

Supplementary Appendix

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Materials and Methods

Ethics statement

All protocols involving specimens from human subjects recruited at Keio University, Fujiwara Clinic, and Satoh Clinic were reviewed and approved by the Institutional Review Boards of The Institute of Medical Science, The University of Tokyo (approval IDs: 2021-1-0416 and 2022-29-0915), and Keio University (approval ID: 20200059), respectively. All human subjects provided written informed consent. All protocols for the use of human specimens were reviewed and approved by the Institutional Review Boards of The Institute of Medical Science, The University of Tokyo (approval IDs: 2021-1-0416, 2021-18-0617 and 2022-29-0915).

Human serum collection

XEC monovalent vaccine sera from fully vaccinated individuals who had received Daiichi-Sankyo XEC vaccine (Daiichi Sankyo cohort) (one 3-dose vaccinated, one 4-dose vaccinated, one 5-dose vaccinated, two 6-dose vaccinated, nine 7-dose vaccinated and eight 8-dose vaccinated; twenty two donors in total, average age: 65.6, range: 28–84, 27.3% male) and those from fully vaccinated individuals who received Meiji Seika Pharma XEC vaccine (Meiji Seika Pharma cohort) (three 5-dose vaccinated, eight 6-dose vaccinated, four 7-dose vaccinated, three 8-dose vaccinated and two 9-dose vaccinated; twenty donors, average age: 44.4, range: 24–62, 45.0% male). For this study, we collected samples before vaccination and three to four weeks (21–28 days) after vaccination.

Sera were inactivated at 56°C for 30 minutes and stored at –80°C until use. The details of the vaccine sera are summarized in **Table S1 and S2**.

Cell culture

The Lenti-X 293T cells (Takara, Cat# 632180) and HOS-ACE2/TMPRSS2 cells (kindly provided by Dr. Kenzo Tokunaga), a derivative of HOS cells (a human osteosarcoma cell line; ATCC CRL-1543) stably expressing human ACE2 and TMPRSS2^{1,2} were maintained in Dulbecco's modified Eagle's medium (DMEM) (high glucose) (Wako, Cat# 044- 29765) containing 10% fetal bovine serum (Sigma-Aldrich Cat# 172012-500ML), 100 units penicillin and 100 ug/ml streptomycin (Sigma-Aldrich, Cat# P4333-100ML).

Pseudovirus preparation

Plasmids expressing the SARS-CoV-2 spike (S) proteins of B.1.1, BA.5, XBB.1.5, JN.1, XEC, LP.8.1, NB.1.8.1, XFG and BA.3.2 were prepared in our previous studies.³⁻¹⁰ Pseudoviruses were prepared as previously described.⁶⁻¹⁰ Briefly, lentivirus (HIV-1)-based, luciferase-expressing reporter viruses were pseudotyped with the SARS-CoV-2 S.

One prior day of transfection, the LentiX-293T cells were seeded at a density of 2×10^6 cells. The LentiX-293T cells were cotransfected with 1 μ g psPAX2-IN/HiBiT (a packaging plasmid encoding the HiBiT-tag-fused integrase¹, 1 μ g pWPI-Luc2 (a reporter plasmid encoding a firefly luciferase gene¹¹ and 500 ng plasmids expressing parental S or its derivatives using TransIT-293 transfection reagent (Mirus, Cat# MIR2704) according to the manufacturer's protocol. Two days post transfection, the culture supernatants were harvested and filtrated. The pseudoviruses were harvested and stored at -80°C until use after filtration.

Neutralization assay

Neutralization assays were performed previously described⁶⁻¹⁰ and mainly conducted by a semi-automated high-throughput method using Fluent780 (Tecan).^{6-10,12} The SARS-CoV-2 spike pseudoviruses (counting $\sim 100,000$ relative light units) and serially diluted (40-fold to 29,160-fold dilution at the final concentration) heat-inactivated sera were manually prepared in a 2-ml 96-well plate (Greiner, Cat# 780271) and in 96-well microplates (ThermoFisher Scientific, Cat# 168136), respectively. The pseudoviruses were dispensed and mixed with the sera in 384-well plates (ThermoFisher Scientific, Cat# 164610) on Fluent780 (Tecan). Pseudoviruses without sera were included as controls. After incubation at 37°C for 1 hour, HOS-ACE2/TMPRSS2 cells (6,000 cells/30 μ l) were added to the 20 μ l mixture of pseudovirus and serum in the 384-well white plate on the device. Two days post infection, the infected cells were lysed with a Bright-Glo luciferase assay system (Promega, Cat# E2620) on Fluent780 (Tecan), and the luminescent signal was measured and processed using an Infinite200 and a Magellan (Tecan). The assay of each serum sample was performed in quadruplicate, and the 50% neutralization titer (NT_{50}) was calculated using Prism 9 (GraphPad Software). The limit of detection (LOD) is determined to be 30 based on our previous report.¹⁰ The raw data of NT_{50} in this study were summarized in **Table S3**.

