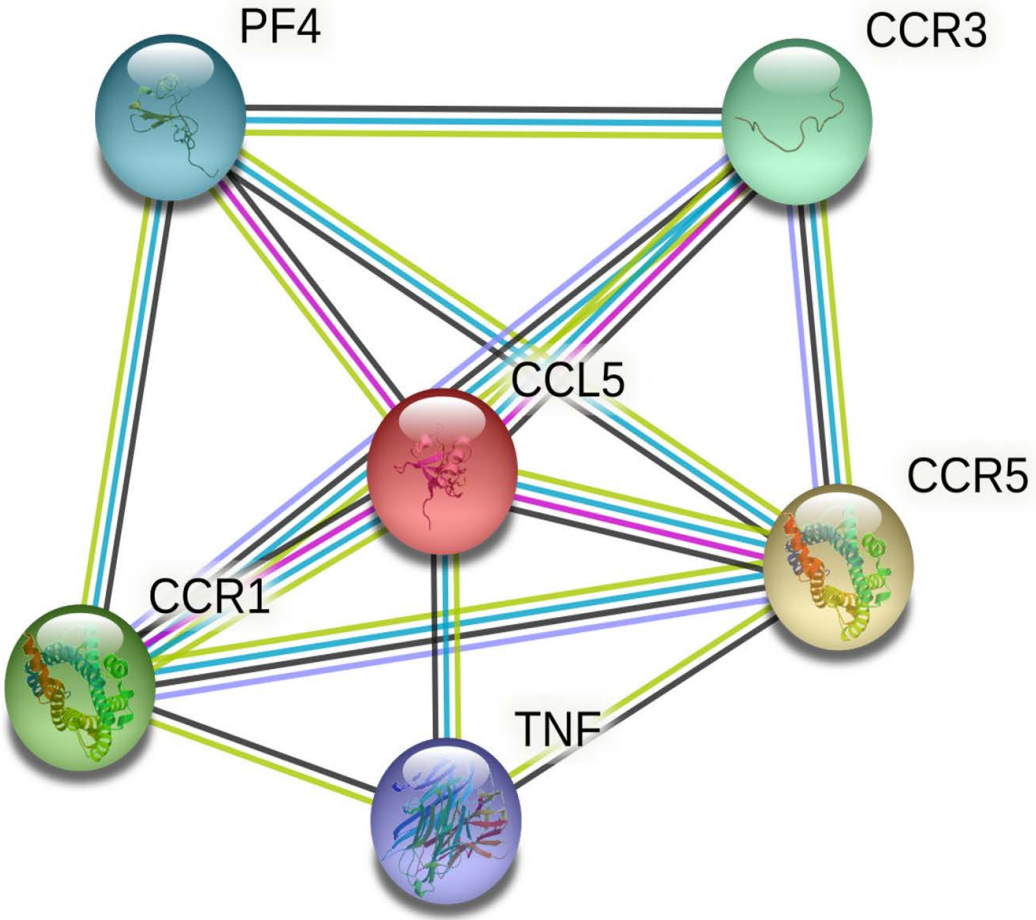
**Figure S1.** Protein-protein interaction network of hub protein concerning CCL5 with minimum required interaction confidence set as 0.7 using String web tool.

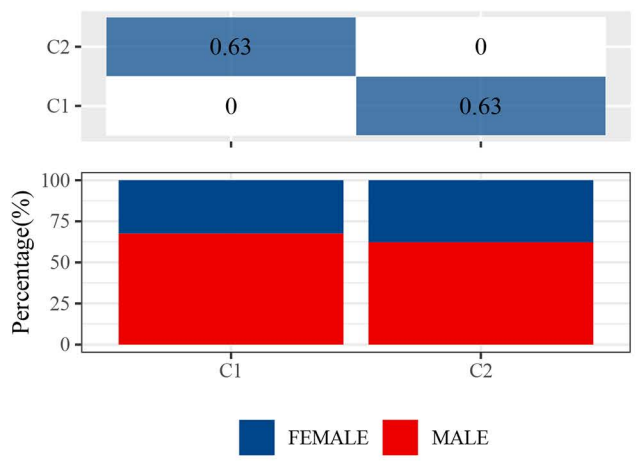
**Figure S2.** Association between *CCL5* mRNA expression and clinicopathological factors in 533 patients with ccRCC from TCGA cohort using Chi-square test.

