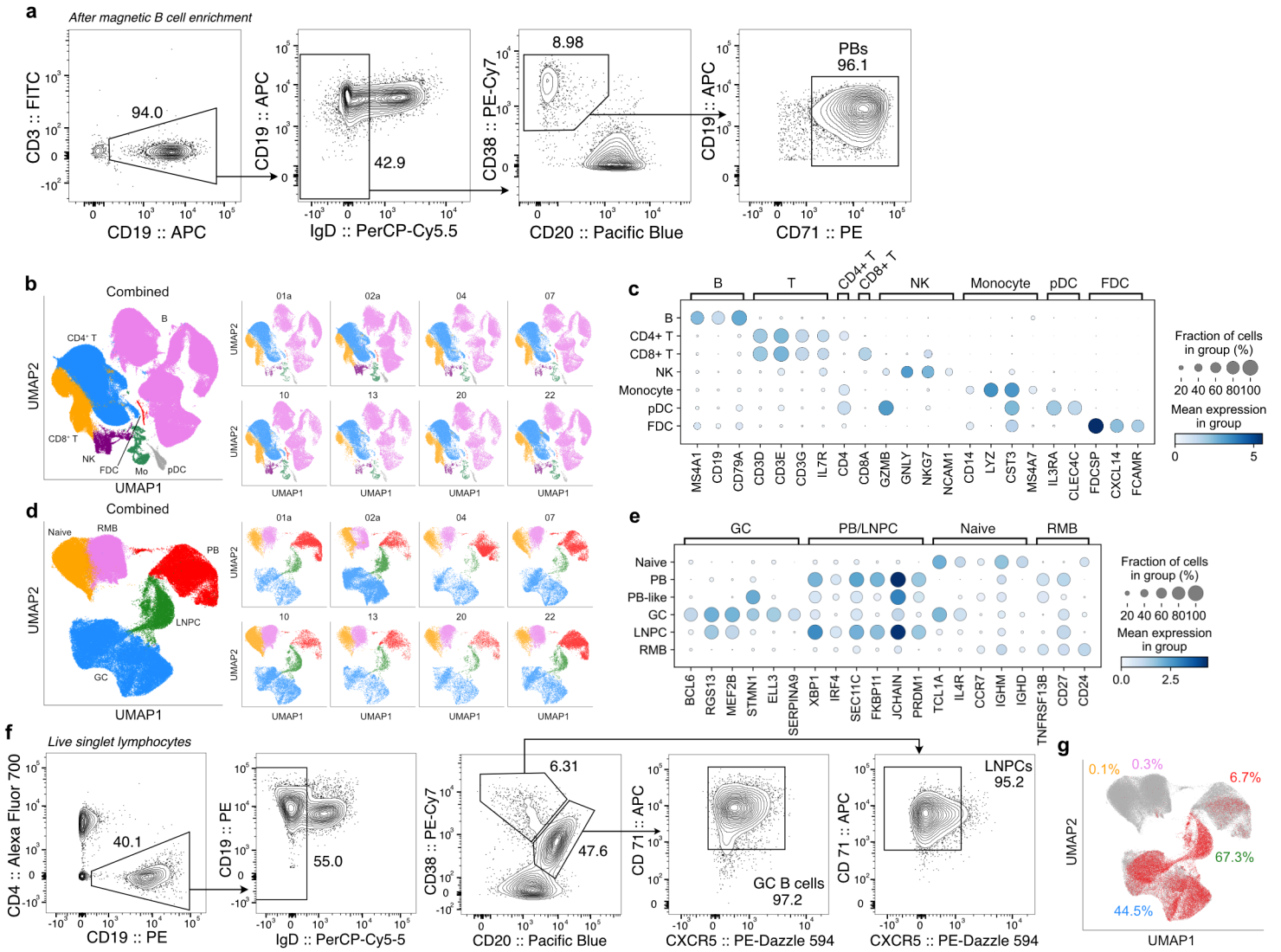
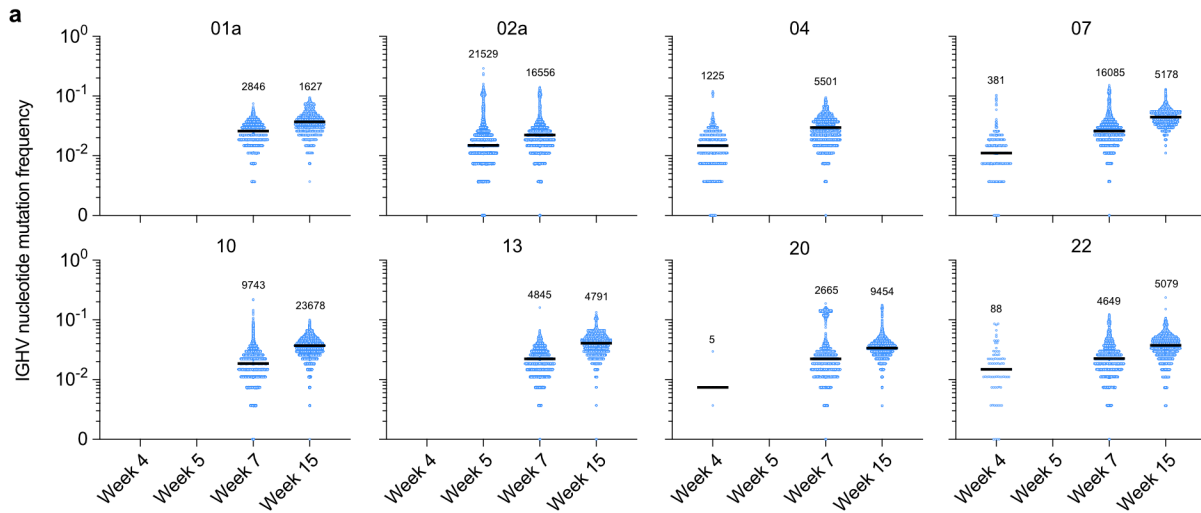


