

Supplementary Materials for

**SARS-CoV-2 spike conformation determines plasma neutralizing activity elicited by  
a wide panel of human vaccines**

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*Sci. Immunol.* **7**, eadf1421 (2022)  
DOI: 10.1126/sciimmunol.adf1421

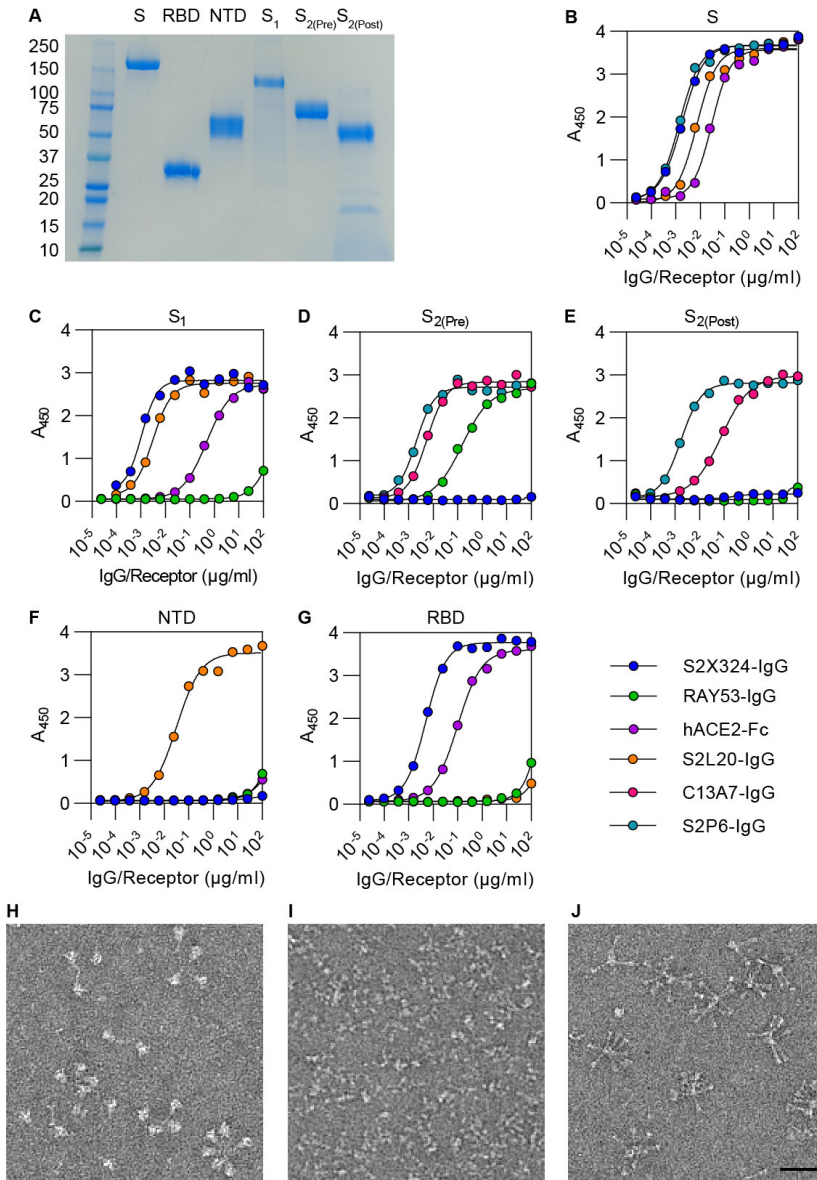
**The PDF file includes:**

Figs. S1 to S13  
Tables S1 to S9

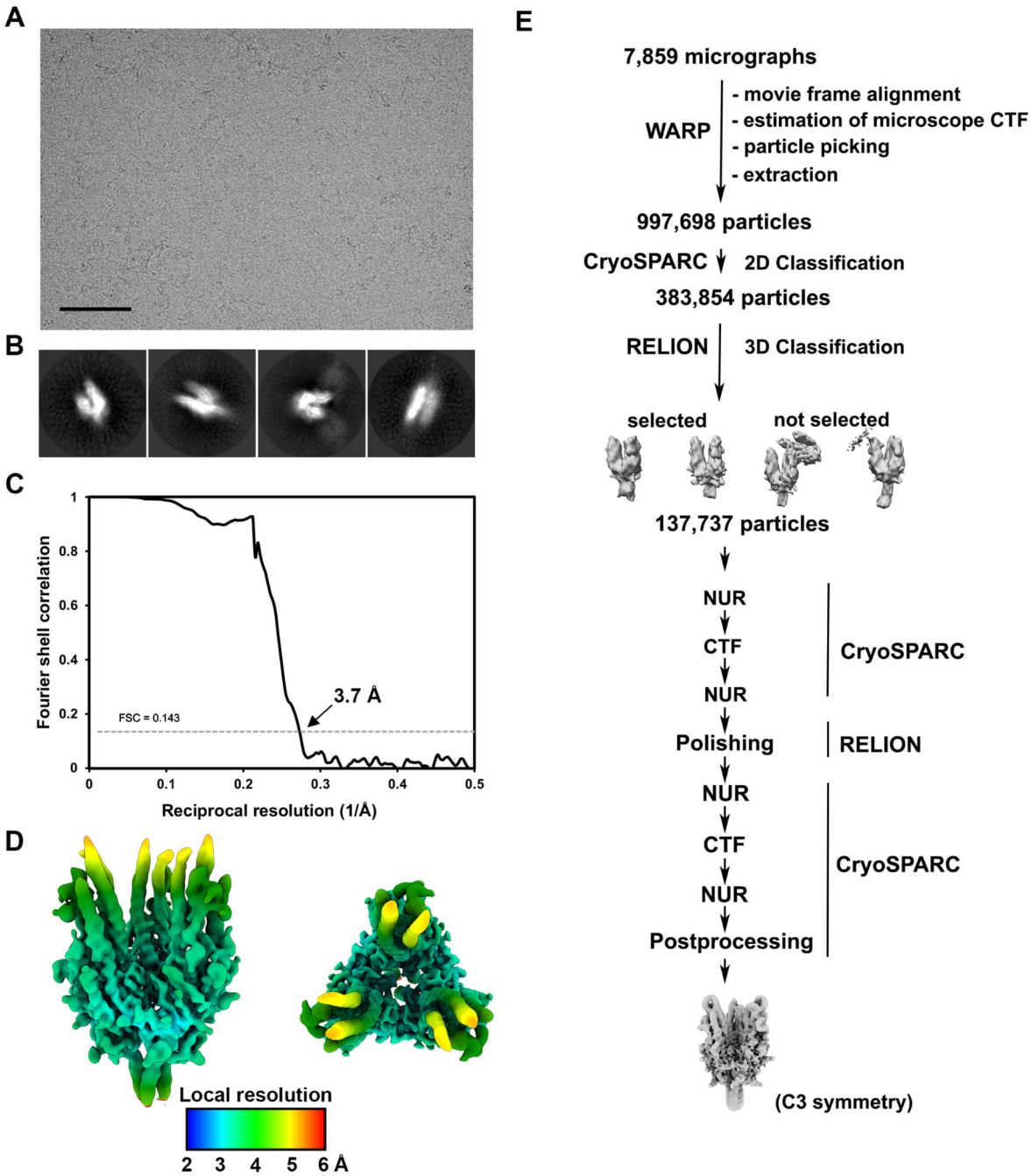
**Other Supplementary Material for this manuscript includes the following:**

Data S1  
MDAR Reproducibility Checklist

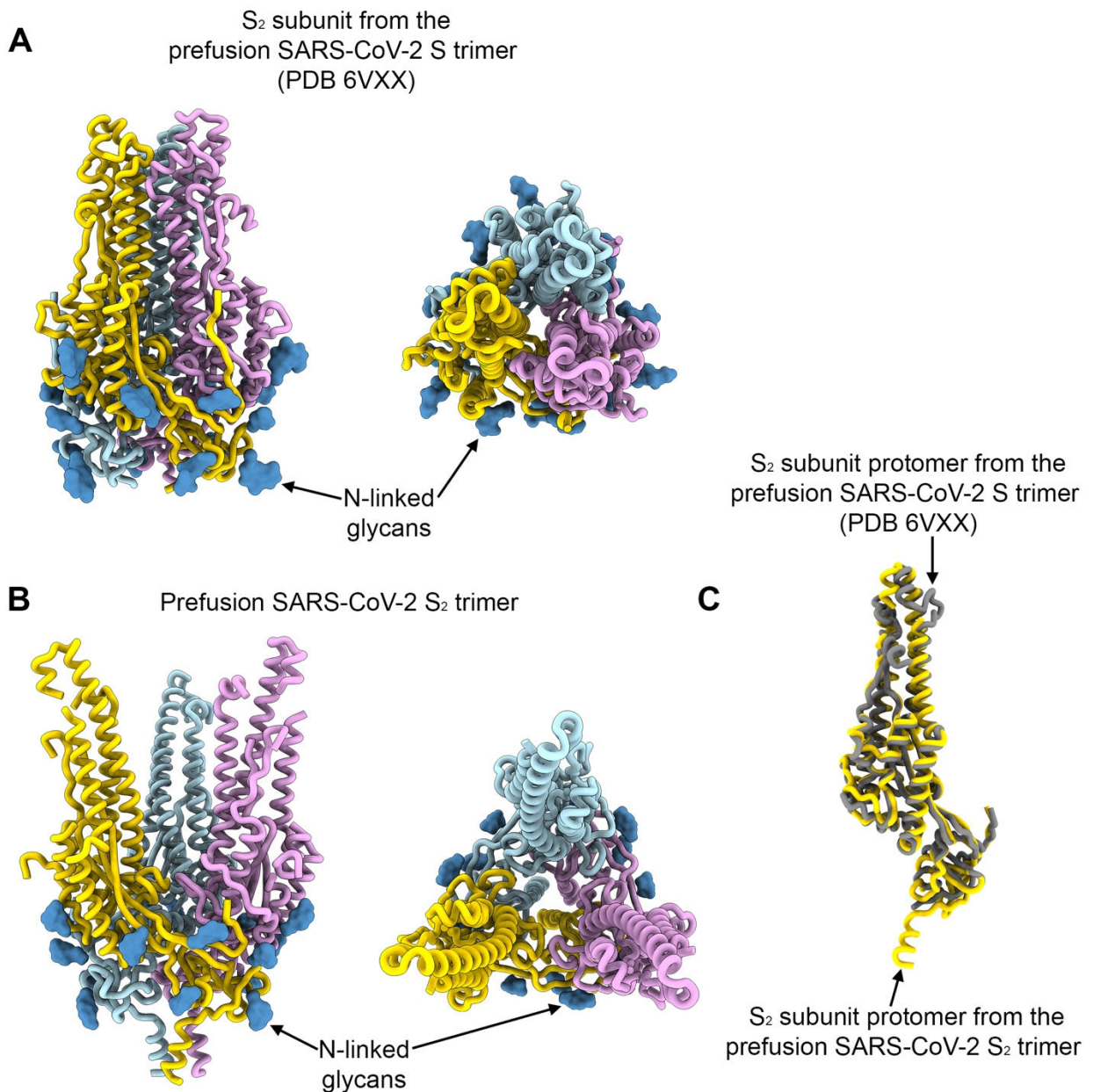
## Supplemental Material



**Figure S1. Biophysical and antigenic characterization of the antigens used for binding and depletion experiments.** **A**, Reducing SDS-PAGE gel of SARS-CoV-2 S, the receptor-binding domain (RBD), the N-terminal domain (NTD), the S<sub>1</sub> subunit, and the S<sub>2</sub> subunit in the prefusion and postfusion conformations. **B-G**, Dose-response ELISA curves for binding of the RBD-targeting S2X324 IgG (80), the prefusion S<sub>2</sub>-targeting RAY-53 IgG (36), the NTD-targeting S2L20 IgG (25), the S<sub>2</sub>-targeting C13A7 IgG (34), the S<sub>2</sub> stem helix-targeting S2P6 IgG (33) and the human ACE2 ectodomain fused to an Fc fragment (hACE2-Fc) to S (B), S<sub>1</sub> (C), S<sub>2(Pre)</sub> (D) S<sub>2(Post)</sub> (E), NTD (F), and RBD (G). **H-J**, Representative negative stain electron micrograph of S (H), S<sub>1</sub> (I), and S<sub>2(Post)</sub> (J). Scale bar: 400 Å .

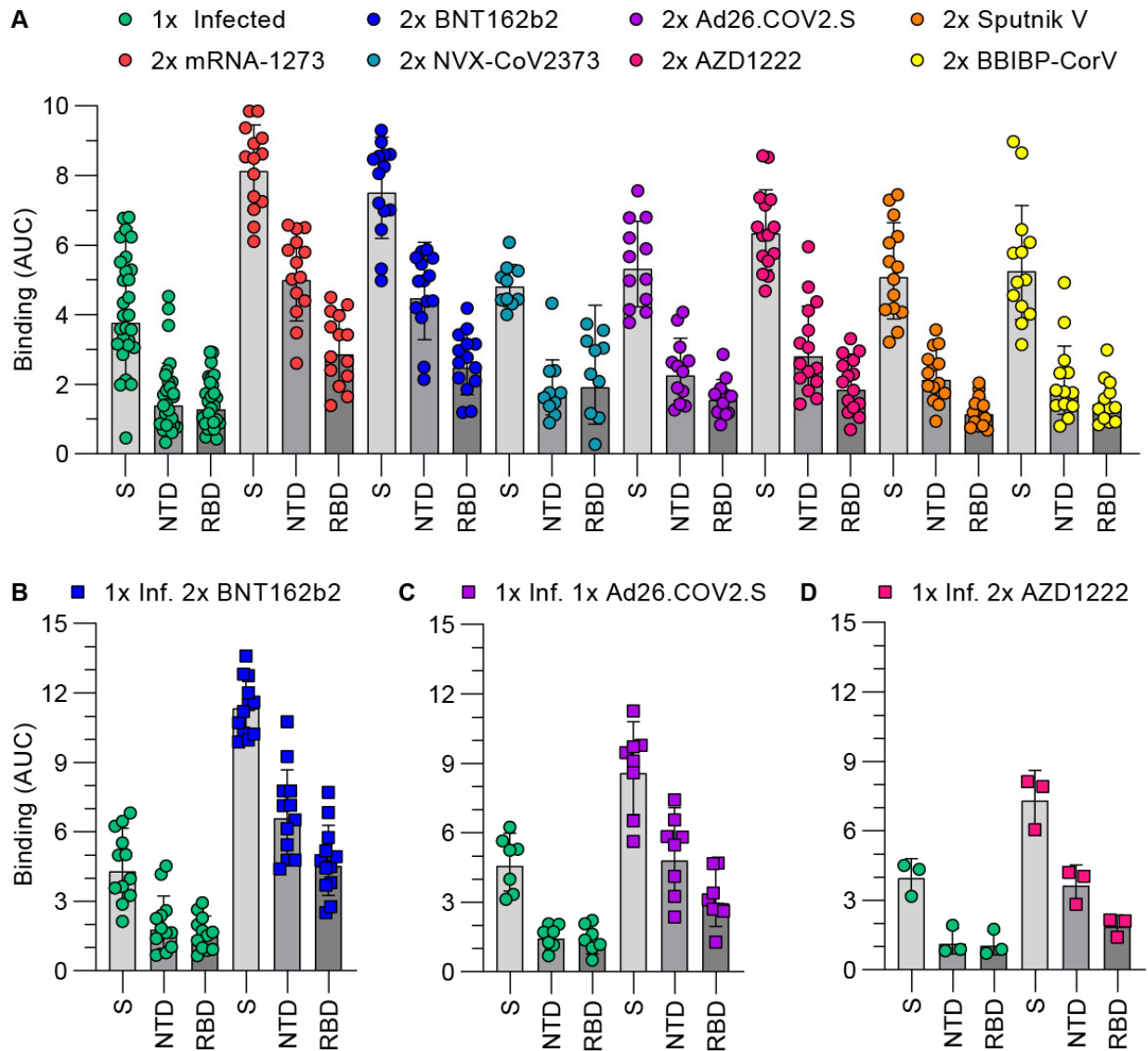


**Figure S2. CryoEM data processing of the prefusion SARS-CoV-2 S<sub>2</sub> subunit trimer dataset.** **A-B**, Representative electron micrograph (A) and 2D class averages (B) of SARS-CoV-2 S<sub>2</sub> embedded in vitreous ice. The scale bar represents 100 nm. **C**, Gold-standard Fourier shell correlation curve for the SARS-CoV-2 S<sub>2</sub> reconstruction. The 0.143 cutoff is indicated by a horizontal dashed line. **D**, Local resolution map calculated using CryoSPARC and plotted onto the unsharpened SARS-CoV-2 S<sub>2</sub> reconstruction viewed from the side (left, along the viral membrane) and the top (right, normal to the viral membrane). **E**, Data processing flowchart. CTF: contrast transfer function; NUR: non-uniform refinement.