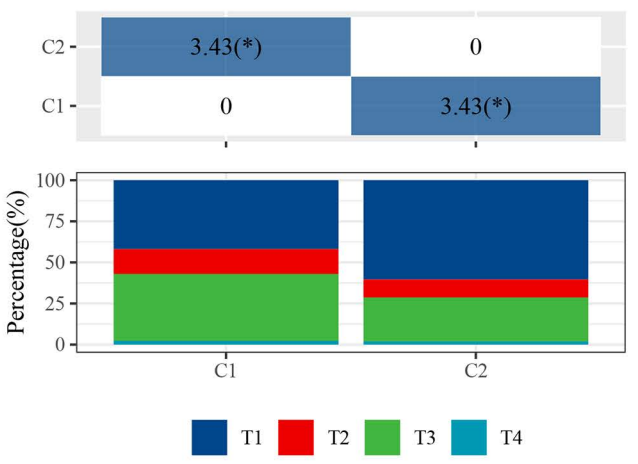
**Figure S3. Prognostic implications of *CCL5* mRNA expression in patients among 33 cancers from TCGA cohort.** (**A-B**) Prognostic value of CCL5 mRNA expression in predicting overall and progression-free survival was assessed using Cox regression analysis and visualized in forest plots. (**C-D**) Histogram showing the predictive value of CCL5 expression in predicting advanced clinical stages and aggressive pathological grade with *P* value converted into $-\log_{10}$(P-value) in the y-coordinate among 33 cancers from TCGA cohort.

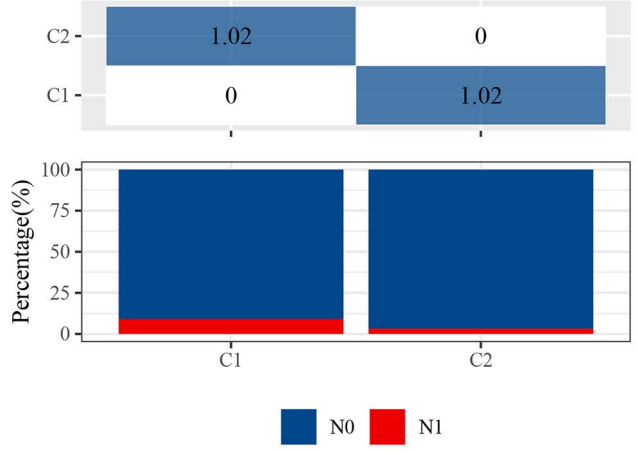
**Figure S4.** Drug sensitivity analysis: the distribution of IC50 score for Axitinib, Pazopanib, Sorafenib and Sunitinib in ccRCC samples of differential CCL5 expression level.

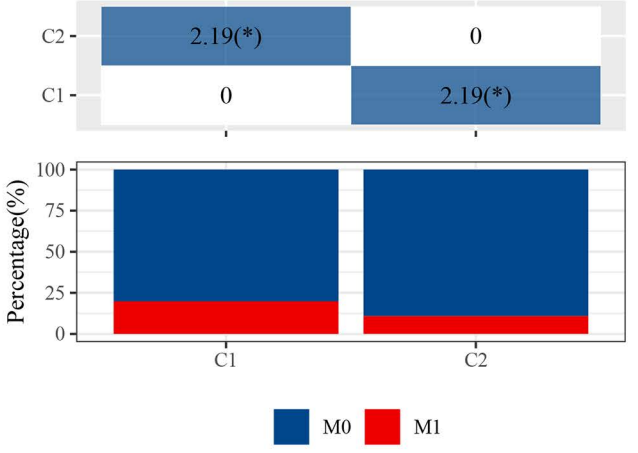
**Figure S5.** KEGG functional enrichment analysis of CCL5 expression in ccRCC

