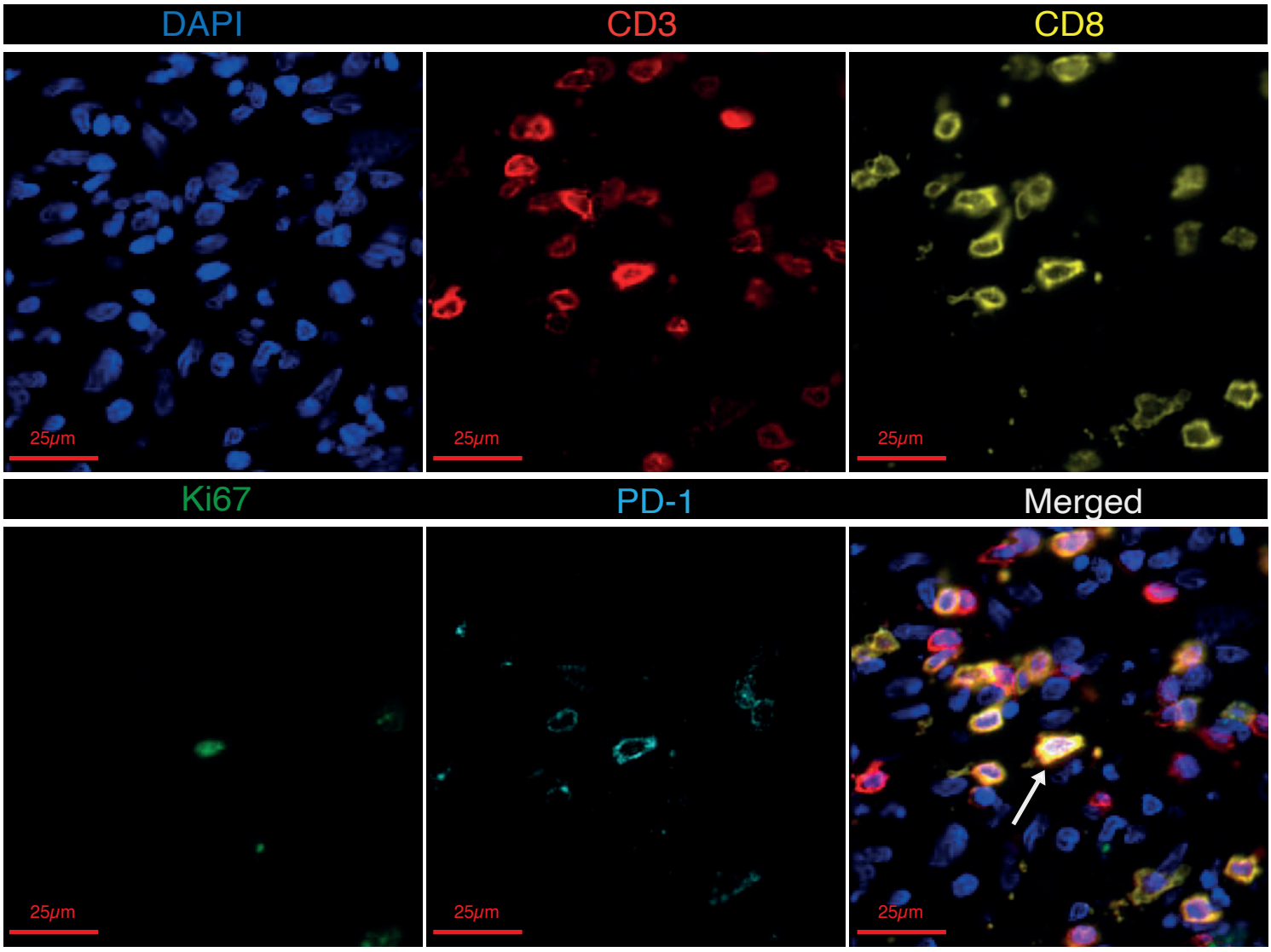
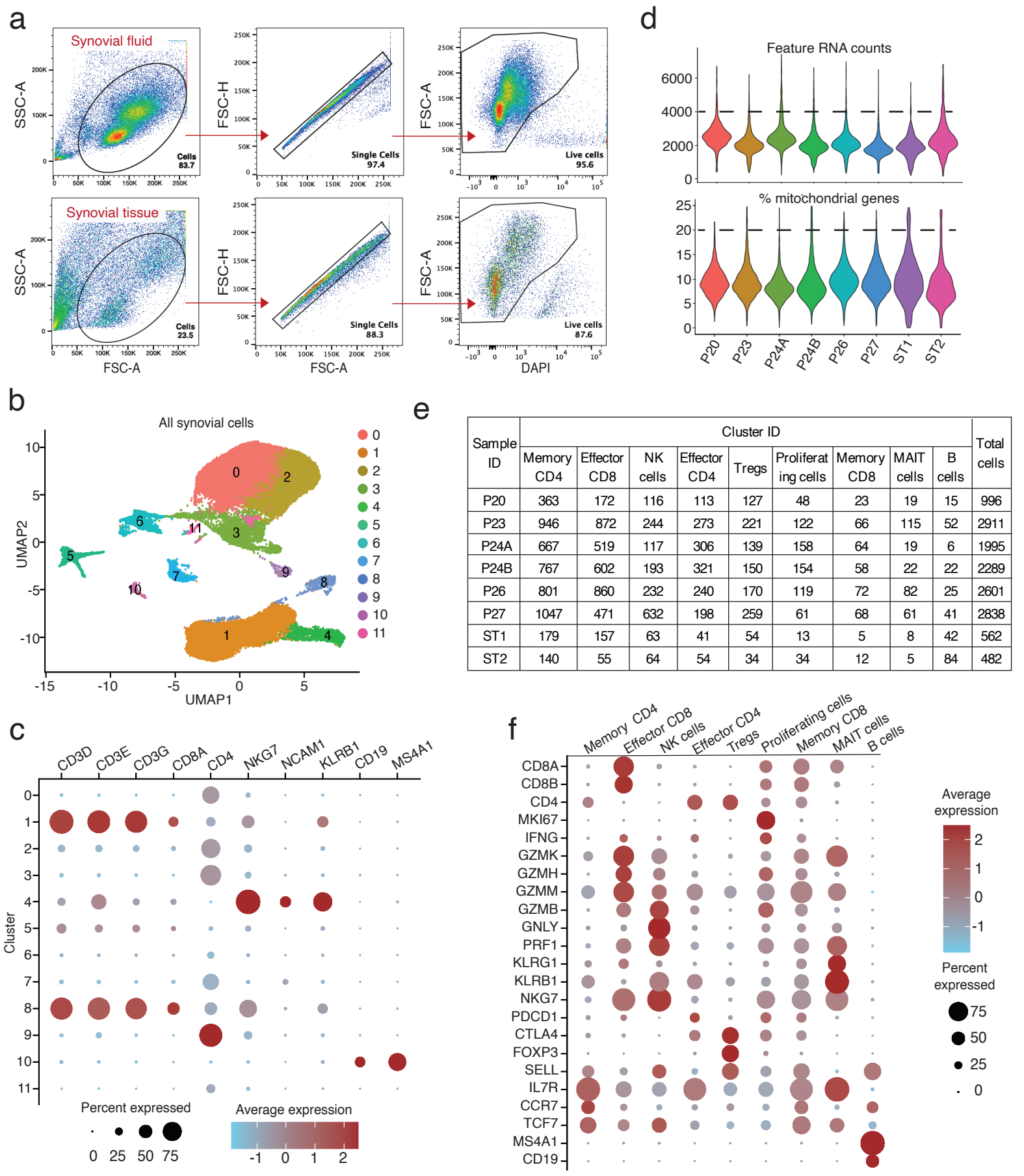


