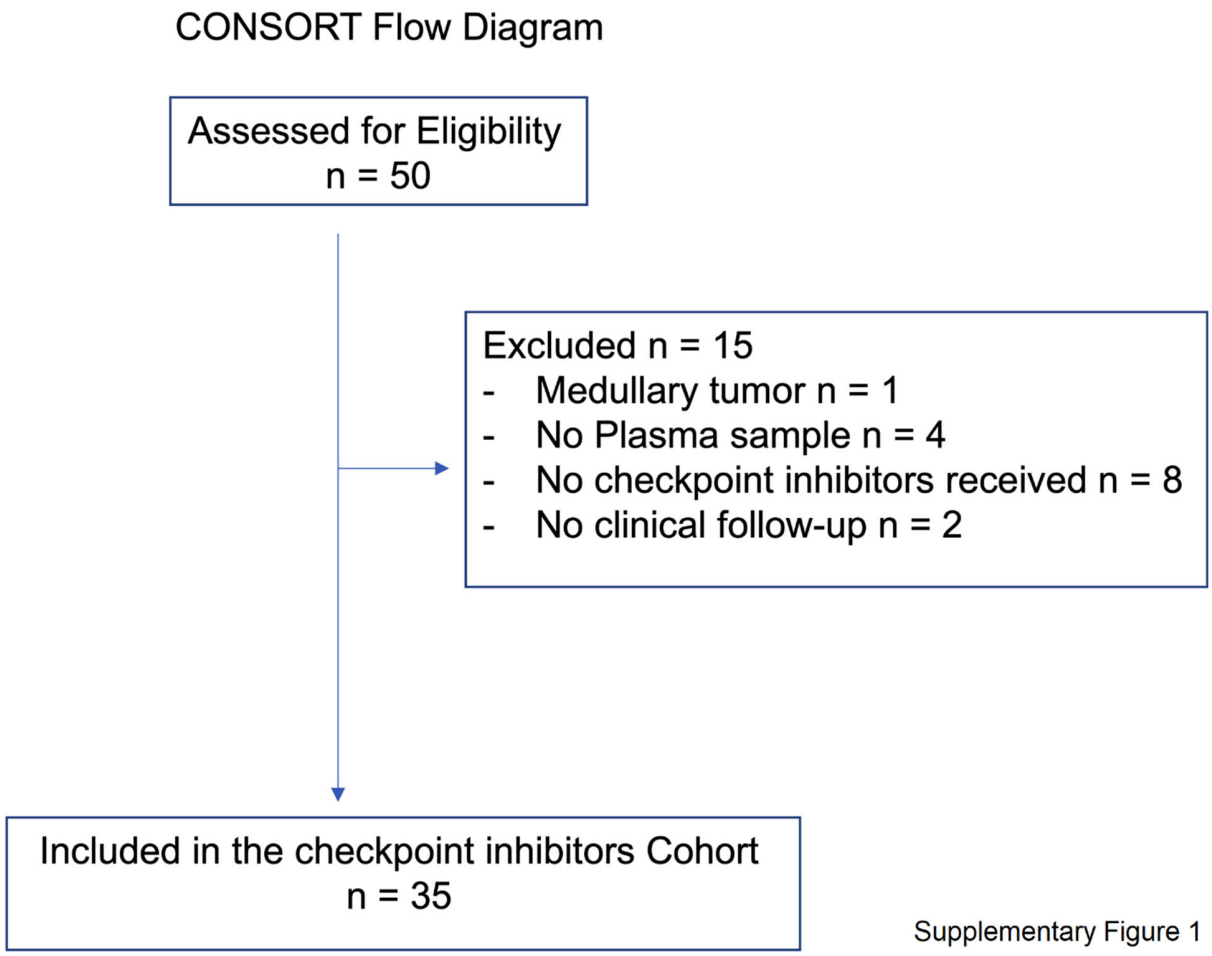
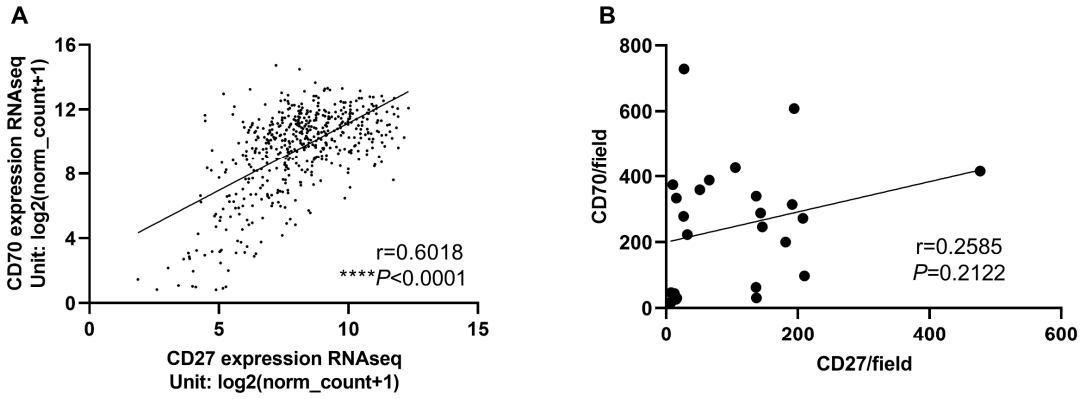


