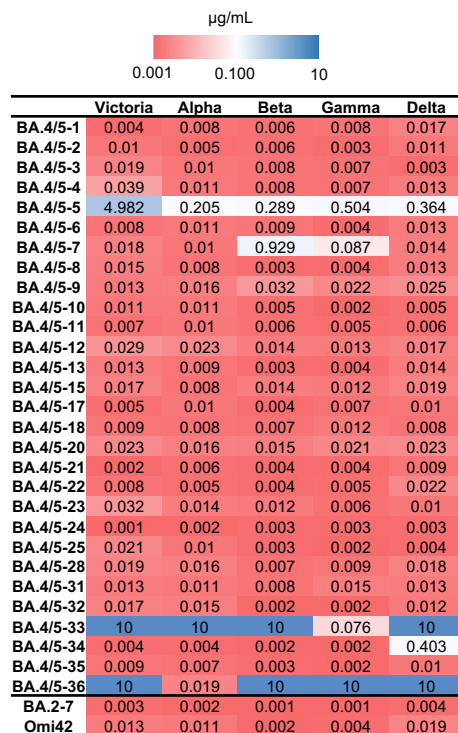
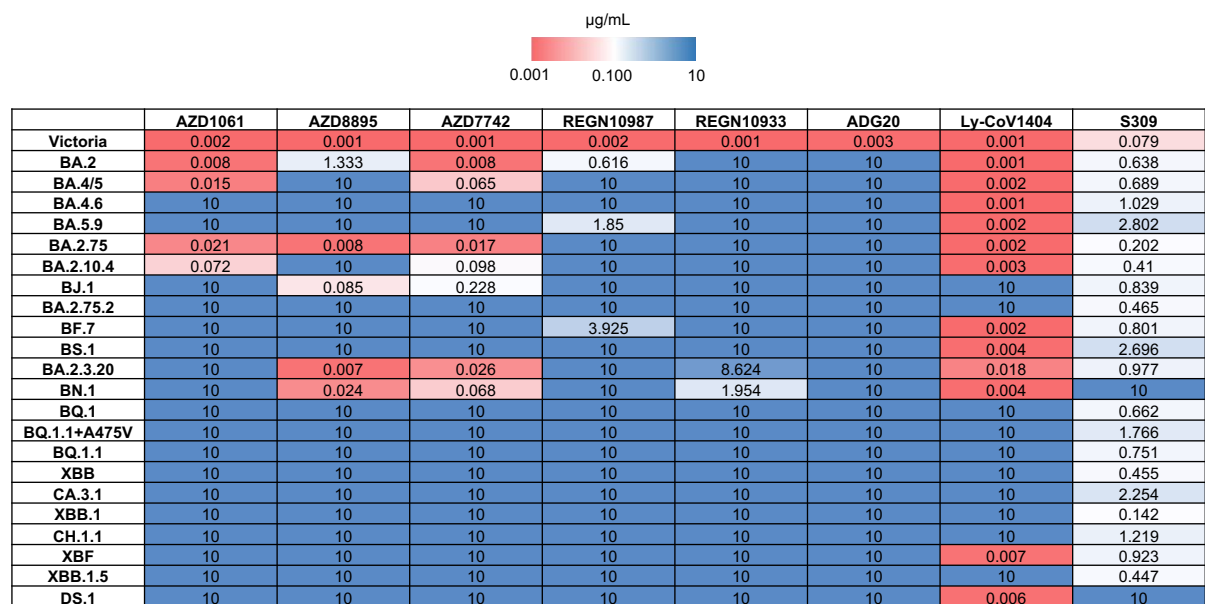