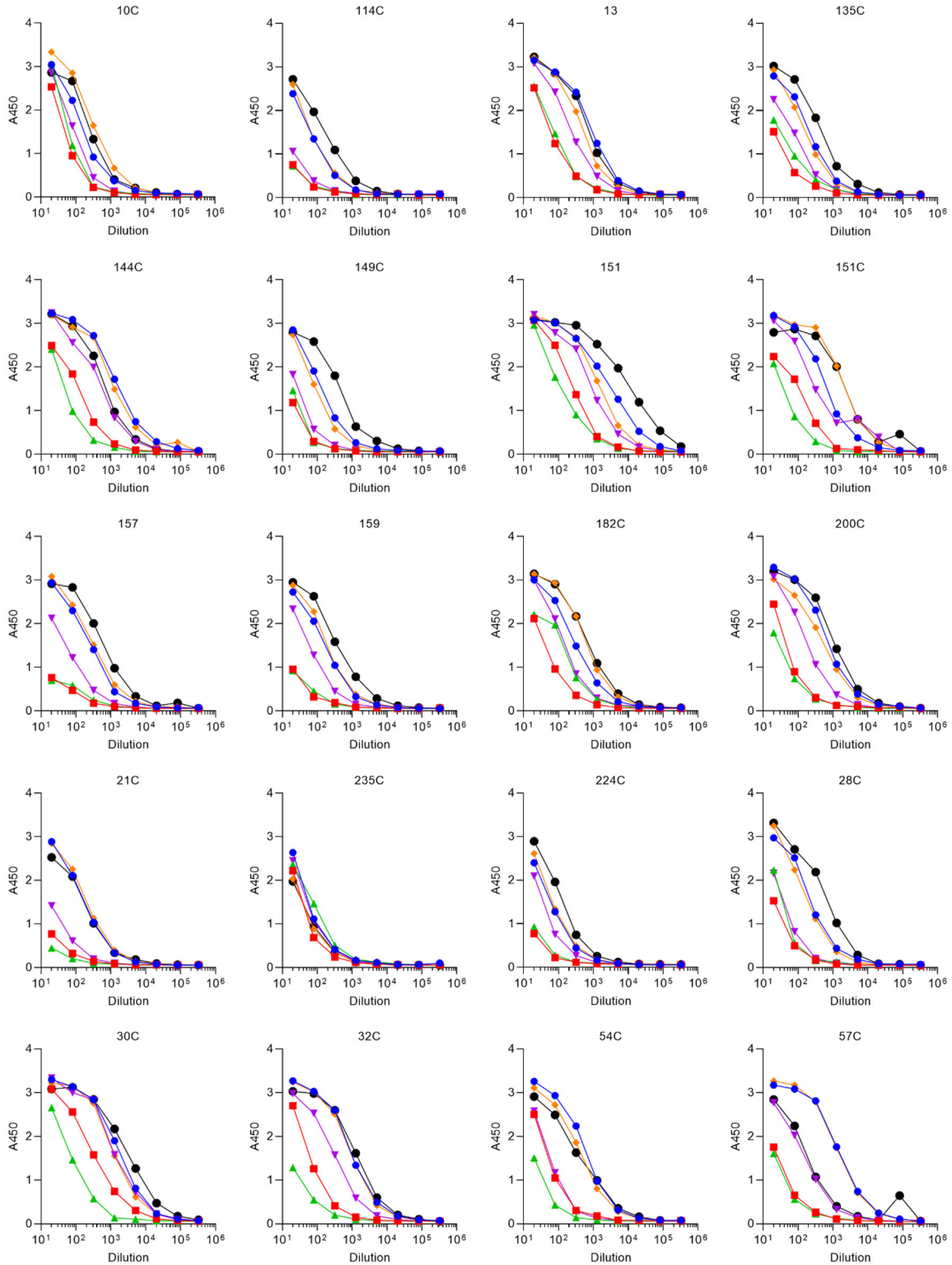
**Figure S3. Comparison of the fusion machinery architecture in prefusion SARS-CoV-2 S and S<sub>2</sub>.** **A**, Ribbon diagram of the S<sub>2</sub> trimer present in the prefusion S ectodomain structure (PDB 6VXX) viewed along two orthogonal orientations. **B**, Ribbon diagram of the S<sub>2</sub> subunit ectodomain trimer structure viewed along two orthogonal orientations. **C**, Superimposition of one protomer from each of the two structures underscoring retention of the overall prefusion tertiary S<sub>2</sub> subunit structure (albeit with some deviation of the quaternary organization of the trimer).

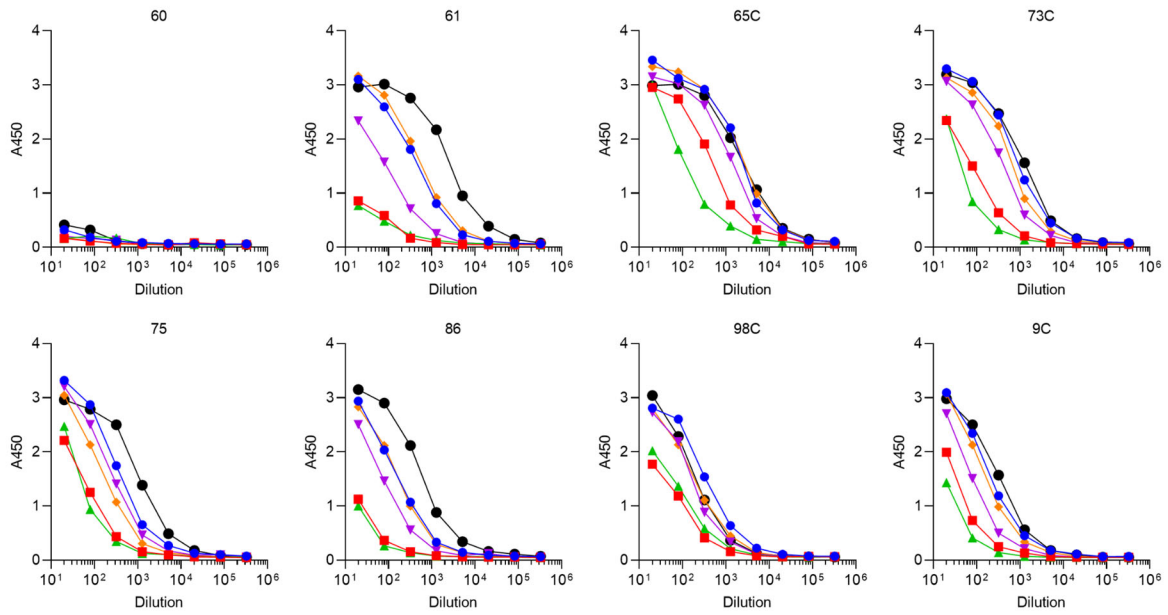




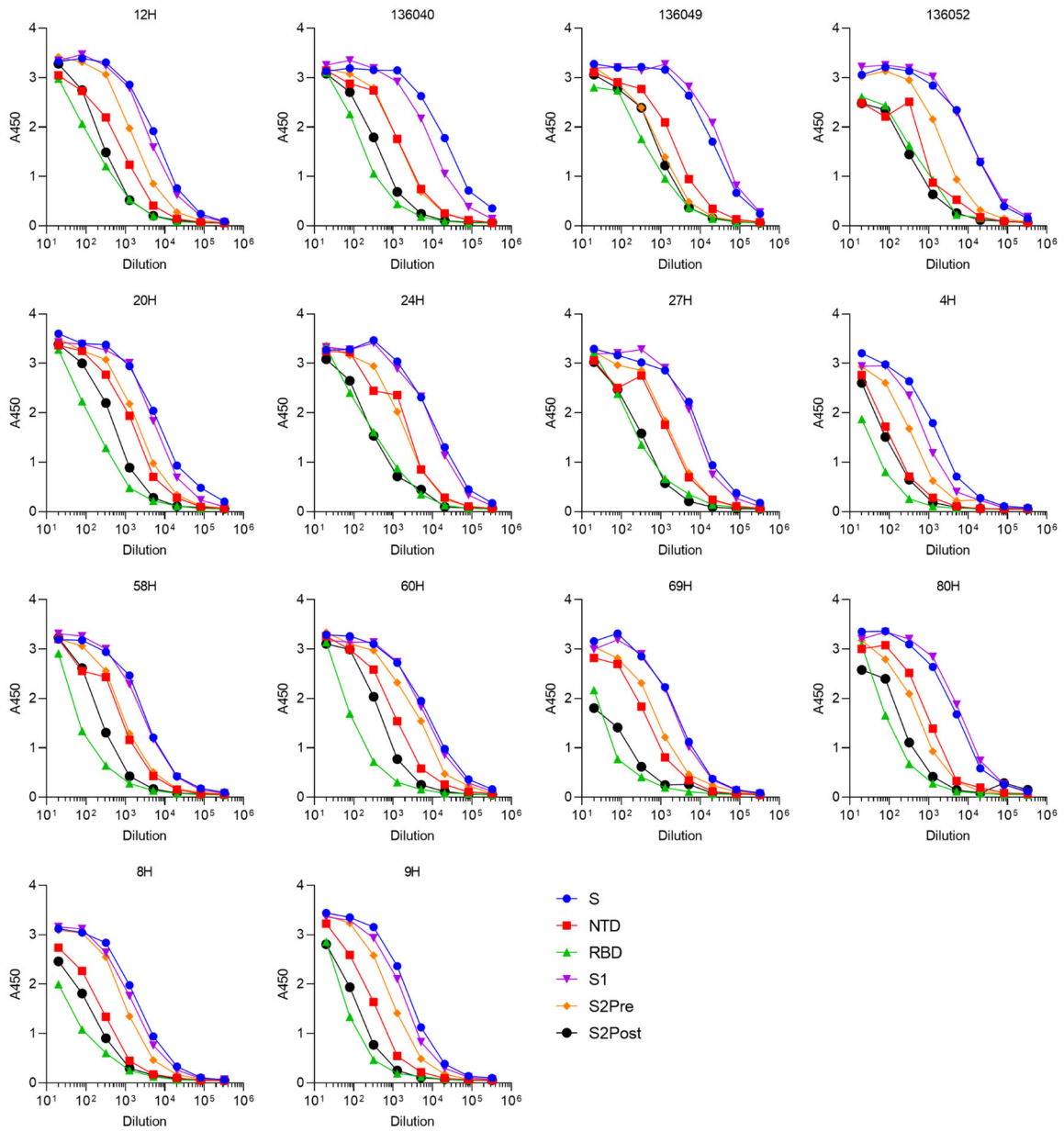
**Figure S4. A**, IgG binding titers elicited by SARS-CoV-2 infection or vaccination against the prefusion S (S), the N-terminal domain (NTD), and the receptor-binding domain (RBD), as measured by ELISA. Individuals were infected with a Wuhan-Hu-1-like strain or vaccinated with two doses of one of seven vaccines. **B-D**, IgG binding titers before and after vaccination with two doses of BNT162b2 (B), one dose of Ad26.COVID.2.S (C), or two doses of AZD1222 (D) in longitudinal cohorts of individuals previously infected with SARS-CoV-2. Each point consists of a representative result from a single patient plasma sample out of at least two experimental replicates consisting of different batches of each antigen. Bars represent geometric means and error bars represent geometric standard deviations. AUCs were determined after log transforming the plasma dilutions and the corresponding dose-response curves are shown in Fig S5-S6.

# A 1x Infected

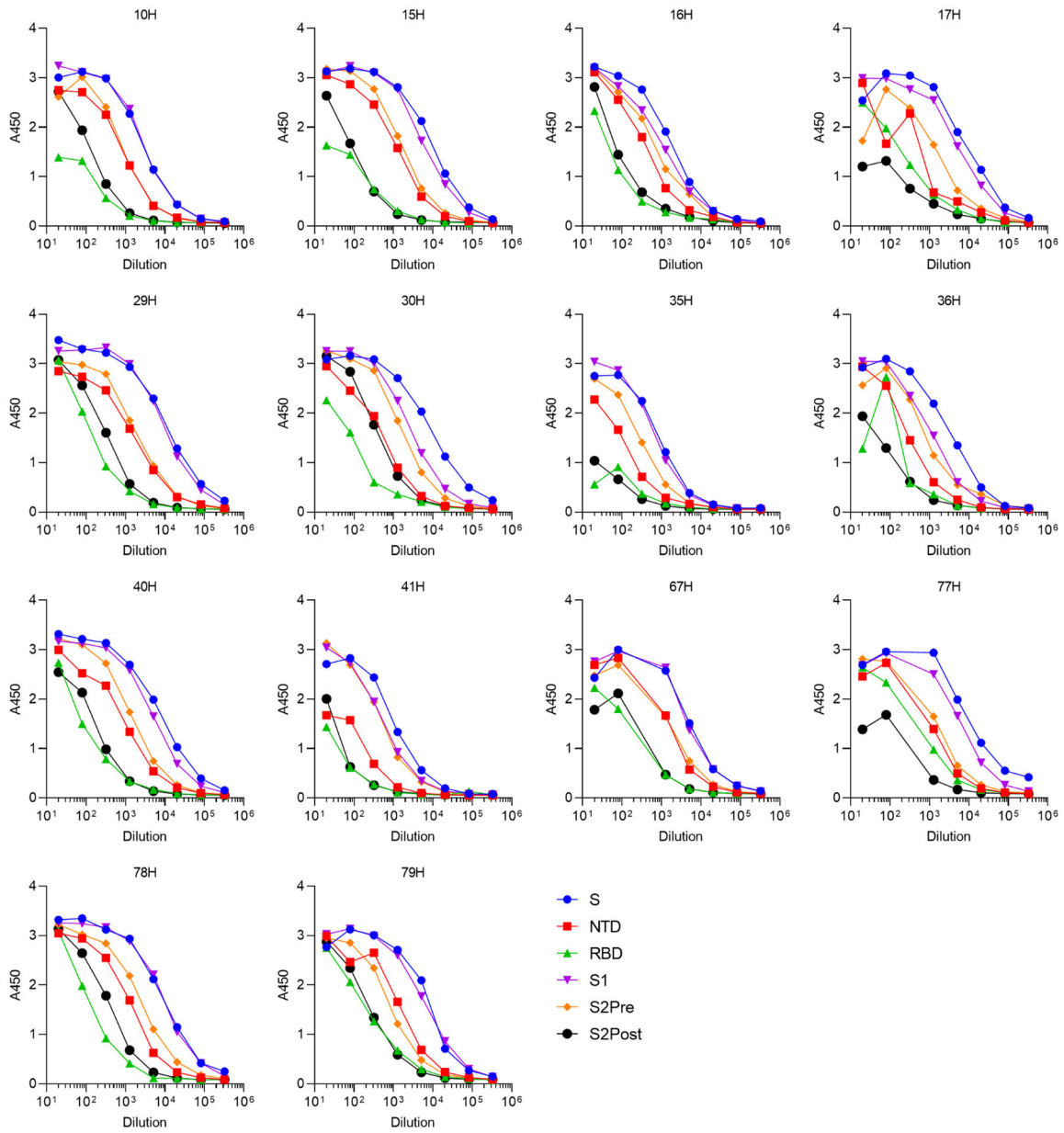




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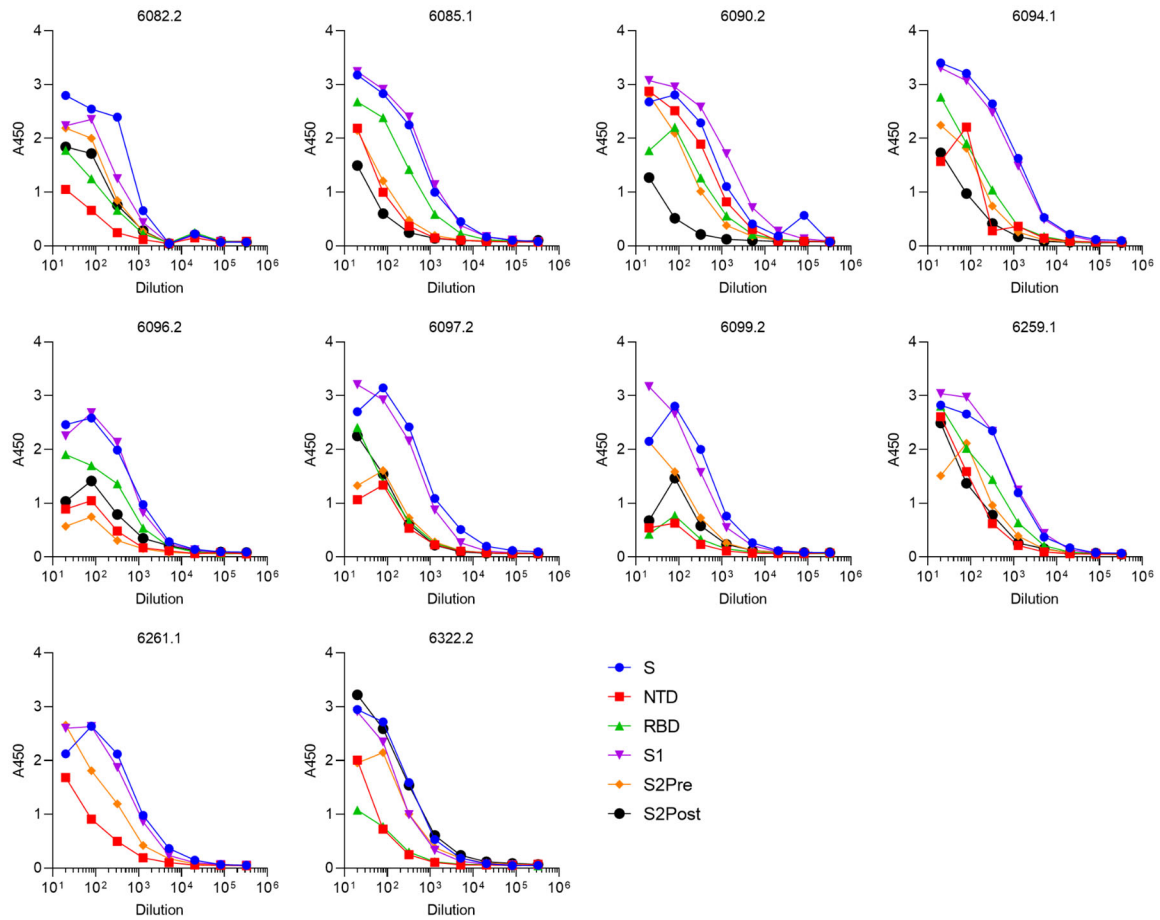


