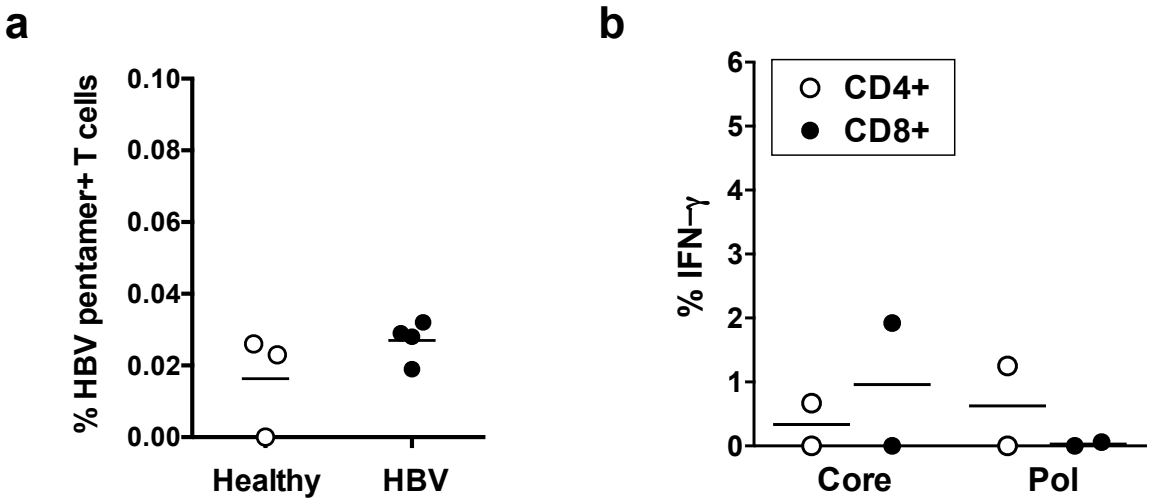
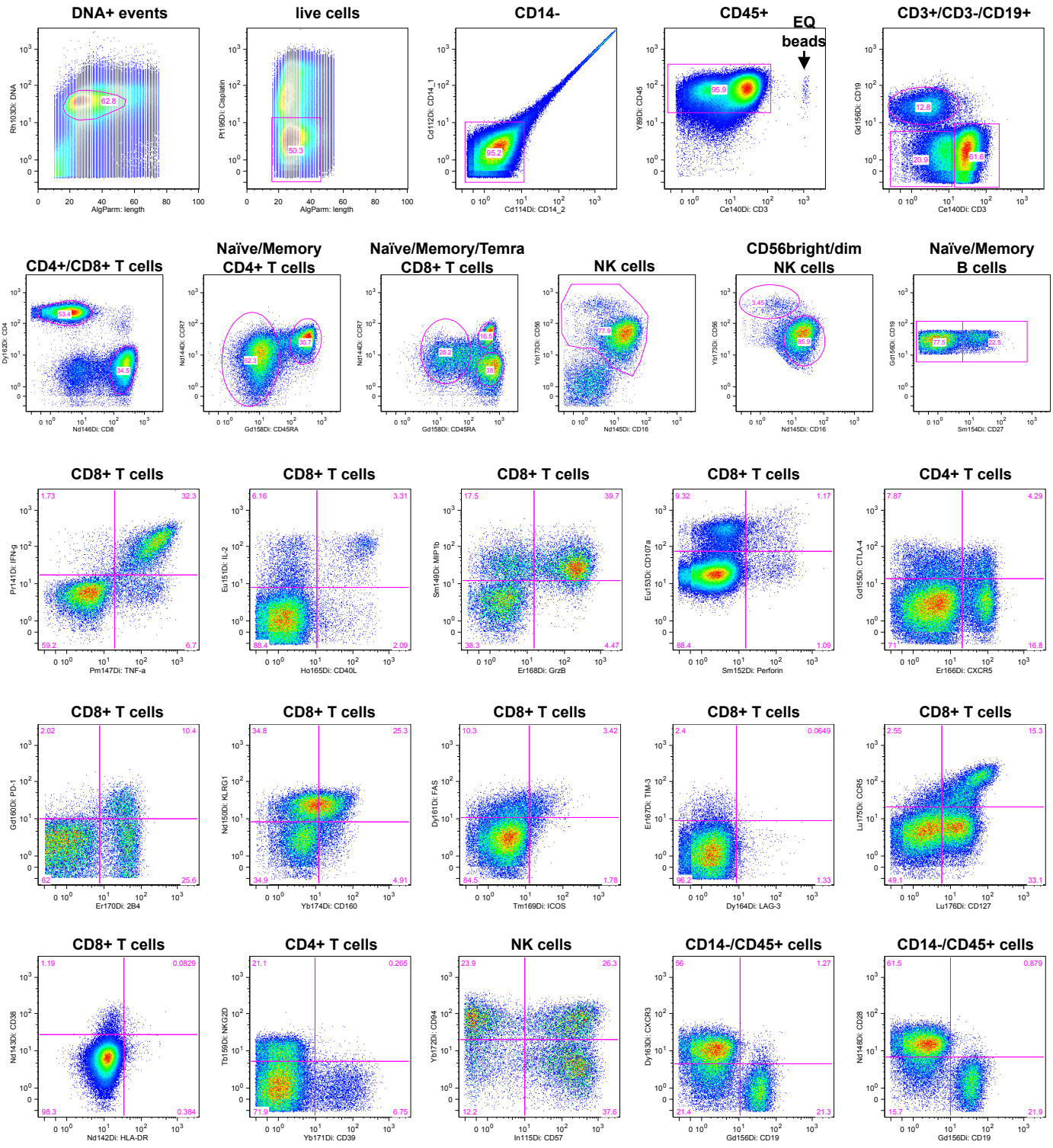