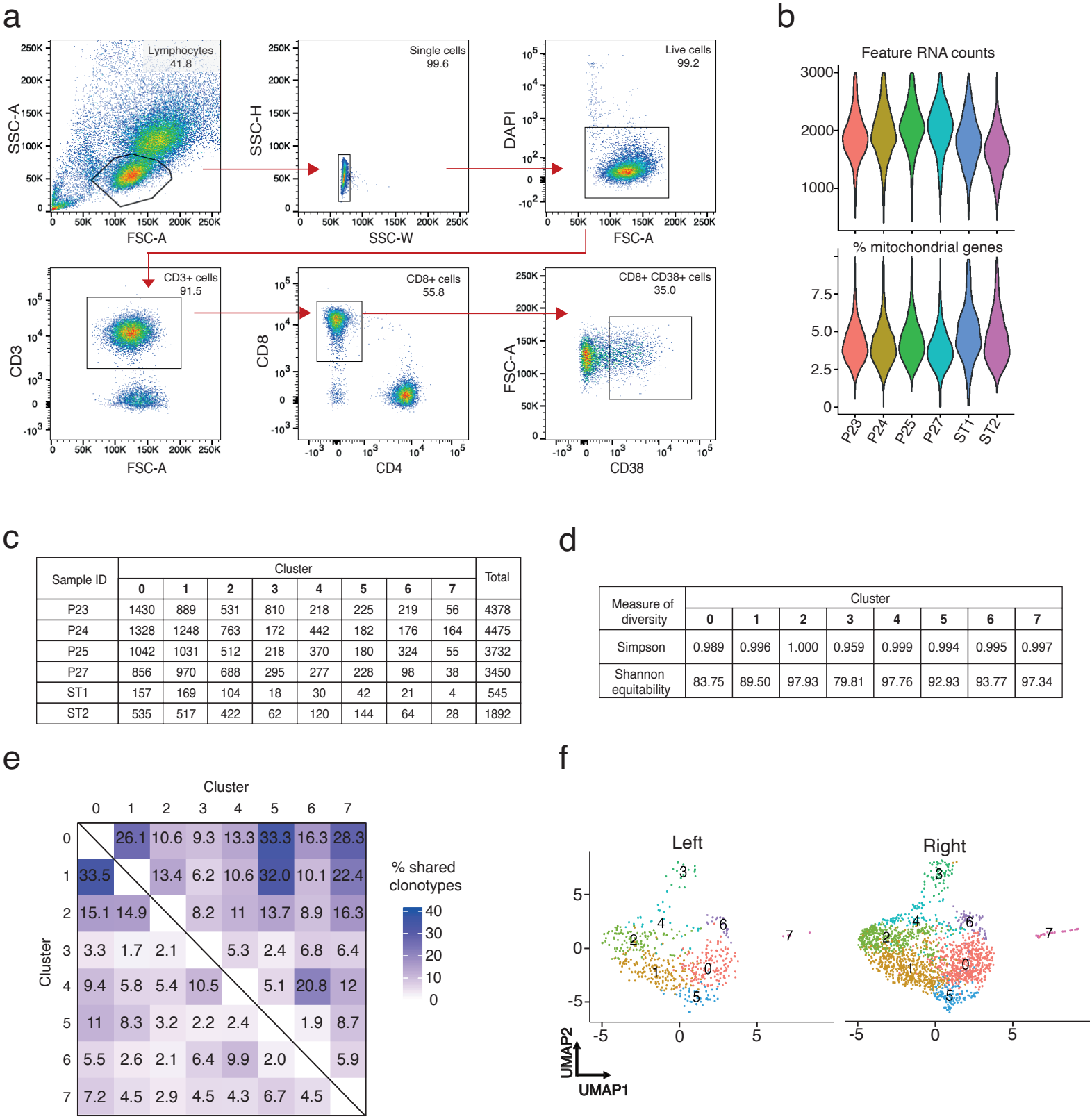
Supplementary figure 1. Multiplexed immunofluorescence of synovial tissue.
Multiplexed immunofluorescence images showing an example of a $Ki67^{+}PD\text{-}1^{+}$ synovial CD8 T cell (white arrow). CD3 staining is shown in red, CD8 in yellow, nuclear stain DAPI in blue, Ki67 in green and PD-1 in cyan.



e

Sample ID	Cluster ID									Total cells
	Memory CD4	Effector CD8	NK cells	Effector CD4	Tregs	Proliferating cells	Memory CD8	MAIT cells	B cells	
P20	363	172	116	113	127	48	23	19	15	996
P23	946	872	244	273	221	122	66	115	52	2911
P24A	667	519	117	306	139	158	64	19	6	1995
P24B	767	602	193	321	150	154	58	22	22	2289
P26	801	860	232	240	170	119	72	82	25	2601
P27	1047	471	632	198	259	61	68	61	41	2838
ST1	179	157	63	41	54	13	5	8	42	562
ST2	140	55	64	54	34	34	12	5	84	482

Supplementary figure 2. Single-cell gene expression analysis of live lymphocytes from ICI-arthritis synovium. **a)** Gating scheme of isolation of live immune cells from ICI-arthritis synovium for scRNA-seq. **b)** UMAP visualization of all live cells from synovial samples that resolved into 12 different cell types. **c)** Dotplot visualization of differentially expressed genes that distinguish lymphocyte markers from other cell types. Color of the dot represents the average expression of the gene across cells in the cluster. Size of the dot represents the percentage of cells in the cluster with that gene detected. **d)** Distribution of all lymphocytes; cells with<4,000 total genes (feature RNA counts) and <20% mitochondrial genes were included in the analysis. **e)** Tabulation of QC filtered lymphocyte numbers contributing to nine distinct clusters from each individual patient. **f)** Dotplot visualization of differentially expressed genes that distinguish lymphocyte clusters.