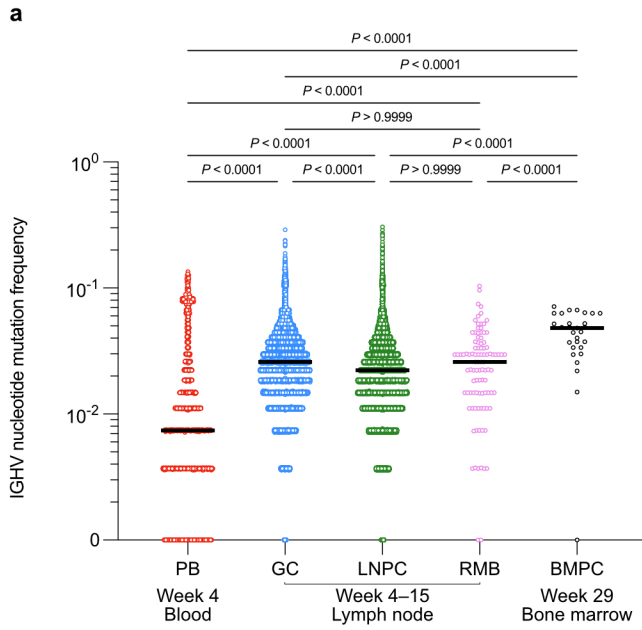
Extended Data Figure 1. Persistence of humoral immune responses to SARS-CoV-2 mRNA vaccination. **a**, Flow cytometry gating strategies for GC B cells (Fig. 1b) and LNPs (defined as CD19⁺ CD3⁺ IgD^{low} CD20^{low} CD38⁺ BLIMP1⁺ CD71⁺ live singlet lymphocytes) in the lymph node. **b**, Kinetics of total (left) and S⁺ LNPs (right) as gated in **a**. **c**, Frequencies of BMPCs secreting IgA antibodies specific for the indicated antigens 29 weeks after immunization. **d**, **e**, Plasma antibody titers against SARS-CoV-2 S measured by ELISA in participants without (red) and with (black) a history of SARS-CoV-2 infection in SARS-CoV-2 vaccinated (left, center) and unvaccinated (right) participants 29 weeks after the first vaccine dose or symptom onset (**d**) and in vaccinated participants over time (**e**). *P* values were determined by Kruskal-Wallis test followed by Dunn's multiple comparison test between unvaccinated and both vaccinated groups (**d**), and by two-sided Mann-Whitney test (**e**). Horizontal lines indicate median values in **c** and **e**. **f**, Flow cytometry gating strategies for MBCs (CD19⁺ CD3⁺ IgD^{low} CD20⁺ CD38⁺ live singlet lymphocytes) and S⁺ MBCs (Fig. 1g) in blood.