Antigenic cartography

Based on the 50% neutralization titers, the antigenic cartography (**Supplementary Figure**) of the viruses and vaccine sera was depicted with the method described by Smith *et al.*¹³ using the Racmacs v1.1.35 on R v4.2.2 (<https://www.r-project.org/>) with 500 optimization runs.

Table S1. Human vaccination sera used in this study

XEC vaccine manufacturers	Donor ID	Sex	Age	Date of 1st vaccination (YYYY-MM-DD)	Date of 2nd vaccination (YYYY-MM-DD)	Date of 3rd vaccination (YYYY-MM-DD)	Date of 4th vaccination (YYYY-MM-DD)	Date of 5th vaccination (YYYY-MM-DD)	Date of 6th vaccination (YYYY-MM-DD)	Date of 7th vaccination (YYYY-MM-DD)	Date of 8th vaccination (YYYY-MM-DD)	Date of 9th vaccination (YYYY-MM-DD)	Date of sampling (before vaccination) (YYYY-MM-DD)	Date of XEC vaccination (YYYY-MM-DD)	Date of sampling (after vaccination) (YYYY-MM-DD)	Time interval between vaccination and the second sampling	Prior infection? (YYYY-MM-DD)
Daiichi-Sankyo	F000100	Male	45	2021-04-28 (P)	2021-05-20 (P)	2022-01-08 (P)	2022-07-15 (P)	2022-12-03 (P)	2023-10-27 (P)	2024-10-01 (D,JN1)	-	-	2025-10-07	2025-10-07	2025-10-29	22	No
Daiichi-Sankyo	F000200	Female	46	2021-04-28 (P)	2021-05-19	2021-12-25 (P)	2022-06-15 (P)	2022-11-21 (P)	2024-10-03 (D,JN1)	-	-	-	2025-10-02	2025-10-02	2025-10-23	21	No
Daiichi-Sankyo	F000300	Male	63	2021-07-03 (M)	2021-07-31 (M)	2022-03-12 (P)	2022-08-18 (M)	2022-11-21 (P)	2024-10-04 (D)	-	-	-	2025-10-01	2025-10-01	2025-10-22	21	Yes (2023-07)
Daiichi-Sankyo	F000400	Female	82	2021-05-20 (P)	2021-06-10 (P)	2022-02-10 (P)	NA	NA	NA	NA	2024-11-11 (P)	-	2025-10-04	2025-10-04	2025-10-27	23	No
Daiichi-Sankyo	F000500	Female	54	2021-05-20 (P)	2021-06-10 (P)	2022-01-28 (P)	2022-08-05 (M)	2022-12-14 (P)	2023-06-21 (M)	2023-11-14 (P)	2024-11-11 (P)	-	2025-10-04	2025-10-04	2025-10-27	23	No
Daiichi-Sankyo	F000868	Female	75	2021-06 (P)	2021-07 (P)	2022-02-08 (P)	2022-07-15 (P)	2022-11-18 (P)	2023-06-06 (P)	2023-10-13 (P)	-	-	2025-10-03	2025-10-03	2025-10-27	24	No
Daiichi-Sankyo	F018678	Female	63	NA	NA	2022-02-15 (P)	2022-07-15 (P)	2022-11-01 (P)	2023-06-27 (P)	2023-09-29 (P)	2024-10-02 (D,JN1)	-	2025-10-03	2025-10-03	2025-10-25	22	Yes (2023-03, 2024-08)
Daiichi-Sankyo	F023012	Female	82	2021-05-21 (P)	2021-06-08 (P)	2022-01-28 (P)	2022-07-15 (P)	2022-11-11 (P)	2023-05-26 (P)	2023-11-07 (P)	-	-	2025-10-07	2025-10-07	2025-10-28	21	No
Daiichi-Sankyo	F035951	Female	74	NA	NA	2022-02-18 (P)	2022-07-19 (P)	2023-01-30 (P)	2023-06-13 (P)	2024-10-04 (D,JN1)	-	-	2025-10-03	2025-10-03	2025-10-24	21	No
Daiichi-Sankyo	F037838	Female	70	2021-06-29 (P)	2021-07-25 (P)	2022-02-09 (P)	2022-08-09 (P)	2022-12-13 (P)	2023-07-11 (P)	2023-11-14 (P)	2024-10-01 (D,JN1)	-	2025-10-01	2025-10-01	2025-10-23	22	No
