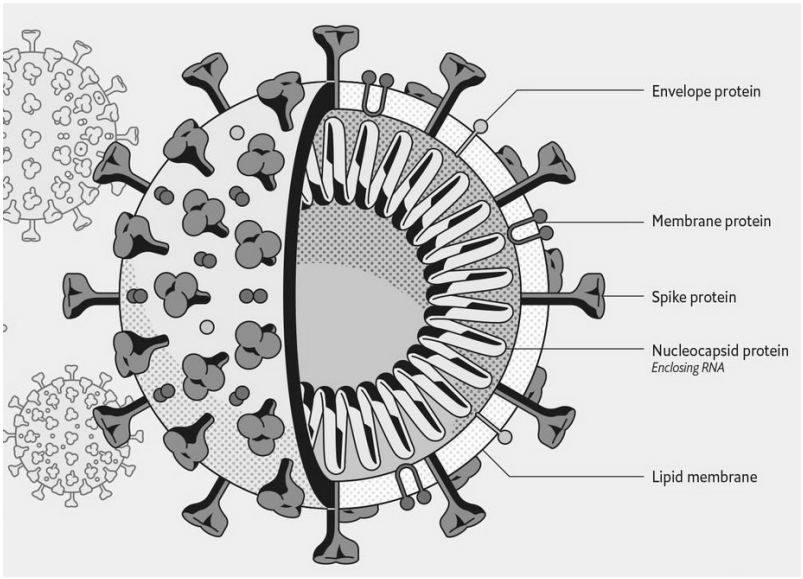
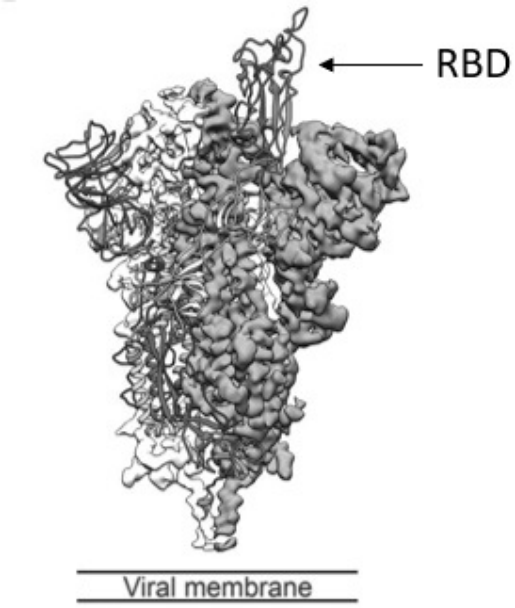
A


Envelope protein
Membrane protein
Spike protein
Nucleocapsid protein
Enclosing RNA
Lipid membrane

B


RBD
Viral membrane

FIGS. 1A-B

C

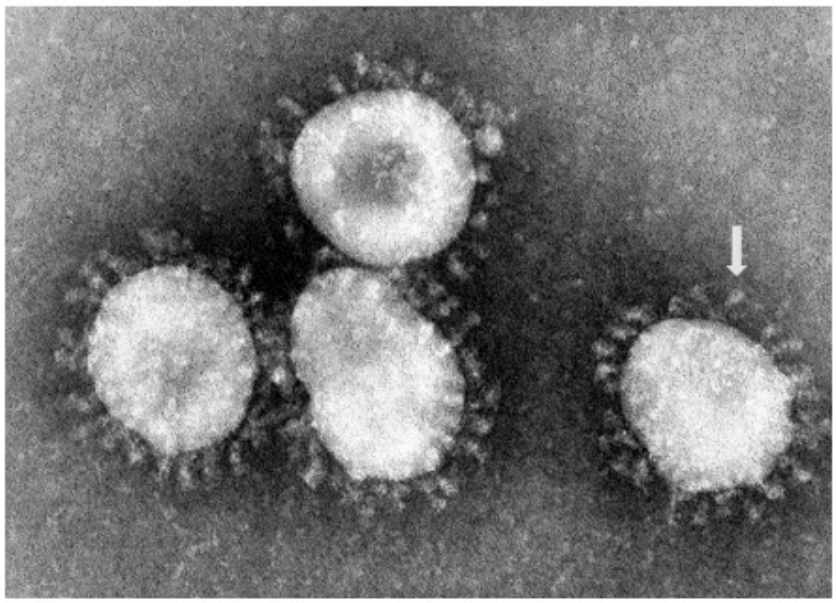
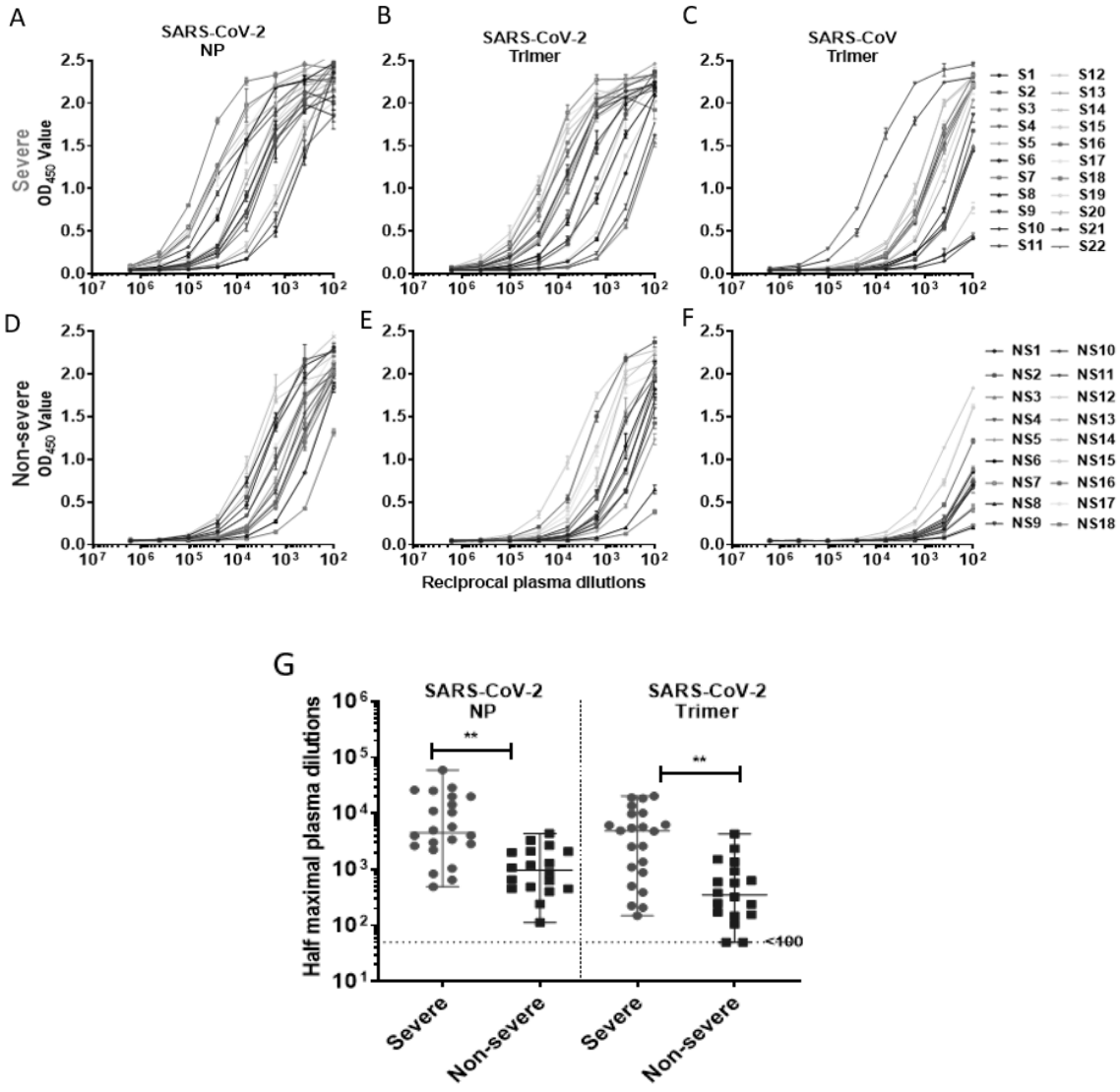
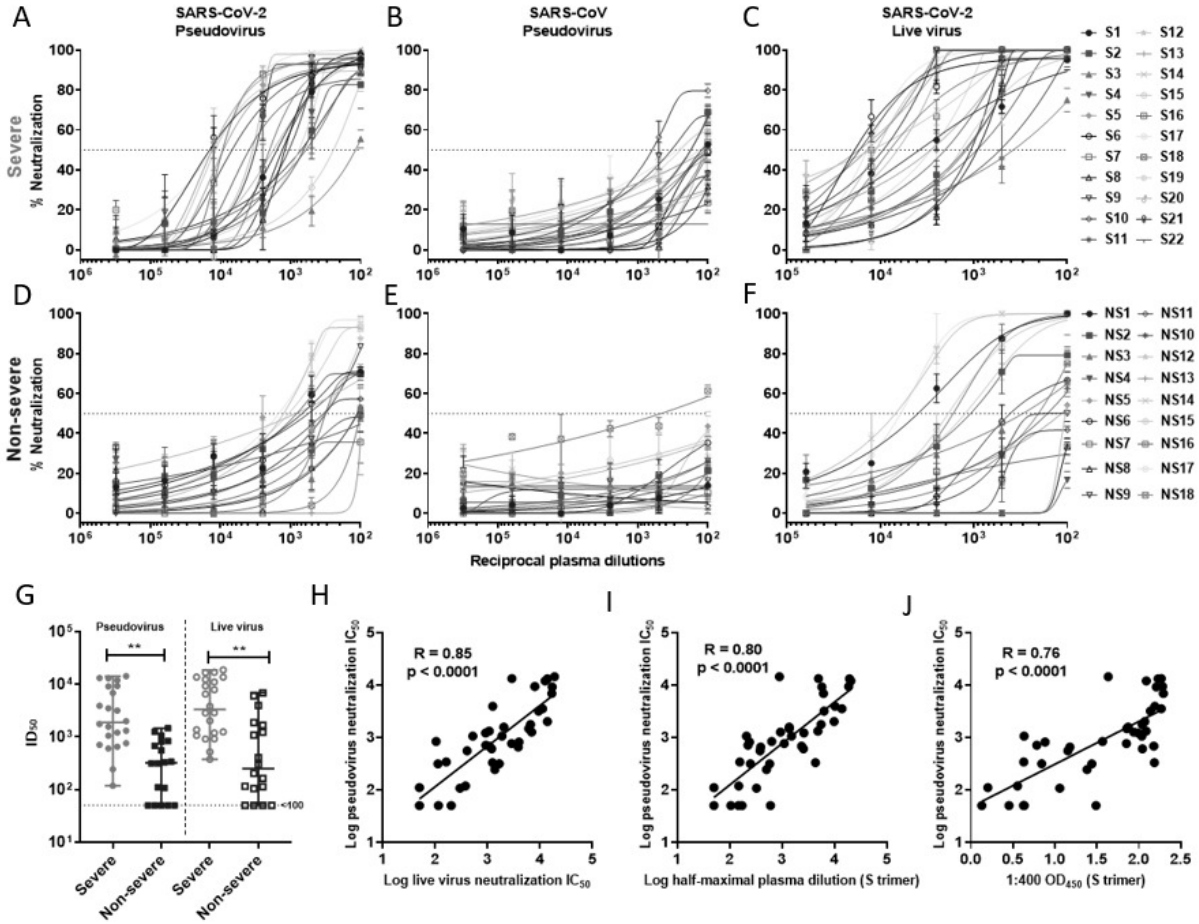


