Supplementary materials

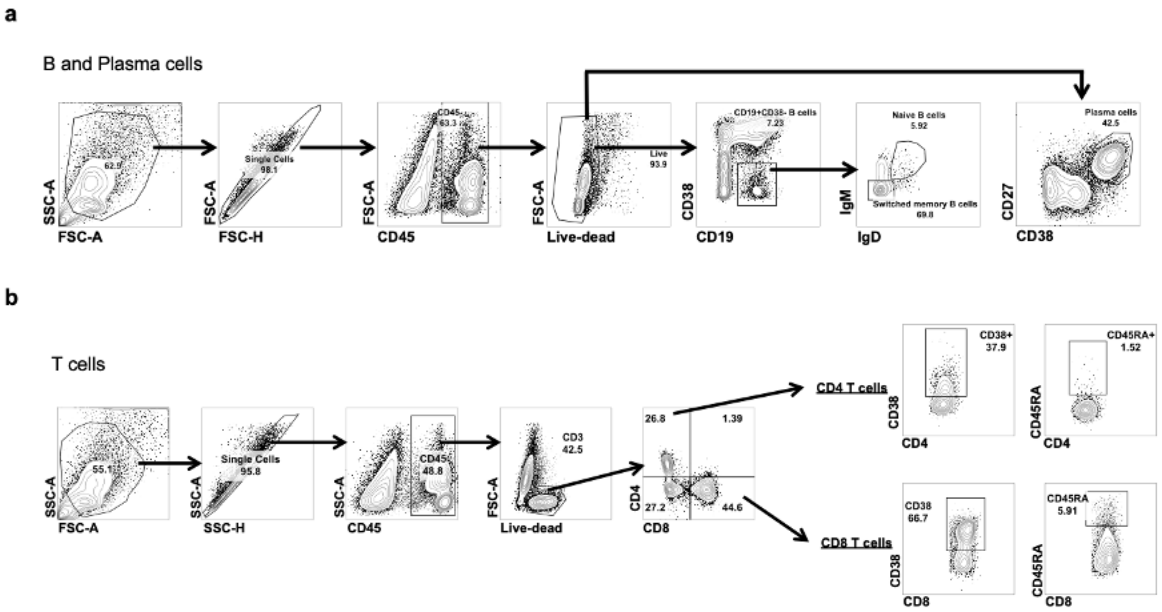

Figure S1. Gating strategy for human intestinal cells

a-b, Representative flow cytometry (FC) plots showing gating strategy used to profile intestinal B cells and plasma cells (**a**), as well as T cells (**b**).

