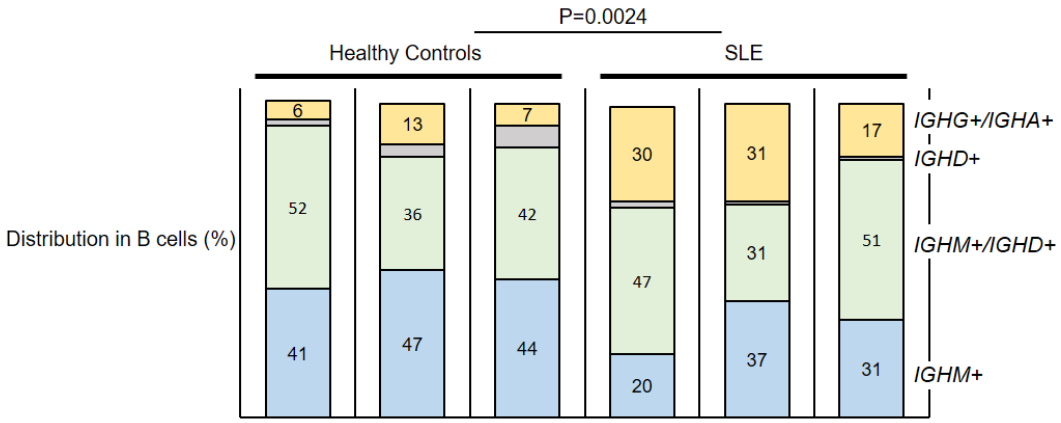
Supplemental Table 1 – Demographics and clinical data of SLE patients

SLE	Race	α-DNA	α - Sm	α - SSA	RD	SLEDAI	AM	IS	CS	IL-4R$^+$ IFNβ$^-$ (%)	IL-4R$^-$ IFNβ$^+$ (%)
SLE#4	AA	-	-	NA	-	2	H	N	N	7.7	18.1
SLE#5	AA	+	+	+	+	4	H	B, MMF	N	17.6	8.0
SLE#6	AA	-	-	+	-	1	H	B, MMF	N	7.8	22.6
SLE#7	AA	-	-	-	-	0	H	N	N	21.3	4.9
SLE#8	AA	+	+	+	+	4	H	N	N	28.9	5.1
SLE#9	AA	+	+	-	-	2	H	MTX	Y	22.3	5.4
SLE#10	AA	+	+	+	-	2	H	N	N	35.4	7.0
SLE#11	AA	+	-	+	+	3	H	B, CTX	Y	3.3	26.6
SLE#12	AA	+	+	+	+	4	H	N	N	0.2	69.7
SLE#13	AA	+	+	-	+	2	H	MTX	N	37.4	7.7
SLE#14	AA	-	-	-	+	2	H	N	Y	7.4	27.0
SLE#15	AA	+	+	+	-	2	H	N	N	2.9	50.3
SLE#16	AA	+	+	+	+	0	H	MMF	Y	0.0	54.9
SLE#17	AA	+	+	+	-	2	H	MTX	Y	29.8	3.4
SLE#18	AA	-	-	+	+	10	H	B, AZA	Y	44.8	1.6
SLE#19	AA	-	+	+	+	4	H	N	N	47.9	5.1
SLE#20	AA	-	+	+	+	5	H	N	N	12.0	30.5
SLE#21	AA	+	+	+	+	6	Q	MMF	N	2.2	45.8
SLE#22	AA	+	+	+	-	6	H	MTX	Y	2.6	44.2
SLE#23	AA	+	+	+	+	5	H	B	Y	10.3	31.5
SLE#24	AA	−	+	-	+	0	H	B	N	25.2	15.0
SLE#25	AA	−	+	+	−	1	H	MMF	Y	14.8	22.8
SLE#26	AA	+	+	-	+	5	H	N	Y	15.8	25.4
SLE#27	AA	-	-	+	-	2	H	N	N	13.3	25.6
SLE#28	AA	+	+	+	-	2	H	N	Y	8.1	24.3
SLE#29	AA	+	+	NA	+	4	H	N	Y	26.4	4.7
SLE#30	AA	+	NA	NA	+	6	H	MMF	Y	6.0	38.3
SLE#31	AA	+	+	NA	+	10	H	MMF	Y	0.4	58.7
SLE#32	AA	+	NA	NA	+	8	H	MTX	Y	6.1	44.4
SLE#33	AA	-	-	-	-	4	N	MTX	Y	15.7	38.6
SLE#34	White	-	-	NA	-	0	H	MTX	N	48.1	3.4
SLE#35	White	-	-	NA	-	0	H	N	N	33.5	1.2
SLE#36	White	+	NA	+	-	0	H	MTX	Y	43.8	1.3
SLE#37	White	-	-	-	-	0	H	N	N	23.3	5.0
SLE#38	White	-	-	NA	-	2	H	AZA	N	14.1	17.3
SLE#39	White	-	-	-	-	6	H	MTX	N	14.2	23.8
SLE#40	White	+	+	NA	+	2	H	N	N	6.9	33.9
SLE#41	White	-	-	NA	-	2	N	LEF	Y	71.1	1.8
SLE#42	White	+	-	-	-	0	H	N	N	13.6	30.9
SLE#43	White	+	+	NA	+	NA	NA	NA	NA	1.4	51.9
SLE#44	White	-	-	-	-	0	N	MTX	Y	54.5	1.6
SLE#45	White	+	-	+	-	0	H	N	N	44.4	4.0
SLE#46	White	-	-	-	-	2	H	MTX	Y	20.4	17.6
SLE#47	White	+	+	-	-	4	Q	N	N	24.9	16.4
SLE#48	White	−	−	−	−	0	H	N	N	49.4	6.7
SLE#49	White	+	+	+	+	2	N	B	N	9.4	8.4
SLE#50	White	-	-	-	-	2	H	N	N	29.0	13.0

