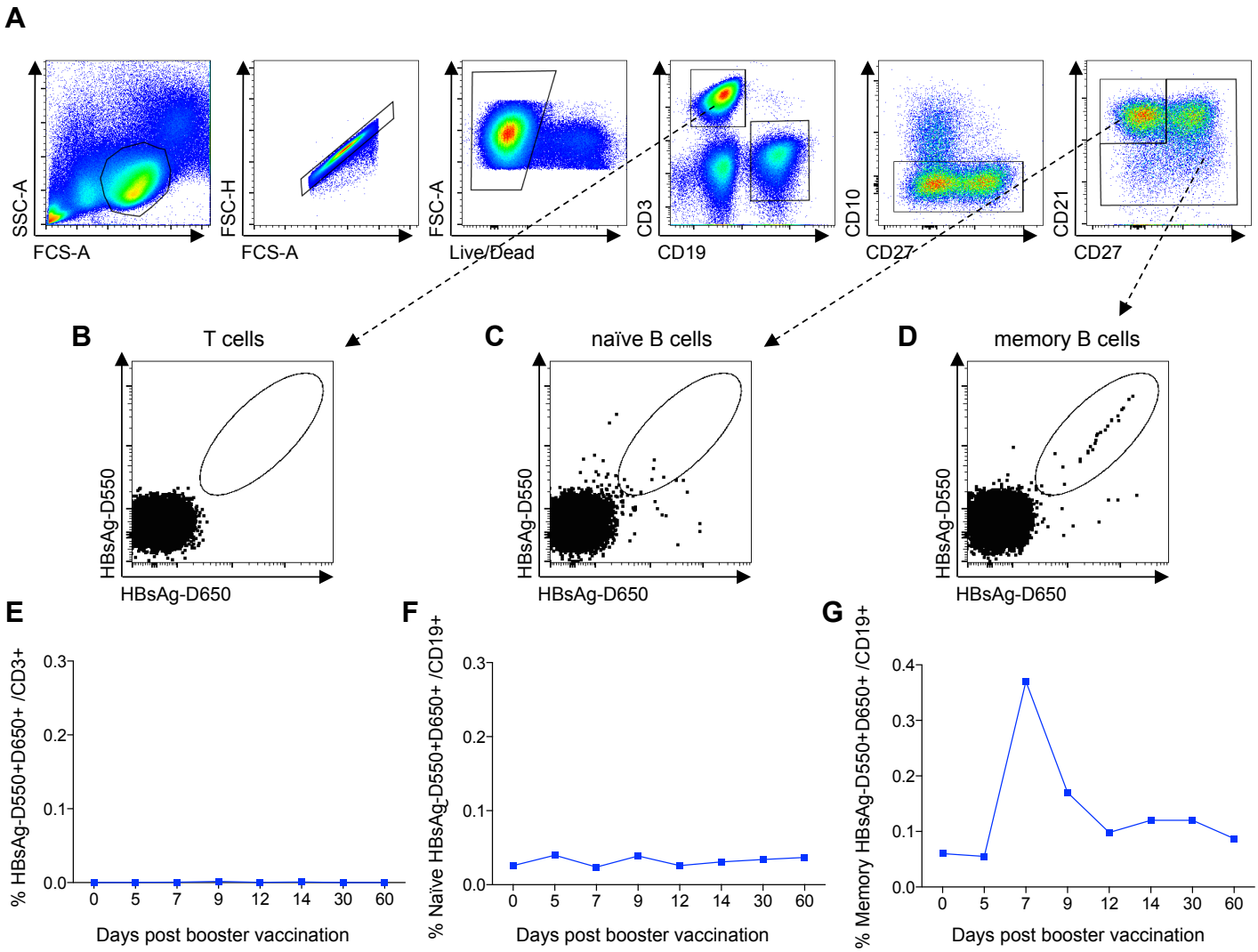
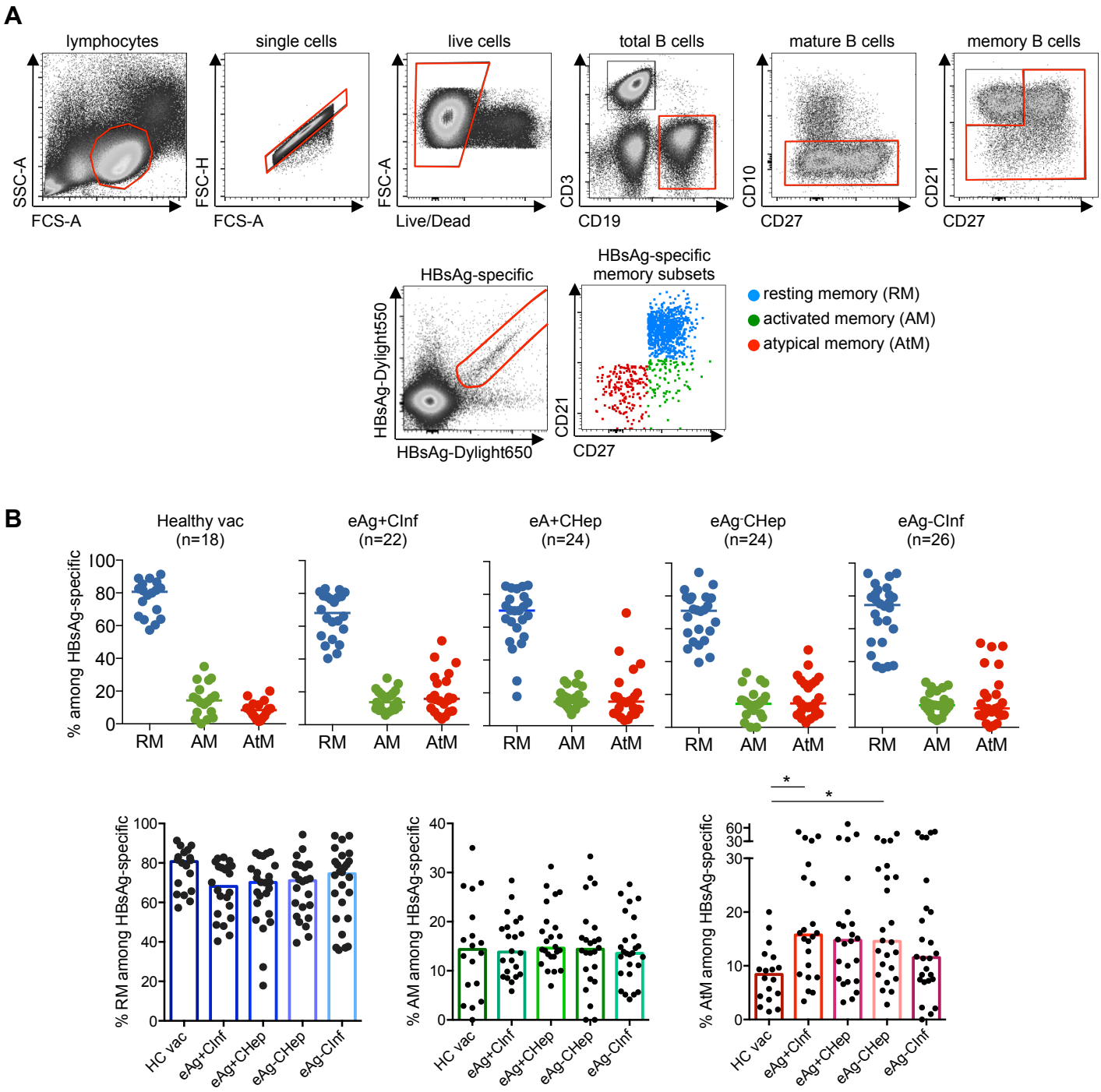