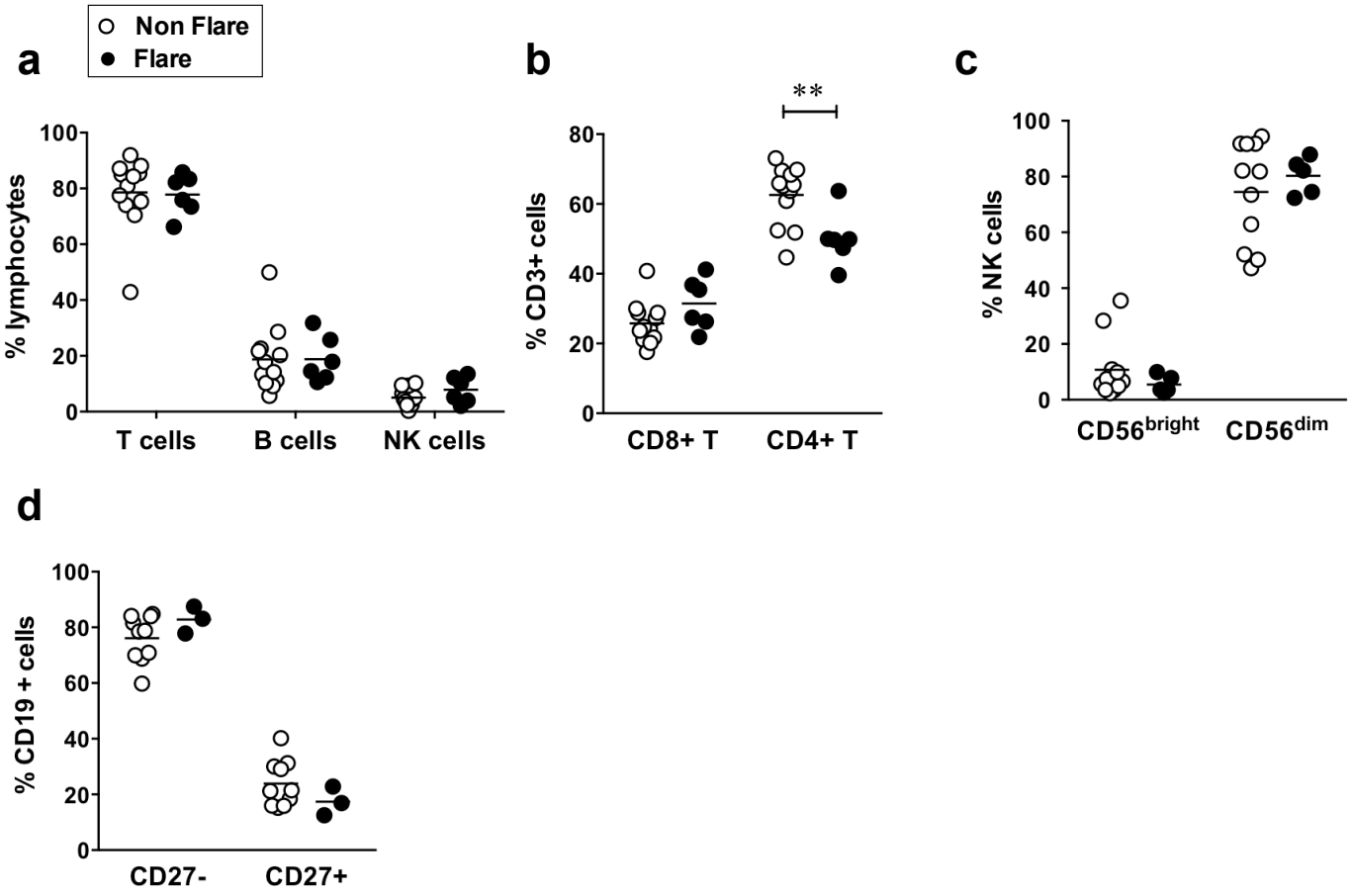
Supplementary Figure S1

(a) The percentage of pentamer+ CD8+ T cells specific for five HLA-A*0201-restricted HBV epitopes ($Core_{18-27}$, $Env_{183-191}$, $Env_{335-343}$, $Pol_{455-463}$ and $Pol_{573-581}$) is shown for HLA-A*02:01+ patients (n=4; NF 2, NF 7, NF 10 and F 5) and HLA-A*02:01+ healthy donors (n=3). PBMCs were stained directly ex vivo and analysed by flow cytometry. **(b)** IFN-γ release by CD4+ and CD8+ T cell lines generated after a 10 day in vitro expansion of PBMCs from patients of the flare group (n=2).