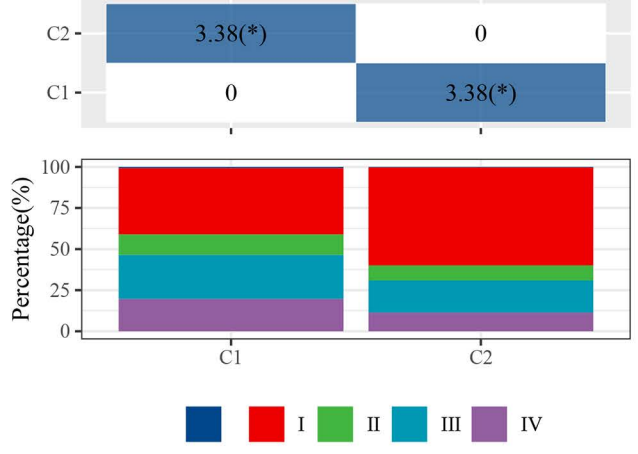

PF4
CCR3
CCL5
CCR5
CCR1
TNF

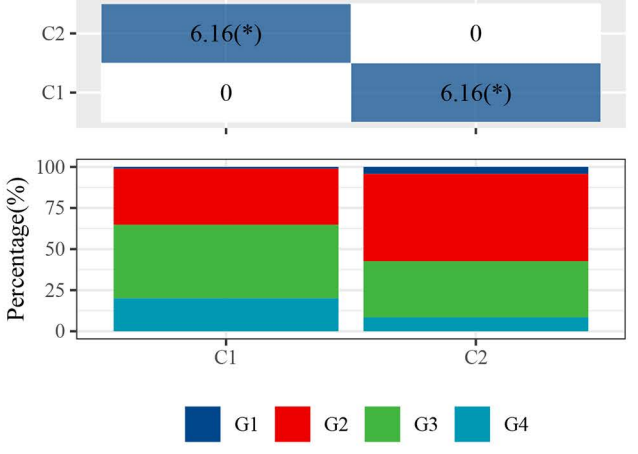

C2
C1
0.63
0
0
0.63
Percentage(%)
100
75
50
25
0
C1
C2
FEMALE
MALE

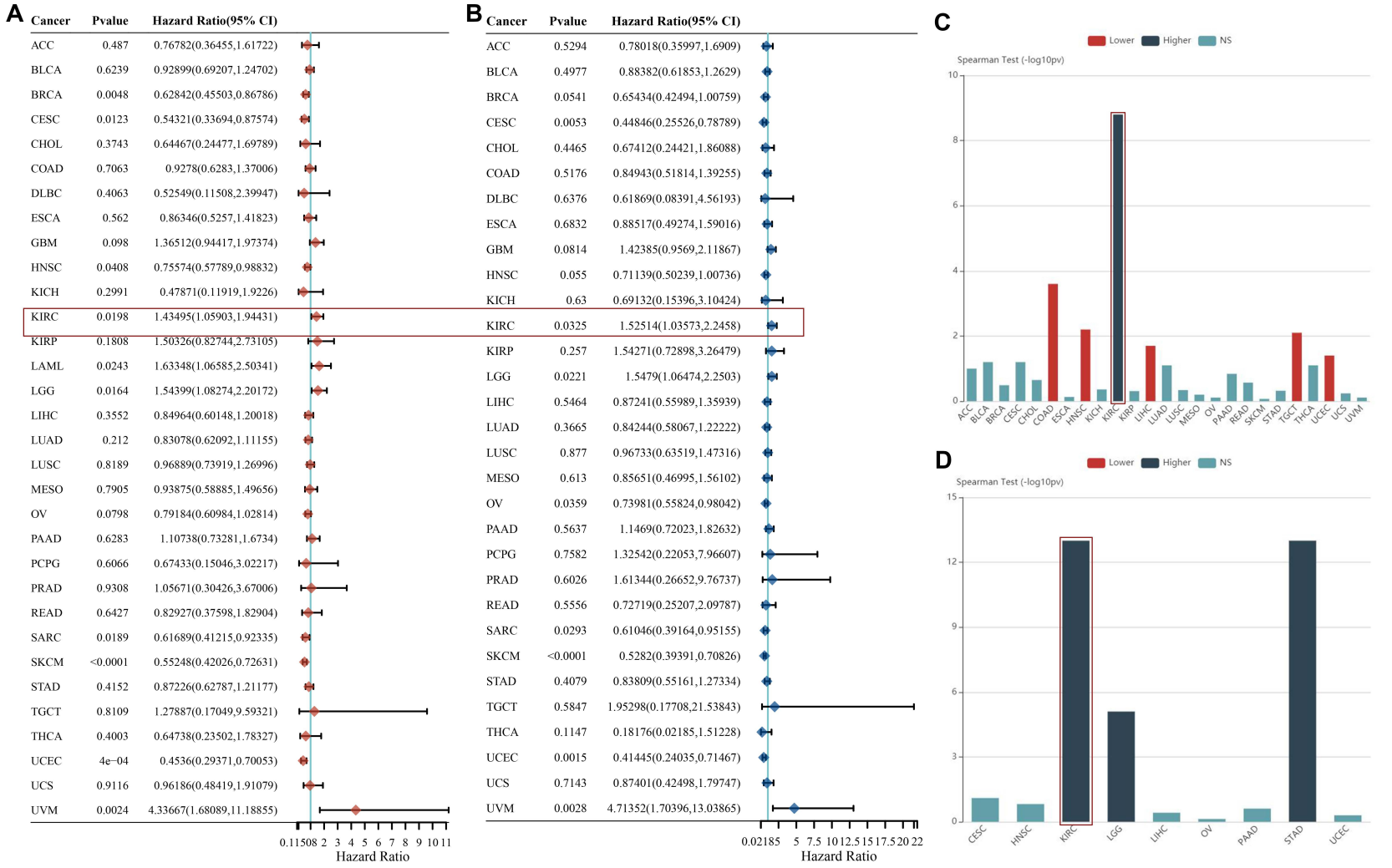

C2
C1
3.43(*)
0
0
3.43(*)
Percentage(%)
100
75
50
25
0
C1
C2
T1
T2
T3
T4

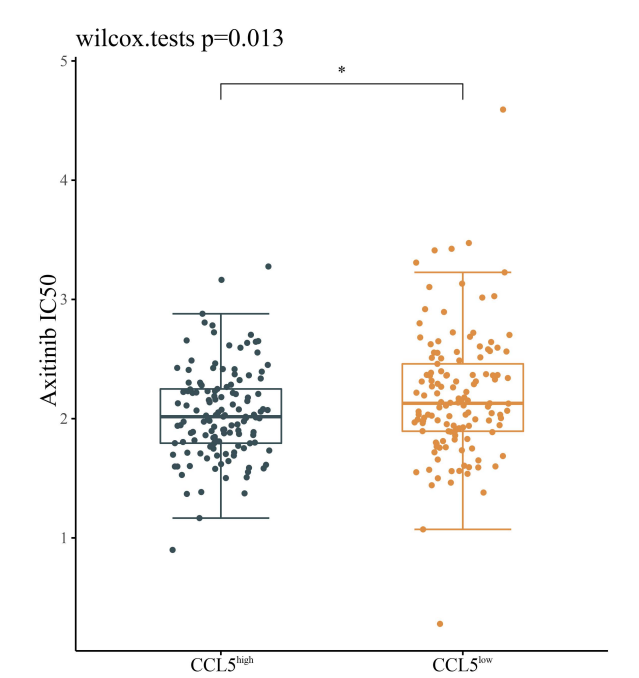

C2
C1
1.02
0
0
1.02
Percentage(%)
100
75
50
25
0
C1
C2
N0
N1

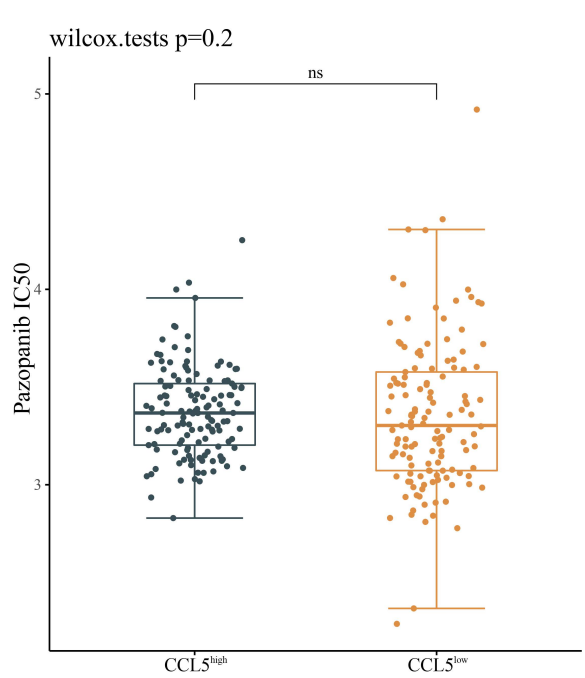

C2
C1
2.19(*)
0
0
2.19(*)
Percentage(%)
100
75
50
25
0
C1
C2
M0
M1

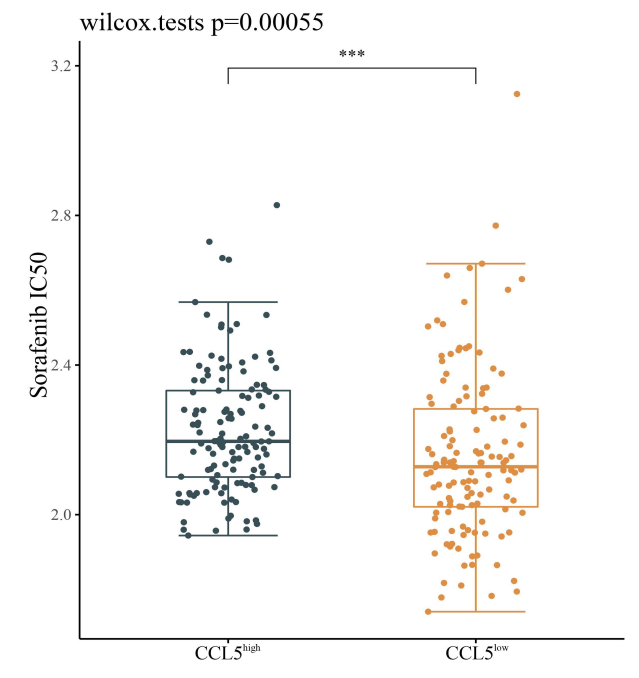

C2
C1
3.38(*)
0
0
3.38(*)
Percentage(%)
100
75
50
25
0
C1
C2
I
II
III
IV

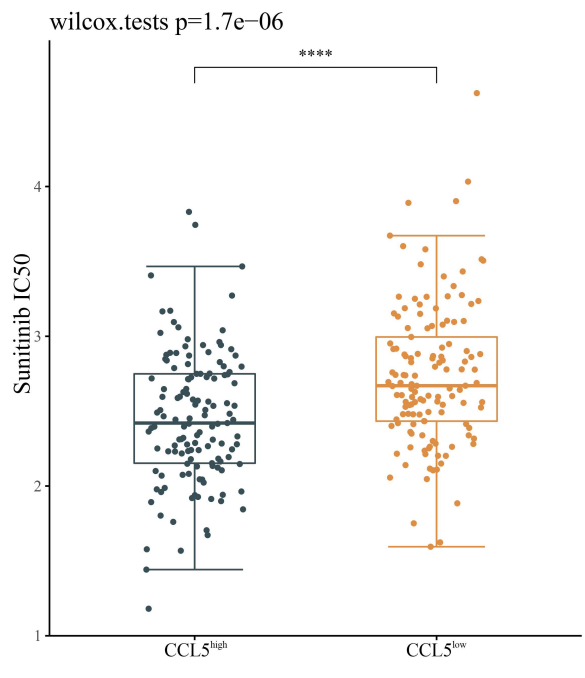

C2
C1
6.16(*)
0
0
6.16(*)
Percentage(%)
100
75
50
25
0
C1
C2
G1
G2
G3
G4

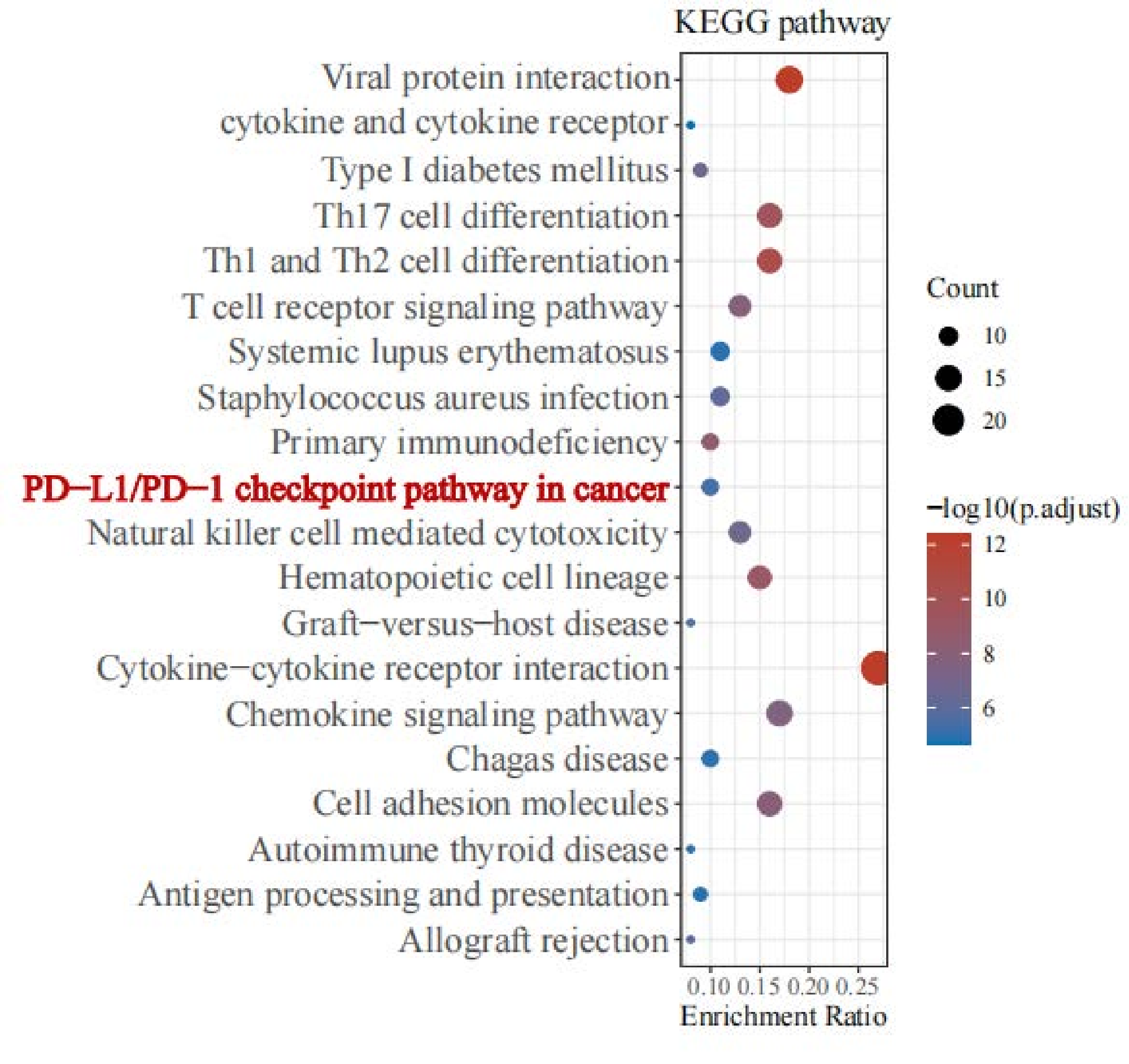

A
Cancer Pvalue Hazard Ratio(95% CI)
ACC 0.487 0.76782(0.36455,1.61722)
BLCA 0.6239 0.92899(0.69207,1.24702)