Supplementary Figure 1. Flow chart for inclusion in the immunotherapy Colcheckpoint cohort

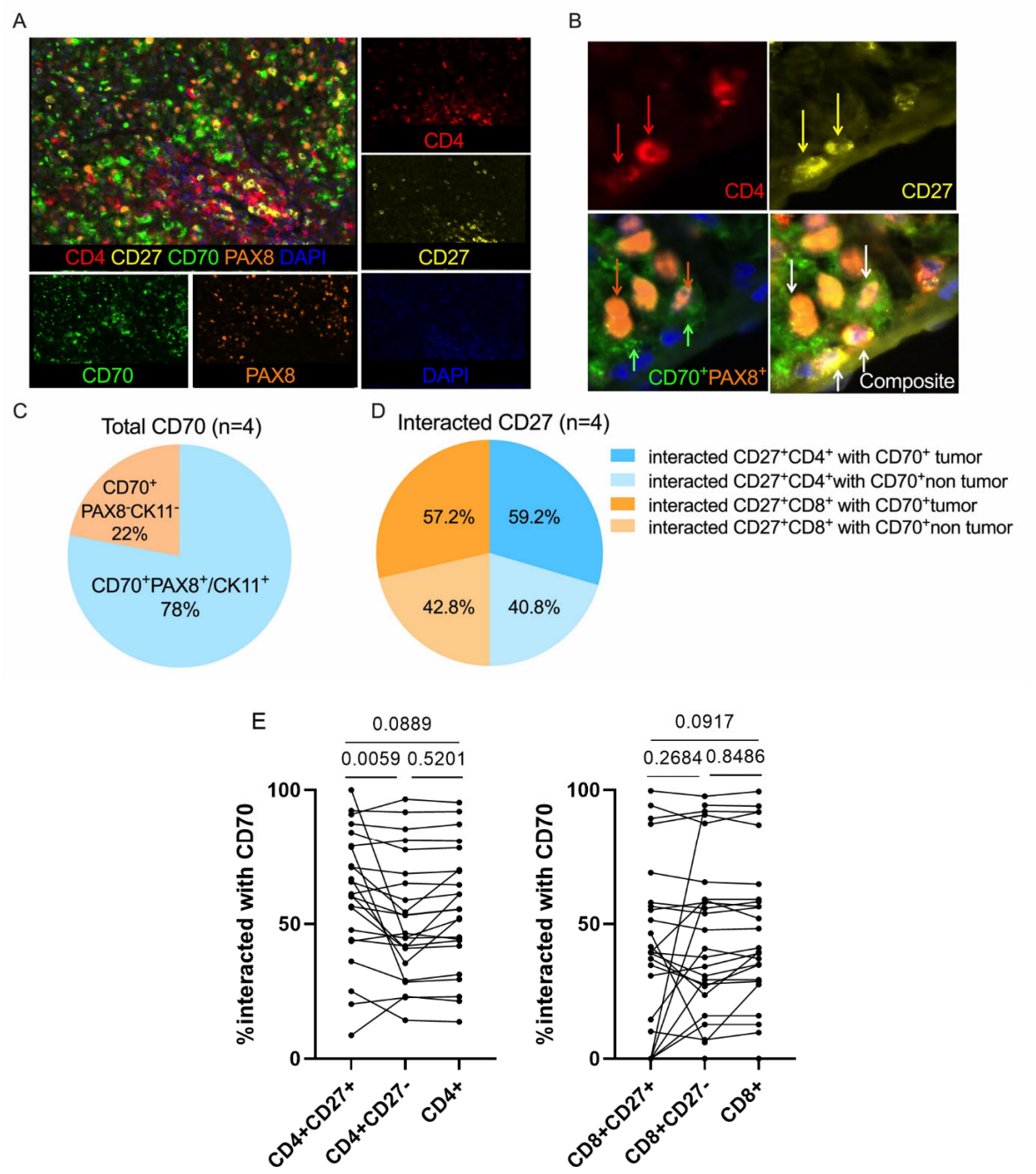
* Only clear cell renal carcinoma and papillary carcinoma were considered for inclusion.