Daiichi-Sankyo	F039982	Female	67	2021-06-25 (P)	2021-07-16 (P)	2022-02-18 (P)	2022-07-19 (P)	2022-12-05 (P)	2023-10-13 (P)	2024-11-12 (P)	-	-	2025-10-01	2025-10-01	2025-10-22	21	No
Daiichi-Sankyo	F050041	Male	74	2021-06-15 (P)	2021-07-16 (P)	2022-02-18 (P)	2022-07-19 (P)	2022-11-18 (P,BA4/5)	2023-06-13 (P,BA4/5)	2024-12-06 (P)	-	-	2025-10-07	2025-10-07	2025-10-28	21	No
Daiichi-Sankyo	F050351	Female	79	NA	NA	NA	2022-07-19 (P)	2022-11-08 (P)	2023-05-16 (P)	2023-09-26 (P)	2024-10-04 (D,JN1)	-	2025-10-07	2025-10-07	2025-10-29	22	No
Daiichi-Sankyo	F052203	Male	80	2021-06-13 (M)	2021-07-14 (M)	2022-01-28 (P)	2022-11-01 (P)	2023-05-23 (P)	2023-10-17 (P)	2024-11-05 (P)	-	-	2025-10-03	2025-10-03	2025-10-28	25	No
Daiichi-Sankyo	F055336	Female	75	2021-06-11 (P)	2021-07-02 (P)	2022-02-04 (P)	2022-07-08 (P)	2022-11-15 (P)	2023-05-19 (P)	2023-10-06 (P)	2024-10-02 (D,JN1)	-	2025-10-01	2025-10-01	2025-10-24	21	No
Daiichi-Sankyo	F072023	Female	57	2021-07-05 (P)	2021-07-26 (P)	2022-02-10 (M)	2022-07-15 (P)	2022-12-23 (P,BA4/5)	2023-07-14 (P,BA1)	2023-11-10 (XBB)	2024-10-01 (D,JN1)	-	2025-10-03	2025-10-03	2025-10-24	21	Yes (2024-02, 2025-02)
Daiichi-Sankyo	F072088	Female	71	2021-06-24 (P)	2021-07-15 (P)	2022-03-04 (P)	2022-08-25 (P)	2023-01-06 (P)	2023-05-16 (P)	2023-09-26 (P)	2024-10-03 (D,JN1)	-	2025-10-04	2025-10-04	2025-10-29	25	No
Daiichi-Sankyo	F075080	Female	75	2021-06-08 (P)	2021-06-29 (P)	2022-07-12 (P)	2022-11-08 (P)	2023-05-16 (P)	2023-09-29 (P)	2024-10-01 (D,JN1)	-	-	2025-10-01	2025-10-01	2025-10-22	21	No
Daiichi-Sankyo	F078713	Female	28	2021-04 (P)	2021-04 (P)	2021-12 (P)	-	-	-	-	-	-	2025-10-03	2025-10-03	2025-10-24	21	Yes (2022-11)
Daiichi-Sankyo	F079661	Male	62	NA	NA	NA	2022-10 (P)	2024-10-01 (D,JN1)	-	-	-	-	2025-10-03	2025-10-03	2025-10-24	21	No
Daiichi-Sankyo	F079996	Male	84	NA	NA	NA	NA	2023-06-13 (P)	2023-10-24 (P)	2024-10-04 (D,JN1)	-	-	2025-10-03	2025-10-03	2025-10-24	21	Yes (2023-01)
Daiichi-Sankyo	F082525	Female	37	NA	NA	NA	2022-10 (P)	-	-	-	-	-	2025-10-03	2025-10-03	2025-10-28	25	Yes (2022-08)
Meiji Seika Pharma	S0015	Female	24	2021-06-18 (P)	2021-07-09 (P)	2022-03-31 (P)	2022-09-29 (P)	2023-10-08 (P)	-	-	-	-	2025-10-04	2025-10-04	2025-10-27	23	Yes (2022-01, 2023-07)
Meiji Seika Pharma	S0019	Male	37	2021-06-19 (M)	2021-07-17 (M)	2022-05-13 (M)	2022-10-28 (M)	2023-10-06 (M)	2024-05-11 (M)	2024-08-03 (P)	2024-10-20 (MSP)	-	2025-09-28	2025-09-28	2025-10-24	26	No
Meiji Seika Pharma	S0049	Female	34	2021-01-01 (P)	NA	NA	NA	NA	NA	NA	NA	2025-10-20 (MSP)	2025-09-29	2025-09-29	2025-10-20	21	Yes (2023-11-01)
Meiji Seika Pharma	S0066	Male	41	2021-07-15 (M)	2021-08-12 (M)	2022-02-15 (M)	2022-10-14 (P)	2023-10-16 (P)	2024-11-04 (MSP)	-	-	-	2025-10-04	2025-10-04	2025-10-25	21	Yes (2023-07-29, 2025-07-18)
Meiji Seika Pharma	S0074	Female	49	2021-07-10 (P)	2021-07-30 (P)	2022-02-10 (M)	2022-10-06 (M)	2023-09-29 (P)	2024-11-16 (MSP)	-	-	-	2025-09-27	2025-09-27	2025-10-18	21	No
