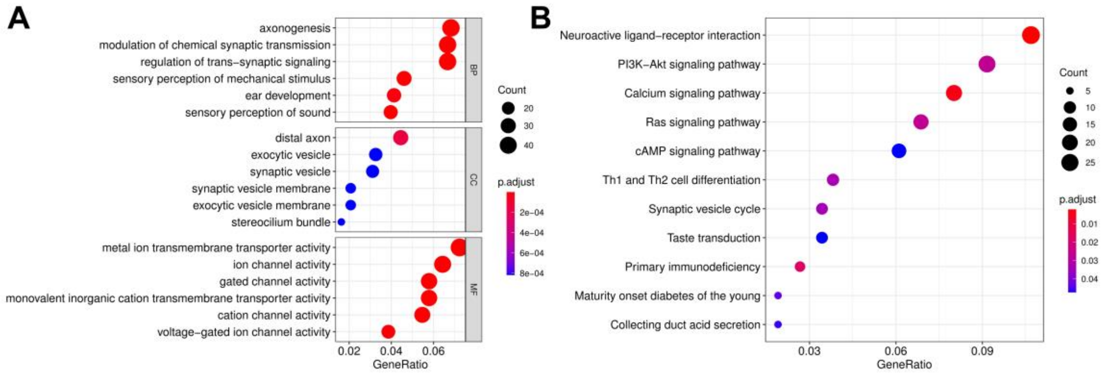
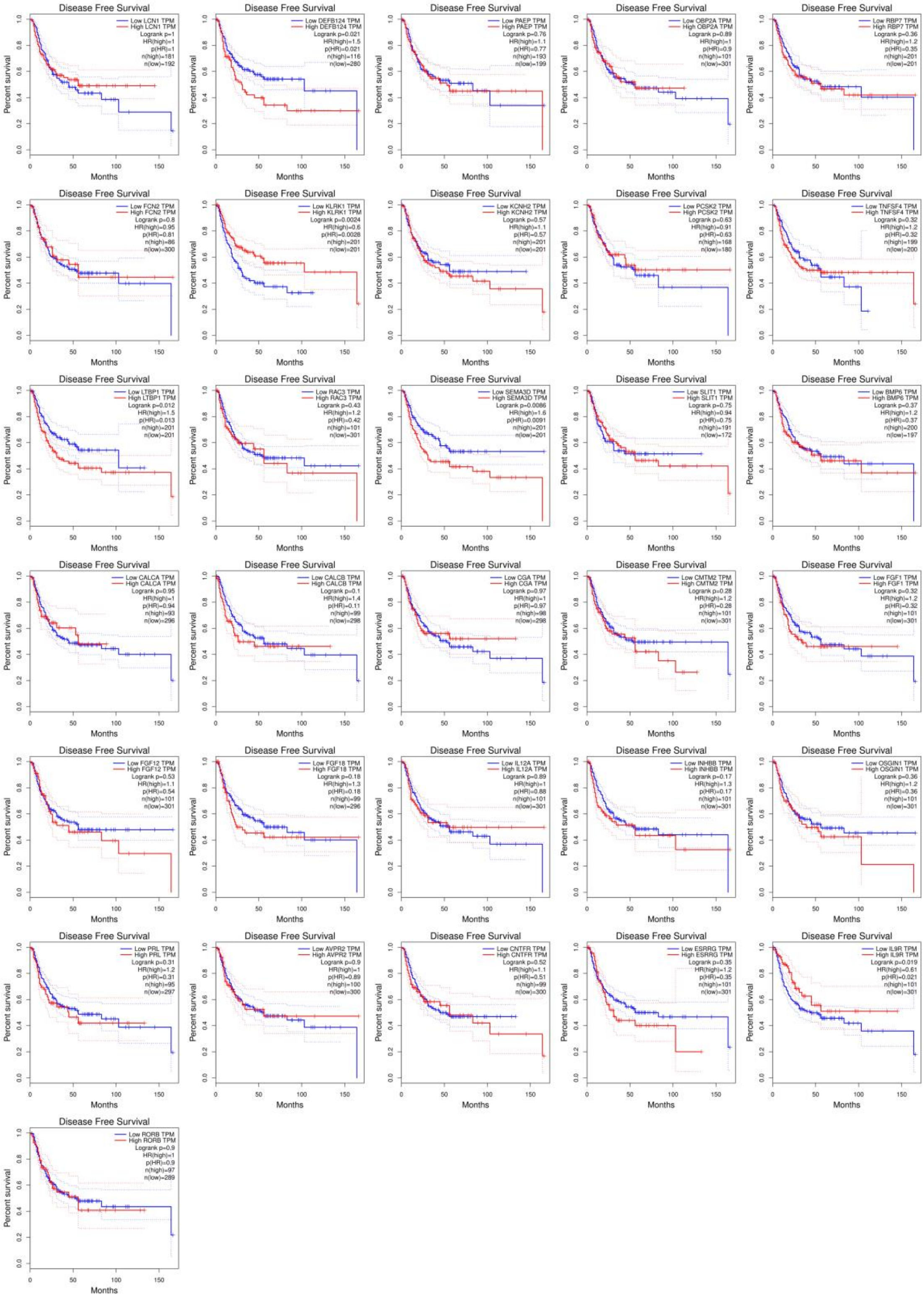
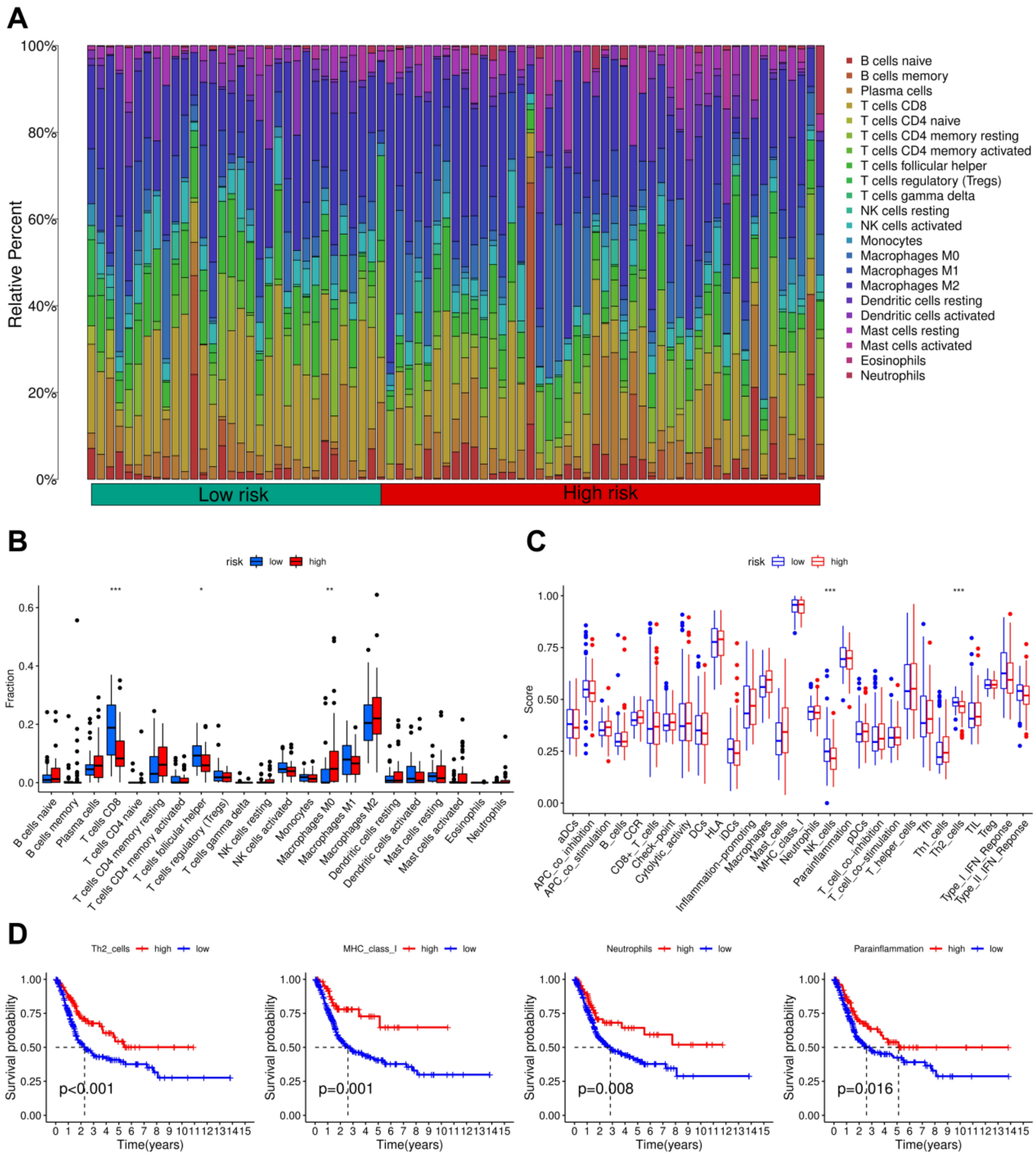


Supplementary Fig. 1. Functional enrichment analysis. (A) Bubble plot revealed GO functional enrichment analysis of DEGs. (B) Bubble plot indicated KEGG functional enrichment analysis of DEGs.

