

**Figure S6**. Interactions between T and myeloid cell populations, related to **Figure 6**. (**A**) Heatmap of pairwise correlation of the proportion of each T cell cluster (relative to total T cells per sample) and myeloid cell cluster (relative to total myeloid cells per cluster) across all samples (Spearman correlation). (**B**) All significant interactions between the PMCH<sup>+</sup> terminally exhausted CD8<sup>+</sup> T cell population (T cell population most enriched in metastatic disease) and the 'TAM.1', 'TAM.2', and 'CD14<sup>+</sup> Monocyte.3' populations (myeloid populations most enriched in metastatic disease), used to derive an interaction gene signature for subsequent analysis in bulk RNA-seq data. (**C**) Flow cytometry of intratumoral cells and healthy donor PBMCs (negative control). The proportion of each CD8<sup>+</sup> T cell population that expresses CTLA4, or of each CD14<sup>+</sup> myeloid population that expresses PD-L1. For CD86 expression on CD14<sup>+</sup> myeloid cells, median fluorescence intensity (MFI) was used because not clearly distinct CD86<sup>+</sup> population could be gated. (two-sided Wilcoxon rank-sum test for pair-wise comparison between the dysfunctional immune population of interest, orange, and the negative controls from healthy donor PBMCs, purple). (**D**) The average proportion of CD163<sup>+</sup> M2-like receptors expressing the specified ligand (PD-L1, PD-L2, Galectin-9, or PVR; out of all CD14<sup>+</sup> myeloid cells) and of PD-1<sup>+</sup> TIM-3<sup>+</sup> terminally exhausted CD8<sup>+</sup> T cells expressing the cognate receptor (PD-1, TIM-3, or TIGIT, out of all CD8<sup>+</sup> T cells), for normal kidney or early stage cCRCC and for locally advanced or metastatic cCRCC, by flow cytometry (two-sided Wilcoxon rank-sum test). (**E**) Multiplex immunofluorescence analysis showing the average density of PD-1<sup>+</sup> TIM-3<sup>+</sup> terminally exhausted CD8<sup>+</sup> T cells and CD163<sup>+</sup> M2-like macrophages. PBMCs: peripheral blood mononuclear cells. For boxplots, hinges are 25th to 75th percentiles; central lines are medians, whiskers are highest and lowest values no greater than 1.5x interquartil