Figure S1. BA.3.2 lineage tree

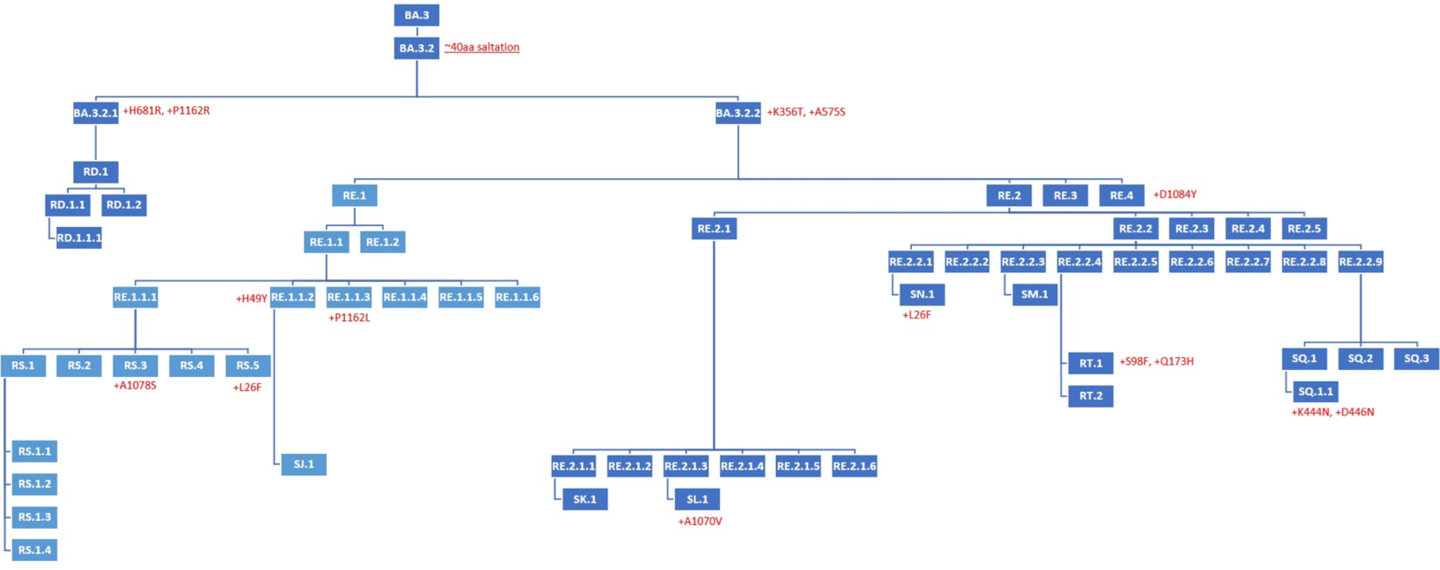


Figure S2. JN.1 mAb -4 and -5 ELISA

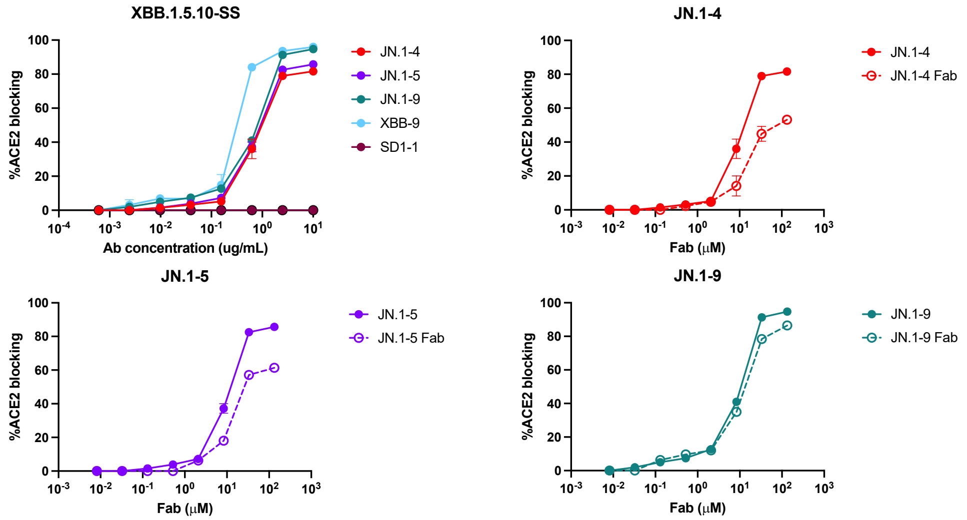
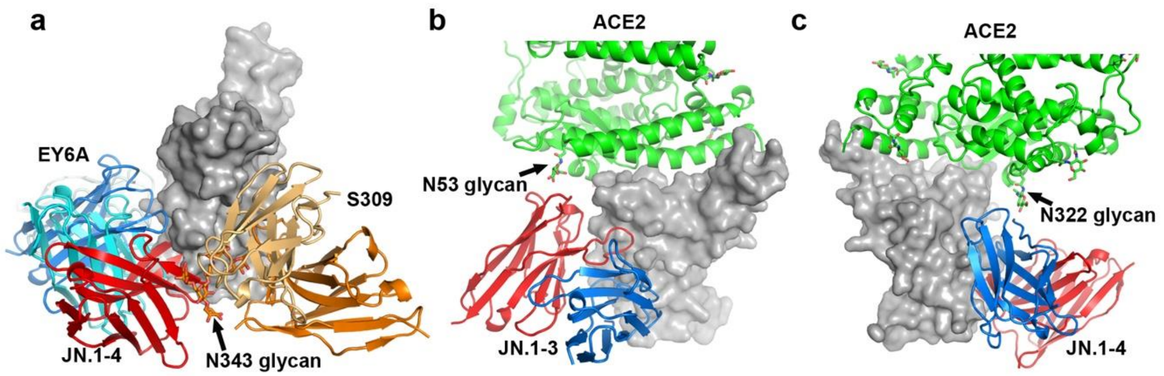
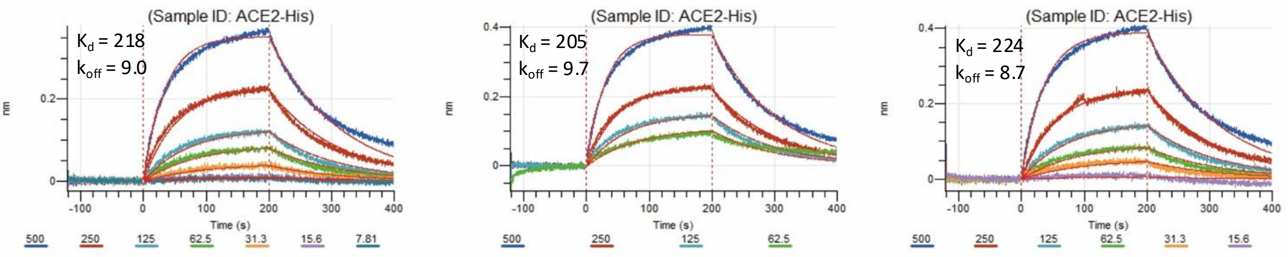


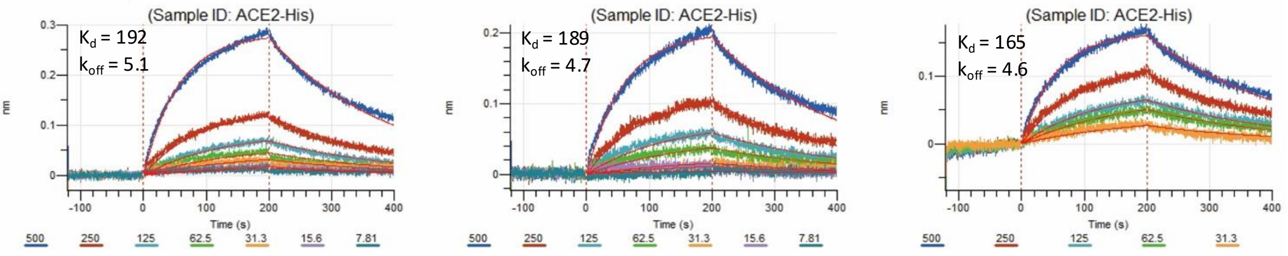