Supplementary figure 2

Supplementary Figure 2 : **Comparative analysis of CD70 and CD27 expression at the mRNA and protein levels**

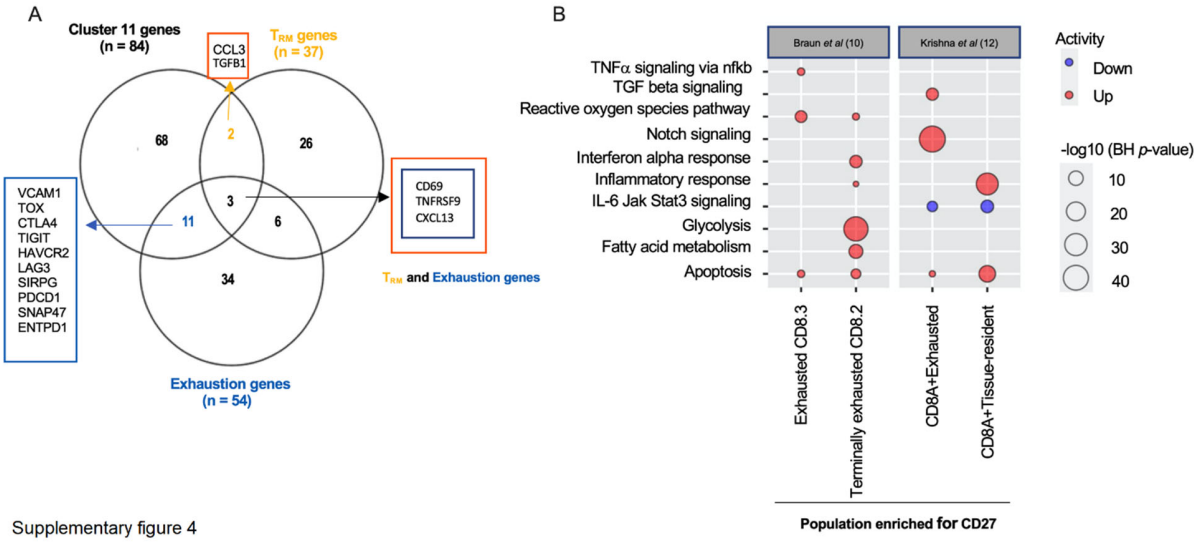
CD70 mRNA and CD27 mRNA expression were plotted from TCGA data base (n = 530 patients) (A). CD70 and CD27 protein expression measured by multiplex in situ immunofluorescence in our series of 25 paients with RCC (B). The Pearson correlation coefficient (r) and significance levels (*p* value) are presented. Values of $p < 0.05$ were considered statistically significant.



Supplementary Figure 3. Interactions of CD27$^+$CD4$^+$ T cells and CD70$^+$ tumor cells in RCC

(A) Representative composite image of 5 fluorescent markers after multispectral imaging and individual markers in the corresponding composite image after spectral unmixing. CD4, red; CD27, yellow; CD70, green; PAX8 (tumor), orange; DAPI, blue. (B) Representative image showing the interaction of CD27-expressing CD4$^+$ T cells with CD70-expressing tumor cells

(CD70⁺PAX8⁺). (C) Average distribution of CD70 expression on PAX8⁺ and/or CK11⁺ tumor cells and nontumor cells (CD70⁺PAX8⁻CK11⁻) in RCC patients (n = 4). (D) Percentages of CD27-expressing CD4⁺ or CD8⁺ cells interacting with CD70⁺ tumor cells (CD70⁺PAX8⁺CK11⁺) and CD70⁺ nontumor cells (CD70⁺PAX8⁻CK11⁻) in RCC patients (n = 4). (E) Specificity of CD27-CD70 interaction by multiplex immunofluorescence analysis. Percentages of CD4⁺CD27⁺, CD4⁺CD27⁻, CD4⁺ T cells and CD8⁺CD27⁺, CD8⁺CD27⁻ and CD8⁺ T cells interacting with CD70⁺ cells in RCC patients. One-way ANOVA was used for statistical analysis. Adjusted P value is presented.

