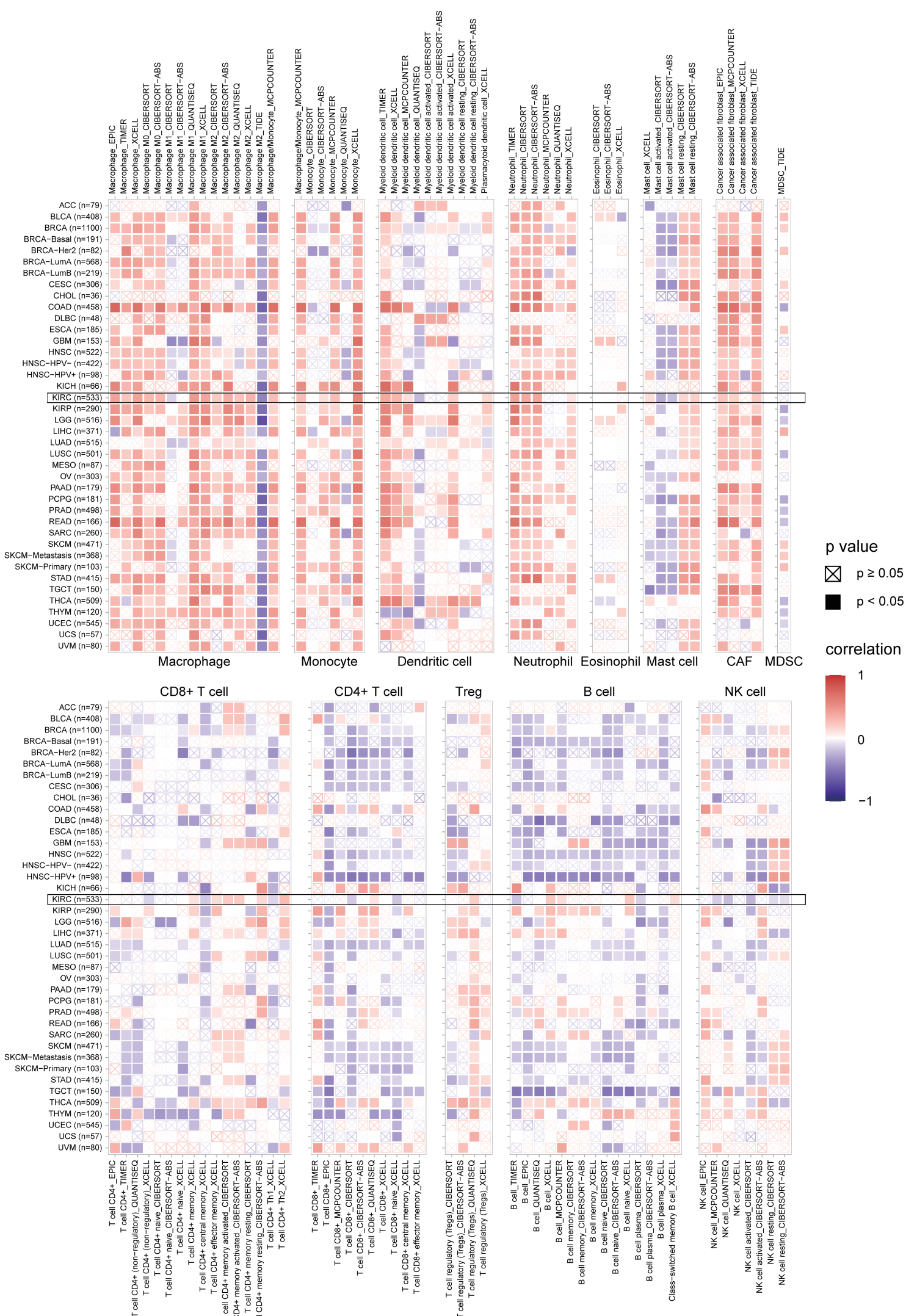
Figure S6. Correlation analysis between TREM1 expression and the infiltration levels of macrophages, monocytes, dendritic cells (DCs), myeloid-derived suppressor cells (MDSCs), neutrophils, eosinophils, CD4+ T cells, CD8+ T cells, T-regulatory lymphocytes (Tregs), NK cells, B cells, mast cells, and cancer-associated fibroblasts (CAFs) in pan-cancer based on TIMER2.0 database. Abbreviation list of tumor cohorts from TCGA is given in Table S1.