Figure S3.



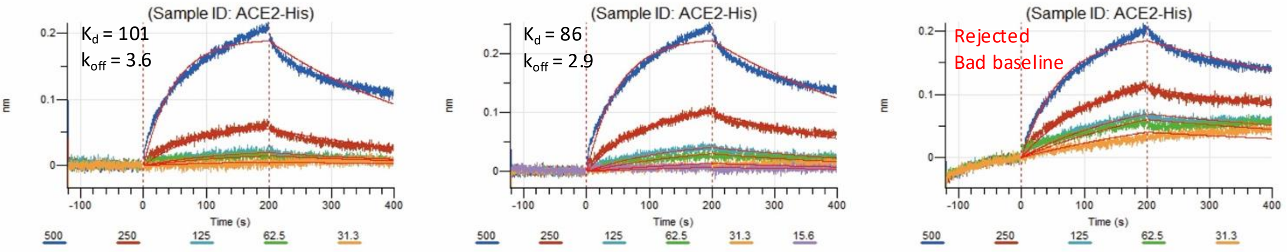
RBD-WH (Measurement 1 to 3, from left to the right)



RBD-BA.1 (Measurement 1 to 3, from left to the right)



RBD-KP.3 (Measurement 1 to 3, from left to the right)



RBD-BA3.2.2 (Measurement 1 to 3, from left to the right)

