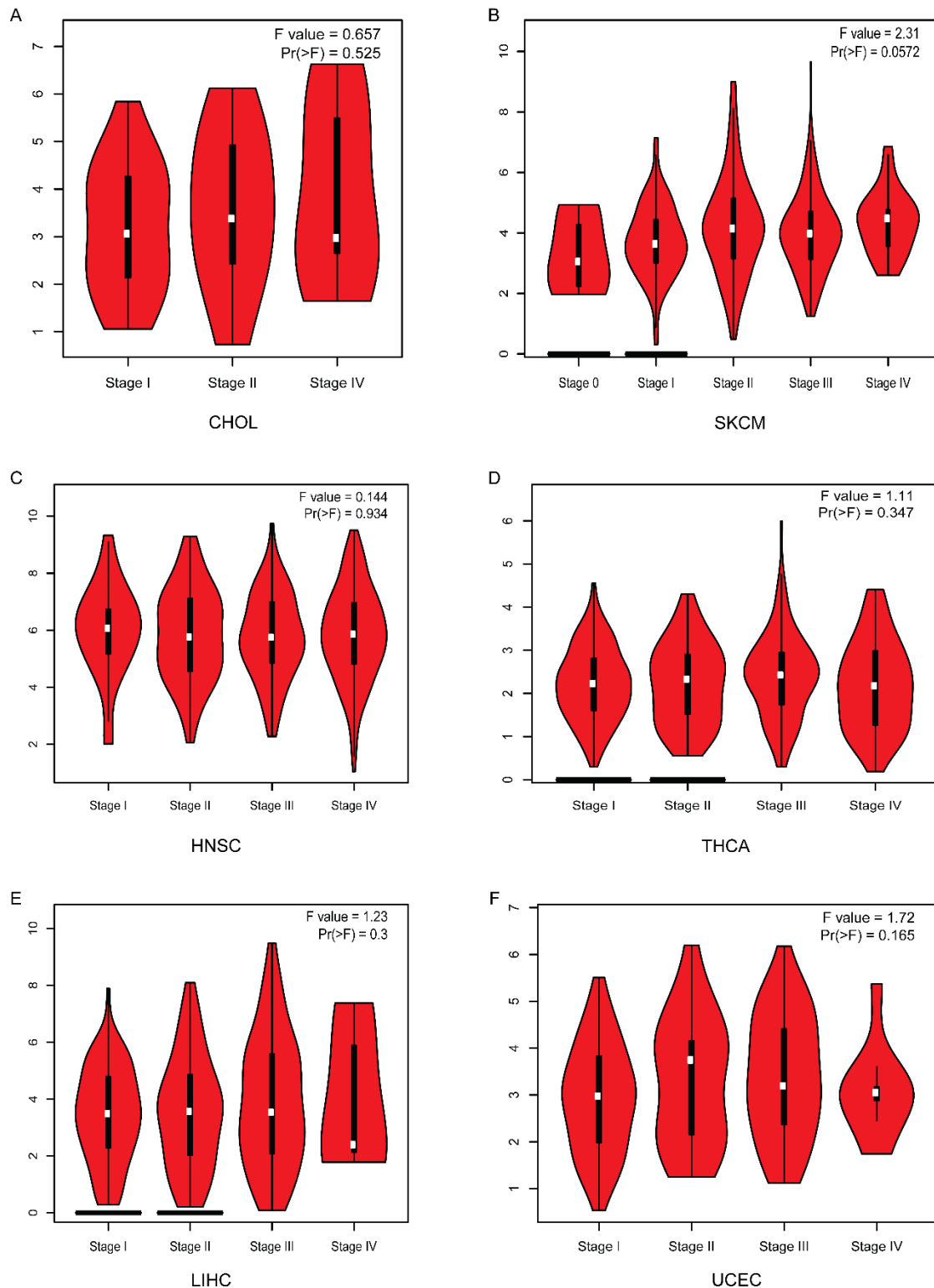
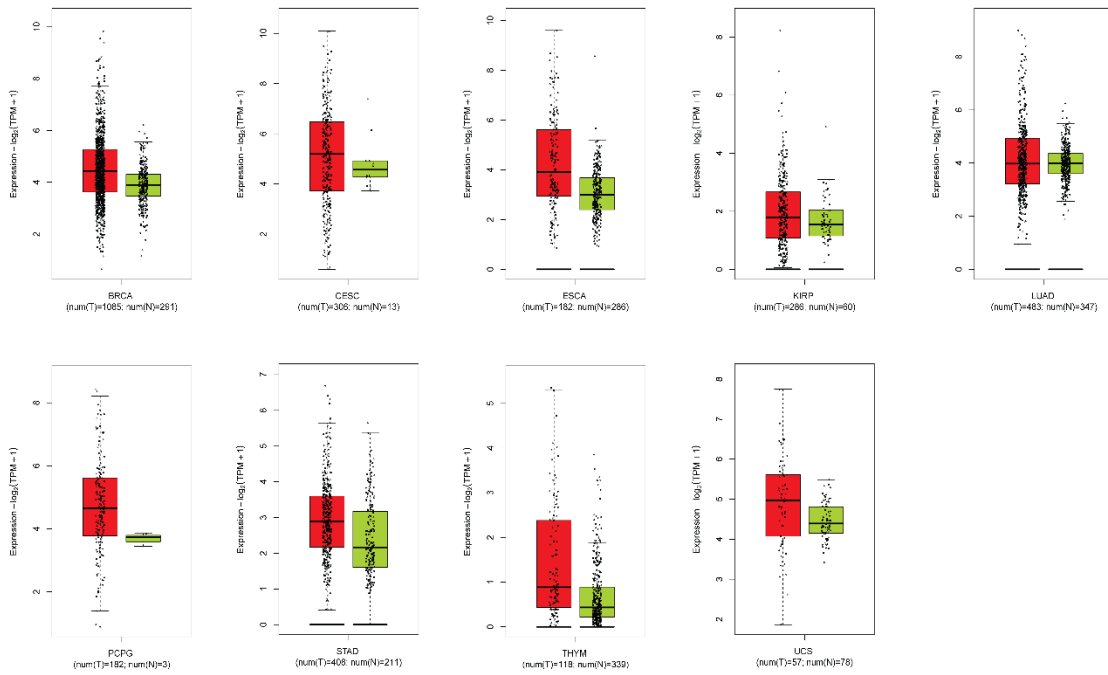




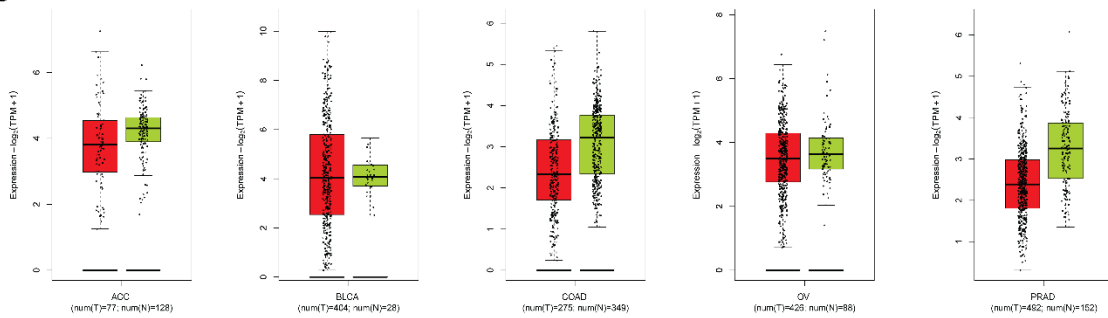
Supplementary Figure 1: TMEM45A expression is correlated with clinical tumor stages in a variety of cancer types. In (A) CHOL ($F = 0.657$, $p = 0.525$), (B) SKCM ($F = 2.31$, $p = 0.0572$), (C) HNSC ($F = 0.144$, $p = 0.934$), (D) THCA ($F = 1.11$, $p = 0.347$), (E) LIHC ($F = 1.23$, $p = 0.3$), and (F) UCEC ($F = 1.72$,

$p = 0.165$). One-way ANOVA was used to assess statistical significance throughout clinical phases, and each panel was annotated with F-statistics and matching $Pr(>F)$ values. The violin contours show data density, the black boxes show the interquartile range, and the white circles show the median. CHOL stands for cholangiocarcinoma; SKCM for skin cutaneous melanoma; HNSC for head and neck squamous cell carcinoma; THCA for thyroid cancer; LIHC for liver hepatocellular carcinoma; and UCEC for uterine corpus endometrial carcinoma.