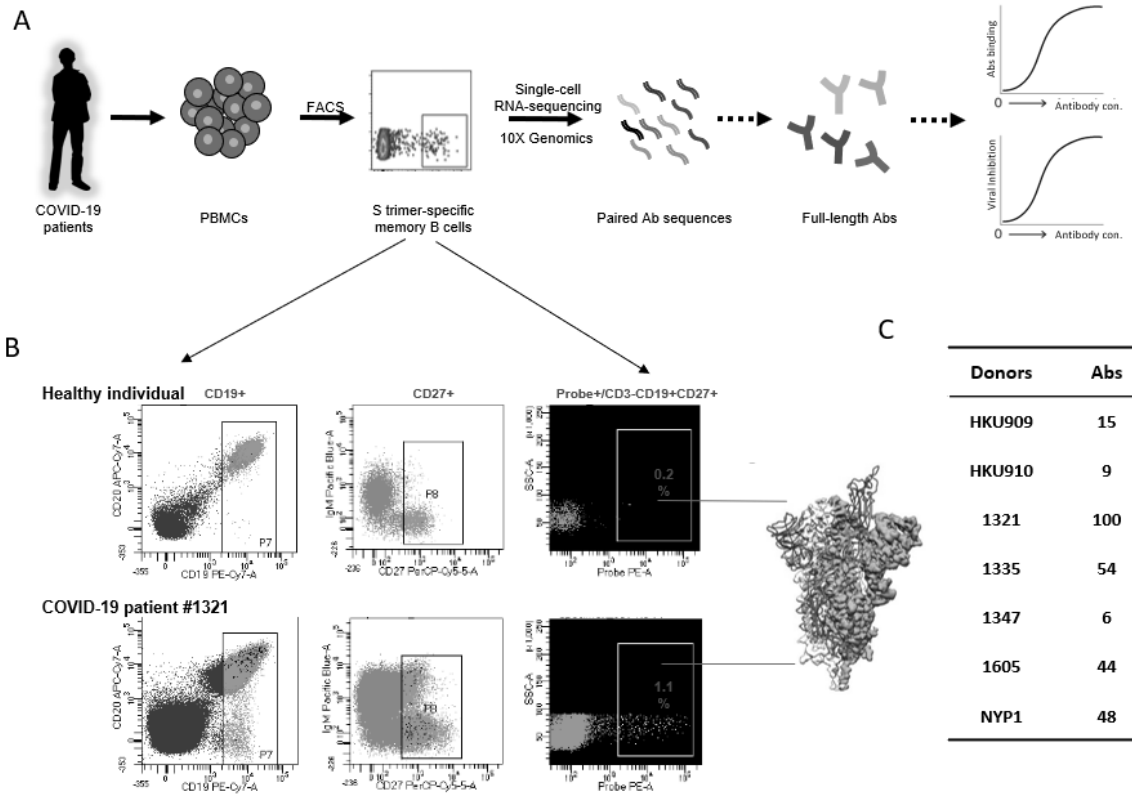
FIG. 1C


A
SARS-CoV-2 NP
B
SARS-CoV-2 Trimer
C
SARS-CoV Trimer
Severe
OD450 Value
S1
S2
S3
S4
S5
S6
S7
S8
S9
S10
S11
S12
S13
S14
S15
S16
S17
S18
S19
S20
S21
S22
D
E
F
Non-severe
OD450 Value
NS1
NS2
NS3
NS4
NS5
NS6
NS7
NS8
NS9
NS10
NS11
NS12
NS13
NS14
NS15
NS16
NS17
NS18
Reciprocal plasma dilutions
G
SARS-CoV-2 NP
SARS-CoV-2 Trimer
Half maximal plasma dilutions
**
**
<100
Severe
Non-severe
Severe
Non-severe

FIGS. 2A-G


A
SARS-CoV-2
Pseudovirus
B
SARS-CoV
Pseudovirus
C
SARS-CoV-2
Live virus
Severe
% Neutralization
D
E
F
Non-severe
% Neutralization
Reciprocal plasma dilutions
S1
S2
S3
S4
S5
S6
S7
S8
S9
S10
S11
S12
S13
S14
S15
S16
S17
S18
S19
S20
S21
S22
NS1
NS2
NS3
NS4
NS5
NS6
NS7
NS8
NS9
NS10
NS11
NS12
NS13
NS14
NS15
NS16
NS17
NS18
G
Pseudovirus
Live virus
ID50
<100
Severe
Non-severe
H
R = 0.85
p < 0.0001
Log pseudovirus neutralization IC50
Log live virus neutralization IC50
I
R = 0.80
p < 0.0001
Log half-maximal plasma dilution (S trimer)
J
R = 0.76
p < 0.0001
1:400 OD450 (S trimer)

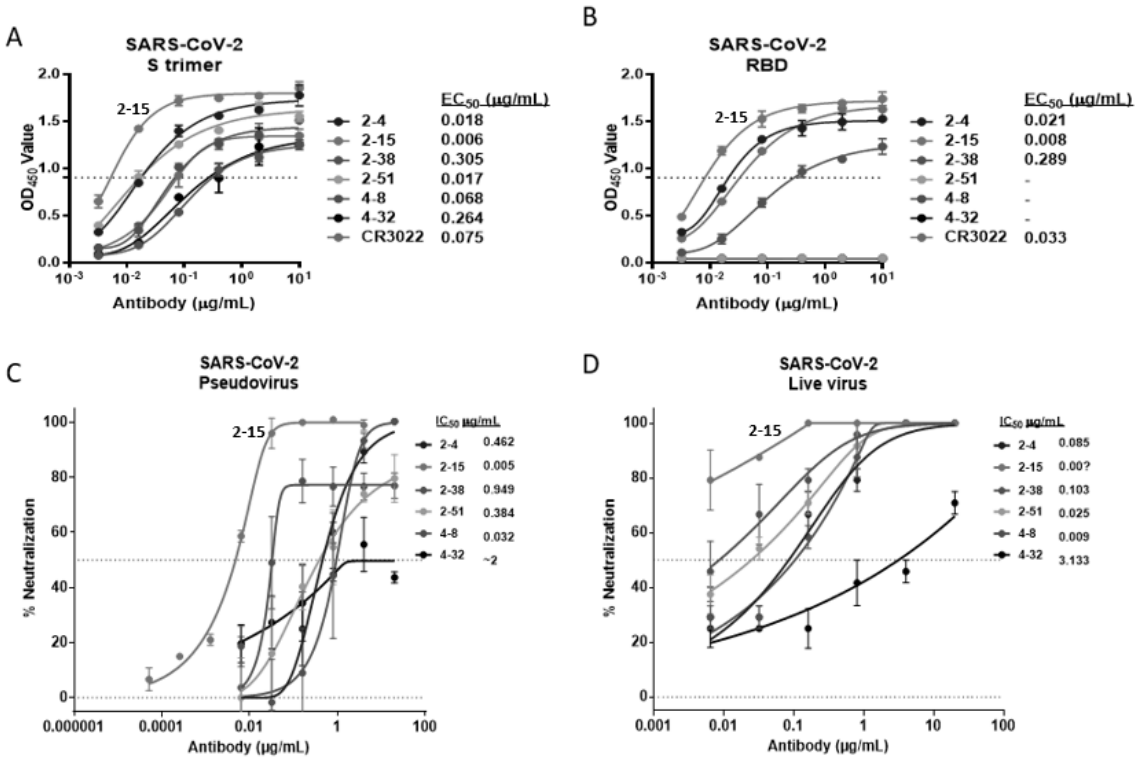
FIGS. 3A-J



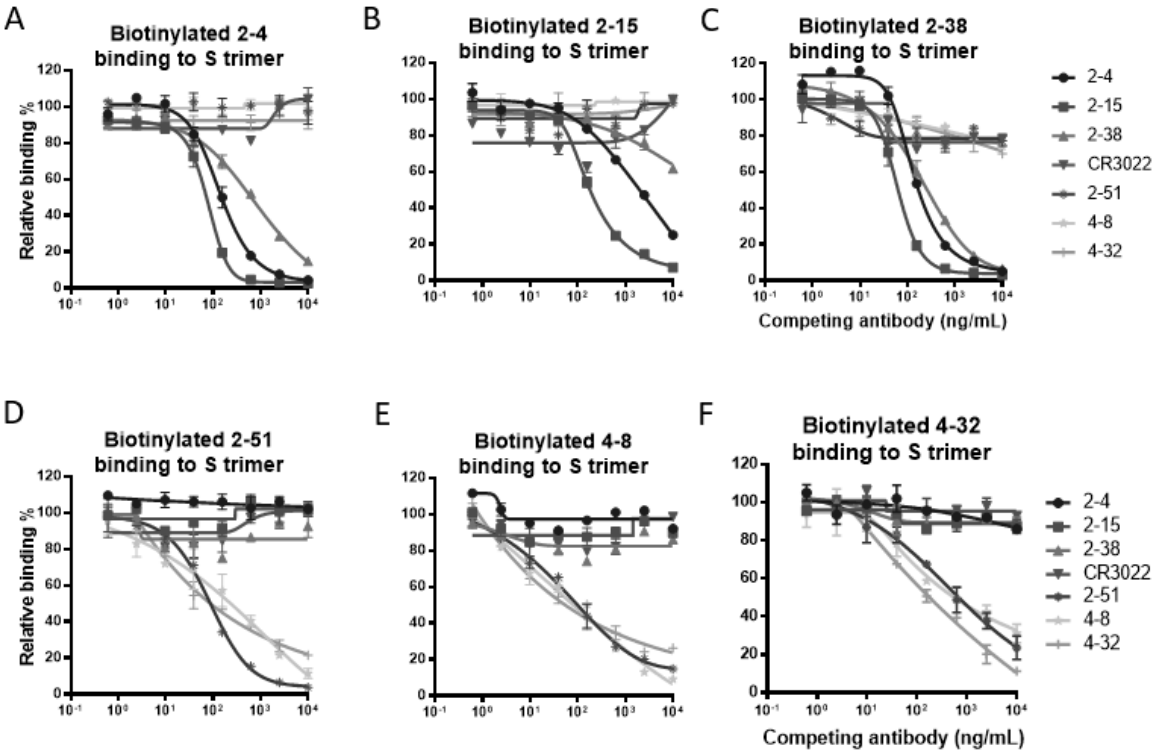
Donors	Abs
HKU909	15
HKU910	9
1321	100
1335	54
1347	6
1605	44
NYP1	48