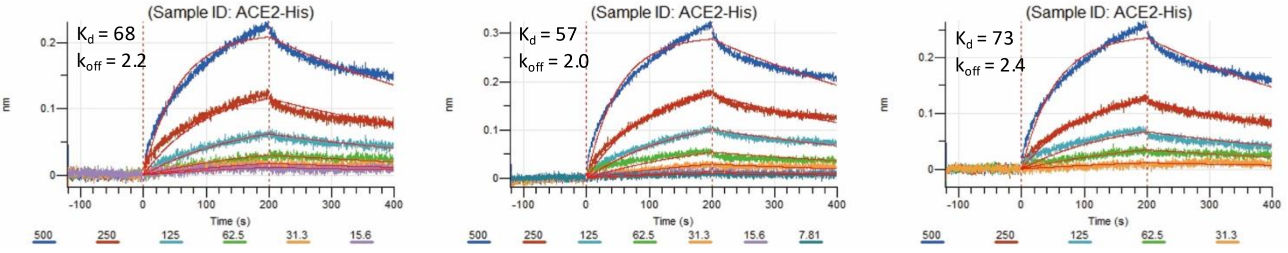


Figure S4. BLI kinetic data for RBD/ACE2 interactions. K_{off} units are E-03/s.

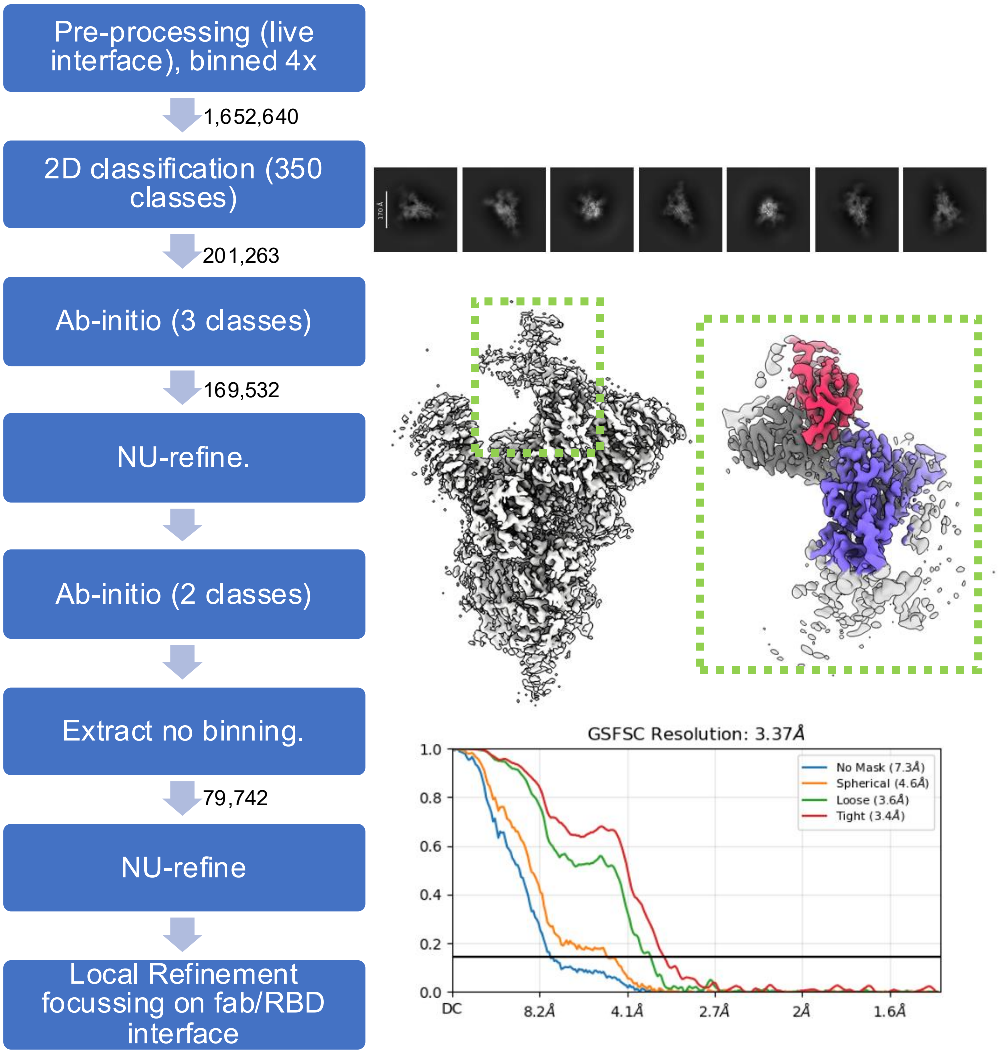


Figure S5. Workflow for processing JN1-9 with KP.3 complex. Numbers of particles after each reduction are written next to processing arrows.

Pre-processing (live interface), binned 4x

1,640,984

2D classification (150 classes)

560,206

Heterogeneous refinement (3 classes from Ab-initio on subset of 200,000)

435,336

NU-refine.