Extended Data Figure 2. Identification of SARS-CoV-2 S-binding B cell clones in the lymph node. **a**, Flow cytometry gating strategies for sorting PBs (defined as $CD19^+ CD3^- IgD^{low} CD20^{low} CD38^+ CD71^+$ live singlet lymphocytes) from blood. **b**, **d** UMAPs of scRNA-seq data from PBs sorted from blood and FNA of draining axillary lymph nodes (**b**), and UMAPs of B cell scRNA-seq clusters (**d**). **c**, **e**, Dot plots for the marker genes used for identifying annotated clusters. **f**, Flow cytometry gating strategies for sorting GC B cells ($CD19^+ CD4^- IgD^{low} CD20^+ CD38^{int} CXCR5^{high} CD71^+$ live singlet lymphocytes) and LNPCs ($CD19^+ CD4^- IgD^{low} CD20^{low} CD38^+ CXCR5^{low} CD71^+$ live singlet lymphocytes) from FNAs. **g**, Visualization of SARS-CoV-2 S-binding clones from all participants on integrated UMAP of B cell clusters. Percentages are of SARS-CoV-2 S-binding clones within GC B cells (blue), LNPCs (green), PBs (red), RMBs (pink) or naive B cells (yellow).



Extended Data Figure 3. Maturation of SARS-CoV-2 S-binding B cells in the lymph node.
a, Comparison of *IGHV* nucleotide mutation frequency of SARS-CoV-2 S-binding GC B cells in each participant at the indicated time points. Horizontal lines represent median values.



Extended Data Figure 4. Evolution of B cell clones induced by SARS-CoV-2 vaccination.
a, Comparison of *IGHV* nucleotide mutation frequency of each B cell subsets. Horizontal lines represent median values. *P* values are determined by Kruskal-Wallis test followed by Dunn's multiple comparison test.

