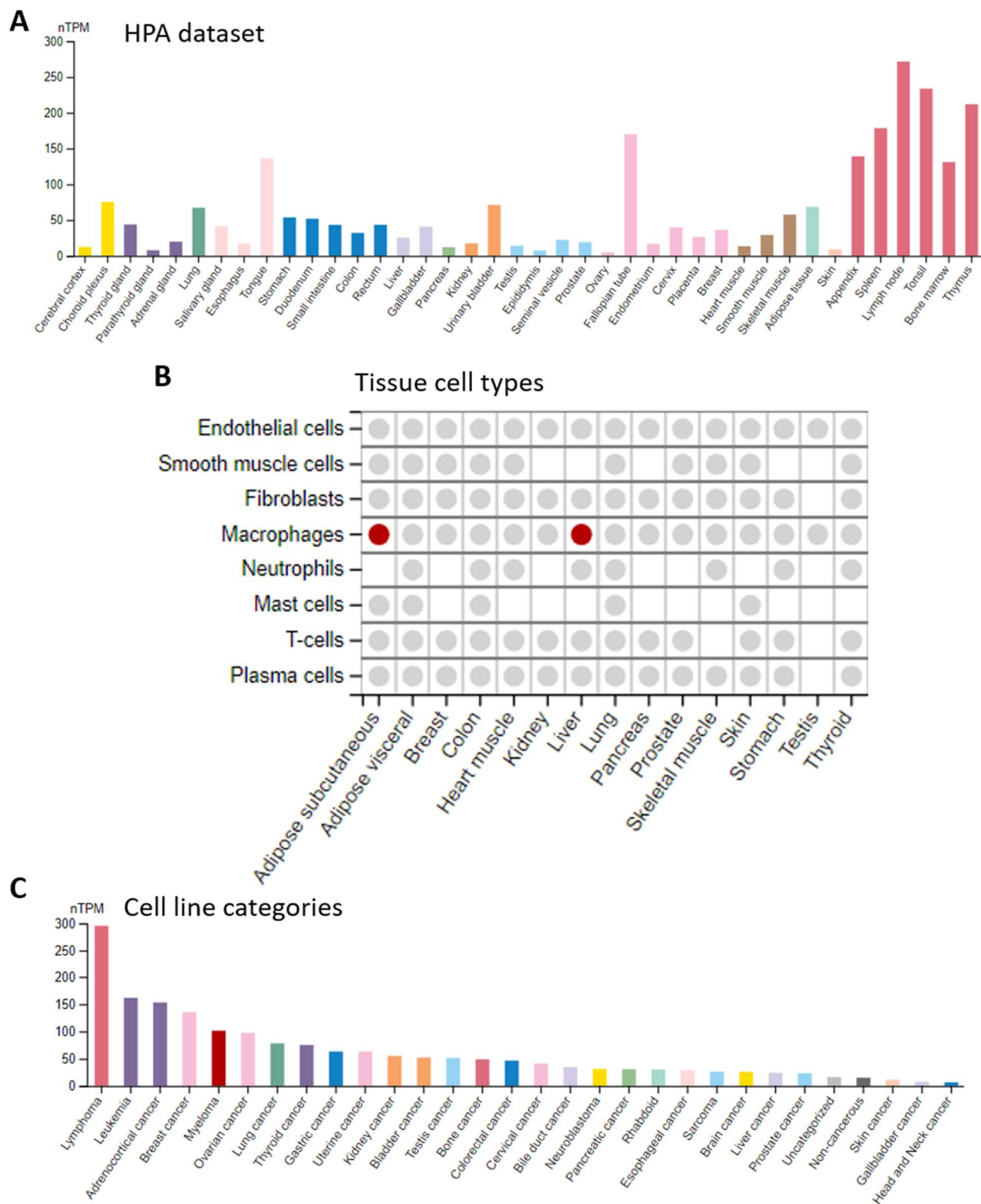


# **Supplementary Material**

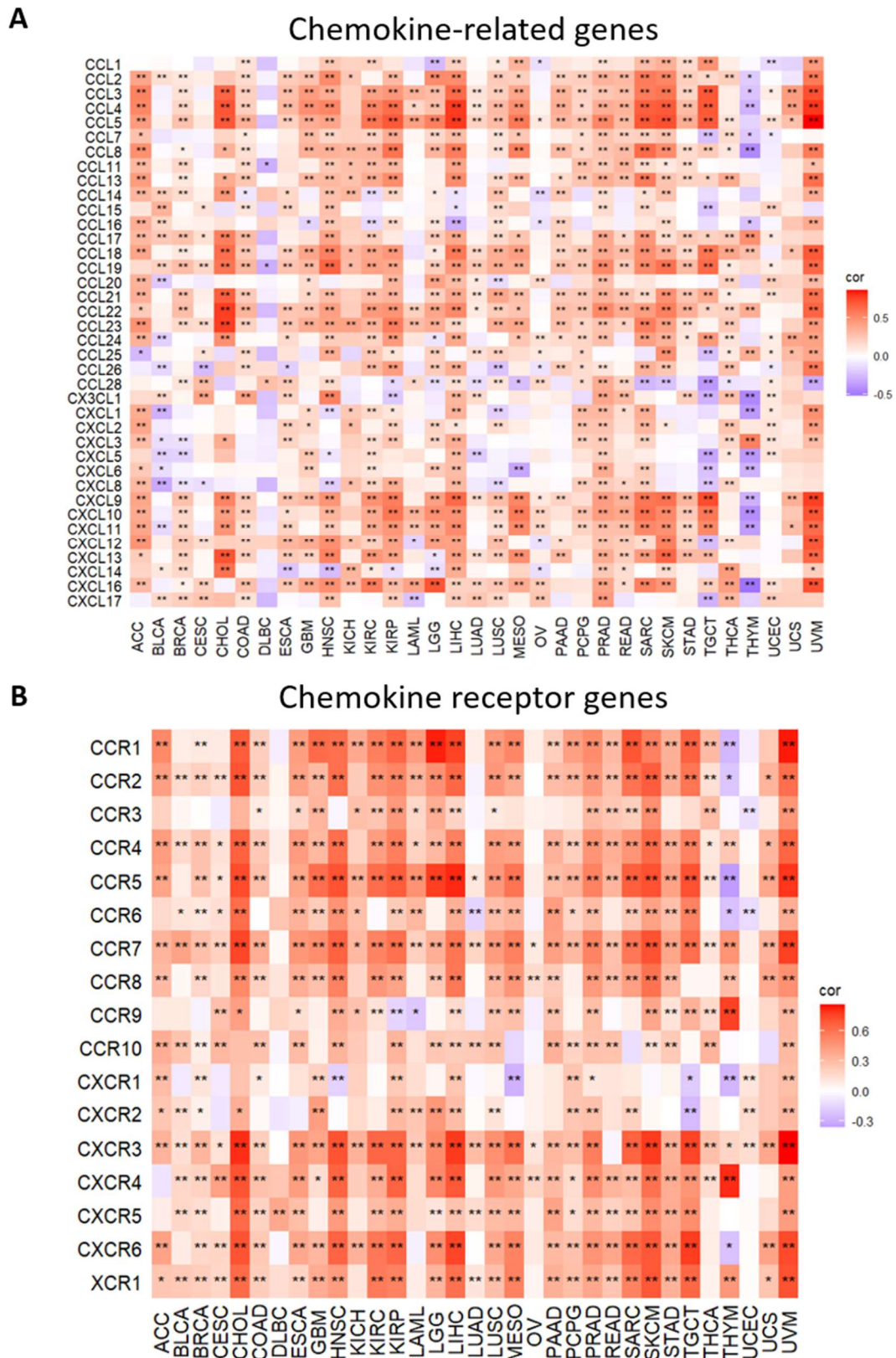
## **A Comprehensive Pan-Cancer Analysis of the Mitochondrial Uncoupling Protein UCP2, with a Focus on Sex and Gender-Related Aspects.**