254 mAbs from 5 ICU patients

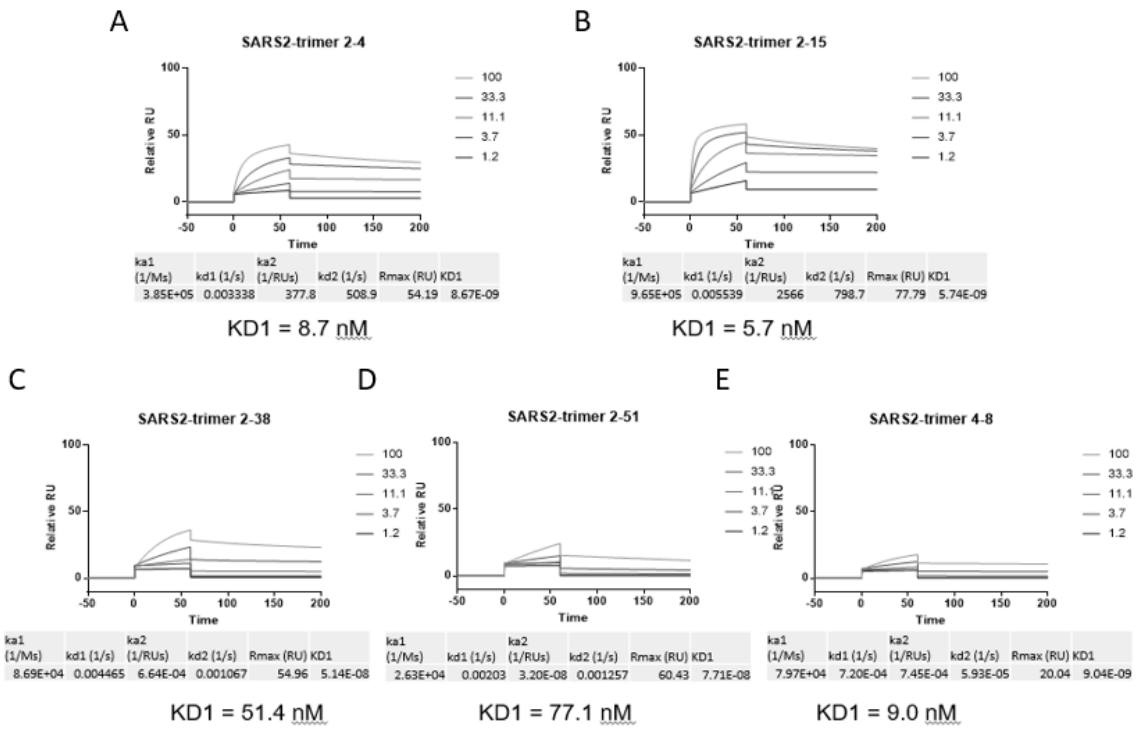
FIGS. 4A-C


A
SARS-CoV-2
S trimer
2-15
OD450 Value
Antibody (µg/mL)
EC50 (µg/mL)
2-4 0.018
2-15 0.006
2-38 0.305
2-51 0.017
4-8 0.068
4-32 0.264
CR3022 0.075
B
SARS-CoV-2
RBD
2-15
OD450 Value
Antibody (µg/mL)
EC50 (µg/mL)
2-4 0.021
2-15 0.008
2-38 0.289
2-51 -
4-8 -
4-32 -
CR3022 0.033
C
SARS-CoV-2
Pseudovirus
2-15
% Neutralization
Antibody (µg/mL)
IC50 µg/mL
2-4 0.462
2-15 0.005
2-38 0.949
2-51 0.384
4-8 0.032
4-32 ~2
D
SARS-CoV-2
Live virus
2-15
% Neutralization
Antibody (µg/mL)
IC50 µg/mL
2-4 0.085
2-15 0.00?
2-38 0.103
2-51 0.025
4-8 0.009
4-32 3.133

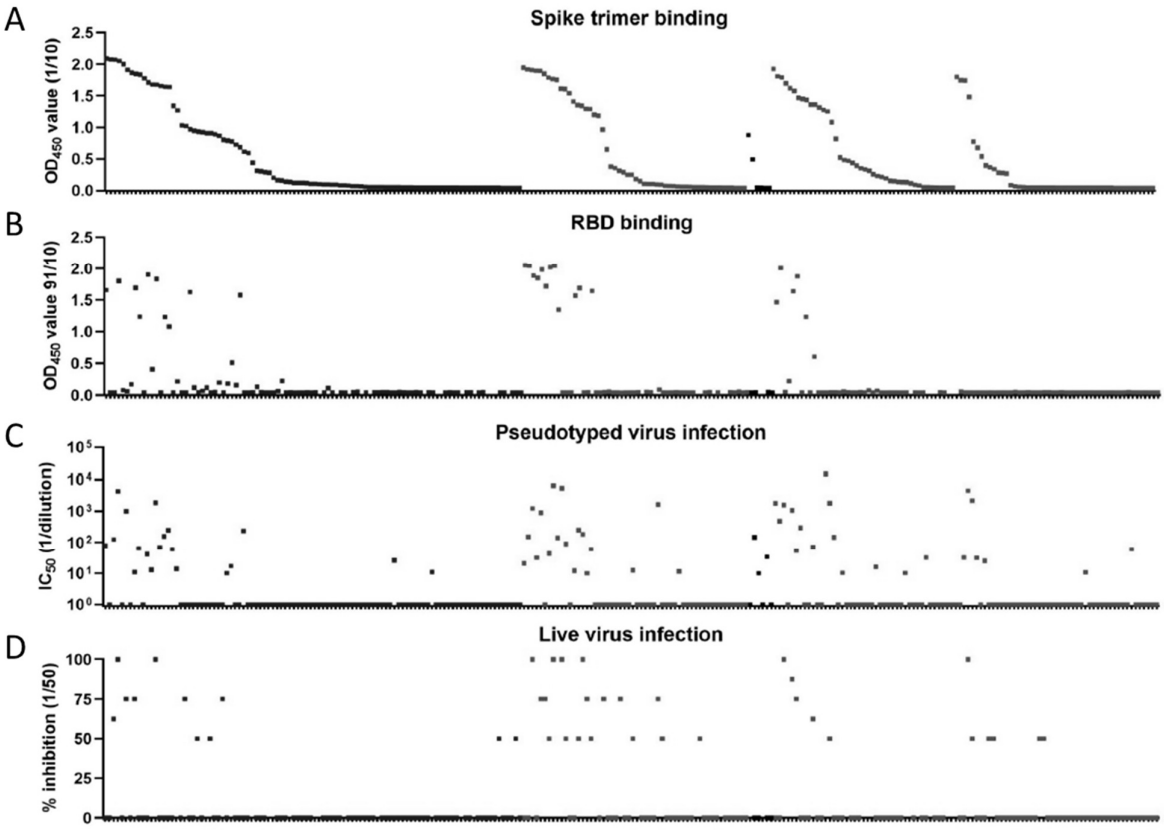
FIGS. 5A-D


A
Biotinylated 2-4 binding to S trimer
Relative binding %
B
Biotinylated 2-15 binding to S trimer
C
Biotinylated 2-38 binding to S trimer
Competing antibody (ng/mL)
2-4
2-15
2-38
CR3022
2-51
4-8
4-32
D
Biotinylated 2-51 binding to S trimer
Relative binding %
E
Biotinylated 4-8 binding to S trimer
F
Biotinylated 4-32 binding to S trimer
Competing antibody (ng/mL)
2-4
2-15
2-38
CR3022
2-51
4-8
4-32

FIGS. 6A-F


A
SARS2-trimer 2-4
Relative RU
Time
100
33.3
11.1
3.7
1.2
ka1 (1/Ms) kd1 (1/s) ka2 (1/RUs) kd2 (1/s) Rmax (RU) KD1
3.85E+05 0.003338 377.8 508.9 54.19 8.67E-09
KD1 = 8.7 nM
B
SARS2-trimer 2-15
ka1 (1/Ms) kd1 (1/s) ka2 (1/RUs) kd2 (1/s) Rmax (RU) KD1
9.65E+05 0.005539 2566 798.7 77.79 5.74E-09
KD1 = 5.7 nM
C
SARS2-trimer 2-38
ka1 (1/Ms) kd1 (1/s) ka2 (1/RUs) kd2 (1/s) Rmax (RU) KD1
8.69E+04 0.004465 6.64E-04 0.001067 54.96 5.14E-08
KD1 = 51.4 nM
D
SARS2-trimer 2-51
ka1 (1/Ms) kd1 (1/s) ka2 (1/RUs) kd2 (1/s) Rmax (RU) KD1
2.63E+04 0.00203 3.20E-08 0.001257 60.43 7.71E-08
KD1 = 77.1 nM
E
SARS2-trimer 4-8
ka1 (1/Ms) kd1 (1/s) ka2 (1/RUs) kd2 (1/s) Rmax (RU) KD1
7.97E+04 7.20E-04 7.45E-04 5.93E-05 20.04 9.04E-09
KD1 = 9.0 nM

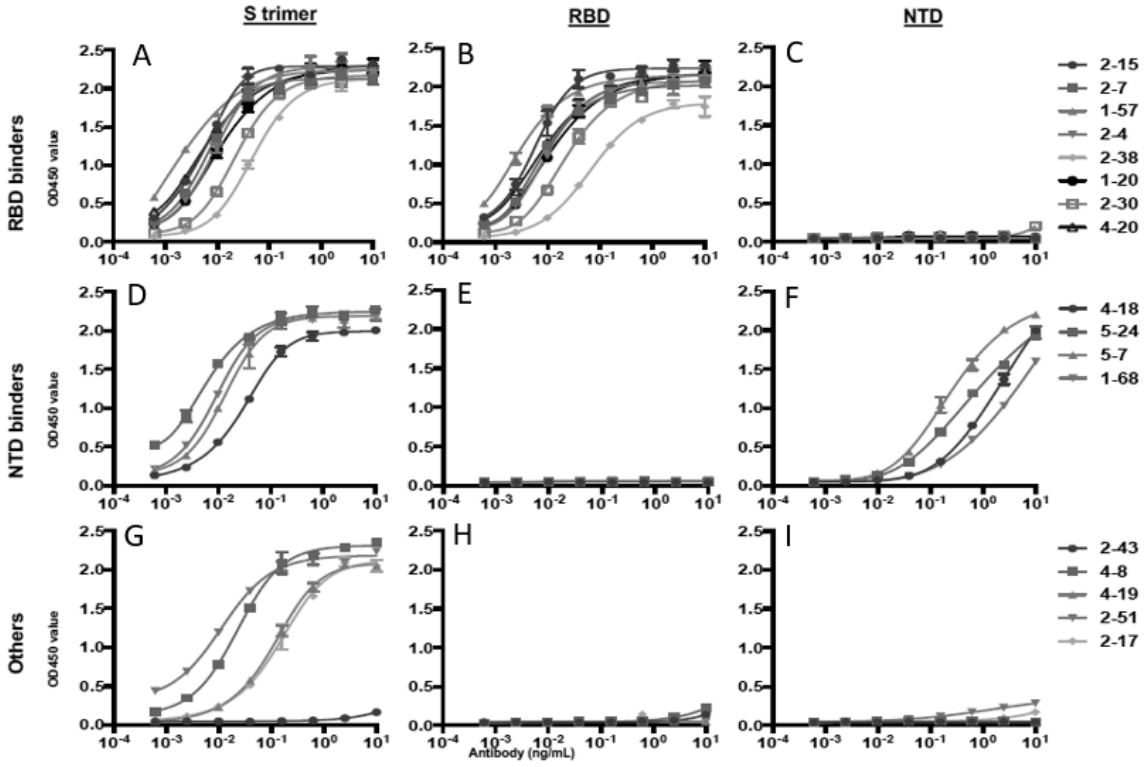
FIGS. 7A-E


A
Spike trimer binding
OD450 value (1/10)
2.5
2.0
1.5
1.0
0.5
0.0
B
RBD binding
OD450 value 91/10)
C
Pseudotyped virus infection
IC50 (1/dilution)
10^5
10^4
10^3
10^2
10^1
10^0
D
Live virus infection
% inhibition (1/50)
100
75
50
25
0