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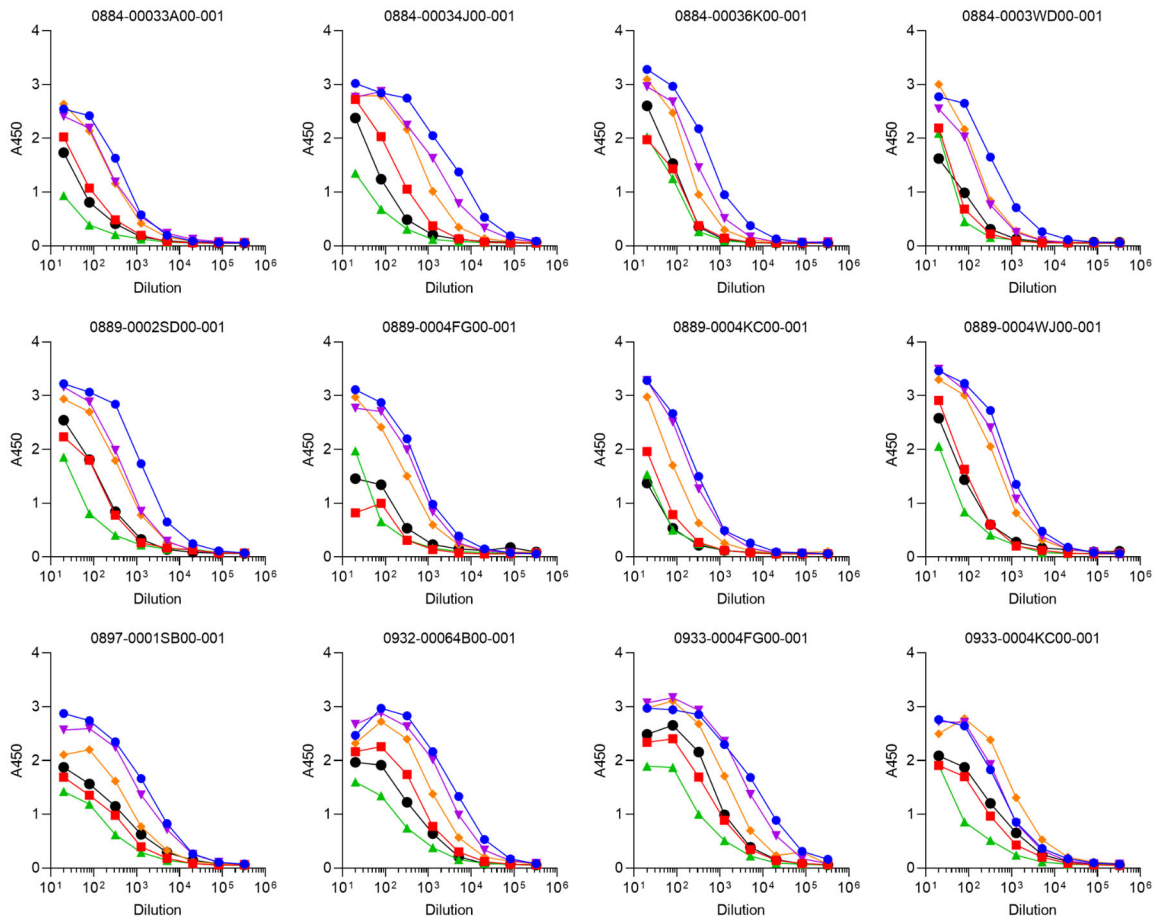




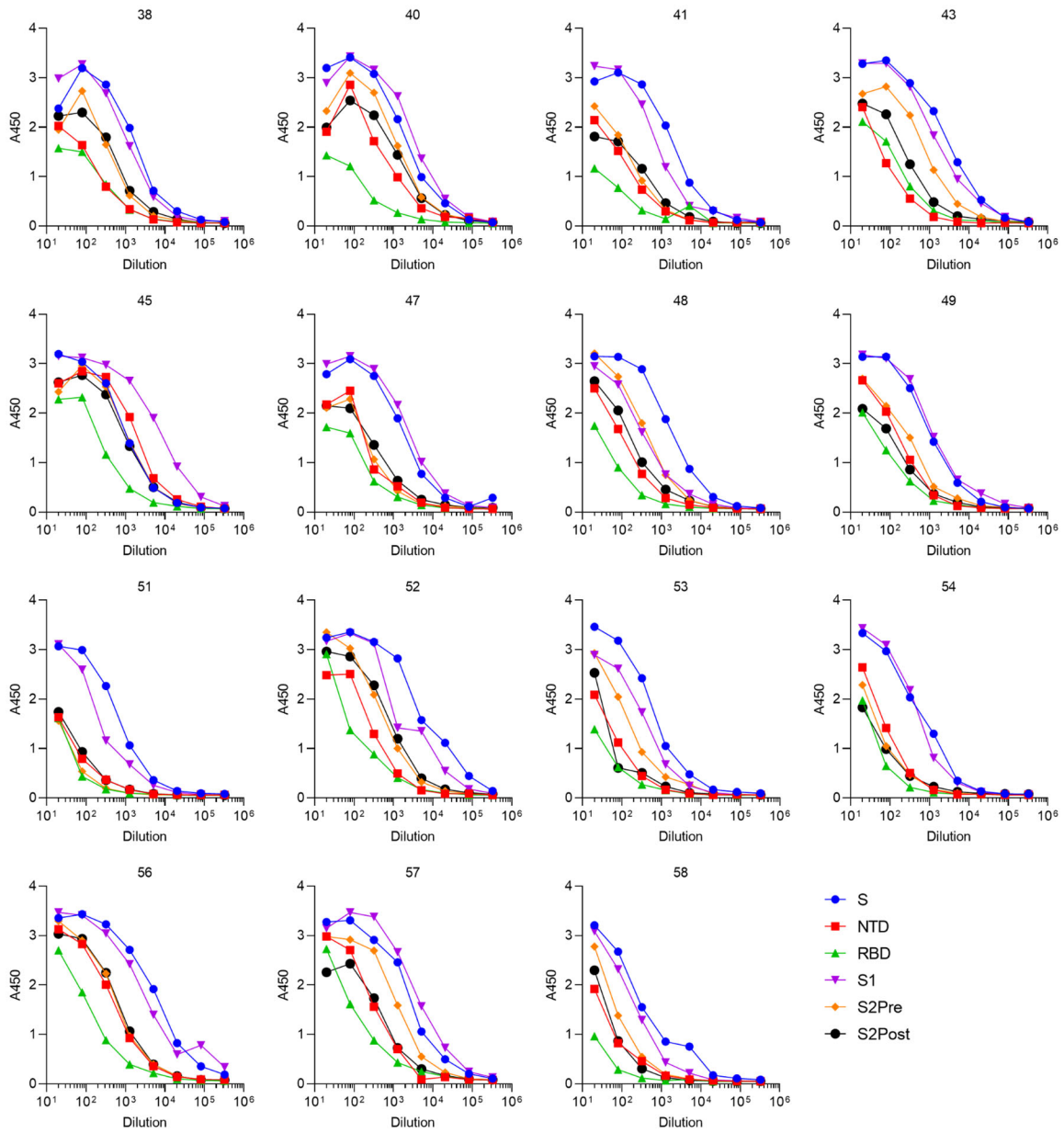
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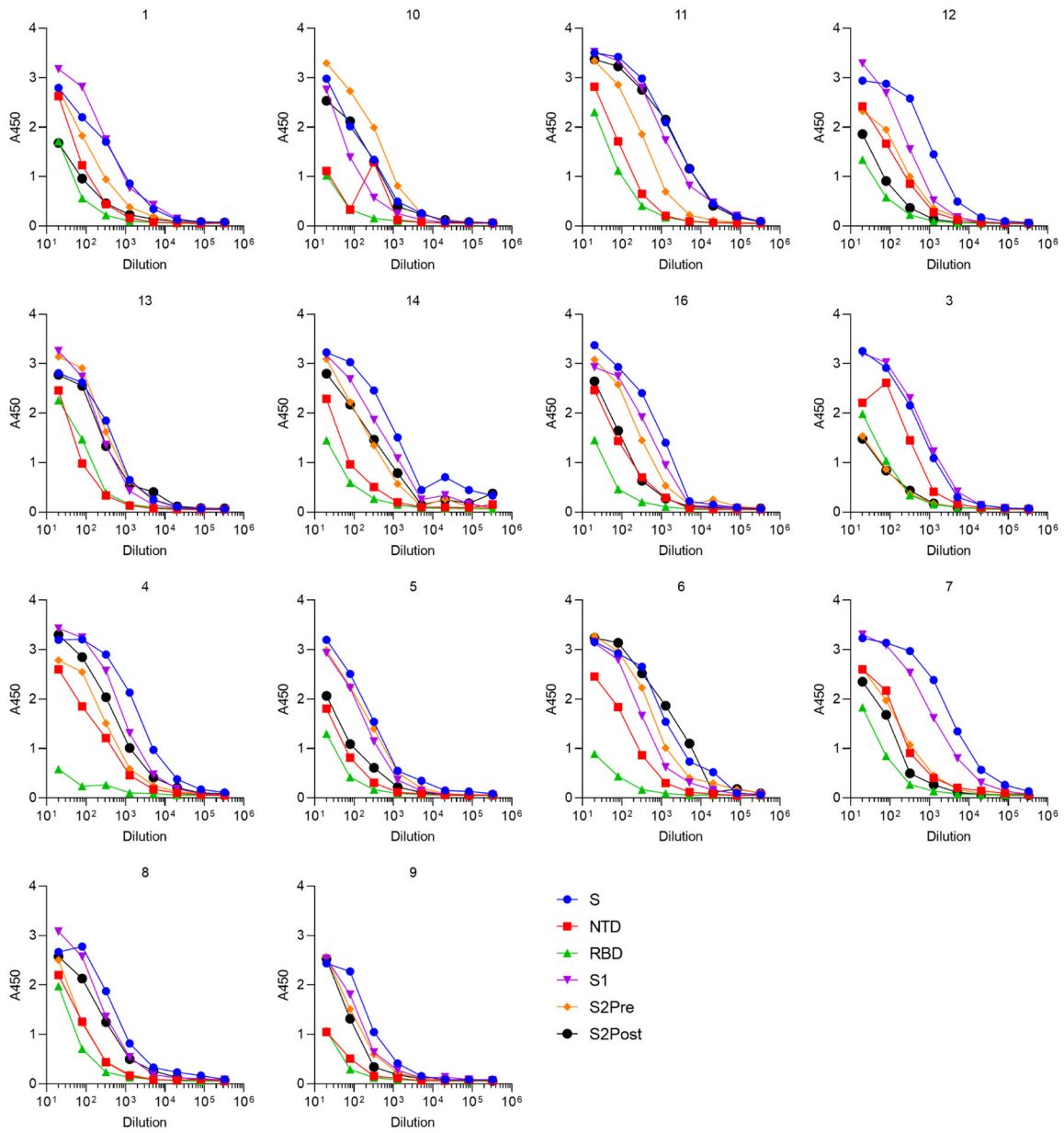
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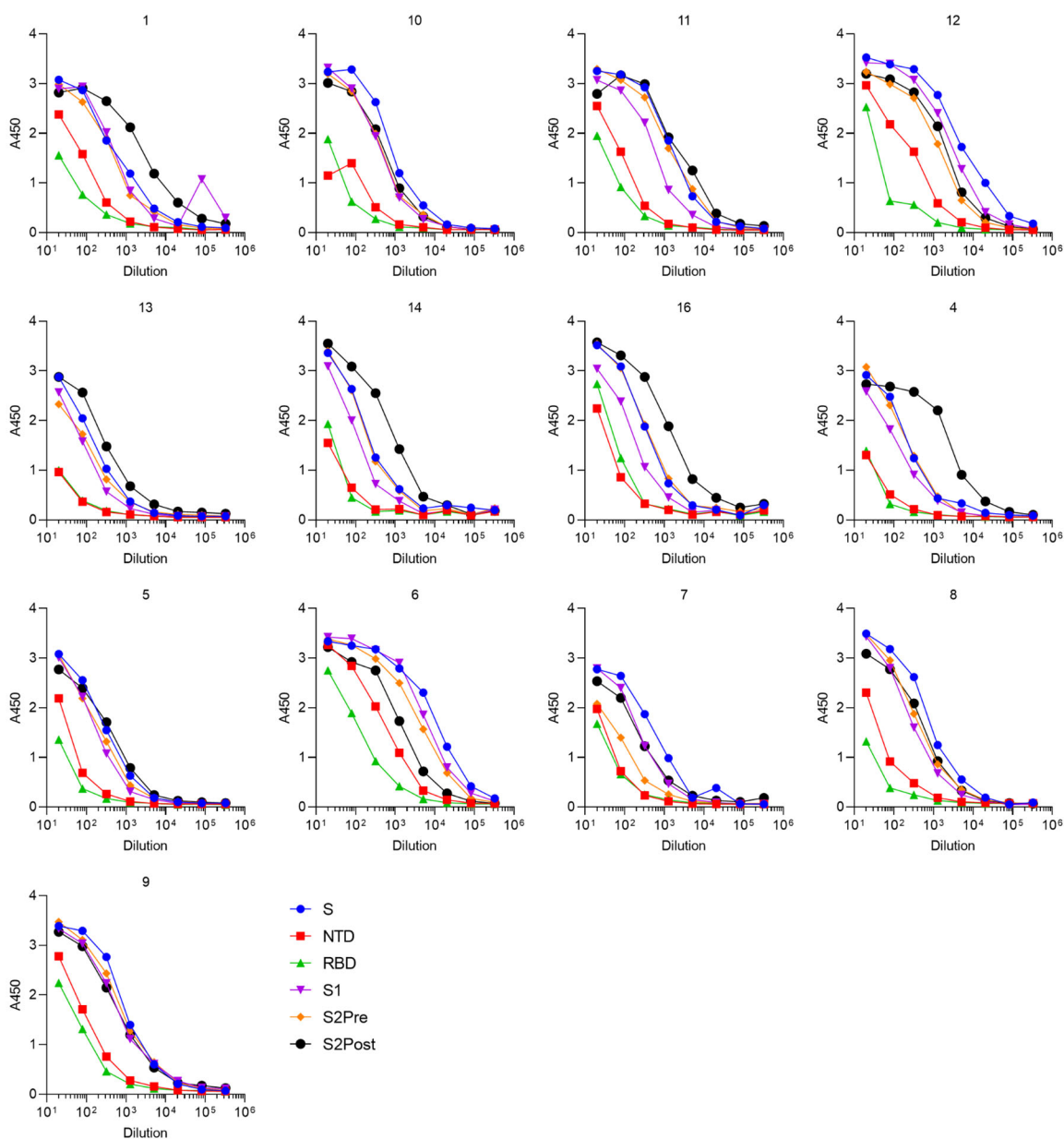
# F 2x AZD1222