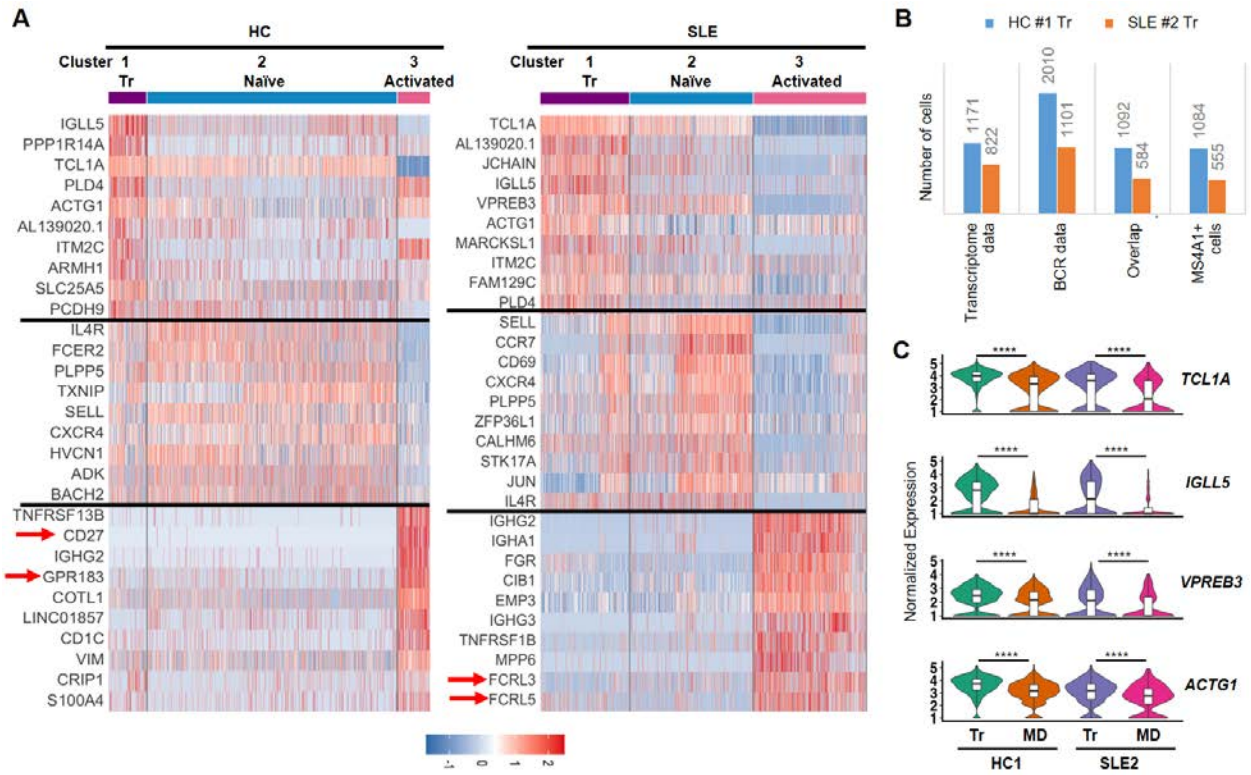
AA = African American; AM = anti-malaria; AZA = azathioprine; B = belimumab; CS = corticosteroid; H = hydroxychloroquine; IS = immune suppressant; Q= quinacrine; LEF = leflunomide; MMF= mycophenolate; MTX = methotrexate; N = No; NA = not available; RD = renal disease; SLEDAI = SLE disease activity index; Y = yes



