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Supplemental information

Antiviral efficacy against and replicative fitness of an XBB.1.9.1 clinical isolate

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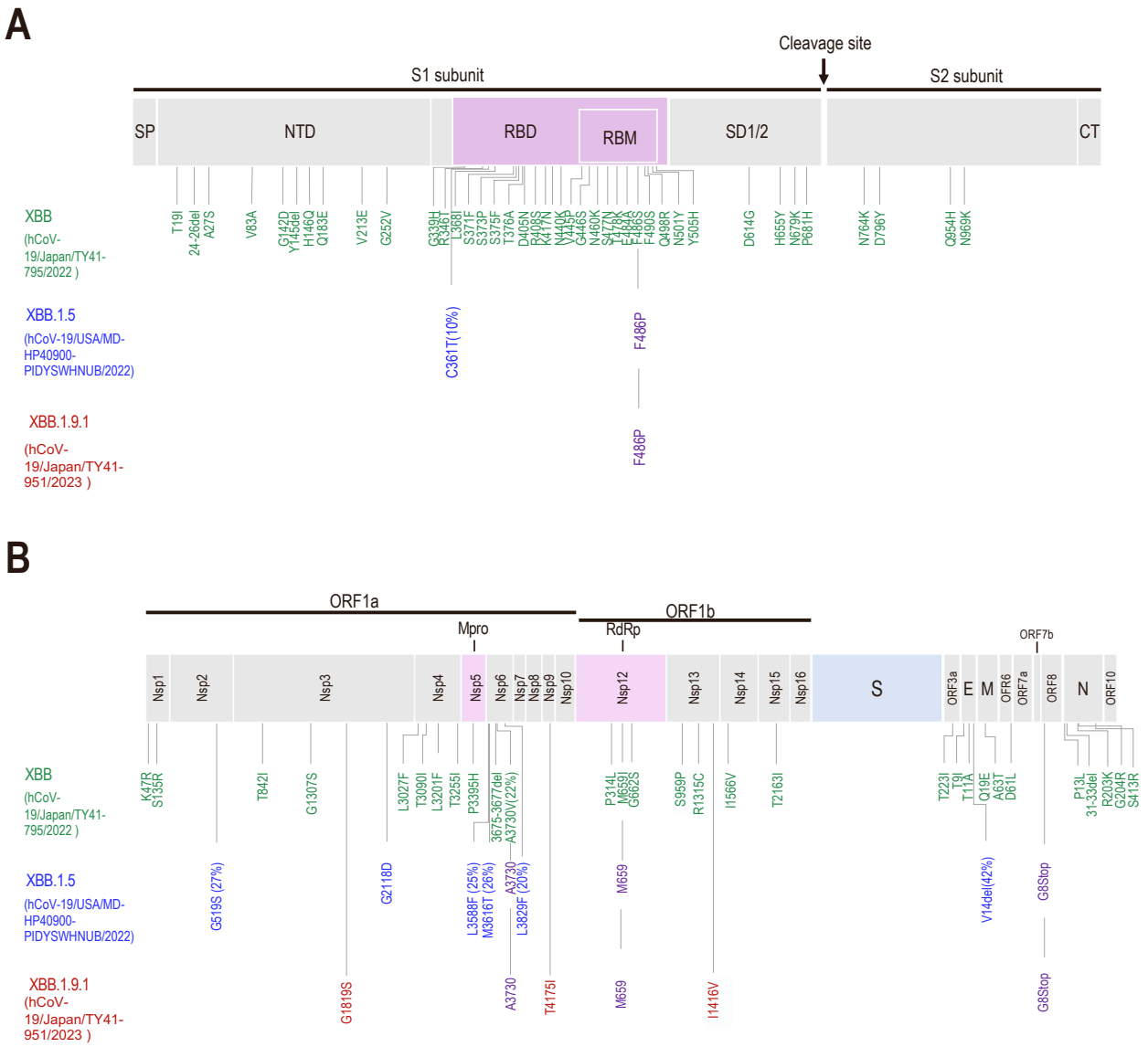

Figure S1. Mutations of Omicron subvariants, related to Figure 1 and 2.