# G 2x Sputnik V



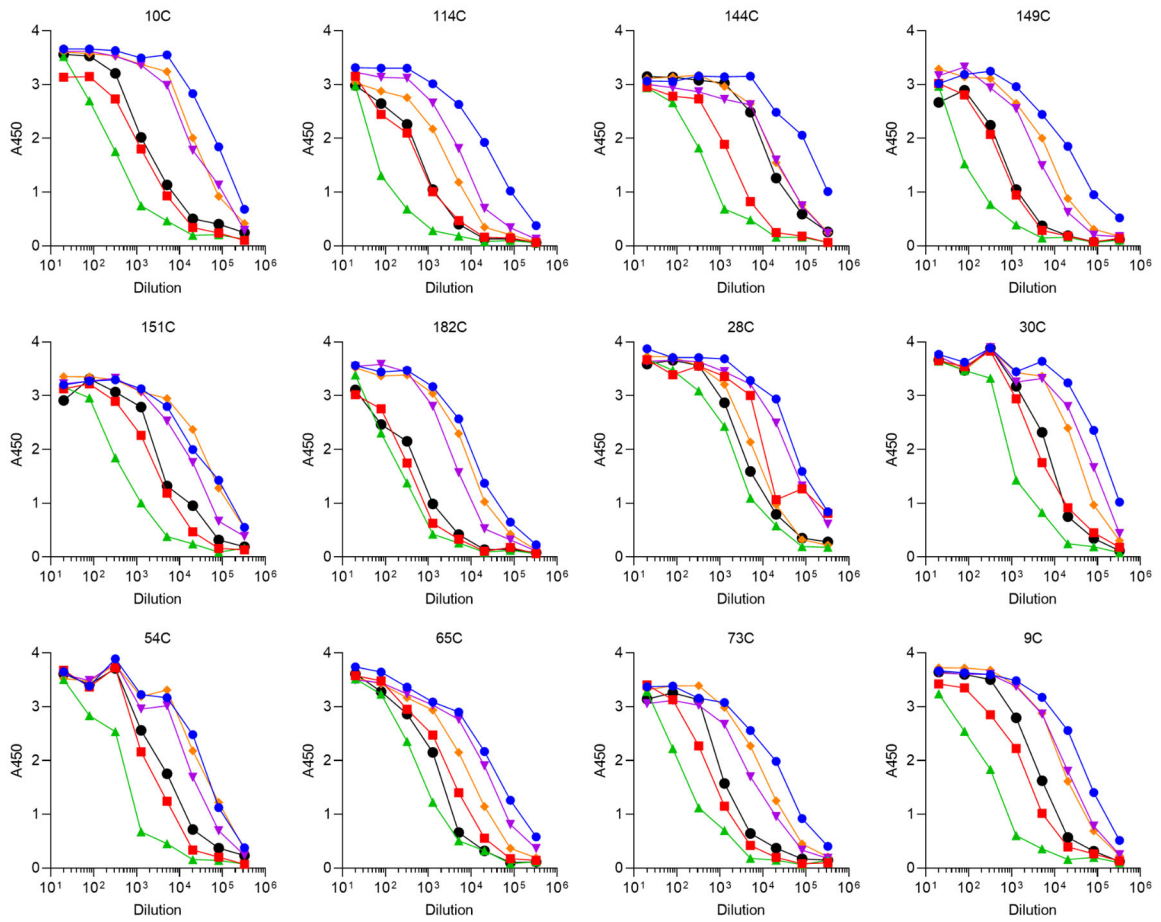
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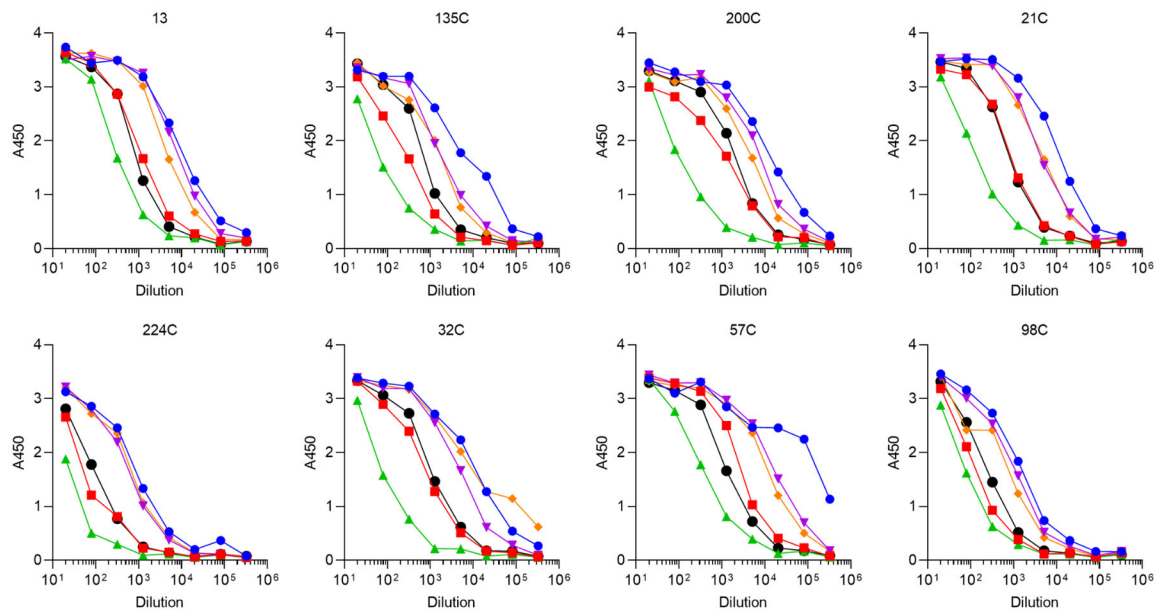
**Figure S5. Analysis of plasma antibody binding titers in previously infected subjects or vaccinees by ELISA. (A-H)** Dose-response curves of plasma antibody binding to the SARS-CoV-2 S, the N-terminal domain (NTD), the receptor-binding domain (RBD), the S<sub>1</sub> subunit, and the S<sub>2</sub> subunit in the prefusion and postfusion conformations. Samples were collected from individuals after SARS-CoV-2 infection (A) or vaccination with two doses of mRNA-1273 (B), BNT162b2 (C), Ad26.COV2.S (D), AZD1222 (E), Sputnik V (F), or BBIBP-CorV (E). Patient demographics can be found in Table S2. Curves are representative of at least two experimental replicates consisting of different batches of each antigen.



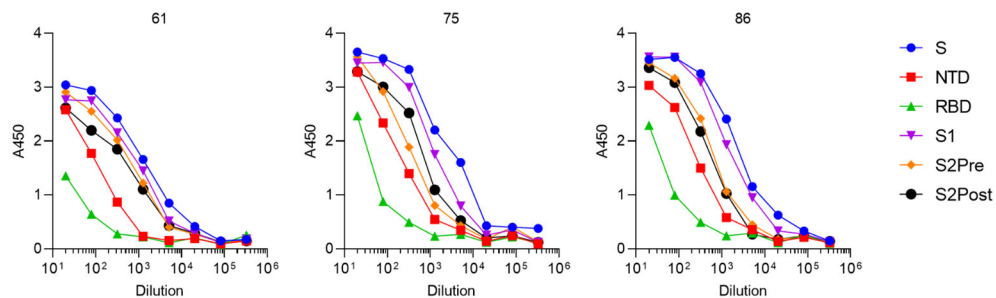
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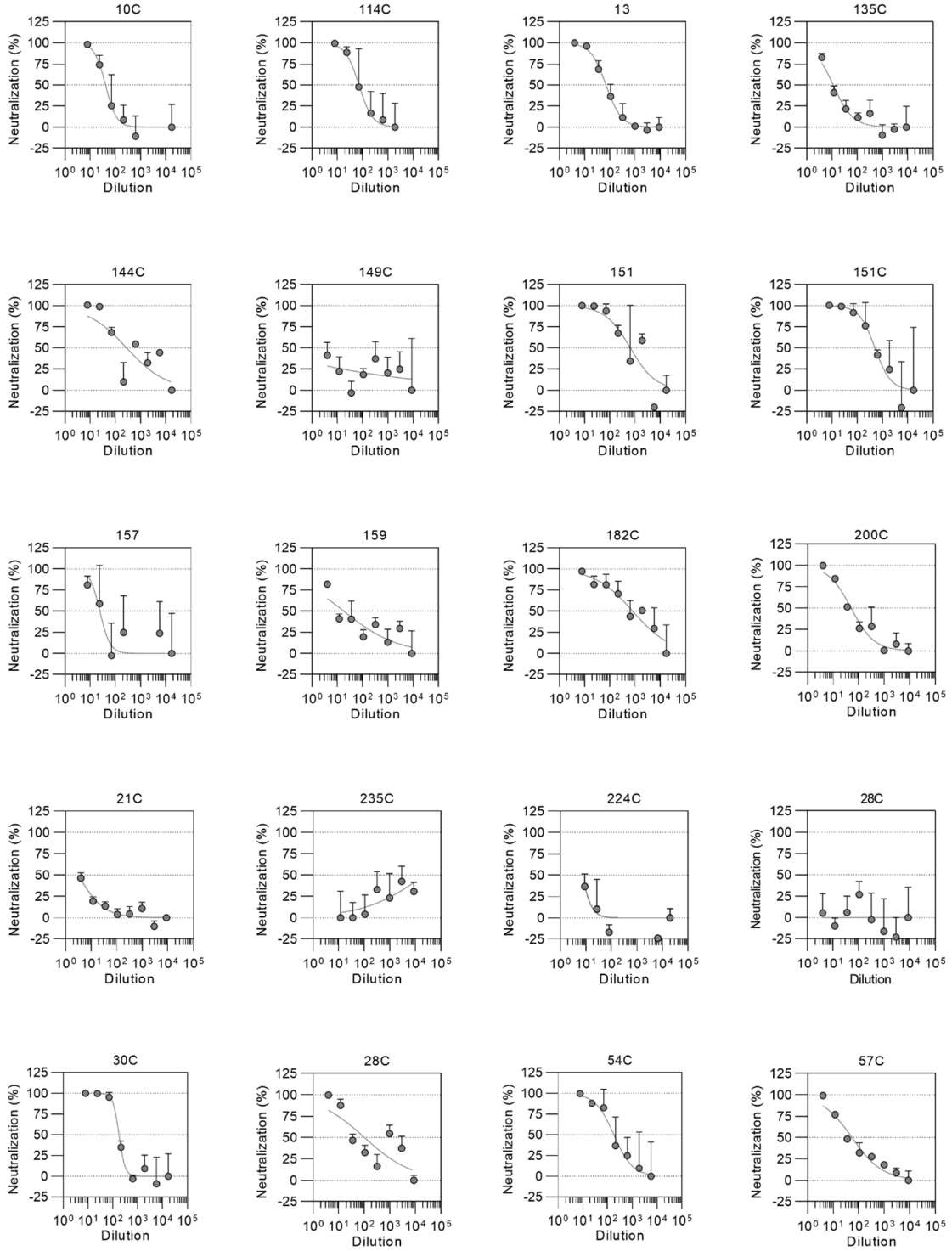


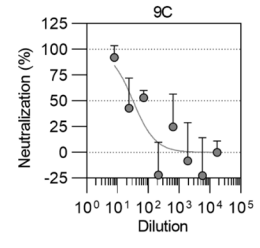
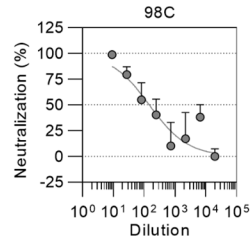
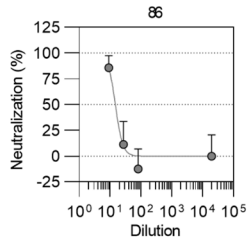
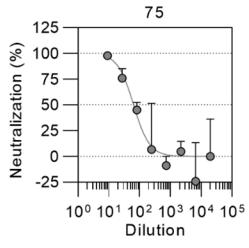
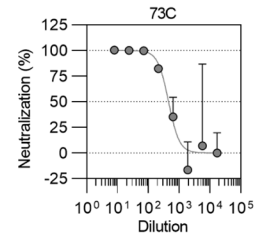
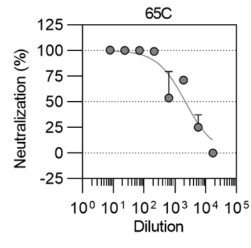
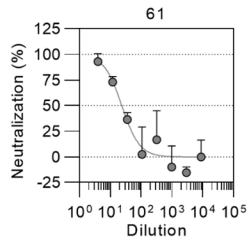
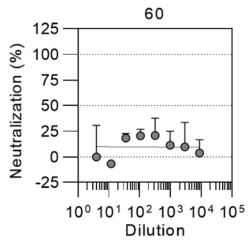
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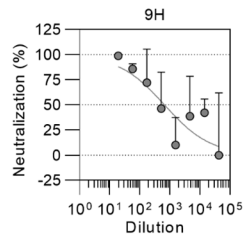
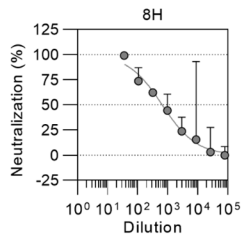
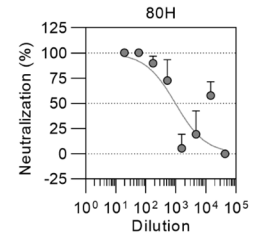
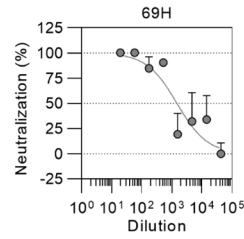
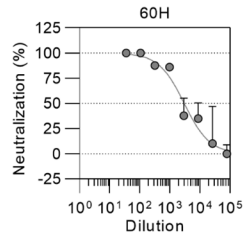
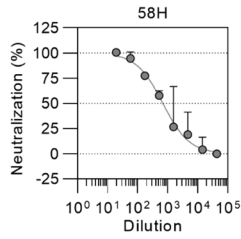
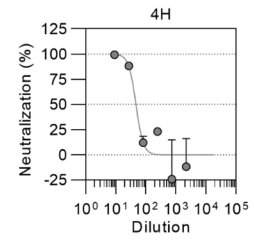
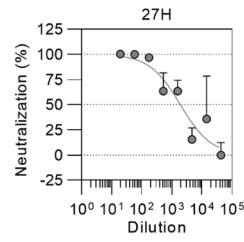
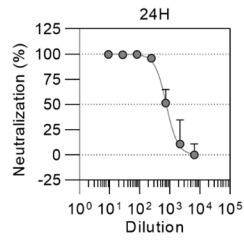
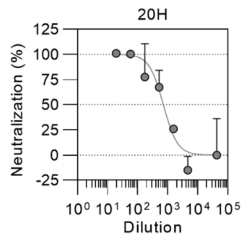
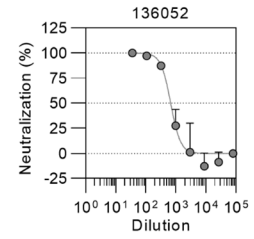
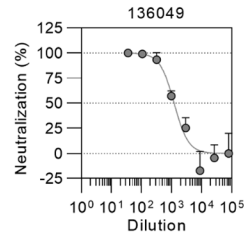
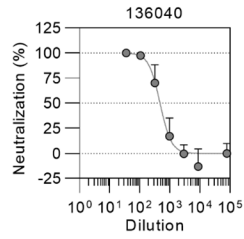
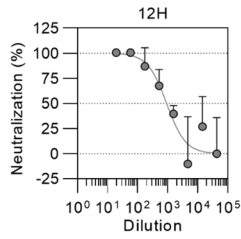
**Figure S6. Analysis of plasma antibody binding titers in previously infected subjects before and after vaccination by ELISA. A-C, Dose-response curves of plasma IgG binding to the SARS-CoV-2 S, the N-terminal domain (NTD), the receptor-binding domain (RBD), the S<sub>1</sub> subunit, and the S<sub>2</sub> subunit in the prefusion and postfusion conformations. Samples were collected from individuals after SARS-CoV-2 infection (Wuhan-Hu-1-like strain) and vaccination with two doses of BNT162b2 (A), one dose of Ad26.COVS (B), or two doses of AZD1222 (C). Patient demographics can be found in Table S2. Curves are representative of at least two experimental replicates consisting of different batches of each antigen.**

# A 1x Infected



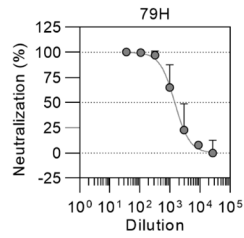
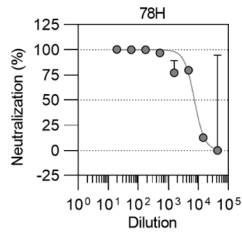
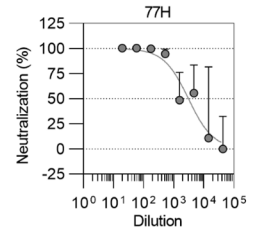
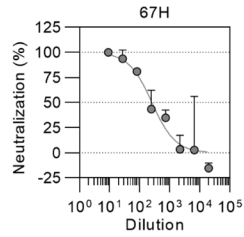
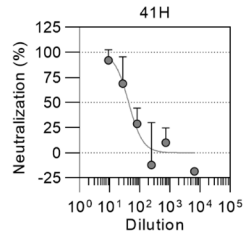
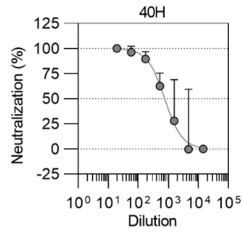
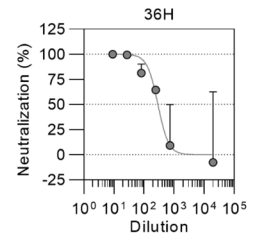
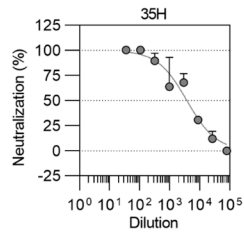
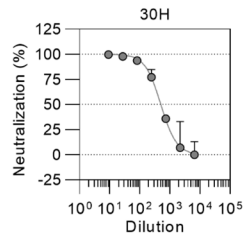
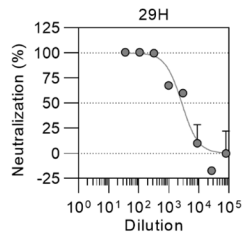
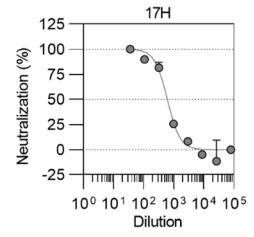
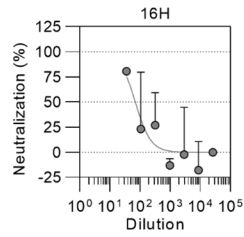
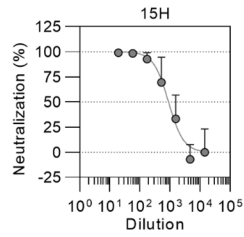
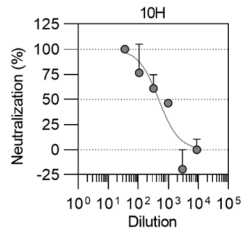


