Supplementary information

Cytotoxic CD8$^+$ T cells target citrullinated antigens in rheumatoid arthritis

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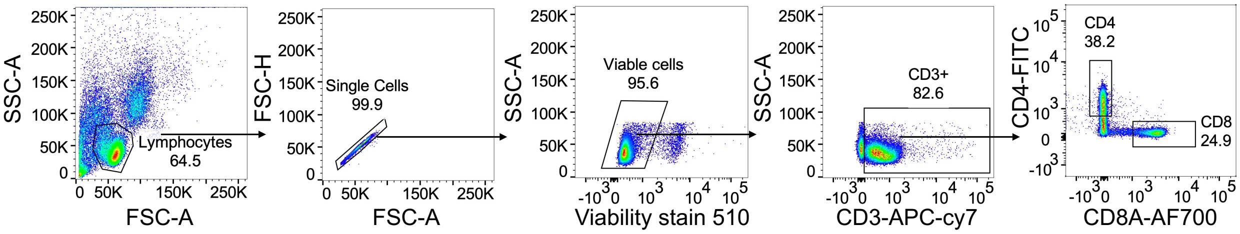
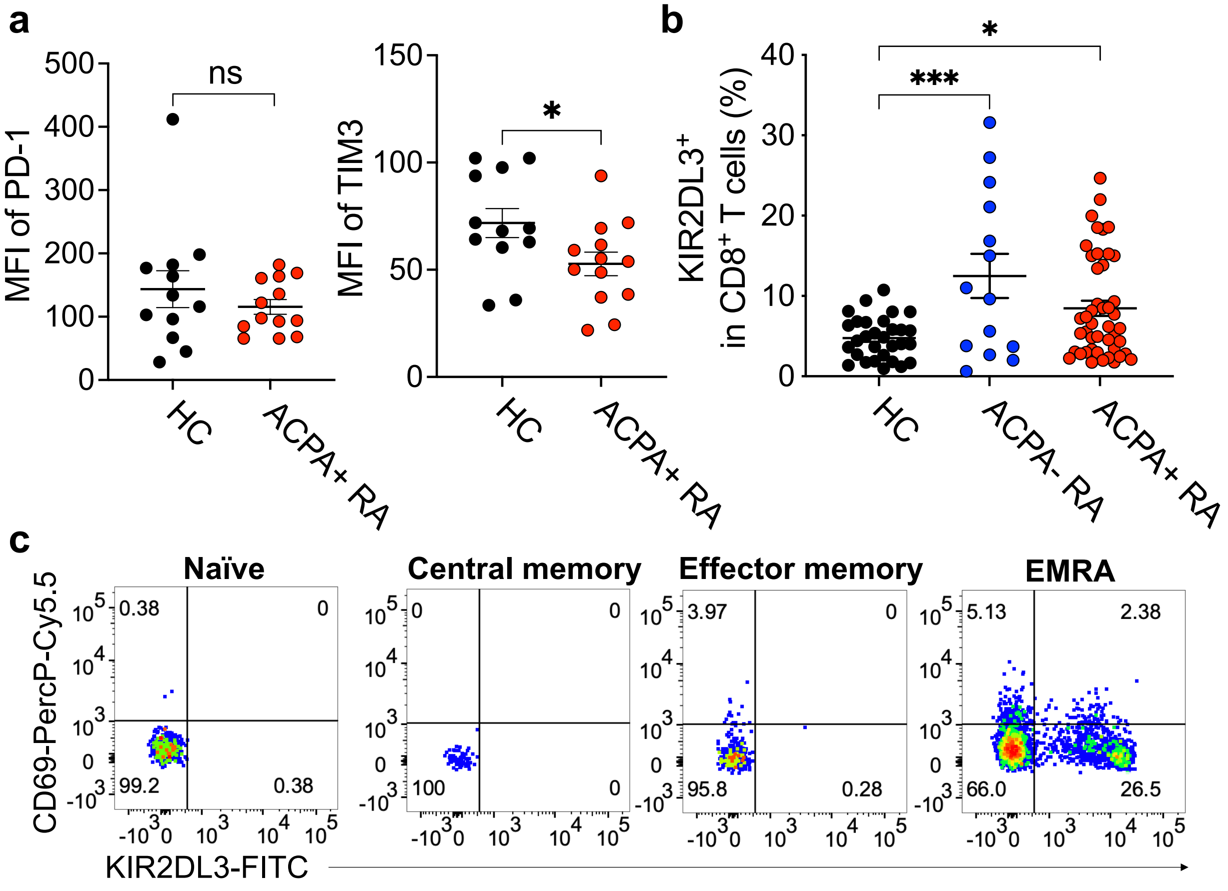
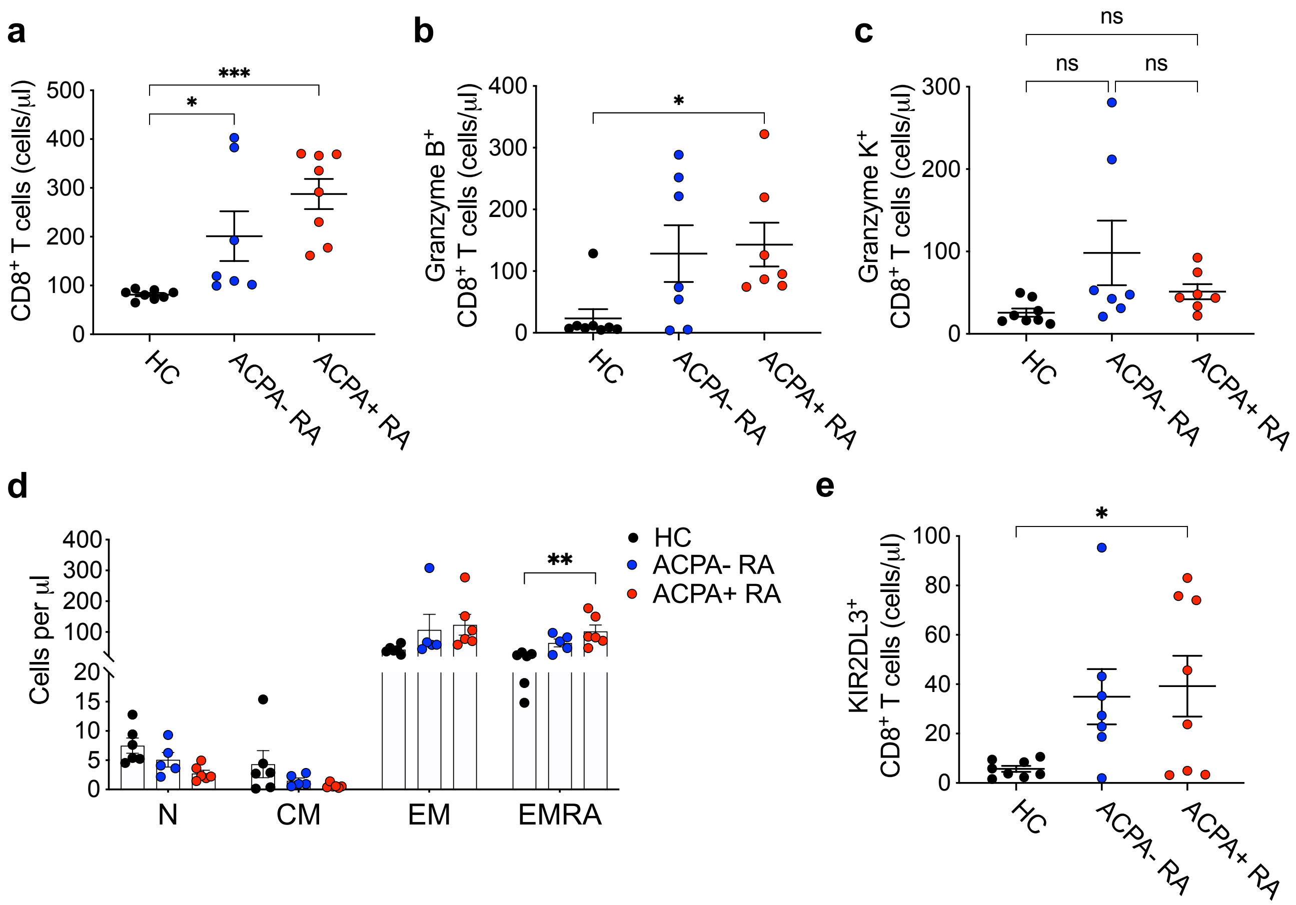
Supplementary Figures



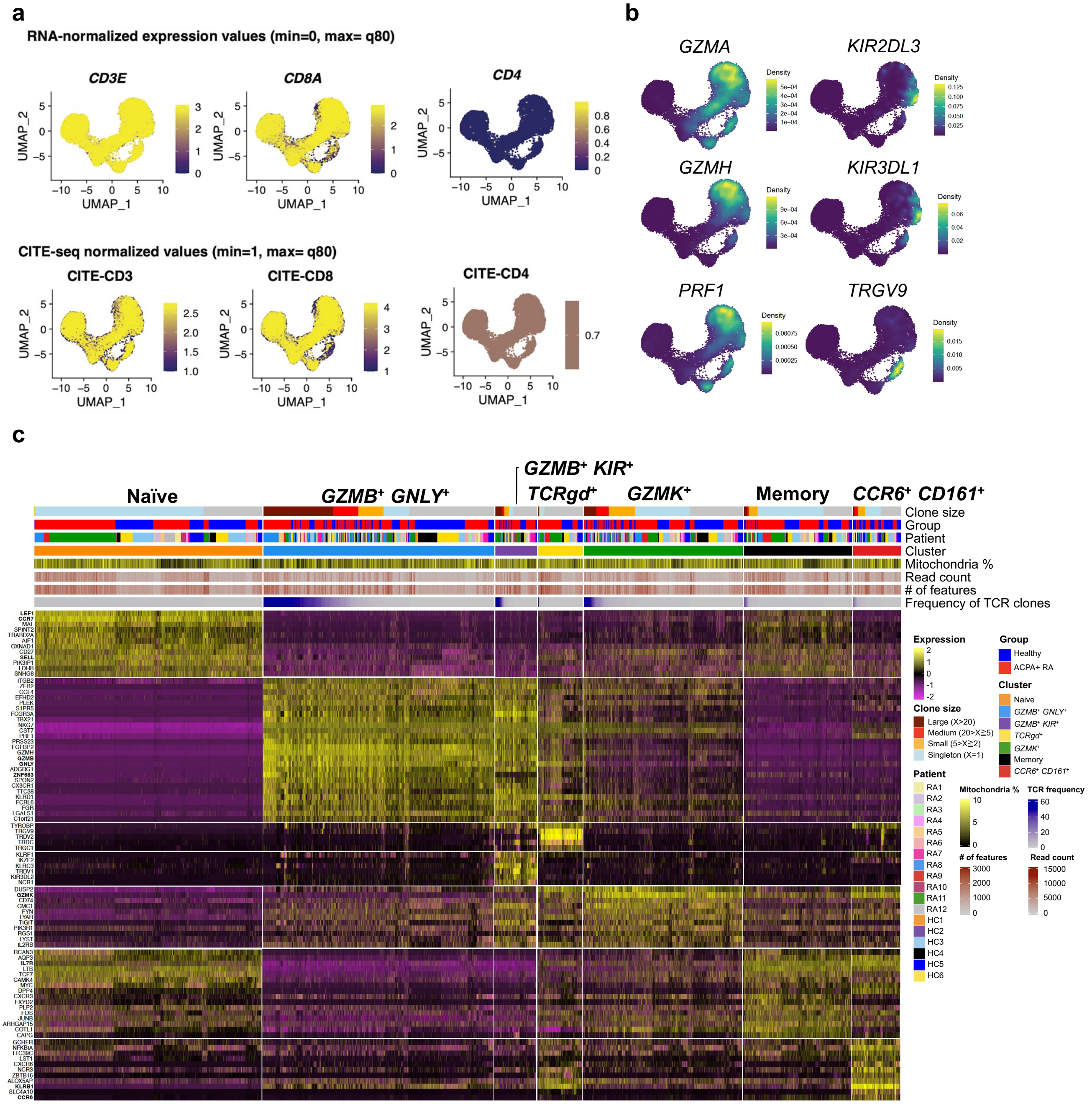
Supplementary Fig. 1: Flow cytometric analysis of CD8$^+$ T cells in ACPA+ RA patient blood. Representative data from ACPA+ RA PBMCs are displayed as flow cytometric plots, and the gating parameters for the CD8$^+$ T cell population indicated.