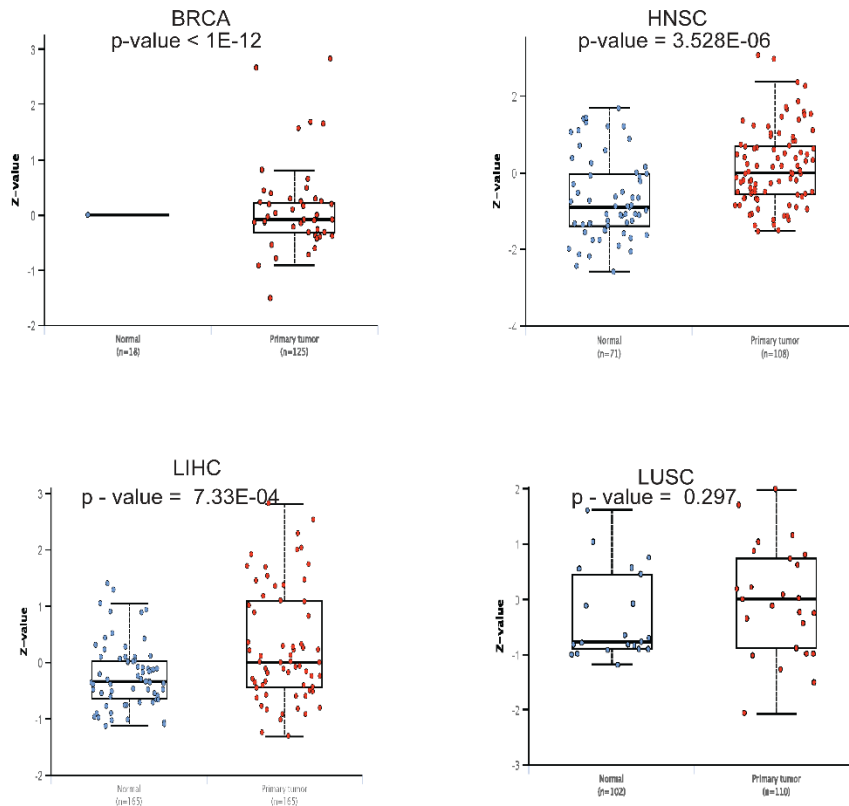
A



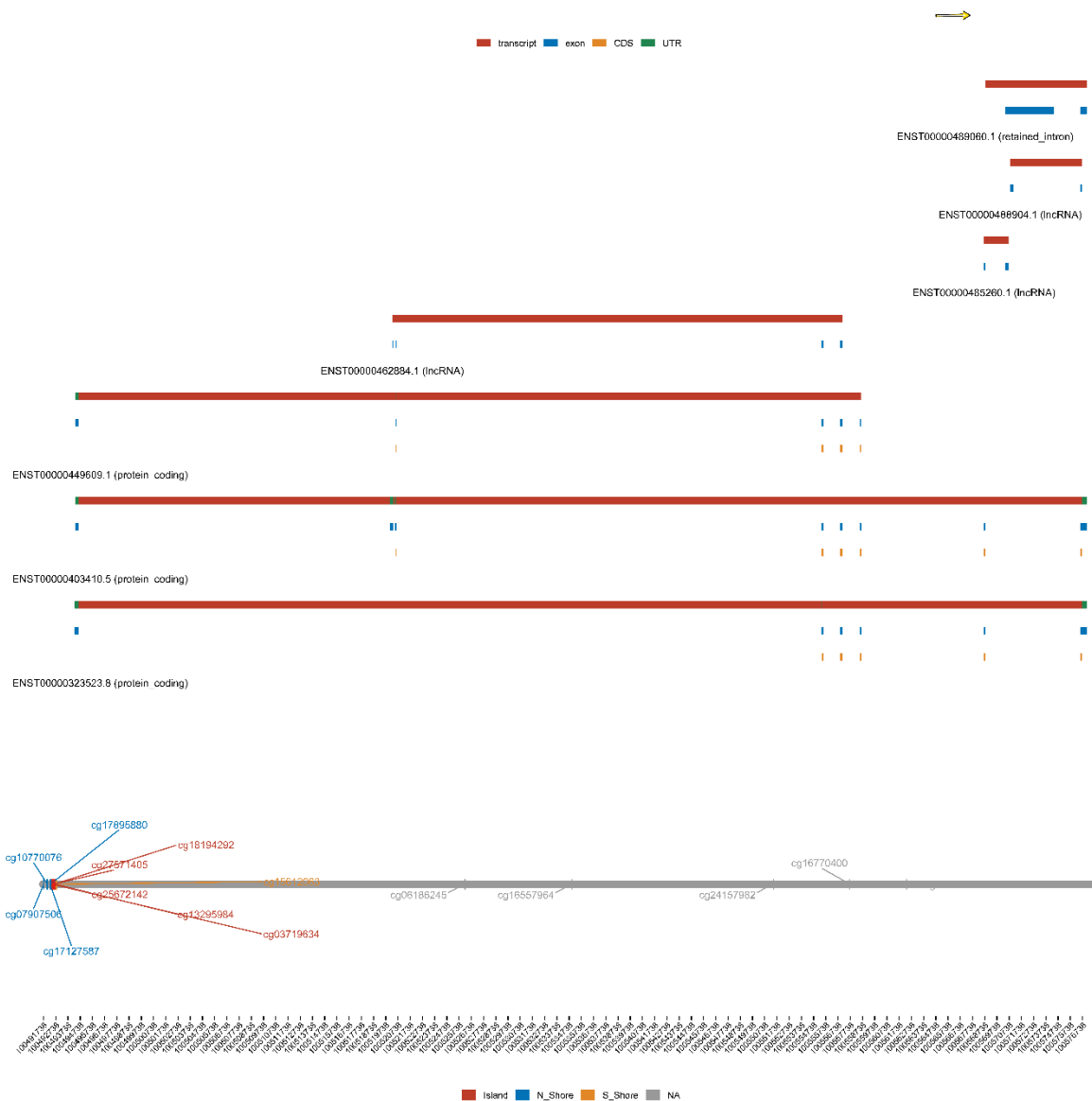
B



Supplementary Figure 2: TMEM45A expression patterns in different TCGA cohorts are not significantly different. Box graphs showing the baseline expression dynamics ($\log_2(\text{TPM}+1)$) of TMEM45A between matching normal (N, green) and tumor (T, red) tissues. (A) Cohorts (BRCA, CESC, ESCA, KIRP, LUAD, PCPG, STAD, THYM, and UCS) with non-significant transcriptome up-regulation. (B) ACC, BLCA, COAD, OV, and PRAD cohorts showing non-significant transcriptome down-regulation. Annotated underneath each acronym are the sample sizes for tumors (num(T)) and normal controls (num(N)). Individual dots show single-specimen values, box bounds show the interquartile range (IQR), and centerlines show the median. ACC stands for Adrenocortical Carcinoma; BLCA for Bladder Urothelial Carcinoma; BRCA for Breast Invasive Carcinoma; CESC for Cervical Squamous Cell Carcinoma and Endocervical Adenocarcinoma; COAD for Colon Adenocarcinoma; ESCA for Esophageal Carcinoma; KIRP for Kidney Renal Papillary Cell Carcinoma; LUAD for Lung Adenocarcinoma; OV for Ovarian Serous Cystadenocarcinoma; PRAD for Prostate Adenocarcinoma; THYM for Thymoma; and UCS for Uterine Carcinoma.



Supplementary Figure 3: TMEM45A's proteomic expression profile in CPTAC cohorts' primary cancers and normal controls. Box plots showing TMEM45A protein expression levels (Z-values) for all accessible cancer types in the CPTAC database. When compared to corresponding normal tissues, initial tumors exhibit considerable protein up-regulation in BRCA ($p < 1 \times 10^{-12}$), HNSC ($p = 3.528 \times 10^{-6}$), and LIHC ($p = 7.33 \times 10^{-4}$), but LUSC exhibits a non-significant change ($p = 0.297$). Below each panel are the sample sizes (n) for primary tumors and normal controls. The UALCAN platform analysis was used to establish statistical significance. Breast Invasive Carcinoma (BRCA); Head and Neck Squamous Cell Carcinoma (HNSC); Lung Squamous Cell Carcinoma (LUSC) and Liver Hepatocellular Carcinoma (LIHC).