## B 2x mRNA-1273

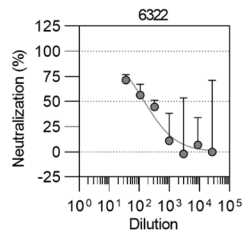
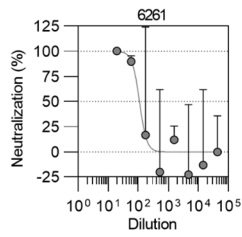
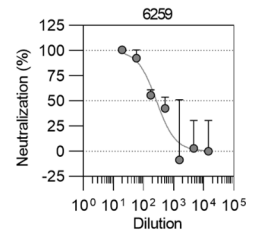
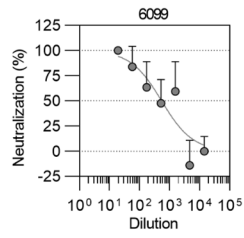
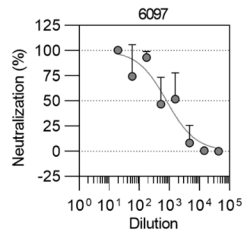
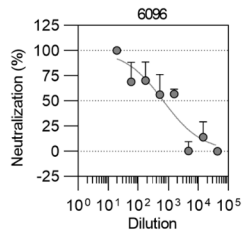
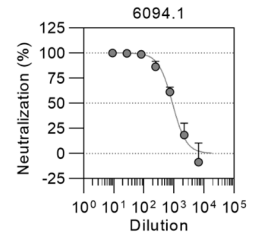
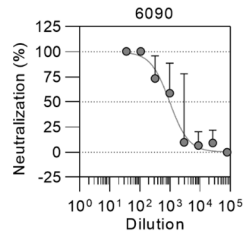
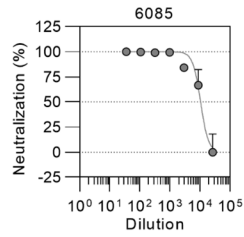
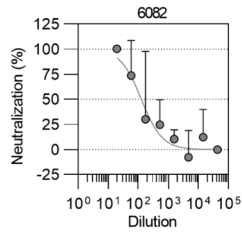




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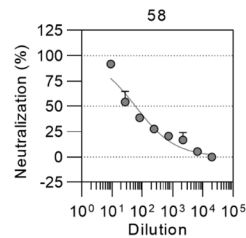
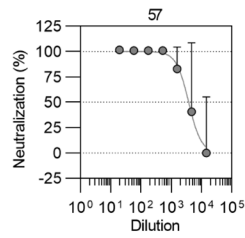
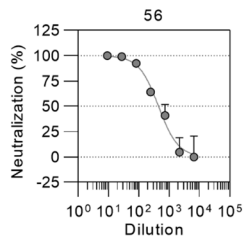
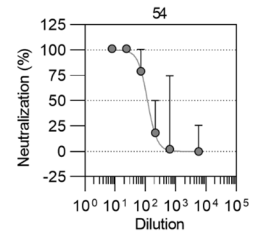
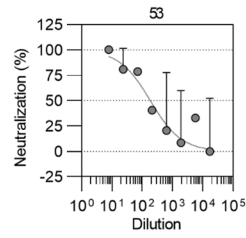
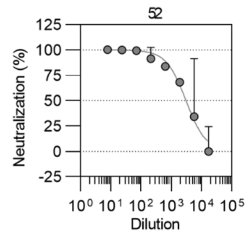
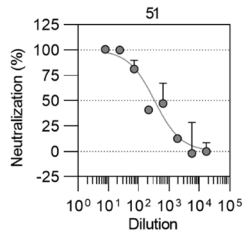
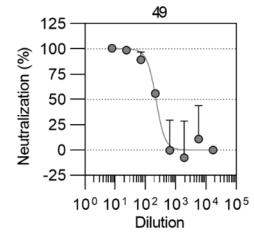
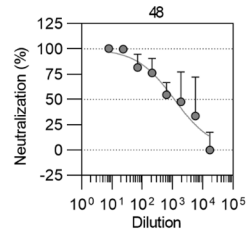
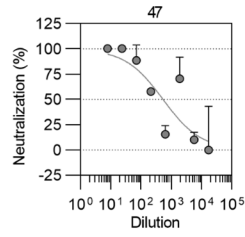
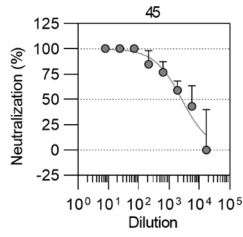
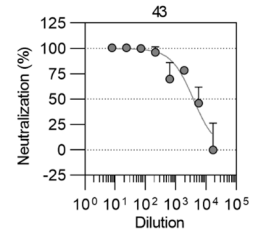
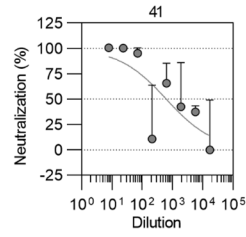
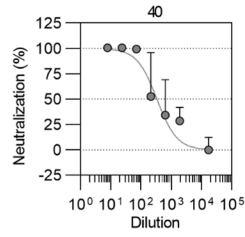
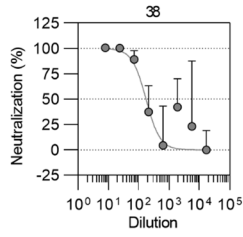


D 2x NVX-CoV2373

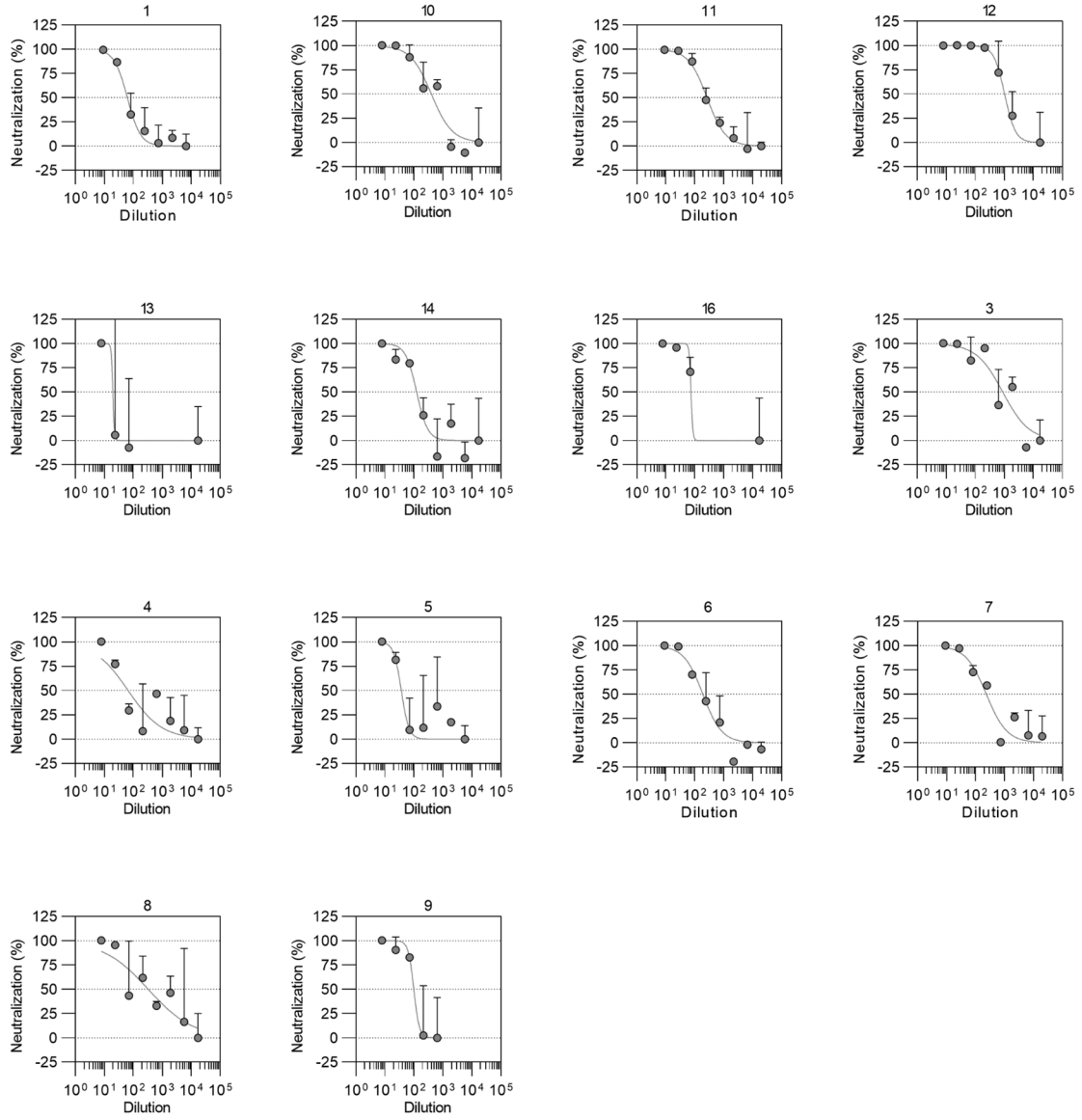




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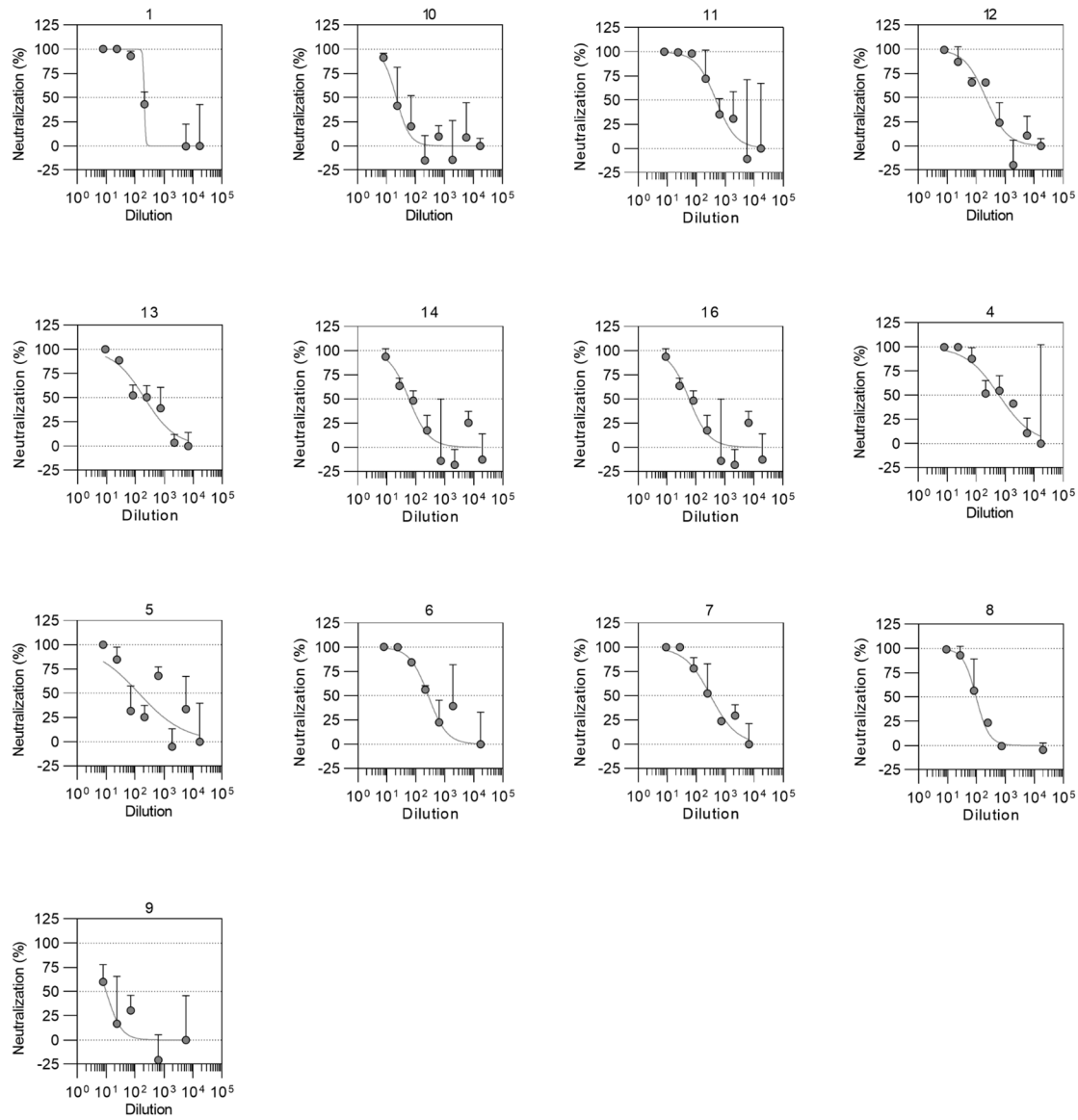


# G 2x Sputnik V



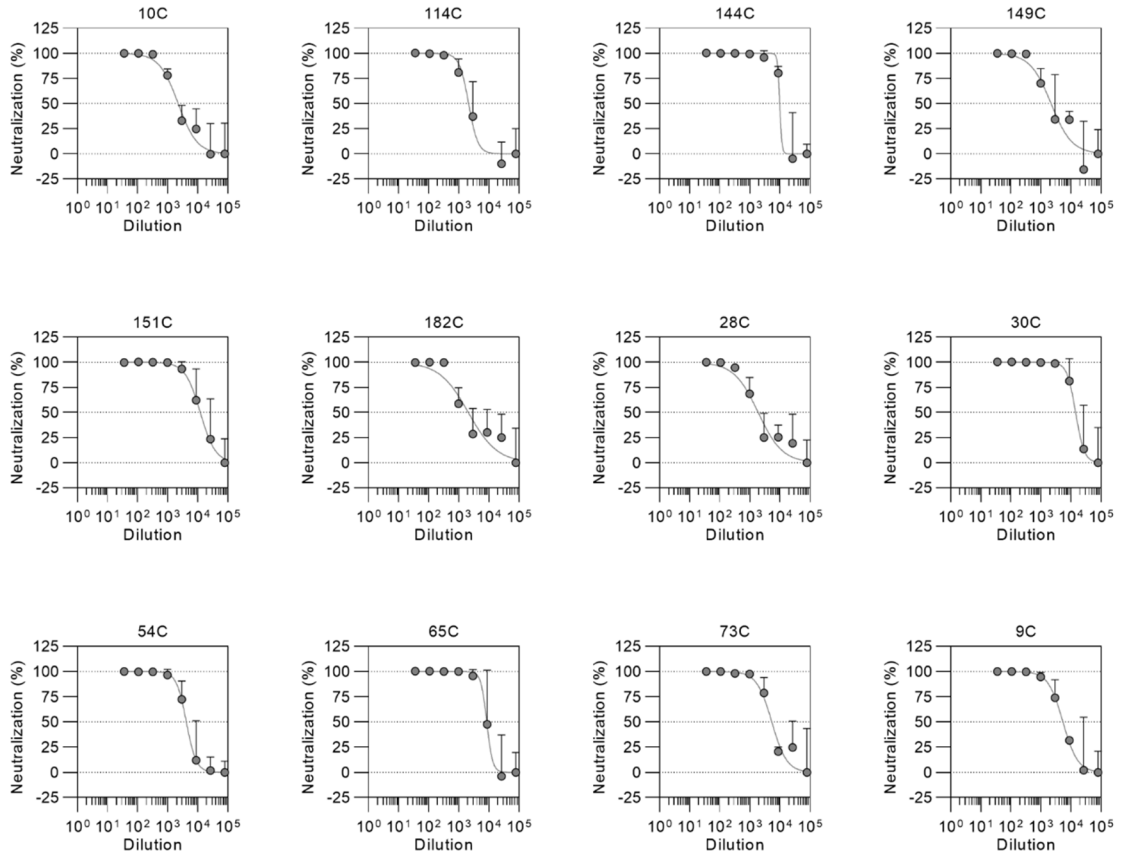


## H 2x BBIBP-CorV

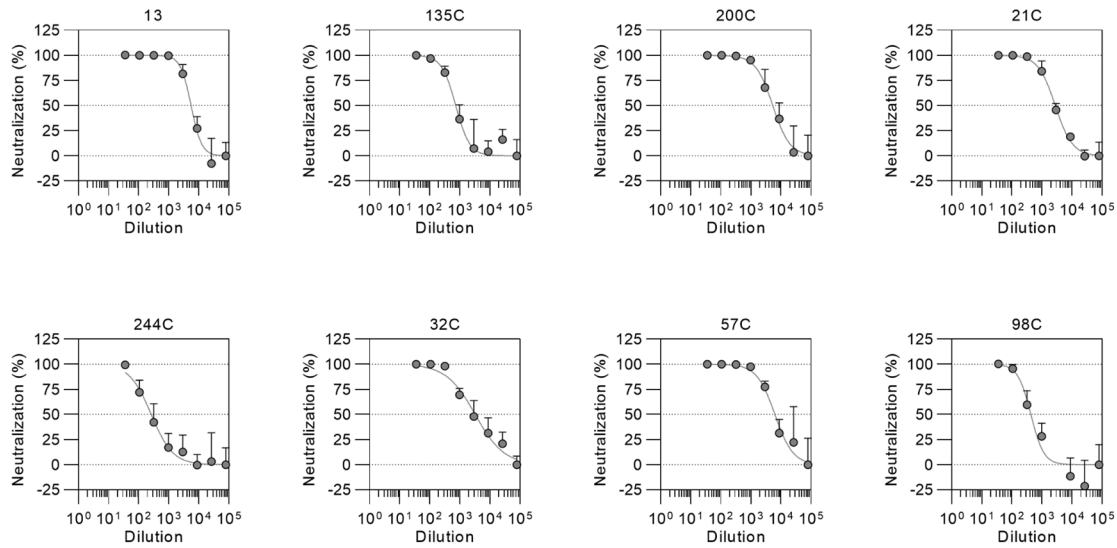


**Figure S7. Evaluation of plasma neutralizing activity in previously infected subjects or vaccinees.** A-E, Normalized dose-response neutralization curves using SARS-CoV-2 Wuhan-Hu-1/G614 S VSV pseudovirus and TMPRSS2-overexpressing VeroE6 target cells. Samples were collected from individuals after SARS-CoV-2 infection (A) or vaccination with two doses of mRNA-1273 (B), BNT162b2 (C), NVX-CoV2373 (D), Ad26.COVS (E), AZD1222 (F), Sputnik V (G), and BBIBP-CorV (H). Patient demographics can be found in Table S2. Points are the means of two-four replicates using the same pseudovirus and error bars are the geometric standard deviations. Curves are representative of at least two experimental replicates consisting of different batches of pseudovirus.