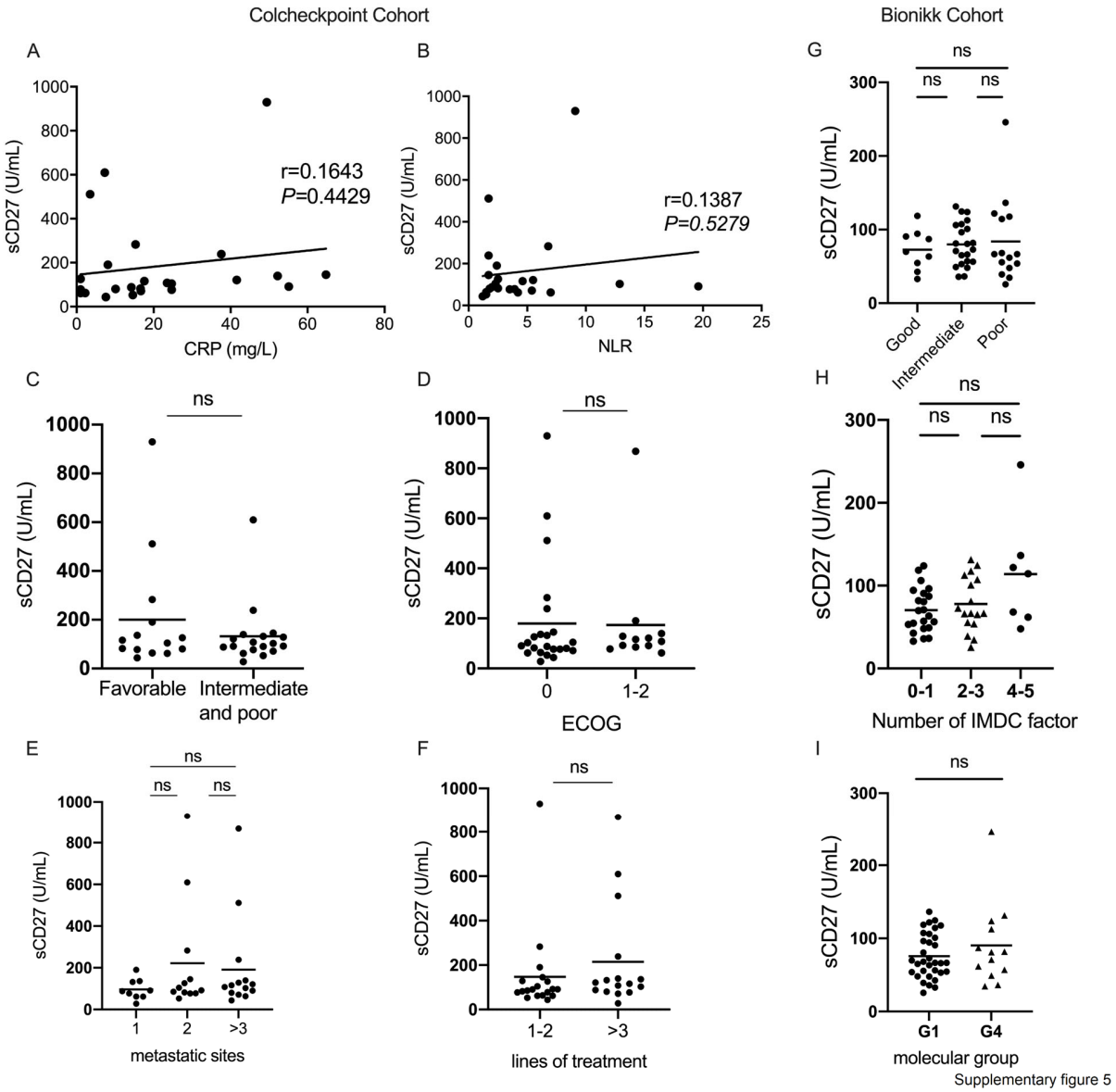


Supplementary figure 4

Supplementary Figure 4. Genes preferentially expressed in Cluster 11 and the apoptotic nature of CD27⁺CD8⁺ T cells identified by public gene dataset analysis

A. Venn diagram analysis (Venny 2.1) of genes significantly upregulated in Cluster 11 (*p* value BH corrected < 0.05) indicated that 14 of the genes corresponded to exhaustion-related genes and 5 corresponded to resident memory T-cell genes. Note that 3 upregulated genes overlapped between exhausted and resident memory T cells.

