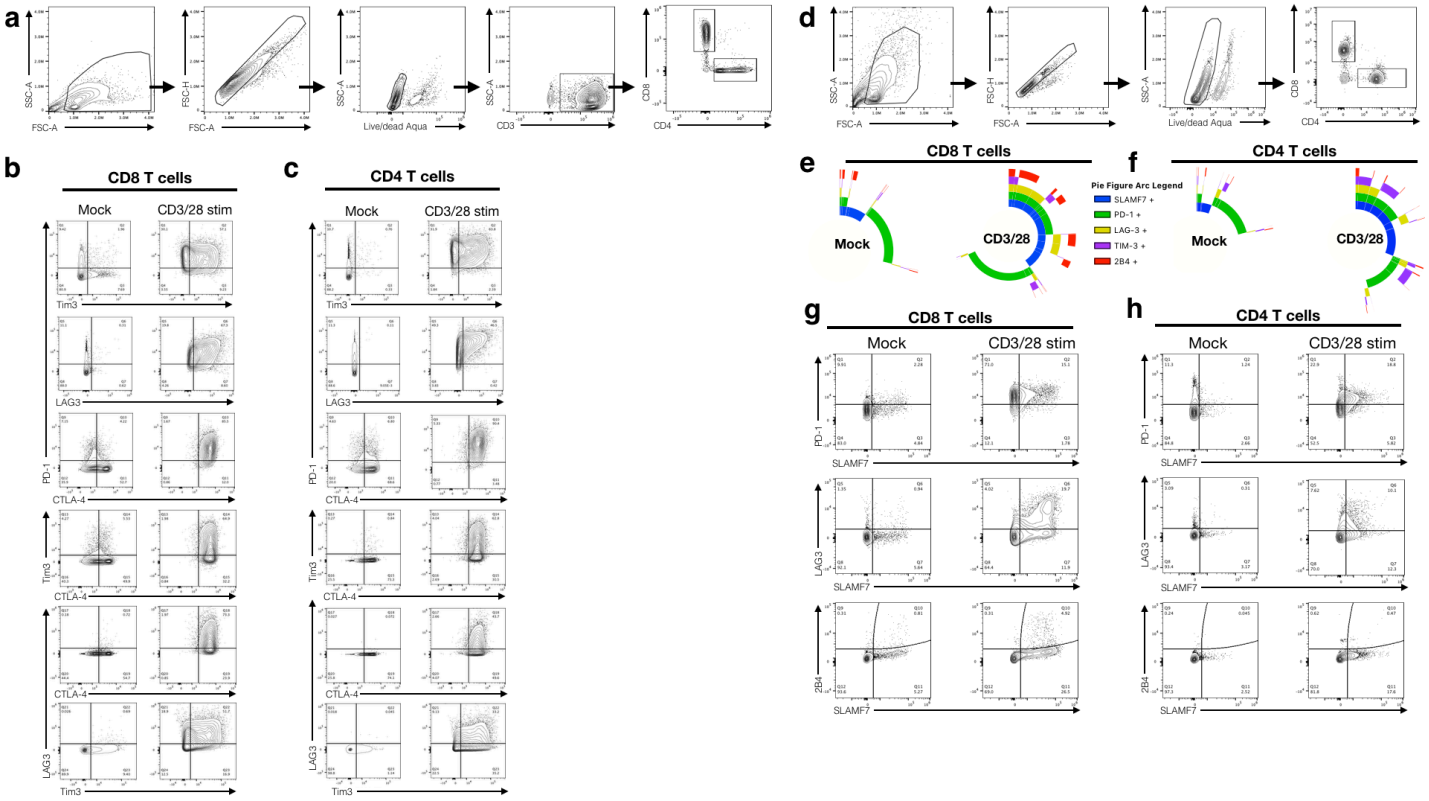
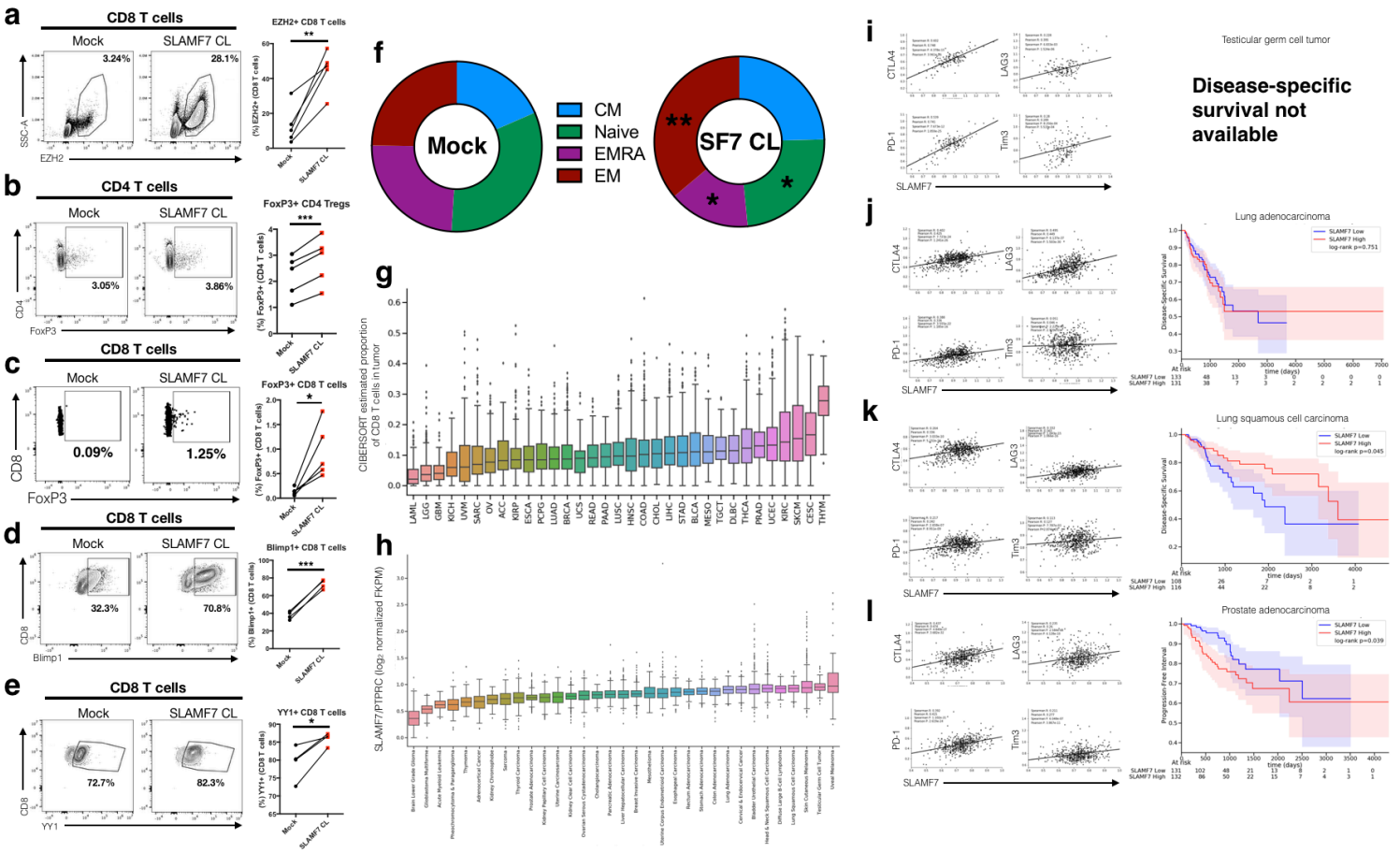
Supplemental figures