Meiji Seika Pharma	S0087	Female	45	2021-08-21 (M)	2021-09-18 (M)	2022-03-30 (P)	2024-03-01 (D)	2024-12-20 (MSP)	-	-	-	-	2025-09-26	2025-09-26	2025-10-20	24	Yes (2022-08-04, 2025-07-04)
Meiji Seika Pharma	S0094	Female	49	2021-05-01 (P)	2021-05-22 (P)	2022-02-06 (P)	2022-08-04 (P)	2023-05-11 (P)	2023-10-26 (P)	2024-11-01 (MSP)	-	-	2025-09-29	2025-09-29	2025-10-27	28	Yes (2022-12-06)
Meiji Seika Pharma	S0112	Male	59	2021-08-16 (P)	2021-09-06 (P)	2022-03-07 (P)	2022-10-25 (P)	2023-10-10 (P)	2024-06-21 (M)	2024-10-07 (M)	2025-04-08 (P)	-	2025-09-26	2025-09-26	2025-10-17	21	Yes (2024-02, 2024-09-04)
Meiji Seika Pharma	S0119	Male	36	2021-07-19 (M)	2021-08-23 (M)	2022-03-09 (M)	2023-11-10 (P)	2023-10-27 (M)	2024-11-22 (MSP)	-	-	-	2025-10-01	2025-10-01	2025-10-27	26	Yes (2023-09-04, 2025-08-02)
Meiji Seika Pharma	S0135	Male	40	2021-07-02 (P)	2021-07-23 (P)	2022-02-16 (M)	2022-11-02 (P)	2023-09-22 (P)	2024-11-03 (MSP)	-	-	-	2025-09-26	2025-09-26	2025-10-21	25	No
Meiji Seika Pharma	S0140	Female	48	2021-07-18 (M)	2021-08-15 (M)	2022-02-26 (M)	2022-10-24 (M)	2023-11-24 (P)	2024-11-12 (MSP)	-	-	-	2025-09-29	2025-09-29	2025-10-27	28	No
Meiji Seika Pharma	S0162	Female	62	2021-07-16 (P)	2021-08-06 (P)	2022-02-28 (M)	2022-10-04 (M)	2023-10-20 (M)	2024-10-21 (P)	-	-	-	2025-09-29	2025-09-30	2025-10-28	28	Yes (2023-04-02)
Meiji Seika Pharma	S0171	Male	40	2021-07-08 (M)	2021-08-03 (M)	2022-04-21 (P)	2022-12-02 (M)	2023-10-16 (P)	2024-10-24 (P)	-	-	-	2025-09-28	2025-09-28	2025-10-25	27	Yes (2022-02-18)
Meiji Seika Pharma	S0185	Female	51	2021-06-24 (M)	2021-07-23 (M)	2022-02-15 (M)	2022-07-15 (P)	2022-11-03 (P)	2023-06-02 (P)	2023-11-07 (P)	2024-07-19 (M)	2024-11-01 (MSP)	2025-09-30	2025-09-30	2025-10-21	21	No
Meiji Seika Pharma	S0194	Male	27	2021-08-29 (P)	2021-09-18 (P)	2022-03-22 (M)	2022-11-11 (P)	2023-09-23 (P)	2024-11-16 (P)	2025-04-12 (MSP)	-	-	2025-09-28	2025-09-28	2025-10-22	24	No
Meiji Seika Pharma	S0197	Female	41	2021-07-04 (P)	2021-07-25 (P)	2022-01-31 (M)	2022-10-02 (M)	2023-09-29 (M)	2024-05-31 (P)	2024-10-03 (P)	2025-03-19 (MSP)	-	2025-09-27	2025-09-27	2025-10-20	23	No
Meiji Seika Pharma	S0219	Female	57	2021-07-12 (M)	2021-08-09 (M)	2022-02-15 (M)	2022-10-08 (P)	2023-10-08 (M)	-	-	-	-	2025-09-29	2025-09-29	2025-10-20	21	No
Meiji Seika Pharma	S0221	Male	45	2021-08-01 (P)	2021-08-22 (P)	2022-03-06 (M)	2022-10-10 (M)	2023-10-28 (M)	2024-06-14 (M)	2024-10-20 (MSP)	-	-	2025-09-28	2025-09-28	2025-10-25	27	Yes (2023-08-30)
Meiji Seika Pharma	S0235	Female	49	2021-08-25 (P)	2021-09-24 (P)	2022-04-07 (N)	2022-12-01 (P)	2023-11-22 (P)	2024-11-16 (MSP)	-	-	-	2025-09-29	2025-09-29	2025-10-21	22	No
Meiji Seika Pharma	S0261	Male	54	2021-07-14 (P)	2021-08-12 (P)	2022-02-24 (M)	2022-10-28 (P)	2023-06-15 (P)	2023-12-28 (P)	2024-11-15 (MSP)	-	-	2025-09-26	2025-09-26	2025-10-20	24	No