BRCA 0.0048 0.62842(0.45503,0.86786)
CESC 0.0123 0.54321(0.33694,0.87574)
CHOL 0.3743 0.64467(0.24477,1.69789)
COAD 0.7063 0.9278(0.6283,1.37006)
DLBC 0.4063 0.52549(0.11508,2.39947)
ESCA 0.562 0.86346(0.5257,1.41823)
GBM 0.098 1.36512(0.94417,1.97374)
HNSC 0.0408 0.75574(0.57789,0.98832)
KICH 0.2991 0.47871(0.11919,1.9226)
KIRC 0.0198 1.43495(1.05903,1.94431)
KIRP 0.1808 1.50326(0.82744,2.73105)
LAML 0.0243 1.63348(1.06585,2.50341)
LGG 0.0164 1.54399(1.08274,2.20172)
LIHC 0.3552 0.84964(0.60148,1.20018)
LUAD 0.212 0.83078(0.62092,1.11155)
LUSC 0.8189 0.96889(0.73919,1.26996)
MESO 0.7905 0.93875(0.58885,1.49656)
OV 0.0798 0.79184(0.60984,1.02814)
PAAD 0.6283 1.10738(0.73281,1.6734)
PCPG 0.6066 0.67433(0.15046,3.02217)
PRAD 0.9308 1.05671(0.30426,3.67006)
READ 0.6427 0.82927(0.37598,1.82904)
SARC 0.0189 0.61689(0.41215,0.92335)
SKCM <0.0001 0.55248(0.42026,0.72631)
STAD 0.4152 0.87226(0.62787,1.21177)