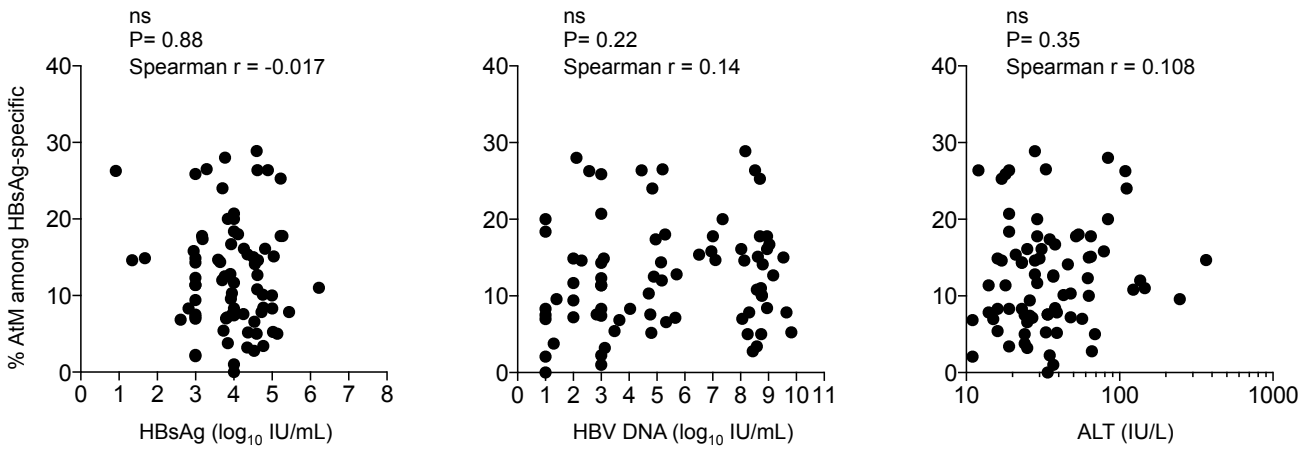
Supplementary Figure 1: Fluorescently labeled HBsAg-baits bind specifically to memory B cells after booster HBV vaccination