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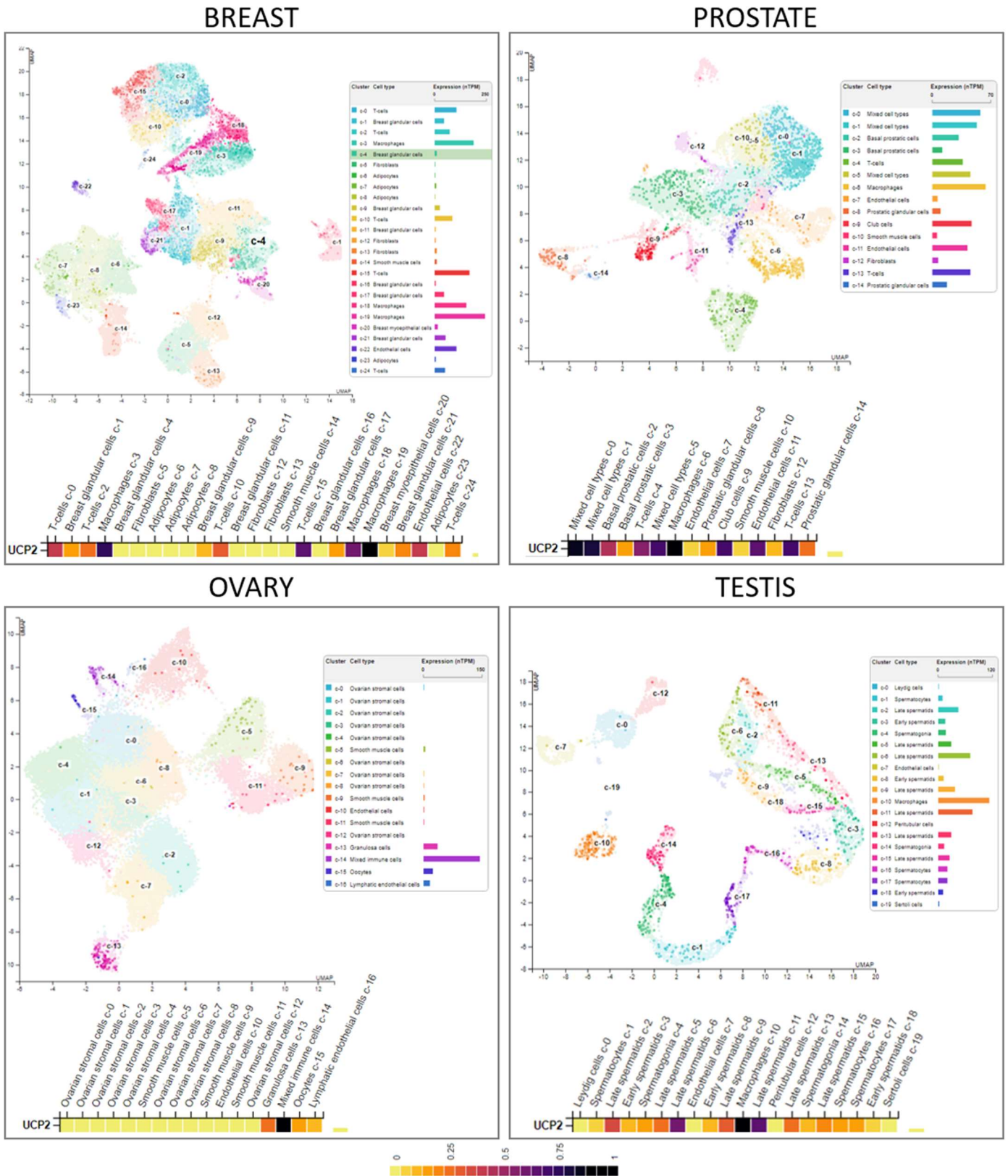
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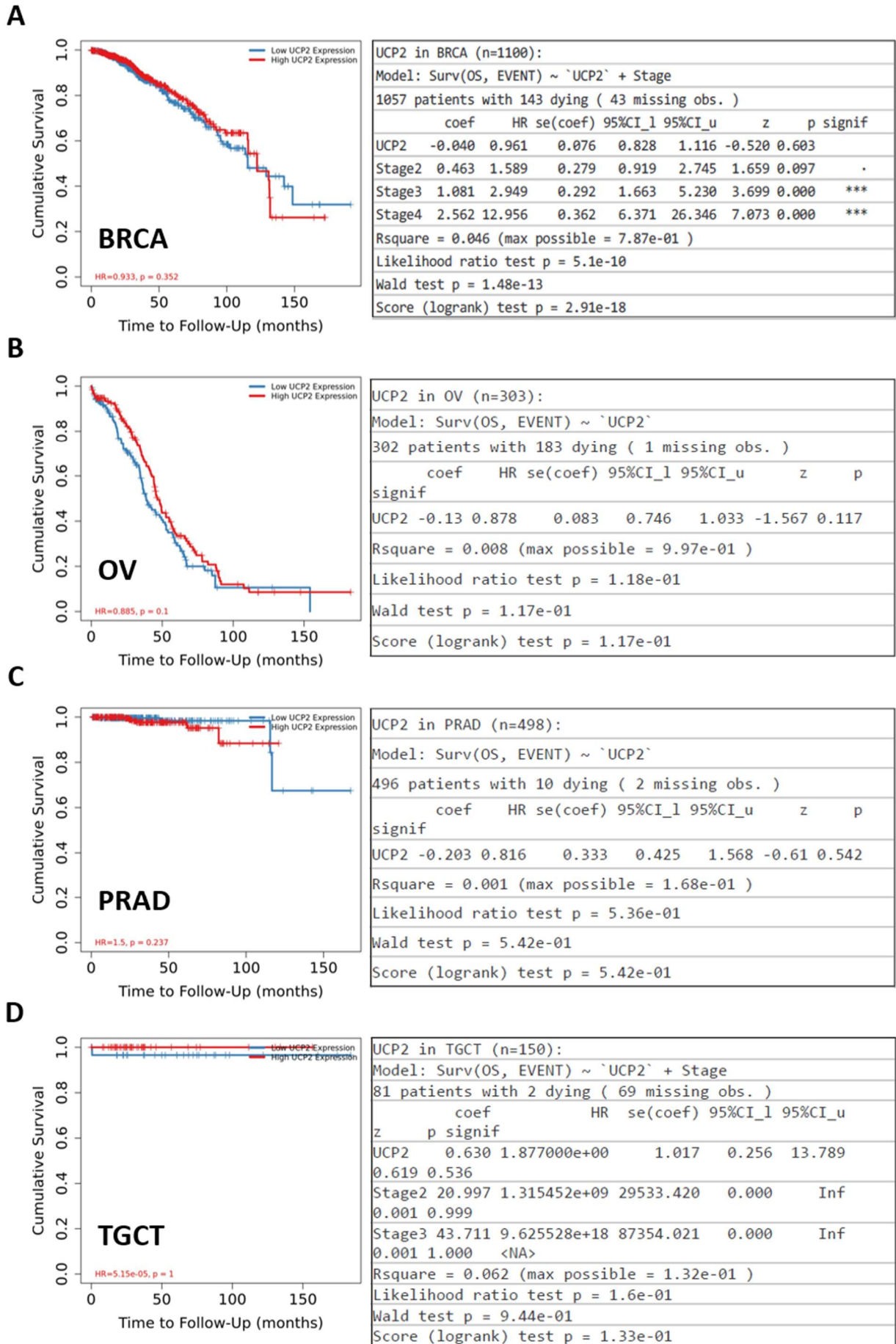
**Fig. S1. UCP2 Expression Across Tissues, Cell Types, and Cancer Cell Lines Based on Human Protein Atlas (HPA) Data** (A) Expression of *UCP2* based on the Human Protein Atlas (HPA) RNA-Seq tissue corresponding to mean values of different individual samples from each tissue. Color coding is based on tissue groups, each consisting of tissue with functional features in common. (B) Expression of *UCP2* based on HPA in different tissue cell types. Colored dots indicate that the selected gene has core cell type specificity in the indicated tissue. Grey dots indicate that the indicated cell type is present within that tissue, but the gene is not predicted to be enriched there. (C) RNA expression of *UCP2* based on HPA in cancer cell lines.