Supplemental Fig. 1

(A) Gating scheme used for assessing T cells in **Fig. 1**.
(B) Co-expression of all combinations of exhaustion markers on CD8⁺ human T cells.
(C) Co-expression of all combinations of exhaustion markers on CD4⁺ human T cells.
(D) Gating scheme used for assessing murine T cells.
(E) SPICE plots of mouse CD8⁺ T cells Mock or CD3/28 stimulated *in vitro* for 6 days. Plots are pooled results from (n=2) mice.
(F) SPICE plots of mouse CD4⁺ T cells Mock or CD3/28 stimulated *in vitro* for 3 days. Plots are pooled results from (n=2) mice.
(G, H) Representative biaxial plots showing SLAMF7 co-expression with exhaustion markers on CD8⁺ (G) and CD4⁺ (H) T cells.
Results in (D-H) are from a single experiment.



Supplemental Fig. 2

(A) Changes in EZH2 expression in Mock and SLAMF7 activated primary human CD8⁺ T cells following 6 days of *in vitro* stimulation.

(B) Changes in FoxP3 expression in CD4⁺ primary human T cells following 6 days of *in vitro* stimulation. (C) Changes in FoxP3 expression in Mock and SLAMF7 activated primary human CD8⁺ T cells following 6 days of *in vitro* stimulation.

(D) Changes in Blimp1 expression in Mock and SLAMF7 activated primary human CD8⁺ T cells following 6 days of *in vitro* stimulation.