TGCT 0.8109 1.27887(0.17049,9.59321)
THCA 0.4003 0.64738(0.23502,1.78327)
UCEC 4e−04 0.4536(0.29371,0.70053)
UCS 0.9116 0.96186(0.48419,1.91079)
UVM 0.0024 4.33667(1.68089,11.18855)
0.1 1 5 0 8 2 3 4 5 6 7 8 9 10 11
Hazard Ratio
B
Cancer Pvalue Hazard Ratio(95% CI)
ACC 0.5294 0.78018(0.35997,1.6909)
BLCA 0.4977 0.88382(0.61853,1.2629)
BRCA 0.0541 0.65434(0.42494,1.00759)
CESC 0.0053 0.44846(0.25526,0.78789)
CHOL 0.4465 0.67412(0.24421,1.86088)
COAD 0.5176 0.84943(0.51814,1.39255)
DLBC 0.6376 0.61869(0.08391,4.56193)
ESCA 0.6832 0.88517(0.49274,1.59016)
GBM 0.0814 1.42385(0.9569,2.11867)
HNSC 0.055 0.71139(0.50239,1.00736)
KICH 0.63 0.69132(0.15396,3.10424)
KIRC 0.0325 1.52514(1.03573,2.2458)
KIRP 0.257 1.54271(0.72898,3.26479)
LGG 0.0221 1.5479(1.06474,2.2503)
LIHC 0.5464 0.87241(0.55989,1.35939)
LUAD 0.3665 0.84244(0.58067,1.22222)
LUSC 0.877 0.96733(0.63519,1.47316)