Extract 2-fold binned

NU-refinement

3D classification

116,770

Extract unbinned

Local refinement

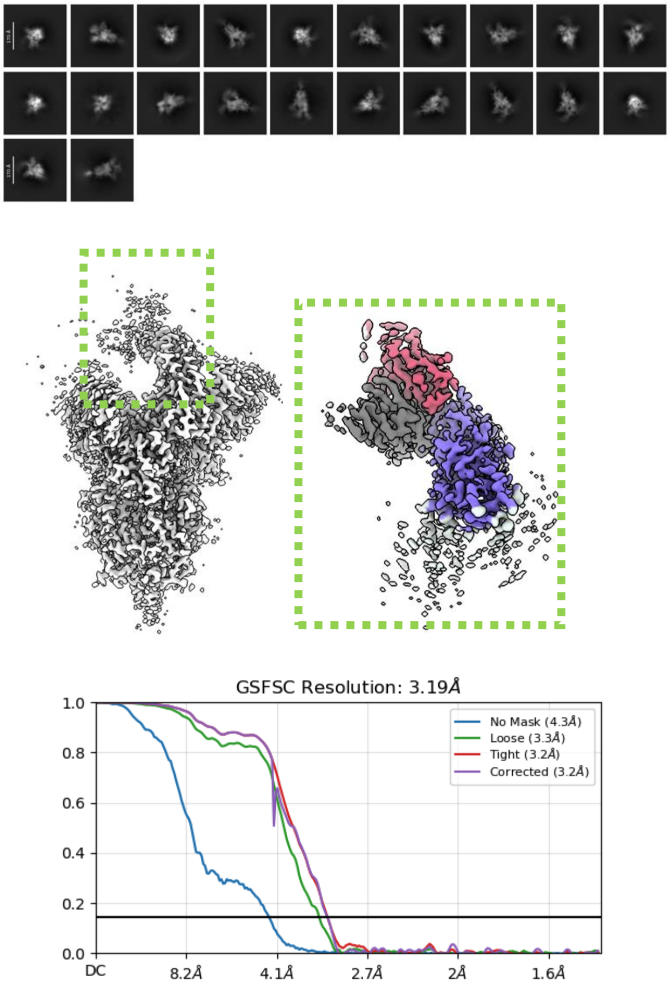


Figure S6. Workflow for processing JN1-10 with KP.3 complex. Numbers of particles after each reduction are written next to processing arrows.