	HC #1	HC #2	HC #3	SLE #1	SLE #2	SLE #3
	Healthy	Healthy	Healthy	SLE	SLE	SLE
Anti-DNA	–	–	–	+	+	+
Ant-Smith	–	–	–	+	+	+
Anti-Ro/SSA	–	–	–	+	–	+
Renal Disease	–	–	–	+	+	+
SLEDAI	0	0	0	2	18	11
Race (Gender)	AA (M)	AA (F)	AA (F)	AA (F)	AA (F)	AA (F)
# of single cell transcriptome data	2211	2598	1896	2935	1618	2533
# of overlapped transcriptome/BCR data	2003	2221	1714	1909	1042	1053
# *MS4A1*+ cells	1990	2111	1587	1900	892	1011

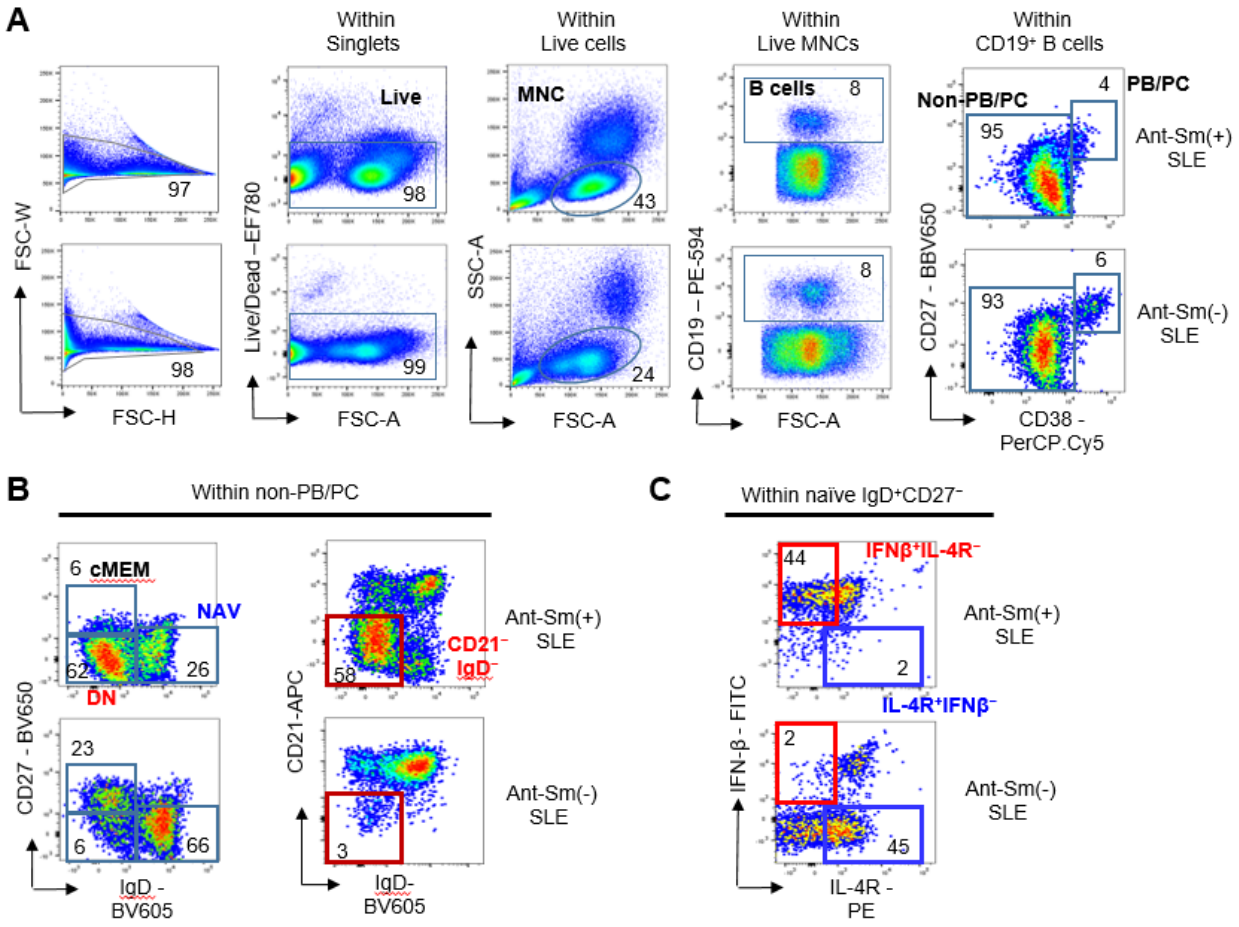
Supplemental Fig. 1. Single cell-RNA-seq analysis showing the distribution of *IGH* genes in B cells of healthy controls and SLE patients.