MESO 0.613 0.85651(0.46995,1.56102)
OV 0.0359 0.73981(0.55824,0.98042)
PAAD 0.5637 1.1469(0.72023,1.82632)
PCPG 0.7582 1.32542(0.22053,7.96607)
PRAD 0.6026 1.61344(0.26652,9.76737)
READ 0.5556 0.72719(0.25207,2.09787)
SARC 0.0293 0.61046(0.39164,0.95155)
SKCM <0.0001 0.5282(0.39391,0.70826)
STAD 0.4079 0.83809(0.55161,1.27334)
TGCT 0.5847 1.95298(0.17708,21.53843)
THCA 0.1147 0.18176(0.02185,1.51228)
UCEC 0.0015 0.41445(0.24035,0.71467)
UCS 0.7143 0.87401(0.42498,1.79747)
UVM 0.0028 4.71352(1.70396,13.03865)
0.02 1 8 5 7.5 10 12.5 15 17.5 20 22
Hazard Ratio
C
Lower Higher NS
Spearman Test (-log10pv)
10 8 6 4 2 0
ACC BLCA BRCA CESC CHOL COAD ESCA HNSC KICH KIRC KIRP LIHC LUAD LUSC MESO OV PAAD READ SKCM STAD TGCT THCA UCEC UCS UVM
D
Lower Higher NS
Spearman Test (-log10pv)
15 12 9 6 3 0
CESC HNSC KIRC LGG LIHC OV PAAD STAD UCEC


wilcox.tests p=0.013
*
Axitinib IC50
5
4
3
2
1
CCL5high
CCL5low


wilcox.tests p=0.2
ns
Pazopanib IC50
5
4
3
CCL5high
CCL5low


wilcox.tests p=0.00055
***
Sorafenib IC50
3.2
2.8
2.4
2.0
CCL5high
CCL5low


wilcox.tests p=1.7e−06
****
Sunitinib IC50
4
3
2
1
CCL5high
CCL5low


KEGG pathway
Viral protein interaction
cytokine and cytokine receptor
Type I diabetes mellitus
Th17 cell differentiation
Th1 and Th2 cell differentiation
T cell receptor signaling pathway
Systemic lupus erythematosus
Staphylococcus aureus infection
Primary immunodeficiency
PD−L1/PD−1 checkpoint pathway in cancer
Natural killer cell mediated cytotoxicity
Hematopoietic cell lineage
Graft−versus−host disease
Cytokine−cytokine receptor interaction
Chemokine signaling pathway
Chagas disease
Cell adhesion molecules
Autoimmune thyroid disease
Antigen processing and presentation
Allograft rejection
0.10 0.15 0.20 0.25
Enrichment Ratio
Count
10
15
20
−log10(p.adjust)
12
10
8
6

