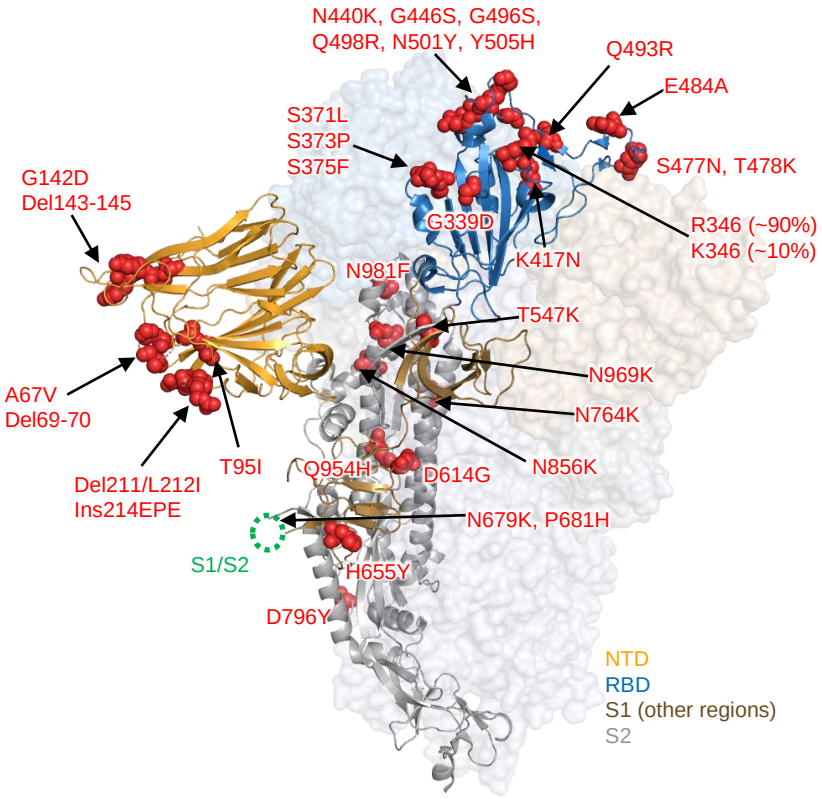
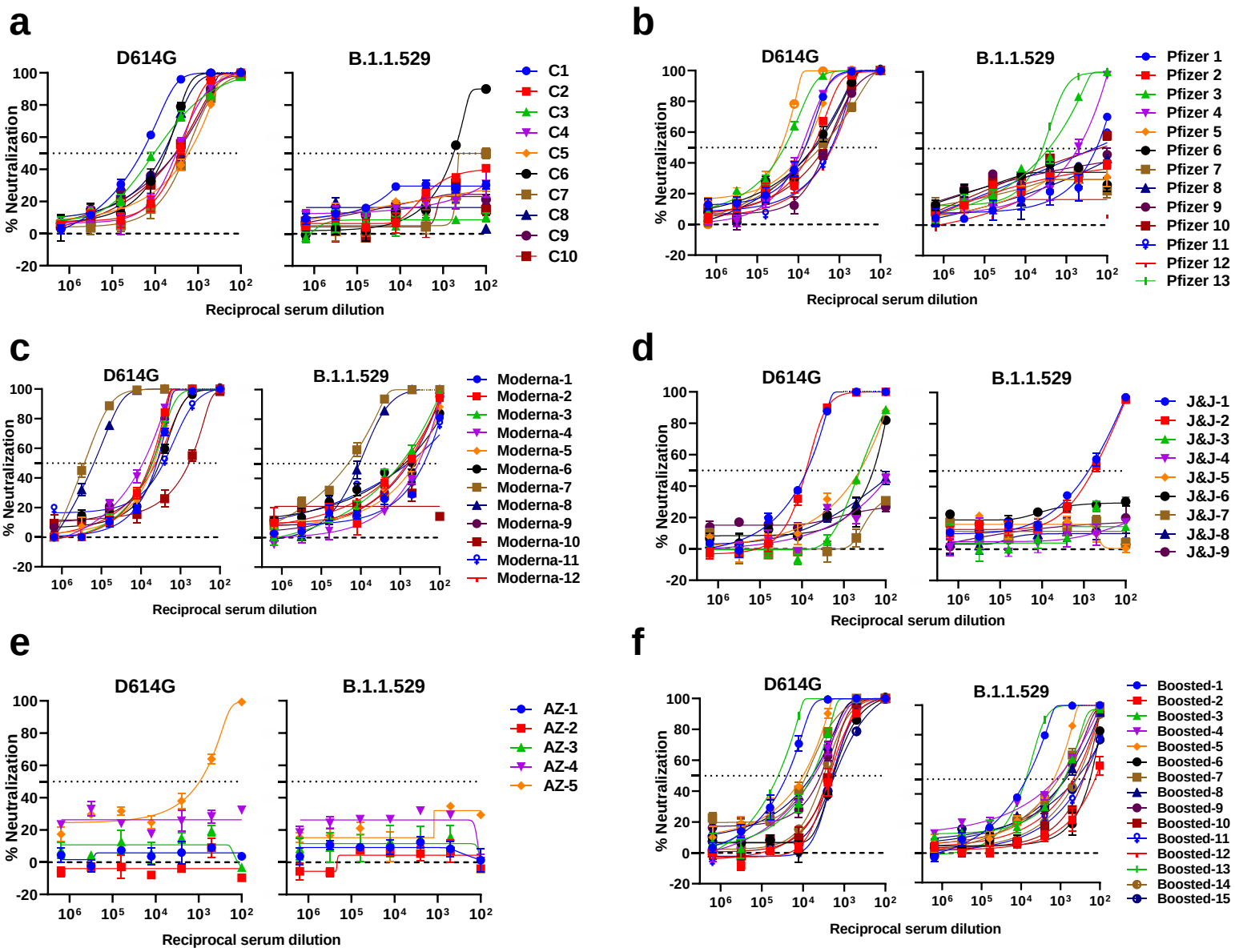
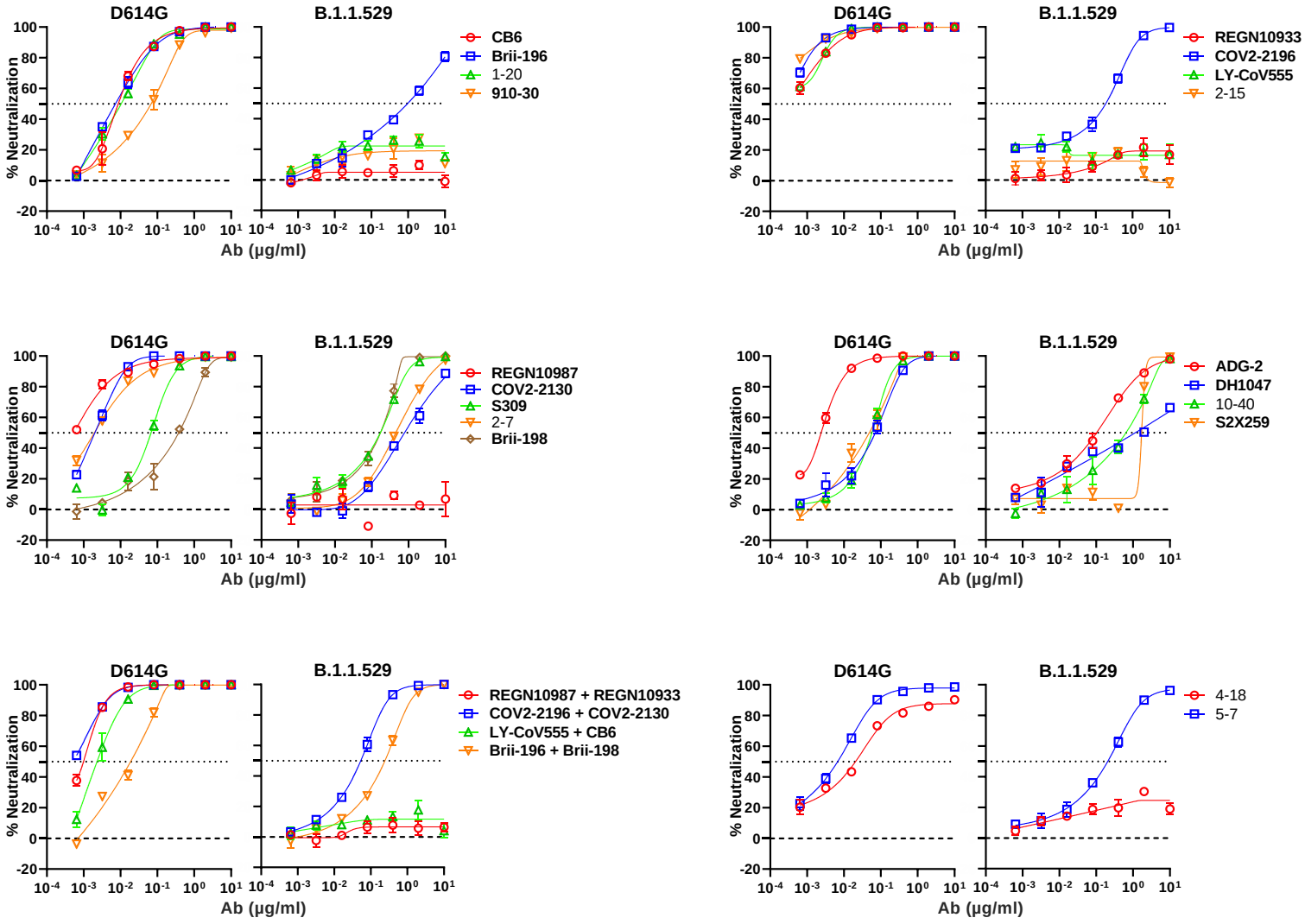


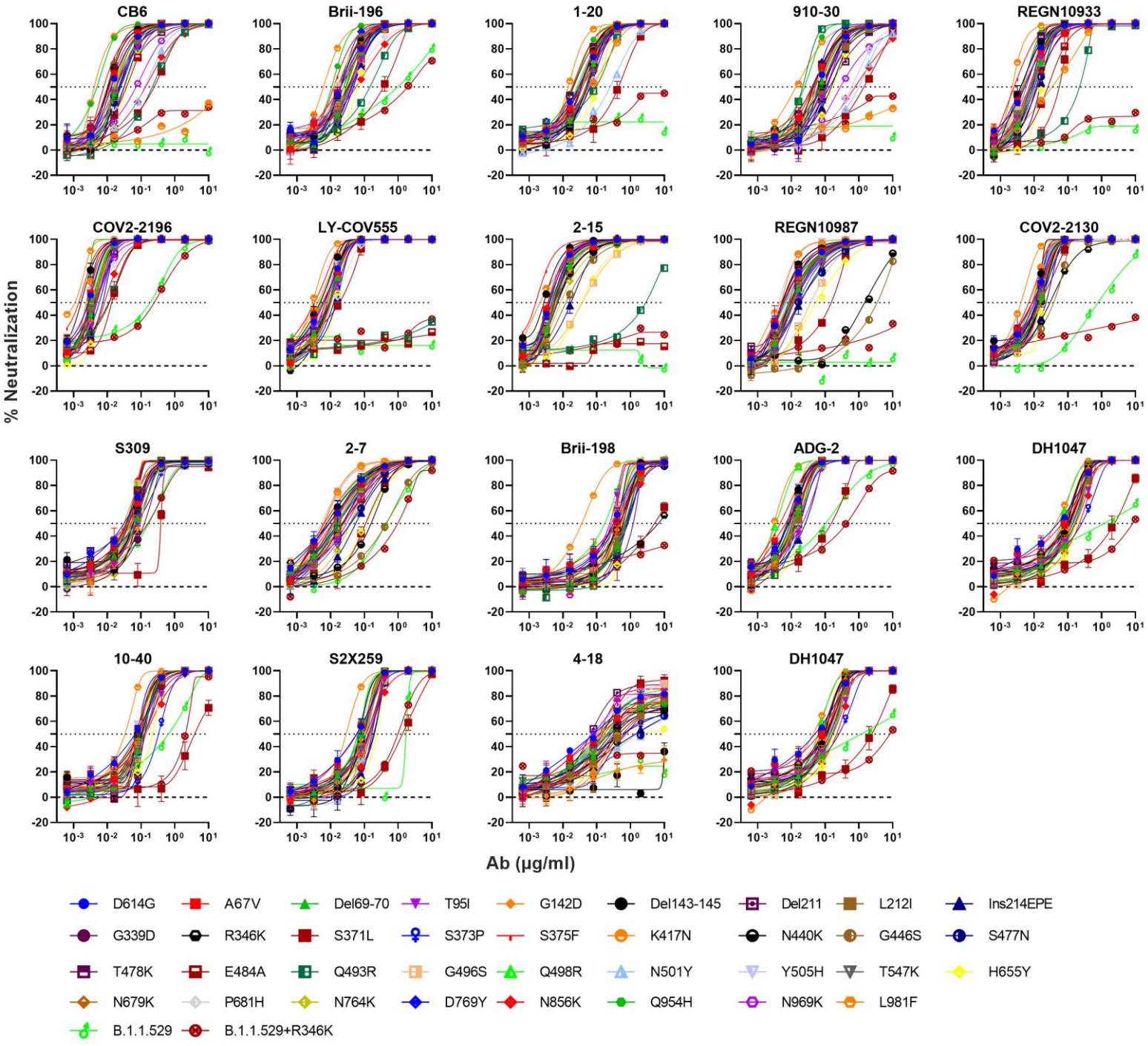
Extended Data Fig. 1. Mutations within B.1.1.529 denoted on the full SARS-CoV-2 spike trimer (PDB: 6zge).



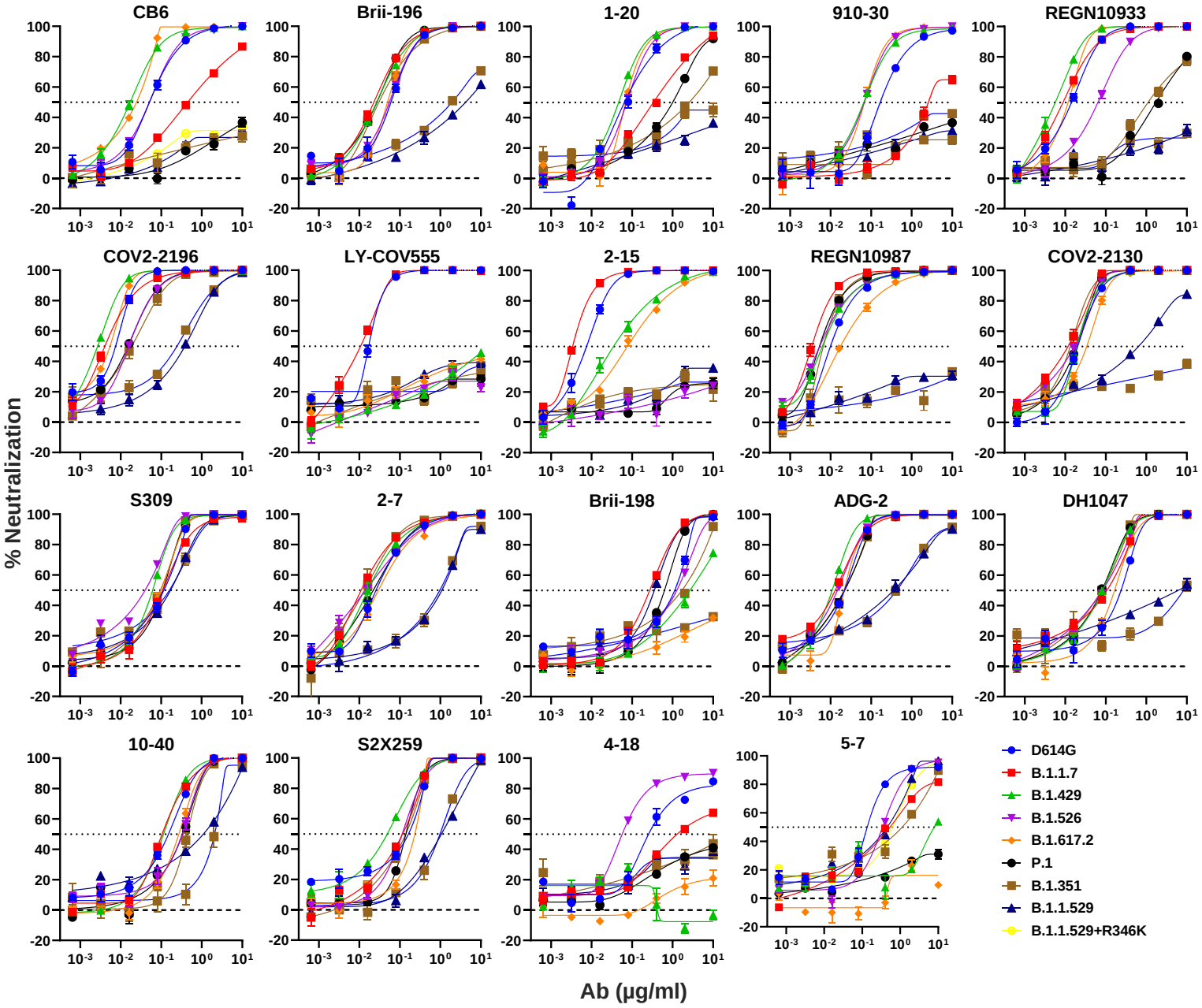