scRNA-seq analysis was carried out using B cells purified from 3 healthy controls (left) and 3 SLE patients (right). All genes that were expressed by ≥ three cells and all cells that expressed ≥ 200 detected genes were kept for subsequent informatics analysis. Only cells that expressed the VDJ regions of BCR as well as *MS4A1* (the coding gene for CD20) were used for further analysis (boxed in yellow). Bar graph showing the distribution of the indicated populations of B cells, determined using the expression of *IGHM* and *IGHD* genes. The numbers shown in each bar graph indicate the percentages of cells in each subset of B cells. Statistical differences in B cell distribution between the average of HC and SLE were determined using a Chi-square test. The demographics and clinical characteristics of each patient are included.



Supplemental Fig. 2. Transcriptomic clustering of *IGHM+IGHD+* B cells into 3 subsets.

B cells isolated from 3 healthy controls and 3 SLE patients were subjected to a droplet-based scRNA-seq analysis. Data analysis was carried out using *IGHM+IGHD+* B cells only. (**A**) Heatmap analysis shwing the differentially expressed genes across 3 subclusters in HCs and SLE patients. In the heatmaps, rows correspond to individual genes found to be selectively upregulated in individual clusters ($p < 0.01$). (**B, C**) Tr B cells isolated from 1 healthy control (HC#1), and 1 autoAb$^+$ SLE patient (SLE#2) were subjected to a droplet-based scRNA-seq analysis. (**B**) Bar graph showing the number of cells that expressed ≥ 200 detected genes and all genes that were expressed by ≥ three cells. Only cells that expressed the VDJ regions of BCR as well as *MS4A1* (the coding gene for CD20) were used for further analysis. (**C**) Violin plots demonstrating the expression of the indicated genes in Tr B cells and *IGHM*$^+$*IGHD*$^+$ B cells in the same individual. The statistical analysis was carried out using the "stat_compare_means" function in ggpubr (v0.4.0) package ****: $p \leq 0.0001$ between the indicated comparisons.



Supplemental Fig. 3. Flow cytometry gating strategy to access the percentages of IL-4R⁻IFN-β⁺ or IL-4R⁺IFN-β⁻ naïve B cells in SLE patients.

Peripheral B cells from SLE patients were analyzed by multi-parameter flow cytometry. (**A**) Representative plots showing the sequential gating strategy to access $CD27^{hi}CD38^{hi}$ plasmablasts/plasma (PB/PC) or all other non-PB/PC B cells. (**B**) Representative pseudo-color flow cytometry plots showing the distribution of $IgD^{+}CD27^{-}$ naïve (NAV), $IgD^{-}CD27^{+}$ classical memory (cMEM) or $IgD^{-}CD21^{-}$ B cells from the non-PB/PC B subset of a representative anti-Sm positive (+) SLE patient and a representative anti-Sm negative (-) SLE patient. (**C**) Representative flow cytometry plots and percentages of $IFN\beta^{+}IL\text{-}4R^{-}$ (red) or $IFN\beta^{-}IL\text{-}4R^{+}$ (blue) subset within the naïve B cells are shown.