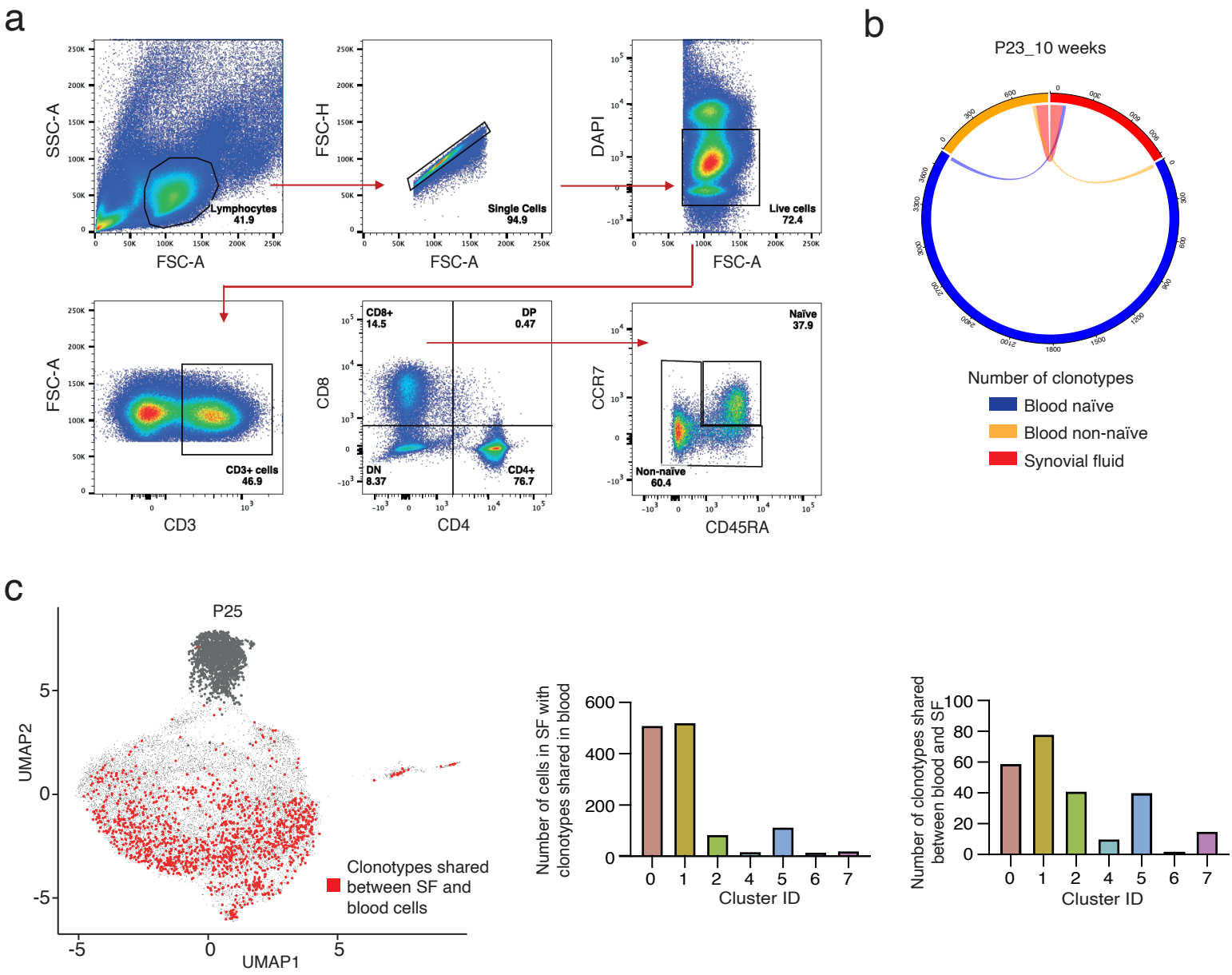
c

Sample ID	Cluster								Total
	0	1	2	3	4	5	6	7	
P23	1430	889	531	810	218	225	219	56	4378
P24	1328	1248	763	172	442	182	176	164	4475
P25	1042	1031	512	218	370	180	324	55	3732
P27	856	970	688	295	277	228	98	38	3450
ST1	157	169	104	18	30	42	21	4	545
ST2	535	517	422	62	120	144	64	28	1892

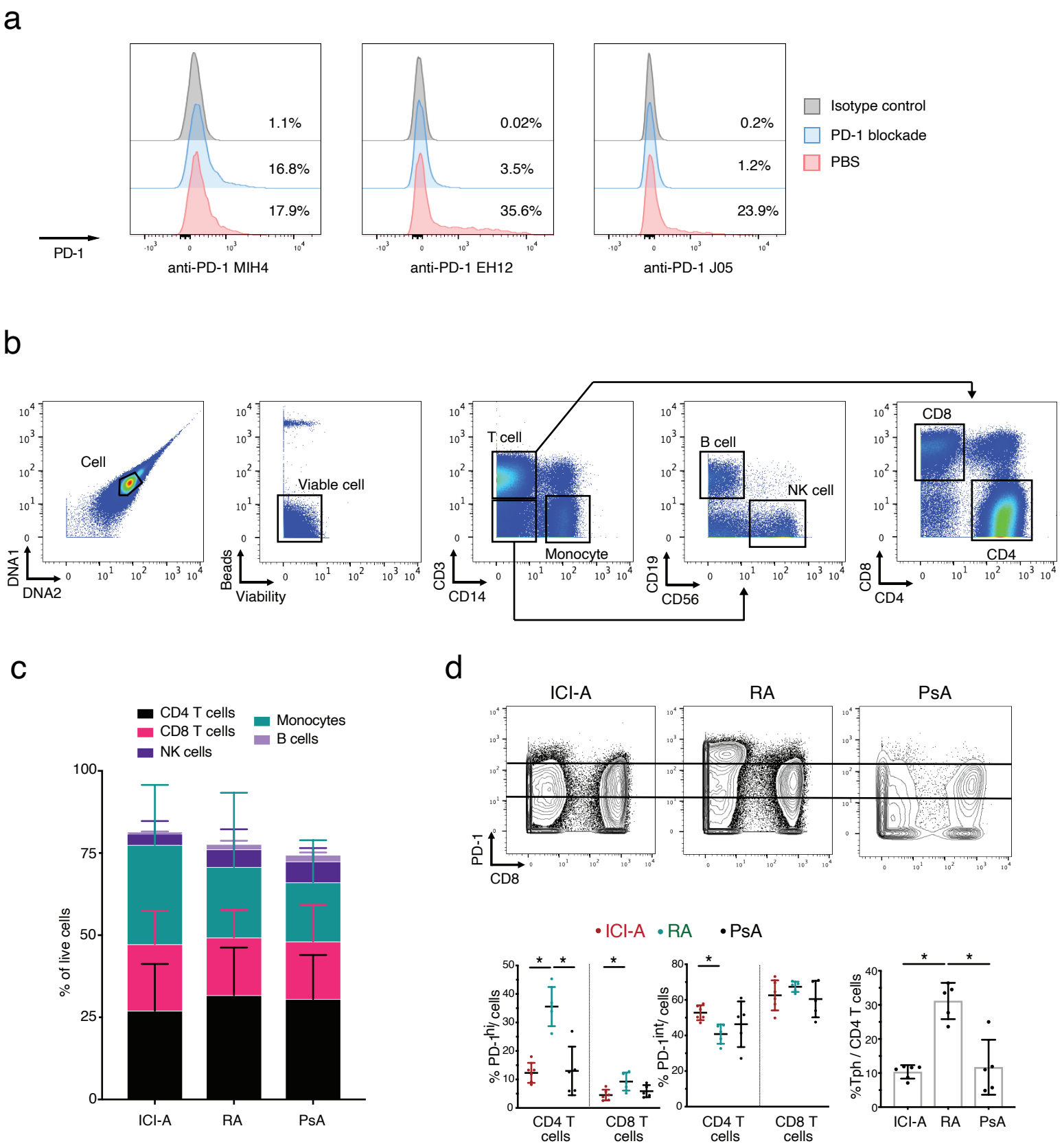
d

Measure of diversity	Cluster							
	0	1	2	3	4	5	6	7
Simpson	0.989	0.996	1.000	0.959	0.999	0.994	0.995	0.997
Shannon equitability	83.75	89.50	97.93	79.81	97.76	92.93	93.77	97.34

