

Figure S1

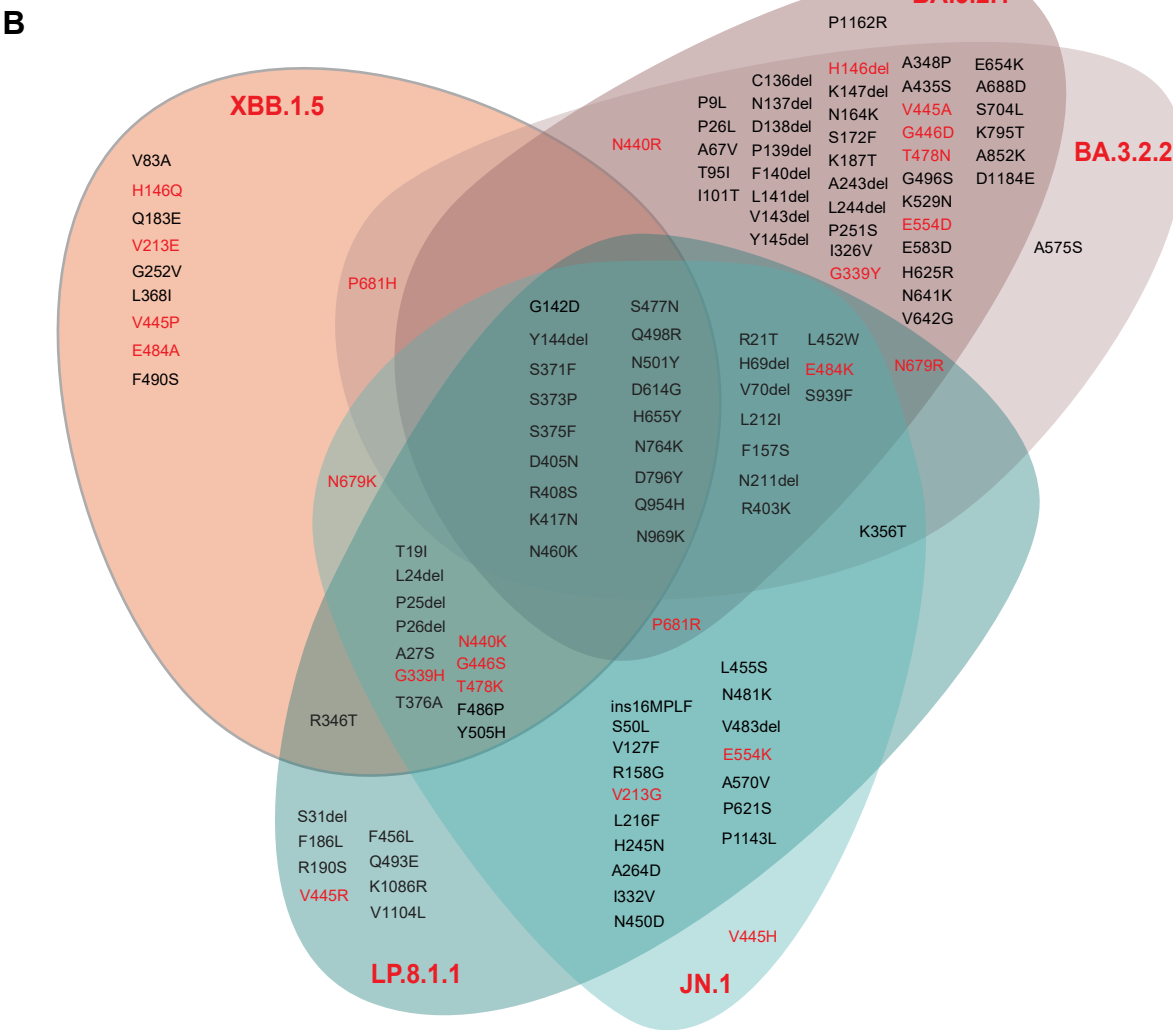
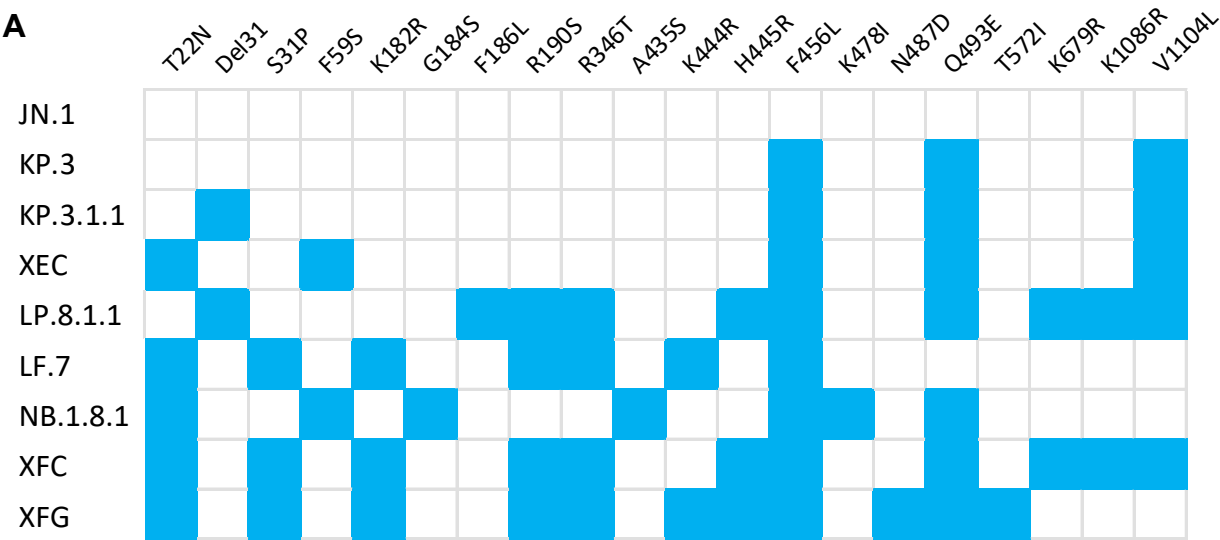