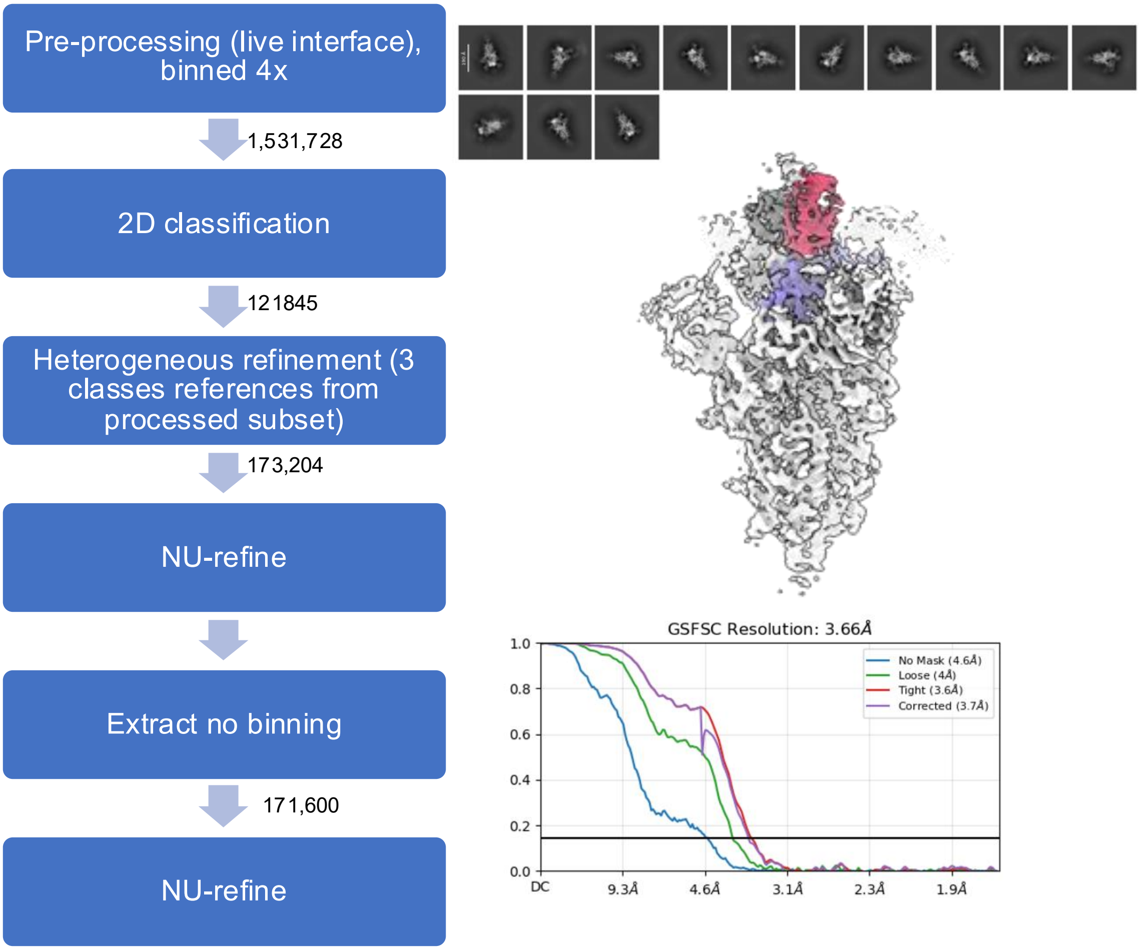


Figure S7. Workflow for processing JN1-3 with KP.3 complex. Numbers of particles after each reduction are written next to processing arrows.

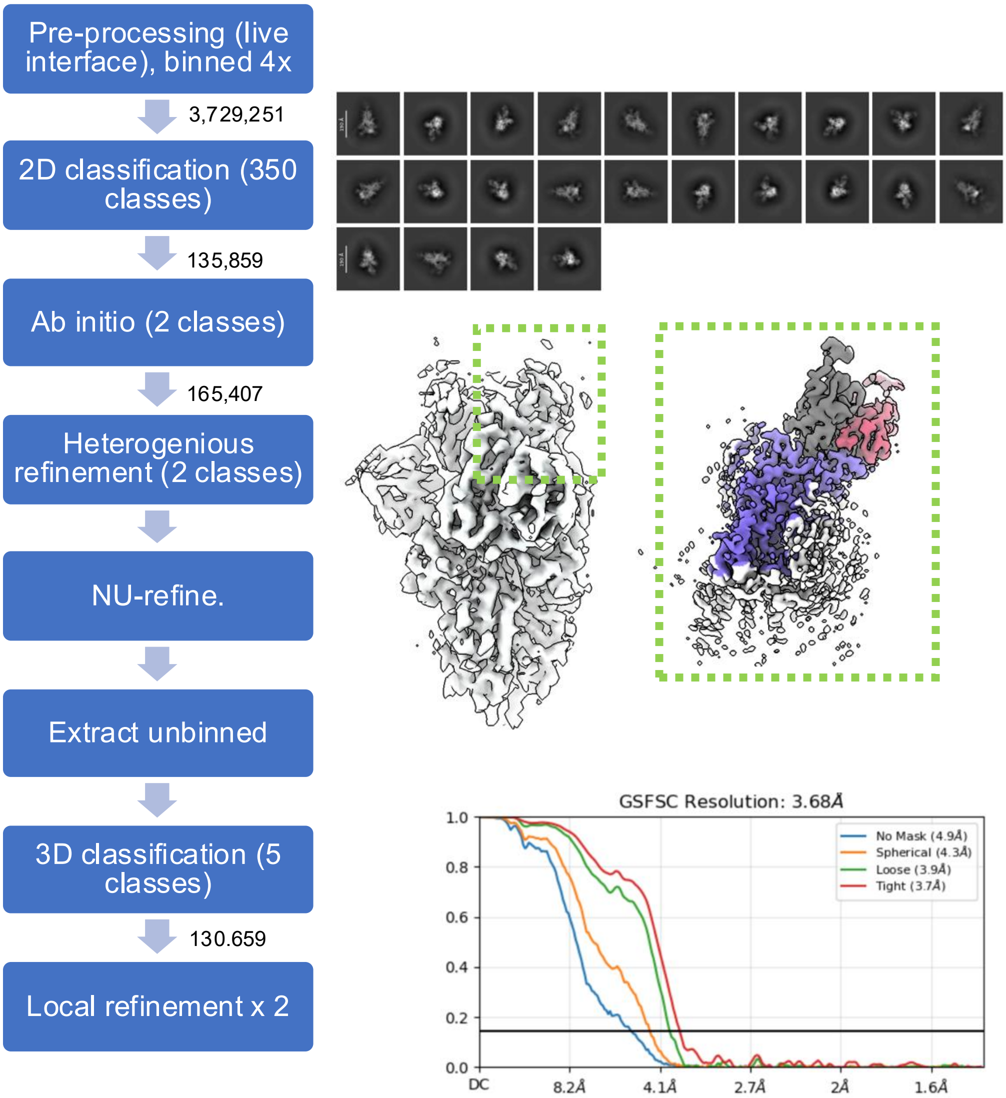


Figure S8. Workflow for processing JN1-6 with KP.3 complex. Numbers of particles after each reduction are written next to processing arrows.