NA, not applicable.

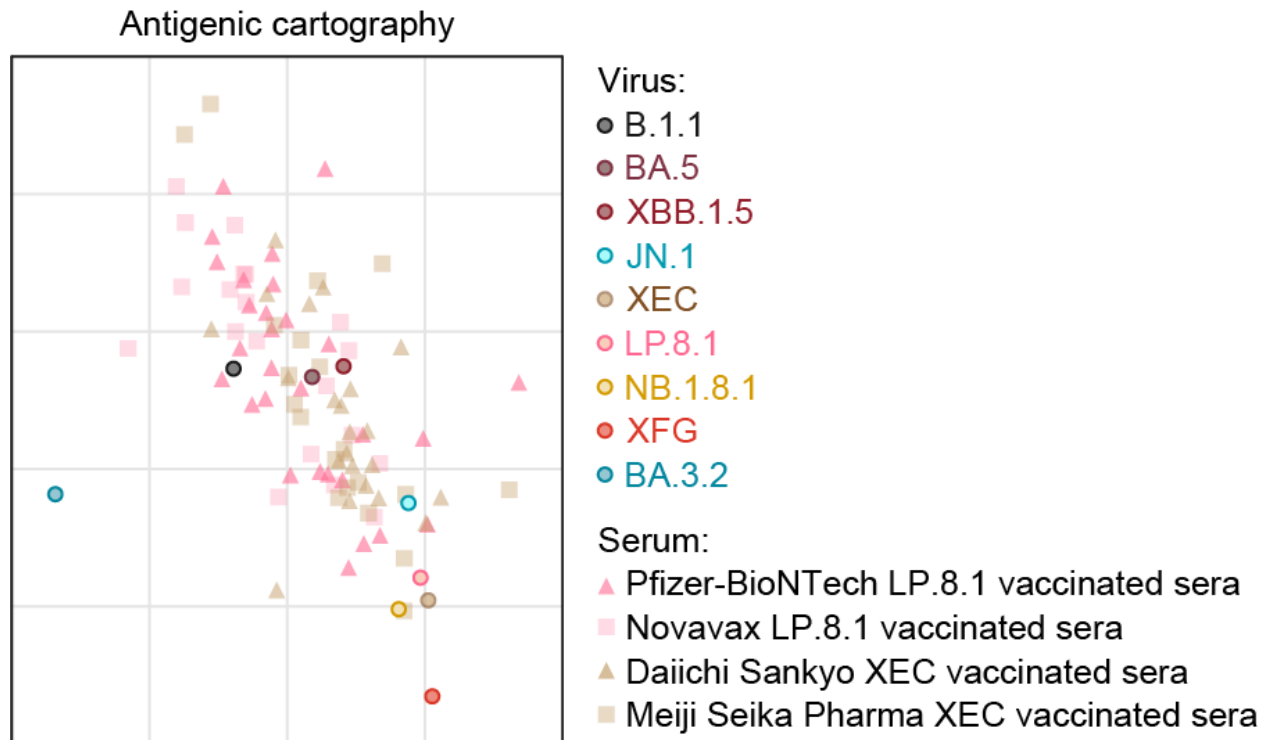
A, Astrazeneca; P, Pfizer/BioNTech; M, Moderna; S, Sinovac; J, Jenner; N, Novavax/Takeda; D, Daiichi-Sankyo; MSP, Meiji Seika Pharma