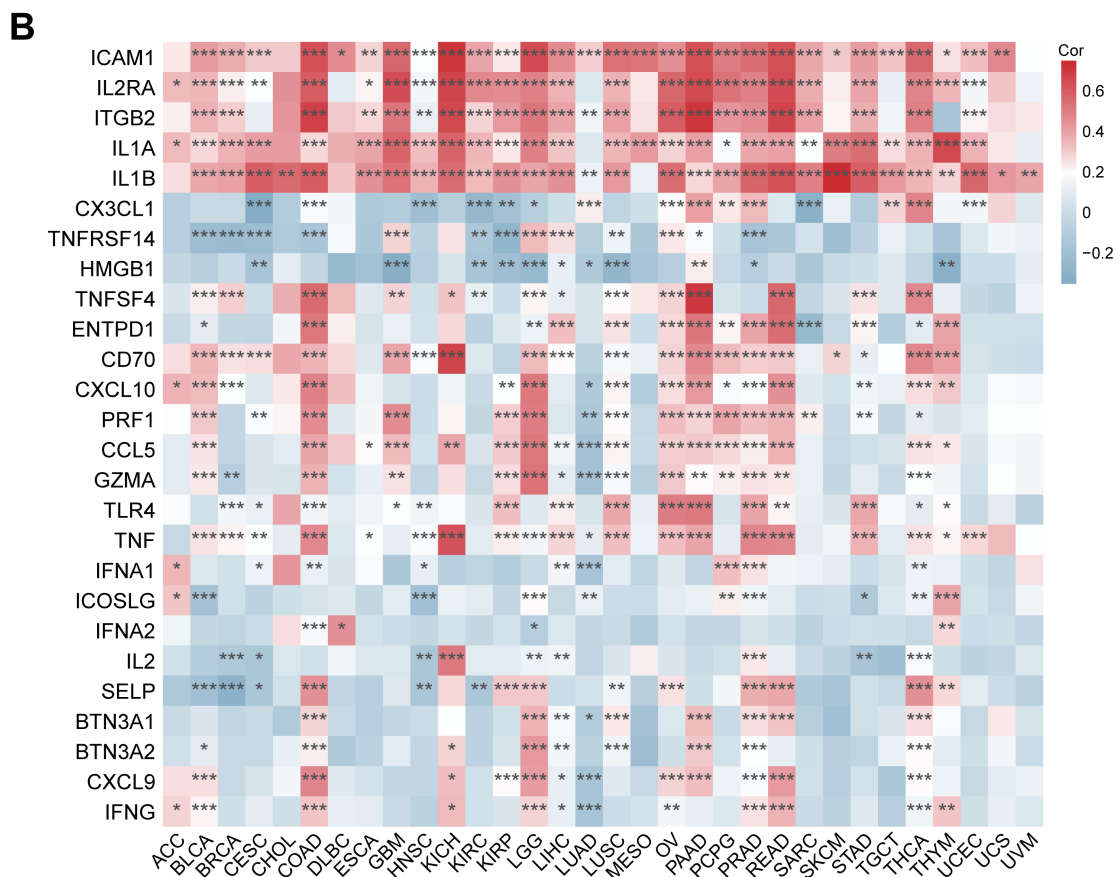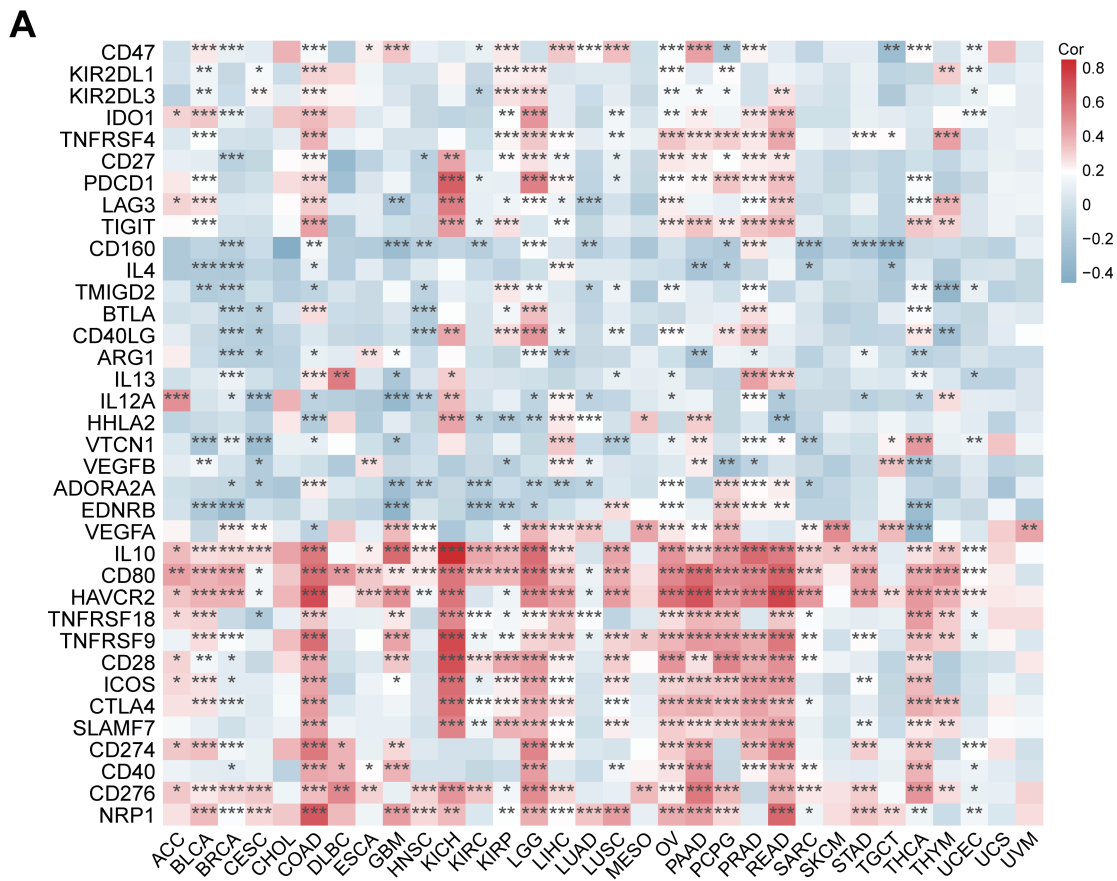
Figure S6. Correlation analysis between TREM1 expression and immunomodulatory genes. **(A, B)** Heatmap displaying the association between TREM1 expression and inhibitory genes **(A)** or immune stimulatory **(B)** in pan-cancer. Abbreviation list of tumor cohorts from TCGA is given in Table S1. *P < 0.05, **P < 0.01, ***P < 0.001.