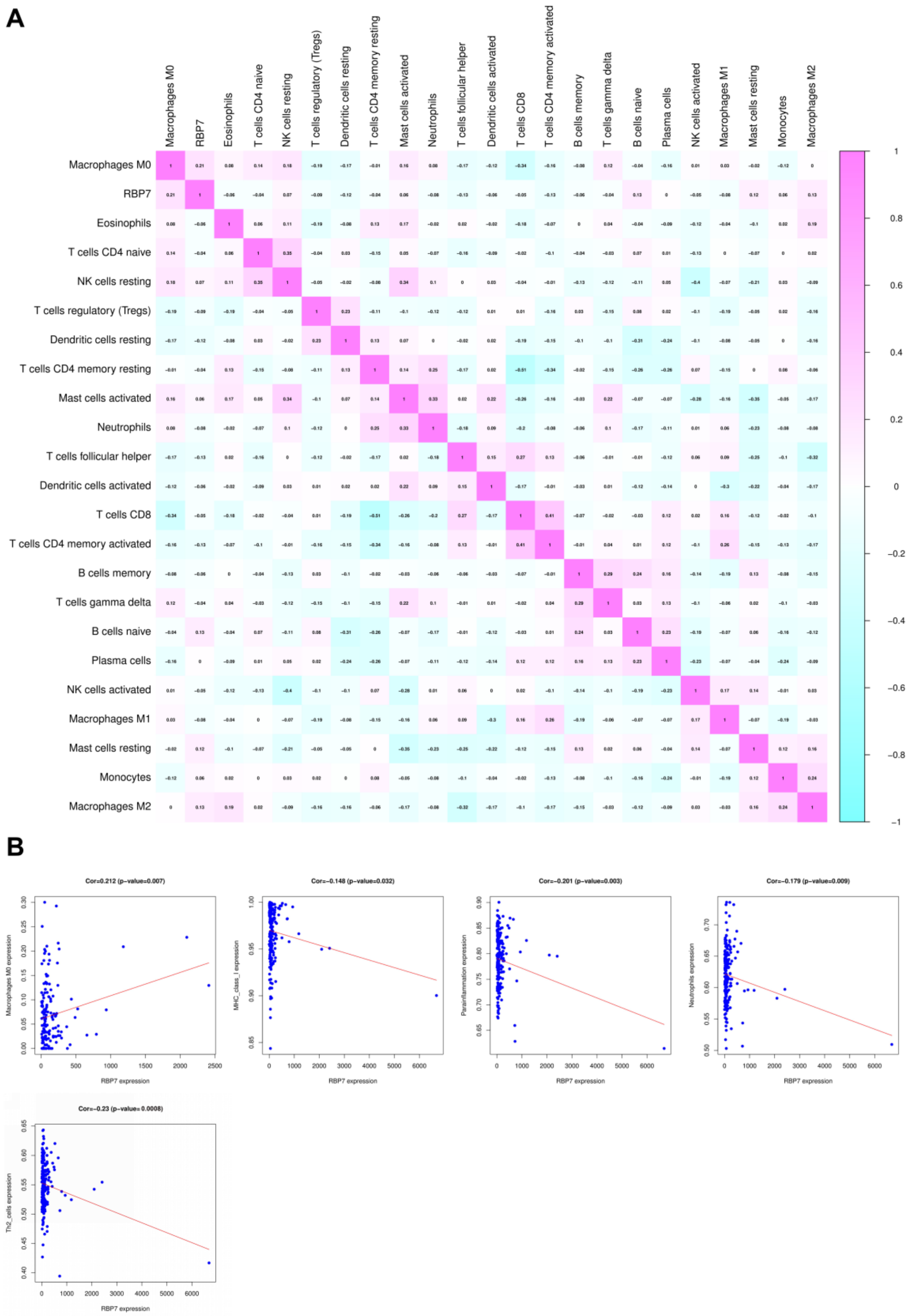


Supplementary Fig. 2. Survival analysis of the 31 DEIGs displayed by differences of disease free survival between low and high TPM of genes.



Supplementary Fig. 3. Immune cells and immune pathways analysis. (A) Distribution of 22 different immune cells' relative percent in low risk and high risk groups. (C) Differences of 22 different immune cells' fraction between low risk and high risk groups. (D) Differences of different immune pathways' ssGSEA score between low risk and high risk groups. (E) High ssGSEA scores of Th2 cells ($p < 0.001$), MHC class I ($p = 0.001$), neutrophils ($p = 0.008$), and parainflammation ($p = 0.016$) were positively correlated with better prognosis of BLCA patients.

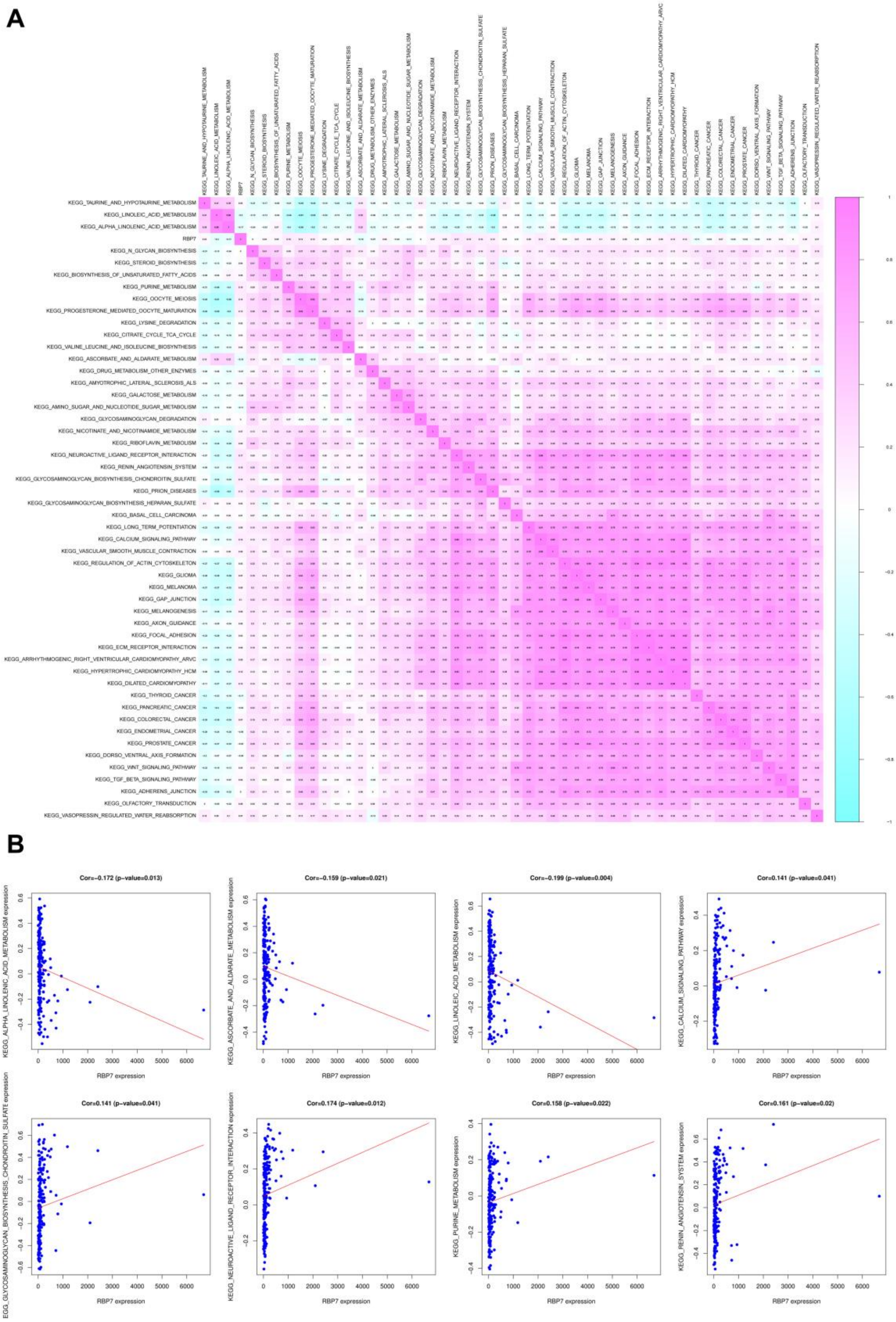
Abbreviations: ssGSEA, single-sample Gene Set Enrichment Analysis.



