**Supplementary Figure 1.** Univariate Cox analysis suggested pathological TNM stage, AJCC stages, ISUP grade and HK3 expression as prognostic indicators in 533 ccRCC patients from TCGA cohort.

**Supplementary Figure 2.** HK3 plays an important role in the immune microenvironment of various cancers.
Supplementary Table 1. Univariate Cox logistic regression analysis of PFS and OS in 377 ccRCC patients from FUSCC cohort (PFS: progression-free survival; OS: overall survival; ccRCC: clear cell renal cell carcinoma; FUSCC: Fudan University Shanghai Cancer Center)

| Covariates                  | PFS          |          |          |          | OS          |          |          |
|-----------------------------|--------------|----------|----------|----------|-------------|----------|----------|
|                             | HR           | 95% CI   | P value  | HR       | 95% CI      | P value  |          |
| Age                         | 1.013        | 1.001-1.025 | **0.029** | 1.015    | 1.002-1.028 | **0.027** |
| Lateral                     | 1.029        | 0.783-1.352 | 0.838    | 0.981    | 0.719-1.339 | 0.903    |
| BMI                         | 0.905        | 0.813-1.051 | 0.091    | 0.947    | 0.886-1.011 | 0.076    |
| pT stage (ref. T1-T2)       | 6.555        | 4.790-8.970 | **<0.001** | 7.968    | 5.689-11.160 | **<0.001** |
| pN stage (ref. N0)          | 7.810        | 5.444-11.204 | **<0.001** | 8.929    | 6.052-13.174 | **<0.001** |
| pM stage (ref. M0)          | 7.864        | 5.732-10.790 | **<0.001** | 10.197   | 7.204-14.433 | **<0.001** |
| AJCC stage (ref. I-II)      | 9.670        | 7.027-13.307 | **<0.001** | 12.994   | 9.066-18.624 | **<0.001** |
| ISUP grade (ref. 1-2)       | 2.742        | 2.049-3.670 | **<0.001** | 3.370    | 2.372-4.788 | **<0.001** |
| HK3 expression (ref. Low)   | 2.852        | 2.131-3.817 | **<0.001** | 2.999    | 1.999-4.497 | **<0.001** |