(A) Spike (S) protein substitutions in the XBB.1.9.1 clinical isolate used in this study. Compared with XBB (hCoV-19/Japan/TY41-795/2022), substitutions are shown in blue for XBB.1.5 (hCoV-19/USA/MD-HP40900-PIDYSWHNUB/2022). The conserved substitutions between XBB.1.5 and XBB.1.9.1 (hCoV-19/Japan/TY41-951/2023) are shown in purple. The S protein comprises two subunits, S1 and S2. The arrow indicates the S1/S2 proteolytic cleavage site. SP, signal peptide; NTD, N-terminal domain; RBD, receptor-binding domain; RBM, receptor-binding motif; SD1/2, subdomain 1 and 2; and CT, cytoplasmic tail.

(B) Non-spike protein substitutions in the XBB.1.9.1 clinical isolate used in this study. Compared with XBB (hCoV-19/Japan/TY41-795/2022), substitutions are shown in blue for XBB.1.5 (hCoV-19/USA/MD-HP40900-PIDYSWHNUB/2022) and red for XBB.1.9.1 (hCoV-19/Japan/TY41-951/2023). The conserved substitutions between XBB.1.5 and XBB.1.9.1 are shown in purple. ORF, open reading frame; Mpro, main protease; RdRp, RNA-dependent RNA polymerase; S, Spike; E, Envelope; M, Membrane; and N, Nucleocapsid.

Table S1. Neutralizing antibody titers of human plasma from individuals who received four doses of COVID-19 monovalent mRNA vaccine, related to Figure 1

Sample ID	Age	Gender	Plasma collection day post-final vaccination	Vaccine	FRNT50: 50% focus reduction neutralization titer			
					SARS-CoV-2/UT-NC002-1T/Human/2020/Tokyo (A)	hCoV-19/Japan/TY41-795/2022 (Omicron XBB)	hCoV-19/USA/MD-HP40900-PIDYSWHNUB/2022 (Omicron XBB.1.5)	hCoV-19/Japan/TY41-951/2023 (Omicron XBB.1.9.1)
HP(H)-019	57	F	50	BNT162b2 x 3, mRNA-1273 x 1	1505	22	37	11
HP(H)-088	46	F	43	BNT162b2 x 3, mRNA-1273 x 1	2085	49	91	29
HP(H)-101	48	M	73	BNT162b2 x 3, mRNA-1273 x 1	949	23	34	<10
HP(H)-131	62	M	62	BNT162b2 x 3, mRNA-1273 x 1	730	17	28	<10
HP(H)-148	44	F	53	BNT162b2 x 3, mRNA-1273 x 1	832	22	42	<10
HP(H)-152	53	F	82	BNT162b2 x 3, mRNA-1273 x 1	1217	51	57	<10
HP(H)-158	29	F	41	BNT162b2 x 3, mRNA-1273 x 1	743	<10	<10	<10
HP(H)-160	62	F	91	BNT162b2 x 4	1430	13	64	<10
HP(H)-172	52	F	76	BNT162b2 x 3, mRNA-1273 x 1	508	20	25	<10
HP(H)-173	39	M	82	BNT162b2 x 3, mRNA-1273 x 1	413	<10	<10	<10
HP(H)-179	51	F	48	BNT162b2 x 3, mRNA-1273 x 1	771	27	48	<10
HP(H)-185	48	F	50	BNT162b2 x 3, mRNA-1273 x 1	3398	54	73	21
HP(H)-189	57	F	68	BNT162b2 x 4	1098	86	31	10
HP(H)-215	49	M	73	BNT162b2 x 3, mRNA-1273 x 1	160	<10	<10	<10
HP(H)-228	49	F	51	BNT162b2 x 3, mRNA-1273 x 1	1492	21	38	<10
HP(H)-241	62	F	57	BNT162b2 x 4	1211	29	34	<10
HP(H)-248	59	F	52	BNT162b2 x 3, mRNA-1273 x 1	754	20	40	<10
HP(H)-252	49	M	77	BNT162b2 x 3, mRNA-1273 x 1	512	19	50	<10
HP(H)-282	43	M	48	BNT162b2 x 3, mRNA-1273 x 1	513	<10	13	<10
HP(H)-297	56	M	45	BNT162b2 x 3, mRNA-1273 x 1	1849	128	250	98
HP(H)-299	53	F	53	BNT162b2 x 3, mRNA-1273 x 1	961	<10	<10	<10
HP(H)-300	72	F	96	BNT162b2 x 4	670	24	51	17

Table S2. Neutralizing antibody titers of human plasma from individuals who received the bivalent (ancestral and BA.4/5) mRNA vaccine after four doses of COVID-19 mRNA vaccine, related to Figure 1