Extended Data Table 1. Demographics of participants

Variable	SARS-CoV-2 mRNA vaccination				Variable	Convalescent (N=48) N (%)
	Total (N=43) N (%)	Blood (N=42) N (%)	Lymph node (N=15) N (%)	Bone marrow (N=11) N (%)		
Age (median [range])	38 (28-73)	37.5 (28-73)	37 (28-52)	36 (28-48)	Age (median [range])	50 (21-69)
Sex					Sex	
Female	21 (48.8)	20 (47.6)	7 (53.8)	6 (54.5)	Female	23 (47.9)
Male	22 (51.2)	22 (52.4)	6 (46.2)	5 (45.5)	Male	25 (52.1)
Race					Race/Ethnicity	
White	34 (79.1)	34 (81)	12 (80)	11 (100)	White	47 (97.9)
Black	6 (14)	6 (14.3)	2 (13.3)	0 (0)	Black	0 (0)
Asian	1 (2.3)	0 (0)	1 (6.7)	0 (0)	Asian	1 (2.1)
Other	2 (4.7)	2 (4.8)	0 (0)	0 (0)	Hispanic	0 (0)
Ethnicity						
Not of Hispanic, Latinx, or Spanish origin	41 (95.3)	40 (95.2)	14 (93.3)	10 (90.9)		
Hispanic, Latinx, Spanish origin	2 (4.7)	2 (4.8)	1 (6.7)	1 (9.1)		
BMI (media [range])	26.8 (21.4-67.4)	26.9 (21.4-67.4)	24.1 (21.4-40.1)	23.9 (21.4-40.1)		
Comorbidities					Comorbidities	
Lung disease	1 (2.3)	1 (2.4)	0 (0)	0 (0)	Asthma	10 (20.8)
Diabetes mellitus	0 (0)	0 (0)	0 (0)	0 (0)	Other lung disease	0 (0)
Hypertension	7 (16.3)	6 (14.3)	2 (13.3)	1 (9.1)	Heart disease	0 (0)
Cardiovascular	0 (0)	0 (0)	0 (0)	0 (0)	Hypertension	7 (14.6)
Liver disease	0 (0)	0 (0)	0 (0)	0 (0)	Diabetes mellitus	3 (6.3)
Chronic kidney disease	0 (0)	0 (0)	0 (0)	0 (0)	Cancer	6 (12.5)
Cancer on chemotherapy	0 (0)	0 (0)	0 (0)	0 (0)	Autoimmune disease	4 (8.3)
Hematological malignancy	0 (0)	0 (0)	0 (0)	0 (0)	Hyperlipidaemia	2 (4.2)
Pregnancy	0 (0)	0 (0)	0 (0)	0 (0)	GERD	5 (10.4)
Neurological	0 (0)	0 (0)	0 (0)	0 (0)	Other	16 (33.3)
HIV	0 (0)	0 (0)	0 (0)	0 (0)	Solid Organ Transplant	1 (2.1)
Hyperlipidemia	1 (2.3)	1 (2.4)	0 (0)	0 (0)		
Gastroesophageal reflux disease	-	-	-	-		
Autoimmune disease	-	-	-	-		
Solid organ transplant recipient	0 (0)	0 (0)	0 (0)	0 (0)		
Bone marrow transplant recipient	0 (0)	0 (0)	0 (0)	0 (0)		
Confirmed SARS-CoV-2 infection	13 (30.2)	13 (31)	0 (0)	0 (0)	Hospitalized for treatment of COVID-19	3 (6.3)
Time from SARS-CoV-2 infection to baseline visit in days (median [range])	234 (70-370)	234 (70-370)	-	-		

Extended Data Table 2. Vaccine side effects

Variable	Total N=43 N (%)	Total N=43 N (%)
	First dose	Second dose
None	2 (4.7)	0 (0)
Chills	9 (20.9)	18 (41.9)
Fever	6 (14)	12 (27.9)
Headache	10 (23.3)	16 (37.2)
Injection site pain/redness/swelling	37 (86)	39 (90.7)
Muscle or joint pain	10 (23.3)	25 (58.1)
Fatigue	13 (30.2)	27 (62.8)
Duration of side effects in hours (median [range])		
Chills	18 (6-72)	24 (0.2-48)
Fever	8 (3-72)	30 (1-48)
Headache	36 (6-120)	24 (4-72)
Injection site pain	48 (0.2-168)	48 (2-144)
Muscle or joint pain	24 (3-72)	24 (1-48)
Fatigue	48 (12-120)	24 (3-144)

Extended Data Table 3. Frequencies of total and SARS-CoV-2 S-binding GC B cells and LNPCs in draining axillary lymph nodes