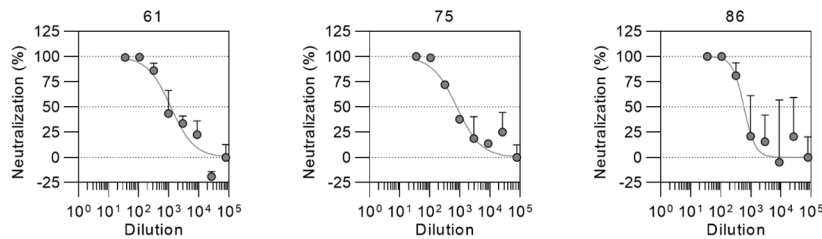
**A** 1x Infected 2x BNT162b2



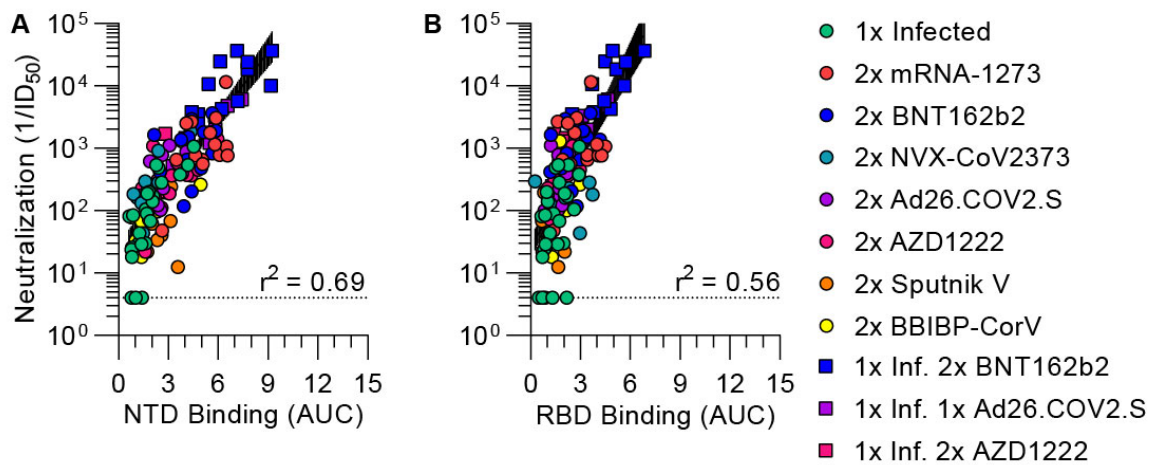
## B 1x Infected 1x Ad26.COV2.S



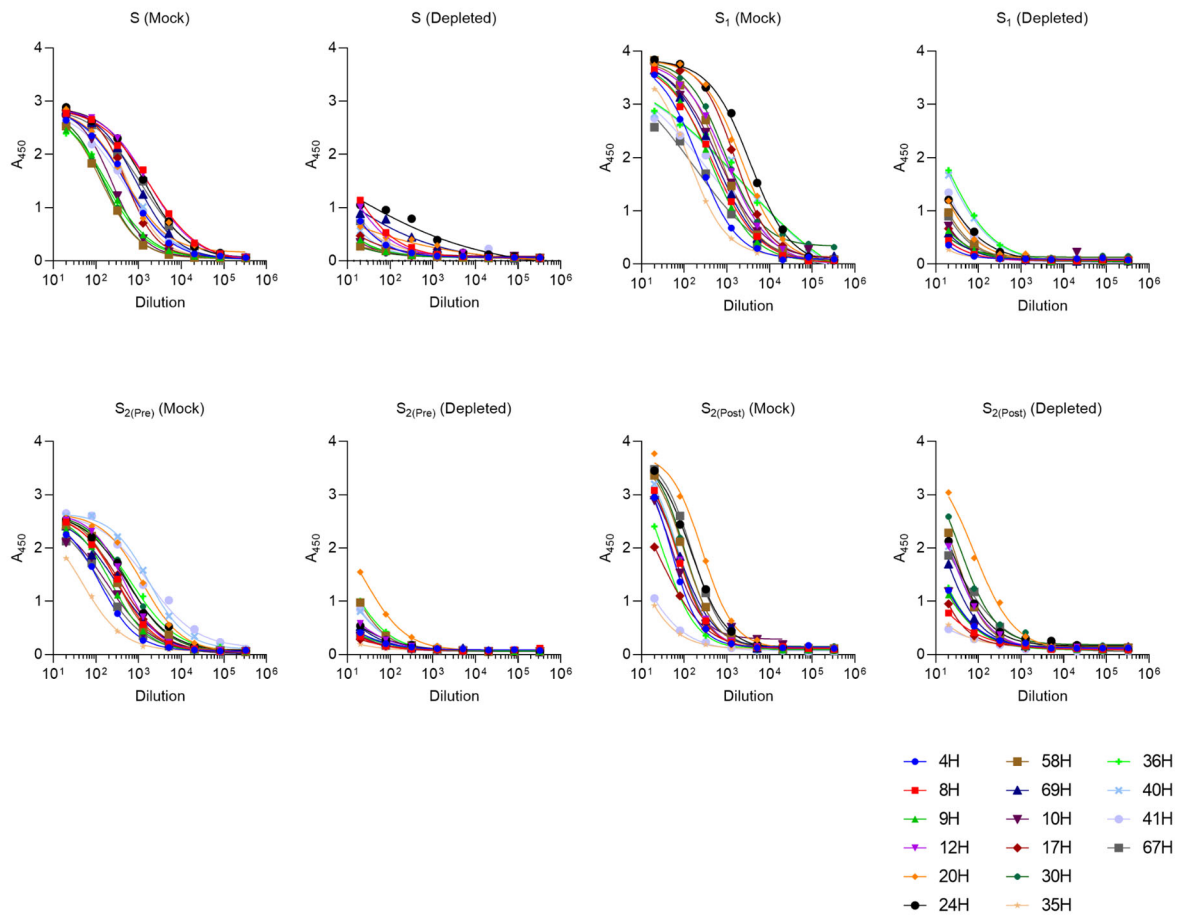
## C 1x Infected 2x AZD1222



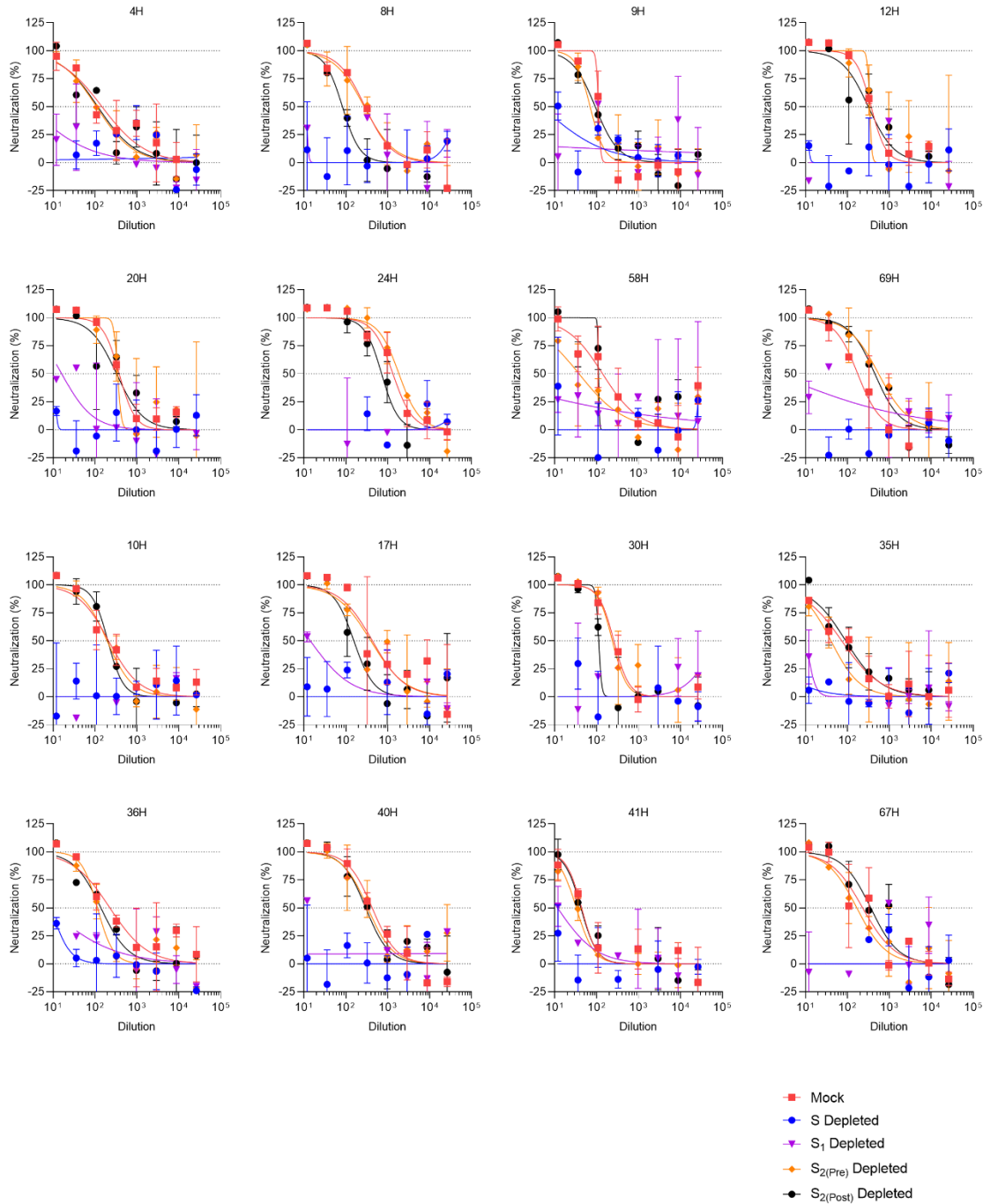
**Figure S8. Evaluation of plasma neutralizing activity in previously infected subjects before and after vaccination. A-C**, Normalized neutralization curves using SARS-CoV-2 Wuhan-Hu-1/G614 S VSV pseudovirus and TMPRSS2-overexpressing VeroE6 target cells. Samples were collected from individuals after SARS-CoV-2 infection (Wuhan-Hu-1-like strain) and vaccination with two doses of BNT162b2 (A), one dose of Ad26.COV2.S (B), or two doses of AZD1222 (C). Patient demographics can be found in Table S2. Points are the means of two-four replicates using the same pseudovirus and error bars are the geometric standard deviations. Curves are representative of at least two experimental replicates consisting of different batches of pseudovirus.



**Figure S9. A-B,** Correlation between NTD plasma IgG binding titers (A) or RBD plasma IgG binding titers (B) and neutralization titers. Binding AUCs were taken on log-transformed data and neutralization titers were log transformed before fitting to linear regression. The black shaded regions represent 95% confidence intervals.

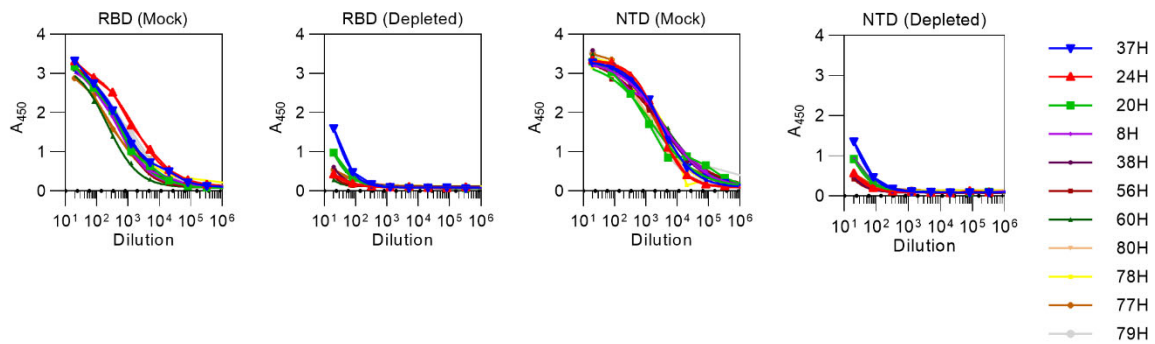


**Figure S10. Analysis of antibody binding titers in vaccinee plasma before or after antigen-specific depletion by ELISA.** Dose-response curves of plasma IgG binding to SARS-CoV-2 S, the S<sub>1</sub> subunit, or the S<sub>2</sub> subunit in the prefusion or postfusion conformation following mock depletion or depletion with each of these antigens. Samples were collected from individuals vaccinated with two doses of mRNA-1273 or BNT162b2. Curves are representative of at least two experimental replicates consisting of different batches of antigens and each color corresponds to one vaccinee.



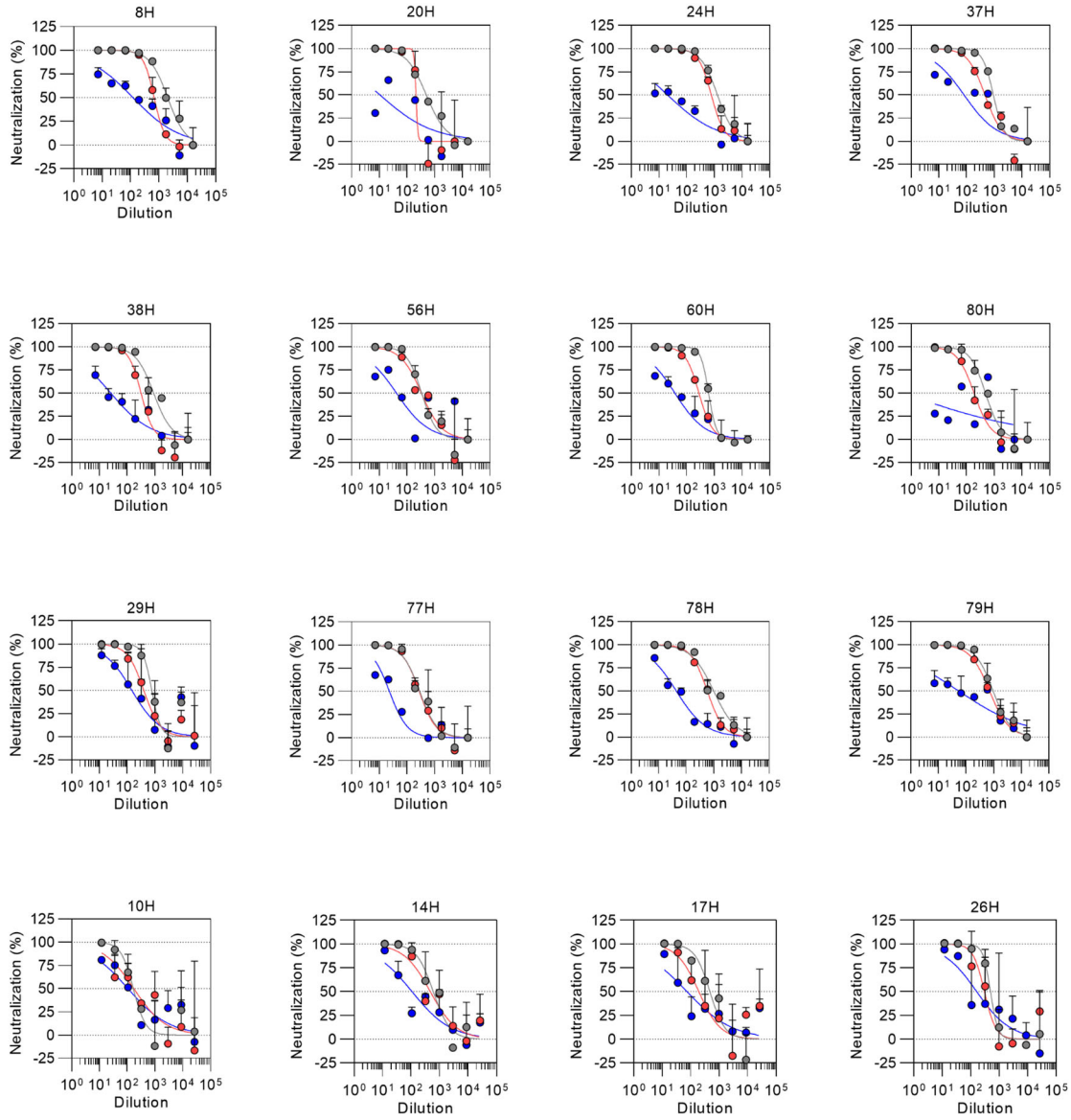
**Figure S11. Evaluation of plasma neutralizing activity in vaccinee plasma before or after antigen-specific depletion.** Normalized neutralization curves using SARS-CoV-2 Wuhan-Hu-1/G614 S VSV pseudovirus using VeroE6-TMPRSS2 target cells following mock depletion or depletion with S, the S<sub>1</sub> subunit, or the S<sub>2</sub> subunit in the prefusion or postfusion conformation. Samples were collected from individuals vaccinated with two doses of mRNA-1273 or BNT162b2. Patient demographics can be found in Table S2. Individual points are the mean of duplicates using the same antigen and error bars are the standard deviation of those duplicates. Curves are

representative of at least two experimental replicates consisting of different batches of antigens and pseudoviruses.