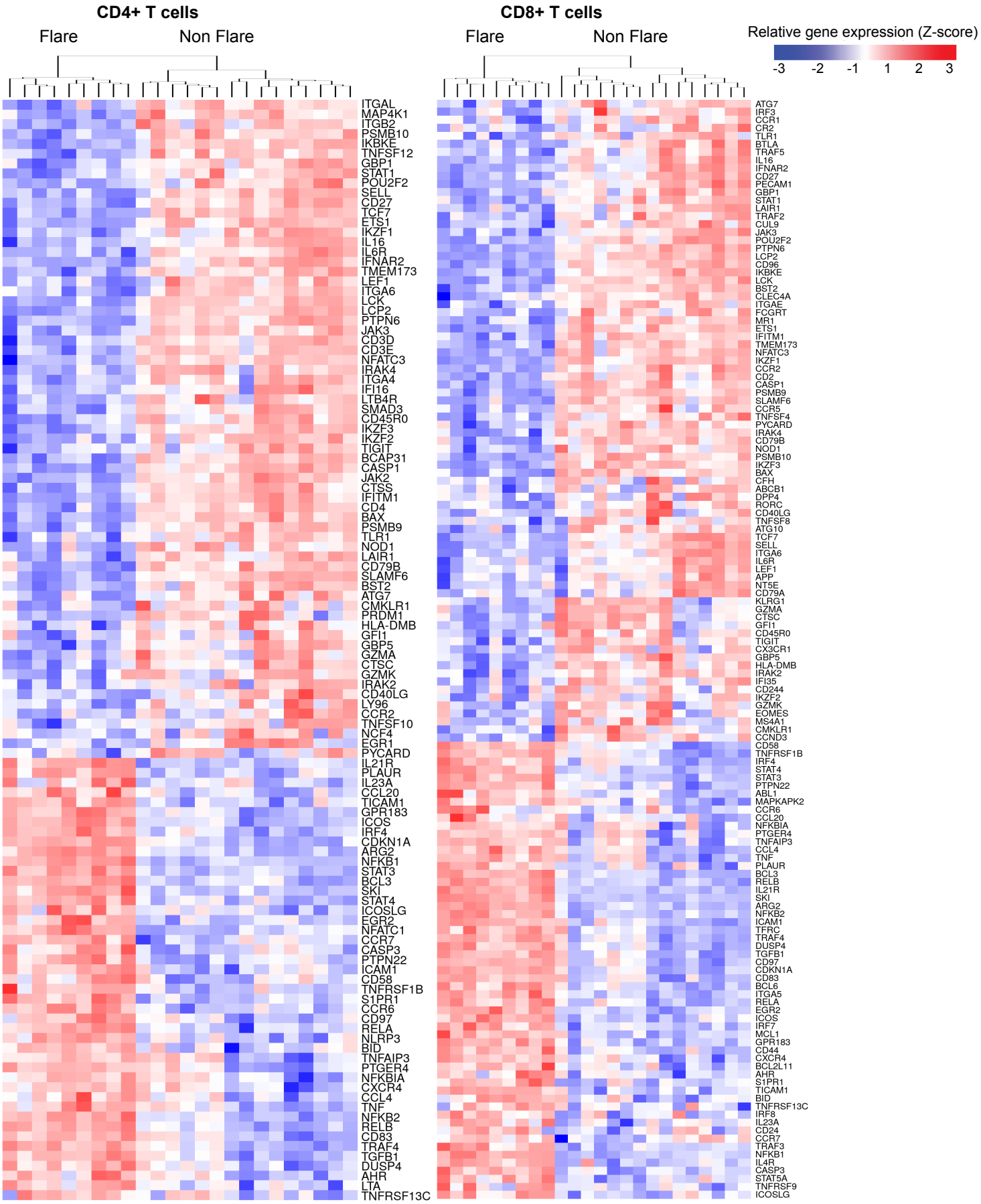


Supplementary Figure S2

Simultaneous detection of lineage markers and molecules involved in cellular, differentiation, exhaustion and activation by CyTOF and gating strategy used to identify the populations of interest in Figure 4. Representative biaxial mass cytometry plots show the staining quality of all markers from the indicated immune cell type.

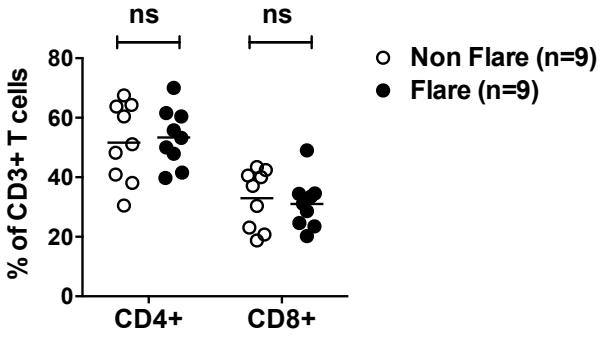


Supplementary Figure S3
Percentage of indicated immune cell subsets identified by CyTOF from patients that do or do not flare upon NUC therapy discontinuation.



Supplementary Figure S4

mRNA expression of immune-regulatory genes was analyzed by NanoString in CD4+ (left) and CD8+ (right) T cells sorted from the peripheral blood of patients that flare (n=9) or do not flare (n=15) upon therapy discontinuation. The differentially expressed genes (>1.5 fold difference, p<0.05, FDR adjusted) in CD4+ and CD8+ T cells from the two patient groups are shown by heat map (log2 transformed, z-score).



Supplementary Figure S5
Percentage of CD4+ and CD8+ T cells identified by flow cytometry in patients from cohort 2 that do or do not flare upon NUC therapy discontinuation.