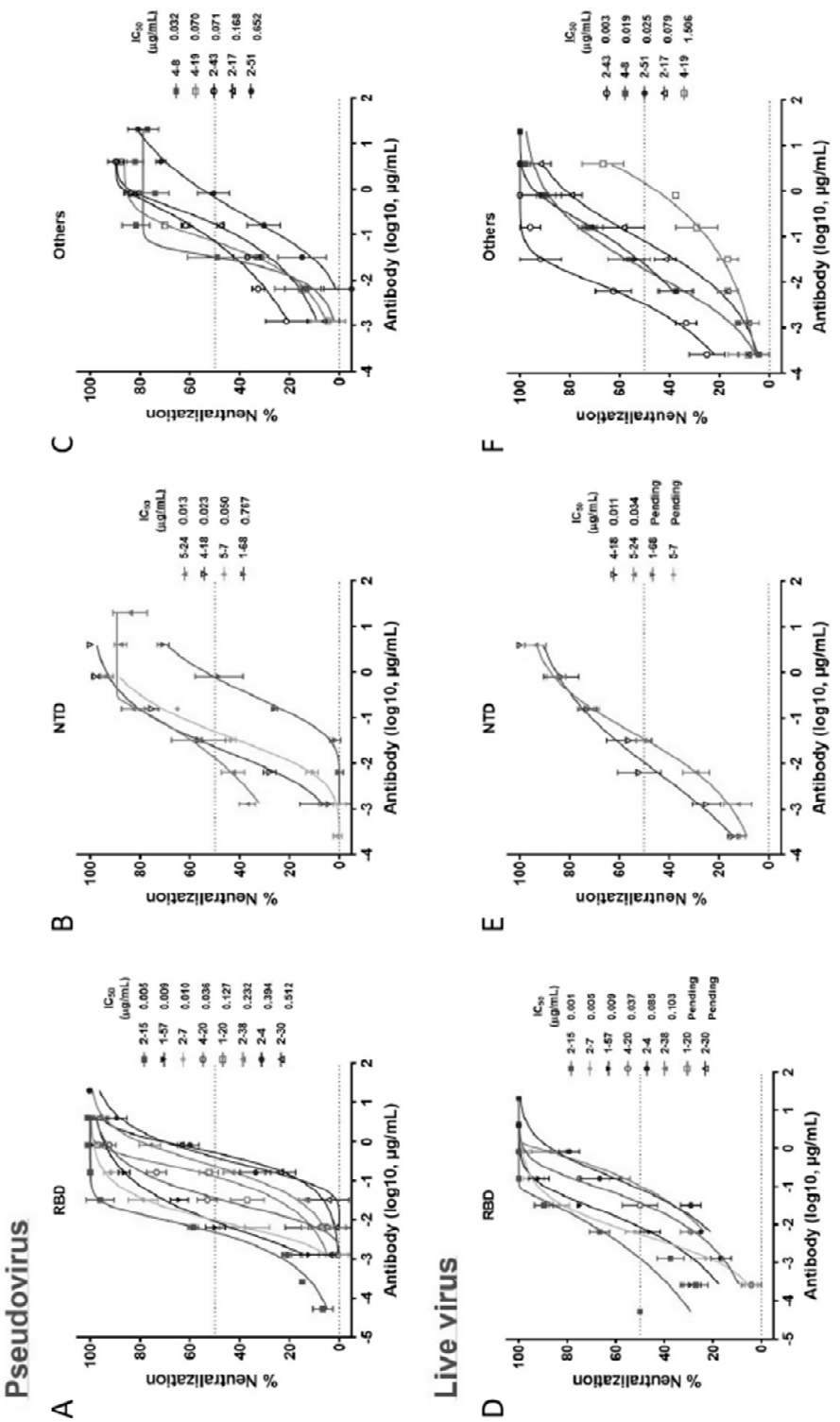
FIGS. 8A-D

Total Abs synthesized	Abs tested	Binding Abs			Neutralizing Abs (pseudovirus)			Neutralizing Abs (live virus, 217 tested)		
		S trimer	RBD	Non-RBD	S trimer	RBD	Non-RBD	S trimer	RBD	Non-RBD
254	254	121	38	83	52	28	24	32	13	19

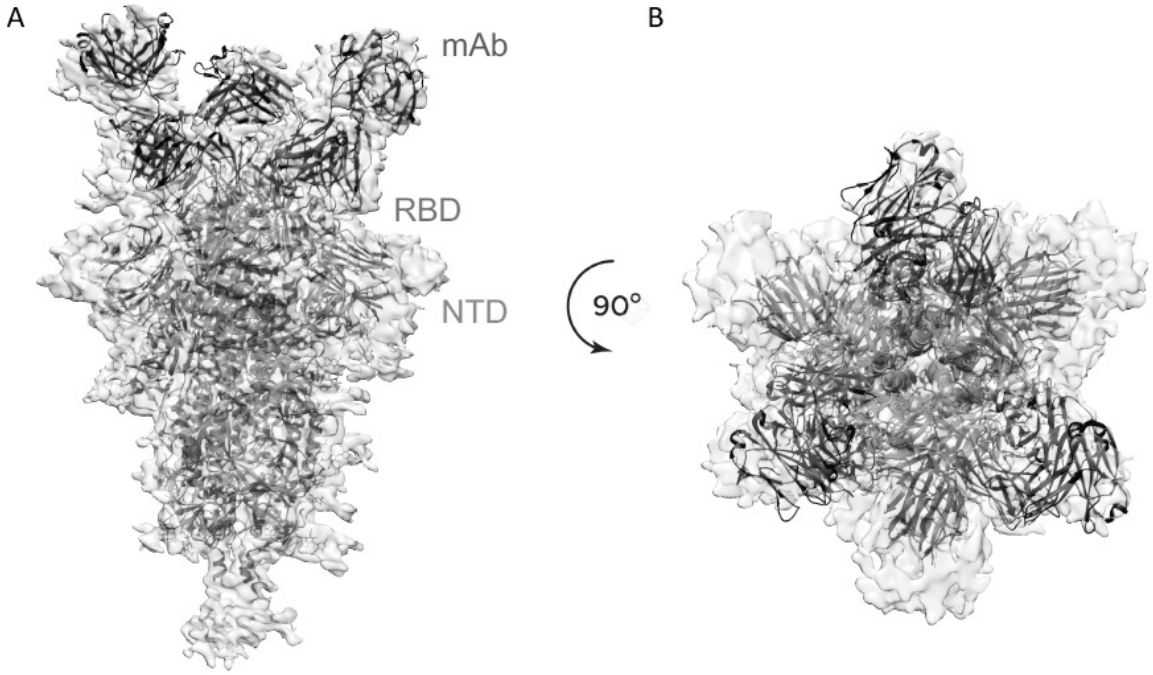
FIG. 9



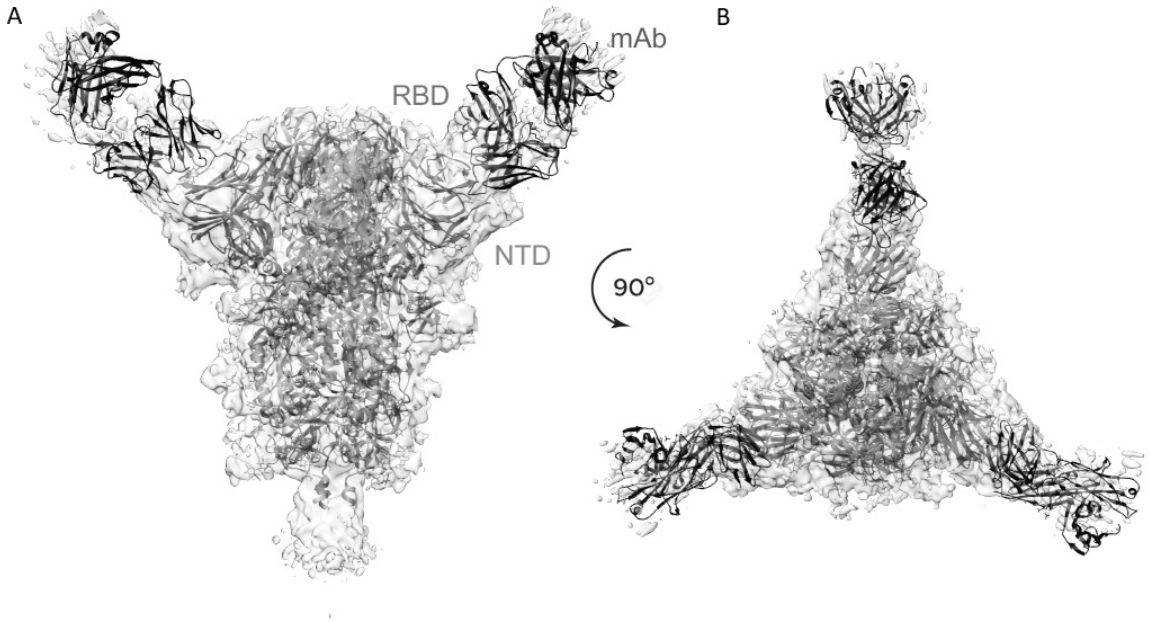
FIGS. 10A-I


Pseudovirus
Live virus
A
RBD
% Neutralization
Antibody (log10, µg/mL)
IC50 (µg/mL)
2-15 0.005
1-57 0.009
2-7 0.010
4-20 0.036
1-20 0.127
2-38 0.232
2-4 0.394
2-30 0.512
B
NTD
IC50 (µg/mL)
5-24 0.013
4-18 0.023
5-7 0.050
1-68 0.767
C
Others
IC50 (µg/mL)
4-8 0.032
4-19 0.070
2-43 0.071
2-17 0.168
2-51 0.652
D
RBD
IC50 (µg/mL)
2-15 0.001
2-7 0.005
1-57 0.009
4-20 0.037
2-4 0.085
2-38 0.103
1-20 Pending
2-30 Pending
E
NTD
IC50 (µg/mL)
4-18 0.011
5-24 0.034
1-68 Pending
5-7 Pending
F
Others
IC50 (µg/mL)
2-43 0.003
4-8 0.019
2-51 0.025
2-17 0.079
4-19 1.506

FIGS. 11A-F



FIGS. 12A-B



FIGS. 13A-B

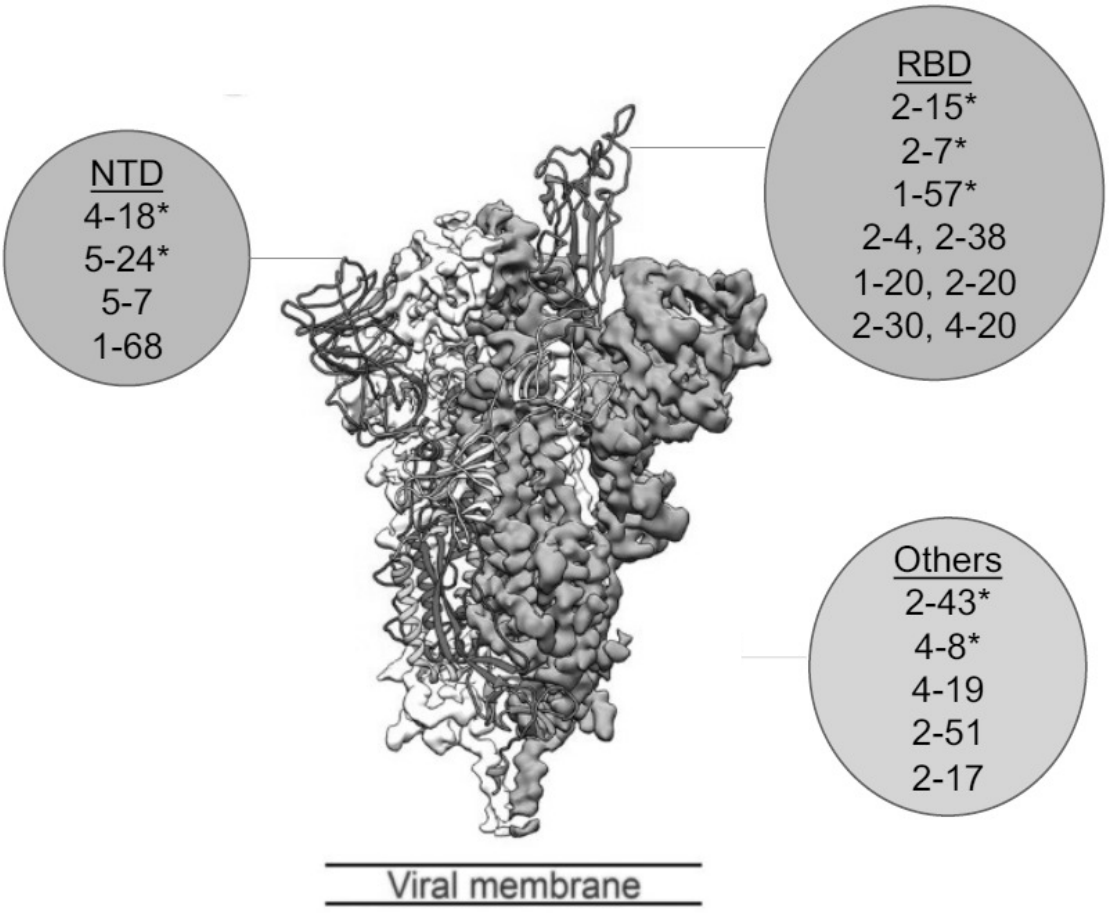

NTD
4-18*
5-24*
5-7
1-68
RBD
2-15*
2-7*
1-57*
2-4, 2-38
1-20, 2-20
2-30, 4-20
Others
2-43*
4-8*
4-19
2-51
2-17
Viral membrane