Participant	LN #	Total GC B cells (% of CD19)						SARS-CoV-2 S-binding GC B cells (% of CD19)						
		Week 3	Week 4	Week 5	Week 7	Week 15	Week 29	Week 3	Week 4	Week 5	Week 7	Week 15	Week 29	
01a	1	15.25	13.69	11.14	31.67	29.13	14.37	3.23	5.41	4.01	13.75	18.06	8.00	
02a	1	8.28	34.16	44.92	21.90	7.17	0.85	1.36	9.66	11.55	5.98	0.01	0.06	
	2		14.08	13.54	23.13				4.66	3.85	9.33			
04	1	4.71	14.02	11.21	43.94	3.75	0.38	0.57	2.84	5.59	6.37	0.70	0.00	
	2					1.09	0.41					0.03	0.00	
07	1	21.14	19.68	11.48	39.22	28.93	28.10	4.59	4.92	3.87	14.55	19.92	14.77	
08	1	9.91	1.31	3.99	12.15		31.34	1.21	0.41	0.91	4.21		23.33	
10	1	7.72	5.92	2.82	7.34	19.33	19.41	1.10	1.47	0.90	3.10	14.19	15.37	
	2		5.70	3.40	4.28	7.14	9.19		1.36	1.04	1.05	2.79	5.90	
13	1	14.99	8.69	7.23	16.02	20.21	0.77	3.53	3.00	2.14	3.70	10.03	0.00	
15	1	13.06	26.89	44.56				2.96	8.01	9.58				
	2		0.23	0.61					0.01	0.02				
16	1	5.20	7.61	17.04		5.82	4.40	0.74	1.50	3.34		2.57	1.48	
	2		1.22	7.44		9.61	3.64		0.24	1.84		5.81	1.06	
20	1	0.41	7.49	2.10	0.52	0.47	0.71	0.03	3.07	0.31	0.04	0.04	0.02	
	2		7.79	3.36	13.67	16.93	20.23		1.28	0.72	4.43	11.08	10.56	
21	1		20.18		14.50		7.03		5.92		5.20		3.33	
22	1	24.69	20.63	19.66	25.86	22.01	0.72	4.44	5.35	4.92	7.33	9.69	0.00	
26	1						1.69						0.29	
28	1	6.40	6.25			12.82	9.46	1.12	1.16			7.26	4.73	
43	1	29.01	29.38	26.09	29.43	35.19		4.43	9.42	6.28	15.26	15.38		

Participant	LN #	Total LNPCs (% of CD19)						SARS-CoV-2 S-binding LNPCs (% of CD19)						
		Week 3	Week 4	Week 5	Week 7	Week 15	Week 29	Week 3	Week 4	Week 5	Week 7	Week 15	Week 29	
01a	1	0.77	4.96	6.00	6.82	8.23	2.33	0.07	0.84	1.15	1.61	2.04	0.78	
02a	1	0.35	2.47	3.52	3.20	0.43	0.22	0.01	0.20	0.40	0.36	0.00	0.00	
	2		2.30	3.74	3.91				0.25	0.28	0.54			
04	1	0.88	1.29	1.57	2.67	0.29	0.08	0.05	0.09	0.43	0.20	0.00	0.01	
	2					0.17	0.14					0.00	0.01	
07	1	0.97	2.74	1.73	3.97	2.02	1.87	0.07	0.26	0.26	0.67	0.32	0.22	
08	1	1.07	2.18	1.53	4.84		3.49	0.07	0.09	0.15	0.74		1.30	
10	1	0.71	4.08	2.31	3.92	4.02	2.42	0.04	0.34	0.33	0.86	1.06	0.76	
	2		2.83	3.51	1.75	1.08	1.40		0.18	0.40	0.16	0.19	0.31	
13	1	0.39	0.94	1.57	5.25	3.02	0.04	0.02	0.21	0.30	0.64	0.44	0.00	
15	1	1.26	1.27	3.60				0.08	0.12	0.29				
	2		1.79	0.64					0.10	0.01				
16	1	0.47	0.88	2.24		1.68	0.60	0.02	0.05	0.12		0.16	0.03	
	2		0.43	1.31		2.91	1.06		0.02	0.11		0.43	0.10	
20	1	0.14	0.46	0.28	0.35	0.34	0.09	0.01	0.01	0.00	0.00	0.00	0.00	
	2		1.73	1.62	4.01	2.48	1.32		0.05	0.08	0.22	0.42	0.29	
21	1		3.42		12.18		1.53		0.38		1.70		0.25	
22	1	1.01	2.92	5.91	7.84	5.84	0.07	0.03	0.16	0.30	0.77	0.82	0.00	
26	1						0.23						0.00	
28	1	0.54	1.54			6.26	1.29	0.03	0.13			1.15	0.25	
43	1	1.14	3.85	3.66	7.75	3.63		0.05	0.63	0.55	2.44	0.93		