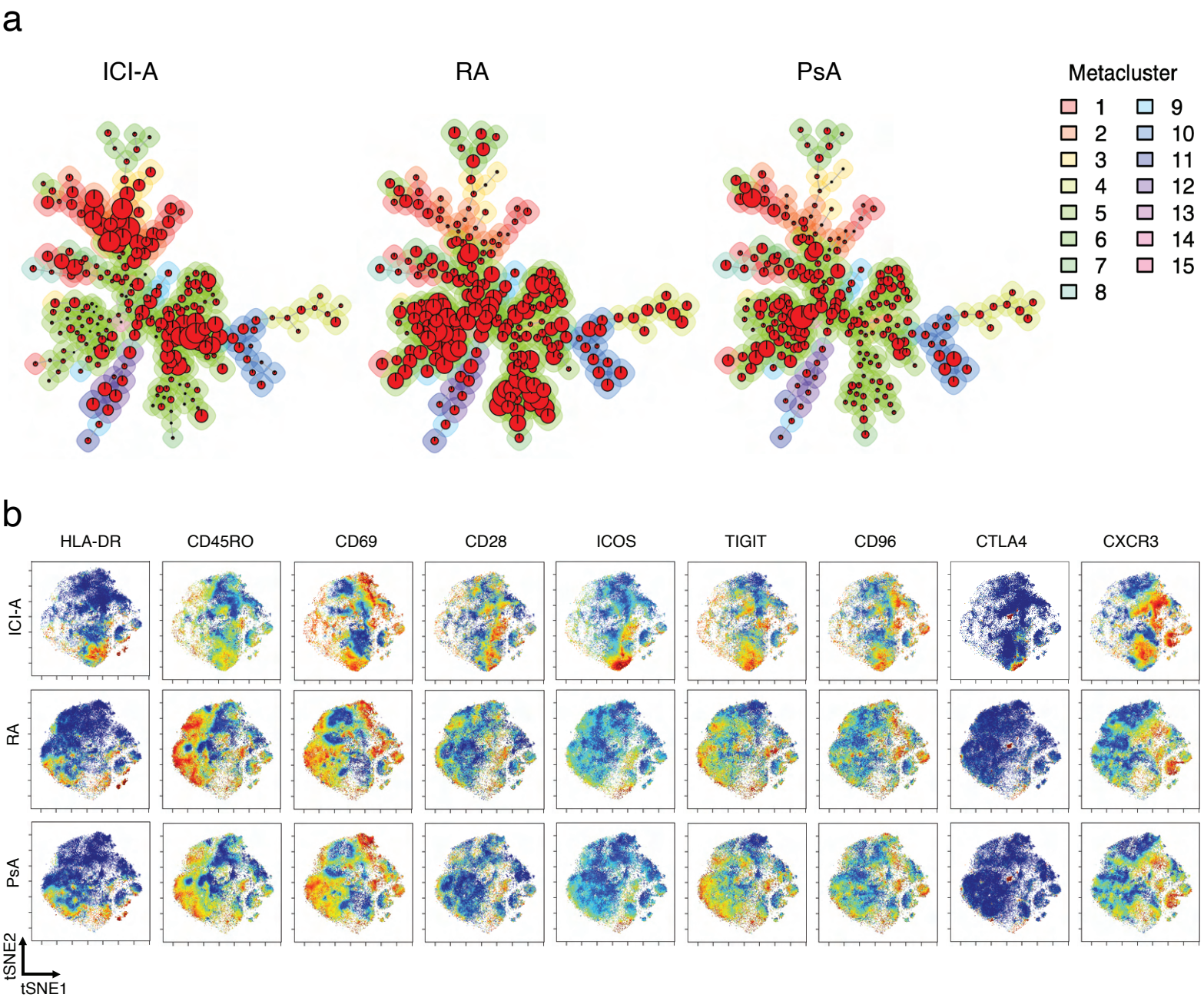
Supplementary figure 3. Single-cell analysis of CD8 T cells from ICI-arthritis synovial fluid and tissue.
a) Gating scheme of CD8 T cell isolation from ICI-arthritis synovium for scRNA-seq. **b)** Distribution of cells that passed quality control having <3,000 total genes (feature RNA counts) and <10% mitochondrial genes. **c)** Tabulation of QC filtered CD8 T cell numbers contributing to eight transcriptomically distinct clusters from each individual patient. **d)** Simpson and Shannon equitability indices calculated for the eight CD8 T cell clusters. **e)** The percentage of clonotypes shared between clusters. The row identity represents the denominator. **f)** Synovial tissue CD8 T cell scRNA-seq clusters from the left and right knee. Cluster IDs for figures (c) - (f): 0 - GZM+, 1 - Transitional, 2 - Tcm, 3 - MAIT, 4 - ZNF683+, 5 - KLRG1+, 6 - Dysfunctional, and 7 - Proliferating.