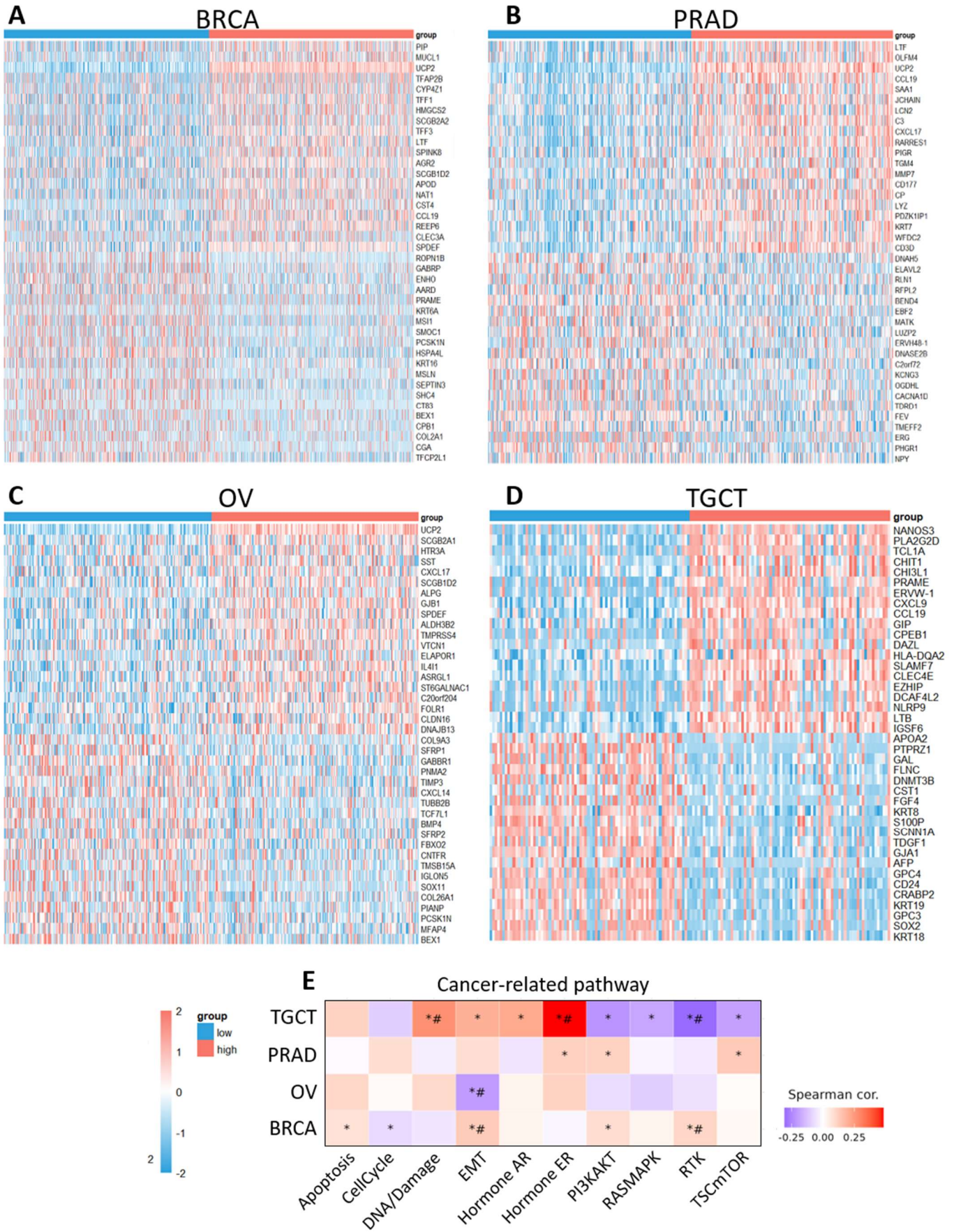
**Fig. S2. Correlation between *UCP2* expression, chemokine genes, and chemokine receptor genes. (A)** Chemokine genes. **(B)** Chemokine receptor genes. Similar clusters were identified using the complete linkage method, with significance levels indicated as \*\* $p < 0.01$  and \* $p < 0.05$ . The heatmap was drawn using the TCGAplot R package (v7.0.1) (<https://github.com/tjhwangxiong/TCGAplot>). Pearson correlation analysis was used to calculate the correlation between *UCP2* expression and these immune-related genes.