Supplementary Figure 4: The TMEM45A locus's genome, transcript architecture, and CpG probe locations. Diagrammatic representation of the TMEM45A gene locus's genomic structure and epigenetic annotation taken from the SMART database. The graphic shows the locations of retained introns, long non-coding RNAs (lncRNAs), and protein-coding transcripts, such as ENST00000449609.1 and ENST00000403410.5. Transcripts, exons, coding sequences (CDS), and untranslated regions (UTRs) are all defined by color-coded characteristics. Certain Illumina HumanMethylation404 CpG probe locations, such as cg07907506, are exactly in line with the relevant genomic coordinates and functional area classifications, such as CpG Islands, N-shores, and S-shores.

TMEM45A										log(TPM/10 ⁻¹)										
BLCA_GSE130801	0	0	3	3	3	0	0	0	0	0	0.82	0.23	0.32	0.33	0.33	3.03	3.03	0.03	0.03	0.03
BRCA_EMTA8B0107	0	0	0.01	0.01	3	3	0	0	0.01	3.05	0.03	0.02	0.04	0.04	0.03	0.41	3.1	3.1	0.18	0.18
BRCA_GSE114727_HiSeq	0	0	3	3	3	3	0	0	0	0.01	0.01	0.03	0	0.02	0.1	0.07	0.07	0.07	0.07	0.07
BRCA_GSE136638_mouse_HiSeq100L4	H	H	H	H	3	3	3	0	0	0	0	0	0	0	0	0	0	0	0	0
BRCA_GSE159536	0	0	3	3	3	3	0	0	0	0.63	0.63	0.63	0.63	0.63	0.61	0.61	0.35	0.35	0.35	0.35
BRCA_GSE143423	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	
BRCA_GSE159873	0.01	0.31	0.32	0.01	0.31	0.01	0.01	0.01	0.01	3.01	0.01	0.04	0.04	0.03	0.8	3.6	0.27	3.1	0.1	0.1
BRCA_GSE150660	0	0	3	3	3	3	0	0	0	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	
BRCA_GSE161325	0.01	0.31	0.31	0.01	0.31	0.01	0.01	0.01	0.01	3.02	3.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	
BRCA_GSE110918	0	0	0.01	0.01	3	3	0	0	0.01	3.05	0.01	0.01	0.01	0.01	0.03	0.37	0.08	0.15	0.15	0.15
BRCA_GSE114962	0	0	3	3	3	3	0	0	0	0	0	0	0	0	0	3	3	0	0	
BRCA_GSE159322	0.07	0.32	0.32	3	3	3	0	0	0	3.44	0.44	0.21	0.17	0.17	0.30	0.30	0.28	0.28	0.22	0.22
BRCA_GSE159324	0	0	3	3	3	3	0	0	0	3.02	0.01	0	0	0	0	3	3	0	0	0
BRCA_GSE160263	0	0	3	3	3	3	0	0	0	0	0	0	0	0	0	3	3	0	0	0
BRCA_GSE111286	H	H	H	H	3	3	3	0	0	0	0	0	0	0	0	0	0	0	0	0
BRCA_GSE121630	0	0	3	3	3	3	0	0	0	3.02	0.01	0	0	0	0	3	3	0	0	0
BRCA_GSE128554	0	0	3	3	3	3	0	0	0	3.26	0	0	0.01	0.01	0.11	0.11	0.11	0.11	0.11	0.11
BRCA_GSE145281_HiSeq1	0	0	3	3	3	3	0	0	0	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
BRCA_GSE150112	0	0	3	3	3	3	0	0	0	3.02	0.02	0.01	0.01	0.01	0.03	0.30	0.03	0.03	0.03	0.03
BRCA_GSE171306	0	0	0.01	3	3	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BRCA_GSE126149_HiSeq100L4	0	0	3	3	3	3	0	0	0	3.05	0.05	0.01	0.01	0.01	0.16	0.16	0.16	0.16	0.16	0.16
BRCA_GSE140028_HiSeq	0	0	3	3	3	3	0	0	0	3.02	0.01	0	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
BRCA_GSE140228_Sequencing	H	H	0.15	0.01	3	3	0	0	0	3.02	0	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE145115	0	0	0.03	0.03	0.03	0.02	0.1	0.1	0.1	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
BRCA_GSE144408	0	0	3	3	3	3	0	0	0	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
BRCA_GSE160830	H	H	0.32	0.04	0.01	0.31	0.01	0.01	0.01	3.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE160833	0	0	3	3	3	3	0	0	0	0.33	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
BRCA_GSE160921	0.01	0.32	0.32	0.01	0.31	0.01	0.01	0.01	0.01	3.01	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE150130	0.01	0.32	0.02	0.01	0.31	0.01	0.01	0.01	0.01	3.51	0.09	0.52	0.52	0.52	0.52	0.52	0.52	0.52	0.52	0.52