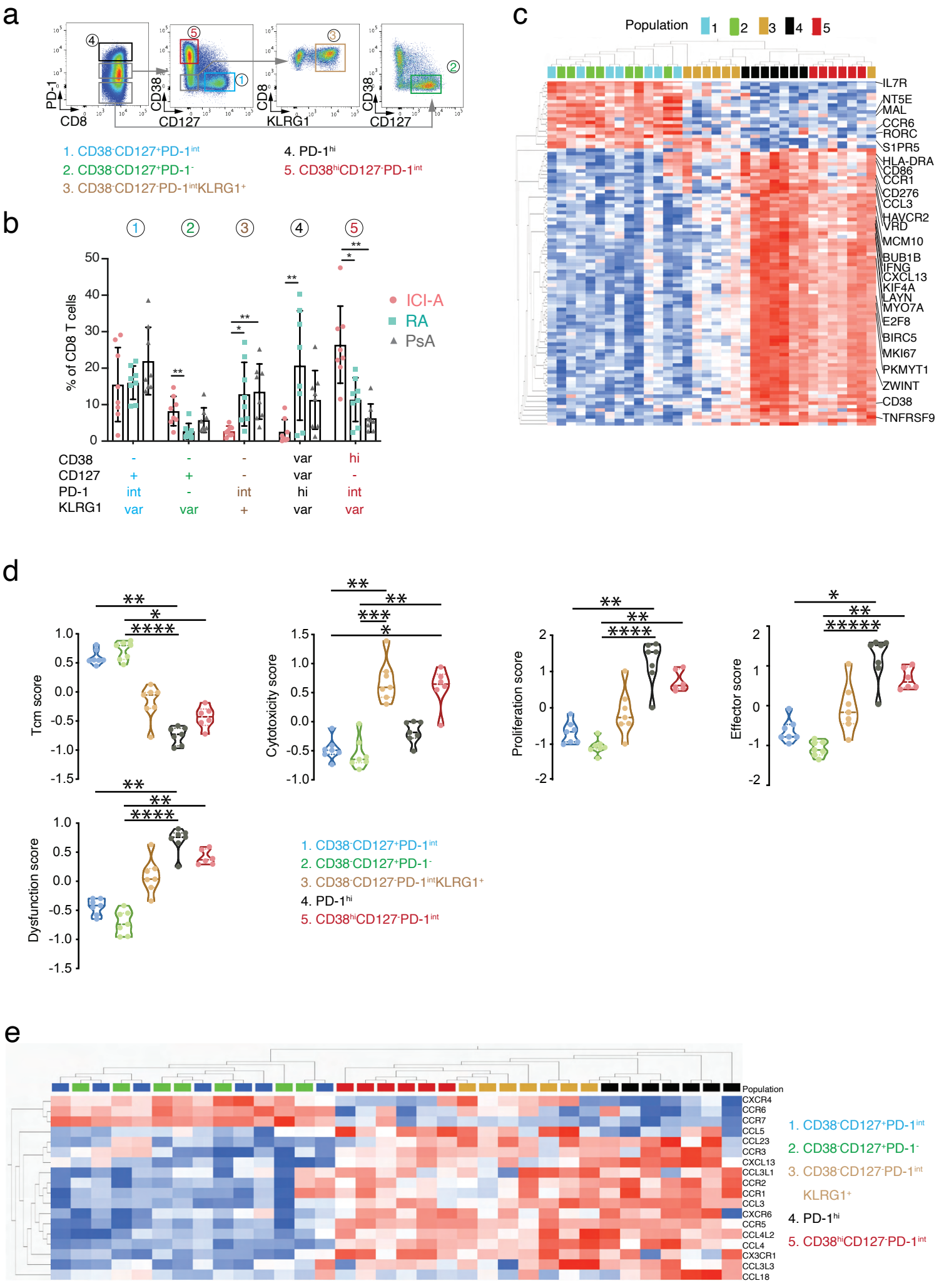
Supplementary figure 4. Single-cell analysis of CD8 T cells from peripheral blood of ICI-arthritis patients.
a) Gating scheme of naïve and non-naïve CD8 T cell isolation from ICI-arthritis blood for scRNA-seq and TCR repertoire analysis. **b)** Circle plot of clonotypes and shared clonotypes between synovial fluid CD8 cells and naïve and non-naïve blood CD8 cells after 10 weeks for P23. **c)** UMAP representation of clonotypes shared between paired synovial fluid CD8 cells and blood naïve and non-naïve CD8 cells in P25. MAIT cells were excluded in the analysis (dark gray dots). Bar graphs show the number of cells contained in the shared clonotypes and the number of shared clonotypes in each cluster. Cluster IDs for figure (c): 0 - GZM+, 1 - Transitional, 2 - Tcm, 3 - MAIT, 4 - ZNF683+, 5 - KLRG1+, 6 - Dysfunctional, and 7 - Proliferating .



Supplementary figure 5. Basic analysis of mass cytometry of ICI-A, RA and PsA synovial fluid.
a) Flow cytometric detection of PD-1 on T cells using indicated detection antibody clones with or without prior incubation with pembrolizumab blockade *in vitro*. **b)** Example gating of mass cytometry data. **c)** Frequency of CD8 T cells, CD4 T cells, B cells, monocytes, and NK cells in ICI-A (n=6), RA (n=5) and PsA (n=5) synovial fluid. **d)** Example gating of high, intermediate and low PD-1 expression levels on T cells from ICI-A, RA and PsA synovial fluid detected by mass cytometry. Quantification of PD-1^{hi} cells, PD-1^{int} cells and PD-1^{hi}CXCR5^{-} CD4 Tph cells are shown. Mean ± SD shown. *p<0.05, **p<0.001 by Kruskal-Wallis test in (d).