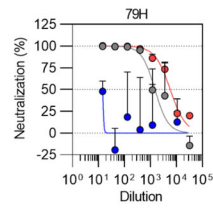
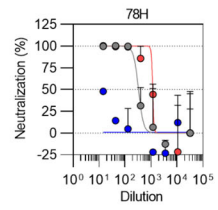
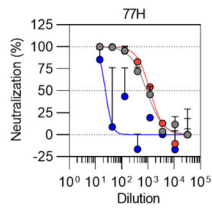
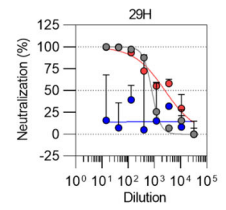
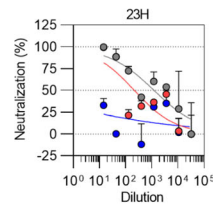
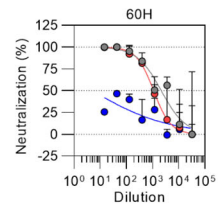
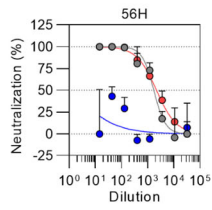
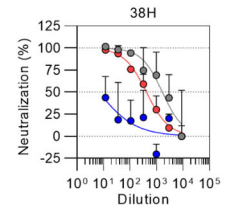
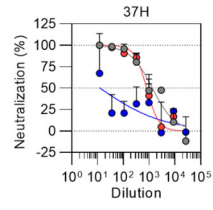
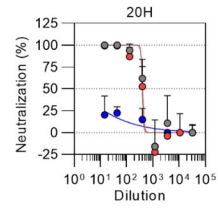
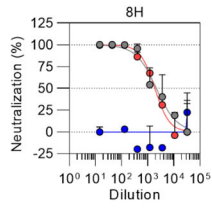
**Figure S12. Analysis of antibody binding titers in vaccinee plasma before or after antigen-specific depletion by ELISA.** Dose-response curves of plasma IgG binding to the RBD or the NTD following mock, RBD, or NTD depletion. Samples were collected from individuals vaccinated with two doses of mRNA-1273 or BNT162b12. Patient demographics can be found in Table S2. Curves are representative of at least two experimental replicates consisting of different batches of antigen and each color corresponds to one vaccinee.

# A G614

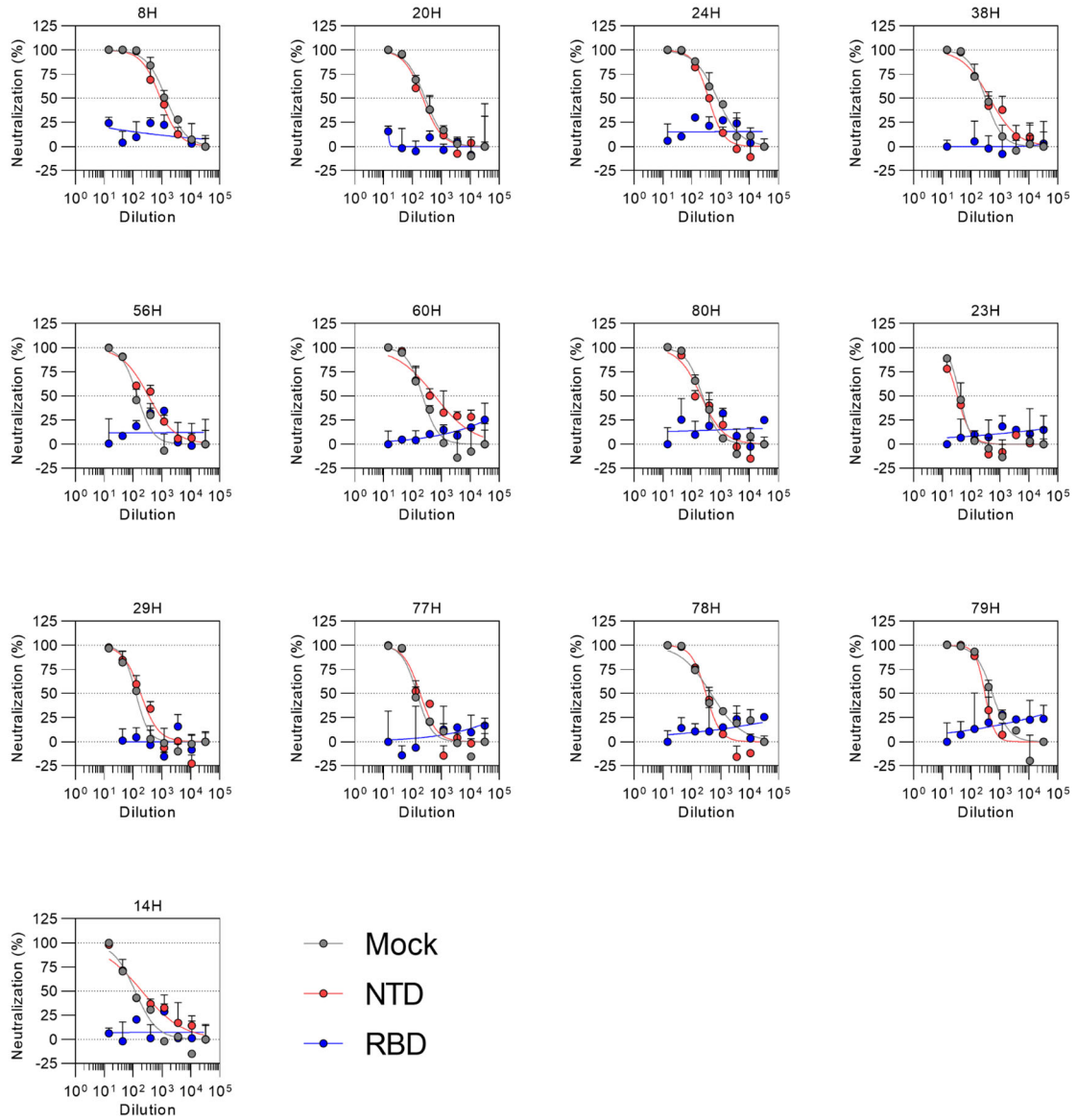




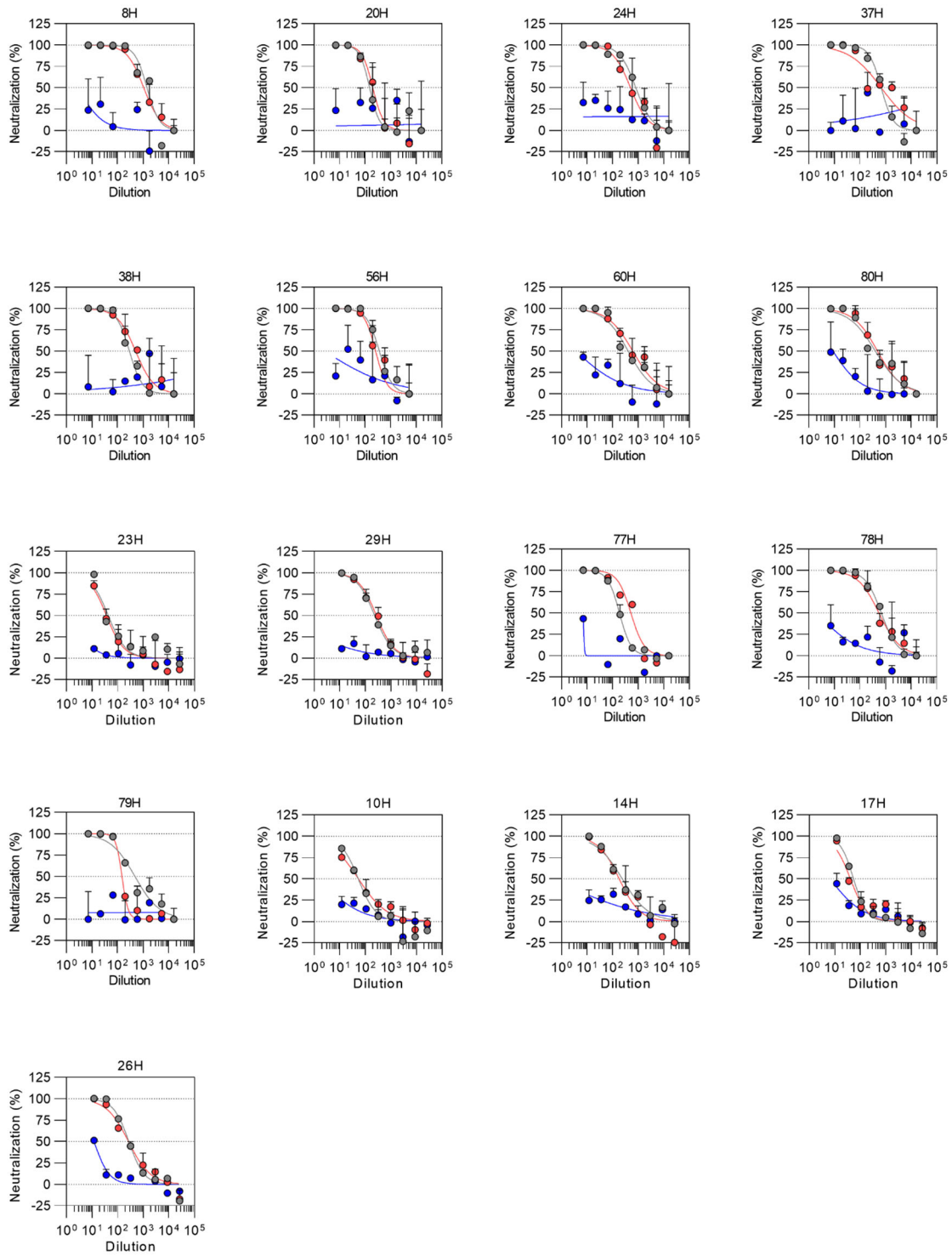
## B Alpha



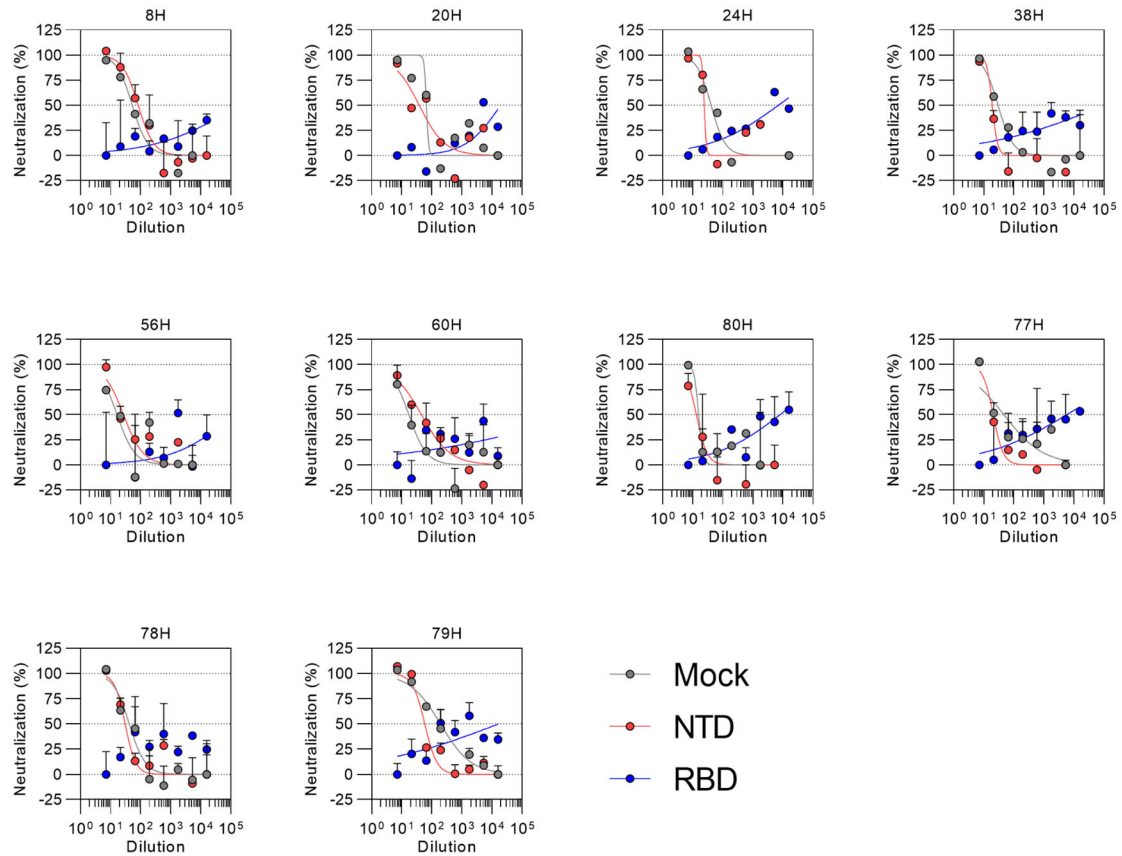
### C Beta



## D Delta



## E Omicron BA.1



**Figure S13. Evaluation of vaccine-elicited plasma neutralizing activity against SARS-CoV-2 variants before and after antigen-specific depletion.** Normalized neutralization curves using SARS-CoV-2 Wuhan-Hu-1/G614 S, Alpha S, Beta S, Delta S, or Omicron BA.1 S VSV pseudoviruses using VeroE6-TMPRSS2 target cells following mock depletion or depletion with the Wuhan-Hu-1 RBD or NTD. Samples were collected from individuals vaccinated with two doses of mRNA-1273 or BNT162b12 and each color corresponds to one vaccinee. Individual points are the mean of duplicates and error bars (top only) are the standard deviation of those duplicates. Each graph is representative of at least two experimental replicates consisting of different batches of pseudoviruses. Patient demographics can be found in Table S2.

**Table S1.** CryoEM data collection and refinement statistics.

	Prefusion SARS-CoV-2 spike S <sub>2</sub> subunit PDB 8DYA EMD-27779
<u>Data collection and processing</u>	
Magnification	105,000
Voltage (kV)	300
Electron exposure (e <sup>-</sup> /Å <sup>2</sup> )	60
Defocus range (µm)	-0.5 - -2.5
Pixel size (Å)	0.843
Symmetry imposed	C3
Final particle images (no.)	137,737
Map resolution (Å)	3.7
FSC threshold	0.143
Map sharpening <i>B</i> factor (Å <sup>2</sup> )	-161
<u>Model building and refinement</u>	
MolProbity score	1.23
Clashscore	1.82
Poor rotamers (%)	0.29
Ramachandran plot	
Favored (%)	95.80
Allowed (%)	3.68
Disallowed (%)	0.52

**Table S2.** Demographics data of enrolled plasma donors. The days since last vaccine dose for NVX-CoV2373 is unknown due to the double-blinded nature of the clinical trial. Subjects received their second vaccine dose on one date and their second placebo dose on another date. The time interval since last vaccine dose for both dates are listed.