	Macrophages M0	RBP7	Eosinophils	T cells CD4 naive	NK cells resting	T cells regulatory (Tregs)	Dendritic cells resting	T cells CD4 memory resting	Mast cells activated	Neutrophils	T cells follicular helper	Dendritic cells activated	T cells CD8	T cells CD4 memory activated	B cells memory	T cells gamma delta	B cells naive	Plasma cells	NK cells activated	Macrophages M1	Mast cells resting	Monocytes	Macrophages M2
Macrophages M0	1	0.21	0.08	0.14	0.18	-0.19	-0.17	-0.01	0.16	0.08	-0.17	-0.12	-0.34	-0.16	-0.08	0.12	-0.04	-0.16	0.01	0.03	-0.02	-0.12	0
RBP7	0.21	1	-0.06	-0.04	0.07	-0.09	-0.12	-0.04	0.06	-0.08	-0.13	-0.06	-0.05	-0.13	-0.06	-0.04	0.13	0	-0.05	-0.08	0.12	0.06	0.13
Eosinophils	0.08	-0.06	1	0.06	0.11	-0.19	-0.08	0.13	0.17	-0.02	0.02	-0.02	-0.18	-0.07	0	0.04	-0.04	-0.09	-0.12	-0.04	-0.1	0.02	0.19
T cells CD4 naive	0.14	-0.04	0.06	1	0.35	-0.04	0.03	-0.15	0.05	-0.07	-0.16	-0.09	-0.02	-0.1	-0.04	-0.03	0.07	0.01	-0.13	0	-0.07	0	0.02
NK cells resting	0.18	0.07	0.11	0.35	1	-0.05	-0.02	-0.08	0.34	0.1	0	0.03	-0.04	-0.01	-0.13	-0.12	-0.11	0.05	-0.4	-0.07	-0.21	0.03	-0.09
T cells regulatory (Tregs)	-0.19	-0.09	-0.19	-0.04	-0.05	1	0.23	-0.11	-0.1	-0.12	-0.12	0.01	0.01	-0.16	0.03	-0.15	0.08	0.02	-0.1	-0.19	-0.05	0.02	-0.16
Dendritic cells resting	-0.17	-0.12	-0.08	0.03	-0.02	0.23	1	0.13	0.07	0	-0.02	0.02	-0.19	-0.15	-0.1	-0.1	-0.31	-0.24	-0.1	-0.08	-0.05	0	-0.16
T cells CD4 memory resting	-0.01	-0.04	0.13	-0.15	-0.08	-0.11	0.13	1	0.14	0.25	-0.17	0.02	-0.51	-0.34	-0.02	-0.15	-0.26	-0.26	0.07	-0.15	0	0.08	-0.06
Mast cells activated	0.16	0.06	0.17	0.05	0.34	-0.1	0.07	0.14	1	0.33	0.02	0.22	-0.26	-0.16	-0.03	0.22	-0.07	-0.07	-0.28	-0.16	-0.35	-0.05	-0.17
Neutrophils	0.08	-0.08	-0.02	-0.07	0.1	-0.12	0	0.25	0.33	1	-0.18	0.09	-0.2	-0.08	-0.06	0.1	-0.17	-0.11	0.01	0.06	-0.23	-0.08	-0.08
T cells follicular helper	-0.17	-0.13	0.02	-0.16	0	-0.12	-0.02	-0.17	0.02	-0.18	1	0.15	0.27	0.13	-0.06	-0.01	-0.01	-0.12	0.06	0.09	-0.25	-0.1	-0.32
Dendritic cells activated	-0.12	-0.06	-0.02	-0.09	0.03	0.01	0.02	0.02	0.22	0.09	0.15	1	-0.17	-0.01	-0.03	0.01	-0.12	-0.14	0	-0.3	-0.22	-0.04	-0.17
T cells CD8	-0.34	-0.05	-0.18	-0.02	-0.04	0.01	-0.19	-0.51	-0.26	-0.2	0.27	-0.17	1	0.41	-0.07	-0.02	-0.03	0.12	0.02	0.16	-0.12	-0.02	-0.1
T cells CD4 memory activated	-0.16	-0.13	-0.07	-0.1	-0.01	-0.16	-0.15	-0.34	-0.16	-0.08	0.13	-0.01	0.41	1	-0.01	0.04	0.01	0.12	-0.1	0.26	-0.15	-0.13	-0.17
B cells memory	-0.08	-0.06	0	-0.04	-0.13	0.03	-0.1	-0.02	-0.03	-0.06	-0.06	-0.03	-0.07	-0.01	1	0.29	0.24	0.16	-0.14	-0.19	0.13	-0.08	-0.15
T cells gamma delta	0.12	-0.04	0.04	-0.03	-0.12	-0.15	-0.1	-0.15	0.22	0.1	-0.01	0.01	-0.02	0.04	0.29	1	0.03	0.13	-0.1	-0.06	0.02	-0.1	-0.03
B cells naive	-0.04	0.13	-0.04	0.07	-0.11	0.08	-0.31	-0.26	-0.07	-0.17	-0.01	-0.12	-0.03	0.01	0.24	0.03	1	0.23	-0.19	-0.07	0.06	-0.16	-0.12
Plasma cells	-0.16	0	-0.09	0.01	0.05	0.02	-0.24	-0.26	-0.07	-0.11	-0.12	-0.14	0.12	0.12	0.16	0.13	0.23	1	-0.23	-0.07	-0.04	-0.24	-0.09
NK cells activated	0.01	-0.05	-0.12	-0.13	-0.4	-0.1	-0.1	0.07	-0.28	0.01	0.06	0	0.02	-0.1	-0.14	-0.1	-0.19	-0.23	1	0.17	0.14	-0.01	0.03
Macrophages M1	0.03	-0.08	-0.04	0	-0.07	-0.19	-0.08	-0.15	-0.16	0.06	0.09	-0.3	0.16	0.26	-0.19	-0.06	-0.07	-0.07	0.17	1	-0.07	-0.19	-0.03
Mast cells resting	-0.02	0.12	-0.1	-0.07	-0.21	-0.05	-0.05	0	-0.35	-0.23	-0.25	-0.22	-0.12	-0.15	0.13	0.02	0.06	-0.04	0.14	-0.07	1	0.12	0.16
Monocytes	-0.12	0.06	0.02	0	0.03	0.02	0	0.08	-0.05	-0.08	-0.1	-0.04	-0.02	-0.13	-0.08	-0.1	-0.16	-0.24	-0.01	-0.19	0.12	1	0.24
Macrophages M2	0	0.13	0.19	0.02	-0.09	-0.16	-0.16	-0.06	-0.17	-0.08	-0.32	-0.17	-0.1	-0.17	-0.15	-0.03	-0.12	-0.09	0.03	-0.03	0.16	0.24	1

Supplementary Fig. 4. Correlation analysis between DEIGs and immune cells and immune pathways expression. (A) Co-expression heatmap showed the correlation between RBP7 expression and 22 different immune cells expression. (B) Correlation between RBP7 expression and Macrophages M0 (R = 0.212, *p* =0.007), Th2 cells (R = -0.148, *p* = 0.032), Parainflammation (R = -0.201, *p* = 0.003), Neutrophils (R = -0.179, *p* = 0.009) and MHC class I (R = -0.23, *p* = 0.0008) expression.

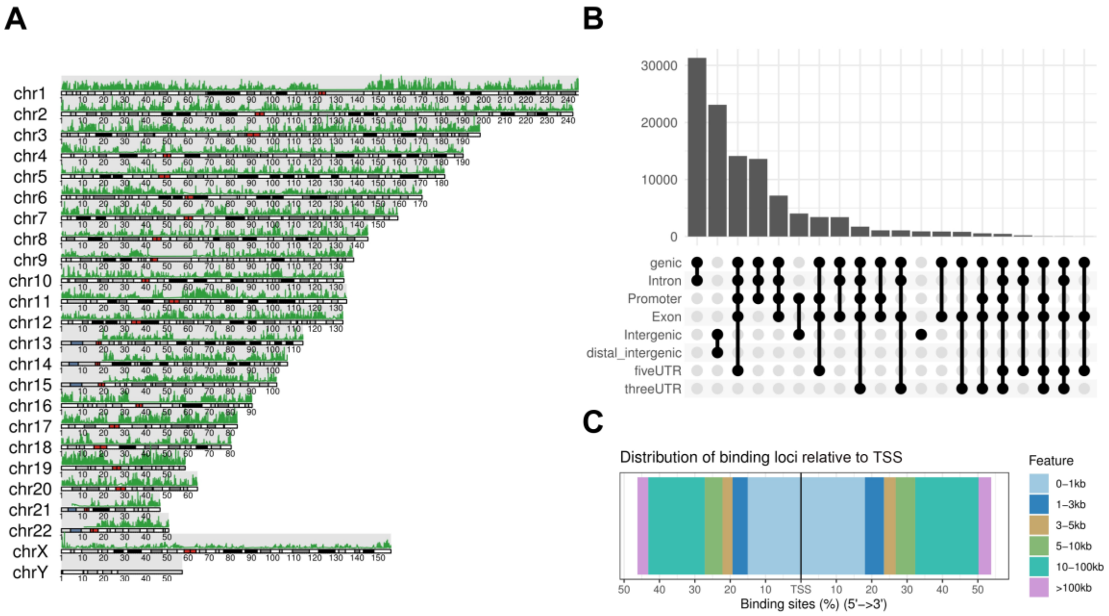
Abbreviation: DEIGs, differentially expressed immune genes.



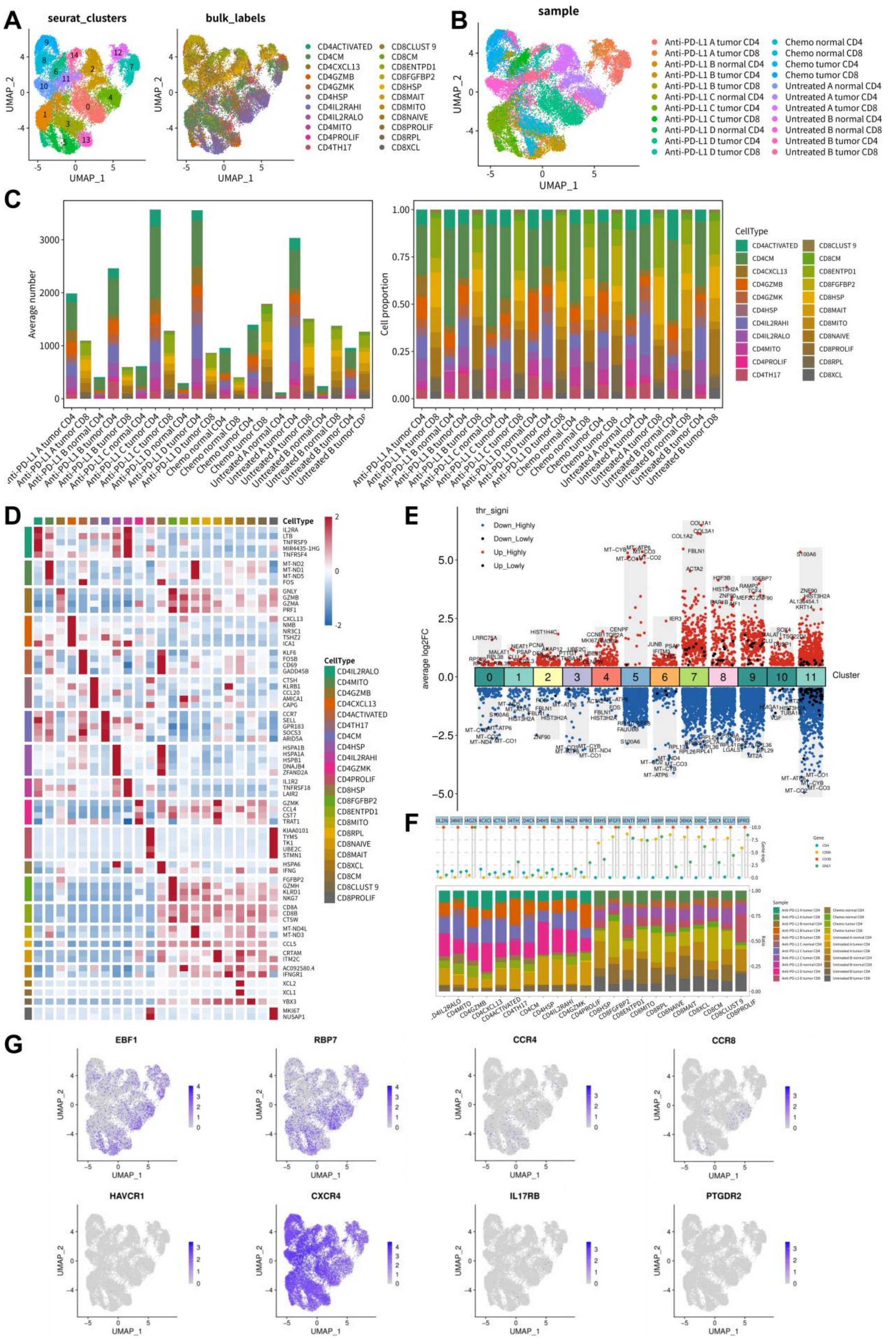
Supplementary Fig. 5. Correlation analysis between DEIGs and KEGG pathways. (A) Co-expression heatmap showed the correlation between RBP7 expression and the 50 KEGG pathways expression. (B) Correlation between RBP7 expression and KEGG_ALPHA_LINOLENIC_ACID_METABOLISM (R