FIG. 14

A

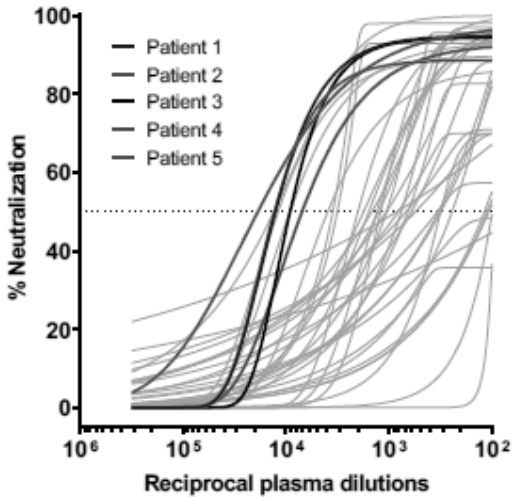
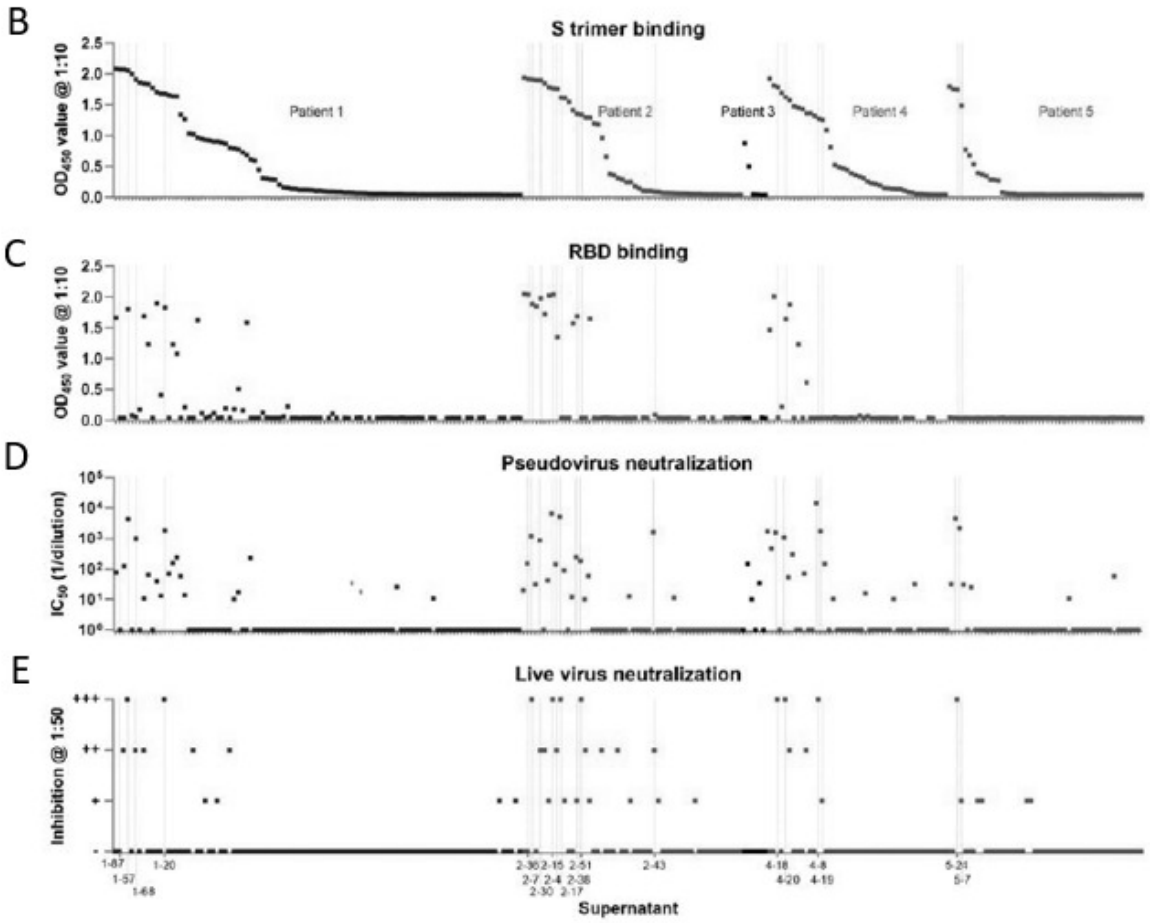
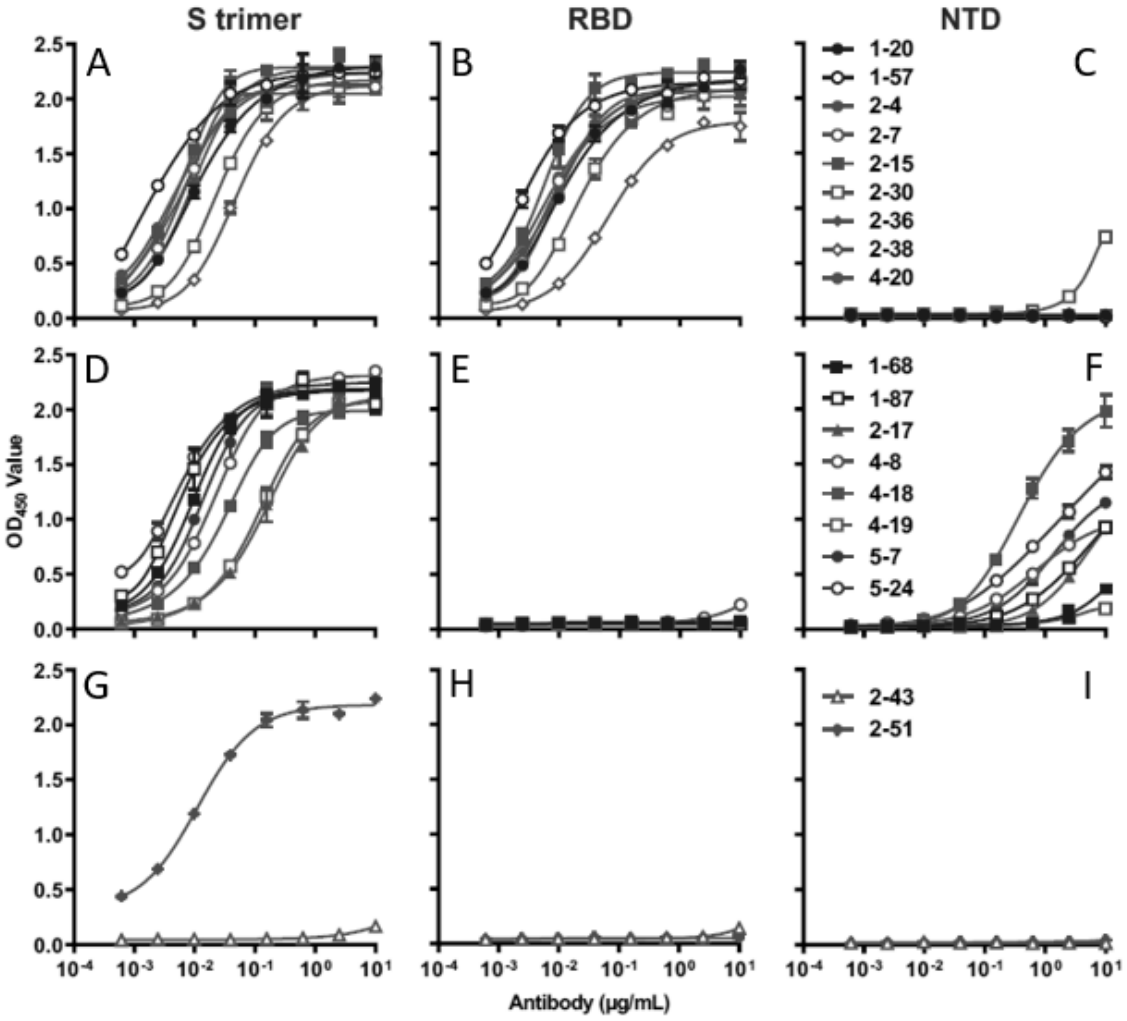

100
80
60
40
20
0
% Neutralization
Patient 1
Patient 2
Patient 3
Patient 4
Patient 5
10⁶
10⁵
10⁴
10³
10²
Reciprocal plasma dilutions

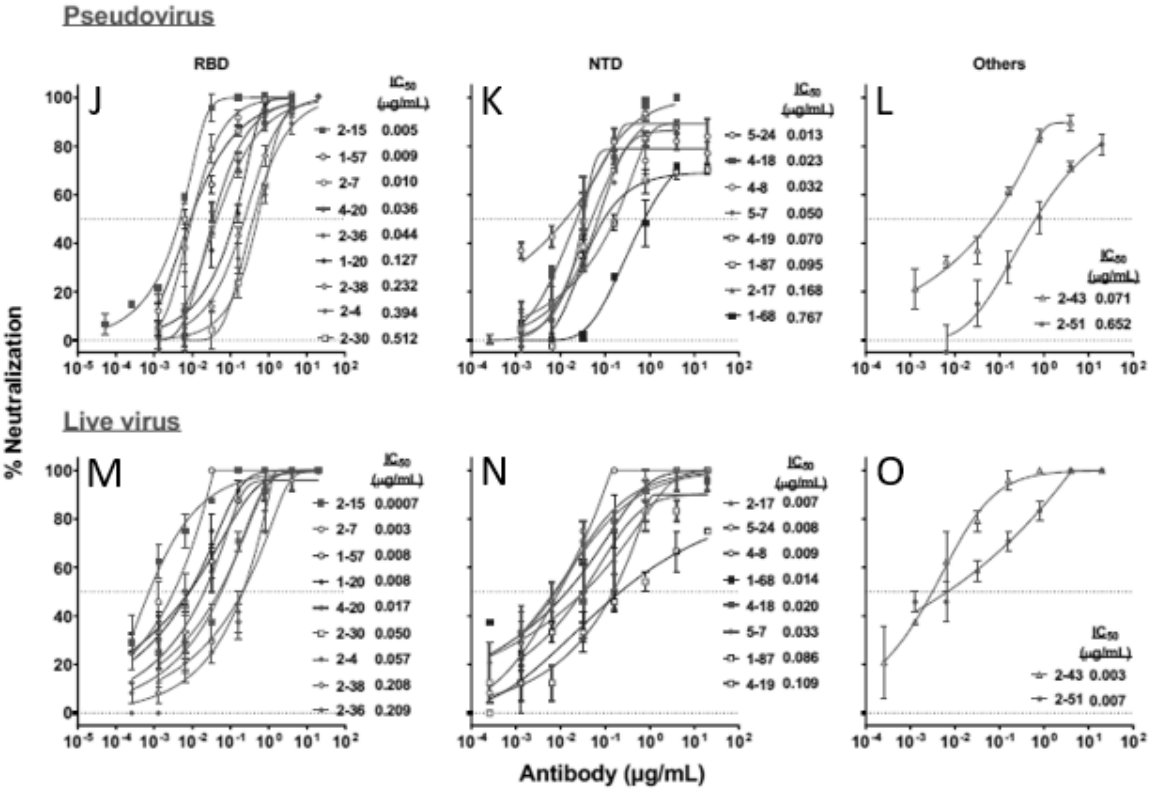
FIG. 15A


B
S trimer binding
OD450 value @ 1:10
Patient 1
Patient 2
Patient 3
Patient 4
Patient 5
C
RBD binding
OD450 value @ 1:10
D
Pseudovirus neutralization
IC50 (1/dilution)
E
Live virus neutralization
Inhibition @ 1:50
Supernatant