Sample ID	Age	Gender	Plasma collection day post-final vaccination	Vaccine	FRNT50: 50% focus reduction neutralization titer			
					SARS-CoV-2/UT-NC002-1T/Human/2020/Tokyo (A)	hCoV-19/Japan/TY41-795/2022 (Omicron XBB)	hCoV-19/USA/MD-HP40900-PIDYSWHNUB/2022 (Omicron XBB.1.5)	hCoV-19/Japan/TY41-951/2023 (Omicron XBB.1.9.1)
HP(H)-019	57	F	50	BNT162b2 x 3, mRNA-1273 x 1	1505	22	37	11
HP(H)-088	46	F	43	BNT162b2 x 3, mRNA-1273 x 1	2085	49	91	29
HP(H)-101	48	M	73	BNT162b2 x 3, mRNA-1273 x 1	949	23	34	<10
HP(H)-131	62	M	62	BNT162b2 x 3, mRNA-1273 x 1	730	17	28	<10
HP(H)-148	44	F	53	BNT162b2 x 3, mRNA-1273 x 1	832	22	42	<10
HP(H)-152	53	F	82	BNT162b2 x 3, mRNA-1273 x 1	1217	51	57	<10
HP(H)-158	29	F	41	BNT162b2 x 3, mRNA-1273 x 1	743	<10	<10	<10
HP(H)-160	62	F	91	BNT162b2 x 4	1430	13	64	<10
HP(H)-172	52	F	76	BNT162b2 x 3, mRNA-1273 x 1	508	20	25	<10
HP(H)-173	39	M	82	BNT162b2 x 3, mRNA-1273 x 1	413	<10	<10	<10
HP(H)-179	51	F	48	BNT162b2 x 3, mRNA-1273 x 1	771	27	48	<10
HP(H)-185	48	F	50	BNT162b2 x 3, mRNA-1273 x 1	3398	54	73	21
HP(H)-189	57	F	68	BNT162b2 x 4	1098	86	31	10
HP(H)-215	49	M	73	BNT162b2 x 3, mRNA-1273 x 1	160	<10	<10	<10
HP(H)-228	49	F	51	BNT162b2 x 3, mRNA-1273 x 1	1492	21	38	<10
HP(H)-241	62	F	57	BNT162b2 x 4	1211	29	34	<10
HP(H)-248	59	F	52	BNT162b2 x 3, mRNA-1273 x 1	754	20	40	<10
HP(H)-252	49	M	77	BNT162b2 x 3, mRNA-1273 x 1	512	19	50	<10
HP(H)-282	43	M	48	BNT162b2 x 3, mRNA-1273 x 1	513	<10	13	<10
HP(H)-297	56	M	45	BNT162b2 x 3, mRNA-1273 x 1	1849	128	250	98
HP(H)-299	53	F	53	BNT162b2 x 3, mRNA-1273 x 1	961	<10	<10	<10
HP(H)-300	72	F	96	BNT162b2 x 4	670	24	51	17

Table S3. Neutralizing antibody titers of human plasma from individuals who were infected with the Omicron BA.2 variant after three doses of COVID-19 mRNA vaccine, related to Figure 1

Sample ID	Age	Gender	Plasma collection day post-onset	Vaccine	FRNT50: 50% focus reduction neutralization titer			
					SARS-CoV-2/UT-NC002-1T/Human/2020/Tokyo (A)	hCoV-19/Japan/TY41-795/2022 (Omicron XBB)	hCoV-19/USA/MD-HP40900-PIDYSWHNUB/2022 (Omicron XBB.1.5)	hCoV-19/Japan/TY41-951/2023 (Omicron XBB.1.9.1)
HPCo-383	56	F	29	mRNA-1273 x 2, BNT162b2 x 1	508	<10	18	<10
HP-S(H)0377	29	M	44	BNT162b2 x 3	693	98	51	44
HP-S(H)0380	22	M	42	BNT162b2 x 3	3574	62	39	20
HP-S(H)0381	22	M	44	BNT162b2 x 3	1094	18	22	12
HP-S(H)0382	21	M	44	BNT162b2 x 3	5413	97	57	218
HP-S(H)0383	18	M	42	BNT162b2 x 3	3838	45	72	160
HP-S(H)0882	23	M	89	BNT162b2 x 3	1022	24	26	<10
HP-S(H)0883	24	M	84	BNT162b2 x 3	3619	86	76	29
HP-S(H)0888	21	M	89	BNT162b2 x 3	6092	66	74	50
HP-S(H)1056	22	M	42	BNT162b2 x 3	6857	112	148	79