BRCA_GSE160822	0	0	3	3	3	3	0	0	0	3.02	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE160834	0	0	3	3	3	3	0	0	0	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE117570	0	0	3	3	3	3	0	0	0	3.02	0	0	0	0.08	0.08	0.08	0.08	0.08	0.08	0.08
BRCA_GSE127464	0.03	0.33	0.33	0.02	0.32	0.02	0.29	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
BRCA_GSE127471	H	H	1	H	0.2	3	3	0	0	0	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE131907	0	0	3	3	3	3	0	0	0	3.04	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
BRCA_GSE130855	0	0	0.01	3	3	3	0	0	0.01	3.43	0.02	0	0	0	0	3	3	0	0	0
BRCA_GSE143422	H	H	1	H	0.15	0.01	0.01	0.01	0.01	3.01	0.01	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
BRCA_GSE146100	0.01	0.33	0.32	0.01	0.31	0.01	0.01	0.01	0.01	3.02	0.01	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE146971	H	H	0.12	0.01	0.31	0.01	0.01	0.01	0.01	3.01	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE146655	0	0	3	3	3	3	0	0	0	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE150660	0	0	3	3	3	3	0	0	0	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
BRCA_GSE150835	H	H	0.01	3	3	3	0	0	0	3.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE160268	0	0	3	3	3	3	0	0	0	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE178021_HiSeq	0	0	3	3	3	3	0	0	0	0	0	0	0	0	0	3	3	0	0	0
BRCA_GSE160664	H	H	1	3	3	3	0	0	0	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE172877	0	0	0.33	0.02	0.32	3	3	0	0	0	0.25	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
BRCA_GSE159607	0	0	3	3	3	3	0	0	0	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE159607	H	H	3	3	3	3	0	0	0	3.08	0.01	0	0	0	0	3	3	0	0	0
BRCA_GSE159828	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0	0.04	0.04	0.04	0.04	0.04	0.04	0.04
BRCA_GSE159830	H	H	3	3	3	3	0	0	0	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE117092	0.01	0.31	0.32	3	3	3	0	0	0	3.04	0.04	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
BRCA_GSE151214	0	0	3	3	3	3	0	0	0	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BRCA_GSE150800	H	H	0.08	0.07	0.08	0.08	0.08	0.08	0.08	0.08	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
BRCA_GSE154703	0	0	3	3	3	3	0	0	0	0.08	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0	3	3	3	3	0	0	0	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BRCA_GSE150722	0	0																		

Supplementary Figure 5: Single-cell expression landscape of *TMEM45A* across the tumor microenvironment (TME). To characterize the cellular distribution of *TMEM45A* at single-cell resolution, scRNA-seq data from 12 representative cancer types (BRCA, STAD, NSCLC, LIHC, HNSC, UCEC, BLCA, KIRC, SKCM, PAAD, SARC, and OV) were analyzed using the TISCH2 database. The heatmap illustrates the correlation between *TMEM45A* mRNA expression and various cell lineages categorized by “Celltype (major-lineage)”. The color scale indicates the expression intensity, with red representing higher expression levels ($\log(\text{TPM}/10+1)$). The vertical axis (rows) lists the individual scRNA-seq datasets across the selected malignancies, while the horizontal axis (columns) represents the major cell populations, including malignant, immune, and stromal cells. Significant enrichment of *TMEM45A* is observed in malignant epithelial cells, endothelial cells, and fibroblasts, with variable expression in myeloid lineages (monocytes/macrophages).