Extended Data Fig. 2. Individual neutralization curves for pseudovirus neutralization assays by serum. Neutralization by **a,** convalescent sera. **b,** Pfizer (BNT162b2) vaccinee sera. **c,** Moderna (mRNA-1273) vaccinee sera. **d,** J&J (Ad26.COV2.S) vaccinee sera. **e,** AstraZeneca (ChAdOx1 nCoV-19) vaccinee sera. **f,** boosted (three homologous BNT162b2 or mRNA-1273 vaccinations) vaccinee sera.



Extended Data Fig. 3. Individual neutralization curves for pseudovirus neutralization assays by monoclonal antibodies.



Extended Data Fig. 4. Individual neutralization curves for pseudovirus neutralization assays by monoclonal antibodies against individual SARS-CoV-2 mutations.



Extended Data Fig. 5. Individual neutralization curves for pseudovirus neutralization assays by monoclonal antibodies against SARS-CoV-2 variants.

Extended Data Table 1. Demographics and vaccination information for serum samples from convalescent patients used in this study.

Convalescent Sample	Days post-symptoms	Age	Gender
C1	18	57	Female
C2	25	51	Male
C3	29	71	Female
C4	32	50	Male
C5	35	59	Male
C6	120	56	Male
C7	105	54	Female
C8	77	51	Female
C9	18	79	Male
C10	9	45	Male

Extended Data Table 2. Demographics and vaccination information for serum samples from vaccinated individuals used in this study.