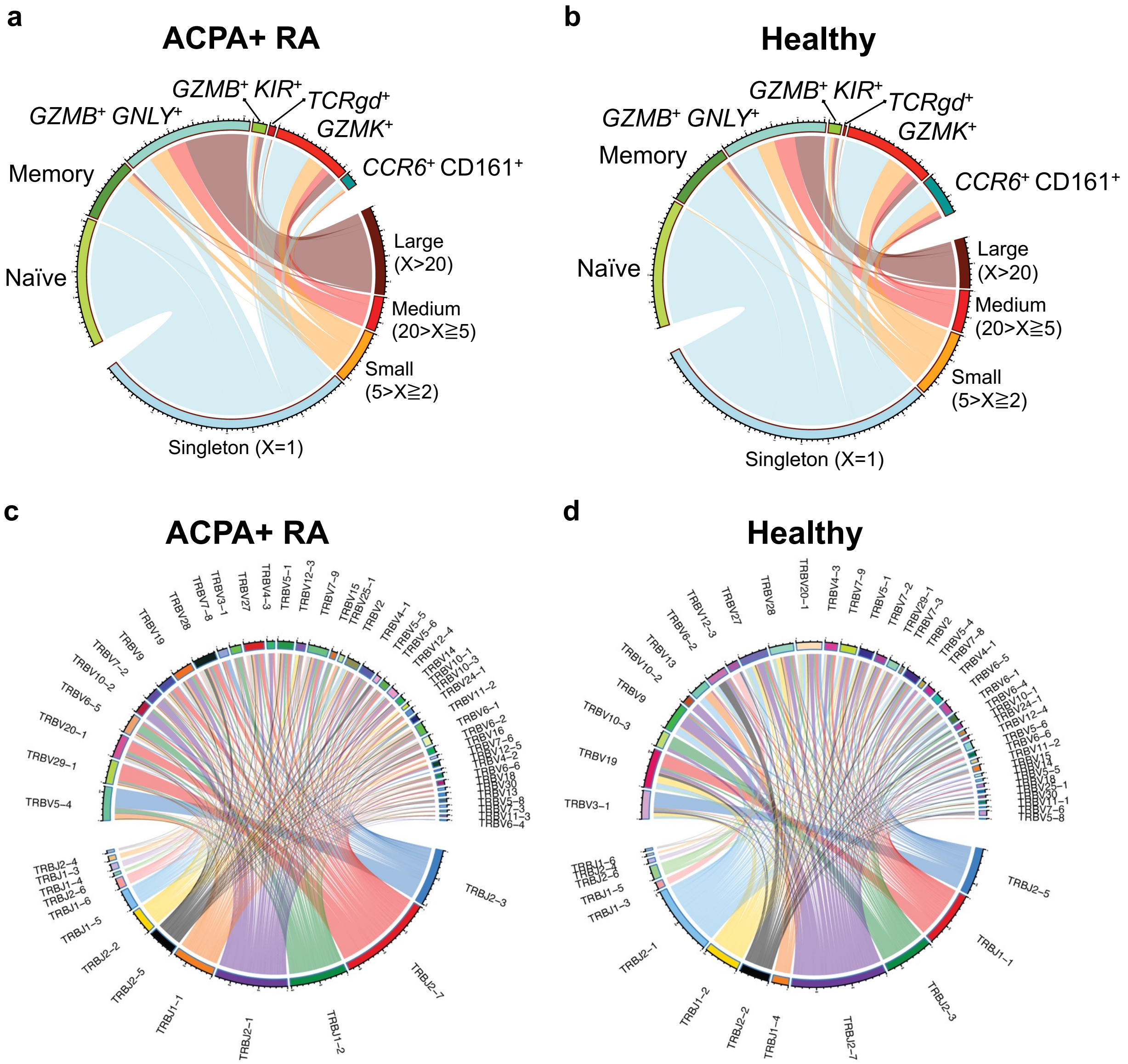
Supplementary Fig. 2: Phenotypic characterization of CD8$^+$ T cells in ACPA+ RA patient blood. a Expression of PD-1 or TIM3 in CD8$^+$ T cells from PBMCs from healthy controls (*n* = 12) or ACPA+ RA patients (*n* = 13) measured by flow cytometry. $^*P$=0.0376. **b** Percentage of KIR2DL3$^+$CD8$^+$ T cells in HC (*n* = 30), ACPA- RA (*n* = 14), or ACPA+ RA (*n* = 45) analyzed by flow cytometry ($^{***}P$=0.0007, or $^*P$=0.0355). **c** Representative dot plots showing expression levels of CD69 and KIR2DL3 in CD8$^+$ T memory subsets (naïve, CM, EM, or EMRA). Data are presented as means ± SEM. $^*P < 0.05$ or $^{***}P < 0.001$ by two-tailed unpaired *t*-test (**a**) or one-way ANOVA (**b**) with Tukey's multiple comparisons test. ns, not significant. Source data are provided as a Source Data file. HC healthy control, ACPA anti-citrullinated protein antibodies, RA rheumatoid arthritis, MFI median fluorescence intensity.



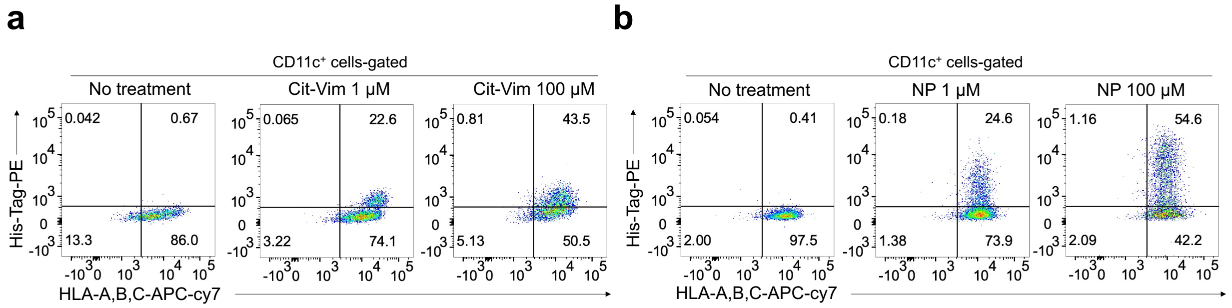
Supplementary Fig. 3: Absolute cell counts of CD8$^+$ T cells in ACPA+ RA patients. Absolute cell numbers of total CD8$^+$ T cells (**a,** HC n = 8, ACPA- RA n = 7, ACPA+ RA n = 8, $^*P$=0.0466, or $^{***}P$=0.0005), granzyme B-expressing CD8$^+$ T cells (**b,** HC n = 8, ACPA- RA n = 7, ACPA+ RA n = 7, $^*P$=0.0473), or granzyme K (**c,** HC n = 8, ACPA- RA n = 7, ACPA+ RA n = 7)-expressing CD8$^+$ T cells, memory CD8$^+$ T cells (**d,** HC n = 6, ACPA- RA n = 5, ACPA+ RA n = 5, $^*P$=0.006), or KIR2DL3$^+$CD8$^+$ T cells (**e,** HC n = 8, ACPA- RA n = 7, ACPA+ RA n = 8, $^*P$=0.0484) per 1 μl assessed by counting beads in each PBMC. Data are presented as means ± SEM. $^*P < 0.05$, $^{**}P < 0.01$, or $^{***}P < 0.001$ by ordinary one-way ANOVA (**a-c, e**) or two-way ANOVA (**d**) with Tukey's multiple comparisons test. ns, not significant. Source data are provided as a Source Data file. HC healthy control, ACPA anti-citrullinated protein antibodies, RA rheumatoid arthritis.



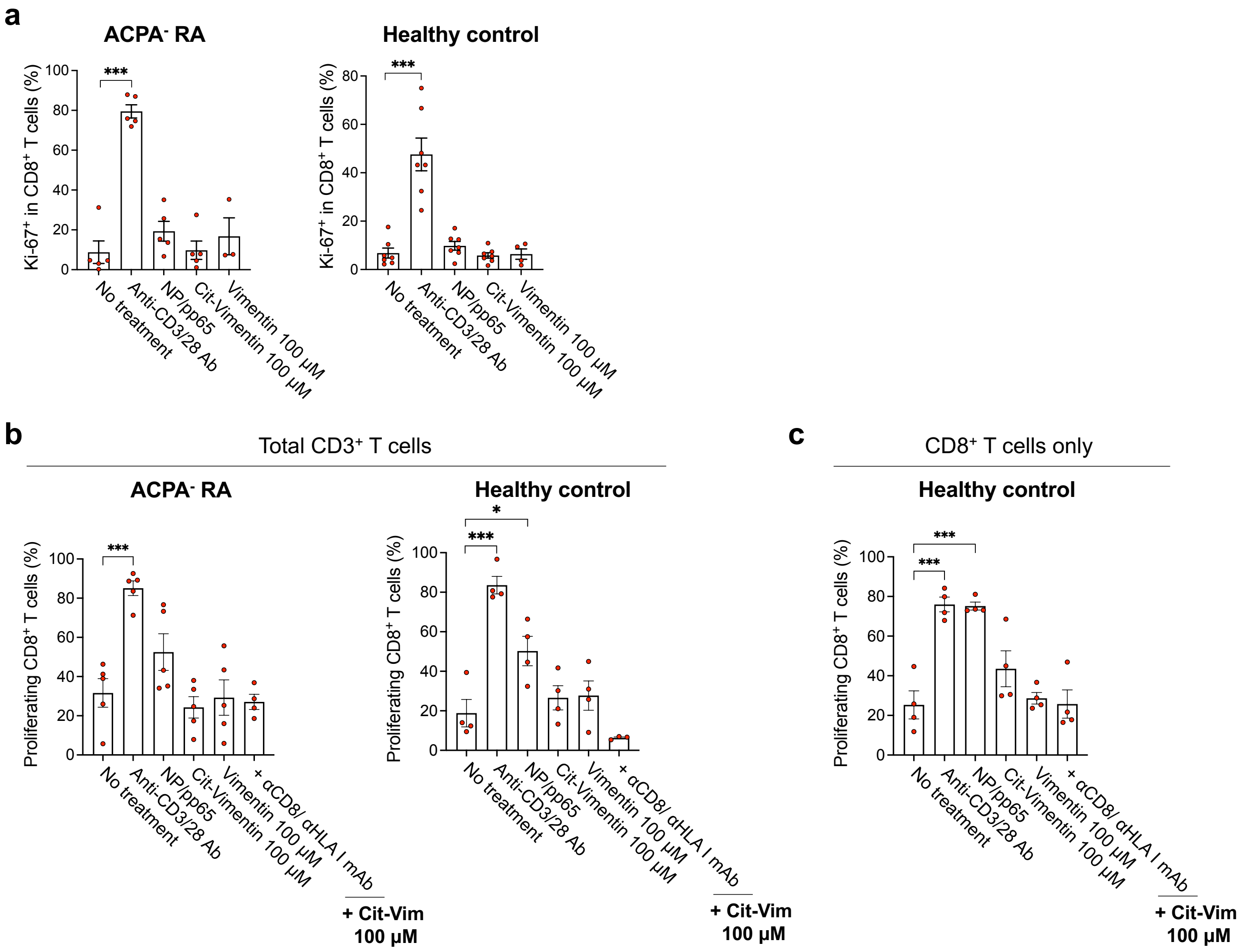
Supplementary Fig. 4: Expression of cell type marker genes in CD8$^+$ T cells from ACPA+ RA and healthy control blood. **a** mRNA and CITE-seq expression of marker genes (*CD3E*, *CD8A*, and *CD4*) used to identify and confirm analysis of CD8$^+$ T cells. Color indicates the expression level of each marker gene. **b** Density plots display marker genes including *GZMA*, *KIR2DL3* or *TRGV9*) in CD8$^+$ T cells. **c** Heatmap of select differentially expressed gene signatures (log2 Fold Change > 0.8) in each cluster with bars; clonal size, patients, clusters, mitochondrial gene percentage, read count, number of features in each cell and frequency of TCR clone. ACPA anti-citrullinated protein antibodies, RA rheumatoid arthritis.



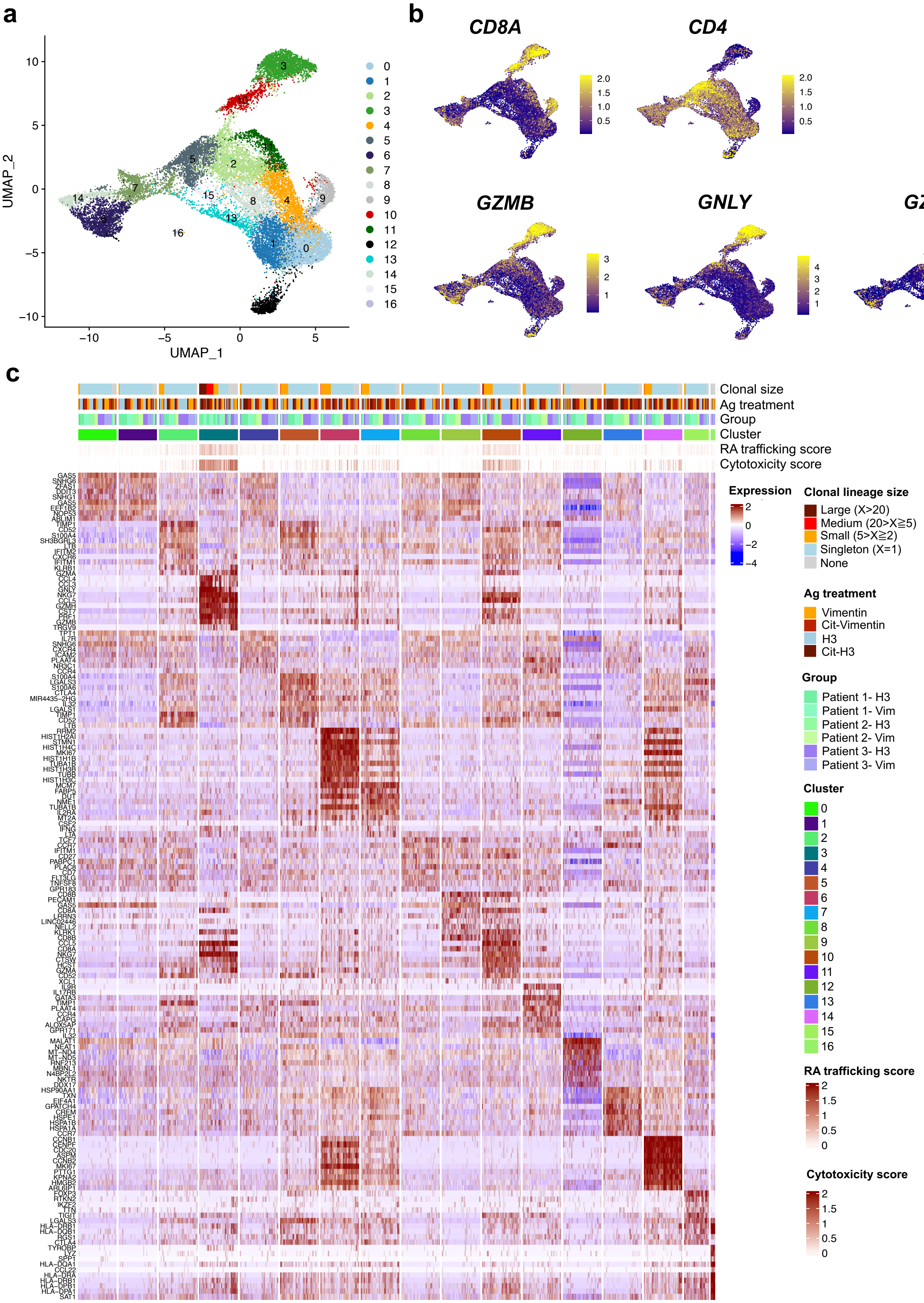
Supplementary Fig. 5: CD8$^+$ T cells expressing cytotoxic mediators are clonally expanded in ACPA+ RA blood. a, b Chord diagrams representing the contribution of each cluster to clonal sizes (**a**) and the shared clonotypes between clusters (**b**). **c** TCR beta chain V- and J-gene usage of CD8$^+$ T cells of ACPA+ RA blood. The width of each band represents the frequency of V- or J- gene usage. ACPA anti-citrullinated protein antibodies, RA rheumatoid arthritis.