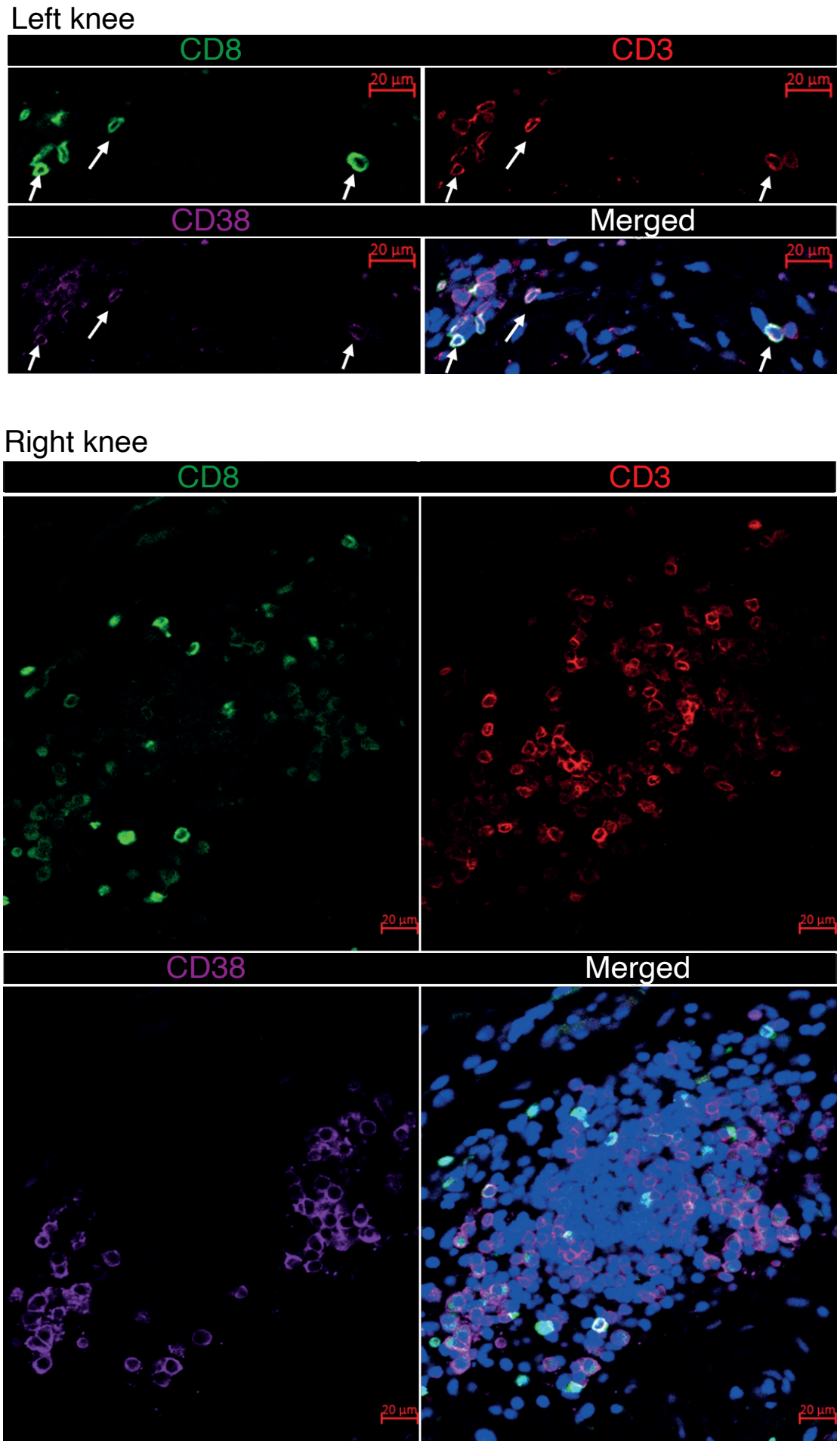


Supplementary figure 6. Unsupervised analysis of mass cytometry of ICI-A, RA and PsA synovial fluid.
a) FlowSOM minimus spanning tree showing metaclusters on CD8 T cells from ICI-A, RA and PsA synovial fluid detected by mass cytometry. **b)** tSNE plots showing expression of indicated markers on CD8 T cells from ICI-A, RA and PsA synovial fluid detected by mass cytometry.