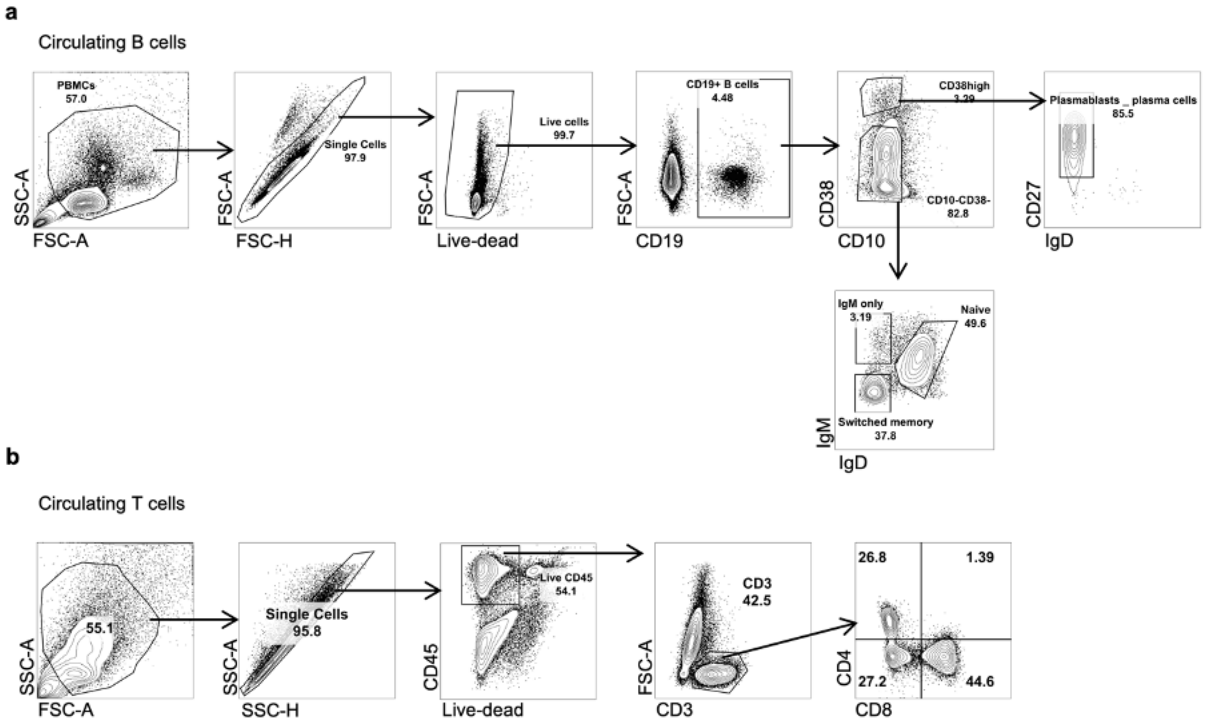

Figure S2. Gating strategy for human circulating cells

a-b, Representative flow cytometry (FC) plots showing gating strategy used to profile circulating B cells and plasma cells (**a**), as well as T cells (**b**).