**Fig. S3. UMAP visualization and RNA expression of cell clusters in BRCA, PRAD, OV, and TGCT patients.** UMAPs plot visualizing the cells in each cluster for BRCA, PRAD, OV, and TGCT patients. Each dot represents a cell, with mouseover revealing read count and cluster membership. Hovering over a cluster name highlights the corresponding cluster in the bar chart below. Each cluster is assigned a unique color. The bar chart shows RNA expression (nTPM) in each cell type cluster for BRCA, PRAD, OV, and TGCT patients.



**Fig. S4. Kaplan-Meier survival and Cox Proportional Hazards Model analysis.** Kaplan-Meier survival and Cox Proportional Hazards Model analysis of UCP2 expression based on BRCA (A), OV (B), PRAD (C), and TGCT (D) cancer stages.



**Fig. S5. Heatmaps of *UCP2* expression and correlation with DEGs and biological pathways in BRCA, TGCT, PRAD, and OV cancers.** (A-D) Heatmaps of *UCP2* expression and correlation with DEGs in BRCA, TGCT, PRAD, and OV, with positive or negative correlations indicated by color. Red indicates a high expression level, while blue indicates a low expression. (E) A heatmap was generated to visualize the biological pathways associated with *UCP2* gene expression in breast, prostate, ovarian, and testicular cancers.

**Table S1: Abbreviations for cancer types in The Cancer Genome Atlas (TCGA) study**

<b>Abbreviation</b>	<b>Study_name</b>
ACC	Adrenocortical carcinoma
BLCA	Bladder urothelial carcinoma
BRCA	Breast invasive carcinoma
CESC	Cervical and endocervical cancers
CHOL	Cholangiocarcinoma
COAD	Colon adenocarcinoma
COADREAD	Colorectal adenocarcinoma
DLBC	Lymphoid Neoplasm Diffuse Large B-cell Lymphoma
ESCA	Esophageal carcinoma
FPPP	FFPE Pilot Phase II
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
TGCT	Testicular Germ Cell Tumors
THCA	Thyroid carcinoma
THYM	Thymoma
UCEC	Uterine Corpus Endometrial Carcinoma
UCS	Uterine Carcinosarcoma
UVM	Uveal Melanoma

**Table S2: UCP2 expression across TCGA cancer types.**

Tumor Type	Expression	p-value
BLCA	Upregulated	0,008182749
BRCA	Upregulated	1,97E-08
CHOL	Upregulated	0,026036071
GBM	Upregulated	0,000299823
ESCA	Upregulated	0,001609326
HNSC	Upregulated	1,34E-12
KICH	Downregulated	0,011135915
KIRC	Downregulated	0,182576863
KIRP	Downregulated	0,151683073
LAML	Downregulated	–
LUAD	Upregulated	2,51E-05
LUSC	Downregulated	3,84E-06
MESO	Upregulated	–
OV	Upregulated	–
PAAD	Downregulated	0,009973904
PCPG	Upregulated	0,565547838
PRAD	Downregulated	3,14E-06
READ	Downregulated	0,145976994
SARC	Upregulated	–
SKCM	Upregulated	0,000117499
STAD	Upregulated	0,001561375
TGCT	Downregulated	–
THCA	Upregulated	5,13E-14
THYM	Downregulated	–
UCEC	Upregulated	6,28E-11
UCS	Downregulated	–
UVM	Upregulated	–
ACC	Downregulated	–
COAD	Upregulated	0,467724262
DLBC	Upregulated	–
LIHC	Upregulated	0,679670549
LGG	Downregulated	–
CESC	Upregulated	0,079269666

- Indicates absence of control data for comparison



**Table S3. Hazard\_Ratio\_Data\_for\_UCP2.**

<b>Cancer</b>	<b>HR (95% CI)</b>	<b>P Value</b>
ACC	1.196 (0.968-1.477)	0,097
BLCA	0.94 (0.82-1.077)	0,37
BRCA	0.984 (0.826-1.173)	0,859
CESC	0.719 (0.574-0.901)	0,004
CHOL	1.031 (0.675-1.575)	0,886
COAD	1.082 (0.844-1.388)	0,534
DLBC	1.381 (1.023-1.865)	0,723
ESCA	1.065 (0.875-1.298)	0,532
GBM	0.841 (0.620-1.140)	0,163
HNSC	0.926 (0.842-1.018)	0,196
KICH	1.649 (0.972-2.804)	0,085
KIRC	1.141 (0.972-1.341)	0,13
KIRP	1.366 (1.056-1.768)	0,018
LAML	1.392 (1.162-1.669)	0
LGG	1.392 (1.162-1.669)	0
LIHC	0.949 (0.898-1.201)	0,808
LUAD	0.766 (0.628-0.933)	0,008
LUSC	1.047 (0.918-1.194)	0,493
MESO	1.207 (0.891-1.636)	0,225
OV	0.849 (0.741-0.973)	0,019
PAAD	0.849 (0.656-1.099)	0,215
PCPG	1.28 (0.639-2.564)	0,487
PRAD	0.995 (0.474-2.091)	0,99
READ	0.874 (0.440-1.740)	0,263
SARC	0.782 (0.646-0.946)	0,011
SKCM	0.895 (0.797-1.008)	0,083
STAD	1.125 (0.907-1.396)	0,282
TGCT	2.336 (0.536-10.186)	0,259
THCA	0.694 (0.409-1.175)	0,173
THYM	0.611 (0.351-1.063)	0,081
UCEC	0.919 (0.713-1.182)	0,601
UCS	0.993 (0.713-1.382)	0,967
UVM	1.124 (0.736-1.717)	0,587