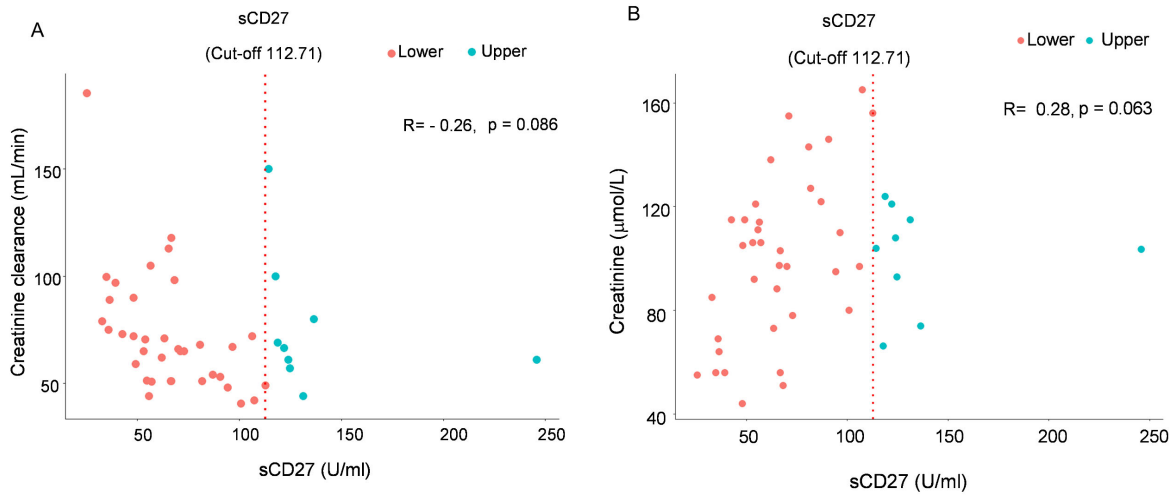
B. Gene set analysis performed on the Braun *et al.* [18] (left) and Krishna *et al. [19]*. datasets (right) using ssGSEA. Bubble size represents the significant (BH adjusted *p* value) activities of hallmark gene sets focused on CD8⁺ T-cell populations (pairwise limma eBayes tests and combined using the function combineMarkers of the package scran).



Supplementary Figure 5. sCD27 is independent of inflammation and other clinical risk factors

Colcheckpoint cohort (A-F): sCD27 was plotted against C Reactive Protein (CRP) (A) and the neutrophil-to-lymphocyte ratio (NLR) (B) in RCC patients. The Pearson correlation coefficient (r) and significance levels (*p* value) are presented. (C) sCD27 levels in RCC patients with favorable and intermediate or poor prognostic outcomes according to the MSKCC risk factor model (n = 32). (D) sCD27 levels in RCC patients according to ECOG performance scores (n = 35). (E) sCD27 levels in RCC patients according to metastatic sites (n = 35). (F) sCD27 levels in RCC patients who received checkpoint inhibitor treatment as different lines of therapy (n = 35).

BIONIKK cohort (G-I): sCD27 levels in RCC patients according to the International Metastatic RCC Database Consortium (IMDC) risk score (G), number of IMDC factors (H) and molecular group stratified by the RNA signature (I). The data are shown as dots with the mean indicated. Significance was determined by an unpaired *t* test. Values of $p < 0.05$ were considered statistically significant.



Supplementary figure 6

Supplementary Figure 6 : Correlation between plasma sCD27 concentrations and kidney function

Plasma sCD27 concentrations were plotted with two parameters reflecting kidney function: creatinine clearance (A) and plasma creatinine (B).

46 plasmas obtained from patients included in the BIONIKK trial before anti-PD-1 treatment were tested for sCD27 and creatinine. Statistical analysis was done with the Pearson's correlation coefficient and correlation test were performed (coefficient and p-value shown on each panel)