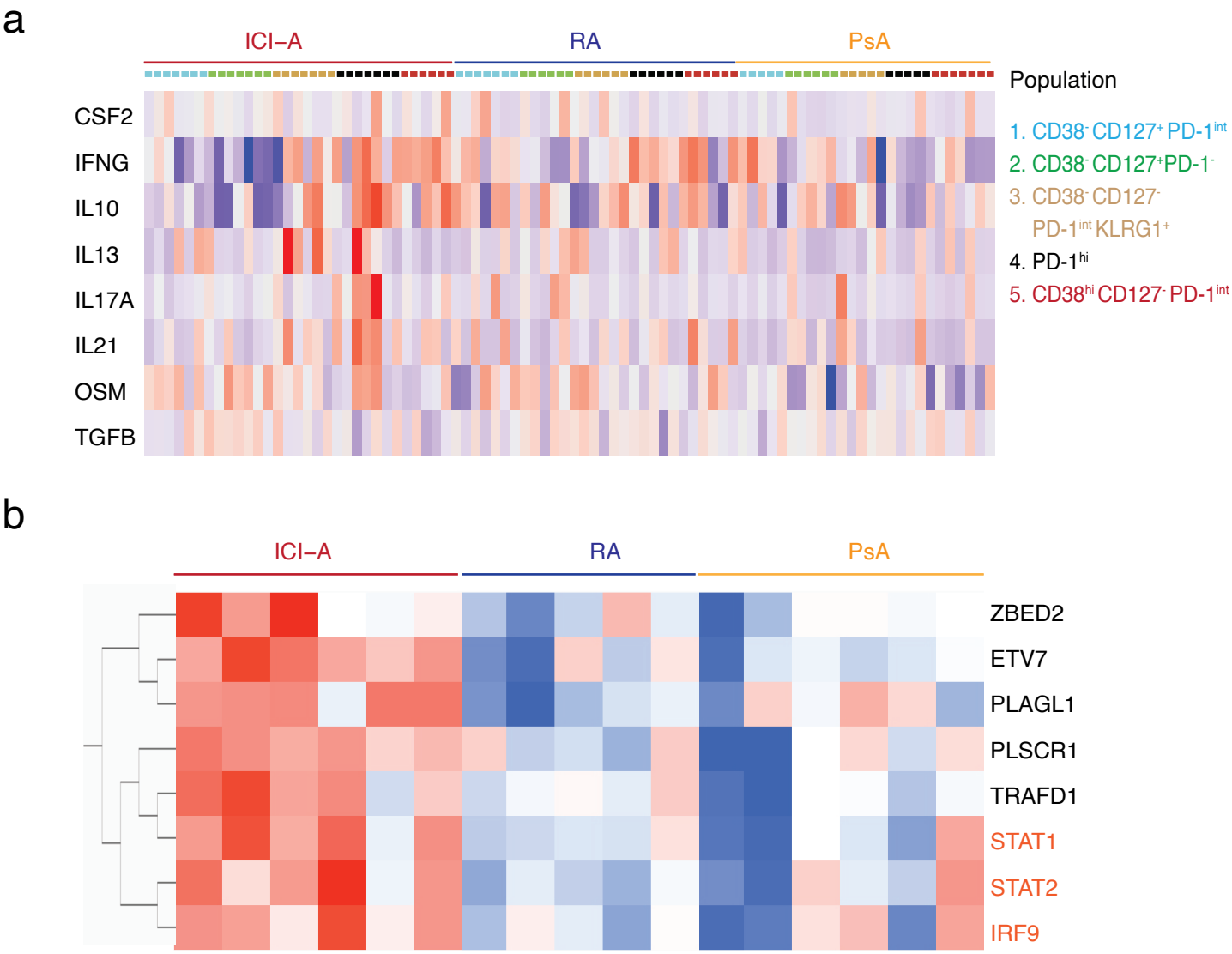


Wang et al. Suppl. Figure 7

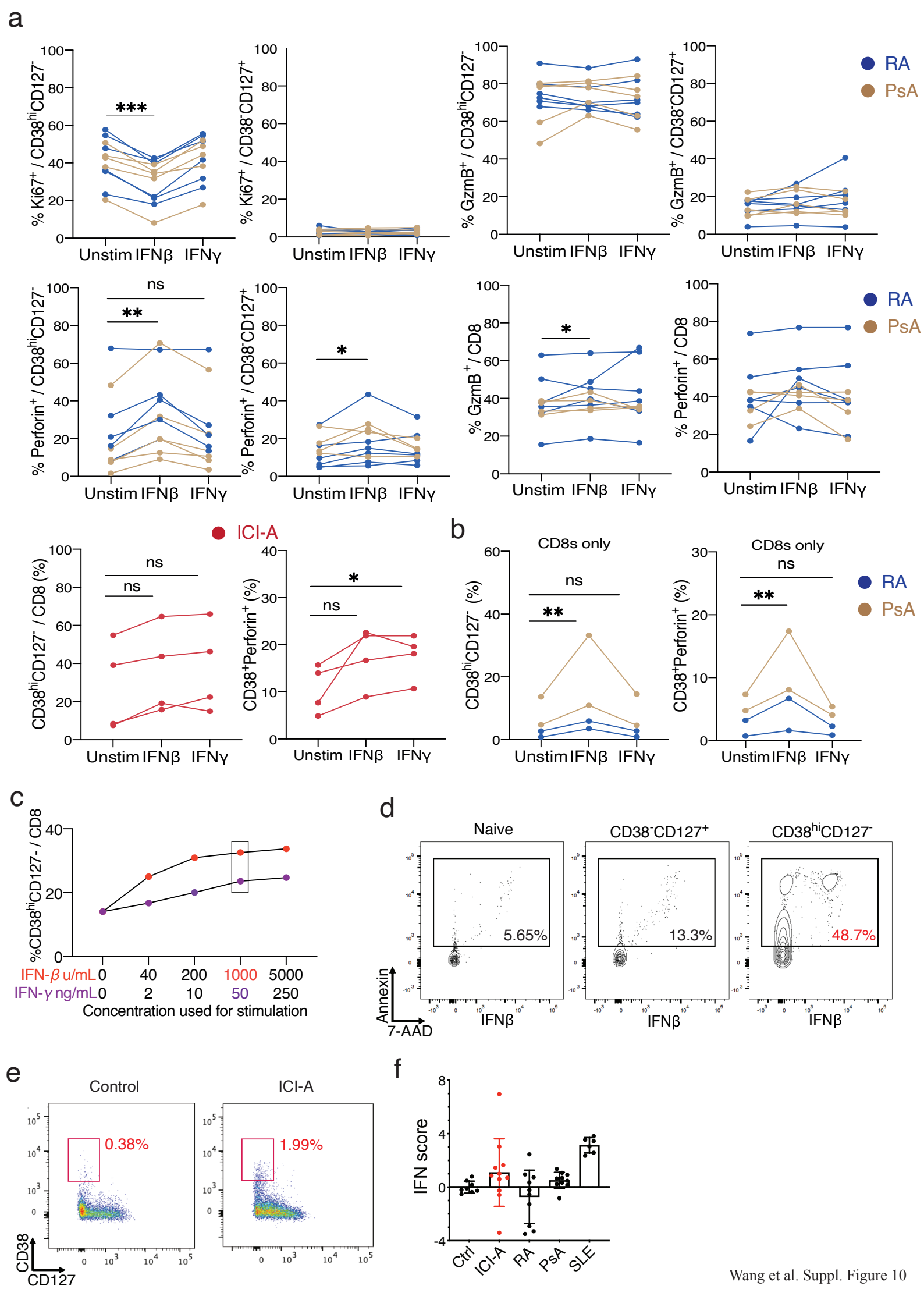
Supplementary figure 7. Transcriptional features of CD8 T cells in ICI-arthritis synovial fluid.
a) Sorting scheme to isolate five CD8 T cell populations with indicated surface phenotypes. **b)** Frequency of sorted CD8 T cell populations in ICI-arthritis (ICI-A), RA and PsA synovial fluid (n=8). **c)** Hierarchical clustering of CD8 T cell populations from ICI-A synovial fluid based on row-normalized mean expression of 100 top variable genes by RNA-seq. Colors indicate cell populations as in (a). **d)** Gene module scores of CD8 T cell populations as in (a) from ICI-A synovial fluid, calculated based on differentially expressed genes. **e)** Hierarchical clustering of CD8 T cell populations from ICI-A synovial fluid based on row-normalized mean expression of differentially expressed chemokines and chemokine receptors measured by RNA-seq. *$p<0.05$, **$p<0.001$, ***$p<0.0001$ by Kruskal-Wallis test in (b) and (d).



Supplementary figure 8. CD38 detection on CD8 T cells in synovium using multiplexed immunofluorescence. Multiplexed immunofluorescence images showing CD38 protein detection on CD8 T cells (marked with white arrows) present in left and right knees of patient. CD8 staining is shown in green, CD3 in red and CD38 in magenta.



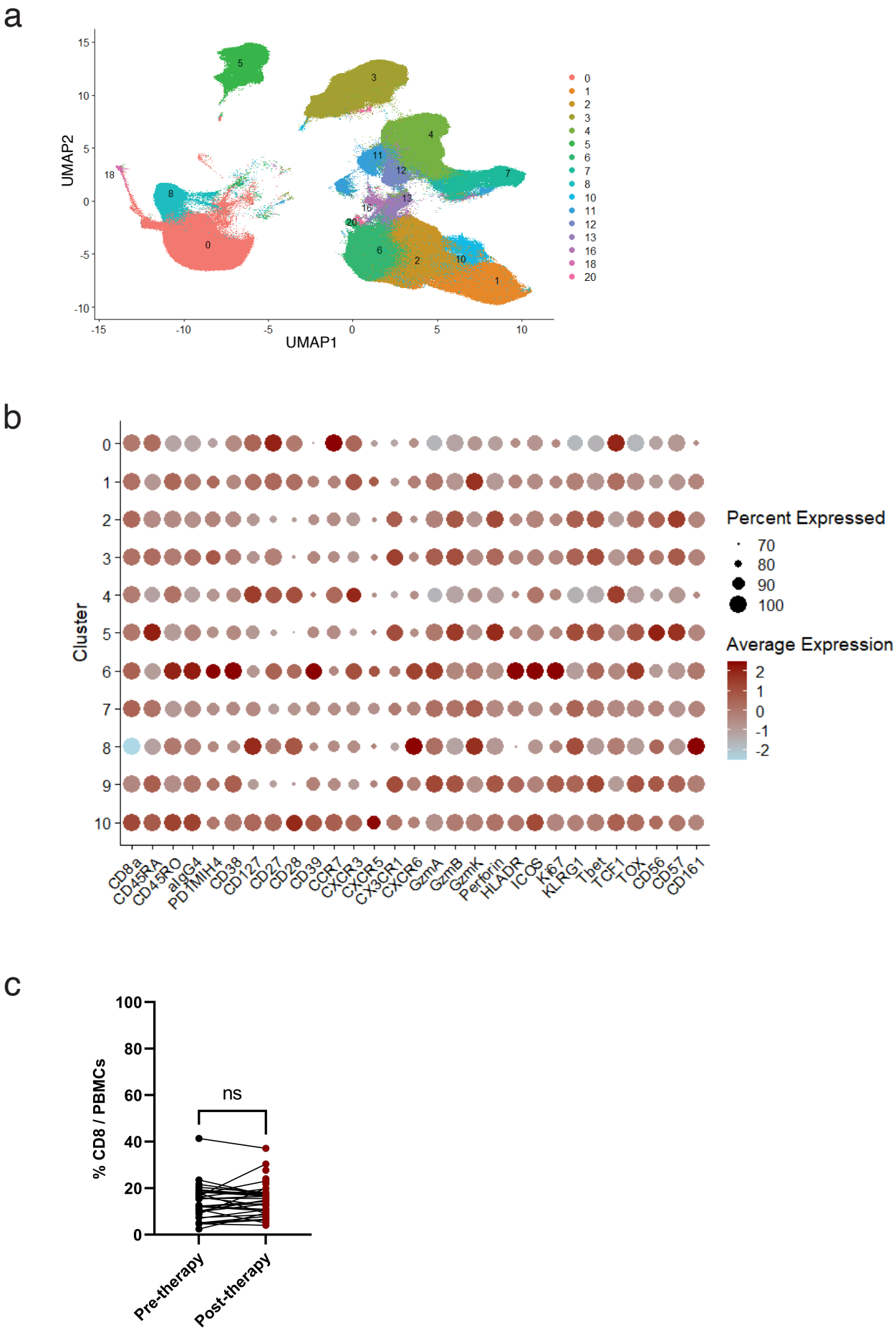
Supplementary figure 9. Distinct activation of IFN-inducible genes in ICI-arthritis.
a) Heatmap showing the expression of cytokine genes across the sorted populations ordered by diseases. **b)** Heatmap showing the expression of differentially transcription factor genes across the sorted populations ordered by diseases. Mean ± SD shown.