= -0.172, *p* =0.013), KEGG_ASCORBATE_AND_ALDARATE_METABOLISM (R = -0.159, *p* = 0.021), KEGG_LINOLEIC_ACID_METABOLISM (R = -0.199, *p* = 0.004), KEGG_GLYCOSAMINOGLYCAN_BIOSYNTHESIS_CHONDROITIN_SULFATE (R = 0.141, *p* = 0.041), NEUROACTIVE_LIGAND_RECEPTOR_INTERACTION (R = 0.174, *p* = 0.012), KEGG_PURINE_METABOLISM (R = 0.158, *p* = 0.022), and KEGG_RENIN_ANGIOTENSIN_SYSTEM (R = 0.161, *p* = 0.02) enrichment.

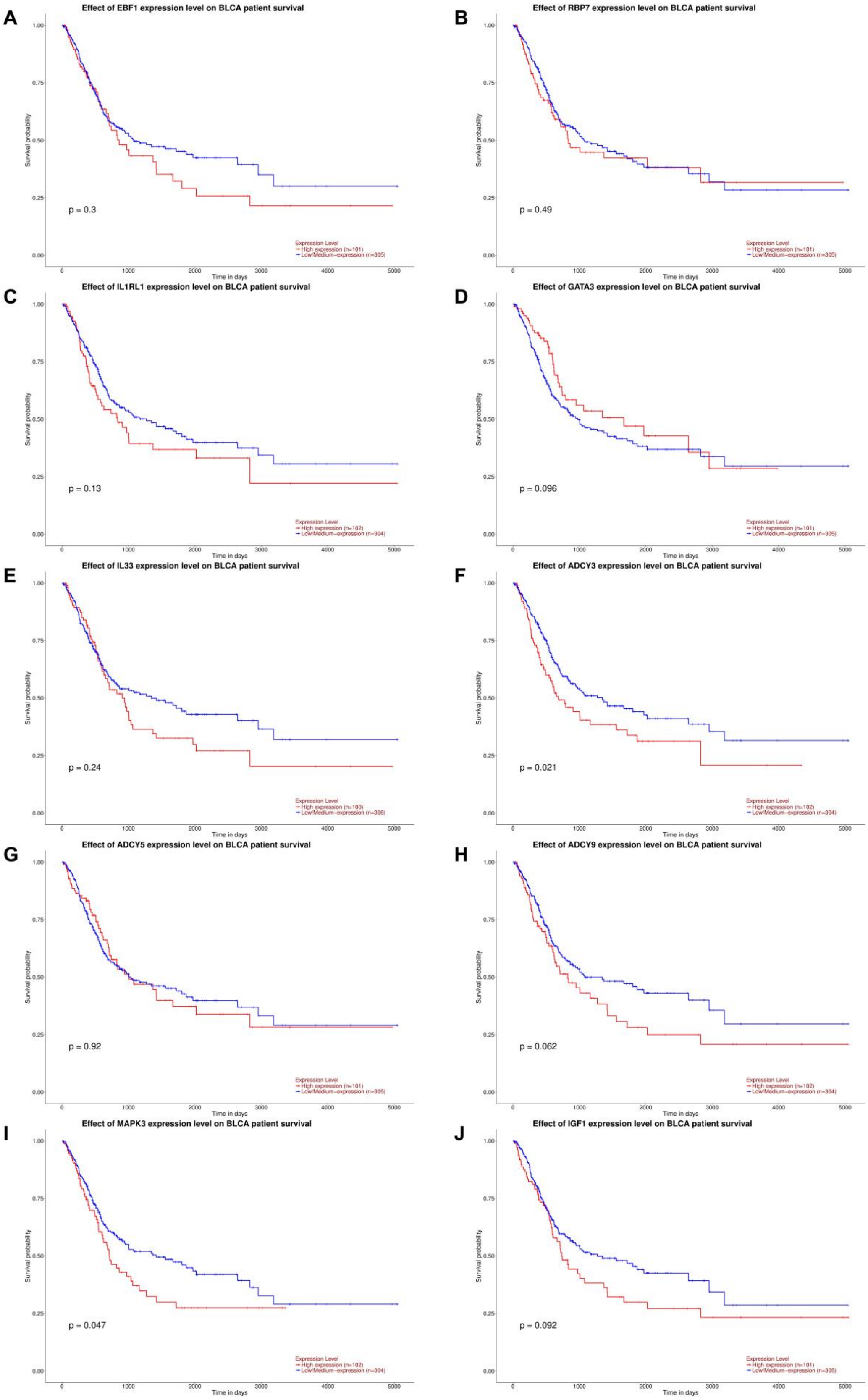
Abbreviation: DEIGs, differentially expressed immune genes; KEGG, Kyoto Encyclopedia of Genes and Genomes.



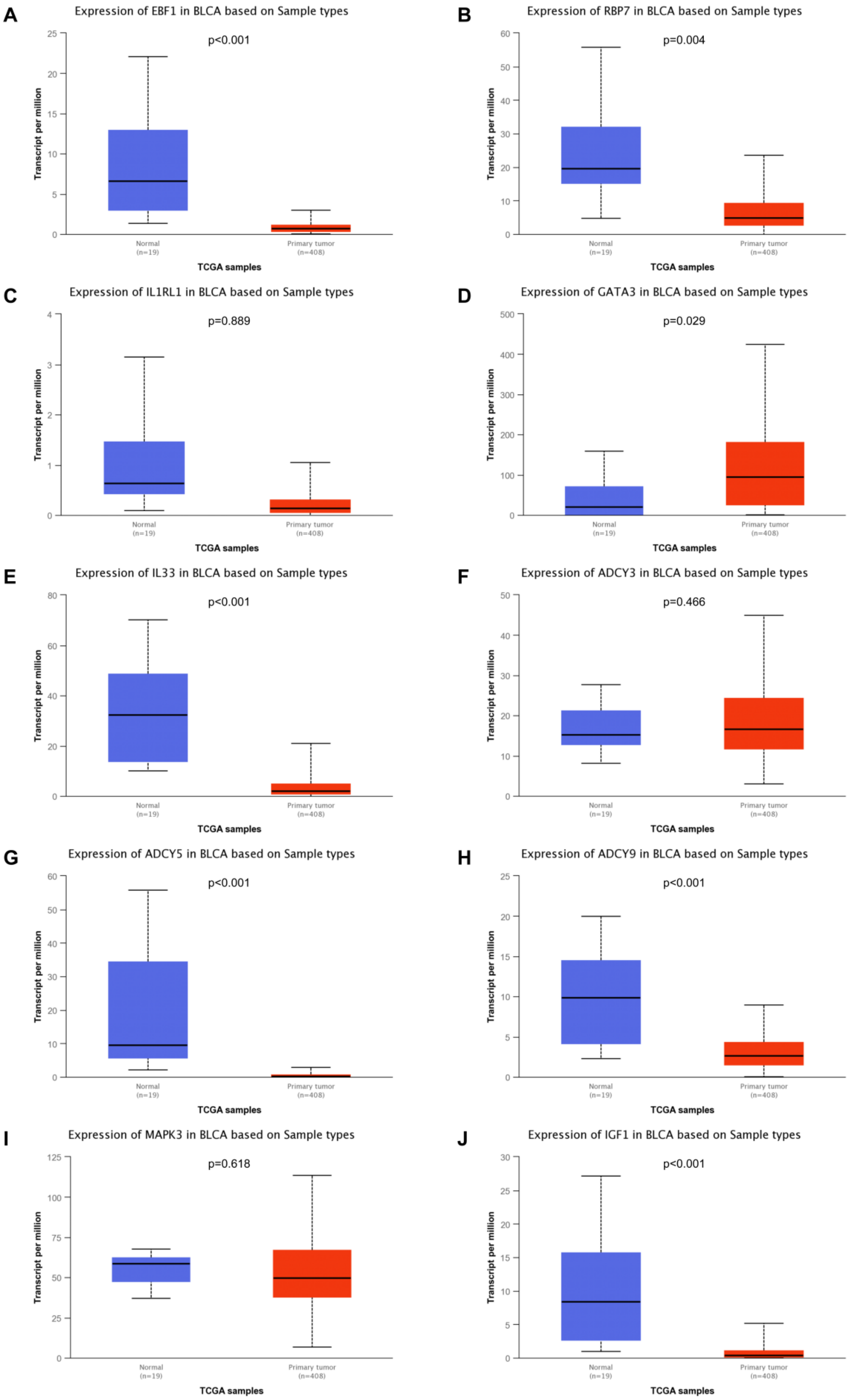
Supplementary Fig. 6. (A) Open chromatin loci on different chromosomes. (B) The venn pie and upsetplot showed the distribution and intersection of different pick types. (C) the distribution of binding loci relative to TSS.