Figure S2

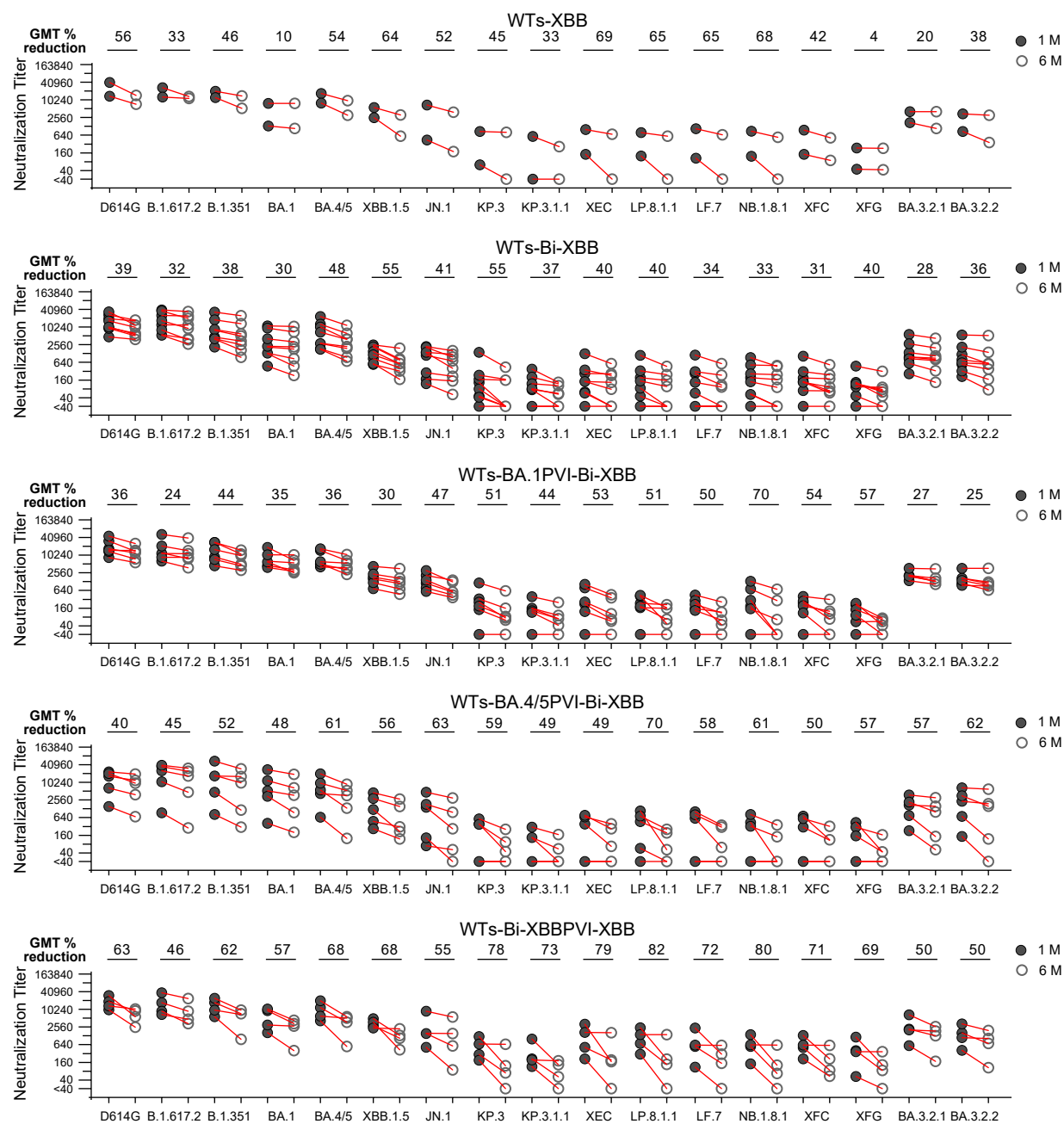


Table S1. SARS-CoV-2 spikes used for pseudoviruses.

Virus name	GenBank or GISAID #
D614G	EPI_ISL_5851484
B.1.617.2	MW934201
B.1.351	MW598419
BA.1	OQ361639
BA.4/5	EPI_ISL_12464782
XBB.1.5	EPI_ISL_15687648
JN.1	OR649559
KP.3	PP599813
KP.3.1.1	PP897603
XEC	PQ147446
LF.7	EPI_ISL_19707256
XFG	EPI_ISL_19724626
XFC	EPI_ISL_19658767
LP.8.1.1	EPI_ISL_19808041
NB.1.8.1	EPI_ISL_19750627
BA.3.2.1	EPI_ISL_19771107
BA.3.2.2	EPI_ISL_19771105

Table S2. Summary of antigenic exposures for each participant

Sample ID	COVID-19 vaccination fall 2023	Number of vaccinations	COVID-19 infection date (month-year)	XBB.1.5 Booster date (month-year)	Days since XBB.1.5 booster vaccination (1 month)	Days since XBB.1.5 booster vaccination (6 months)