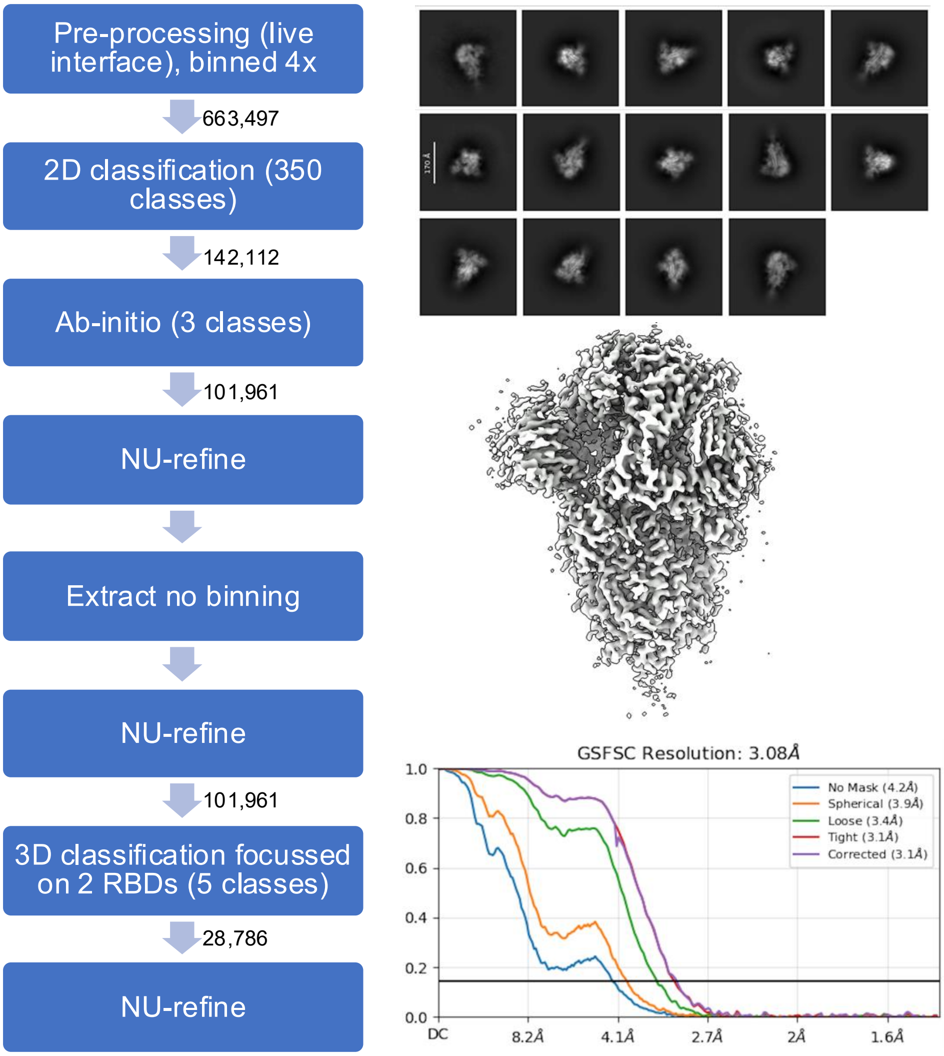


Figure S9. Workflow for cryoEM processing of BA.3.2.2 Spike. Numbers of particles after each reduction are written next to processing arrows. The 2D class averages selected for final processing, final volume and gold standard FSC plot are shown on the right.

Table S1. Patient sample information for Sera PV NT

Participant number	Sampling date	Timepoint	Latest received vaccine
1	9/25/2024	V3+336	Unknown
2	9/27/2024	V3+1052	Unknown
3	10/02/2024	V3+1063	Unknown
4	10/07/2024	V5+370	Unknown
5	04/10/2025	V6+184	Unknown
6	04/10/2025	V6+170	JN.1
7	04/11/2025	V6+163	JN.1
8	04/11/2025	V6 +163	JN.1
9	4/24/2025	V6+191	JN.1
10	4/24/2025	V6+170	JN.1
11	4/24/2025	V6+191	Unknown
12	4/24/2025	V6+192	JN.1
13	4/25/2025	V6 + 183	JN.1
14	4/25/2025	V6+ 186	JN.1
15	4/25/2025	V3 + 1268	Unknown
16	4/25/2025	V7 + 188	JN.1
17	4/28/2025	V6+180	JN.1
18	4/28/2025	V6+205	JN.1
19	4/30/2025	V6+162	Unknown
20	05/01/2025	V3+1232	Unknown
21	05/02/2025	V4 + 892	Unknown
22	05/02/2025	V6 +178	JN.1
23	05/02/2025	V3 + 1269	Unknown
24	05/02/2025	V6 + 178	JN.1
25	05/07/2025	V8+27	JN.1
26	05/08/2025	V6+191	JN.1
27	05/08/2025	V6+143	JN.1
28	05/08/2025	V6+189	JN.1
29	05/12/2025	V6+ 195	JN.1
30	5/16/2025	V5+535	Unknown
31	5/16/2025	V6+171	JN.1
32	5/22/2025	V6+ 220	JN.1
33	10/10/2024	V5+ 342	Unknown
34	10/11/2024	V5+ 364	Unknown
35	10/17/2024	V3 + 1036	Unknown
36	11/29/2024	V6+30	JN.1
37	12/06/2024	V6+38	JN.1
38	10/31/2024	V7 + 26	JN.1
39	11/14/2024	V6+31	JN.1
40	11/21/2024	V6+30	JN.1
41	11/25/2024	V6 +26	JN.1

