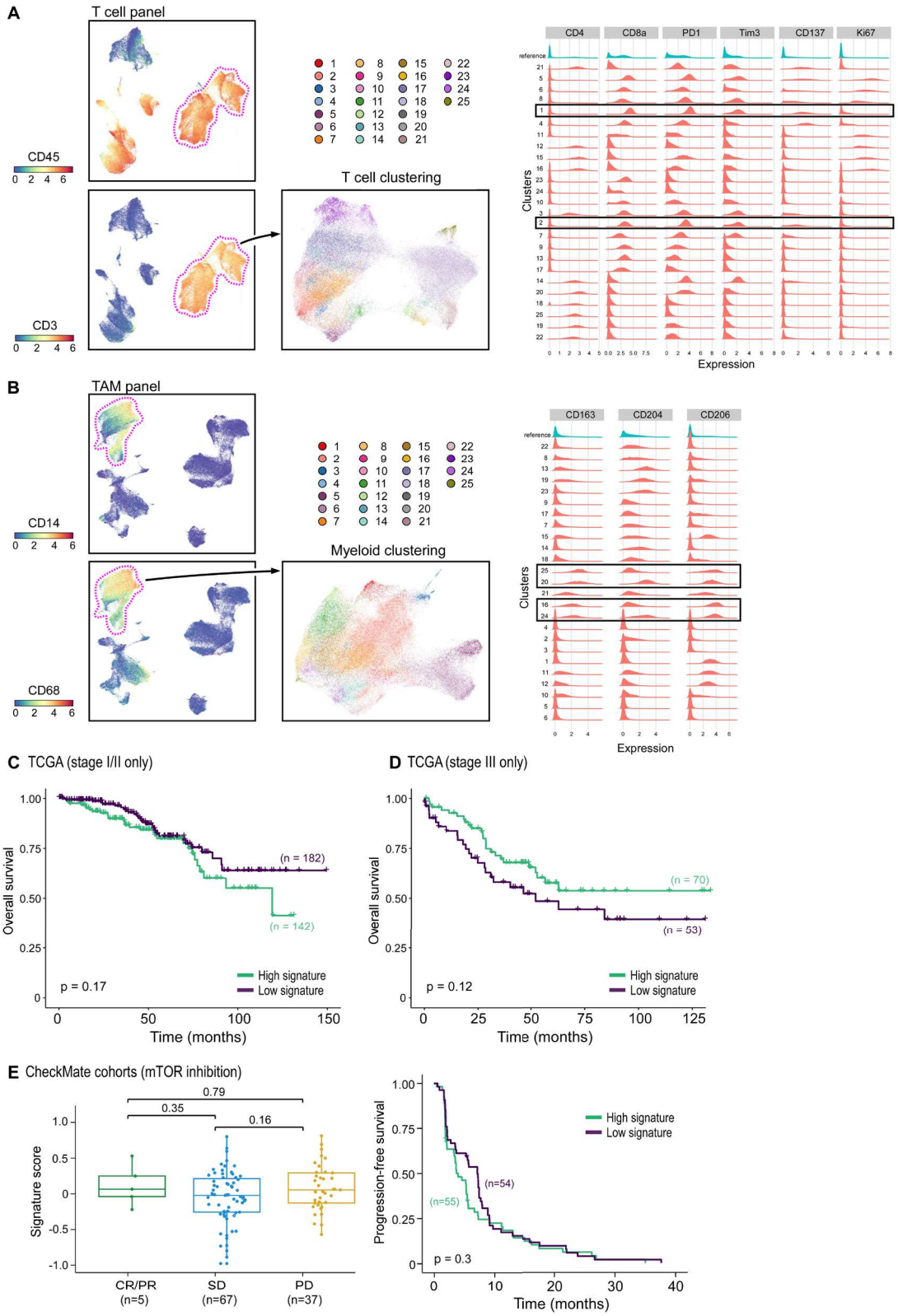


**Figure S7**. Analysis of dysfunctional immune populations in external cohorts, related to **Figure 7**. **(A-B)** Analysis of previously generated mass cytometry data from ccRCC tumors (and normal kidney samples), from Chevrier et al., 2017. **A,** Gating for the T cell panel. An initial clustering step was performed to identify CD45$^+$ CD3$^+$ T cells. T cells were then re-clustered, and terminally exhausted CD8$^+$ T cell clusters were selected based on expression of CD8, PD-1, TIM-3, CD137, and absence of CD4 or KI-67 expression. **B,** Gating for the TAM panel. An initial clustering step was performed to identify myeloid cells, expressing, for example, markers such as CD14 and CD68. Myeloid cells were then re-clustered, and M2-like macrophages were selected based on high expression of CD163 (they also expressed other M2-like markers, including CD204 or CD206). For **(C)** stage I/II and **(D)** stage III ccRCC tumors from the TCGA KIRC cohort, there was no significant difference in overall survival in patient with tumors that had a high terminal exhaustion/TAM interaction gene signature (≥ median) vs. low signature. **(E)** Gene expression signature analysis of tumors from the CheckMate cohorts of advanced ccRCC revealed no association of the terminal exhaustion / TAM interaction signature with response (two-sided Wilcoxon rank-sum test; boxplots hinges are 25th to 75th percentiles; central lines are medians, whiskers are highest and lowest values no greater than 1.5x interquartile range, and dots are outliers) or progression free survival (two-sided log-rank test) following treatment with mTOR inhibition. CR/PR: complete response/partial response; SD: stable disease; PD: progressive disease.