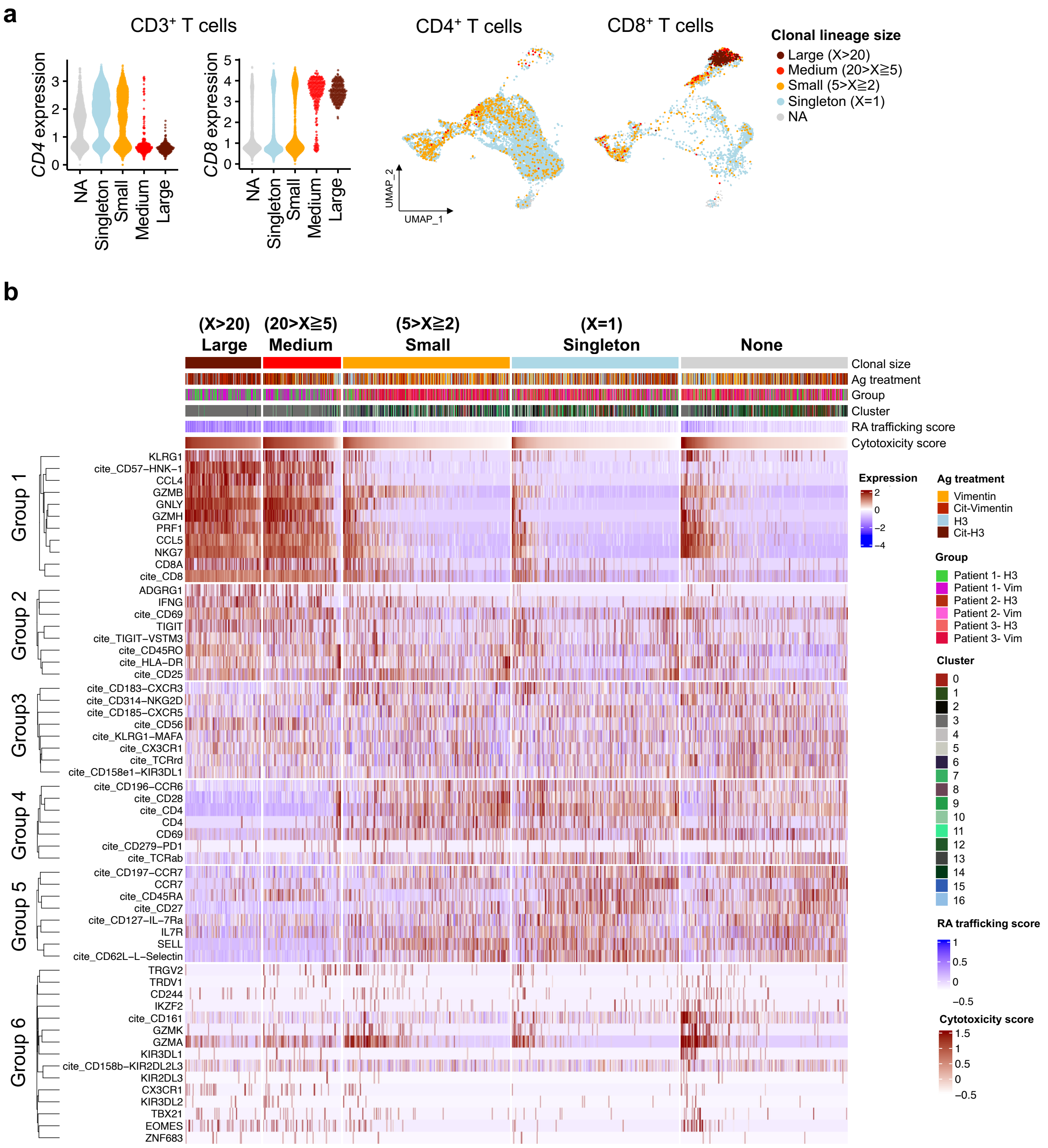
Supplementary Fig. 6: CD11c$^+$ cells from ACPA+ RA patients endocytose cit-vimentin. a,b, Representative flow cytometric plots of protein endocytosis by CD11c$^+$ cells in ACPA+ RA PBMCs show antigen-presenting cells uptake recombinant His-tagged cit-vimentin protein (**a**), or NP protein (**b**) in a dose-dependent manner (1 or 100 μM) after 16 hr of culture. Cit-Vim citrullinated vimentin.



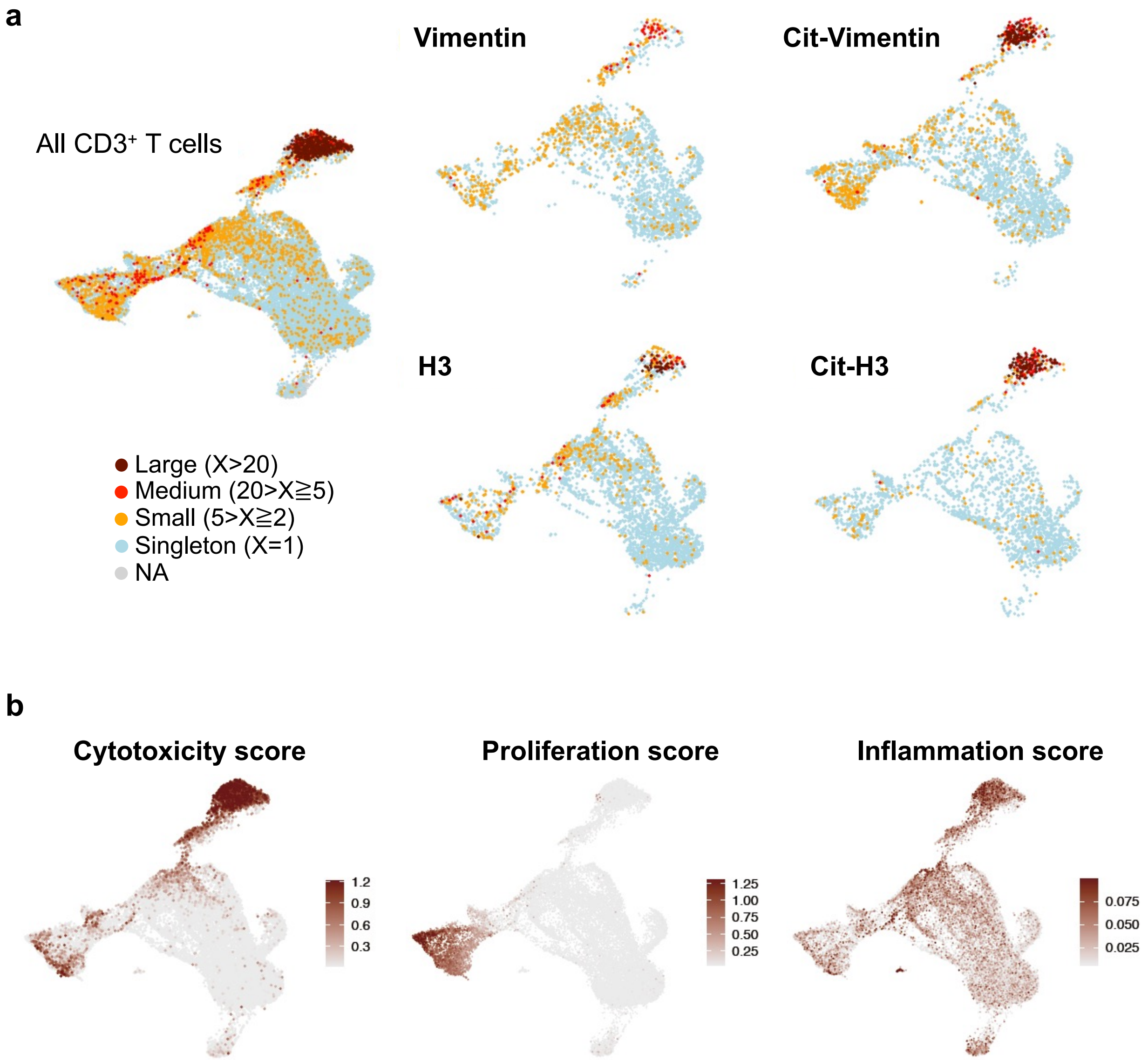
Supplementary Fig. 7: Citrullinated vimentin does not induce the proliferation of ACPA- RA or HC CD8$^+$ T cells. a Percentage of Ki-67$^+$CD8$^+$ T cells in ACPA- RA (*n* = 5) or HC (*n* = 7) PBMCs after stimulation with anti-CD3/28 antibodies, NP (Influenza)/ pp65 (CMV) proteins (50 µM of each), citrullinated vimentin (100 µM), or native vimentin (100 µM) for 16 hr. $^{***}P < 0.0001$. **b, c** Quantification of the proliferating CD8$^+$ T cells in co-culture of monocyte-derived dendritic cells (MoDCs) with ACPA- RA or HC total CD3$^+$ T cells (**b**, $^{***}P=0.0002$ in ACPA- RA, $^{***}P=0.0002$, or $^{*}P=0.0214$ in HC) or CD8$^+$ T cells only (**c**, n = 4, $^{***}P=0.0007$, or $^{***}P=0.0005$). For **b**, no treatment, anti-CD3/28 Ab, NP/pp65, cit-vimentin or native vimentin n = 5, cit-vimentin with anti-CD8/ HLA class I antibodies n = 4 in ACPA- RA and no treatment, anti-CD3/28 Ab, NP/pp65, cit-vimentin or native vimentin n = 4 and cit-vimentin with anti-CD8/ HLA class I antibodies n = 3 in HC. Bars represent means ± SEM. $^{*}P < 0.05$ or $^{***}P < 0.001$ by ordinary one-way ANOVA with Tukey's multiple comparisons test. Source data are provided as a Source Data file. ACPA anti-citrullinated protein antibodies, RA rheumatoid arthritis. mAb monoclonal antibody.


a
UMAP_2
UMAP_1
10
5
0
−5
−10
−10
−5
0
5
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
b
CD8A
CD4
GZMB
GNLY
GZMK
2.0
1.5
1.0
0.5
3
2
1
4
c
Clonal size
Ag treatment
Group
Cluster
RA trafficking score
Cytotoxicity score
GAS5
SNHG6
ZFAS1
DDIT3
SNHG1
GAS5
EEF1B2
NOP53
ABLIM1
TIMP1
CD52
S100A4
SH3BGRL3
LTB
IFITM2
CXCR6
IFITM1
KLRB1
GZMA
CCL4
CCL3
GNLY
NKG7
CCL5
GZMH
CST7
PRF1
GZMB
TRGV9
TPT1
IL7R
SNHG6
CXCR4
ICAM2
PLAAT4
NR3C1
CCR4
S100A4
LGALS3
S100A6
CTLA4
MIR4435−2HG
IL32
LGALS1
TIMP1
CD52
LTB
RRM2
HIST1H2AI
STMN1
HIST1H4C
MKI67
HIST1H1B
TUBA1B
HIST1H3B
TUBB
HIST1H3C
MCM7
FABP5
DUT
NME1
TUBA1B
IL2RA
MT2A
CSF2
IFNG
LTA
TCF7
CCR7
IFITM1
CD27
PABPC1
PLAC8
CD7
FLT3LG
TNFSF8
GPR183
CD8B
PECAM1
GAS5
CD8A
LRRN3
LINC02446
NELL2
KLRK1
CD8B
CCL5
CD8A
NKG7
CTSW
HCST
GZMA
CD52
XCL1
IL9R
IL17RB
GATA3
TIMP1
PLAAT4
CCR4
CAPG
ALOX5AP
GPR171
IL32
MALAT1
NEAT1
MT−ND4
MT−ND5
RNF213
MBNL1
N4BP2L2
NKTR
DDX17
HSP90AA1
TXN
EIF4A1
GPATCH4
CREM
HSPE1
HSPA1B
HSPA1A
CCR7
CCNB1
CENPF
CDC20
ASPM
CCNB2
MKI67
PTTG1
KPNA2
HMGB2
ARL6IP1
FOXP3
RTKN2
IKZF2
TTN
TIGIT
LGALS3
HLA−DRB1
HLA−DQB1
RGS1
CTLA4
TYROBP
LYZ
SPP1
HLA−DQA1
CCL22
HLA−DRA
HLA−DRB1
HLA−DPB1
HLA−DPA1
SAT1
Expression
2
0
−2
−4
Clonal lineage size
Large (X>20)
Medium (20>X≥5)
Small (5>X≥2)
Singleton (X=1)
None
Ag treatment
Vimentin
Cit-Vimentin
H3
Cit-H3
Group
Patient 1- H3
Patient 1- Vim
Patient 2- H3
Patient 2- Vim
Patient 3- H3
Patient 3- Vim
Cluster
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
RA trafficking score
2
1.5
1
0.5
0
Cytotoxicity score
2
1.5
1
0.5
0