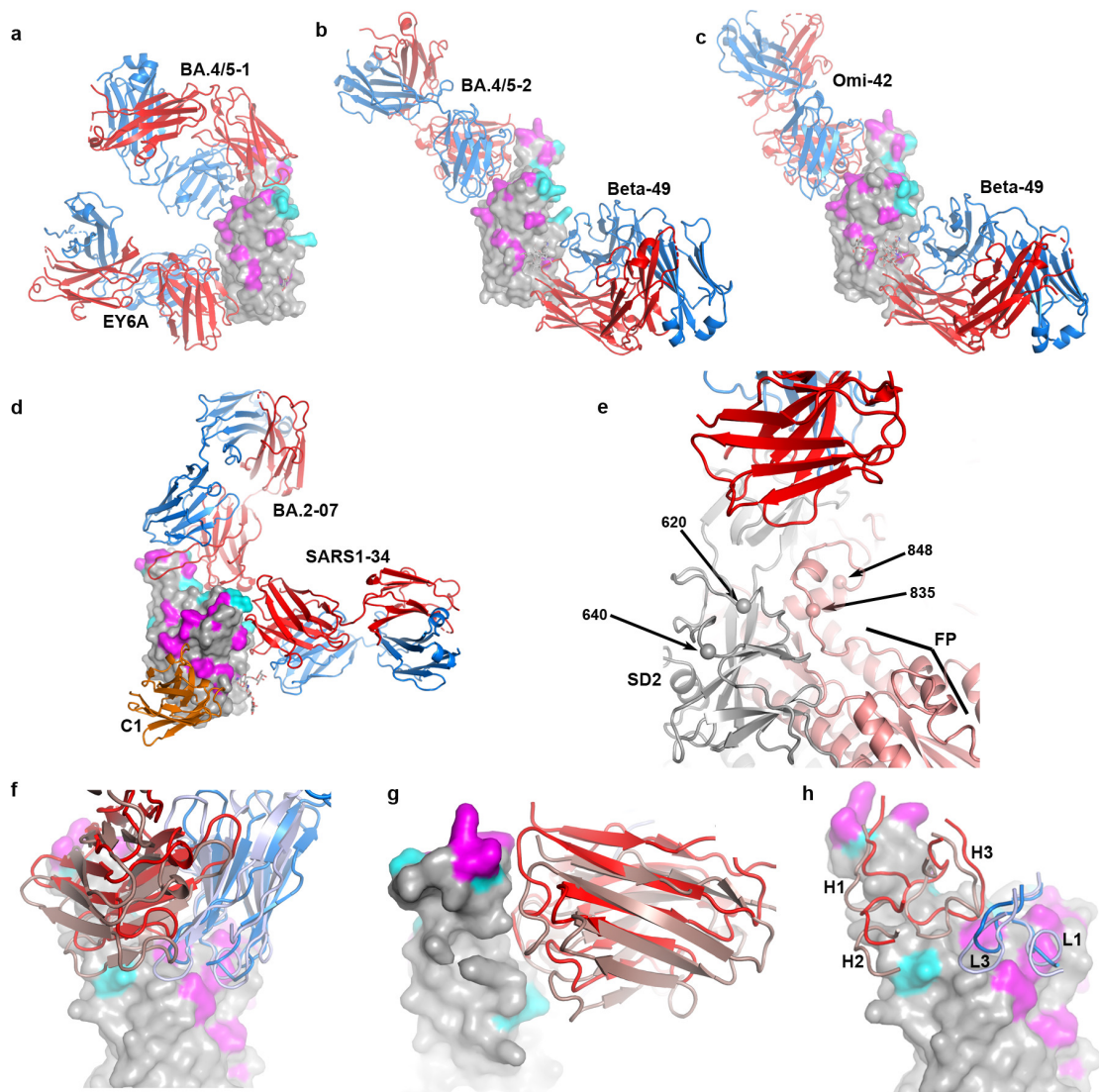
a



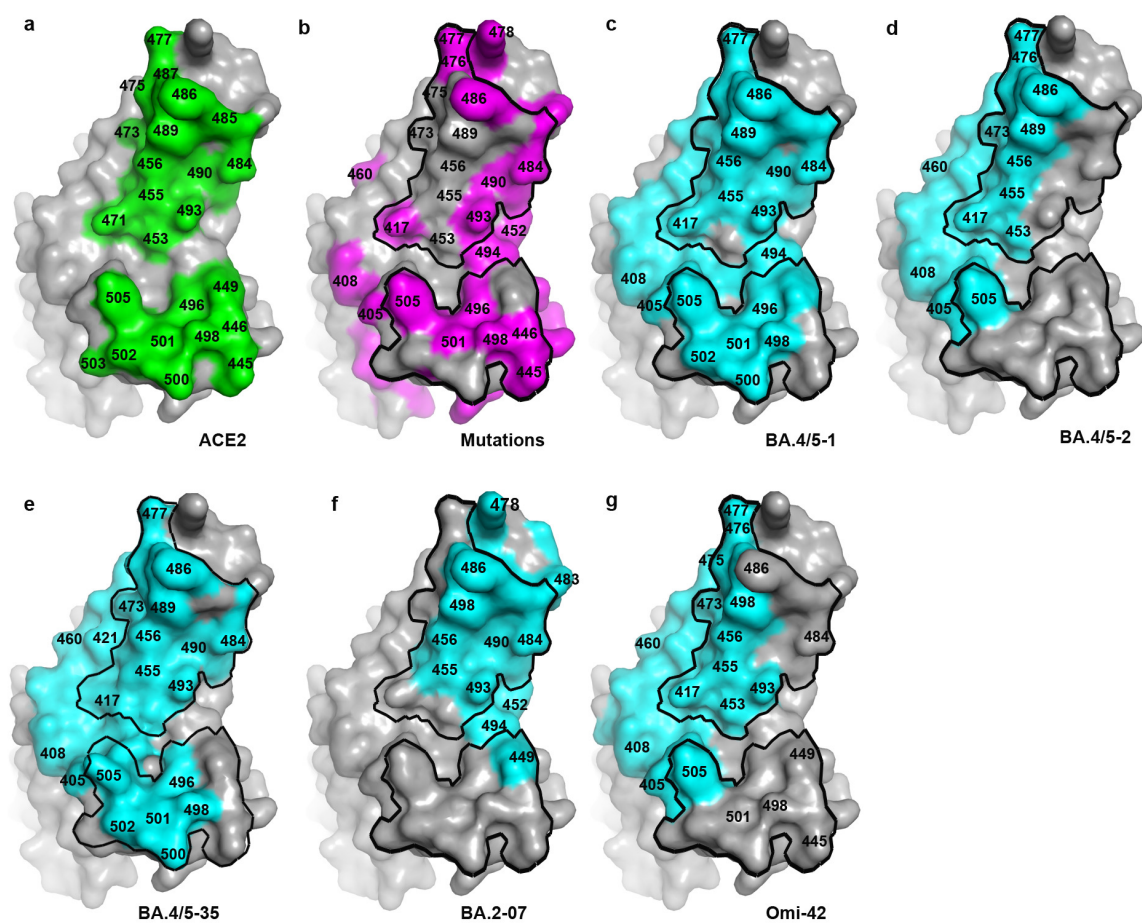
b



Extended Data Fig. 1



Extended Data Fig. 2



Extended Data Fig. 3

Extended Data Table 1 Ig variable gene usage for BA.4/5 mAb

Ab id.	Protein-Specific	Heavy Chain					Light Chain		
		V-REGION Nb of AA changes	V-GENE and allele	J-GENE and allele	D-GENE and allele	Light Chain	V-REGION Nb of AA changes	V-GENE and allele	J-GENE and allele
BA.4/5-1	RBD	5	4-39*01 F	4*02 F	1-26*01 F	K	7	1-NL1*01 F	2*01 F
BA.4/5-2	RBD	14	3-30*03 F, or 3-30*18 F or 3-30-5*01 F	6*02 F	2-15*01 F	K	5	3-11*01 F	3*01 F
BA.4/5-3	RBD	16	4-61*02 F, or 4-61*11	4*02 F	1-26*01 F	K	9	1-5*01 F	1*01 F
BA.4/5-4	RBD	11	1-3*01 F, or 1-3*04	6*03 F	6-25*01 F	K	5	1-5*01 F	4*01 F
BA.4/5-5	Non-RBD/NTD	10	4-59*01 F, or 4-61*01 F	4*02 F	1-26*01 F	λ	6	2-23*02 F	2*01 F, or 3*01 F
BA.4/5-6	RBD	10	3-53*04 F	4*02 F	4-17*01 F	K	9	3-20*01 F	2*02
BA.4/5-7	RBD	14	3-53*02 F	4*02 F	4-17*01 F	K	5	3-15*01 F	1*01 F
BA.4/5-8	RBD	6	3-66*02 F	6*02 F	1-26*01 F	K	4	1-33*01 F, or 1D-33*01 F	2*01 F
BA.4/5-9	RBD	13	1-46*01 F, or 1-46*02 F or 1-46*03 F	4*02 F	4-23*01 ORF	K	6	3-11*01 F	2*03
BA.4/5-10	RBD	2	3-66*02 F	6*02 F	1-26*01 F	K	5	1-33*01 F, or 1D-33*01 F	2*01 F
BA.4/5-11	RBD	6	3-33*01 F, or 3-33*03 F or 3-33*06 F	3*02 F	3-22*01 F	K	3	1-39*01 F, or 1D-39*01 F	2*01 F
BA.4/5-12	RBD	9	3-30*03 F, or, 3-30*18 F, or 3-30-5*01 F	6*02 F	3-9*01 F	K	8	1-33*01 F, or 1D-33*01 F	5*01 F
BA.4/5-13	RBD	9	1-69*01 F, or 1-69D*01 F	6*02 F	5-18*01 F	λ	14	1-33*01 F, or 1D-33*01 F	3*01 F