**Table S4. Hazard\_Ratio\_Data\_for\_UCP2 adjusted by age.**

<b>Cancer</b>	<b>HR (95% CI)</b>	<b>P Value</b>
ACC	1.261 (0.997-1.595)	0,053
BLCA	0.93 (0.808-1.069)	0,305
BRCA	0.97 (0.813-1.158)	0,736
CESC	0.729 (0.581-0.914)	0,006
CHOL	1.032 (0.672-1.531)	0,886
COAD	1.084 (0.852-1.397)	0,49
DLBC	1.955 (0.278-13.681)	0,499
ESCA	1.068 (0.874-1.305)	0,521
GBM	1.278 (1.028-1.589)	0,027
HNSC	0.934 (0.831-1.051)	0,258
KICH	1.547 (0.931-2.574)	0,082
KIRC	1.152 (0.972-1.368)	0,102
KIRP	1.384 (1.067-1.796)	0,014
LAML	1.742 (1.260-2.409)	0,001
LGG	1.599 (1.324-1.931)	0
LIHC	1.032 (0.863-1.233)	0,733
LUAD	0.727 (0.593-0.891)	0,002
LUSC	1.043 (0.915-1.188)	0,528
MESO	1.176 (0.860-1.608)	0,311
OV	0.871 (0.758-1.001)	0,051
PAAD	0.869 (0.677-1.116)	0,271
PCPG	1.163 (0.572-2.365)	0,677
PRAD	0.993 (0.474-2.082)	0,986
READ	0.838 (0.513-1.369)	0,48
SARC	0.742 (0.609-0.905)	0,003
SKCM	0.9 (0.801-1.011)	0,076
STAD	1.129 (0.913-1.397)	0,282
TGCT	2.789 (0.686-11.336)	0,152
THCA	0.845 (0.421-1.805)	0,635
THYM	0.74 (0.384-1.425)	0,368
UCEC	0.919 (0.672-1.257)	0,598
UCS	0.944 (0.67-1.331)	0,744
UVM	1.251 (0.802-1.951)	0,323

**Table S5. Number of alive, deceased, and total females and males affected by the indicated cancer in the TCGA dataset.**

<b>Database</b>	<b>alive</b>	<b>dead</b>	<b>total</b>	<b>female</b>	<b>male</b>
TCGA-GBM	30	123	153	54	99
TCGA-THCA	485	16	501	366	135
TCGA-LUAD	318	182	500	270	230
TCGA-LUSC	282	212	494	128	366
TCGA-COAD	340	98	438	204	234
TCGA-READ	133	26	159	71	88
TCGA-HNSC	281	218	499	133	366
TCGA-STAD	208	146	354	125	229
TCGA-LIHC	235	130	365	119	246
TCGA-PAAD	84	92	176	80	96
TCGA-KICH	55	9	64	26	38
TCGA-KIRC	355	173	528	184	344
TCGA-KIRP	241	44	285	76	209
TCGA-BLCA	227	179	406	107	299
TCGA-PRAD	484	10	494	0	494
TCGA-TGCT	130	4	134	0	134
TCGA-BRCA	923	152	1075	1063	12
TCGA-CESC	220	71	291	291	0
TCGA-UCEC	450	91	541	541	0
TCGA-OV	143	230	373	373	0
TCGA-SKCM	73	29	102	42	60