BA1/2, BA.1/2 bivalent vaccine; BA4/5, BA.4/5 bivalent vaccine; XBB, XBB.1.5 monovalent vaccine; JN1, JN.1 monovalent vaccine

Table S2. Raw data of 50% neutralization titer																				
XEC-based vaccine		B.1.1		BA.5		XBB.1.5		JN.1		XEC		LP.8.1		NB.1.8.1		XFG		BA.3.2		
manufacturers	Donor ID	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
Daiichi-Sankyo	F000100	615.1	3055	551.6	5566	463.5	4607	156.1	2963	81.15	3209	91.24	3380	40	3010	40	1853	105	1195	
Daiichi-Sankyo	F000200	1959	3003	2931	5960	1320	4789	673.7	2697	464.3	2450	521.2	2252	412.3	2093	259.9	1412	669.9	1255	
Daiichi-Sankyo	F000300	2251	2221	3712	4556	2717	3550	1152	2556	601.1	1487	564.5	1371	556.8	1565	110.6	1036	989.3	1064	
Daiichi-Sankyo	F000400	116.8	184.6	80.38	200.5	136.6	126.4	40	144.7	40	96.35	40	102.3	40	99.64	40	107.2	40	40	
Daiichi-Sankyo	F000500	3867	3766	917.4	1218	127.5	426.4	40	2369	40	1597	40	1538	40	1836	40	1874	830.3	737.1	
Daiichi-Sankyo	F000868	657.5	1789	1368	4868	934.5	4526	346.4	2843	40	825.8	79.73	869.5	65.63	646.4	40	292.9	285.6	1148	
Daiichi-Sankyo	F018678	1066	1136	2385	3655	1841	2433	1118	2182	840.2	2124	962.2	2098	1052	2194	997	2297	614.5	901	
Daiichi-Sankyo	F023012	112.5	331.1	98.7	608.9	108.8	477.8	40	305.9	40	90.78	40	77.37	40	88.64	40	40	40	208.3	
Daiichi-Sankyo	F035951	1017	1481	1411	3959	567.8	2868	477.4	3125	266.1	2551	294.9	2185	263.7	2013	84.83	346.3	446.7	1176	
Daiichi-Sankyo	F037838	1019	3377	1679	11237	923	6023	316.2	7233	40	4515	63.04	3963	74.83	5126	40	2607	377.9	2613	
Daiichi-Sankyo	F039982	109.3	683.6	84.11	989.3	62	729	40	1074	40	847.1	40	765.9	40	903.2	40	314.6	40	224.2	
Daiichi-Sankyo	F050041	1266	3612	1432	8617	801.2	7305	132.1	3879	69.46	3082	99.78	3295	81.74	2751	40	1622	233.5	1891	
Daiichi-Sankyo	F050351	1256	1810	2428	3743	1859	3312	1178	7683	274.6	5953	369.9	4152	287.1	7101	86.32	3242	564.1	1008	
Daiichi-Sankyo	F052203	355.6	962.7	302.6	1736	155.8	1429	51.74	1033	40	167.4	40	236.9	40	99.02	40	61.24	49.67	351.6	
Daiichi-Sankyo	F055336	378	415.1	193	294.7	72.74	147.2	40	110.8	40	58.66	40	77.42	40	76.7	40	53.52	136.9	112.4	
Daiichi-Sankyo	F072023	132.4	282.2	125.6	716.8	135.2	680	182.2	1291	106.5	996.4	99.15	776.2	114	752.4	94.93	440	40	141.5	
Daiichi-Sankyo	F072088	3867	7878	4132	10557	1642	6290	452.9	4367	185.3	4051	196.8	3088	152.3	3110	96.82	1215	1236	2672	
Daiichi-Sankyo	F075080	212.9	323.1	405	869.1	366.4	823.2	105.9	893.9	40	571.8	68.69	549	86.41	714.3	86.83	649.7	74.39	173.5	
Daiichi-Sankyo	F078713	176.6	3116	80.49	7233	104.9	4320	40	2825	40	1542	40	1955	40	1412	40	523.1	40	1871	
Daiichi-Sankyo	F079661	1324	1517	2064	3219	1572	2580	1132	2340	684.7	1968	645.6	1812	688.4	1916	561.3	1396	428	501.5	