Supplementary Table S1

Metal	Antibody	Clone	Company
89Y	CD45	HI30	Fluidigm
112/114Cd	Qdot800-CD14	TüK4	Termo Fisher
115In	CD57	HCD57	Biolegend
139La	CD7	M-T701	BD Biosciences
140Ce	CD3	UCHT1	BioXcell
141Pr	IFN-γ	4S.B3	eBioscience
142Nd	HLA-DR	L243	Biolegend
143Nd	CD38	HIT2	Biolegend
144Nd	CCR7	150503	R&D
145Nd	CD16	3G8	Biolegend
146Nd	CD8	SK1	Biolegend
147Sm	TNF-α	MAb11	eBioscience
148Nd	CD28	CD28.2	Biolegend
149Sm	MIP1-β	D21-1351	BD Biosciences
150Nd	KLRG1	13F2F12	eBioscience
151Eu	IL-2	MQ1-17H12	eBioscience
152Sm	Perforin	B-D48	abcam
153Eu	CD107a	H4A3	BD Biosciences
154Sm	CD27	LG.7F9	eBioscience
155Gd	CTLA-4	BN13	BD Biosciences
156Gd	CD19	HIB19	Biolegend
158Gd	CD45RA	HI100	Biolegend
159Tb	NKG2D	1D11	Biolegend
160Gd	PD-1	eBioJ105	eBioscience
161Dy	FAS (CD95)	DX2	Biolegend
162Dy	CD4	SK3	Biolegend
163Dy	CXCR3	1C6	BD Biosciences
164Dy	LAG-3	874501	R&D
165Ho	CD40L (CD154)	24-31	eBioscience
166Er	CXCR5	RF8B2	BD Biosciences
167Er	TIM-3	344823	R&D
168Er	Granzyme B	CLB-GB11	abcam
169Tm	ICOS	C398.4A	Biolegend
170Er	2B4	C1.7	Biolegend
171Yb	CD39	A1	Biolegend
172Yb	CD94	DX22	Biolegend
173Yb	CD56	NCAM16.2	BD Biosciences
174Yb	CD160	688327	R&D
175Lu	CCR5	HEK/1/85a	Acris
176Yb	CD127	A019D5	Biolegend

Intracellular antibodies