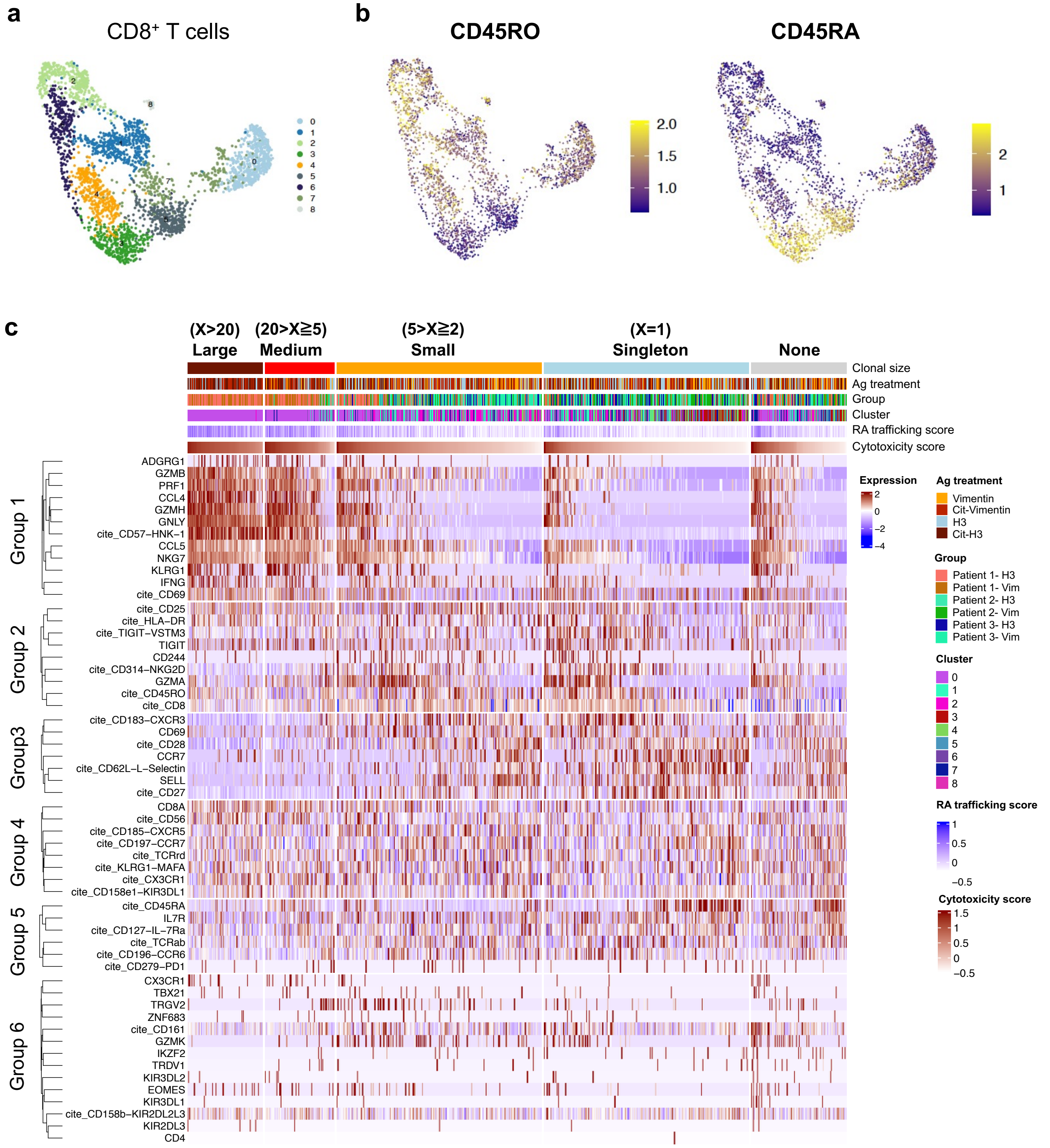
Supplementary Fig. 8: Single-cell RNA sequencing of CD3$^+$ T cells stimulated by native or citrullinated antigens. **a** UMAP plot representing 17 distinct clusters of CD3$^+$ T cells (n = 13,354) stimulated by native or citrullinated proteins. **b** Expression of *CD8A*, *CD4*, *GZMB*, *GNLY* or *GZMK* in the clusters. Color shows the expression level of each marker. **c** Heatmap showing transcriptional differences in each cluster. Top bars indicate clonal size, Protein treatment, patient group, clusters and scoring scale for RA trafficking and cytotoxicity. Individual T cells are ordered by clonal size in each cluster. RA rheumatoid arthritis, Vim vimentin, Ag antigen.



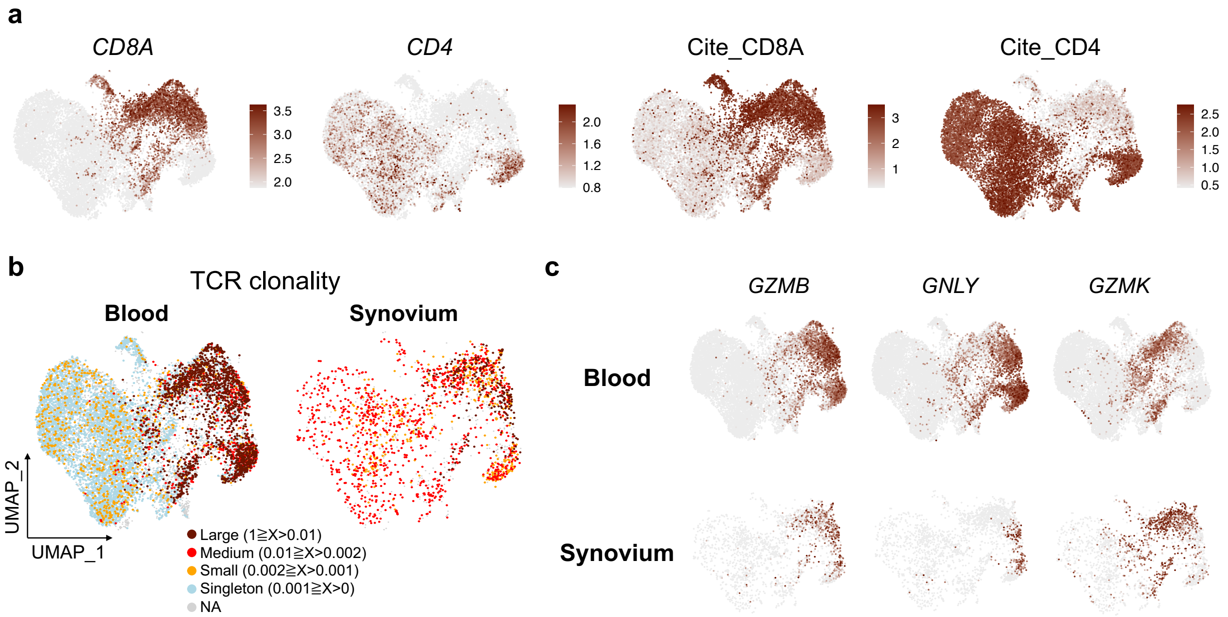
Supplementary Fig. 9: Clonal lineages of CD4$^+$ and CD8$^+$ T cells stimulated by native or citrullinated antigens. a Distribution of each clonal family in *CD4*$^+$ (n = 7,885) or *CD8*$^+$ (n = 3,284) T cells. **b** Heatmap representing 6 groups determined by unsupervised clustering based on the level of RNA and CITE-seq antibodies (cite_). Individual T cells are ordered by cytotoxicity score in each cluster. Ag antigen, Vim vimentin.



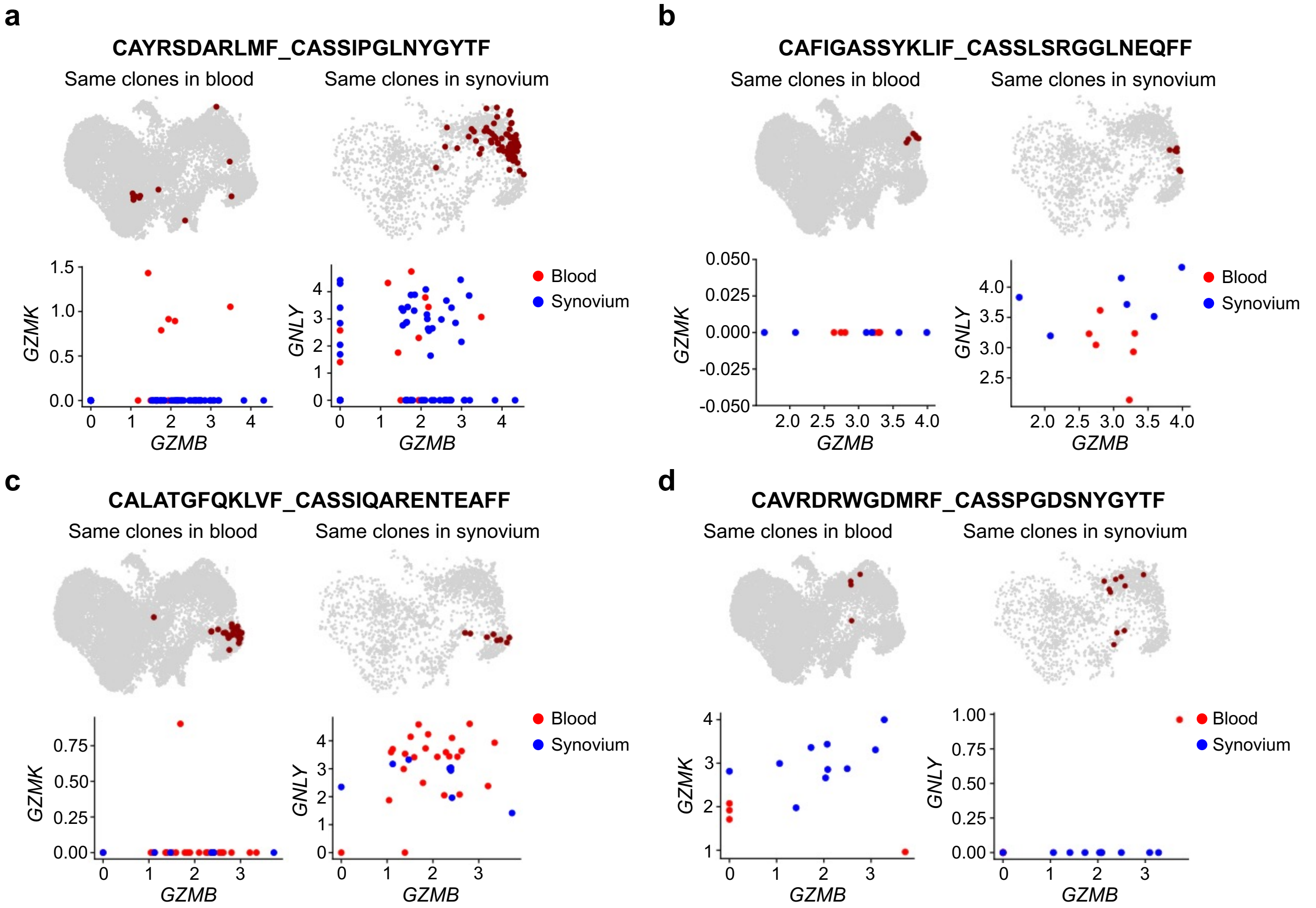
Supplementary Fig. 10: Citrullinated antigens stimulate clonal expansion of CD3$^+$ T cells with high cytotoxicity scores. a UMAP plots of all CD3$^+$ T cells stimulated by native or citrullinated Vimentin or H3 integrated with TCR clonality. **b** UMAP plots showing cytotoxicity, proliferation, or inflammation score. The score was calculated by the expression level of canonical marker genes. Cit- citrullinated.