BA.4/5-15	RBD	6	3-9*01 F	6*02 F	3-9*01 F	λ	9	1-44*01 F	1*01 F
BA.4/5-17	RBD	8	3-53*04 F	6*02 F	6-19*01 F	λ	4	1-51*01 F	1*01 F
BA.4/5-18	RBD	11	1-69*01 F, or 1-69D*01 F	6*02 F	5-18*01 F	K	18	1-33*01 F, or 1D-33*01 F	3*01 F
BA.4/5-20	RBD	11	3-9*01 F	6*02 F	3-9*01 F	λ	8	1-44*01 F	1*01 F
BA.4/5-21	RBD	11	3-9*01 F	4*02 F	3-22*01 F	K	12	1-9*01 F	4*01 F
BA.4/5-22	RBD	13	1-69*01 F, or 1-69D*01 F	4*02 F	5-12*01 F	K	11	2-30*01 F	1*01 F
BA.4/5-23	RBD	15	3-53*01 F	4*02 F	4-17*01 F	K	12	3-20*01 F	1*01 F
BA.4/5-24	RBD	9	3-9*01 F	5*02 F	3-22*01 F	K	17	1-9*01 F	3*01 F, or 4*01 F
BA.4/5-25	RBD	16	1-69*09 F	4*02 F	5-18*01 F	K	9	1-5*01 F	2*02
BA.4/5-28	RBD	10	3-66*01 F, or 3-66*04 F	6*02 F	1-1*01 F	λ	16	3-21*04 F	2*01 F, or 3*01 F or 3*02 F
BA.4/5-31	RBD	6	4-39*01 F	4*02 F	1-26*01 F	K	15	1-NL1*01 F	2*01 F
BA.4/5-32	RBD	12	3-66*02 F	3*01 F	3-10*02 F	λ	10	3-21*02 F	1*01 F
BA.4/5-33	NTD	13	3-23*04 F	4*02 F	5-18*01 F	K	5	3-15*01 F	2*01 F
BA.4/5-34	RBD	12	1-69*01 F, or 1-69D*01 F	4*02 F	5-12*01 F	K	8	2-30*01 F	1*01 F
BA.4/5-35	RBD	12	3-66*01 F, or 3-66*04 F	4*02 F	1-26*01 F	K	6	3-15*01 F	2*01 F
BA.4/5-36	NTD	13	4-4*02 F	3*02 F	2-21*01 F	K	16	1-5*01 F	1*01 F

Extended Data Table 2 Mutations in RBD for variants shown in Fig. 2a. Indicated mutations are those additional mutations relative to the sequence of BA.2

Variant			Mutations in RBD area				
BA.2	G339D		T376A D405N R408S			E484A	Q493R
Victoria							
BA.1	G339D			G446S		E484A	Q493R G496S
BA.1.1	G339D R346K			G446S		E484A	Q493R G496S
BA.2.12.1	G339D		T376A D405N R408S		L452Q	E484A	Q493R