Daiichi-Sankyo	F079996	1367	2868	1931	7390	992.5	3971	580.9	3321	255.9	2435	210.1	2326	302.7	2420	40	852.9	480.8	1032	
Daiichi-Sankyo	F082525	321	3228	335.3	8720	262.4	5768	104.5	3829	69.19	4316	64.84	4329	82.05	4476	40	4648	108	1582	
Meiji Seika Pharma	S0015	392.5	660.5	402.1	917.9	189.2	650.4	129.6	657.4	99.7	427.1	109.3	749	99.49	455.1	40	282.3	154.1	257.2	
Meiji Seika Pharma	S0019	780.4	869.6	450.8	556.1	113.4	210.5	57.81	67.17	40	40	40	40	40	40	40	40	64.4	80.81	
Meiji Seika Pharma	S0049	977.3	1630	1774	4021	2090	3232	1436	3812	1158	3332	1881	4932	909.5	3696	781.9	2041	578.2	1247	
Meiji Seika Pharma	S0066	1929	2729	3215	3851	3151	3156	1145	2280	521.3	959.5	610.1	1167	771.4	1372	225.9	447	581.8	750.8	
Meiji Seika Pharma	S0074	1323	1823	1240	2296	696.5	1489	401.4	1976	194.4	1298	287.5	1894	297.6	1834	207.2	1441	521.9	921.8	
Meiji Seika Pharma	S0087	1616	1958	3224	4959	2302	2523	2082	2947	1380	2736	1771	2362	1190	2548	415.3	862.7	974.5	1158	
Meiji Seika Pharma	S0094	905.1	796.8	709.2	1099	360.5	752.7	254	877.1	116.8	618.4	148.6	1027	105.1	791.4	59.41	500.7	148.8	309.6	
Meiji Seika Pharma	S0112	870.4	1112	870.5	1641	477.1	1016	381.8	2202	260.8	2247	244.9	2763	295.7	2372	133	2276	190	345.3	
Meiji Seika Pharma	S0119	2489	1947	2674	2274	1599	1661	1236	1171	563.7	635.8	678.1	1021	524.2	616.7	170.6	198.3	792.2	672.2	
Meiji Seika Pharma	S0135	1688	1357	1599	1719	934.8	1110	449.8	872.5	136.3	672.9	153	320.5	132.2	784	89.58	349.8	506.6	440.6	
Meiji Seika Pharma	S0140	1821	2105	521.5	601.2	166.9	303.4	746.6	1072	832.9	991.8	1005	1702	573.9	683.4	588.9	712.9	134	132.6	
Meiji Seika Pharma	S0162	182	563.2	701.1	2746	655.3	2111	157.9	943.9	91.88	425.6	120.5	496.3	83.47	309.9	117.8	321.6	40	392.6	
Meiji Seika Pharma	S0171	1275	1624	1341	1785	1063	1649	293.3	501.2	142.5	428.1	195.5	482.4	297.5	453.4	124.3	226.8	317.8	325.6	
Meiji Seika Pharma	S0185	771.1	1491	599	1602	315.3	1129	179.6	979.1	78.25	700.4	96.23	415.2	93.45	759.6	83.9	329.2	233.6	456.6	
Meiji Seika Pharma	S0194	957.3	1239	1313	1852	965.7	1294	1248	2217	563.5	1291	803.7	2041	557.6	1409	478.5	1174	213.2	185.9	
Meiji Seika Pharma	S0197	172.9	260.7	186.1	360.6	164	307.6	346.8	1205	266.9	1283	179.9	1015	315.4	1412	169.9	741.9	105.7	248.5	
Meiji Seika Pharma	S0219	566.2	1117	300.9	620	210	910.9	63.98	527.4	40	248.5	40	282.2	40	246	40	81.44	115.3	248.7	
Meiji Seika Pharma	S0221	2101	3288	3443	4551	2230	5230	1100	2212	486.2	1195	635.8	698.7	328.2	698	114.1	321.3	586.8	774.1	
Meiji Seika Pharma	S0235	1280	1841	1535	2532	795.6	1442	257.9	342	40	70.03	40	86.63	40	77.32	40	40.03	184.7	213.2	
Meiji Seika Pharma	S0261	567.9	779.6	310	895.6	216.9	644.8	72.23	985.1	83.37	540.1	92.31	985.8	63.8	564.6	82.11	410.1	85.38	227.8	