(E) Changes in YY1 expression in Mock and SLAMF7 activated primary human CD8⁺ T cells following 6 days of *in vitro* stimulation.

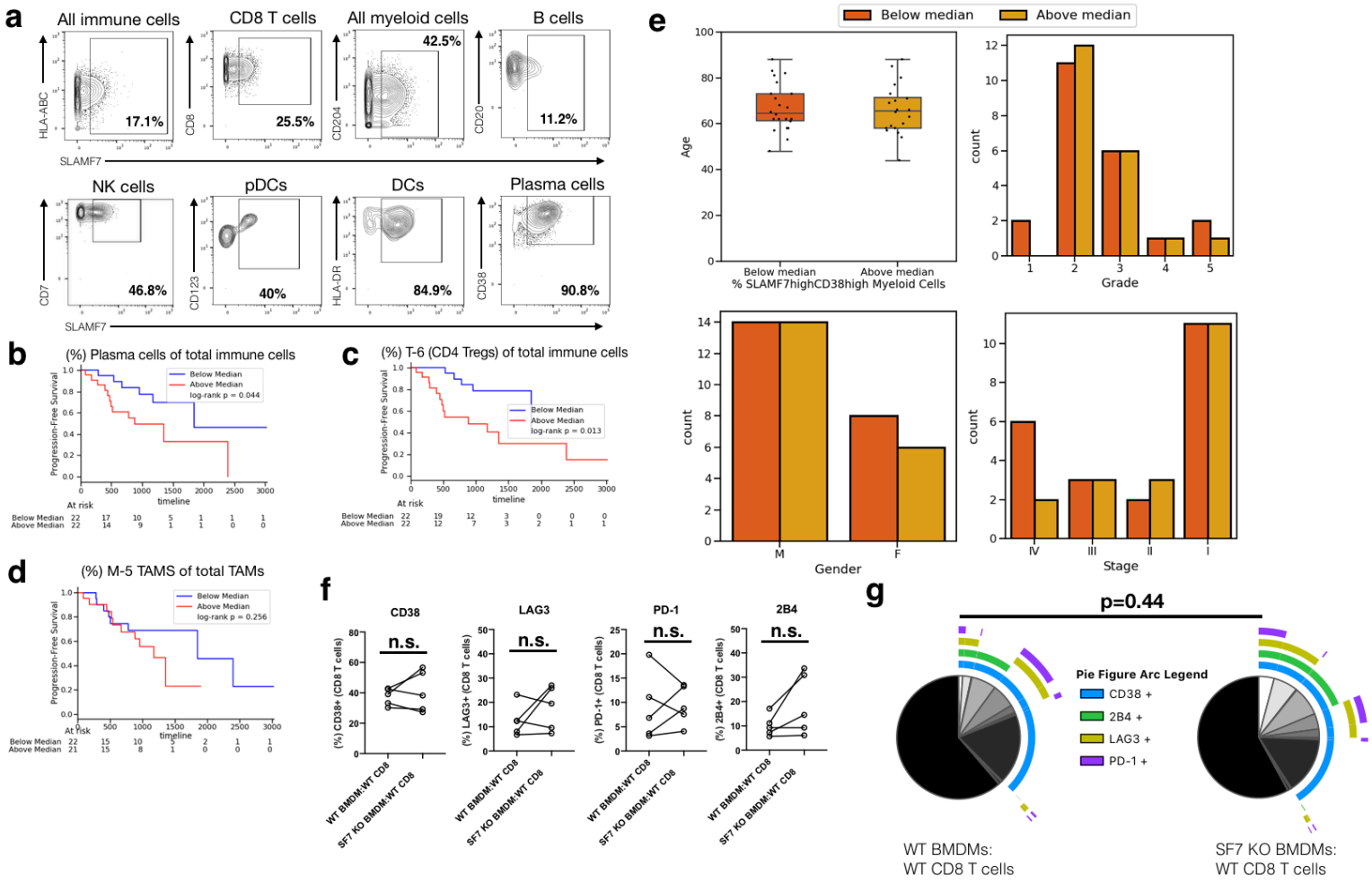
(F) Changes in primary human CD8⁺ T cell subsets following 6 days of SLAMF7 activation. Results shown are the averages of three individual donors run in duplicate. Asterisks in the SF7 CL donut graph indicate significant changes from Mock.

(G) CIBERSORT-generated estimations of CD8⁺ T cell compositions from bulk RNA-seq data from TCGA participants was acquired from the Genomic Data Commons (GDC). TCGA abbreviations are available at: https://gdc.cancer.gov/resources-tcga-users/tcga-code-tables/tcga-study-abbreviations.