1	Pfizer	5		Sep-25	35	197
2	Pfizer	4		Nov-25	11	223
3	Pfizer	6		Nov-25	30	198
4	Pfizer	5		Oct-25	22	227
5	Moderna	5		Nov-25	9	190
6	Pfizer	6		Oct-25	28	203
7	Pfizer	5	Nov-25	Nov-25	7	159
8	Pfizer	5		Oct-25	52	241
9	Pfizer	6		Oct-25	40	166
10	Pfizer	5		Oct-25	23	177
11	Pfizer	5	Mar-25	Nov-25	32	158
12	Pfizer	5	Feb-25	Oct-25	20	202
13	Pfizer	6	Jan-25	Sep-25	46	186
14	Pfizer	5	Dec-25	Oct-25	28	238
15	Pfizer	6	Dec-25	Oct-25	20	248
16	Pfizer	5	Jan-25	Oct-25	16	191
17	Moderna	7	Apr-25	Sep-25	56	202
18	Moderna	7	May-25	Oct-25	11	188
19	Pfizer	5	May-25	Oct-25	26	201
20	Pfizer	5	May-25	Oct-25	36	191
21	Moderna	5	Jun-25	Oct-25	27	215
22	Pfizer	5	Oct-25	Oct-25	21	204
23	Pfizer	5	Nov-25	Oct-25	28	203
24	Pfizer	5	Jul-25	Oct-25	16	162
25	Pfizer	6	Dec-25	Oct-25	21	202