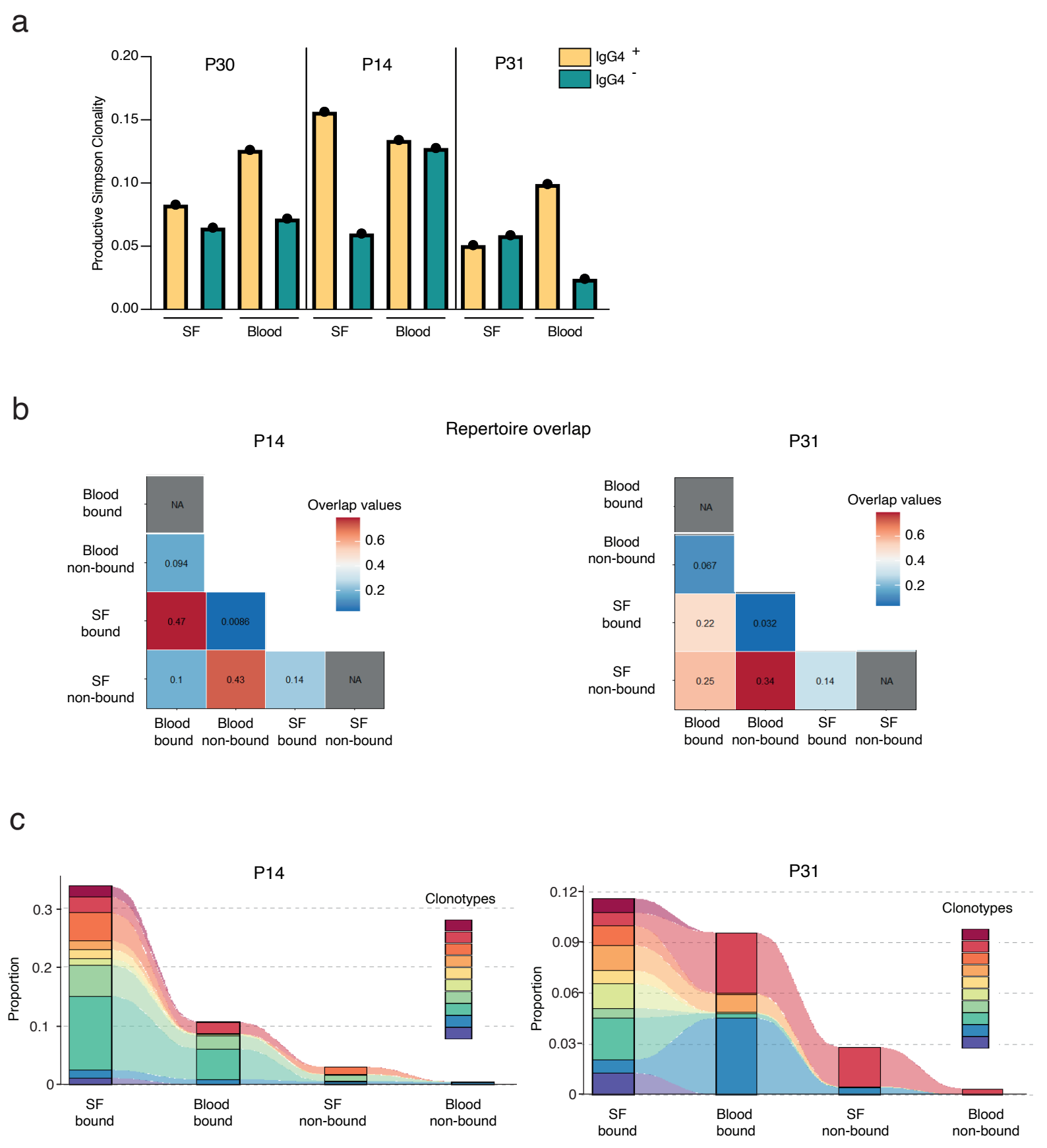
Wang et al. Suppl. Figure 10

Supplementary figure 10. Expression of intracellular markers with or without IFN treatment in SFMC and PBMC from various disease conditions.

a) Frequency of $Ki67^+$, granzyme B^+, $Perforin^+$ and cells in indicated CD8 T cell subsets from total SFMC (RA in blue, PsA in gold and ICI-A in red) cultured with IFN-β or IFN-γ for 72 hours. **b)** Frequency of $CD38^{hi}CD127^-$ and $CD38^+Perforin^+$ cells in cultured CD8 T cells from SF (RA in blue, PsA in gold) with IFN-β or IFN-γ for 72 hours. Lines link the same patient sample under the different conditions in (a) and (b). **c)** Titration curve of cytokine concentrations for IFN stimulation experiments (IFN-β in red and IFN-γ in purple). Black box indicates concentration used in all experiments. **d)** Representative flow cytometry plots of Annexin versus 7-AAD gating on indicated PBMC-derived CD8 T cell subsets treated with IFN-β for cytotoxicity assays. See Fig. 4e. **e)** Representative flow cytometric plot of CD38 and CD127 expression on gated CD8 T cells from PBMC from healthy control and ICI-arthritis (ICI-A) patients. **f)** 8 gene-derived IFN score of PBMC from controls (n=8), ICI-A (n=11), RA (n=10), PsA (n=10), and SLE (n=6) patients. *$p<0.05$, **$p<0.001$, ***$p<0.0001$ by Kruskal-Wallis test in (a) and (b).



Supplementary figure 11. Features of CD8 T cells following ICI treatment.
a) UMAP visualization of total PBMCs analysed by CyTOF. **b)** Dotplot depicting expression of listed markers in CD8 T cells divided by the clusters visualized in Figure 5a. **c)** Frequency of CD8 T cells among total PBMCs pre and post initiation of therapy. Black lines connect paired patients before and 6-weeks post initiation of therapy. ns = not significant by Kruskal Wallis test.



Supplementary figure 12. TCR repertoire overlap in drug-bound synovial fluid and blood CD8 T cells.
a) Productive Simpson clonality of all 3 patients in both blood and synovial fluid (SF). Values closer to zero are more polyclonal. **b)** Plot denoting the Morisita index value for each comparison demonstrating the repertoire overlap. Each plot depicts 1 patient each. See Fig. 5h. **c)** Alluvial plot demonstrating the location and overlap of the top 10 most abundant TCR clones in anti-PD-1 bound and not bound blood and synovial fluid. Each plot depicts 1 patient each.