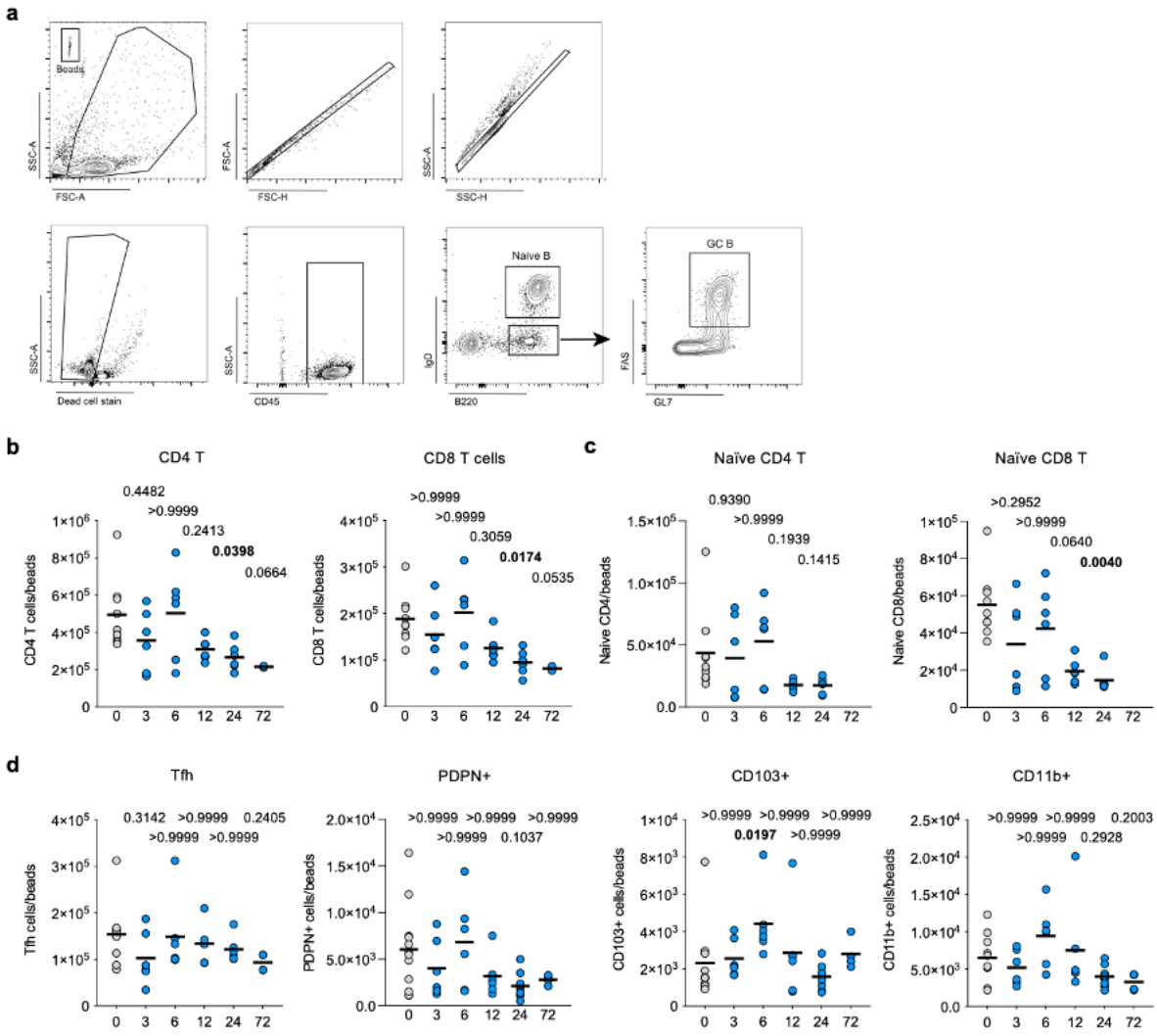

Figure S3. Kinetic profiling of mouse PPs after anti-α4β7 administration

a, Representative flow cytometry (FC) plots showing gating strategy used to profile mouse B cells. **b**, Frequency of CD4 T cells and CD8 T cells from isolated PPs of untreated mice (grey) and at 3, 6, 12, 24 and 72 hours after anti-α4β7 administration. **c**, Frequency of Naïve CD4 and CD8 T cells after anti-α4β7 administration. **d**, Frequency of T follicular helper, PDPN+, CD103+ and CD11b+ cells after anti-α4β7 administration. Data shown as individual values and mean. Unpaired non-parametric analysis was done using Kruskal-Wallis test and Dunn's multiple comparisons test. The *p* values are indicated.

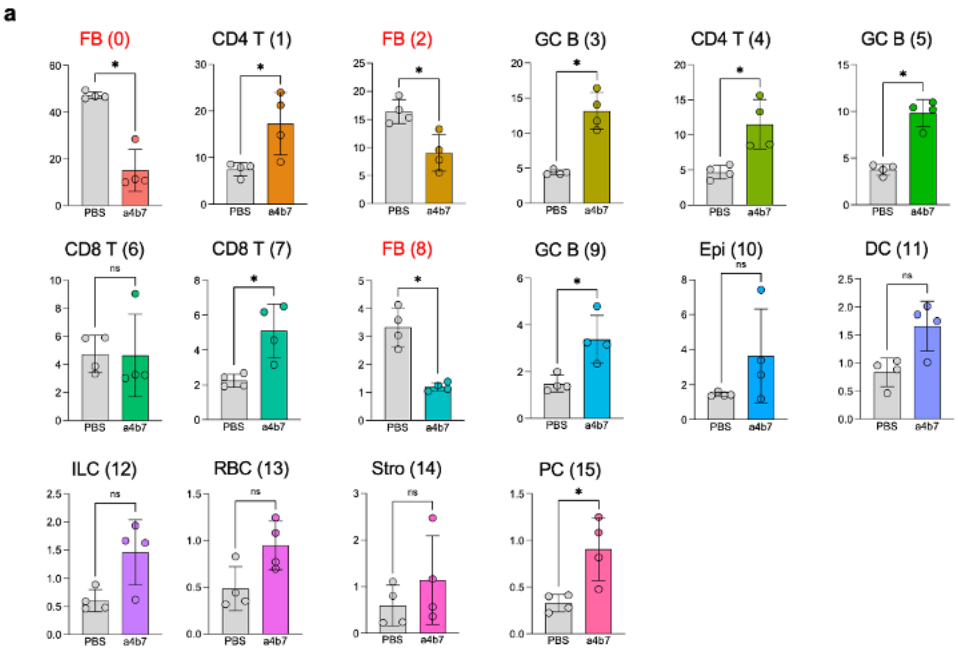

Figure S4. Frequency of single-cell RNAseq clusters

a, Bar plots for the frequency of cell clusters among total cells from Figure 4. Data shown as individual values and mean. Unpaired analysis was done using Mann Whitney test.