Table S2. Patient sample information for antibody isolation

C-COV19	Antigen use for sorting	Timepoint	Infection_status	Variant	Swab Date	Date of 1st post infection sample	Isolated antibodies
1	JN.1-SS KP.3-SS	V5+89	PCR+24	GE.1.2	17/12/2023	10/01/2024	JN.1-1 and 3
2	JN.1-SS KP.3-SS	V5+93	PCR+21	EG.5	29/12/2023	19/01/2024	JN.1-4 and 5
3	JN.1-SS KP.3-SS	V5	PCR+33	JN.1	19/01/2024	21/02/2024	JN.1-6
4	JN.1-SS KP.3-SS		PCR+35	JN.1	16/02/2024	22/03/2024	JN.1-8 to 13

Table S3. JN.1 mAb spreadsheet

Ab id.	Sample grouping	Heavy chain					Light chain				
		V-GENE and allele	V-REGION Nb of AA changes	J-GENE and allele	D-GENE and allele	CDR3-IMGT length	Light Chain	V-GENE and allele	V-REGION Nb of AA changes	J-GENE and allele	CDR3-IMGT length
JN.1-1	GE.1.2	5-51*01 F	5	4*02 F	4-17*01 F	8	K	3-15*01 F	13	1*01 F	10
JN.1-3	GE.1.2	5-51*01 F	8	4*02 F	4-17*01 F	8	K	3-15*01 F	11	1*01 F	10
JN.1-4	EG.5	4-61*01 F	21	4*02 F	3-3*01 F	6	L	6-57*03 F	14	2*01 F, or 3*01 F	9
JN.1-5	EG.5	4-59*01 F, or 4-59*02 F or 4-59*12 (F) or 4-61*12 F	44	4*02 F	3-3*01 F	7	L	6-57*03 F	19	2*01 F, or 3*01 F	9
JN.1-6	JN.1	3-49*04 F	5	3*02 F	3-10*01 F	10	L	3-1*01 F	6	1*01 F	9
JN.1-8	JN.1	4-30-4*09 F, or 4-31*03 F	7	1*01 F	5-12*01 F	7	L	2-14*03 F	4	2*01 F, or 3*01 F	20
JN.1-9	JN.1	4-30-2*07 F, or 4-30-4*01 F	9	4*02 F	3-3*01 F	13	L	1-40*02 F	1	2*01 F, or 3*01 F	12
JN.1-10	JN.1	4-30-2*07 F, or 4-30-4*01 F	8	3*02 F	3-3*01 F	7	L	1-40*01 F, or 1-40*02 F	7	2*01 F, or 3*01 F or 3*02 F	11
JN.1-11	JN.1	4-30-4*09 F, or 4-31*03 F	15	4*02 F	3-16*01 F	13	L	1-40*01 F	13	2*01 F, or 3*01 F	11
JN.1-12	JN.1	4-30-4*09 F, or 4-31*03 F	11	5*02 F	6-13*01 F	16	L	1-40*02 F	6	2*01 F, or 3*01 F	12
JN.1-13	JN.1	4-30-4*09 F, or 4-31*03 F	8	4*02 F	2-8*01 F	13	L	2-14*03 F	6	2*01 F, or 3*01 F	10

Table S4. JN.1 mAb neutralisation heat map

	Pseudo-virus IC50 (µg/ml)																		
	Victoria	**BA.2**	**BA.4**	**XBB.1.5**	**XBB.1.5.10**	**XBB.1.5.70**	**BA.2.86**	**JN.1**	**KP.2**	**LB.1**	**KP.3**	**KP.3.1.1**	**XEC**	**LP.8.1**	**LP.8.1.1**	**LP.8.1.2**	**NB.1.8.1**	**XFG**	**BA.3.2.2**
JN.1-1	0.040	0.005	0.011	0.909	0.447	0.403	0.013	0.025	10	10	0.010	0.019	0.014	10	10	10	0.010	10	0.097
JN.1-3	0.041	0.003	0.007	0.016	0.017	0.017	0.007	0.006	10	10	0.008	0.006	0.006	10	10	10	0.005	10	0.041
JN.1-4	0.081	0.074	0.152	0.082	0.206	0.314	0.028	0.050	0.015	0.056	0.062	0.046	0.102	0.035	0.067	0.070	0.107	0.042	3.891
JN.1-5	0.203	0.179	0.132	0.228	0.275	0.297	0.014	0.067	0.018	0.064	0.066	0.050	0.123	0.042	0.079	0.088	0.182	0.041	5.357
JN.1-6	10	10	0.159	0.002	0.001	0.001	0.012	0.020	0.001	0.002	0.012	0.007	0.013	0.006	0.020	10	10	10	10
JN.1-8	10	0.007	0.012	0.008	0.009	0.004	0.010	0.013	0.007	0.011	0.034	0.023	0.046	0.023	0.028	0.023	0.045	0.021	10
JN.1-9	10	0.001	0.002	0.003	0.004	0.005	0.002	0.002	0.002	0.006	0.005	0.005	0.005	0.004	0.008	0.008	0.004	0.005	10
JN.1-10	10	0.001	0.002	0.002	0.003	0.004	0.019	0.022	0.013	0.032	0.021	0.026	0.026	0.007	0.013	0.007	0.090	0.011	10
JN.1-11	10	0.001	0.001	0.001	0.003	0.004	0.001	0.002	0.002	0.004	0.003	0.006	0.007	0.003	0.004	0.003	0.008	0.002	10
JN.1-12	10	0.001	0.001	0.002	0.003	0.004	0.008	0.012	0.007	0.018	0.006	0.017	0.021	0.149	0.088	0.103	0.032	0.085	10
JN.1-13	10	0.002	0.002	0.003	0.005	0.004	0.002	0.003	0.004	0.006	0.003	0.006	0.003	0.004	0.004	0.005	0.005	0.006	10