BA.4/5	G339D		T376A D405N R408S		L452R	E484A F486V	R493Q
BA.4.6	G339D R346T		T376A D405N R408S		L452R	E484A F486V	R493Q
BA.5.9	G339D R346I		T376A D405N R408S		L452R	E484A F486V	R493Q
BA.2.75	G339H		T376A D405N R408S	G446S	N460K	E484A	R493Q
BA.2.10.4	G339D		T376A D405N R408S	G446S		E484A F486P	R493Q S494P
BJ.1	G339H R346T L368I		T376A D405N R408S	V445P G446S		V483A E484A	F490V R493Q
BA.2.75.2	G339H R346T		T376A D405N R408S	G446S	N460K	E484A F486S	R493Q
BF.7	G339D R346T		T376A D405N R408S		L452R	E484A F486V	R493Q
BS.1	G339D R346T		T376A D405N R408S		L452R N460K	G476S E484A	Q493R
BA.2.3.20	G339D		T376A D405N R408S K444R		N450D L452M N460K	E484R	R493Q
BN.1	G339H R346T K356T		T376A D405N R408S	G446S	N460K	E484A F490S	R493Q
BQ.1	G339D		T376A D405N R408S K444T		L452R N460K	E484A F486V	R493Q
BQ.1.1 +A475V	G339D R346T		T376A D405N R408S K444T		L452R N460K A475V	E484A F486V	R493Q
BQ.1.1	G339D R346T		T376A D405N R408S K444T		L452R N460K	E484A F486V	R493Q
XBB	G339H R346T L368I		T376A D405N R408S	V445P G446S	N460K	E484A F486S F490S	R493Q
CA.3.1	G339H R346T		T376A D405N R408S K444M	G446S	L452R N460K	E484A F486S	R493Q
XBB.1	G339H R346T L368I		T376A D405N R408S	V445P G446S	N460K	E484A F486S F490S	R493Q
CH.1.1	G339H R346T		T376A D405N R408S K444T	G446S	L452R N460K	E484A F486S	R493Q
XBF	G339H R346T		T376A D405N R408S	G446S	N460K	E484A F486P F490S	R493Q
XBB.1.5	G339H R346T L368I		T376A D405N R408S	V445P G446S	N460K	E484A F486P F490S	R493Q
DS.1	G339H R346T K356T R403K		T376A D405N R408S	G446S	N460K	E484A F486S F490S	R493Q