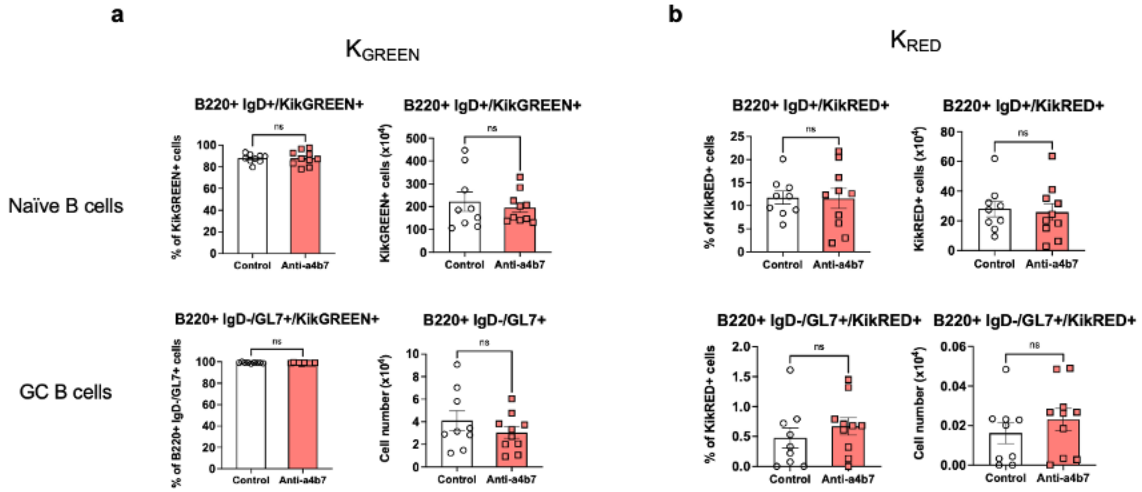

Figure S5. B cell monitoring in mesenteric lymph nodes after photoconversion

Cell frequency and absolute cell number of K_{GREEN} (**a**) and K_{RED} (**b**) Naïve B cells and GC B cells from non-photoconverted mesenteric lymph nodes. Mice were treated with anti-α4β7 or Isotype control as in Figure 5. Data shown as individual values, mean and SD. Unpaired analysis was done using Mann Whitney test.

Table S1. COHORT 1 (Mount Sinai) used for flow cytometry studies.

	Vedolizumab treated	TNFi treated	Untreated	p-value
Number of patients	56	10	17	NA
Age (mean ± SD)	38.39 ± 13.43	29.94 ± 9.72	40.92 ± 19.1	0.15
Sex, n M / F	29 / 27	15 / 7	13 / 4	0.01
Disease activity/extent*, n				
Not active	3	2	3	
E1	5	1	5	
E2	22	4	6	
E3	26	3	3	0.1

*extent of active disease at time of endoscopy

SD = Standard deviation. Age is at the time of first biopsy analyzed. For continuous variables used One-way ANOVA, for categorical variables used Chi-square test for trend.

Table S2. COHORT 2 (Mount Sinai) used for histology studies

	Vedolizumab responder	Vedolizumab non-responder	p-value
Number of patients	12	22	NA
Age (mean ± SD)	37.4 ± 17.7	41.5 ± 17.9	0.52
Sex, n M / F	4 / 8	15 / 7	0.08
Disease extent, n			
E1	0	1	
E2	4	10	
E3	8	11	0.29
MES (pre), n			
0	0	0	
1	1	0	
2	5	5	
3	3	9	0.09
Unknown	3	8	
MES (post), n			
0	11	3	
1	1	3	
2	0	7	
3	0	7	<0.0001
Unknown	0	2	