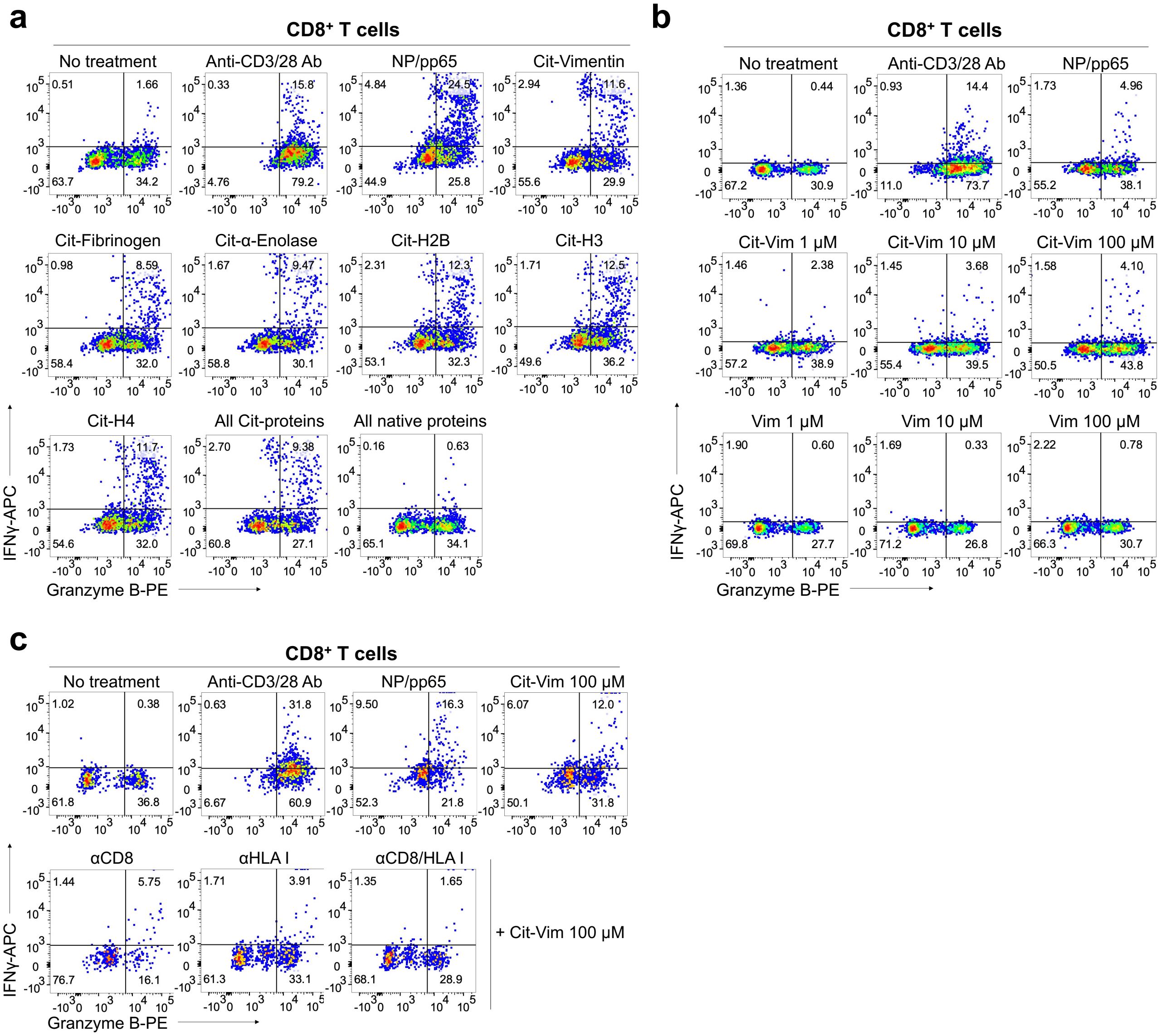
Supplementary Fig. 11: Phenotype of CD8$^+$ T cells stimulated by native or citrullinated antigens. a UMAP plot of CD8$^+$ T cells having 9 transcriptionally different clusters. **b** Expression level of CD45RO and CD45RA CITE-seq antibodies in CD8$^+$ T cells. **c** Heatmap of 6 groups by unsupervised clustering using the level of RNA and CITE-seq antibodies (cite_). RA rheumatoid arthritis, Vim vimentin, Cit- citrullinated.



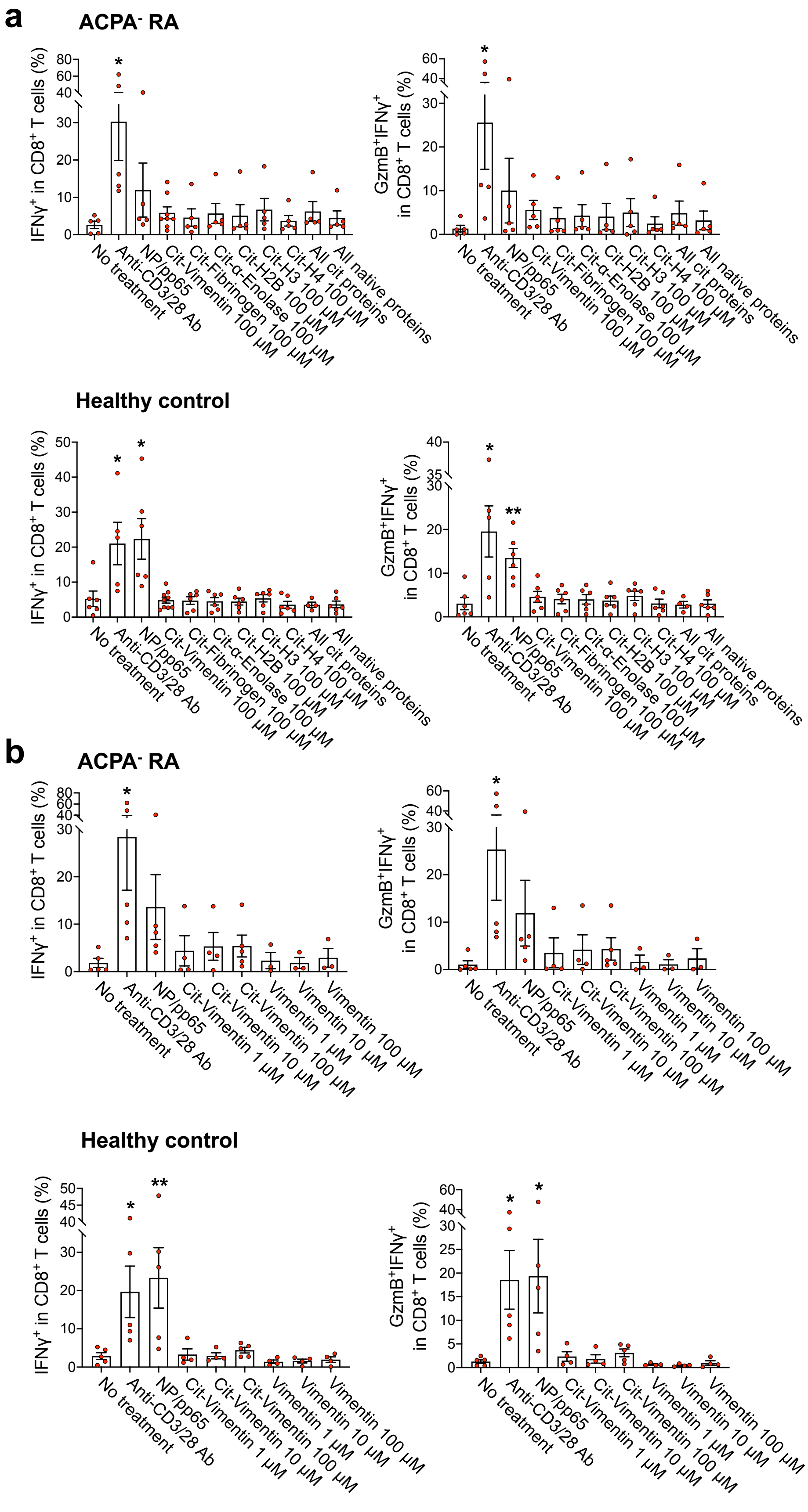
Supplementary Fig. 12: Integrated analysis of single cell RNA-seq data from paired RA blood and synovium CD8$^+$ T cells. a UMAP plots representing the expression levels of CD8A and CD4 in mRNA and CITE-seq Abs. **b** UMAP plots of ACPA+ RA blood (*n* = 3) and synovium (n = 4) CD8$^+$ T cells integrated with TCR clonality (*n* = 9,360 paired *TCRαβ* sequences). Color indicates the groups by the ratio of clonotypes in total cells. **c** UMAP plots showing the expression of *GZMB*, *GNLY* and *GZMK* in integrated blood and synovial CD8$^+$ T cells. Scale bars represent the normalized expression values. TCR T cell receptor.



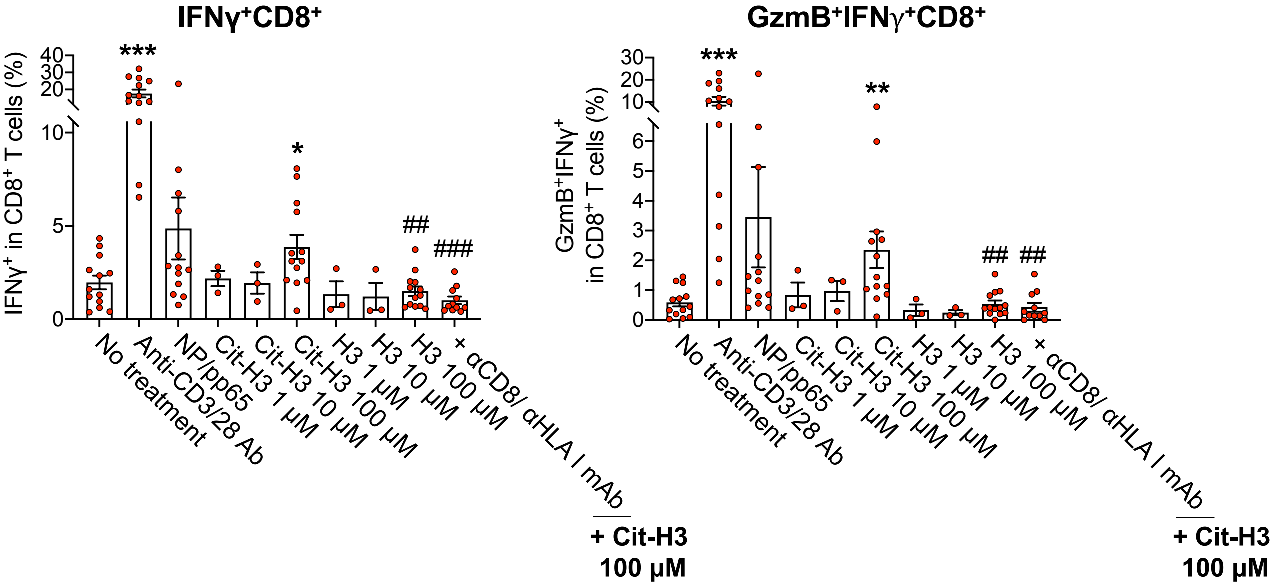
Supplementary Fig. 13: Shared T cell clonotypes between ACPA+ RA blood and matched synovium. a-d Mapping of shared clonotypes in the matched blood and synovium from ACPA+ RA patients. The frequent clonotypes are represented as CDR3 alpha-beta sequences. Dot plots show the expression level of *GZMB*, *GZMK*, and/or *GNLY* in the same clonotypes located in either blood (red) and synovium (blue). Source data are provided as a Source Data file.



Supplementary Fig. 14: ACPA+ RA patient blood CD8$^+$ T cells are activated by citrullinated proteins in a CD8:HLA class I-dependent manner. a-c Representative flow cytometric plots of ACPA+ RA blood CD8$^+$ T cells stimulated with citrullinated proteins (**a**), a range of concentrations of cit-vimentin or native vimentin (**b**), and in the presence of anti-CD8/ HLA class I-blocking antibodies (**c**). Ab antibody, Vim vimentin, Cit- citrullinated.