IC50 (µg/ml)

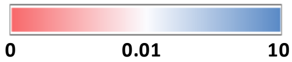


Table S5. Affinity measurement

Loading	Analyte	K_d (nM)				k_{off} (1/s)			
		1	2	3	Avg	1	2	3	Avg
RBD-WH	ACE2-His	218	205	224	216	8.95E-03	9.72E-03	8.71E-03	9.12E-03
RBD-BA.1	ACE2-His	192	189	165	182	5.07E-03	4.67E-03	4.58E-03	4.77E-03
RBD-KP.3	ACE2-His	101	85.7	–	93	3.55E-03	2.91E-03	–	3.23E-03
RBA-BA.3.2.2	ACE2-His	68.2	57.2	72.6	66	2.16E-03	2.02E-03	2.36E-03	2.18E-03

Table S6. Data collection, structure determination and refinement statistics

Method	X-ray Crystallography	Cryo-EM					
Structure	Delta-RBD/JN.1-4 Fab		KP.3-RBD/JN.1-9 Fab local refinement	KP.3-RBD/JN.1-10 Fab local refinement	KP.3-RBD/JN.1-6 Fab local refinement	KP.3-RBD/JN.1-3 Fab	BA.3.2.2 Spike
PDB/EMBD ID	9TXF		9SF7/ EMD-54815	29RE/ EMD-57321	9SF5/ EMD-54814	9SHB/ EMD-54894	29SU/ EMD-57358
Data collection							
Space group	$P2_1$	Voltage (kV)	300	300	300	300	300
Cell dimensions		Frames (EER fractions)	50	50	50	50	50
a, *b*, *c* (Å)	42.3, 182.4, 102.3	Dose rate (e^-/Å^2/s)	9.5	9.5	9.2	8.5	9.3
a, b, g (°)	90, 99.7, 90	Total dose (e^-/Å^2)	50	50	50	50	50
Resolution (Å)	68–2.32 (2.36–2.32)[a]	Calibrated pixel size (Å^2)	0.7303	0.7303	0.7303	0.729	0.7303
R_{merge}	0.179 (-–)	Defocus (µm), 0.3 increments	-0.8 to -2.6	-0.8 to -2.6	-0.8 to -2.6	-0.8 to -2.6	-0.8 to -2.6
R_{pim}	0.073 (0.898)	Movies	7,574	9,189	18,432	6,672	1,977
$I/s(I)$	8.1 (0.6)	Particles (final)	108,638	116,770	130,659	171,600	28,786
$CC_{1/2}$	0.998 (0.316)	Symmetry	C1	C1	C1	C1	C1
Completeness (%)	100 (98.3)	Map resolution (Å)	3.5	3.2	3.7	3.7	3.1
Redundancy	7.0 (7.2)	Sharpening B-factor (Å^2)	68	95	122	82	41
Refinement							
Resolution (Å)	68–2.32	Resolution (Å)	3.5	3.2	3.7	3.7	3.1
No. reflections	63,620/ 1,979	No. residues	3,291	3,320	3,388	3,412	2,999
R_{work} / R_{free}	0.215/ 0.249	*B* factors (Å^2)	53	52	62	116	83.4
No. atoms		r.m.s. deviations					
Protein	9,582	Bond lengths (Å)	0.002	0.002	0.003	0.002	0.003
Ligand/ion/water	292	Bond angles (°)	0.4	0.4	0.5	0.5	0.5
B factors (Å^2)		Clash score	5.4	6.0	6.2	5.5	2.9
Protein	68	Ramachandran outlier (%)	0	0	0	0	0
Ligand/ion/water	56	Rotamer outlier (%)	1.1	1.7	1.6	1.9	1.7
r.m.s. deviations		d FSC model (0.5, Å)	3.9	3.3	3.9	7.9	3.1
Bond lengths (Å)	0.002	CC (mask)	0.67	0.82	0.80	0.56	0.84
Bond angles (°)	0.5						