Vaccine Sample	Vaccine type	Days post-vaccination (after last dose)	Documented COVID Infection	Age	Gender
Moderna vaccinee #1	mRNA-1273	31	No	72	Male
Moderna vaccinee #2	mRNA-1273	19	No	38	Female
Moderna vaccinee #3	mRNA-1273	6	No	42	Male
Moderna vaccinee #4	mRNA-1273	81	No	40	Female
Moderna vaccinee #5	mRNA-1273	123	No	40	Female
Moderna vaccinee #6	mRNA-1273	177	No	40	Female
Moderna vaccinee #7	mRNA-1273	29	No	57	Female
Moderna vaccinee #8	mRNA-1273	74	No	57	Female
Moderna vaccinee #9	mRNA-1273	32	No	66	Female
Moderna vaccinee #10	mRNA-1273	72	No	63	Male
Moderna vaccinee #11	mRNA-1273	74	No	68	Female
Moderna vaccinee #12	mRNA-1273	58	No	46	Female
Pfizer vaccinee #1	BNT162b2	21	No	62	Male
Pfizer vaccinee #2	BNT162b2	36	No	62	Male
Pfizer vaccinee #3	BNT162b2	26	No	38	Male
Pfizer vaccinee #4	BNT162b2	66	No	38	Male
Pfizer vaccinee #5	BNT162b2	22	No	57	Female
Pfizer vaccinee #6	BNT162b2	61	No	57	Female
Pfizer vaccinee #7	BNT162b2	20	No	55	Male
Pfizer vaccinee #8	BNT162b2	16	No	64	Female
Pfizer vaccinee #9	BNT162b2	32	No	68	Male
Pfizer vaccinee #10	BNT162b2	20	No	35	Male
Pfizer vaccinee #11	BNT162b2	15	No	48	Female
Pfizer vaccinee #12	BNT162b2	21	No	45	Male
Pfizer vaccinee #13	BNT162b2	213	Yes	66	Male
J&J vaccinee #1 (BEI Cat. #NRH-10818)	Ad26.COV2.S	55	Yes	50	Female
J&J vaccinee #2 (BEI Cat. #NRH-10819)	Ad26.COV2.S	61	Yes	50	Female
J&J vaccinee #3 (BEI Cat. #NRH-10835)	Ad26.COV2.S	186	Unknown	43	Female
J&J vaccinee #4 (BEI Cat. #NRH-10845)	Ad26.COV2.S	69	Unknown	28	Female
J&J vaccinee #5 (BEI Cat. #NRH-10823)	Ad26.COV2.S	50	No	42	Female
J&J vaccinee #6 (BEI Cat. #NRH-10834)	Ad26.COV2.S	175	Unknown	43	Female
J&J vaccinee #7 (BEI Cat. #NRH-10839)	Ad26.COV2.S	39	No	47	Male
J&J vaccinee #8 (BEI Cat. #NRH-10844)	Ad26.COV2.S	60	Unknown	28	Female
J&J vaccinee #9 (BEI Cat. #NRH-10824)	Ad26.COV2.S	51	No	43	Male
AZ vaccinee #1 (BEI Cat. #NRH-10817)	ChAdOx1 nCoV-19	158	Unknown	73	Male
AZ vaccinee #2 (BEI Cat. #NRH-10814)	ChAdOx1 nCoV-19	152	Unknown	36	Female
AZ vaccinee #3 (BEI Cat. #NRH-10815)	ChAdOx1 nCoV-19	159	Unknown	36	Female
AZ vaccinee #4 (BEI Cat. #NRH-10811)	ChAdOx1 nCoV-19	142	Yes	26	Female
AZ vaccinee #5 (BEI Cat. #NRH-3083)	ChAdOx1 nCoV-19	91	Unknown	56	Female

Extended Data Table 2 (continued). Demographics and vaccination information for serum samples from vaccinated individuals used in this study.