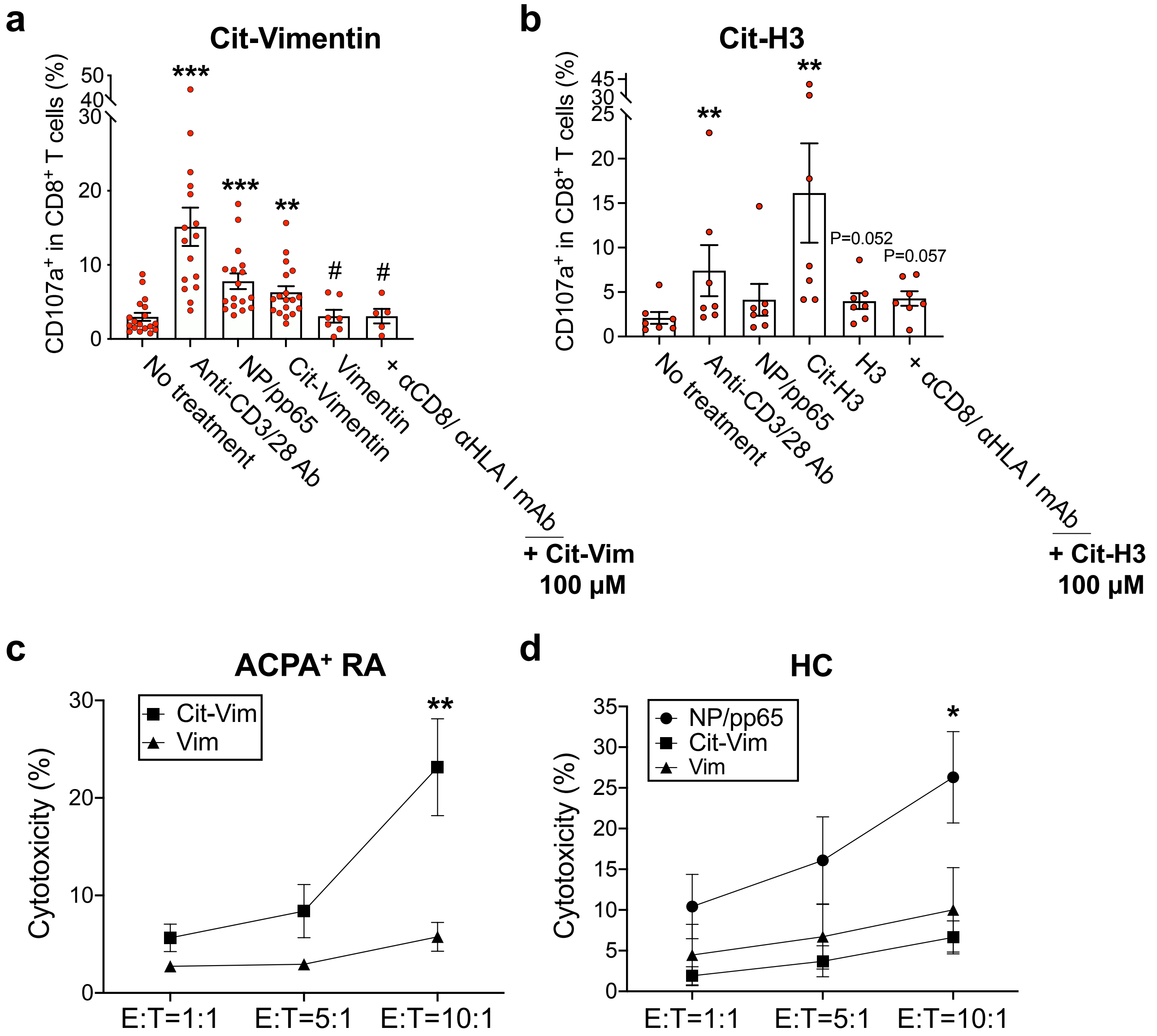

a
ACPA- RA
IFNγ+ in CD8+ T cells (%)
GzmB+IFNγ+ in CD8+ T cells (%)
0
10
20
30
40
60
80
*
**
No treatment
Anti-CD3/28 Ab
NP/pp65
Cit-Vimentin 100 μM
Cit-Fibrinogen 100 μM
Cit-α-Enolase 100 μM
Cit-H2B 100 μM
Cit-H3 100 μM
Cit-H4 100 μM
All cit proteins
All native proteins
Healthy control
35
45
50
b
ACPA- RA
Cit-Vimentin 1 μM
Cit-Vimentin 10 μM
Cit-Vimentin 100 μM
Vimentin 1 μM
Vimentin 10 μM
Vimentin 100 μM
Healthy control
5
15
25

Supplementary Fig. 15: ACPA- RA patient CD8$^+$ T cells react with viral but not citrullinated antigens. a Percentages of IFNγ and/ or GzmB-expressing CD8$^+$ T cells from PBMCs of ACPA- RA or HCs were measured by intracellular staining after stimulation with anti-CD3/28 antibodies, NP (Influenza)/ pp65 (CMV) proteins (50 μM of each), citrullinated proteins (vimentin, fibrinogen, α-enolase, and histones H2B, H3 or H4) (100 μM), all citrullinated proteins (20 μM each), or all native proteins (20 μM each) for 16 hr. For ACPA- RA, no stimulation (n = 5), anti-CD3/28 Abs (n = 5), NP/pp65 (n = 5), cit-vimentin (IFNγ$^+$ n = 8, GzmB$^+$IFNγ$^+$ n = 5), cit-fibrinogen, α-enolase, and histones H2B, H3 or H4 (n = 5), all cit proteins (n = 5), or all native proteins (n = 5); $^*P$=0.0296, or $^*P$=0.0498. For HC, no stimulation (n = 6), anti-CD3/28 Abs (n = 5), NP/pp65 (n = 6), cit-vimentin (IFNγ$^+$ n = 9, GzmB$^+$IFNγ$^+$ n = 6), cit-fibrinogen, α-enolase, and histones H2B, H3 or H4 (n = 6), all cit proteins (n = 4), or all native proteins (n = 6); $^*P$=0.0274, $^*P$=0.0201, $^*P$=0.0150, or $^{**}P$=0.0023. **b** Quantification of IFNγ$^+$ or IFNγ$^+$GzmB$^+$ CD8$^+$ T cells in ACPA- RA or HC PBMCs stimulated for 16 hr with cit-vimentin or native vimentin in a concentration-dependent manner. No stimulation (ACPA- RA and HC n = 5), anti-CD3/28 Abs (ACPA- RA and HC n = 5), NP/pp65 (ACPA- RA and HC n = 5), cit-vimentin 1 or 10 μM (ACPA- RA and HC n = 4), cit-vimentin 100 μM (ACPA- RA and HC n = 5), vimentin 1,10 or 100 μM (ACPA- RA n = 3 and HC n = 4). In ACPA- RA, $^*P$=0.0462, or $^*P$=0.05. In HC, $^*P$=0.0385, $^{**}P$=0.033, $^*P$=0.024, or $^*P$=0.0491. For **a, b,** data are presented as means ± SEM. By two-tailed unpaired *t*-test: $^*P < 0.05$ or $^{**}P < 0.01$ versus no treatment. Source data are provided as a Source Data file. ACPA anti-citrullinated protein antibodies, RA rheumatoid arthritis, Ab antibody.



Supplementary Fig. 16: ACPA+ RA blood CD8$^+$ T cells react with cit-H3.

Percentage of IFNγ or GzmB expressing CD8$^+$ T cells in ACPA+ RA blood measured by intracellular staining after stimulation with a range of concentrations of citrullinated histone H3 (cit-H3) or native H3 protein in presence or absence of anti-CD8/HLA class I-blocking antibodies for 16 hrs. No stimulation (n = 13), anti-CD3/28 Abs (n = 13), NP/pp65 (n = 13), cit-H3 or native H3 1 or 10 μM (n = 3), cit-H3 or native H3 100 μM (n = 13), cit-H3 with anti-CD8/ HLA class I antibodies (n = 11). For IFNγ$^+$CD8$^+$, $^{***}P$<0.0001, $^{*}P$=0.0172, $^{\#\#}P$=0.0023, or $^{\#\#\#}P$=0.0007. For GzmB$^+$IFNγ$^+$CD8$^+$, $^{***}P$<0.0001, $^{**}P$=0.0098, $^{\#\#}P$=0.0077, or $^{\#\#}P$=0.0099. Data are presented as means ± SEM. By two-tailed unpaired *t*-test: $*P < 0.05$, $**P < 0.01$ or $***P < 0.001$ versus no treatment, and $^{\#\#}P < 0.01$ or $^{\#\#\#}P < 0.001$ versus cit-H3 100 μM. Source data are provided as a Source Data file. Ab antibody.



Supplementary Fig. 17: Citrullinated antigens stimulate ACPA+ RA blood CD8$^+$ T cells to exhibit cytotoxic activity and mediate cell killing. a, b Flow cytometry analysis of CD107a$^+$ expression by CD8$^+$ T cells was used as a measure of degranulation activity. ACPA+ RA blood samples were stimulated with citrullinated or native forms of the RA autoantigens vimentin and histone H3 (100 µM each), with or without anti-CD8/ HLA class I-blocking antibodies, and flow cytometry analysis performed to quantitate CD107a$^+$CD8$^+$ T cells. For (**a**), no stimulation (n = 18), anti-CD3/28 Abs (n = 16), NP/pp65 (n = 17), cit-vimentin (n = 18), vimentin (n = 7), cit-vimentin with anti-CD8/ HLA class I antibodies (n = 5); $^{***}P < 0.0001$, $^{***}P=0.0003$, $^{**}P=0.0021$, $^{\#}P=0.0364$, or $^{\#}P=0.0494$. For (**b**), n = 7; $^{***}P < 0.0001$, or $^{*}P=0.028$. **c, d** Antigen-independent cytotoxic activity of cit-vimentin, native vimentin, or viral protein stimulated $CD8^+$ T cells from ACPA+ RA (**c**) or HC (**d**) blood against the DLD-1 cell line was determined using a lactate dehydrogenase (LDH) release assay. For (**c**), cit-vimentin (n = 7) and vimentin (n = 5); $^{**}P=0.0025$. For (**d**), NP/pp65 (n = 14), cit-vimentin or vimentin (n = 3). E:T ratio means effector/target cell ratio. Data are presented as means ± SEM. For (**a, b**), using two-tailed unpaired *t*-test: $^{*}P < 0.05$, $^{**}P < 0.01$, or $^{***}P < 0.001$ versus no treatment; $^{\#}P < 0.05$ versus cit-vimentin; *P* value represented on the graph was compared with cit-vimentin. For (**c, d**), using two-way ANOVA with Tukey's multiple comparisons test: $**P < 0.01$. Source data are provided as a Source Data file. HC healthy control, ACPA anti-citrullinated protein antibodies, RA rheumatoid arthritis, mAb monoclonal antibody, Cit-Vim citrullinated vimentin.

Supplementary Tables

Supplementary Table 1. Demographic characteristics of RA patients.

	RA patients
Total Number	59
Gender, Female/Male	4/55
Age (years) - mean±SD	66.15±12.24
Dis duration (years) - mean±SD	11.35±10.69
Disease activity	
ACPA positive (%)	76.27
RF positive (%)	73.33
CDAI score - mean±SD	15.17±15.95
MTX use (%)	51.11
MTX duration (years)	4.96±4.9

Supplementary Table 2 Differentially expressed genes in each cluster identified in ACPA+ RA as compared to HC blood. Differentially expressed genes in each cluster were selected with Log2 Fold change > 0.8. Wilcoxon Rank Sum test and the Benjamini–Hochberg method to adjust the *P* values for multiple testing. Avg average, Pct percentage, p_val_adj adjusted *P* value.

Gene	Avg_log2FC	Pct.1	Pct.2	p_val_adj	Cluster
CCR7	2.17188736	0.952	0.528	0	Naïve
LEF1	2.00017763	0.954	0.652	0	Naïve
ACTN1	1.50463023	0.94	0.711	0	Naïve
NELL2	1.42062488	0.889	0.612	0	Naïve
MAL	1.32861183	0.804	0.643	0	Naïve
LTB	1.29286009	0.964	0.78	0	Naïve
SELL	1.25489209	0.951	0.817	0	Naïve
NOSIP	1.2525314	0.947	0.812	0	Naïve
OXNAD1	1.2385171	0.956	0.681	0	Naïve
PIK3IP1	1.1523528	0.96	0.805	0	Naïve
AIF1	1.14401643	0.867	0.767	0	Naïve
TRABD2A	1.07210543	0.915	0.757	0	Naïve
LDLRAP1	1.05680921	0.928	0.822	0	Naïve
CD27	1.03820024	0.934	0.718	0	Naïve
SPINT2	1.02349056	0.967	0.724	0	Naïve
SNHG8	0.99485116	0.993	0.924	0	Naïve
NDFIP1	0.97624462	0.986	0.869	0	Naïve
ABLIM1	0.96524899	0.787	0.402	0	Naïve
CD8B	0.90637784	0.98	0.9	0	Naïve
CAMK4	0.85677228	0.958	0.737	0	Naïve
ARMH1	0.82194778	0.793	0.738	0	Naïve
HSPB1	0.79107008	0.972	0.821	0	Naïve
PCED1B	0.76851258	0.867	0.737	0	Naïve
RCAN3	0.74887121	0.782	0.717	0	Naïve
LDHB	0.74089477	0.961	0.907	0	Naïve
TCF7	0.95014837	0.841	0.758	3.76E-301	Naïve
CD55	0.86560341	0.88	0.786	3.17E-286	Naïve
SATB1	0.76575809	0.749	0.593	1.77E-205	Naïve
FLT3LG	0.71486197	0.879	0.791	1.39E-199	Naïve
S100B	0.81117364	0.72	0.75	1.09E-184	Naïve

FGFBP2	2.64092332	0.994	0.896	0	*GZMB+ GNLY+*
GZMH	2.48081498	0.982	0.899	0	*GZMB+ GNLY+*
GNLY	2.2873411	0.956	0.666	0	*GZMB+ GNLY+*
GZMB	2.20826241	0.949	0.829	0	*GZMB+ GNLY+*
ZNF683	1.93895227	0.954	0.888	0	*GZMB+ GNLY+*
NKG7	1.86436384	0.999	0.888	0	*GZMB+ GNLY+*
PRF1	1.71556813	0.988	0.773	0	*GZMB+ GNLY+*
ADGRG1	1.69693841	0.956	0.796	0	*GZMB+ GNLY+*
LGALS1	1.62412354	0.905	0.789	0	*GZMB+ GNLY+*
SPON2	1.56725113	0.933	0.694	0	*GZMB+ GNLY+*
PRSS23	1.46520941	0.945	0.865	0	*GZMB+ GNLY+*
FCGR3A	1.40710564	0.927	0.738	0	*GZMB+ GNLY+*
CX3CR1	1.31747937	0.874	0.788	0	*GZMB+ GNLY+*
ZEB2	1.29236084	0.834	0.797	0	*GZMB+ GNLY+*
PLEK	1.27834466	0.87	0.707	0	*GZMB+ GNLY+*
CST7	1.25537403	0.993	0.952	0	*GZMB+ GNLY+*
CCL4	1.25062717	0.856	0.876	0	*GZMB+ GNLY+*
ITGB1	1.21597628	0.94	0.911	0	*GZMB+ GNLY+*
KLRD1	1.21207058	0.915	0.787	0	*GZMB+ GNLY+*
EFHD2	1.17334611	0.876	0.717	0	*GZMB+ GNLY+*
FCRL6	1.15172947	0.935	0.93	0	*GZMB+ GNLY+*
TBX21	1.15137019	0.938	0.891	0	*GZMB+ GNLY+*
GZMA	1.14945792	0.986	0.847	0	*GZMB+ GNLY+*
S100A4	1.13366146	0.995	0.937	0	*GZMB+ GNLY+*
ITGB2	1.07810461	0.995	0.959	0	*GZMB+ GNLY+*
FLNA	1.06917519	0.974	0.941	0	*GZMB+ GNLY+*
S1PR5	1.01688766	0.906	0.847	0	*GZMB+ GNLY+*
SLC9A3R1	0.98919573	0.974	0.894	0	*GZMB+ GNLY+*
CCL5	0.97731527	0.994	0.97	0	*GZMB+ GNLY+*
HOPX	0.97559354	0.913	0.871	0	*GZMB+ GNLY+*
FCGR3A	1.78521332	0.98	0.784	3.47E-253	*GZMB+ KIR+*
TTC38	1.06213688	0.961	0.761	3.68E-205	*GZMB+ KIR+*
KIR3DL2	0.78538508	0.816	0.57	4.05E-177	*GZMB+ KIR+*
TRDV1	1.75850042	0.823	0.758	3.73E-166	*GZMB+ KIR+*
NKG7	1.08540583	0.999	0.916	6.13E-161	*GZMB+ KIR+*
S1PR5	0.96269525	0.953	0.86	1.03E-154	*GZMB+ KIR+*
GZMB	1.12077486	0.971	0.859	1.27E-147	*GZMB+ KIR+*
KLRC3	1.17386824	0.793	0.594	2.35E-140	*GZMB+ KIR+*
ADGRG1	0.93451484	0.941	0.837	1.72E-135	*GZMB+ KIR+*