PBMCs of a subject receiving an HBV-booster vaccination were stained longitudinally with live/dead, anti-CD3, anti-CD19, anti-CD10, anti-CD27, anti-CD21, HBsAg-D550 and HBsAg-D650. **A)** shows the gating strategy for detection of HBsAg-specific memory B cells (MBCs); plots reshown from Fig 7A. HBsAg-D550 and HBsAg-D650 binding to T cells (**B**), to naïve B cells (**C**), and to MBCs (**D**) are shown. Longitudinal detection over 60 days post-booster vaccination of double positive HBsAg-D550^{+}D650^{+} T cells (**E**), naïve B cells (**F**) and MBCs (**G**) are shown.



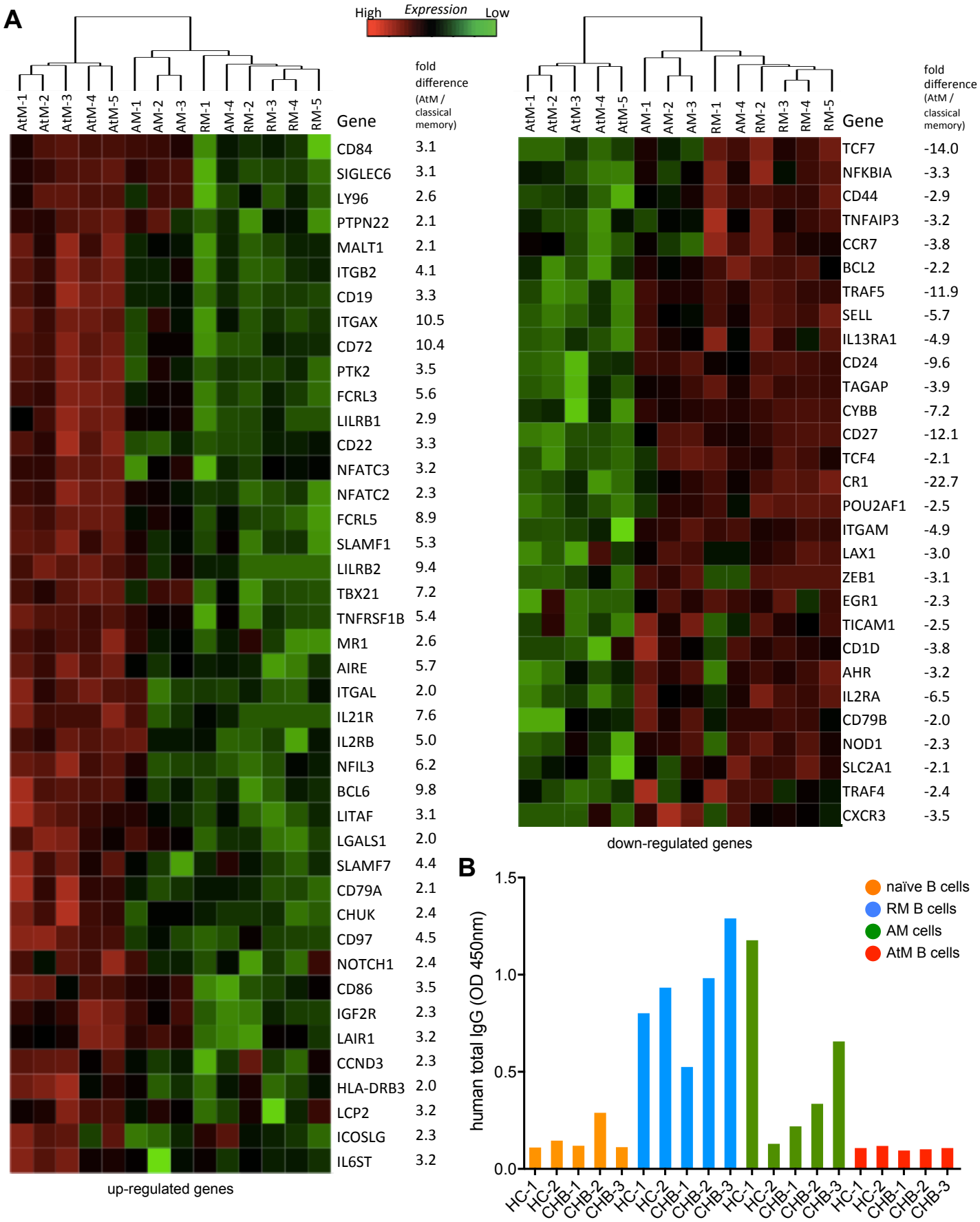
Supplementary Figure 2: Manual gating strategy and frequency of different memory B cell subsets among HBsAg-specific B cells in chronic HBV patients