	TNF inhibitor responders	TNF inhibitor non-responder	p-value
Number of patients	11	15	NA
Age (mean ± SD)	43.2 ± 17.4	34 ± 13.0	0.20
Sex, n M / F	5 / 6	10 / 5	0.43
TNF used			
Infliximab*	8	11	
Adalimumab*	3	4	>0.99
Disease extent			
E1	0	0	
E2	6	4	
E3	5	11	0.15
MES (post), n			
0	5	0	
1	4	2	
2	0	2	
3	0	11	<0.0001
Unknown	2	0	

*or biosimilar

SD = Standard deviation; MES = Mayo Endoscopic Score. Age is at the time of first biopsy analyzed. If no in mayo endoscopic score in report, assigned 3 if reported as severe and/or ulcerations. For continuous variables used Mann Whitney test, for categorical variables used Fisher's exact or Chi-square test for trend

Table S3. COHORT 3 (Validation cohort, Belgium) used for histology studies

	Vedolizumab responder	Vedolizumab non-responder	p-value
Number of patients	9	12	NA
Age (mean ± SD)	50.8 ± 18.36	43.27 ± 10.8	0.24
Sex, n M / F	5 / 4	7 / 5	>0.9999
Disease extent, n			
E1	3	2	
E2	5	5	
E3	1	5	0.13
MES (pre), n			
0	0	0	
1	0	0	
2	1	6	
3	8	6	0.06
Unknown	0	0	
MES (post), n			
0	4	3	
1	3	2	
2	2	1	
3	0	6	0.04
Unknown	0	0	

SD = Standard deviation; MES = Mayo Endoscopic Score. Age is at the time of first biopsy analyzed. If no in mayo endoscopic score in report, assigned 3 if reported as severe and/or ulcerations. For continuous variables used Mann Whitney test, for categorical variables used Fisher's exact or Chi-square test for trend.

Table S4. Antibodies used for Flow cytometry of human samples.

Marker	Fluorochrome	Manufacturer	Clone
CD19	PE.Cy7	Biolegend	SJ25C1
CD38	APC	Biolegend	HB-7
CD10	APC.Cy7	Biolegend	HI10a
CD27	PerCP.Cy5.5	Biolegend	O323
IgD	PB	Biolegend	IA6-2
IgM	A700	Biolegend	MHM-88
IgA	FITC	SouthernBiotech	Polyclonal
Beta7-integrin	PE	Biolegend	FIB504
Beta7-integrin	FITC	Biolegend	FIB504
CD3	PB	Biolegend	UCHT1
CD4	A700	Biolegend	RPA-T4
CD8	APC.CY7	Biolegend	SK1
CD45RA	PE.Cy7	Biolegend	HI100
TIGIT	BV605	Biolegend	A15153G
ICOS	APC.Cy7	Biolegend	C398.4A
CXCL13	APC	Invitrogen	53610
PD1	PE	Biolegend	EH12.2H7
PD1	APC	Biolegend	EH12.2H7
CXCR3	PE	Biolegend	G025H7
CCR9	PE	Biolegend	L053E8
CXCR4	PE	Biolegend	12G5

Table S5. Antibodies used for Flow cytometry of murine samples.

Marker	Fluorochrome	Manufacture	Clone
B220	Pacific Blue	Biolegend	RA3-6B2
B220	APC	Biolegend	RA3-6B2
CD3	PerCP cy5.5	Biolegend	17A2
CD3	Pacific Blue	Biolegend	17A2
CD31	Alexa fluor488	Biolegend	MEC13.3
CD4	PE-Cy7	Biolegend	GK1.5
CD44	APC	Biolegend	IM7
CD45	Alexa fluor700	Biolegend	30-F11
CD62L	PE	Biolegend	MEL-14
CD8	Alexa fluor488	Biolegend	53-6.7
CXCR5	BV421	Biolegend	L138D7
Epcam	APC	Biolegend	G8.8
FAS	FITC	Biolegend	SA367H8
GL7	APC	Biolegend	GL7
IgA	PE	eBioscience	mA-6E1
IgD	PerCP cy5.5	Biolegend	11-26c.2a
PD1	APC	Biolegend	RMP1-30
PDPN	PE-Cy7	Biolegend	8.1.1