CST7	0.93584796	0.991	0.962	1.76E-130	*GZMB+ KIR+*
PRF1	1.01856434	0.989	0.828	4.97E-124	*GZMB+ KIR+*
TBX21	0.78939386	0.944	0.903	1.23E-123	*GZMB+ KIR+*
C1orf21	0.7426384	0.904	0.855	7.30E-122	*GZMB+ KIR+*
KLRD1	1.06721614	0.936	0.819	3.51E-117	*GZMB+ KIR+*
FGR	0.87854003	0.909	0.886	2.99E-115	*GZMB+ KIR+*
FCRL6	0.8177497	0.964	0.93	9.00E-114	*GZMB+ KIR+*
FGFBP2	0.8305155	0.983	0.922	9.59E-108	*GZMB+ KIR+*
CCL5	0.78234757	0.995	0.976	9.86E-99	*GZMB+ KIR+*
PLEK	0.84156567	0.912	0.747	7.33E-93	*GZMB+ KIR+*
GZMH	0.76278171	0.967	0.921	9.21E-89	*GZMB+ KIR+*
CMC1	0.83244954	0.816	0.632	8.14E-75	*GZMB+ KIR+*
CCL4	0.8534083	0.916	0.868	2.86E-68	*GZMB+ KIR+*
IKZF2	0.77393067	0.693	0.574	4.91E-65	*GZMB+ KIR+*
TIGIT	1.00714799	0.741	0.696	9.89E-58	*GZMB+ KIR+*
ZEB2	0.80594977	0.82	0.807	3.56E-55	*GZMB+ KIR+*
CD63	0.7813272	0.859	0.812	1.37E-53	*GZMB+ KIR+*
GNLY	0.80162342	0.881	0.744	2.43E-53	*GZMB+ KIR+*
KLRF1	0.93276105	0.648	0.531	5.53E-38	*GZMB+ KIR+*
NCR1	0.82343017	0.592	0.417	5.63E-19	*GZMB+ KIR+*
TYROBP	0.84125194	0.66	0.688	3.20E-12	*GZMB+ KIR+*
TRDV2	1.99128693	0.913	0.407	0	*TCRgd+*
TRGV9	1.92133086	0.852	0.666	1.24E-221	*TCRgd+*
TYROBP	1.33879925	0.875	0.677	2.75E-189	*TCRgd+*
MAP3K8	0.63507239	0.974	0.865	1.50E-171	*TCRgd+*
S100B	0.62382483	0.867	0.736	5.13E-162	*TCRgd+*
DUSP2	1.05992088	0.996	0.965	4.05E-146	*TCRgd+*
KLRB1	1.04734785	0.882	0.763	1.68E-121	*TCRgd+*
MATK	0.71312879	0.949	0.881	6.32E-108	*TCRgd+*
KLRG1	0.85459333	0.913	0.73	2.58E-103	*TCRgd+*
KLRD1	0.77247908	0.933	0.819	1.04E-102	*TCRgd+*
ID2	0.92916918	0.965	0.78	3.99E-97	*TCRgd+*
ALOX5AP	0.80492512	0.915	0.815	1.02E-71	*TCRgd+*
GNLY	0.74442669	0.879	0.743	5.58E-71	*TCRgd+*
CST7	0.58130969	0.99	0.962	1.93E-64	*TCRgd+*
NKG7	0.57142342	0.998	0.916	3.11E-63	*TCRgd+*
DUSP1	0.82391136	0.98	0.889	2.01E-61	*TCRgd+*
KRT10	0.55492149	0.988	0.941	6.52E-59	*TCRgd+*
TRDC	1.1402084	0.663	0.562	4.61E-51	*TCRgd+*

PRELID1	0.56047116	0.969	0.858	2.82E-46	*TCRgd+*
ANXA1	0.52941704	0.973	0.894	4.07E-45	*TCRgd+*
APOBEC3G	0.53168543	0.853	0.825	6.76E-42	*TCRgd+*
ZFP36	0.52644306	0.981	0.916	3.04E-38	*TCRgd+*
IL2RB	0.53117476	0.928	0.861	1.33E-31	*TCRgd+*
CD300A	0.51766821	0.7	0.544	1.28E-24	*TCRgd+*
NCR3	0.5182753	0.65	0.648	2.80E-12	*TCRgd+*
TRGC1	0.68535161	0.565	0.393	4.71E-10	*TCRgd+*
KLRC1	0.58682728	0.394	0.33	7.14E-06	*TCRgd+*
GZMK	1.99717379	0.895	0.768	0	*GZMK+*
DUSP2	1.35848465	0.991	0.96	0	*GZMK+*
CD74	1.07464734	0.946	0.907	0	*GZMK+*
COTL1	0.66638748	0.93	0.872	7.40E-248	*GZMK+*
RGS1	0.83275317	0.705	0.643	9.78E-207	*GZMK+*
FYN	0.81771733	0.904	0.784	1.04E-193	*GZMK+*
CMC1	1.0803568	0.754	0.615	1.22E-184	*GZMK+*
CCL4	0.63132847	0.892	0.866	3.33E-149	*GZMK+*
CCL5	0.52091684	0.989	0.975	5.05E-143	*GZMK+*
LYAR	0.58186799	0.882	0.839	3.17E-104	*GZMK+*
IL10RA	0.51340213	0.945	0.897	4.31E-87	*GZMK+*
TIGIT	0.68709491	0.686	0.701	1.23E-81	*GZMK+*
LYST	0.56801848	0.693	0.615	2.91E-77	*GZMK+*
PIK3R1	0.57399294	0.74	0.748	1.04E-46	*GZMK+*
LTB	1.07119384	0.977	0.804	0	Memory
IL7R	1.03381631	0.981	0.791	0	Memory
COTL1	0.76448942	0.959	0.871	0	Memory
CAPG	0.55036677	0.898	0.714	0	Memory
AQP3	0.54135708	0.898	0.798	5.71E-169	Memory
LGALS3	0.58233773	0.816	0.783	2.94E-168	Memory
JUNB	0.65509324	0.997	0.977	3.32E-153	Memory
ARHGAP15	0.76563726	0.913	0.809	2.03E-151	Memory
PTGER2	0.55948452	0.912	0.815	5.78E-145	Memory
LDHB	0.60480366	0.963	0.915	1.60E-143	Memory
CXCR3	0.64707736	0.868	0.738	4.90E-143	Memory
FXYD2	0.72697369	0.762	0.702	1.39E-142	Memory
FOS	0.59514237	0.921	0.784	6.91E-139	Memory
TIMP1	0.619823	0.838	0.698	3.64E-115	Memory
PLP2	0.68495292	0.86	0.759	9.64E-105	Memory
TCF7	0.53829795	0.884	0.763	1.00E-100	Memory

KLRB1	2.46140509	0.967	0.757	0	*CCR6+ CD161+*
LST1	0.65603783	0.865	0.596	1.93E-208	*CCR6+ CD161+*
IL7R	1.23562461	0.984	0.806	4.41E-207	*CCR6+ CD161+*
DPP4	0.91774681	0.888	0.701	1.12E-188	*CCR6+ CD161+*
TYROBP	1.19564119	0.884	0.675	1.58E-184	*CCR6+ CD161+*
MYC	0.7221775	0.942	0.667	4.50E-178	*CCR6+ CD161+*
TTC39C	0.78485329	0.964	0.854	2.13E-173	*CCR6+ CD161+*
GZMK	1.10947754	0.925	0.783	1.66E-162	*CCR6+ CD161+*
NFKBIA	1.35943949	0.936	0.831	2.11E-147	*CCR6+ CD161+*
NCR3	1.36753518	0.838	0.637	1.26E-143	*CCR6+ CD161+*
DUSP1	1.12077918	0.982	0.888	3.22E-142	*CCR6+ CD161+*
AQP3	1.08914582	0.927	0.804	1.39E-133	*CCR6+ CD161+*
LGALS3	0.95770062	0.805	0.786	3.32E-125	*CCR6+ CD161+*
SLAMF1	0.66166051	0.811	0.609	1.59E-108	*CCR6+ CD161+*
ALOX5AP	0.97222512	0.922	0.813	6.24E-106	*CCR6+ CD161+*
GCHFR	0.84474297	0.805	0.628	2.54E-105	*CCR6+ CD161+*
KLRG1	0.91738742	0.904	0.73	1.29E-93	*CCR6+ CD161+*
CXCR6	0.89331155	0.719	0.547	7.54E-90	*CCR6+ CD161+*
CCR6	0.81160558	0.728	0.758	1.09E-88	*CCR6+ CD161+*
LTB	0.80620585	0.967	0.817	1.07E-75	*CCR6+ CD161+*
ZBTB16	0.90784986	0.697	0.641	6.60E-71	*CCR6+ CD161+*
CD69	0.83337076	0.925	0.84	3.02E-52	*CCR6+ CD161+*
GBP5	0.60826196	0.851	0.675	5.81E-48	*CCR6+ CD161+*
FOS	0.65314205	0.928	0.794	1.06E-43	*CCR6+ CD161+*
ERN1	0.83350715	0.73	0.697	4.33E-36	*CCR6+ CD161+*
SLC4A10	0.89645098	0.615	0.378	8.03E-31	*CCR6+ CD161+*
JAML	0.6162617	0.669	0.581	7.01E-29	*CCR6+ CD161+*
ZFP36L1	0.69958413	0.82	0.735	5.53E-26	*CCR6+ CD161+*
TMIGD2	0.72239382	0.697	0.714	9.21E-26	*CCR6+ CD161+*
DDIT4	0.7047064	0.984	0.947	1.59E-17	*CCR6+ CD161+*

Supplementary Table 3. HLA typing of ACPA+ RA patients. 12 ACPA+ RA patients were randomly selected and sequenced to get HLA types.