Table S3. Cohort comparison summary

Vaccine strain	Vaccine manufacturers	Average age	% male	Average times of vaccination	Average times of infection
XEC	Daiichi Sankyo	65.6	27.3	6.9	0.4
XEC	Meiji Seika Pharma	44.4	45.0	6.7	0.8
LP.8.1	Pfizer/BioNTech	33.8	37.9	5.2	0.8
LP.8.1	Novavax	44.5	45.0	6.4	0.5



Supplemental figure. Antigenic cartography

Antigenic map based on the serum neutralization data from the neutralization assay. Virus positions are represented by closed circles. Both axes represent antigenic distance with one antigenic distance unit (AU) in any direction corresponding to a 2-fold change in NT50.

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Supplementary References

1. Ozono S, Zhang Y, Ode H, et al. SARS-CoV-2 D614G spike mutation increases entry efficiency with enhanced ACE2-binding affinity. *Nat Commun* 2021; **12**(1): 848.
2. Ferreira I, Kemp SA, Datir R, et al. SARS-CoV-2 B.1.617 Mutations L452R and E484Q Are Not Synergistic for Antibody Evasion. *J Infect Dis* 2021; **224**(6): 989-94.
3. Motozono C, Toyoda M, Zahradnik J, et al. SARS-CoV-2 spike L452R variant evades cellular immunity and increases infectivity. *Cell Host Microbe* 2021; **29**(7): 1124-36 e11.
4. Kimura I, Yamasoba D, Tamura T, et al. Virological characteristics of the SARS-CoV-2 Omicron BA.2 subvariants, including BA.4 and BA.5. *Cell* 2022; **185**(21): 3992-4007 e16.
5. Uriu K, Ito J, Zahradnik J, et al. Enhanced transmissibility, infectivity, and immune resistance of the SARS-CoV-2 omicron XBB.1.5 variant. *Lancet Infect Dis* 2023; **23**(3): 280-1.
6. Kaku Y, Okumura K, Padilla-Blanco M, et al. Virological characteristics of the SARS-CoV-2 JN.1 variant. *Lancet Infect Dis* 2024; **24**(2): e82.
7. Kaku Y, Okumura K, Kawakubo S, et al. Virological characteristics of the SARS-CoV-2 XEC variant. *Lancet Infect Dis* 2024; **24**(12): e736.
8. Chen L, Kaku Y, Okumura K, et al. Virological characteristics of the SARS-CoV-2 LP.8.1 variant. *Lancet Infect Dis* 2025; **25**(4): e193.
9. Uriu K, Okumura K, Uwamino Y, et al. Virological characteristics of the SARS-CoV-2 NB.1.8.1 variant. *Lancet Infect Dis* 2025; **25**(8): e443.
10. Kaku Y, Fujiwara M, Uriu K, et al. Humoral immunity induced by LP.8.1 monovalent vaccines against a broad range of SARS-CoV-2 variants including XEC, NB.1.8.1, XFG, and BA.3.2. *bioRxiv* 2025: 2025.11.18.689152.
11. Ozono S, Zhang Y, Tobiume M, Kishigami S, Tokunaga K. Super-rapid quantitation of the production of HIV-1 harboring a luminescent peptide tag. *J Biol Chem* 2020; **295**(37): 13023-30.
12. Garcia-Beltran WF, St Denis KJ, Hoelzemer A, et al. mRNA-based COVID-19 vaccine boosters induce neutralizing immunity against SARS-CoV-2 Omicron variant. *Cell* 2022; **185**(3): 457-66 e4.
13. Smith DJ, Lapedes AS, de Jong JC, et al. Mapping the antigenic and genetic evolution of influenza virus. *Science* 2004; **305**(5682): 371-6.