FIGS. 15B-E

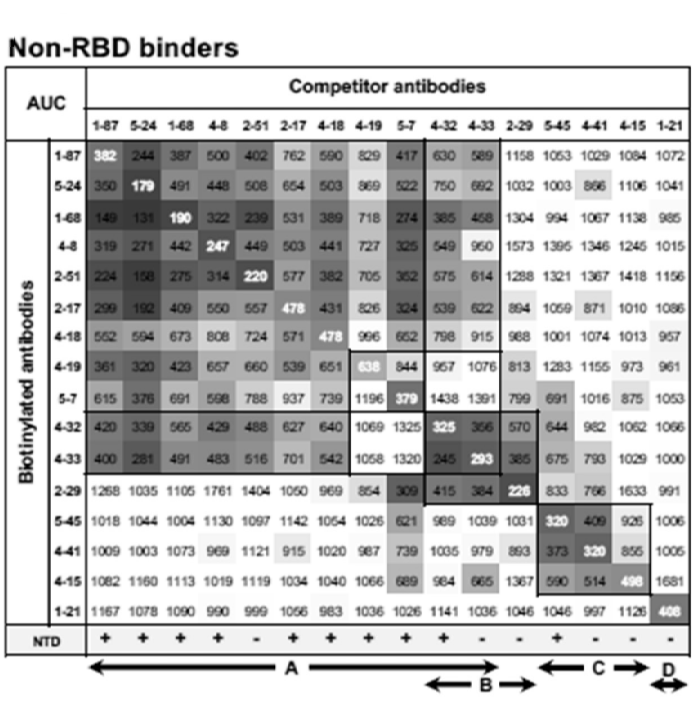

S trimer
RBD
NTD
A
B
C
D
E
F
G
H
I
1-20
1-57
2-4
2-7
2-15
2-30
2-36
2-38
4-20
1-68
1-87
2-17
4-8
4-18
4-19
5-7
5-24
2-43
2-51
OD450 Value
Antibody (μg/mL)

FIGS. 16A-I

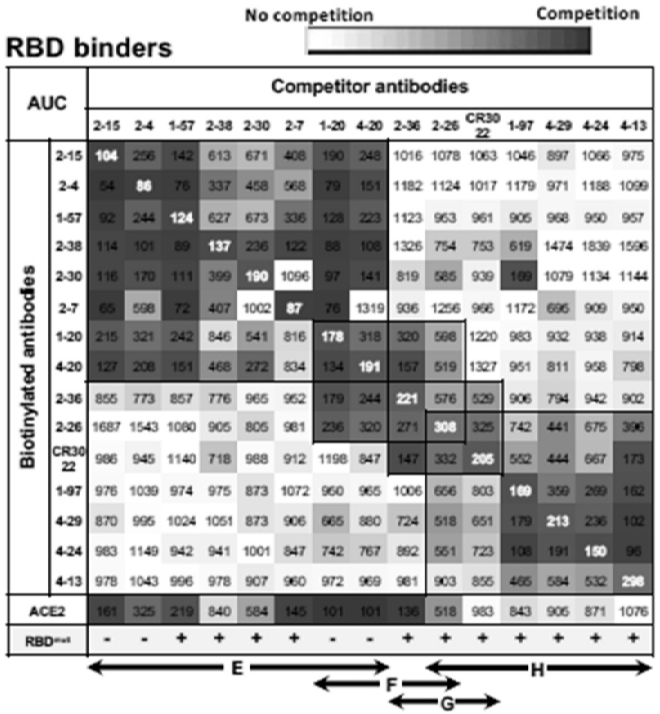

Pseudovirus
RBD
NTD
Others
J
K
L
M
N
O
% Neutralization
Antibody (μg/mL)
IC50 (μg/mL)
2-15 0.005
1-57 0.009
2-7 0.010
4-20 0.036
2-36 0.044
1-20 0.127
2-38 0.232
2-4 0.394
2-30 0.512
5-24 0.013
4-18 0.023
4-8 0.032
5-7 0.050
4-19 0.070
1-87 0.095
2-17 0.168
1-68 0.767
2-43 0.071
2-51 0.652
Live virus
2-15 0.0007
2-7 0.003
1-57 0.008
1-20 0.008
4-20 0.017
2-30 0.050
2-4 0.057
2-38 0.208
2-36 0.209
2-17 0.007
5-24 0.008
4-8 0.009
1-68 0.014
4-18 0.020
5-7 0.033
1-87 0.086
4-19 0.109
2-43 0.003
2-51 0.007

FIGS. 16J-O

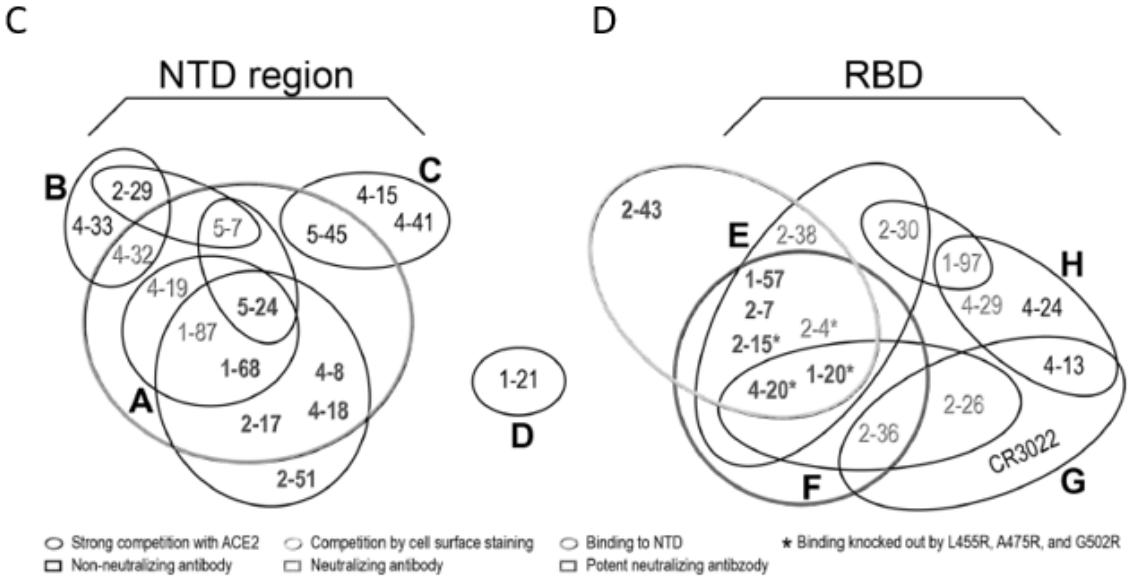
A


Non-RBD binders
AUC
Competitor antibodies
1-87 5-24 1-68 4-8 2-51 2-17 4-18 4-19 5-7 4-32 4-33 2-29 5-45 4-41 4-15 1-21
Biotinylated antibodies
1-87 382 244 387 500 402 762 590 829 417 630 589 1158 1053 1029 1084 1072
5-24 350 179 491 448 508 654 503 869 522 750 692 1032 1003 866 1106 1041
1-68 149 131 190 322 239 531 389 718 274 385 458 1304 994 1087 1138 985
4-8 319 271 442 247 449 503 441 727 325 549 960 1573 1395 1346 1245 1015
2-51 224 158 275 314 220 577 382 705 352 575 614 1288 1321 1367 1418 1156
2-17 299 192 409 550 557 478 431 826 324 539 622 894 1059 871 1010 1086
4-18 552 594 673 808 724 571 478 996 652 798 915 988 1001 1074 1013 957
4-19 361 320 423 657 660 539 651 638 844 957 1076 813 1283 1155 973 961
5-7 615 376 691 598 788 937 739 1196 379 1438 1391 799 691 1016 875 1053
4-32 420 339 565 429 488 627 640 1069 1325 325 356 570 644 982 1062 1066
4-33 400 281 491 483 516 701 542 1058 1320 245 293 385 675 793 1029 1000
2-29 1268 1035 1105 1761 1404 1050 969 854 309 415 384 226 833 766 1633 991
5-45 1018 1044 1004 1130 1097 1142 1054 1026 621 989 1039 1031 320 409 926 1006
4-41 1009 1003 1073 969 1121 915 1020 987 739 1035 979 893 373 320 855 1005
4-15 1082 1160 1113 1019 1119 1034 1040 1066 689 984 665 1367 590 514 498 1681
1-21 1167 1078 1090 990 999 1056 983 1036 1026 1141 1036 1046 1046 997 1126 408
NTD + + + + - + + + + + - - + - - -
A
B
C
D

B


No competition
Competition
RBD binders
AUC
Competitor antibodies
2-15 2-4 1-57 2-38 2-30 2-7 1-20 4-20 2-36 2-26 CR3022 1-97 4-29 4-24 4-13
Biotinylated antibodies
2-15 104 256 142 613 671 408 190 248 1016 1078 1063 1046 897 1066 975
2-4 54 86 76 337 458 568 79 151 1182 1124 1017 1179 971 1188 1099
1-57 92 244 124 627 673 336 128 223 1123 963 961 905 968 950 957
2-38 114 101 89 137 236 122 88 108 1326 754 753 619 1474 1839 1596
2-30 116 170 111 399 190 1096 97 141 819 585 939 189 1079 1134 1144
2-7 65 598 72 407 1002 87 76 1319 936 1256 966 1172 696 909 950
1-20 215 321 242 846 541 816 178 318 320 598 1220 983 932 938 914
4-20 127 208 151 468 272 834 134 191 157 519 1327 951 811 958 798
2-36 855 773 857 776 965 952 179 244 221 576 529 906 794 942 902
2-26 1687 1543 1080 905 805 981 236 320 271 308 325 742 441 675 396
CR3022 986 945 1140 718 988 912 1198 847 147 332 295 552 444 667 173
1-97 976 1039 974 975 873 1072 960 965 1006 656 803 169 359 269 162
4-29 870 995 1024 1051 873 906 665 880 724 518 651 179 213 236 102
4-24 983 1149 942 941 1001 847 742 767 892 551 723 108 191 150 96
4-13 978 1043 996 978 907 960 972 969 981 903 855 465 584 532 298
ACE2 161 325 219 840 584 145 101 101 136 518 983 843 905 871 1076
RBDwt - - + + + + - - + + + + + + +
E
F
G
H

FIGS. 17A-B


C
NTD region
B
C
A
D
2-29
4-33
4-32
5-7
4-15
4-41
5-45
4-19
5-24
1-87
1-68
4-8
4-18
2-17
2-51
1-21
D
RBD
2-43
E
2-38
2-30
1-97
H
1-57
2-7
2-15*
2-4*
4-29
4-24
4-20*
1-20*
4-13
2-26
2-36
CR3022
F
G
Strong competition with ACE2
Non-neutralizing antibody
Competition by cell surface staining
Neutralizing antibody
Binding to NTD
Potent neutralizing antibzody
★ Binding knocked out by L455R, A475R, and G502R