Extended Data Table 3. Data collection, structure determination and refinement statistics

Method	X-ray Crystallography				Cryo-EM		
Structure	Delta-RBD/BA.4/5-1/EY6A	Delta-RBD/BA.4/5-2/Beta-49	Delta-RBD/BA.4/5-35	Delta-RBD/Omi-42/Beta-49	BA.4-spike/BA.4/5-5	BA.2.12.1-Spike/BA.2-07	Delta-RBD/BA.2-07/SARS 1-34/C1
PDB/EMBD ID	8CBD	8CBE	8CMA	8CBF	8CIN	8CIM	8CII
Data collection							
Space group	C2	P2 ₁ 2 ₁ 2	C2	P2 ₁ 2 ₁ 2	Voltage (kV)	300	300
Cell dimensions					Frames (EER fractions)	50	50
a, b, c (Å)	242.0, 139.4, 168.5	179.9, 147.0, 52.2	195.8, 85.1, 57.0	177.0, 144.3, 49.7	Dose rate (e ⁻ /Å ² /s)	11.7	9.1
a, b, γ (°)	90, 115.6, 90	90, 90, 90	90, 102.0, 90	90, 90, 90	Total dose (e ⁻ /Å ²)	50	50
Resolution (Å)	75–3.52 (3.58–3.52) ^a	60–3.16 (3.21–3.16)	48–3.29 (3.35–3.29)	75–2.33 (2.37–2.33)	Calibrated pixel size (Å ²)	0.7303	0.7303
R _{merge}	0.325 (---)	0.345 (---)	0.298 (---)	0.300 (---)	Defocus (μm)	0.8-2.6	0.8-2.6
R _{pim}	0.133 (1.192)	0.098 (0.994)	0.121 (1.270)	0.086 (1.760)	Movies	10,383	10,619
I/s(I)	4.9 (0.4)	6.1 (0.5)	5.6 (0.5)	7.1 (0.4)	Particles (final)	108,365	61,491
CC _{1/2}	0.984 (0.351)	0.991 (0.322)	0.982 (0.340)	0.998 (0.332)	Symmetry	C3	C3
Completeness (%)	99.7 (98.4)	100 (99.2)	98.9 (94.6)	99.8 (93.3)	Map resolution (Å)	2.7	3.0
Redundancy	7.1 (6.7)	13.3 (13.2)	7.0 (6.8)	13.0 (8.7)	Sharpening B-factor (Å ²)	70.2	65.6
Refinement							
Resolution (Å)	75–3.52	57–3.16	48–3.29	72–2.33	Resolution (Å)	2.7	2.9
No. reflections	59185/3023	23351/1206	13161/681	51927/2733	No. protein atoms	35187	29925
R _{work} / R _{free}	0.219/0.267	0.227/0.268	0.231/0.268	0.215/0.255	B factors (Å ²)	132	72
No. atoms					r.m.s. deviations		
Protein	24090	8087	4718	8033	Bond lengths (Å)	0.006	0.004
Ligand/ion/water	14	49	14	342	Bond angles (°)	0.6	0.5
B factors (Å ²)					Clash score	5.2	4.5
Protein	169	108	125	62	Ramachandran outlier (%)	0	0
Ligand/ion/water	207	123	192	64	Rotamer outlier (%)	1.45	0.8
r.m.s. deviations					d FSC model (0.5)	3.0	3.2
Bond lengths (Å)	0.003	0.002	0.002	0.004	CC (mask)	0.87	0.81
Bond angles (°)	0.5	0.5	0.4	0.6			