(H) *SLAMF7* $\log_2$ FKPM mRNA expression was divided by *PTPRC* $\log_2$ FKPM mRNA expression to normalize for total immune cell contributions, and results were plotted for all TCGA participants by cancer type.

(I-L) Left, co-expression of SLAMF7 mRNA with various exhaustion marker mRNA from Testicular Germ Cell Tumor (n=139) (I), Lung Adenocarcinoma (n=539) (J), Lung Squamous Cell Carcinoma (n=490) (K), and Prostate Adenocarcinoma (n=550) (L), displayed as in **Figure 5**. Right, Kaplan-Meier curves showing disease specific survival for the top and bottom SLAMF7 expressing quartiles in Lung Adenocarcinoma (J) and Lung Squamous Cell Carcinoma (K). Prostate Adenocarcinoma (L) is shown as progression free survival. Accurate, disease specific survival data not available for Testicular Germ Cell Tumor (I). Log-rank test is used to compare groups in (I-L) and shaded regions represent 95% confidence interval. Center line in box plots represents the median, the entire box represents the first and fourth quartiles, and the whiskers show the min and max, excluding outliers.

Results in (A-E) are from a single experiment, representative of 5 independent experiments (A, B, D, E) or 3 independent experiments (C). Groups in (A-E) compared using a two-way paired student's t-test. Groups in (F) compared using a two-way ANOVA with Sidak's multiple comparison test. *p<0.05; **p<0.01; ***p<0.001.



Supplemental Fig. 3

(A) Representative gates of SLAMF7^{+} cells from various immune cell types from Chevrier et al., 2017 CyTOF dataset.
(B-D) Kaplan-Meier progression free survival curves with ccRCC patients stratified by percent of plasma cells from total immune cells (B), percent total CD4^{+} Tregs from total immune cells (C), and percent total M-5 TAMs per total TAMs (D). Log-rank test is used to compare groups in (B-D).
(E) Demographic and clinical parameter comparison between ccRCC patients in the “above median” and “below median” groups of patients stratified by SLAMF7^{high}CD38^{high} TAMs shown in **Figure 6e**.
(F) Changes in expression of exhaustion markers on CD8^{+} T cells from co-cultured with bone marrow-derived macrophages (BMDMs) from WT or SLAMF7$^{-/-}$ mice (n=5). Groups compared using a paired student’s t-test. (G) SPICE plots of data from (F) compared using Permutation test.

Rank	Population 1	Population 2	Spearman Coefficient	Pearson Coefficient	P-value
1	T-0	SF7^{high}CD38^{high} TAMs	0.71	0.78	1.02E-15
2	T-0	SF7+ Myeloid cells	0.67	0.77	2.03E-15
3	T-0	SF7+ M-2 TAMs	0.56	0.69	3.65E-11
4	T-0	SF7+ M-1 TAMs	0.59	0.67	1.5E-09
5	T-0	SF7+ M-0 TAMs	0.53	0.64	2.91E-09
6	T-0	SF7+ all immune cells	0.63	0.63	1.49E-09
7	T-1	SF7+ Myeloid cells	0.57	0.58	6.29E-08
8	T-0	SF7+ M-3 TAMs	0.52	0.55	9.46E-07
9	T-1	SF7^{high}CD38^{high} TAMs	0.59	0.52	2.49E-06
10	T-1	SF7+ M-0 TAMs	0.47	0.47	3.96E-05
1	T-4	SF7+ NK cells	-0.61	-0.69	1.03E-11
2	T-4	SF7+ DN T cells	-0.54	-0.62	3.7E-09
3	T-4	SF7+ CD8 T cells	-0.49	-0.59	2.93E-08
4	T-3	SF7+ M-2 TAMs	-0.58	-0.57	2.08E-07
5	T-4	SF7+ all immune cells	-0.55	-0.56	1.84E-07
6	T-3	SF7+ Myeloid cells	-0.52	-0.54	8E-07
7	T-3	SF7+ M-8 TAMs	-0.44	-0.49	3.42E-05
8	T-3	SF7+ all immune cells	-0.45	-0.47	2.11E-05
9	T-3	SF7+ M-10 TAMs	-0.42	-0.47	3.61E-05
10	T-3	SF7^{high}CD38^{high} TAMs	-0.49	-0.47	3.78E-05

Supplementary Table 1. Top 10 positive and negative correlations between SLAMF7^{+} cell populations and T cell subsets ranked by Pearson coefficient. Related to Figure 6c.