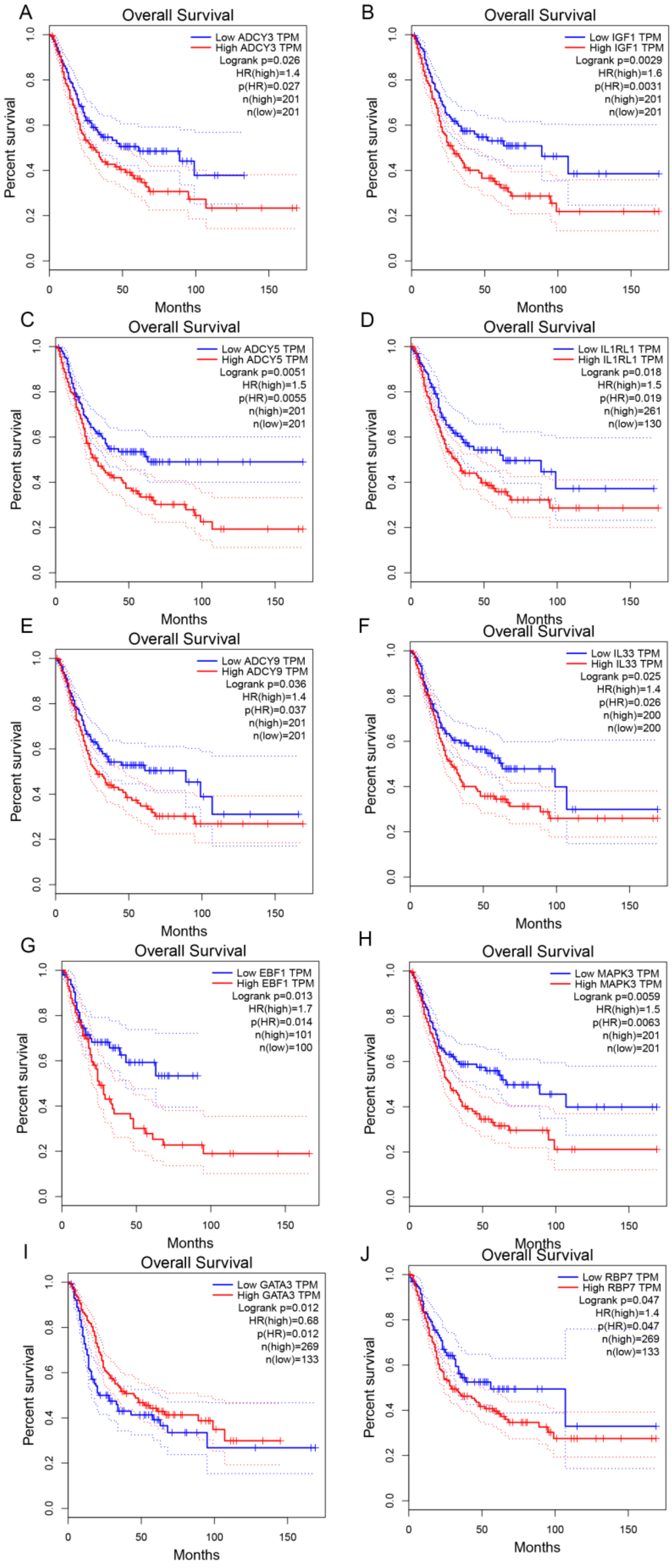
Supplementary Fig. 7. Single-cell RNA sequencing of BLCA infiltrating T cells. (A) t-SNE dimension reduction analysis showing 15 seurat clusters and 22 bulk labels of CD4 and CD8 cells in 22 BLCA samples. (B) The average number and cell propotion of 22 different types of cells in each sample. (C) Top 5 marker genes of each cell type in a heatmap. (D) Marker genes of each cluster in a point plot. (E) Four marker genes (CD4, CD8A, CD3D and GNLY) expression and sample ratio in each cell type. (F) The distribution of 8 marker genes including EBF1 and RBP7.



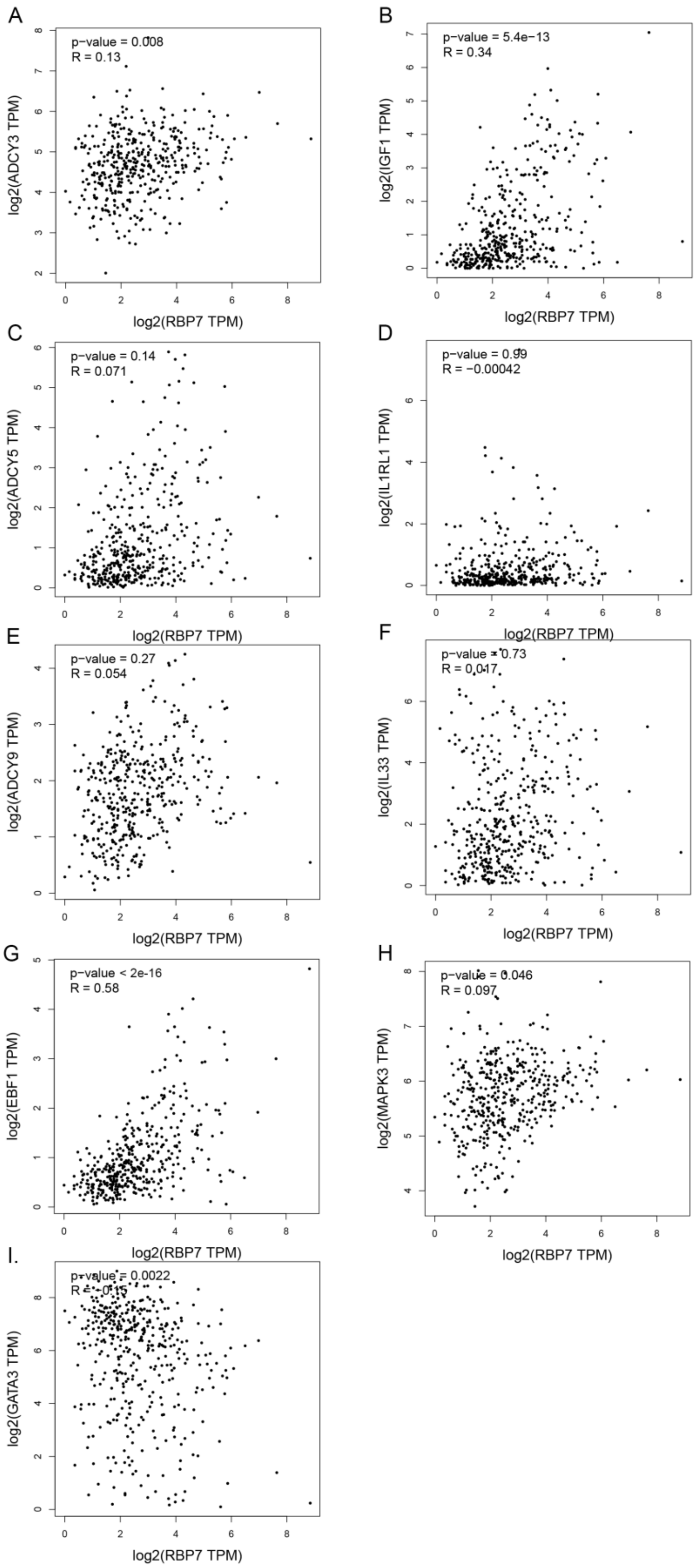
Supplementary Fig. 8. UALCAN database validation. BLCA patients' prognosis between high and low/medium ADCY3 (A), RBP7 (B), IL1RL1 (C), GATA3 (D), IL33(E), ADCY3 (F),ADCY5 (G), ADCY9 (H), MAPK3 (I) and IGF1 (J) expression levels.



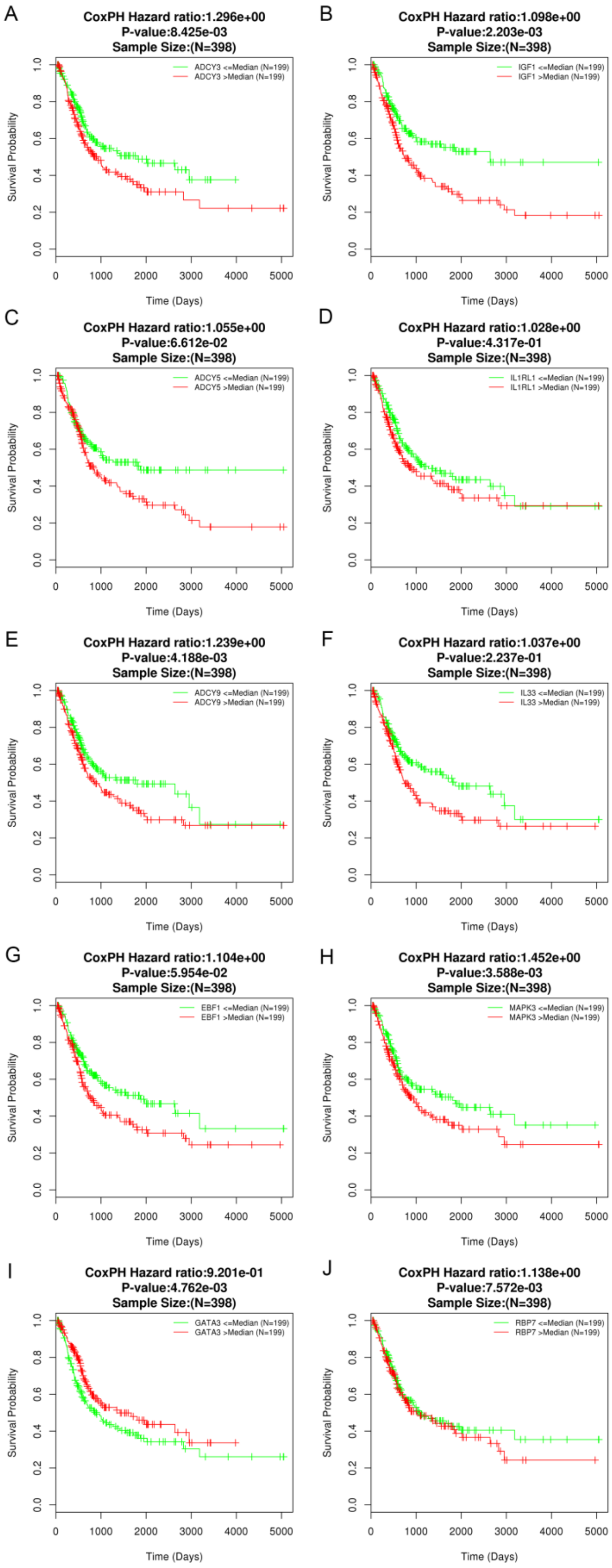
Supplementary Fig. 9. UALCAN database validation. ADCY3 (A), RBP7 (B), IL1RL1 (C), GATA3 (D), IL33(E), ADCY3 (F), ADCY5 (G), ADCY9 (H), MAPK3 (I) and IGF1 (J) expression levels between normal and BLCA primary tumor tissues.