A) PBMCs were stained with live/dead, anti-CD3, anti-CD19, anti-CD10, anti-CD27, anti-CD21, HBsAg-DyLight550 and HBsAg-DyLight650. Gating strategy of dual-stained HBsAg-specific B cells and their distribution into different subsets of memory B cells [resting (RM), activated (AM) and atypical (AtM) memory B cells]. Plots reshown from Fig 7A and Sfig 1A. Last two FACS plots (below; HBsAg-specific) are showing downsampled memory B cells concatenated from 96 CHB samples. **B)** Frequency of RM, AM and AtM B cells among HBsAg-specific cells in healthy and HBV patients with HBeAg+ chronic infection, HBeAg+ chronic hepatitis, HBeAg- chronic hepatitis and HBeAg- chronic infection. Data are presented as median and statistical analysis was performed by the Kruskal-Wallis test followed by Dunn's multiple comparisons test (B); *, $P < 0.05$.



Supplementary Figure 3: No correlation of HBsAg-specific B cells with AtM phenotype and virological/ biochemical parameters

Correlation of frequency of AtM among HBsAg-specific B cells with serum HBsAg (left), HBV-DNA (middle) and ALT (right) levels measured in 76 patients with chronic HBV infection. Spearman's Rank correlation.



Supplementary Figure 4: Gene expression profile and functionality of AtM B cells versus RM and AM B cells in chronic HBV infection.

A) Three different memory B cell (MBC) subsets (based on the expression of CD21 and CD27) from 5 chronic HBV patients were FACS sorted and analyzed for their immune genes expression profile by NanoString technology. A total of 588 immune genes was analyzed. **Left**: 42 genes were >2-fold up regulated ($p<0.05$) in AtM compared to the two classical MBCs. **Right**: 29 genes were >2-fold down regulated in AtM compared to the classical MBCs. **B)** 2000 naïve, RM, AM and AtM B cells were FACS sorted and cultured in the presence of CpG, sCD40L, IL-2, IL-10, IL-15 for 4 days and subsequently with IL-2, IL-6, IL-10 and IL-15 for another 3 days. Total human IgG was measured in the supernatants by ELISA assay.

Supplementary Table 1: List of antibodies used in this study

Antigen	Fluorochrome	Manufacturer	Clone	Catalog number
CD3	BV605	BioLegend	OKT3	317322
CD3	BV500	BD Biosciences	UCH-T1	561416
CD10	PE-CF594	BD Biosciences	HI10A	562396
CD19	BV510	BD Biosciences	SJ25C1	562947
CD21	BV421	BD Biosciences	B-LY4	562966
CD23	BUV395	BD Biosciences	M-L233	564203
CD24	PerCP-Cy5.5	BioLegend	ML5	311116
CD27	BV650	BD Biosciences	L128	563228
CD38	PE-Cy7	BioLegend	HB-7	356608
CD39	BV711	BD Biosciences	TU66	563680
CD69	APC-Cy7	BioLegend	FN50	310914
CD73	BV605	BD Biosciences	AD2	563199
CD95	BV737	BD Biosciences	DX2	564710
HLA-DR	AF700	BioLegend	L243	307626
IgG	BV786	BD Biosciences	G18-145	564230
CD279 (PD-1)	FITC	BD Biosciences	MIH4	557860
CD4	BV650	BD Biosciences	SK3	563876
CD8	PE-Cy7	BD Biosciences	RPA-T8	557746
CD197 (CCR7)	Biotin (plus APC-streptavidin from BD Biosciences; cat no 554067)	BD Biosciences	3D12	557648
CD45RA	FITC	BD Biosciences	HI100	555488