Table S3. Demographic information of the antigenic exposure groups

		Overall	WTs-XBB	WTs-Bi-XBB	WTs-BA.1PVI-Bi-XBB	WTs-BA.4/SPVI-Bi-XBB	WTs-Bi-XBBPVI-XBB
		N=25	N=2	N=8	N=6	N=5	N=4
Age group	18-44	9 (36.0%)	1 (50.0%)	2 (22.2%)	2 (33.3%)	2 (40.0%)	2 (50.0%)
	45-64	15 (60.0%)	0 (0%)	7 (77.8%)	3 (50.0%)	3 (60.0%)	2 (50.0%)
	65+	2 (8.0%)	1 (50.0%)	0 (0%)	1 (16.7%)	0 (0%)	0 (0%)
	Median age (IQR)	47 (39 - 57)	54 (45 - 63)	49 (45 - 55)	46 (41 - 53)	57 (43 - 62)	45 (38 - 54)
Gender	Female	17 (68.0%)	2 (100%)	6 (75.0%)	4 (66.7%)	2 (40.0%)	3 (75.0%)
	Male	8 (32.0%)	0 (0%)	2 (25.0%)	2 (33.3%)	3 (60.0%)	1 (25.0%)
Race							
	White	18 (72.0%)	2 (100%)	4 (50.0%)	5 (83.3%)	4 (80.0%)	3 (75.0%)
	Black	3 (12.0%)	0 (0%)	2 (25.0%)	0 (0%)	0 (0%)	1 (25.0%)
Ethnicity	Asian	4 (16.0%)	0 (0%)	2 (25.0%)	1 (16.7%)	1 (20.0%)	0 (0%)
	Hispanic	1 (4.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (25.0%)
	Non Hispanic	24 (96.0%)	2 (100%)	8 (100%)	6 (100%)	5 (100%)	3 (75.0%)
Primary vaccine series							
Pfizer BNT162b2		25 (100%)	2 (100%)	8 (100%)	6 (100%)	5 (100%)	4 (100%)
First booster (after primary series)							
Pfizer BNT162b2		24 (96.0%)	2 (100%)	8 (100%)	6 (100%)	4 (80.0%)	4 (100%)
Moderna mRNA-1273		1 (4.0%)	0 (0%)	0 (0%)	0 (0%)	1 (20.0%)	0 (0%)
Second booster							
Pfizer BNT162b2		9 (36.0%)	1 (50.0%)	3 (37.5%)	2 (33.3%)	2 (40.0%)	1 (25.0%)
Pfizer bivalent (original and Omicron BA.4/BA.5)		14 (56.0%)	0 (0%)	5 (62.5%)	4 (66.7%)	2 (40.0%)	3 (75.0%)
Moderna bivalent (original and Omicron BA.4/BA.5)		1 (4.0%)	0 (0%)	0 (0%)	0 (0%)	1 (20.0%)	0 (0%)
Pfizer monovalent XBB.1.5		1 (4.0%)	1 (50.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Third booster							
Pfizer BNT162b2		1 (4.0%)	0 (0%)	0 (0%)	0 (0%)	1 (20.0%)	0 (0%)
Pfizer bivalent (original and Omicron BA.4/BA.5)		7 (28.0%)	0 (0%)	3 (37.5%)	2 (33.3%)	1 (20.0%)	1 (25.0%)
Pfizer monovalent XBB.1.5		15 (60.0%)	1 (50.0%)	5 (62.5%)	4 (66.7%)	2 (40.0%)	3 (75.0%)
Moderna monovalent XBB.1.5		1 (4.0%)	0 (0%)	0 (0%)	0 (0%)	1 (20.0%)	0 (0%)
Unboosted		1 (4.0%)	1 (50.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fourth booster							
Pfizer bivalent (original and Omicron BA.4/BA.5)		2 (8.0%)	0 (0%)	0 (0%)	0 (0%)	2 (40.0%)	0 (0%)
Pfizer monovalent XBB.1.5		6 (24.0%)	0 (0%)	3 (37.5%)	2 (33.3%)	0	1 (25.0%)
Unboosted		17 (68.0%)	2 (100%)	5 (62.5%)	4 (66.7%)	3 (60.0%)	3 (75.0%)
Fifth booster							
Moderna monovalent XBB.1.5		2 (8.0%)	0 (0%)	0 (0%)	0 (0%)	2 (40.0%)	0 (0%)
Unboosted		23 (92.0%)	2 (100%)	8 (100%)	6 (100%)	3 (60.0%)	4 (100%)
Days between Fall 2023 vaccination and first serum sample collection							
Median (IQR)		26 (20 - 32)	23 (17 - 29)	26 (19 - 33)	24 (20 - 31)	27 (26 - 36)	21 (20 - 23)
Days between Fall 2023 vaccination and second serum sample collection							
Median (IQR)		201 (188 - 204)	210 (204 - 217)	194 (174 - 209)	197 (187 - 229)	201 (191 - 202)	203 (192 - 203)
Days between SARS-CoV-2 infection and first serum sample collection							
Median (IQR)		570 (480 - 832)	-	1095 (1095 - 1095)	672 (651 - 674)	551 (524 - 553)	230 (99 - 351)
Days between SARS-CoV-2 infection and second serum sample collection							
Median (IQR)		729 (664 - 832)	-	1247 (1247 - 1247)	836 (817 - 874)	708 (702 - 726)	394 (254 - 530)
Infecting variant*							
D614G		1/16 (6.25%)	0/2 (0%)	1/8 (12.5%)	0/6 (0%)	0/5 (0%)	0/4 (0%)
BA.1		6/16 (37.5%)	0/2 (0%)	0/8 (0%)	6/6 (100%)	0/5 (0%)	0/4 (0%)
BA.2/BA.4		1/16 (6.25%)	0/2 (0%)	0/8 (0%)	0/6 (0%)	1/5 (20.0%)	0/4 (0%)
BA.4/5		4/16 (25.0%)	0/2 (0%)	0/8 (0%)	0/6 (0%)	4/5 (80.0%)	0/4 (0%)
XBB		4/16 (25.0%)	0/2 (0%)	0/8 (0%)	0/6 (0%)	0/5 (0%)	4/4 (100%)