**Supplementary Table 2.** Antibodies used in immunohistochemistry, immunofluorescence and flow cytometry assays.

| Markers | Antibody names | Provider | Host | Catalog No. |
|---|---|---|---|---|
| CCL5 | Anti-Human CCL5 Antibody | CST | Rb | 36467 |
| CD68 | Anti-Human CD68 Antibody | Abcam | Ms | ab955 |
| CD45 | APC-Cy7 Anti-Human CD45 Antibody | Biolegend | Ms | 368516 |
| CD45 | PE-Cy7 Anti-Human CD45 Antibody | Biolegend | Ms | 368532 |
| CD14 | FITC Anti-Human CD14 Antibody | BD | Ms | 555397 |
| CD3 | PE-Cy7 anti-human CD3 Antibody | Biolegend | Ms | 100220 |
| CD4 | Brilliant Violet® 421 Anti-Human CD4 Antibody | BD | Ms | 562424 |
| CD8 | BB515 Anti-Human CD8 Antibody | BD | Ms | 564526 |
| CD19 | PerCP/Cy5.5 anti-human CD19 Antibody | Biolegend | Ms | 363016 |
| CD11c | Brilliant Violet® 605 Anti-Human IL-2 Antibody | Biolegend | Ms | 301636 |
| CD80 | PE-Cy7 Anti-Human CD80 Antibody | Biolegend | Ms | 305218 |
| CD86 | Brilliant Violet® 650 Anti-Human CD86 Antibody | Biolegend | Ms | 305428 |
| CD68 | Alexa Fluor® 647 Anti-Human CD68 Antibody | BD | Ms | 562111 |
| PRF-1 | Alexa Fluor® 647 Anti-Human Perforin Antibody | BD | Ms | 563576 |
| CD69 | CD69 (H1.2F3) Hamster mAb (FITC Conjugate) | CST | Rb | 39443 |
| TNF-α | Alexa Fluor® 647 anti-human TNF-α Antibody | Biolegend | Ms | 502916 |
| IFN-γ | IFN-γ (D3H2) XP® Rabbit mAb | CST | Rb | 8455 |
| PD-L1 | PD-L1 (E1L3N®) XP® Rabbit mAb | CST | Rb | 13684 |
| Ki67 | Ki-67 (D3B5) Rabbit mAb | CST | Rb | 9129 |
| GAPDH | GAPDH (D16H11) XP® Rabbit mAb | CST | Rb, Ms | 5174 |
| IgG | Goat Anti-Rabbit IgG conjugated with HRP | Abcam | Rb | ab205718 |
| / | Human Exhausted T Cell Antibody Sampler Kit | CST | Rb, Ms | 81490 |

**Table S3**. Univariate Cox regression analyses of PFS and OS in 290 enrolled ccRCC patients from FUSCC cohort.

| | PFS | | OS | |
|---|---|---|---|---|
| Covariates | HR (95%CI) | *P* value | HR (95%CI) | *P* value |
| Age at surgery | 1.010 (0.996-1.023) | 0.151 | 1.013 (0.999-1.027) | 0.067 |
| BMI ($kg/m^2$) | 0.954 (0.690-1.318) | 0.775 | 0.898 (0.636-1.268) | 0.541 |
| Sex (Ref. Male) | 0.862 (0.623-1.192) | 0.369 | 0.982 (0.700-1.379) | 0.919 |
| Laterality (Ref. left) | 1.071 (0.794-1.444) | 0.653 | 0.922 (0.667-1.274) | 0.623 |
| T stage (T1-T2) | 1.451 (0.814-2.586) | 0.207 | **1.538 (1.006-2.341)** | **0.047** |
| N stage (Ref. N0) | **2.207 (1.384-3.520)** | **0.001** | **2.150 (1.325-3.490)** | **0.002** |
| M stage (Ref. M0) | **1.854 (1.123-3.058)** | **0.016** | **1.735 (1.004-2.998)** | **0.048** |
| ISUP grade (Ref. 1-2) | **2.030 (1.441-2.860)** | **<0.001** | **1.481 (1.017-2.157)** | **0.041** |
| AJCC stage(Ref. I-II) | **2.239 (1.095-4.581)** | **0.027** | **3.480 (1.641-7.382)** | **0.001** |
| CCL5 expression (Ref. Low) | **1.642 (1.209-2.230)** | **0.002** | **1.523 (1.092-2.124)** | **0.013** |

Abbreviations: PFS: progression free survival; OS: overall survival; ccRCC: clear cell renal cell carcinoma; FUSCC, Fudan University Shanghai Cancer Center; HR: hazard ratio; CI: confidence interval; BMI: body mass index; ISUP: International Society of Urological Pathology

**P* value less than 0.05 was considered as statistically significance, and marked in bold.