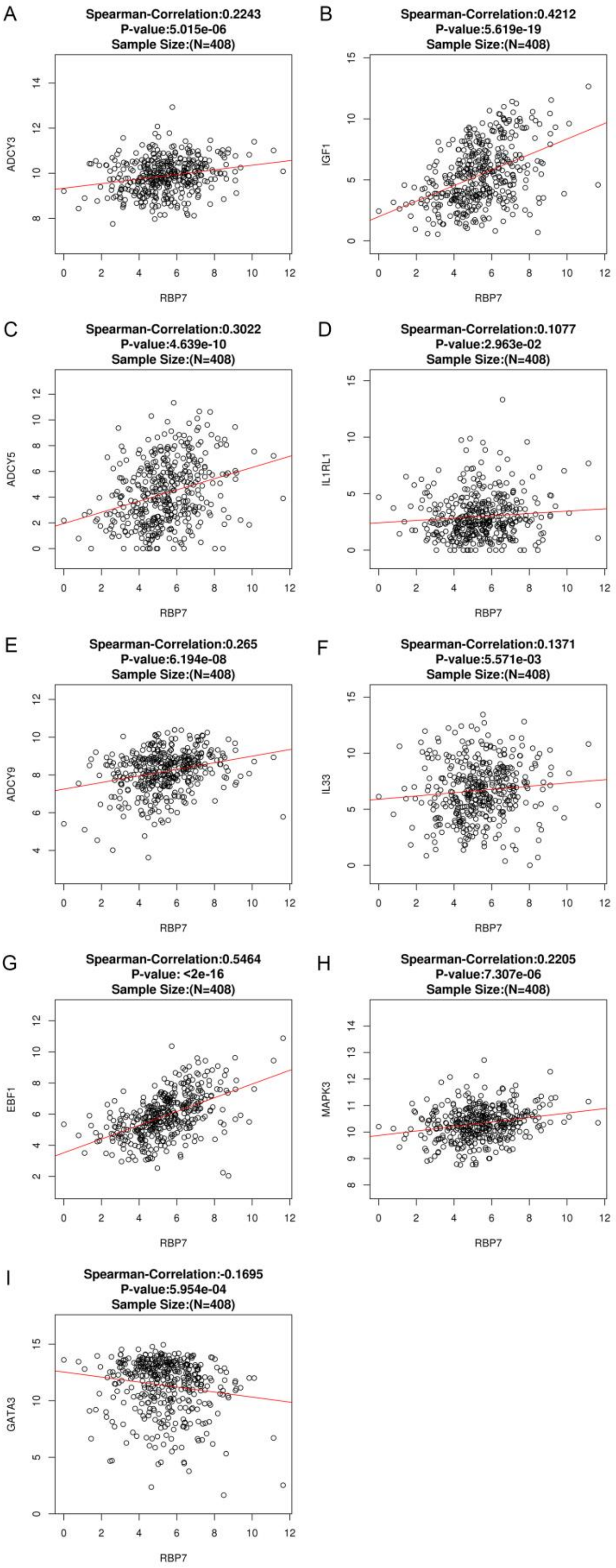
Supplementary Fig. 10. GEPIA database validation. Correlation of ADCY3 (A), IGF1 (B), ADCY5 (C), IL1RL1 (D), ADCY9 (E), IL33 (F), EBF1 (G), MAPK3 (H), GATA3 (I) and RBP7 (J) expression with BLCA patients’ prognosis.


A
p−value = 0.008
R = 0.13
log2(ADCY3 TPM)
log2(RBP7 TPM)
B
p−value = 5.4e−13
R = 0.34
log2(IGF1 TPM)
log2(RBP7 TPM)
C
p−value = 0.14
R = 0.071
log2(ADCY5 TPM)
log2(RBP7 TPM)
D
p−value = 0.99
R = −0.00042
log2(IL1RL1 TPM)
log2(RBP7 TPM)
E
p−value = 0.27
R = 0.054
log2(ADCY9 TPM)
log2(RBP7 TPM)
F
p−value = 0.73
R = 0.017
log2(IL33 TPM)
log2(RBP7 TPM)
G
p−value < 2e-16
R = 0.58
log2(EBF1 TPM)
log2(RBP7 TPM)
H
p−value = 0.046
R = 0.097
log2(MAPK3 TPM)
log2(RBP7 TPM)
I.
p−value = 0.0022
R = −0.15
log2(GATA3 TPM)
log2(RBP7 TPM)

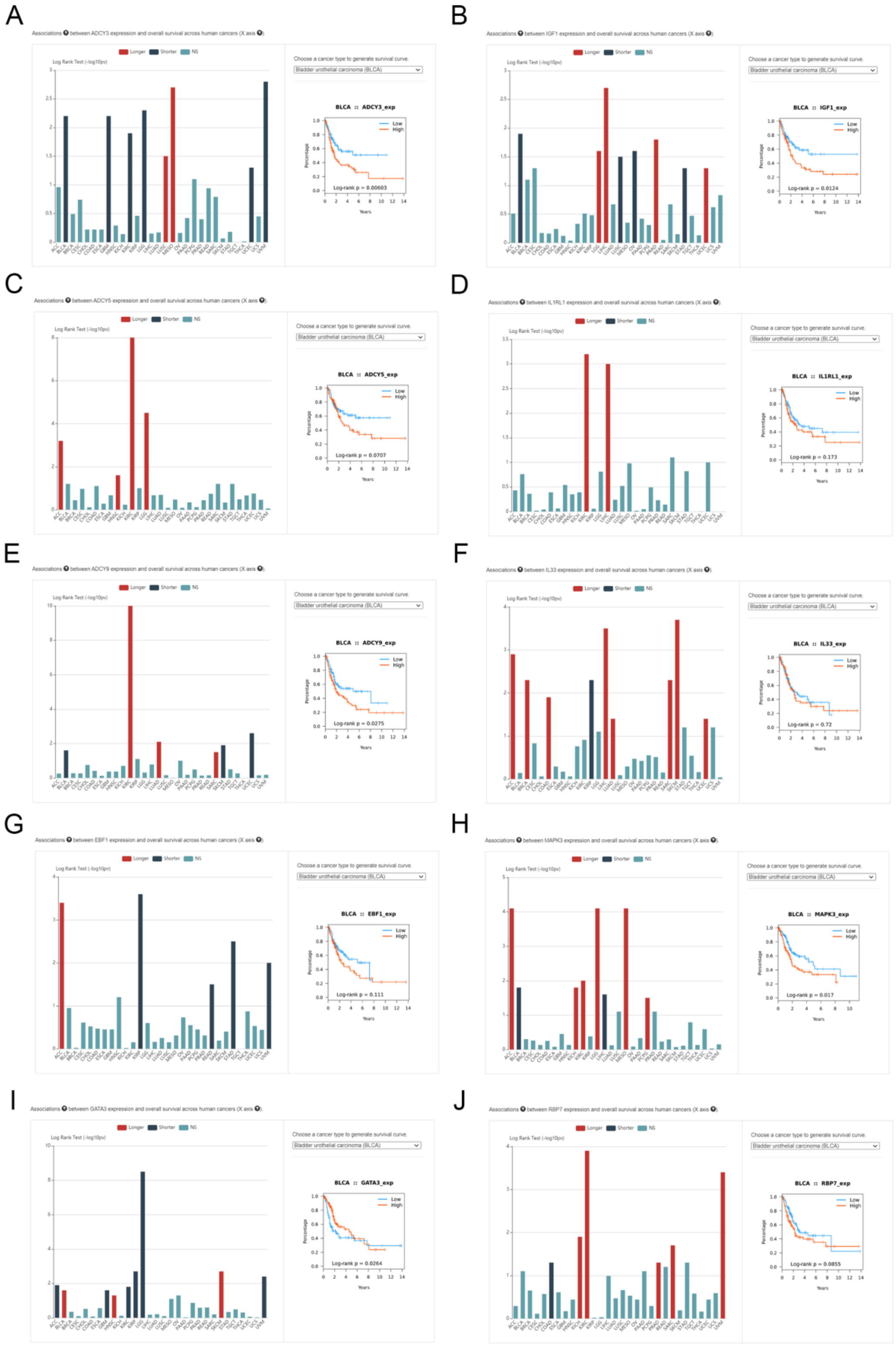
Supplementary Fig. 11. GEPIA database validation. Correlation of ADCY3 (A), IGF1 (B), ADCY5 (C), IL1RL1 (D), ADCY9 (E), IL33 (F), EBF1 (G), MAPK3 (H), and GATA3 (I) expression with RBP7 expression.