* Variants assigned based on date of infection

IQR, Interquartile range

Table S4. Comparison of neutralization titers against XBB.1.5 variant after XBB.1.5 booster

Dunn's multiple comparisons test	1 month	6 months
D614G vs. XBB.1.5	0.06	0.0151
B.1.617.2 vs. XBB.1.5	0.06	0.0135
B.1.351 vs. XBB.1.5	0.69	0.1293
BA.1 vs. XBB.1.5	>0.9999	>0.9999
BA.4/5 vs. XBB.1.5	>0.9999	>0.9999
XBB.1.5 vs. JN.1	>0.9999	>0.9999
XBB.1.5 vs. KP.3	0.00	0.0008
XBB.1.5 vs. XEC	0.04	0.0665
XBB.1.5 vs. KP.3.1.1	<0.0001	<0.0001
XBB.1.5 vs. NB.1.8.1	0.00	0.0025
XBB.1.5 vs. LP.8.1.1	0.01	0.0101
XBB.1.5 vs. LF.7	0.00	0.0084
XBB.1.5 vs. XFG	<0.0001	<0.0001
XBB.1.5 vs. XFC	0.00	0.0435
XBB.1.5 vs. BA.3.2.2	>0.9999	>0.9999
XBB.1.5 vs. BA.3.2.1	>0.9999	>0.9999

Table S5. Comparison of geometric mean neutralization titers for each variant at one month and six months

Wilcoxon matched-pairs signed rank test	P-Value
D614G 1M vs. D614G 6M	<0.0001
B.1.617.2 1M vs. B.1.617.2 6M	<0.0001
B.1.351 1M vs. B.1.351 6M	<0.0001
BA.1 1M vs. BA.1 6M	<0.0001
BA.4/5 1M vs. BA.4/5 6M	<0.0001
XBB.1.5 1M vs. XBB.1.5 6M	<0.0001
JN.1 1M vs. JN.1 6M	<0.0001
KP.3 1M vs. KP.3 6M	<0.0001
KP.3.1.1 1M vs. KP.3.1.1 6M	<0.0001
XEC 1M vs. XEC 6M	<0.0001
LP.8.1.1 1M vs. LP.8.1.1 6M	<0.0001
LF.7 1M vs. LF.7 6M	<0.0001
NB.1.8.1 1M vs. NB.1.8.1 6M	<0.0001
XFG 1M vs. XFC 1M	<0.0001
XFC 1M vs. XFC 6M	<0.0001
BA.3.2.1 1M vs. BA.3.2.1 6M	<0.0001
BA.3.2.2 1M vs. BA.3.2.2 6M	<0.0001