Boosted Sample	Vaccine/boost type	Days post-boost (after last dose)	Documented COVID Infection	Age	Gender
Boosted sera #1	mRNA-1273/mRNA-1273	28	No	66	Female
Boosted sera #2	BNT162b2/BNT162b2	30	No	68	Male
Boosted sera #3	BNT162b2/BNT162b2	14	No	64	Female
Boosted sera #4	BNT162b2/BNT162b2	34	No	55	Male
Boosted sera #5	BNT162b2/BNT162b2	34	No	45	Male
Boosted sera #6	BNT162b2/BNT162b2	15	No	50	Female
Boosted sera #7	BNT162b2/BNT162b2	15	No	48	Female
Boosted sera #8	BNT162b2/BNT162b2	29	No	71	Male
Boosted sera #9	BNT162b2/BNT162b2	90	No	59	Male
Boosted sera #10	BNT162b2/BNT162b2	33	No	45	Male
Boosted sera #11	BNT162b2/BNT162b2	87	No	66	Female
Boosted sera #12	BNT162b2/BNT162b2	84	No	26	Male
Boosted sera #13	mRNA-1273/mRNA-1273	23	No	28	Female
Boosted sera #14	BNT162b2/BNT162b2	14	No	78	Male
Boosted sera #15	BNT162b2/BNT162b2	14	No	75	Female

Extended Data Table 3. Oligos used to construct spike expression plasmids.

Oligo name	Targeted mutations	Oligo sequence
O_single_mutant1	A67V	ATGTGACCTGGTTCCATGTGATCCATGTGTCTGGCACCAATGGCACC
O_single_mutant2	Del69-70	CTGGTTCCATGCCATCTCTGGCACCAATGGCAC
O_single_mutant3	T95I	CTTTGCCAGCATCGAGAAGAGCAACATCATC
O_single_mutant4	Del143-145	TGTAATGACCCATTCCTGGGACACAAGAACAACAAGTCCTGGATG
O_single_mutant5	G142D	GTAATGACCCATTCCTGGACGTCTACTACCACAAG
O_single_mutant6	Del211	ACACACACCAATCCTGGTGAGGGACCTG
O_single_mutant7	L212I	CACACCAATCAACATCGTGAGGGACCTGCC
O_single_mutant8	Ins214EPE	ACCAATCAACCTGGTGAGGGAGCCCGAGGACCTGCCACAGGGCTT
O_single_mutant9	G339D	CTGTGTCCATTTGACGAGGTGTTCAATGCCAC
O_single_mutant10	R346K	TGTTCAATGCCACCAAGTTTGCCTCTGTCTATGCCTG
O_single_mutant11	S371F	CTCTGTGCTCTACAACTTTGCCTCCTTCAGCAC
O_single_mutant12	S371L	CTCTGTGCTCTACAACCTGGCCTCCTTCAGCAC
O_single_mutant13	S373P	CTCTACAACTCTGCCCCCTTCAGCACCTTCAAG
O_single_mutant14	S375F	CAACTCTGCCTCCTTCTTCACCTTCAAGTGTTATGG
O_single_mutant15	K417N	CCCCTGGACAAACAGGCAACATTGCTGACTACAACTACAAACTGC
O_single_mutant16	N440K	CCTGGAACAGCAACAAGCTGGACAGCAAGGTG
O_single_mutant17	G446S	GGACAGCAAGGTGAGCGGCAACTACAACTAC
O_single_mutant18	S477N	GATTTACCAGGCTGGCAACACACCATGTAATG
O_single_mutant19	T478K	CAGGCTGGCAGCAAGCCATGTAATGGAGTGGA
O_single_mutant20	E484A	GTAATGGAGTGGCCGGCTTCAACTGTTAC