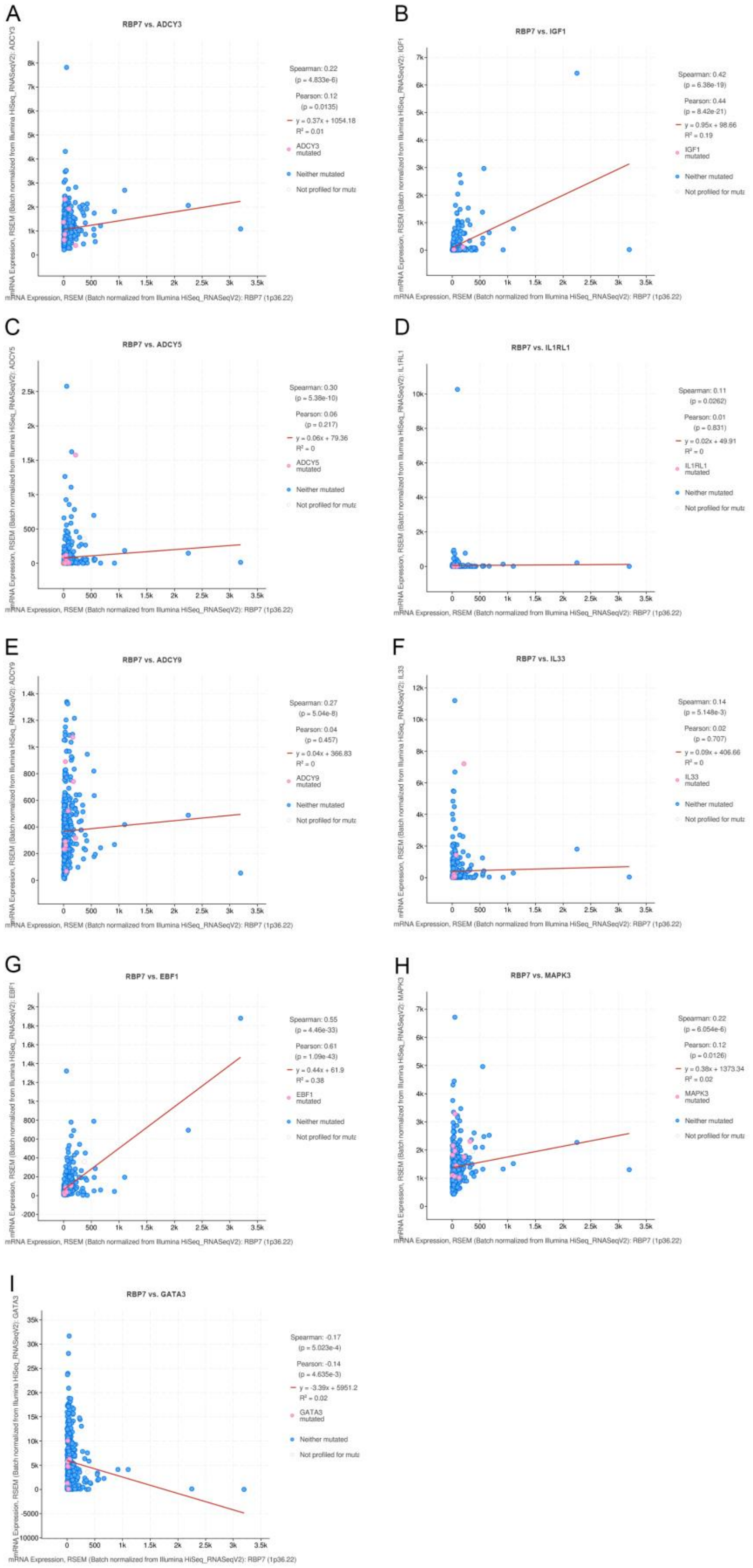
Supplementary Fig. 12. LinkedOmics database validation. Correlation of ADCY3 (A), IGF1 (B), ADCY5 (C), IL1RL1 (D), ADCY9 (E), IL33(F), EBF1 (G), MAPK3 (H), GATA3 (I), and RBP7 (J) expression with BLCA patients’ prognosis.


A
Spearman-Correlation:0.2243
P-value:5.015e-06
Sample Size:(N=408)
ADCY3
RBP7
B
Spearman-Correlation:0.4212
P-value:5.619e-19
Sample Size:(N=408)
IGF1
RBP7
C
Spearman-Correlation:0.3022
P-value:4.639e-10
Sample Size:(N=408)
ADCY5
RBP7
D
Spearman-Correlation:0.1077
P-value:2.963e-02
Sample Size:(N=408)
IL1RL1
RBP7
E
Spearman-Correlation:0.265
P-value:6.194e-08
Sample Size:(N=408)
ADCY9
RBP7
F
Spearman-Correlation:0.1371
P-value:5.571e-03
Sample Size:(N=408)
IL33
RBP7
G
Spearman-Correlation:0.5464
P-value: <2e-16
Sample Size:(N=408)
EBF1
RBP7
H
Spearman-Correlation:0.2205
P-value:7.307e-06
Sample Size:(N=408)
MAPK3
RBP7
I
Spearman-Correlation:-0.1695
P-value:5.954e-04
Sample Size:(N=408)
GATA3
RBP7

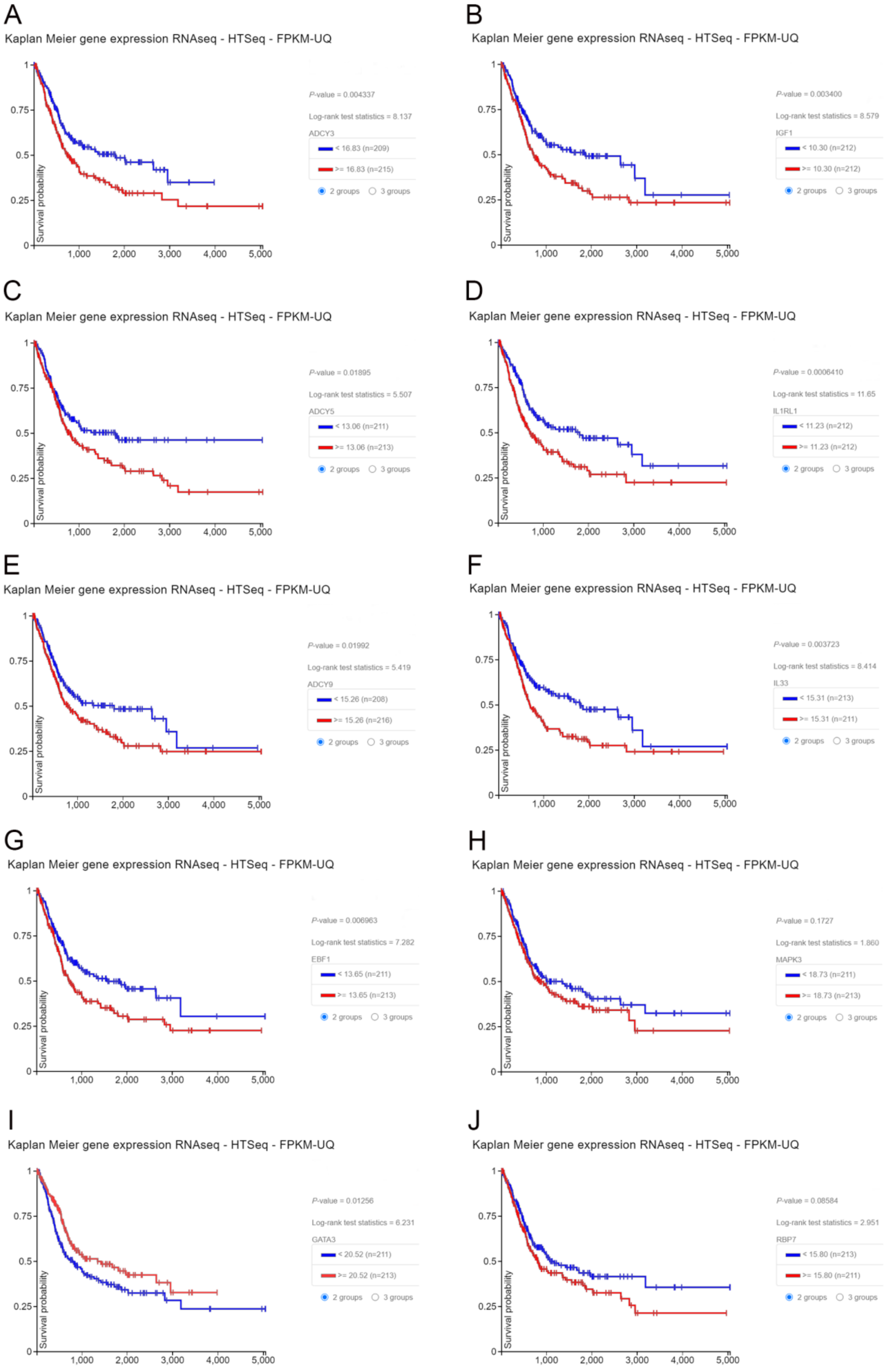
Supplementary Fig. 13. LinkedOmics database validation. Correlation of ADCY3 (A), IGF1 (B), ADCY5 (C), IL1RL1 (D), ADCY9 (E), IL33 (F), EBF1 (G), MAPK3 (H), and GATA3 (I) expression with RBP7 expression.