Extended Data Table 4. Frequencies of CD14⁺ cells in lymph node samples

Participant	LN #	CD14 (% of live singlet)					
		Week 3	Week 4	Week 5	Week 7	Week 15	Week 29
01a	1	0.21	0.06	0.15	0.15	0.16	0.21
02a	1	0.16	0.17	0.07	0.25	0.17	0.30
	2		0.14	0.14	0.71		
04	1	0.19	0.37	0.72	0.14	1.00	0.16
	2					0.33	0.25
07	1	0.19	0.15	0.42	0.66	0.04	4.38
08	1	0.27	0.17	0.34	0.81		1.01
10	1	0.22	0.07	0.08	0.21	0.03	0.23
	2		0.09	0.05	0.13	0.03	0.26
13	1	0.57	0.34	0.43	0.33	1.63	1.04
15	1	0.07	0.19	0.08			
	2		0.14	0.24			
16	1	0.26	0.14	0.06		1.21	0.50
	2		0.11	0.14		0.51	0.32
20	1	0.21	0.15	0.29	0.41	0.84	0.11
	2		0.11	0.16	0.11	0.29	0.16
21	1		0.13		0.11		0.51
22	1	0.18	0.16	0.20	0.36	0.28	0.24
26	1						0.03
28	1	0.14	0.22			0.66	0.66
43	1	0.52	0.32	0.98	0.09	0.01	

Extended Data Table 5. Cell counts and frequencies of overall and B cell clusters in scRNA-seq of PBs sorted from blood and FNA from lymph nodes

Sample	Overall cluster	Cell count (% of whole cells)
PBs sorted from blood	B	27420 (96.5%)
	CD4+ T	35 (0.1%)
	CD8+ T	87 (0.3%)
	NK	730 (2.6%)
	Monocyte	142 (0.5%)
	pDC	6 (0%)
Lymph node	FDC	0 (0%)
	B	139287 (48.1%)
	CD4+ T	108647 (37.5%)
	CD8+ T	29986 (10.4%)
	NK	4983 (1.7%)
	Monocyte	4260 (1.5%)
Combined	pDC	2164 (0.7%)
	FDC	349 (0.1%)
	B	166707 (52.4%)
	CD4+ T	108682 (34.2%)
	CD8+ T	30073 (9.5%)
	NK	5713 (1.8%)
	Monocyte	4402 (1.4%)
	pDC	2170 (0.7%)
	FDC	349 (0.1%)

Participants	B cell cluster	Total cells (each B cell cluster out of whole B cells)	SARS-CoV-2 S-binding cells (S-binding cells out of total cells within each cluster)
01a	GC	4050 (25.5%)	2258 (55.8%)
	LNPC	1113 (7%)	891 (80.1%)
	Naïve	2034 (12.8%)	0 (0%)
	PB	6183 (38.9%)	424 (6.9%)
	PB-like	2 (0%)	0 (0%)
	RMB	2495 (15.7%)	15 (0.6%)
02a	GC	17869 (56.5%)	7663 (42.9%)
	LNPC	3101 (9.8%)	2285 (73.7%)
	Naïve	4161 (13.2%)	2 (0%)
	PB	1837 (5.8%)	246 (13.4%)
	PB-like	1 (0%)	0 (0%)
	RMB	4671 (14.8%)	32 (0.7%)
04	GC	3694 (30%)	1602 (43.4%)
	LNPC	392 (3.2%)	109 (27.8%)
	Naïve	2059 (16.7%)	1 (0%)
	PB	4363 (35.5%)	212 (4.9%)
	PB-like	0 (0%)	-
	RMB	1788 (14.5%)	5 (0.3%)
07	GC	6313 (37.1%)	3695 (58.5%)
	LNPC	716 (4.2%)	492 (68.7%)
	Naïve	3314 (19.5%)	0 (0%)
	PB	3667 (21.6%)	160 (4.4%)
	PB-like	9 (0.1%)	0 (0%)
	RMB	2989 (17.6%)	10 (0.3%)
10	GC	8505 (24.2%)	3099 (36.4%)
	LNPC	2419 (6.9%)	1424 (58.9%)
	Naïve	13382 (38%)	13 (0.1%)
	PB	1497 (4.3%)	59 (3.9%)
	PB-like	2 (0%)	0 (0%)
	RMB	9365 (26.6%)	18 (0.2%)
13	GC	3635 (29.7%)	1385 (38.1%)
	LNPC	907 (7.4%)	671 (74%)
	Naïve	2637 (21.5%)	6 (0.2%)
	PB	1861 (15.2%)	38 (2%)
	PB-like	3 (0%)	0 (0%)
	RMB	3211 (26.2%)	1 (0%)
20	GC	3256 (27.2%)	1641 (50.4%)
	LNPC	659 (5.5%)	363 (55.1%)
	Naïve	3100 (25.9%)	0 (0%)
	PB	1178 (9.9%)	23 (2%)
	PB-like	0 (0%)	-
	RMB	3766 (31.5%)	3 (0.1%)
22	GC	5281 (26.9%)	2087 (39.5%)
	LNPC	1576 (8%)	1089 (69.1%)
	Naïve	2072 (10.6%)	0 (0%)
	PB	6633 (33.8%)	660 (10%)
	PB-like	2 (0%)	0 (0%)
	RMB	4036 (20.6%)	14 (0.3%)
Combined	GC	52603 (33.8%)	23430 (44.5%)
	LNPC	10883 (7%)	7324 (67.3%)
	Naïve	32759 (21%)	22 (0.1%)
	PB	27219 (17.5%)	1822 (6.7%)
	PB-like	19 (0%)	0 (0%)
	RMB	32321 (20.7%)	98 (0.3%)