<b>Vaccine</b>	<b>Sample</b>	<b>Age</b>	<b>Sex</b>	<b>Days Since Symptom Onset or Last Vaccine Dose</b>
<b>1x Infected</b>	10C	31	F	31
	114C	54	F	41
	13	54	M	32
	135C	43	M	49
	144C	30	M	48
	149C	25	M	40
	151	67	M	-
	151C	69	F	41
	157	42	F	-
	159	37	F	-
	182C	75	M	78
	200C	61	M	42
	21C	36	F	26
	235C	65	M	31
	224C	57	F	68
	28C	64	F	42
	30C	60	F	35
	32C	36	M	30
	54C	37	M	36
	57C	56	F	35

	60	36	M	-
	61	33	F	-
	65C	73	M	42
	73C	60	M	49
	75	24	F	-
	86	22	M	-
	98C	33	M	38
	9C	37	F	41
<b>2x mRNA-1273</b>	12H	42	F	10
	136040	40	M	20
	136049	26	F	18
	136052	47	M	21
	20H	33	F	6
	24H	24	M	7
	27H	59	M	11
	4H	23	M	6
	58H	50	F	15
	60H	42	F	8
	69H	68	F	13
	80H	35	F	50
	8H	79	M	11
	9H	75	F	7
<b>2x BNT162b2</b>	10H	33	M	14
	15H	52	M	9
	16H	46	F	6

	17H	76	M	17
	29H	64	M	12
	30H	61	F	10
	35H	60	M	33
	36H	37	M	9
	40H	38	F	13
	41H	36	F	13
	67H	40	F	13
	77H	28	F	14
	78H	22	M	15
	79H	27	F	20
<b>2x NXV-CoV2373</b>	6082.2	21	M	103
	6085.1	36	M	17 or 92
	6090.2	36	F	55
	6094.1	46	F	22 or 127
	6096.2	18	M	155
	6097.2	18	M	78
	6099.2	20	M	69 or 156
	6259.1	42	F	67
	6261.1	60	M	191
	6322.2	41	F	168
<b>2x Ad26.COVS.S</b>	0884-00033A00-001	38	M	14
	0884-00034J00-001	72	F	14
	0884-00036K00-001	43	F	12



	0884-0003WD00-001	54	M	13
	0889-0002SD00-001	43	M	14
	0889-0004FG00-001	28	F	16
	0889-0004KC00-001	36	F	13
	0889-0004WJ00-001	48	F	14
	0897-0001SB00-001	41	F	15
	0932-00064B00-001	60	F	13
	0933-0004FG00-001	51	M	14
	0933-0004KC00-001	26	F	14
<b>2x AZD1222</b>	38	29	F	30
	40	51	F	30
	41	39	F	30
	43	47	M	30
	45	48	F	30
	47	31	F	30
	48	37	F	30
	49	36	F	30
	51	29	F	30
	52	46	M	30
	53	37	F	30
	54	29	F	30
	56	45	F	30
	57	45	F	30
	58	28	F	30
	1	-	-	60-90

<b>2x Sputnik V</b>	10	-	-	60-90
	11	-	-	60-90
	12	-	-	60-90
	13	-	-	60-90
	14	-	-	60-90
	16	-	-	60-90
	3	-	-	60-90
	4	-	-	60-90
	5	-	-	60-90
	6	-	-	60-90
	7	-	-	60-90
	8	-	-	60-90
	9	-	-	60-90
	<b>2x BBIBP-CorV</b>	1	47	F
10		27	M	84
11		28	F	102
12		36	M	22
13		26	F	102
14		26	F	100
16		39	M	97
4		25	F	74
5		26	F	71
6		34	F	82
7		29	M	76
8		34	F	15

	9	33	F	15
<b>1x Infected, 2x BNT162b2</b>	10C	31	F	10
	114C	54	F	31
	144C	30	M	12
	149C	25	M	10
	151C	69	F	15
	182C	75	M	10
	28C	64	F	21
	30C	60	F	11
	54C	37	M	10
	65C	73	M	15
	73C	60	M	32
	9C	37	F	13
	<b>1x Infected, 1x Ad26.COVS</b>	13	54	M
135C		43	M	19
200C		61	M	42
21C		36	F	18
224C		57	F	112
32C		36	M	18
57C		56	F	17
98C		33	M	12
<b>1x Infected, 2x AZD1222</b>	61	33	F	30
	75	24	F	30
	86	22	M	30

**Table S3.** Analysis of statistical significance of differences observed for infection and vaccine-elicited antibody binding titers compared by vaccine, separated by antigen, and determined by Turkey's multiple comparisons test. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, and \*\*\*\*P < 0.0001. ns: non-significant

<b>S</b>	<b>mRNA-1273</b>	<b>BNT162b2</b>	<b>NVXCoV2373</b>	<b>Ad26COV2S</b>	<b>AZD1222</b>	<b>Sputnik V</b>	<b>BBIBP-CorV</b>
<b>Infected</b>	****	****	ns	ns	***	ns	ns
<b>mRNA-1273</b>		ns	****	***	ns	****	***
<b>BNT162b2</b>			***	*	ns	**	*
<b>NVXCoV2373</b>				ns	ns	ns	ns
<b>Ad26COV2S</b>					ns	ns	ns
<b>AZD1222</b>						ns	ns
<b>Sputnik V</b>							ns
<b>S<sub>1</sub></b>	<b>mRNA-1273</b>	<b>BNT162b2</b>	<b>NVXCoV2373</b>	<b>Ad26COV2S</b>	<b>AZD1222</b>	<b>Sputnik V</b>	<b>BBIBP-CorV</b>
<b>Infected</b>	****	****	ns	*	****	ns	ns
<b>mRNA-1273</b>		ns	****	****	ns	****	****
<b>BNT162b2</b>			**	**	ns	***	***
<b>NVXCoV2373</b>				ns	ns	ns	ns
<b>Ad26COV2S</b>					ns	ns	ns
<b>AZD1222</b>						ns	ns
<b>Sputnik V</b>							ns
<b>S<sub>2</sub>(Pre)</b>	<b>mRNA-1273</b>	<b>BNT162b2</b>	<b>NVXCoV2373</b>	<b>Ad26COV2S</b>	<b>AZD1222</b>	<b>Sputnik V</b>	<b>BBIBP-CorV</b>
<b>Infected</b>	**	ns	ns	ns	ns	ns	ns
<b>mRNA-1273</b>		ns	****	ns	*	***	ns
<b>BNT162b2</b>			****	ns	ns	*	ns
<b>NVXCoV2373</b>				ns	ns	ns	ns
<b>Ad26COV2S</b>					ns	ns	ns
<b>AZD1222</b>						ns	ns
<b>Sputnik V</b>							ns
<b>S<sub>2</sub>(Post)</b>	<b>mRNA-1273</b>	<b>BNT162b2</b>	<b>NVXCoV2373</b>	<b>Ad26COV2S</b>	<b>AZD1222</b>	<b>Sputnik V</b>	<b>BBIBP-CorV</b>
<b>Infected</b>	ns	*	****	**	ns	ns	ns
<b>mRNA-1273</b>		ns	ns	ns	ns	ns	ns
<b>BNT162b2</b>			ns	ns	ns	ns	***
<b>NVXCoV2373</b>				ns	ns	ns	****
<b>Ad26COV2S</b>					ns	ns	****
<b>AZD1222</b>						ns	*
<b>Sputnik V</b>							*
<b>NTD</b>	<b>mRNA-1273</b>	<b>BNT162b2</b>	<b>NVXCoV2373</b>	<b>Ad26COV2S</b>	<b>AZD1222</b>	<b>Sputnik V</b>	<b>BBIBP-CorV</b>
<b>Infected</b>	****	****	ns	ns	**	ns	ns
<b>mRNA-1273</b>		ns	****	****	****	****	****
<b>BNT162b2</b>			****	****	**	****	****
<b>NVXCoV2373</b>				ns	ns	ns	ns
<b>Ad26COV2S</b>					ns	ns	ns
<b>AZD1222</b>						ns	ns
<b>Sputnik V</b>							ns
<b>RBD</b>	<b>mRNA-1273</b>	<b>BNT162b2</b>	<b>NVXCoV2373</b>	<b>Ad26COV2S</b>	<b>AZD1222</b>	<b>Sputnik V</b>	<b>BBIBP-CorV</b>
<b>Infected</b>	****	***	ns	ns	ns	ns	ns
<b>mRNA-1273</b>		ns	ns	***	*	****	****
<b>BNT162b2</b>			ns	*	ns	***	**
<b>NVXCoV2373</b>				ns	ns	*	ns
<b>Ad26COV2S</b>					ns	ns	ns
<b>AZD1222</b>						ns	ns
<b>Sputnik V</b>							ns

**Table S4.** Analysis of statistical significance of differences observed for infection and vaccine-elicited antibody binding titers compared by antigen, separated by vaccine, and determined by paired Turkey's multiple comparisons test. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, and \*\*\*\*P < 0.0001. ns: non-significant

<b>Infected</b>	<b>S<sub>1</sub></b>	<b>S<sub>2</sub>(Pre)</b>	<b>S<sub>2</sub>(Post)</b>	<b>NTD</b>	<b>RBD</b>
<b>S</b>	****	ns	ns	****	****
<b>S<sub>1</sub></b>		****	****	****	****
<b>S<sub>2</sub>(Pre)</b>			ns	****	****
<b>S<sub>2</sub>(Post)</b>				****	****
<b>NTD</b>					ns
<b>mRNA-1273</b>	<b>S<sub>1</sub></b>	<b>S<sub>2</sub>(Pre)</b>	<b>S<sub>2</sub>(Post)</b>	<b>NTD</b>	<b>RBD</b>
<b>S</b>	ns	****	****	****	****
<b>S<sub>1</sub></b>		***	****	****	****
<b>S<sub>2</sub>(Pre)</b>			****	ns	****
<b>S<sub>2</sub>(Post)</b>				****	**
<b>NTD</b>					****
<b>BNT162b2</b>	<b>S<sub>1</sub></b>	<b>S<sub>2</sub>(Pre)</b>	<b>S<sub>2</sub>(Post)</b>	<b>NTD</b>	<b>RBD</b>
<b>S</b>	*	****	****	****	****
<b>S<sub>1</sub></b>		****	****	****	****
<b>S<sub>2</sub>(Pre)</b>			****	**	****
<b>S<sub>2</sub>(Post)</b>				***	ns
<b>NTD</b>					***
<b>NVX-CoV2373</b>	<b>S<sub>1</sub></b>	<b>S<sub>2</sub>(Pre)</b>	<b>S<sub>2</sub>(Post)</b>	<b>NTD</b>	<b>RBD</b>
<b>S</b>	ns	***	***	****	***
<b>S<sub>1</sub></b>		**	**	****	***
<b>S<sub>2</sub>(Pre)</b>			ns	ns	ns
<b>S<sub>2</sub>(Post)</b>				ns	ns
<b>NTD</b>					ns
<b>Ad26.COVS.S</b>	<b>S<sub>1</sub></b>	<b>S<sub>2</sub>(Pre)</b>	<b>S<sub>2</sub>(Post)</b>	<b>NTD</b>	<b>RBD</b>
<b>S</b>	**	**	****	****	****
<b>S<sub>1</sub></b>		ns	****	****	****
<b>S<sub>2</sub>(Pre)</b>			****	****	****
<b>S<sub>2</sub>(Post)</b>				ns	**
<b>NTD</b>					**
<b>AZD1222</b>	<b>S<sub>1</sub></b>	<b>S<sub>2</sub>(Pre)</b>	<b>S<sub>2</sub>(Post)</b>	<b>NTD</b>	<b>RBD</b>
<b>S</b>	ns	****	****	****	****
<b>S<sub>1</sub></b>		****	****	****	****
<b>S<sub>2</sub>(Pre)</b>			ns	*	****
<b>S<sub>2</sub>(Post)</b>				ns	***
<b>NTD</b>					**
<b>Sputnik V</b>	<b>S<sub>1</sub></b>	<b>S<sub>2</sub>(Pre)</b>	<b>S<sub>2</sub>(Post)</b>	<b>NTD</b>	<b>RBD</b>
<b>S</b>	**	**	**	****	****
<b>S<sub>1</sub></b>		ns	ns	****	****
<b>S<sub>2</sub>(Pre)</b>			ns	*	***
<b>S<sub>2</sub>(Post)</b>				ns	**
<b>NTD</b>					**
<b>BBIBP-CorV</b>	<b>S<sub>1</sub></b>	<b>S<sub>2</sub>(Pre)</b>	<b>S<sub>2</sub>(Post)</b>	<b>NTD</b>	<b>RBD</b>
<b>S</b>	***	*	ns	****	****
<b>S<sub>1</sub></b>		ns	ns	****	****
<b>S<sub>2</sub>(Pre)</b>			ns	****	****
<b>S<sub>2</sub>(Post)</b>				****	****
<b>NTD</b>					ns

**Table S5.** Analysis of statistical significance of differences observed for infection and vaccine-elicited antibody binding ratios compared by vaccine, separated by antigen, and determined by Turkey's multiple comparisons test. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, and \*\*\*\*P < 0.0001. ns: non-significant

<b>S/S<sub>2</sub>(Post)</b>	<b>mRNA-1273</b>	<b>BNT162b2</b>	<b>NVXCoV2373</b>	<b>Ad26COV2S</b>	<b>AZD1222</b>	<b>Sputnik V</b>	<b>BBIBP-CorV</b>
<b>Infected</b>	****	****	****	****	****	***	ns
<b>mRNA-1273</b>		ns	ns	ns	ns	ns	****
<b>BNT162b2</b>			ns	ns	*	**	****
<b>NVXCoV2373</b>				ns	ns	*	****
<b>Ad26COV2S</b>					ns	ns	****
<b>AZD1222</b>						ns	***
<b>Sputnik V</b>							**
<b>S<sub>1</sub>/S<sub>2</sub>(Post)</b>	<b>mRNA-1273</b>	<b>BNT162b2</b>	<b>NVXCoV2373</b>	<b>Ad26COV2S</b>	<b>AZD1222</b>	<b>Sputnik V</b>	<b>BBIBP-CorV</b>
<b>Infected</b>	****	****	****	****	****	****	ns
<b>mRNA-1273</b>		ns	ns	ns	ns	ns	****
<b>BNT162b2</b>			ns	ns	*	***	****
<b>NVXCoV2373</b>				ns	*	***	****
<b>Ad26COV2S</b>					ns	ns	****
<b>AZD1222</b>						ns	***
<b>Sputnik V</b>							*
<b>S<sub>2</sub>(Pre)/S<sub>2</sub>(Post)</b>	<b>mRNA-1273</b>	<b>BNT162b2</b>	<b>NVXCoV2373</b>	<b>Ad26COV2S</b>	<b>AZD1222</b>	<b>Sputnik V</b>	<b>BBIBP-CorV</b>
<b>Infected</b>	****	****	*	****	ns	ns	ns
<b>mRNA-1273</b>		*	ns	ns	*	ns	****
<b>BNT162b2</b>			***	ns	****	****	****
<b>NVXCoV2373</b>				ns	ns	ns	ns
<b>Ad26COV2S</b>					**	**	****
<b>AZD1222</b>						ns	ns
<b>Sputnik V</b>							ns

**Table S6.** Analysis of statistical significance of differences observed for infection and vaccine-elicited antibody binding titers compared by antigen, separated by vaccine, and determined by paired Turkey's multiple comparisons test. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, and \*\*\*\*P < 0.0001. ns: non-significant

<b>Infected, BNT162b2</b>	<b>S<sub>1</sub></b>	<b>S<sub>2</sub>(Pre)</b>	<b>S<sub>2</sub>(Post)</b>
<b>S</b>	****	**	****
<b>S<sub>1</sub></b>		ns	****
<b>S<sub>2</sub>(Pre)</b>			****
<b>Infected, Ad26.COV2.S</b>	<b>S<sub>1</sub></b>	<b>S<sub>2</sub>(Pre)</b>	<b>S<sub>2</sub>(Post)</b>
<b>S</b>	**	*	****
<b>S<sub>1</sub></b>		ns	***
<b>S<sub>2</sub>(Pre)</b>			**
<b>Infected, AZD1222</b>	<b>S<sub>1</sub></b>	<b>S<sub>2</sub>(Pre)</b>	<b>S<sub>2</sub>(Post)</b>
<b>S</b>	ns	ns	ns
<b>S<sub>1</sub></b>		ns	ns
<b>S<sub>2</sub>(Pre)</b>			ns

**Table S7.** Analysis of statistical significance of differences observed for antibody binding titers in previously infected individuals elicited before and after vaccination compared by antigen, separated by vaccine, and determined by paired Turkey's multiple comparisons test. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, and \*\*\*\*P < 0.0001. ns: non-significant

<b>Infected, 2x BNT162b2</b>	
<b>S</b>	****
<b>S<sub>1</sub></b>	****
<b>S<sub>2</sub>(Pre)</b>	****
<b>S<sub>2</sub>(Post)</b>	*
<b>Infected, 1x Ad26.COVS.2</b>	
<b>S</b>	***
<b>S<sub>1</sub></b>	***
<b>S<sub>2</sub>(Pre)</b>	***
<b>S<sub>2</sub>(Post)</b>	ns
<b>Infected, 2x AZD1222</b>	
<b>S</b>	ns
<b>S<sub>1</sub></b>	ns
<b>S<sub>2</sub>(Pre)</b>	ns
<b>S<sub>2</sub>(Post)</b>	ns

**Table S8.** Analysis of statistical significance of differences observed for infection and vaccine-elicited antibody neutralizing titers. Determined by Turkey's multiple comparisons test. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, and \*\*\*\*P < 0.0001. ns: non-significant

<b>Neut.</b>	<b>mRNA-1273</b>	<b>BNT162b2</b>	<b>NVXCoV2373</b>	<b>Ad26COVS.2</b>	<b>AZD1222</b>	<b>Sputnik V</b>	<b>BBIBP-CorV</b>
<b>Infected</b>	****	*	ns	ns	ns	ns	ns
<b>mRNA-1273</b>		ns	*	**	**	***	**
<b>BNT162b2</b>			ns	ns	ns	ns	ns
<b>NVXCoV2373</b>				ns	ns	ns	ns
<b>Ad26COVS.2</b>					ns	ns	ns
<b>AZD1222</b>						ns	ns
<b>Sputnik V</b>							ns

**Table S9.** Analysis of statistical significance of differences observed for infection and vaccine-elicited antibody neutralizing titers in previously infected individuals. Determined by Turkey's multiple comparisons test. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, and \*\*\*\*P < 0.0001. ns: non-significant

<b>Neutralization</b>	<b>Ad26.COVS.2</b>	<b>AZD1222</b>
<b>BNT162b2</b>	*	ns
<b>Ad26.COVS.2</b>		ns