Sample ID	A/1	A/2	B/1	B/2	C/1	C/2
JG330	A*29:02:01:01	A*32:01:01:01	B*35:03:01:01	B*44:02:01:01	C*12:03:01:01	C*05:01:01:02
JG331	A*24:07:01	A*11:02:01	B*15:35	B*55:02:01:03	C*07:02:01:01	C*01:02:01:01
JG332	A*24:02:01:01	A*01:01:01:01	B*27:05:02:05	B*08:01:01:01	C*02:02:02:01	C*07:01:01:01
JG127	A*03:01:01:01	A*01:01:01:01	B*35:01:01:05	B*52:01:01:02	C*04:01:01:11	C*12:02:02:01
JG128	A*23:01:01:01	A*11:01:01:01	B*07:02:01:01	B*35:01:01:05	C*07:02:01:03	C*04:01:01:01
JG129	A*23:01:01:01	A*68:01:01:02	B*49:01:01:01	B*15:220:01:01	C*07:01:01:16	C*04:01:01:01
JG143	A*02:01:01:01	A*74:01:01:01	B*42:01:01	B*27:05:02:01	C*17:01:01:02	C*15:02:01:01
JG147	A*11:01:01:01	A*02:06:01:01	B*40:01:02:01	B*51:01:01:05	C*03:04:01:02	C*15:02:01:03
JG149	A*24:02:01:01	A*31:01:02:01	B*08:01:01:01	B*57:01:01:01	C*07:01:01:01	C*06:02:01:01
JG159	A*29:02:01:02	A*29:02:01:01	B*45:01:01:01	B*44:03:01:01	C*06:02:01:01	C*16:01:01:01
JG262	A*03:01:01:01	A*01:01:01:01	B*40:01:02:01	B*08:01:01:01	C*03:04:01:01	C*07:01:01:01
JG272	A*30:01:01:01	A*30:01:01:01	B*53:01:01:01	B*44:03:01:10	C*04:01:01:14	C*17:01:01:02
Sample ID	**DPA1/1**	**DPA1/2**	**DPB1/1**	**DPB1/2**	**DQA1/1**	**DQA1/2**
JG330	DPA1*02:02:02:01	DPA1*01:03:01:05	DPB1*05:01:01:01	DPB1*04:02:01:02	DQA1*03:01:01	DQA1*05:05:01:02
JG331	DPA1*02:02:02:01	X	DPB1*05:01:01:01	DPB1*01:01:01:04	DQA1*03:03:01:02	DQA1*06:01:01:02
JG332	DPA1*01:03:01:01	DPA1*1:03:01:05	DPB1*02:01:02:05/416:01	DPB1*04:02:01:02/105:01/665:01	DQA1*03:01:01	DQA1*01:01:01:05
JG127	DPA1*01:03:01:04	DPA1*01:03:01:02	DPB1*04:01:01:06	DPB1*04:01:01:05	DQA1*01:01:01:05	DQA1*03:01:01
JG128	DPA1*02:06	DPA1*01:03:01:04	DPB1*04:01:01:06	DPB1*04:01:01:05	DQA1*01:02:01:03	DQA1*03:01:01
JG129	DPA1*02:01:08:02	DPA1*02:01:01:01	DPB1*01:01:01:01	DPB1*11:01:01:01	DQA1*03:03:01:01	DQA1*01:02:01:04
JG143	DPA1*02:01:08:02	DPA1*01:03:01:01	DPB1*01:01:01:01	DPB1*02:01:02:05	DQA1*04:01:01:04	DQA1*04:01:01:02
JG147	DPA1*02:02:02:01	DPA1*02:02:02:01	DPB1*05:01:01:01	DPB1*03:01:01:01	DQA1*03:03:01:03	DQA1*03:03:01:03
JG149	DPA1*01:03:01:04	DPA1*01:03:01:02	DPB1*04:01:01:06	DPB1*04:01:01:05	DQA1*05:01:01:02	DQA1*03:03:01:01
JG159	DPA1*01:03:01:02	DPA1*01:03:01:01	DPB1*16:01:01:01	DPB1*04:01:01:05	DQA1*03:03:01:01	DQA1*02:01:01:01
JG262	DPA1*01:03:01:03	DPA1*01:03:01:02	DPB1*03:01:01:01	DPB1*04:01:01:05	DQA1*03:01:01	DQA1*05:01:01:02
JG272	DPA1*01:03:01:02	DPA1*02:01:08:02	DPB1*104:01:01:01	DPB1*01:01:01:01	DQA1*01:02:01:03	DQA1*05:05:01:01
Sample ID	**DQB1/1**	**DQB1/2**	**DRB1/1**	**DRB1/2**	**DRB345/1**	**DRB345/2**
JG330	DQB1*03:02:01:01	DQB1*03:01:01:03	DRB1*04:01:01:03	DRB1*11:04:01	DRB4*01:03:01:10	DRB3*02:02:01:04
JG331	DQB1*04:02:01:09	DQB1*03:01:01:12	DRB1*04:05:01:01	DRB1*12:02:01:01	DRB4*01:03:01:01	DRB3*03:01:03
JG332	DQB1*03:02:01:01	DQB1*05:01:01:03	DRB1*04:01:01:03	DRB1*01:01:01	DRB4*01:03:01:10	Absent

JG127	DQB1*05:01:01:03	DQB1*03:02:01:02	DRB1*01:01:01	DRB1*04:04:01	DRB4*01:03:03	Absent
JG128	DQB1*06:02:01:01	DQB1*03:02:01:02	DRB1*15:01:01:05	DRB1*04:04:01	DRB5*01:01:01:01	DRB4*01:03:01:01
JG129	DQB1*02:02:01:02	DQB1*05:01:01:03	DRB1*09:01:02:01	DRB1*13:02:01:02	DRB4*01:01:01:01	DRB3*03:01:01:01
JG143	DQB1*04:02:01:08	DQB1*04:02:01:04	DRB1*08:11	DRB1*03:02:01	DRB3*01:62	Absent
JG147	DQB1*04:01:01:02	DQB1*04:01:01:02	DRB1*04:05:01:03	DRB1*04:05:01:02	DRB4*01:03:01:01	DRB4*01:03:01:01
JG149	DQB1*02:01:01	DQB1*03:01:01:01	DRB1*03:01:01:01	DRB1*04:01:01:01	DRB3*01:01:02:01	DRB4*01:03:01:10
JG159	DQB1*03:01:01:01	DQB1*02:02:01:01	DRB1*04:01:01:03	DRB1*07:01:01:04	DRB4*01:03:01:10	DRB4*01:01:01:01
JG262	DQB1*03:02:01:02	DQB1*02:01:01	DRB1*04:04:01	DRB1*03:01:01:01	DRB4*01:03:01:10	DRB3*01:01:02:01
JG272	DQB1*06:02:01:01	DQB1*03:01:01:03	DRB1*15:03:01:02	DRB1*13:03:01	DRB5*01:01:01:01	DRB3*01:01:02:03

Supplementary Table 4. Antibodies used in flow cytometry experiments.

Marker	Clone	Fluorescence	Company	Dilution
CD3	SK7	APC-H7	BD Biosciences	1:200
CD4	RPA-T4	FITC Pacific Blue	BD Biosciences BioLegend	1:200 1:200
CD8	RPA-T8	Alexa Fluor 700	BD Biosciences	1:200
CD69	FN50	PerCP-Cy5.5	BD Biosciences	1:200
GPR56	CG4	PE	BioLegend	1:200
TCRγδ	B1	FITC	BD Biosciences	1:200
Granzyme K	G3H69	Alexa Fluor 647	BD Biosciences	1:150
Granzyme B	GB11	PE FITC	BD Biosciences	1:200 1:200
CCR7	150503	PE	BD Biosciences	1:150
CD45RA	HI100	Brilliant Violet 421 FITC	BioLegend BD Biosciences	1:200 1:200
PD-1	NAT105	PerCP-Cy5.5	BioLegend	1:200
TIM3	F38-2E2	APC	BioLegend	1:200
CD158b (KIR2DL2/L3)	DX27	FITC	BioLegend	1:200
His-tag	J095G46	PE	BioLegend	1:100
HLA-A,B,C	W6/32	APC-Cy7	BioLegend	1:200
Ki-67	Ki-67	Brilliant Violet 421	BioLegend	1:100
IFNγ	4S.B3 B27 B27	APC-Cy7 PE APC	BioLegend BioLegend BD Biosciences	1:200 1:200 1:150
CD107a	H4S3	APC-Cy7	BioLegend	1:200

Supplementary Table 5. CITE-seq antibodies used in 10X single cell RNA sequencing.

TotalSeqC-Barcode	Specificity	Clone	Reactivity	Barcode sequence
34	CD3	UCHT1	Human	CTCATTGTAACTCCT
45	CD4	SK3	Human	GAGGTTAGTGATGGA
46	CD8	SK1	Human	GCGCAACTTGATGAT
50	CD19	HIB19	Human	CTGGGCAATTACTCG
63	CD45RA	HI100	Human	TCAATCCTTCCGCTT
84	CD56	QA17A16	Human	TTCGCCGCATTGAGT
85	CD25	BC96	Human	TTTGTCCTGTACGCC
87	CD45RO	UCHL1	Human	CTCCGAATCATGTTG
88	PD-1	EH12.2H7	Human	ACAGCGCCGTATTTA
89	TIGIT	A15153G	Human	TTGCTTACCGCCAGA
139	TCRrd	B1	Human	CTTCCGATTCATTCA
140	CXCR3	G025H7	Human	GCGATGGTAGATTAT
143	CCR6	G034E3	Human	GATCCCTTTGTCACT
144	CXCR5	J252D4	Human	AATTCAACCGTCGCC
146	CD69	FN50	Human	GTCTCTTGGCTTAAA
147	CD62L	DREG-56	Human	GTCCCTGCAACTTGA
148	CD197/CCR7	G043H7	Human	AGTTCAGTCAACCGA
149	CD161	HP-3G10	Human	GTACGCAGTCCTTCT
154	CD27	O323	Human	GCACTCCTGCATGTA
159	HLA-DR	L243	Human	AATAGCGAGCAAGTA
165	NKG2D	1D11	Human	CGTGTTTGTTCCTCA
168	CD57	QA17A04	Human	AACTCCCTATGGAGG
179	CX3CR1	K0124E1	Human	AGTATCGTCTCTGGG
224	TCRab	IP26	Human	CGTAACGTAGAGCGA
246	CD122	TU27	Human	TCATTTCCTCCGATT
250	KLRG1	2F1/KLRG1	Human/Mouse	GTAGTAGGCTAGACC
386	CD28	CD28.2	Human	TGAGAACGACCCTAA
389	CD38	HIT2	Human	TGTACCCGCTTGTGA
390	IL-7Ra	A019D5	Human	GTGTGTTGTCCTATG
592	CD158b/KIR2DL2/L3	DX27	Human	GACCCGTAGTTTGAT
599	CD158e1/KIR3DL1	DX9	Human	GGACGCTTTCCTTGA

Supplementary Table 6. Gene list used to measure a score of synovial trafficking, cytotoxicity, proliferation or inflammation.

RA trafficking	Cytotoxicity	Proliferation	Inflammation
CXCR1	*GNLY*	*HMGB2*	*AGER*
CXCR2	*GZMA*	*CDK1*	*ALOX12*
CXCR3	*GZMB*	*NUSAP1*	*ALOX15*
CXCR4	*GZMH*	*UBE2C*	*ALOX5*
CXCR5	*GZMM*	*BIRC5*	*AREG*
CCR1	*GZMK*	*TPX2*	*ATF2*
CCR2	*NKG7*	*TOP2A*	*BCL2L1*
CCR3	*KLRB1*	*NDC80*	*BCL6*
CCR4	*KLRD1*	*CKS2*	*BIRC2*
CCR5	*KLRK1*	*NUF2*	*C1QA*
CCR6	*NCR1*	*CKS1B*	*C1QB*
CCR10	*SLAMF6*	*MKI67*	*C1R*
CX3CR1	*SLAMF7*	*TMPO*	*C1S*
CCL2	*TYROBP*	*CENPF*	*C2*
CCL3	*KIR3DL1*	*TACC3*	*C3*
CCL4	*KIR3DL2*	*SMC4*	*C3AR1*
CCL5		*CCNB2*	*C5*
CCL19		*CKAP2L*	*CCL17*
CCL20		*CKAP2*	*CCL19*
CXCL10		*AURKB*	*CCL2*
CXCL16		*BUB1*	*CCL20*
		KIF11	*CCL22*
		ANP32E	*CCL23*
		TUBB4B	*CCL24*
		GTSE1	*CCL3*
		KIF20B	*CCL4*
		HJURP	*CCL5*
		CDCA3	*CCR1*
		CDC20	*CCR2*
		TTK	*CCR3*
		CDC25C	*CCR4*
		KIF2C	*CCR7*
		RANGAP1	*CD4*

		NCAPD2	*CD40*
		DLGAP5	*CD40LG*
		CDCA2	*CD55*
		CDCA8	*CD86*
		ECT2	*CDC42*
		KIF23	*CEBPB*
		HMMR	*CFB*
		AURKA	*CFD*
		PSRC1	*CFL1*
		ANLN	*CREB1*
		LBR	*CSF1*
		CKAP5	*CSF2*
		CENPE	*CXCL10*
		CTCF	*CXCL3*
		NEK2	*CXCL9*
		G2E3	*CXCR1*
		GAS2L3	*CXCR2*
		CBX5	*CXCR4*
		CENPA	*CYSLTR1*
			CYSLTR2
			DAXX
			DDIT3
			ELK1
			FASLG
			FLT1
			FOS
			FXYD2
			GNAQ
			GNAS
			GNB1
			GRB2
			HDAC4
			HIF1A
			HLA-DRA
			HLA-DRB1
			HMGB1
			HMGB2
			HMGN1
			HRAS

			HSH2D
			HSPB1
			IFI44
			IFIT1
			IFIT2
			IFIT3
			IFNG
			IL10
			IL10RB
			IL12A
			IL13
			IL15
			IL17A
			IL18
			IL18RAP
			IL1A
			IL1B
			IL1R1
			IL1RAP
			IL1RN
			IL2
			IL21
			IL22
			IL22RA2
			IL23A
			IL23R
			IL3
			IL4
			IL5
			IL6
			IL6R
			IL7
			IRF1
			IRF3
			IRF5
			IRF7
			ITGB2
			JUN
			KEAP1

			LIMK1
			LTA
			LTB
			LTB4R
			LTB4R2
			LY96
			MAFF
			MAFG
			MAFK
			MAP2K1
			MAP2K4
			MAP2K6
			MAP3K1
			MAP3K5
			MAP3K7
			MAP3K9
			MAPK1
			MAPK14
			MAPK3
			MAPK8
			MAPKAPK2
			MAPKAPK5
			MASP2
			MAX
			MEF2A
			MEF2C
			MEF2D
			MKNK1
			MMP9
			MRC1
			MX1
			MX2
			MYC
			MYD88
			NFATC3
			NFE2L2
			NFKB1
			NLRP3
			NOD1

			NOD2
			NR3C1
			OAS2
			OASL
			PDGFA
			PLA2G4A
			PLCB1
			PPP1R12B
			PRKCA
			PRKCB
			PTGDR2
			PTGER2
			PTGER4
			PTGIR
			PTGS1
			PTGS2
			PTK2
			RAC1
			RAF1
			RAPGEF2
			RELA
			RELB
			RHOA
			RIPK1
			RIPK2
			ROCK2
			RPS6KA5
			SHC1
			SMAD7
			STAT1
			STAT2
			STAT3
			TBXA2R
			TCF4
			TGFB1
			TGFB3
			TGFBR1
			TLR1
			TLR2

			TLR3
			TLR4
			TLR5
			TLR6
			TLR8
			TLR9
			TNF
			TNFAIP3
			TNFSF14
			TOLLIP
			TRADD
			TRAF2
			TREM2
			TSLP
			TYROBP