Supplementary Materials

Supplementary Figure 1. Negative control of NKG2A IHC staining and confirmation of NKG2A⁺CD8⁺ T cells and NKG2A⁺NK cells. (A) Negative control of NKG2A IHC staining in ccRCC tissues in ZSHC cohort. (B) Flow cytometry of fresh ccRCC tissues confirmed the existence of NKG2A⁺CD8⁺ T cells and NKG2A⁺NK cells. (C) Fresh ccRCC samples were performed with flow cytometry to assess the expression of NKG2A on CD8⁺ T cells and NK cells. Green boxplots represent CD8⁺ T cells, while red boxplots represent NK cells.

Supplementary Figure 2. Multivariate analysis of NKG2A⁺CD8⁺ T cells infiltration and clinicopathological characteristics. Multivariate analysis revealed NKG2A⁺CD8⁺ T cells infiltration as an independent prognostic factor for OS (black), but not for RFS (blue). Multivariate Cox proportional hazards regression analysis.

Supplementary Figure 3. The immune contexture and genomic alteration based on NKG2A⁺CD8⁺ T cells infiltration. (A) Distribution of various immune cells in different infiltration groups of NKG2A⁺CD8⁺ T cells in ZSHC cohort; Green boxplots represent patients with low infiltration of NKG2A⁺CD8⁺ T cells, while red boxplots represent patients with high infiltration. Mann-Whitney U test. (B) The landscape of genomic alterations according to
NKG2A^+CD8^+ T cells infiltration in TCGA-KIRC. Chi-square test. *P<0.05, **P<0.01, ***P<0.001, ns refers to no significance.

Supplementary Figure 4. CD8^+ T cells infiltration or NKG2A expression alone could not predict prognosis of ccRCC patients treated with Nivolumab or Everolimus in CheckMate cohort. (A-B) OS of patients treated with Nivolumab based on NKG2A expression (A) or CD8^+ T cells infiltration (B). (C-D) OS of patients treated with Everolimus based on NKG2A expression (C) or CD8^+ T cells infiltration (D).

Supplementary Figure 5. Association between NKG2A^+CD8^+ T cells infiltration and previously reported immunotherapy biomarker. Heatmap quantifying the expression level of previously reported biomarker of immunotherapy in CheckMate cohort. Mann-Whitney U test. *P<0.05, **P<0.01, ***P<0.001, ns refers to no significance.

Supplementary Table 1. Therapeutic regimens of patients in ZSHC-mRCC (ICB).

Supplementary Table 2. IHC antibodies information.
Supplementary Table 3. Gene list of NKG2A+CD8+ T cells and NKG2A+NK cells signature

Supplementary Table 4. Flow cytometry antibodies information

Supplementary Table 5. Gene signature and data availability

Supplementary Table 6. Clinical characteristics of patients in ZSHC

Supplementary Table 7. Clinical characteristics of patients in ZSHC-mRCC