Supplementary Table1: Abbreviations of cancers in TCGA

Abbreviation	Detail
ACC	Adrenocortical carcinoma
BLCA	Bladder Urothelial Carcinoma
BRCA	Breast invasive carcinoma
CESC	Cervical squamous cell carcinoma and endocervical adenocarcinoma
CHOL	Cholangio carcinoma
COAD	Colon adenocarcinoma
COADREAD	Colon adenocarcinoma/Rectum adenocarcinoma Esophageal carcinoma
DLBC	Lymphoid Neoplasm Diffuse Large B-cell Lymphoma
ESCA	Esophageal carcinoma
GBM	Glioblastoma multiforme
GBMLGG	Glioma
HNSC	Head and Neck squamous cell carcinoma
KICH	Kidney Chromophobe
KIPAN	Pan-kidney cohort (KICH+KIRC+KIRP)
KIRC	Kidney renal clear cell carcinoma
KIRP	Kidney renal papillary cell carcinoma
LAML	Acute Myeloid Leukemia
LGG	Brain Lower Grade Glioma
LIHC	Liver hepatocellular carcinoma
LUAD	Lung adenocarcinoma
LUSC	Lung squamous cell carcinoma
MESO	Mesothelioma
OV	Ovarian serous cystadenocarcinoma
PAAD	Pancreatic adenocarcinoma
PCPG	Pheochromocytoma and Paraganglioma
PRAD	Prostate adenocarcinoma
READ	Rectum adenocarcinoma
SARC	Sarcoma
SKCM	Skin Cutaneous Melanoma
STAD	Stomach adenocarcinoma
STES	Stomach and Esophageal carcinoma
TGCT	Testicular Germ Cell Tumors
THCA	Thyroid carcinoma
THYM	Thymoma
UCEC	Uterine Corpus Endometrial Carcinoma
UCS	Uterine Carcinosarcoma
UVM	Uveal Melanoma

Supplementary Table2: Oligo sequences used in quantitative real-time PCR

Taget		Primer
ACTB	Forward	CATGTACGTTGCTATCCAGGC
	Reverse	CTCCTTAATGTCACGCACGAT
TREM1	Forward	GAACTCCGAGCTGCAACTAAA
	Reverse	TCTAGCGTGTAGTCACATTTCAC