FIGS. 17C-D

A

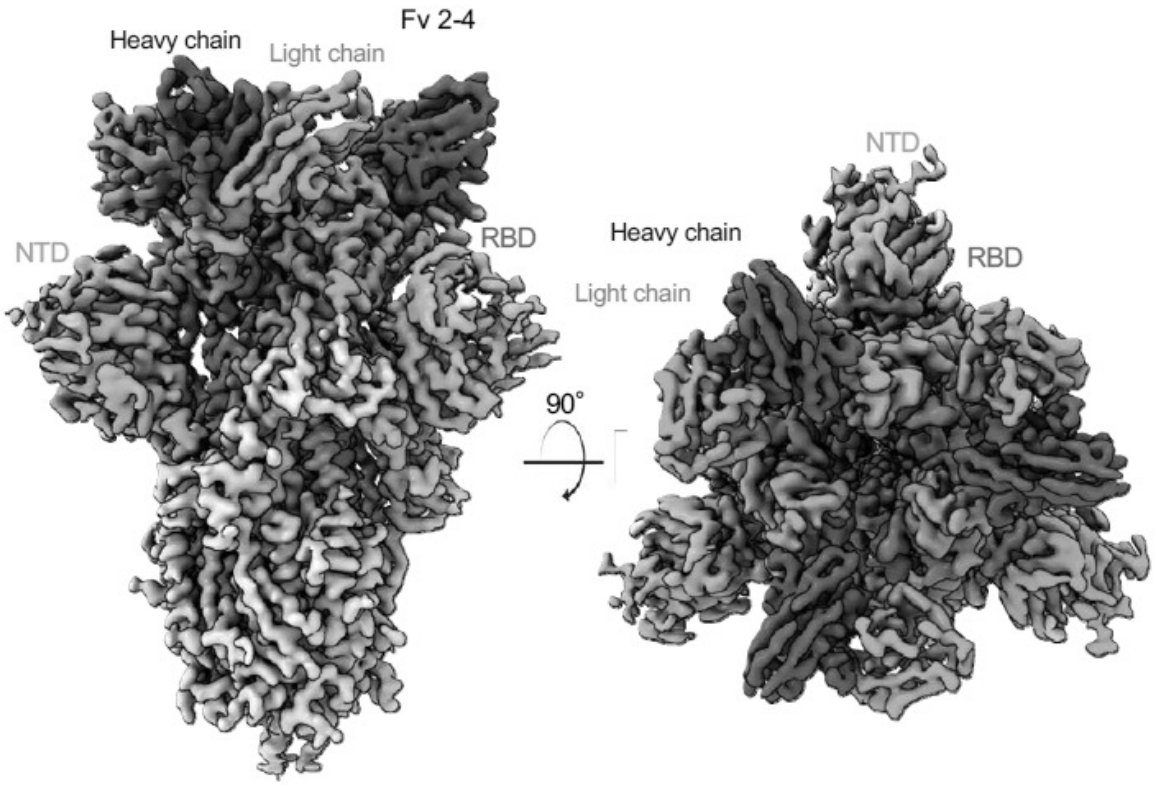

Fv 2-4
Heavy chain
Light chain
NTD
RBD
90°
NTD
Heavy chain
RBD
Light chain

FIG. 18A

B

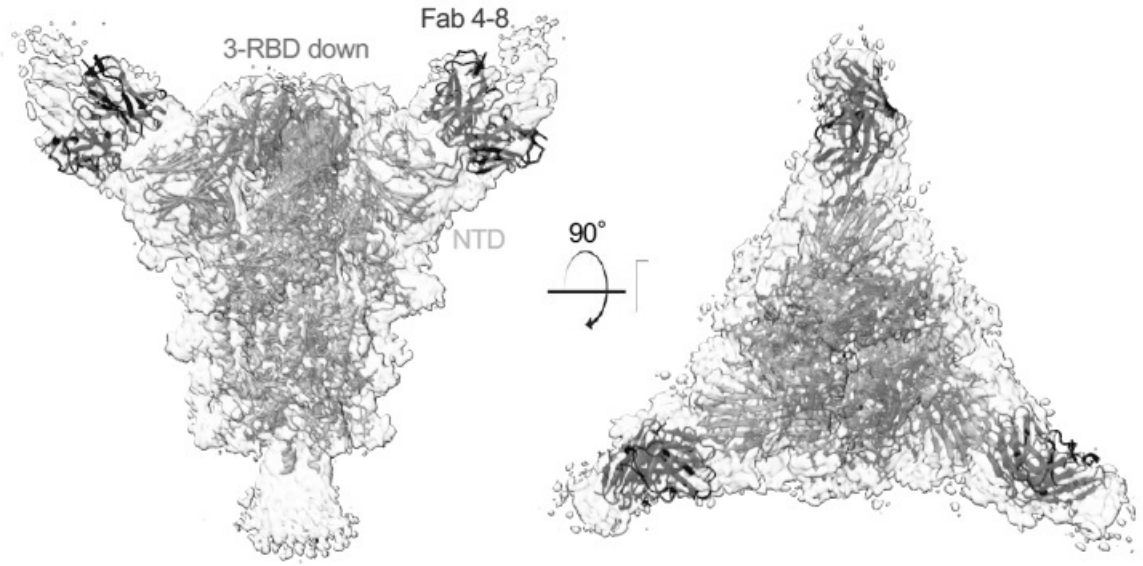


FIG. 18B

C

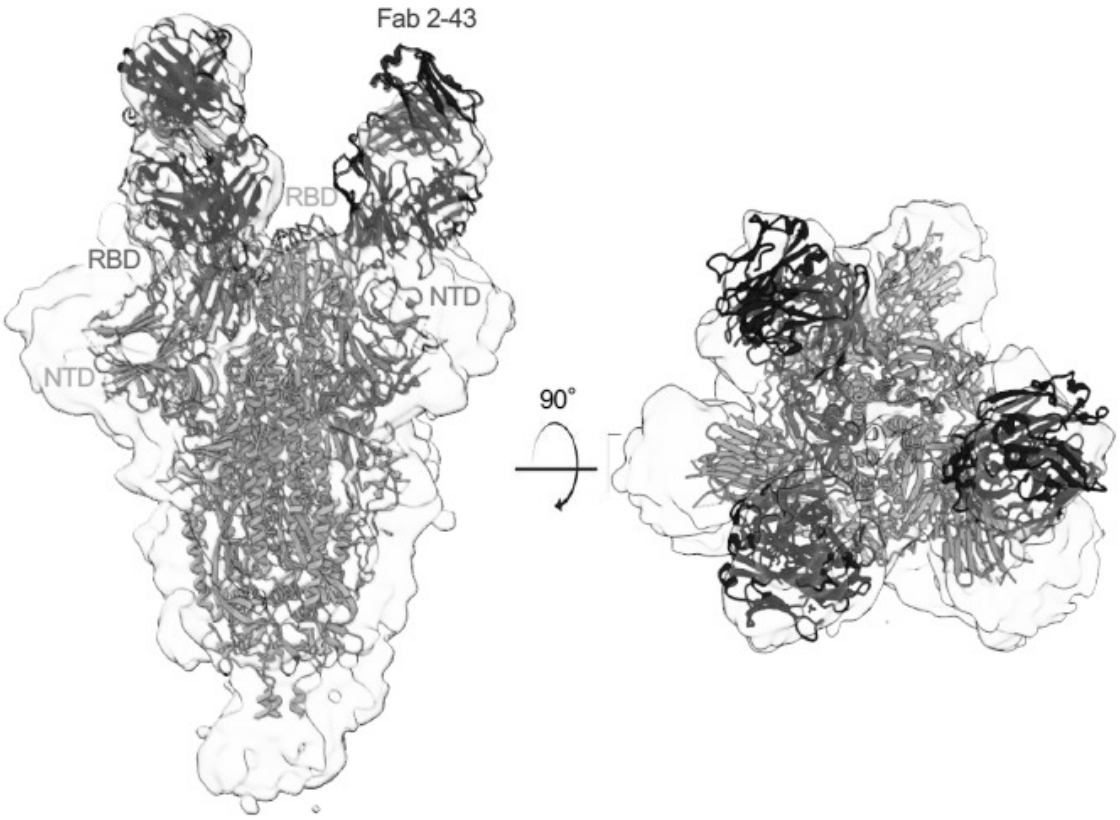


FIG. 18C

D

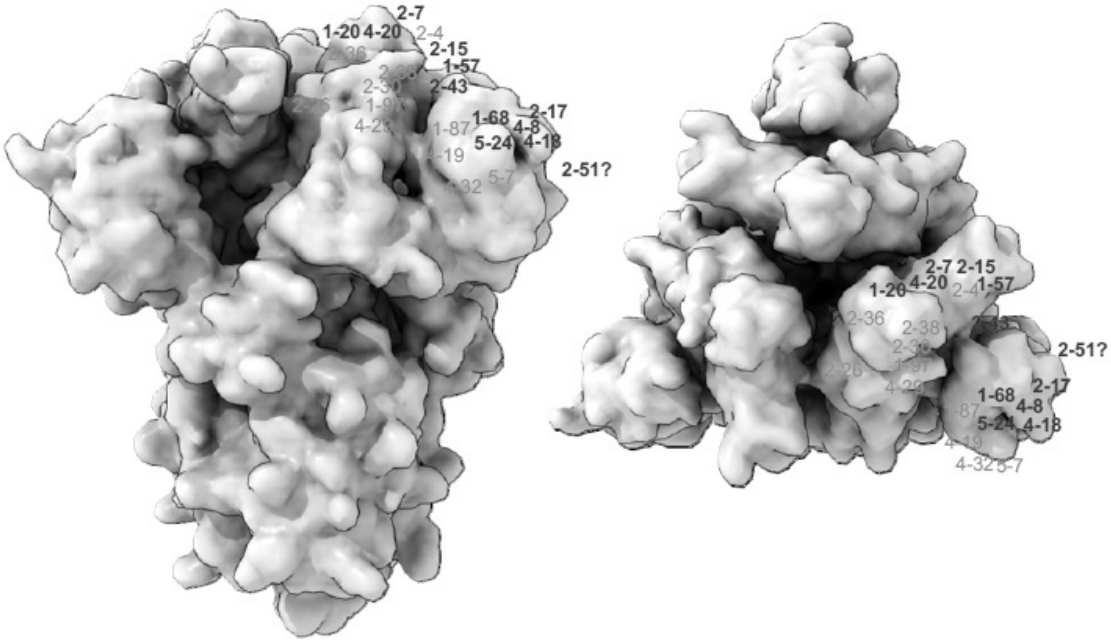

2-7
1-20
4-20
2-4
2-15
1-57
2-43
1-68
2-17
4-8
5-24
4-18
2-51?
1-87
4-19
5-7
1-32
2-7
2-15
1-20
4-20
1-57
2-4
2-36
2-38
2-51?
2-17
1-68
4-8
5-24
4-18
5-7

FIG. 18D

Patient Information

Patient	Age	Sex & Race	Days from symptom onset to:	Biomarker	Complications	Outcome
1	57	Female, Hispanic	Admission: 7 MV: 12 Ab isolation: 18	hsCRP = 208 mg/L ESR = 58 mm/hr IL-6 = 23 pg/mL Ferritin = 766 ng/mL D-dimer = 3.4 µg/mL FEU	ARDS	Discharged on day 30
2	71	Female, Hispanic	Admission: 20 MV: 20 Ab isolation: 29	hsCRP = 33 mg/L ESR > 130 mm/hr IL-6 = 13 pg/mL Ferritin = 425 ng/mL D-dimer = 5.7 µg/mL FEU	ARDS Ventilator associated pneumonia	Discharged on day 45
3	61	Male, White	Admission: 10 MV: 10 Ab isolation: 21	hsCRP = 51 mg/L ESR = 57 mm/hr IL-6 > 315 pg/mL Ferritin = 3,238 ng/mL D-dimer = 7.4 µg/mL FEU	ARDS Acute kidney injury (hemodialysis) Sepsis	Death on day 28
4	51	Male, Black	Admission: 7 MV: 10 Ab isolation: 25	hsCRP = 88 mg/L ESR = 110 mm/hr IL-6 = 77 pg/mL Ferritin = 510 ng/mL D-dimer = 13.4 µg/mL FEU	ARDS Acute kidney injury (no hemodialysis) Ventilator associated pneumonia	Discharged on day 51
5	50	Male, White	Admission: 5 MV: 7 Ab isolation: 32	hsCRP = 2 mg/L ESR = 63 mm/hr	ARDS Neuropathy	Discharged on day 27

Abbreviation: ARDS, acute respiratory distress syndrome; MV, mechanical ventilation; hsCRP, high sensitivity C-reactive protein, ULN>10 mg/L; ESR, erythrocyte sedimentation rate, ULN=20 mm/hr; Interleukin 6, ULN= 5 pg/mL; Ferritin, ULN=150 ng/mL; D-dimer quantitative ULN= 0.8µg/mL FEU.