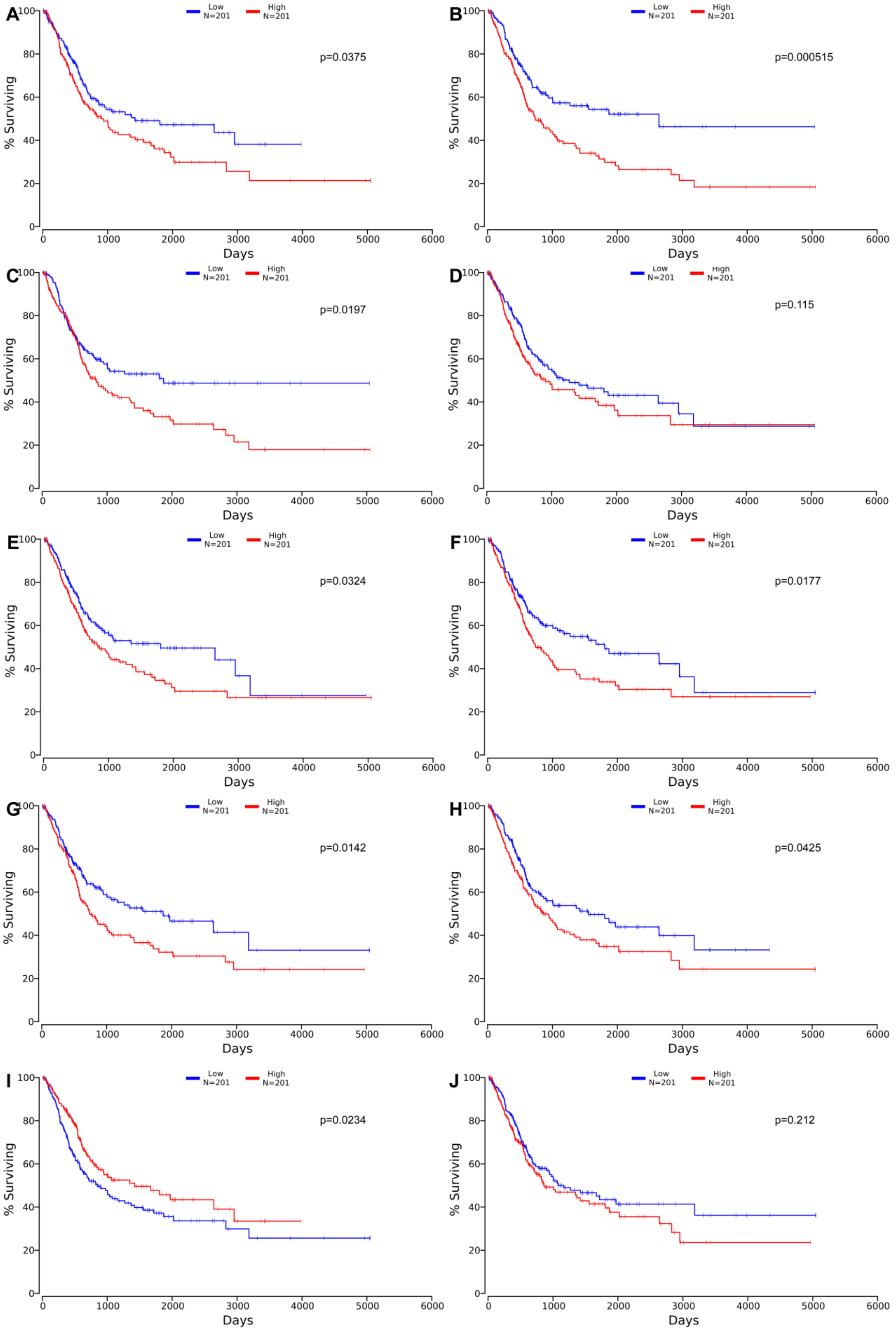
Supplementary Fig. 14. TISIDB database validation. Correlation of ADCY3 (A), IGF1 (B), ADCY5 (C), IL1RL1 (D), ADCY9 (E), IL33(F), EBF1 (G), MAPK3 (H), GATA3 (I), and RBP7 (J) expression with BLCA patients' prognosis.



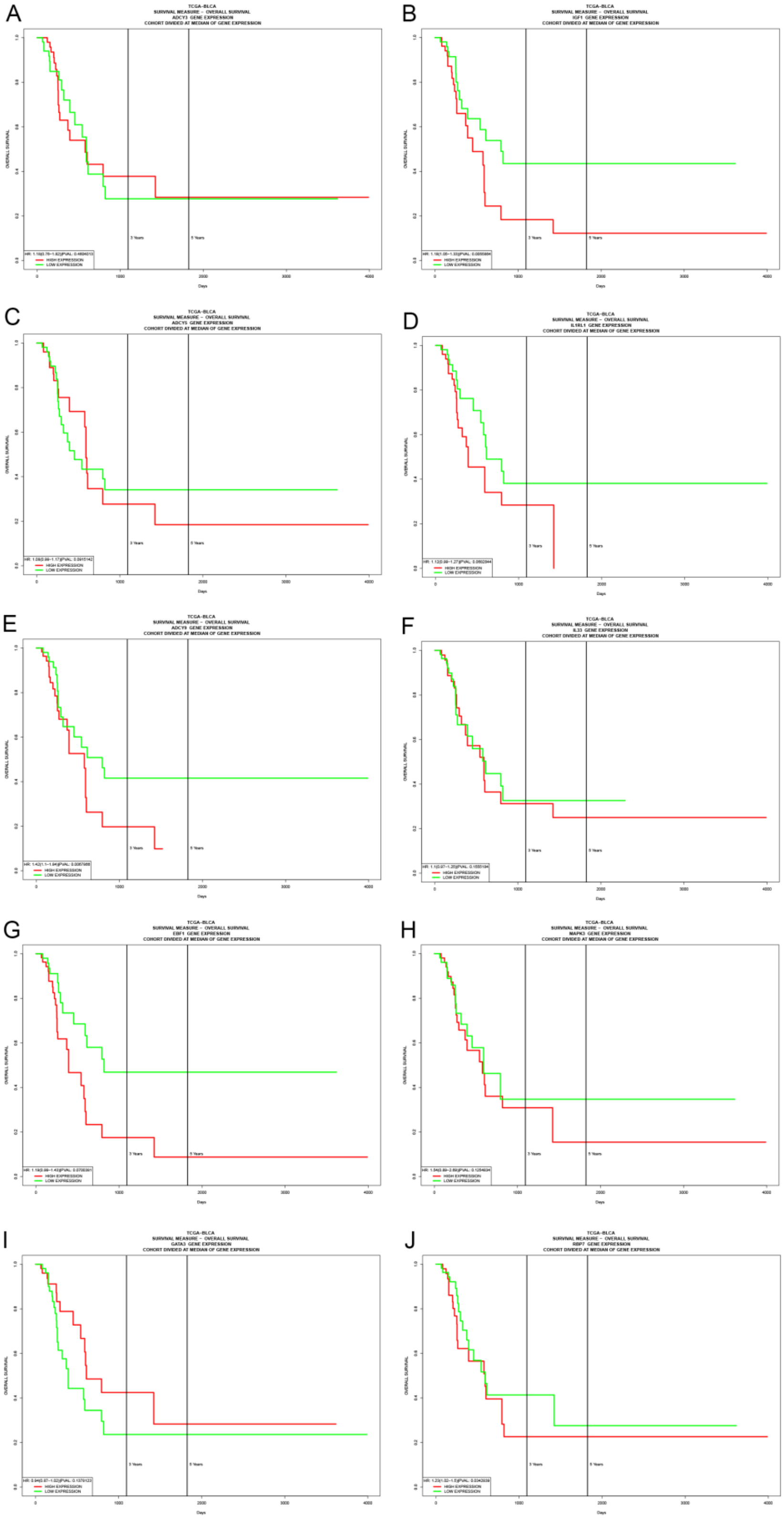
Supplementary Fig. 15. cBioportal database validation. Correlation of ADCY3 (A), IGF1 (B), ADCY5 (C), IL1RL1 (D), ADCY9 (E), IL33 (F), EBF1 (G), MAPK3 (H), and GATA3 (I) expression with RBP7 expression.



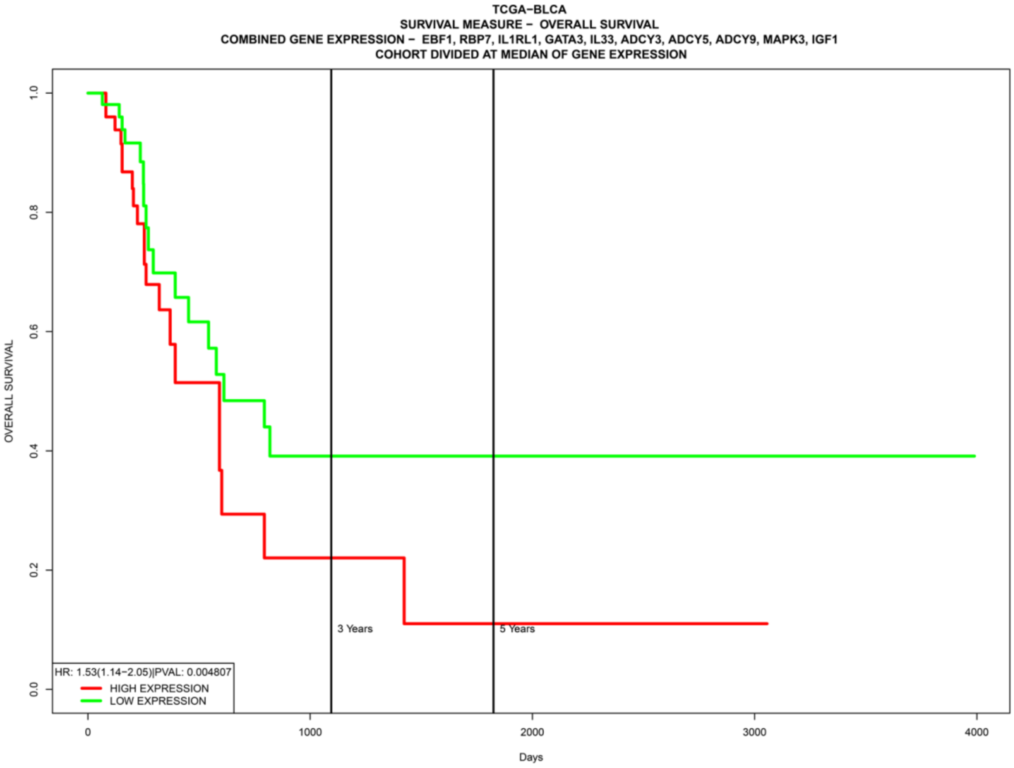
Supplementary Fig. 16. UCSC Xena database validation. Correlation of ADCY3 (A), IGF1 (B), ADCY5 (C), IL1RL1 (D), ADCY9 (E), IL33 (F), EBF1 (G), MAPK3 (H), GATA3 (I), and RBP7 (J) with BLCA patients' prognosis.



Supplementary Fig. 17. OncoLnc database validation. Correlation of ADCY3 (A), IGF1 (B), ADCY5 (C), IL1RL1 (D), ADCY9 (E), IL33 (F), EBF1 (G), MAPK3 (H), GATA3 (I) and RBP7 (J) with BLCA patients' prognosis.



Supplementary Fig. 18. PROGgeneV2 database validation. Correlation of IGF1 (B), ADCY9 (E) and RBP7 (J) expression with BLCA patients' prognosis.



Supplementary Fig. 19. PROGgeneV2 database validation. Correlation of combined gene expression (EBF1, RBP7, IL1RL1, GATA3, IL33, ADCY3, ADCY5, ADCY9, MAPK3, and IGF1) with prognosis of BLCA patients.