O_single_mutant21	Q493R	GTTACTTTCCACTCAGATCCTATGGCTTCCAAC
O_single_mutant22	G496S	CACTCCAATCCTATAGCTTCCAACCAACCAATG
O_single_mutant23	Q498R	CAATCCTATGGCTTCAGACCAACCAATGGAGTGGG
O_single_mutant24	N501Y	CTTCCAACCAACCTACGGAGTGGGCTACCAACC
O_single_mutant25	Y505H	AATGGAGTGGGCCACCAACCATACAGG
O_single_mutant26	T547K	CTTCAATGGACTGAAGGGCACAGGAGTGCTGAC
O_single_mutant27	H655Y	CTGATTGGAGCAGAGTACGTGAACAACTCCTATG
O_single_mutant28	N679K	CCAGACCCAGACCAAGAGCCCAAGGAGGGCA
O_single_mutant29	P681H	CCCAGACCAACAGCAGAAGGAGGGCAAGGTCTGTGGC
O_single_mutant30	N764K	GTACCCAACTTAAGAGGGCTCTGACAGGC
O_single_mutant31	D769Y	GACACCTCCAATCAAGTACTTTGGAGGCTTC
O_single_mutant32	N856K	GTGCCCAGAAGTTCAAGGGACTGACAGTGCTG
O_single_mutant33	Q954H	CAAGATGTGGTGAACCACAATGCCCAGGCTCTG
O_single_mutant34	N969K	GCAACTTTCCAGCAAGTTTGGAGCCATCTCCTC
O_single_mutant35	L981F	GTGCTGAATGACATCTTCAGCAGACTGGACAAGGTGGAGG
O_multiple_oligo1	A67V, Del69-70	TGGTTCCATGTGATCTCTGGCACCAATGG
O_multiple_oligo2	T95I	CTTTGCCAGCATCGAGAAGAGCAAC
O_multiple_oligo3	G142D, Del143-145	GACCCATTCCTGGACCACAAGAACAACAAGTC
O_multiple_oligo4	L212I, Ins214EPE	CACACACCAATCATCGTGAGGGAGCCCGAGGACCTGCCACAGGGCTTC
O_multiple_oligo5	G339D	TGTGTCCATTTGACGAGGTGTTCAATG
O_multiple_oligo6	S371L, S373P, S375F	TGTGCTCTACAACCTGGCCCCCTTCTTCACCTTCAAGTGTTATG
O_multiple_oligo7	K417N	GGACAAACAGGCAACATTGCTGACTACA
O_multiple_oligo8	N440K, G446S	GCAACAAGCTGGACAGCAAGGTGAGCGGCAACTACAA
O_multiple_oligo9	S477N, T478K, E484A	ACCAGGCTGGCAACAAGCCATGTAATGGAGTGGCCGGCTTCAACTGT
O_multiple_oligo10	Q493R, G496S, Q498R, N501Y, Y505H	TACTTTCCACTCAGATCCTATAGCTTCAGACCAACCTACGGAGTGGGCCACCAACCATACAGG GTGGTGGTGCTGTCCTTTGA
O_multiple_oligo11	T547K	GGACTGAAGGGCACAGGAG
O_multiple_oligo12	D614G	CTCTACCAGGGCGTGAACTGTAC
O_multiple_oligo13	H655Y	TTGGAGCAGAGTACGTGAACAACTC
O_multiple_oligo14	N679K, P681H	CAGACCAAGAGCCACAGGAGGGCAAGG
O_multiple_oligo15	N764K	CCAACTTAAGAGGGCTCTGACAG
O_multiple_oligo16	D796Y	CCTCCAATCAAGTACTTTGGAGGCTTC
O_multiple_oligo17	N856K	CAGAAGTTCAAGGGACTGACAGTGCTG
O_multiple_oligo18	Q954H	GTGGTGAACCACAATGCCCAGGCTC
O_multiple_oligo19	N969K	AACTTTCCAGCAAGTTTGGAGCCATCTCCTC
O_multiple_oligo20	L981F	AATGACATCTTCAGCAGACTGGACAAGGTGGAGGCTGAGGTCCAGATTG