Supplementary Table3: Detailed information of TME-related signatures

Pathway	Description	Genes
MHCI	anti-tumor microenvironment	HLA-A, HLA-B, HLA-C, B2M, TAP1, TAP2, TAPBP
MHCII	anti-tumor microenvironment	HLA-DRA, HLA-DRB1, HLA-DMA, HLA-DPA1, HLA-DPB1, HLA-DMB, HLA-DQB1, HLA-DQA1, CIITA
Co-activation molecules	anti-tumor microenvironment	CD28, CD40, TNFRSF4, ICOS, TNFRSF9, CD27, CD80, CD86, CD40LG, CD83, TNFSF4, ICOSLG, TNFSF9, CD70
Effector cells	anti-tumor microenvironment	IFNG, GZMA, GZMB, PRF1, GZMK, ZAP70, GNLY, FASLG, TBX21, EOMES, CD8A, CD8B
Effector cell traffic	anti-tumor microenvironment	CXCL9, CXCL10, CXCL11, CX3CL1, CCL3, CCL4, CX3CR1, CCL5, CXCR3
NK cells	anti-tumor microenvironment	NKG7, CD160, CD244, NCR1, KLRC2, KLRK1, CD226, GZMH, GNLY, IFNG, KIR2DL4, EOMES, GZMB, FGFBP2, KLRF1, SH2D1B, NCR3
T cells	anti-tumor microenvironment	TBX21, ITK, CD3D, CD3E, CD3G, TRAC, TRBC1, TRBC2, CD28, CD5, TRAT1
B cells	anti-tumor microenvironment	CD19, MS4A1, TNFRSF13C, CR2, TNFRSF17, TNFRSF13B, CD22, CD79A, CD79B, BLK, FCRL5, PAX5, STAP1
M1 signature	anti-tumor microenvironment	NOS2, TNF, IL1B, SOCS3, CMKLR1, IRF5, IL12A, IL12B, IL23A
Th1 signature	anti-tumor microenvironment	IFNG, IL2, CD40LG, IL21, TBX21, STAT4, IL12RB2
Antitumor cytokines	anti-tumor microenvironment	TNF, IFNB1, IFNA2, CCL3, TNFSF10, IL21
Checkpoint molecules	pro-tumor microenvironment	PDCD1, CD274, CTLA4, LAG3, PDCD1LG2, BTLA, HAVCR2, TIGIT, VSIR, C10orf54
Treg	pro-tumor microenvironment	FOXP3, CTLA4, IL10, TNFRSF18, CCR8, IKZF4, IKZF2
Treg and Th2 traffic	pro-tumor microenvironment	CCL17, CCL22, CCL1, CCL28, CCR4, CCR8, CCR10
Neutrophil signature	pro-tumor microenvironment	MPO, ELANE, PRTN3, CTSG, CXCR1, CXCR2, FCGR3B, CD177, FFAR2, PGLYRP1
Granulocyte traffic	pro-tumor microenvironment	CXCL8, CXCL1, CXCL2, CXCL5, CCL11, KITLG, CXCR1, CXCR2, CCR3
Immune Suppression by Myeloid Cells	pro-tumor microenvironment	IDO1, ARG1, IL10, CYBB, PTGS2, IL4I1, IL6
Myeloid cells traffic	pro-tumor microenvironment	CSF2, CSF3, CXCL12, CCL26, IL6, CXCL8, CXCL5, CSF1R, CSF2RA, CSF3R, CXCR4, IL6R, CXCR2, CCL15, CSF1

Pathway	Description	Genes
Tumor-associated Macrophages	pro-tumor microenvironment	IL10, MRC1, MSR1, CD163, CSF1R, IL4I1, SIGLEC1, CD68
Macrophage and DC traffic	pro-tumor microenvironment	CCL2, CCL7, CCL8, XCL1, CCR2, XCR1, CSF1R, CSF1
Th2 signature	pro-tumor microenvironment	IL4, IL5, IL13, IL10, GATA3, CCR4
Protumor cytokines	pro-tumor microenvironment	IL10, TGFB1, TGFB2, TGFB3, IL22, MIF, IL6
Cancer-associated fibroblasts	angiogenesis fibrosis	COL1A1, COL1A2, COL5A1, ACTA2, FGF2, FAP, LRP1, CD248, COL6A1, COL6A2, COL6A3, CXCL12, FBLN1, LUM, MFAP5, MMP3, MMP2, PDGFRB, PDGFRA
Matrix	angiogenesis fibrosis	FN1, COL1A1, COL1A2, COL4A1, COL3A1, VTN, LGALS7, LGALS9, LAMA3, LAMB3, LAMC2, TNC, ELN, COL5A1, COL11A1
Matrix remodeling	angiogenesis fibrosis	CA9, MMP9, MMP2, MMP1, MMP3, MMP12, MMP7, MMP11, PLOD2, ADAMTS4, ADAMTS5, LOX
Angiogenesis	angiogenesis fibrosis	VEGFA, VEGFB, VEGFC, PDGFC, CXCL8, CXCR2, FLT1, PGF, CXCL5, KDR, ANGPT1, ANGPT2, TEK, VWF, CDH5
Endothelium	angiogenesis fibrosis	NOS3, KDR, FLT1, VCAM1, VWF, CDH5, MMRN1, ENG, CLEC14A, MMRN2
Tumor proliferation rate	malignant cell properties	MKI67, ESCO2, CETN3, CDK2, CCND1, CCNE1, AURKA, AURKB, E2F1, MYBL2, BUB1, PLK1, CCNB1, MCM2, MCM6
EMT signature	malignant cell properties	SNAI1, SNAI2, TWIST1, TWIST2, ZEB1, ZEB2, CDH2