Extended Data Table 6. Description of monoclonal antibodies derived from GC B cells and LNPCs

		01a (N=145) N (%)	02a (N=410) N (%)	04 (N=124) N (%)	07 (N=201) N (%)	10 (N=249) N (%)	13 (N=108) N (%)	20 (N=99) N (%)	22 (N=167) N (%)
Heavy chain isotype	IGHG	109 (75.2%)	387 (94.4%)	102 (82.3%)	146 (72.6%)	200 (80.3%)	102 (94.4%)	90 (90.9%)	144 (86.2%)
	IGHA	35 (24.1%)	11 (2.7%)	15 (12.1%)	54 (26.9%)	43 (17.3%)	5 (4.6%)	6 (6.1%)	22 (13.2%)
	IGHM	1 (0.7%)	11 (2.7%)	7 (5.6%)	1 (0.5%)	2 (0.8%)	1 (0.9%)	3 (3%)	1 (0.6%)
	IGHD	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Light chain isotype	IGKC	102 (70.3%)	223 (54.4%)	61 (49.2%)	133 (66.2%)	183 (73.5%)	66 (61.1%)	69 (69.7%)	73 (43.7%)
	IGLC	43 (29.7%)	187 (45.6%)	63 (50.8%)	68 (33.8%)	66 (26.5%)	42 (38.9%)	30 (30.3%)	94 (56.3%)
Compartment	GC B cell	85 (58.6%)	248 (60.5%)	95 (76.6%)	134 (66.7%)	151 (60.6%)	68 (63%)	59 (59.6%)	82 (49.1%)
	LNPC	60 (41.4%)	162 (39.5%)	29 (23.4%)	67 (33.3%)	98 (39.4%)	40 (37%)	40 (40.4%)	85 (50.9%)
Time point	Week 4			45 (36.3%)					
	Week 5		180 (43.9%)						
	Week 7	84 (57.9%)	230 (56.1%)	79 (63.7%)	142 (70.6%)	115 (46.2%)	67 (62%)	34 (34.3%)	108 (64.7%)
	Week 15	61 (42.1%)			59 (29.4%)	134 (53.8%)	41 (38%)	65 (65.7%)	59 (35.3%)

Extended Data Table 7. Processing of BCR and 5' gene expression data from scRNA-seq

Participant	Time point	Compartment	BCR		5' gene expression			
			Pre-QC number of cells	Post-QC number of cells	Pre-QC number of cells	Post-QC number of cells	Median number of UMIs per cell	Median number of genes per cell
01a	Week 4	PB	6211	5562	8106	6251	14020	2470
	Week 7	FNA	5637	5198	16493	15065	10069	3904
	Week 15	FNA	5044	4667	14544	13664	9803	3908
02a	Week 4	PB	3981	3016	2847	1952	8589.5	1967.5
	Week 5	FNA	18943	16664	27065	24827	22731	8519
	Week 7	FNA	26710	20982	39293	35052	20904	7936
04	Week 4	PB	5347	4321	8571	4486	12855.5	2546
	Week 4	FNA	5205	4868	11272	10312	11384	4267
	Week 7	FNA	5771	5142	13993	13063	10733	3926
07	Week 4	PB	4123	3610	6284	3745	14059	2602
	Week 7	FNA	7284	6515	14466	13282	10986	4173
	Week 15	FNA	8343	7457	16367	15340	10717	4183
10	Week 4	PB	3228	2535	2336	1565	13046	2386
	Week 7	FNA	20154	18088	33178	30545	22459.5	8451
	Week 15	FNA	23419	20133	35386	31771	23104	8657.5
13	Week 4	PB	2241	1897	3072	2258	12423.5	2433
	Week 7	FNA	8448	7320	14126	13264	10978	4145
	Week 15	FNA	3098	2716	8730	6927	5615	2186
20	Week 4	PB	2962	2175	2011	1346	13254	2343
	Week 7	FNA	5086	4595	15171	14459	10989.5	3758
	Week 15	FNA	8754	7739	18876	17299	11520.5	4065
22	Week 4	PB	6517	5313	9504	6850	11730	2251.5
	Week 7	FNA	9580	7904	22879	21692	9700	3756
	Week 15	FNA	4780	4138	16233	13141	10014.5	3802

Extended Data Table 8. Processing of BCR reads from bulk-seq

Participant	Time point	Compartment	Cell count	Sequence count			
				Input	Preprocessed	Post QC	Unique VDJ
01a	Week 7	GC B cell	16920	1234529	4950	4018	2510
		LNPC	3307	1350772	11799	9851	3592
	Week 15	GC B cell	10440	1031639	1274	897	612
		LNPC	2139	1659983	6337	5348	2122
	Week 29	BMPC	16000000	2224729	142929	127601	65389
	02a	Week 5	GC B cell	75639	2323018	60305	50108
LNPC			7983	2062756	80227	61617	14236
Week 7		GC B cell	65172	2264893	47141	38634	21203
		LNPC	8730	2041016	71862	54796	13202
Week 29		BMPC	200000	1132888	63177	55882	35438
04		Week 4	GC B cell	27014	1191023	3115	2207
	LNPC		2312	1012560	9807	8276	2955
	Week 7	GC B cell	37948	1354770	16773	13798	8757
		LNPC	2495	917541	11273	9403	3361
	Week 29	BMPC	200000	1526703	11664	10357	9241
	07	Week 7	GC B cell	67030	1330762	37376	32737
LNPC			7131	1360131	29602	21560	6666
Week 15		GC B cell	36501	1160090	6994	5377	3762
		LNPC	2108	1798209	19416	14404	3801
Week 29		BMPC	100000	1212296	19112	17647	14378
10		Week 7	GC B cell	37570	2771591	43545	36356
	LNPC		13131	2747041	119842	90279	20947
	Week 15	GC B cell	103688	2599601	78901	65390	34232
		LNPC	15757	2472177	102827	77796	20465
13	Week 7	GC B cell	26603	1448419	13749	11614	6413
		LNPC	6798	1528468	35222	25799	6997
	Week 15	GC B cell	38318	1424118	13795	11862	7757
		LNPC	3801	1263065	26314	19482	5107
	Week 29	BMPC	100000	3206444	21006	19123	14894
	20	Week 7	GC B cell	16773	1249336	10208	8084
LNPC			3967	1248043	38803	28898	7185
Week 15		GC B cell	63961	999961	24525	20745	12230
		LNPC	6877	1324665	3196	1998	1323
Week 29		BMPC	200000	1307413	602	491	380
22		Week 7	GC B cell	17676	1344080	15060	12556
	LNPC		4823	1068783	26503	20779	4907
	Week 15	GC B cell	48264	891196	22310	17775	8612
		LNPC	10443	1290422	28342	19770	6665
	Week 29	BMPC	200000	2185196	115201	105375	64106