FIG. 19

Summary of mAb screening.

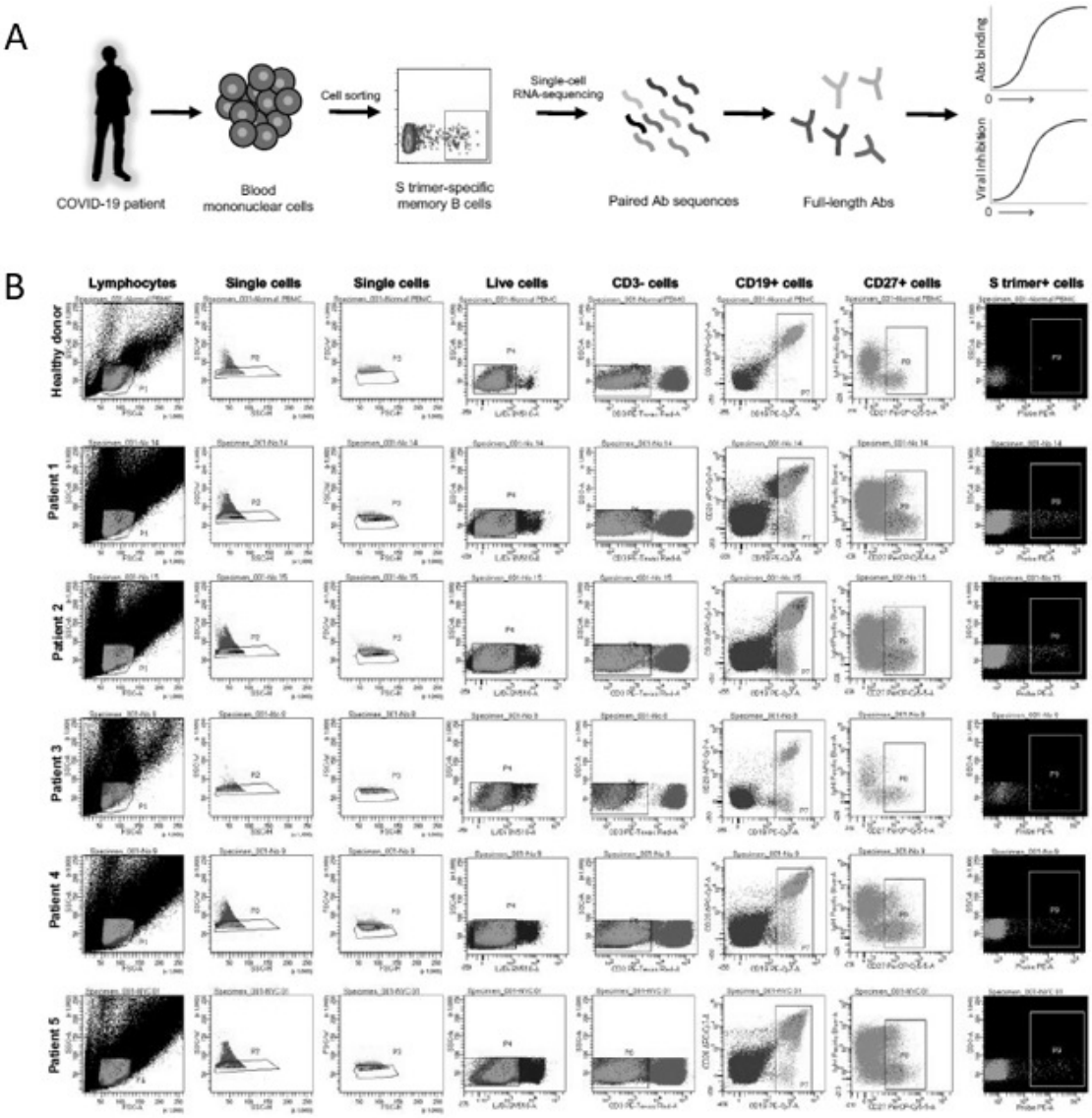
	Abs	Binding Abs			Neutralizing Abs	
		S trimer	RBD	Non-RBD	Pseudovirus	Live virus
Total	252	121	38	83	61	41
Patient 1	100	45	19	26	19	11
Patient 2	54	29	12	17	18	18
Patient 3	6	2	0	2	3	0
Patient 4	44	32	7	25	14	6
Patient 5	48	13	0	13	7	6

FIG. 20

Cryo-EM data collection, refinement, and validation statistics.

	SARS-CoV-2 spike with Fab 2-4 (EMDB-22156) (PDB 6XEY)	SARS-CoV-2 spike RBD up with Fab 4-8 EMDB-22158	SARS-CoV-2 spike RBD down with Fab 4-8 EMDB-22159	SARS-CoV-2 spike with Fab 2-43 EMDB-22157
Data collection and processing				
Magnification	81,000	81,000	81,000	81,000
Voltage (kV)	300	300	300	300
Electron exposure (e–/Å^2)	51.30	51.30	51.30	53.43
Defocus range (μm)	-0.4 to -3.5	-0.4 to -3.5	-0.4 to -3.5	-0.4 to -3.5
Pixel size (Å)	1.058	1.058	1.058	1.058
Symmetry imposed	C3	C1	C3	C1
Initial particle images (no.)	556,983	256,848	256,848	709,052
Final particle images (no.)	83,927	105,278	47,555	18,885
Map resolution (Å)	3.25	4.0	3.9	7.8
FSC threshold	0.143	0.143	0.143	0.143
Map resolution range (Å)	406.3-3.25	406.3-4.0	406.3-3.9	406.3-7.8
Refinement				
Initial model used (PDB code)	6VSB			
Model resolution (Å)	3.7			
FSC threshold	0.5			
Model resolution range (Å)	406.3-3.25			
Map sharpening *B* factor (Å^2)	-97.5			
Model composition				
Non-hydrogen atoms	28,672			
Protein residues	3785			
Ligands	63			
B factors (Å^2)				
Protein	60.89			
Ligand	50.00			
R.m.s. deviations				
Bond lengths (Å)	0.012			
Bond angles (°)	1.879			
Validation				
MolProbity score	1.05			
Clashscore	0.16			
Poor rotamers (%)	0.25			
Ramachandran plot				
Favored (%)	92.09			
Allowed (%)	7.77			
Disallowed (%)	0.13			

FIG. 21


A
COVID-19 patient
Blood mononuclear cells
Cell sorting
S trimer-specific memory B cells
Single-cell RNA-sequencing
Paired Ab sequences
Full-length Abs
Abs binding
Viral inhibition
0
B
Lymphocytes
Single cells
Single cells
Live cells
CD3- cells
CD19+ cells
CD27+ cells
S trimer+ cells
Healthy donor
Patient 1
Patient 2
Patient 3
Patient 4
Patient 5

FIGS. 22A-B

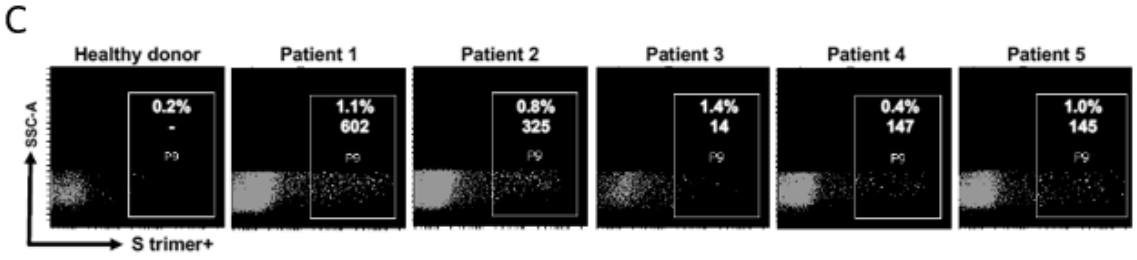
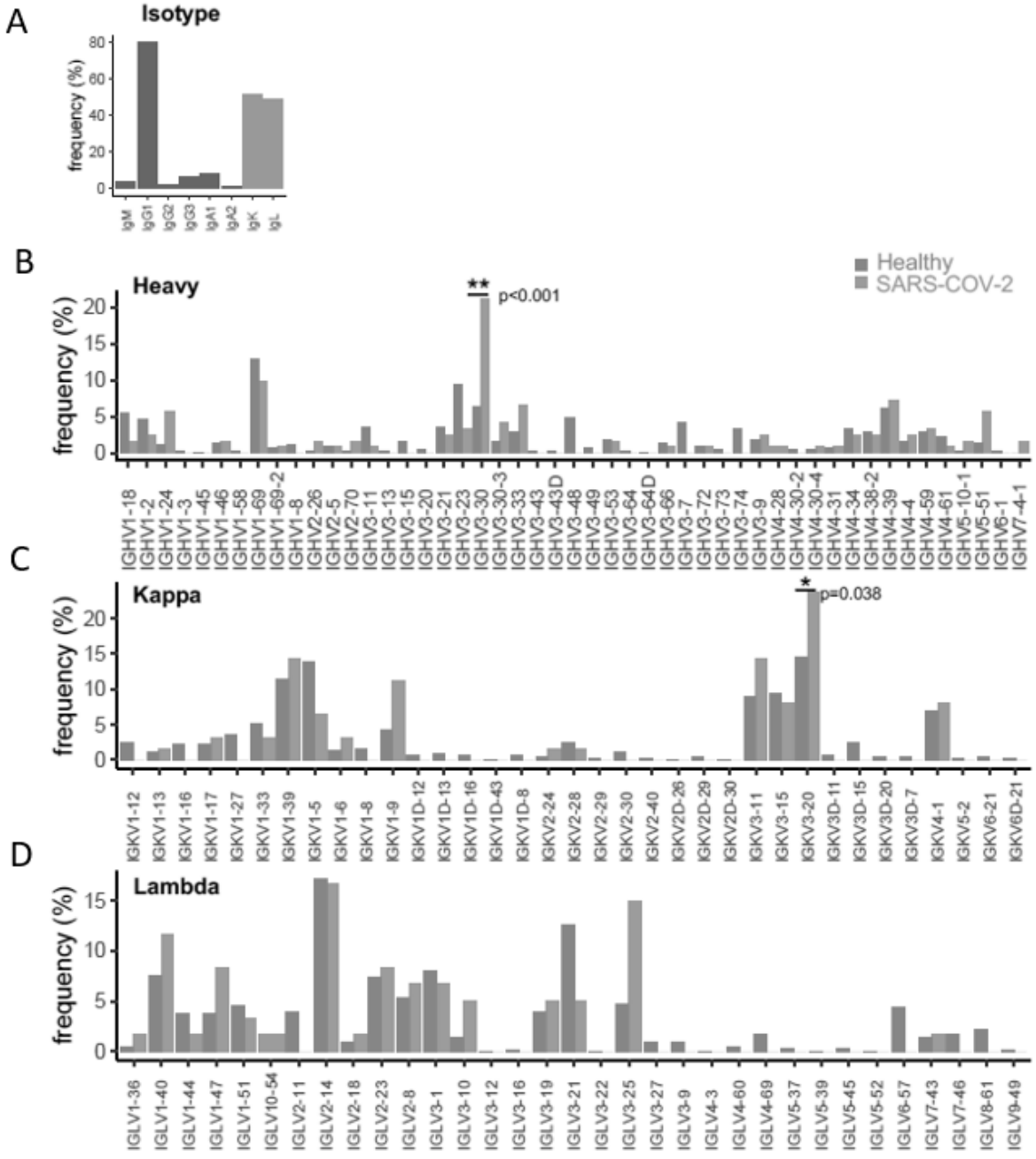
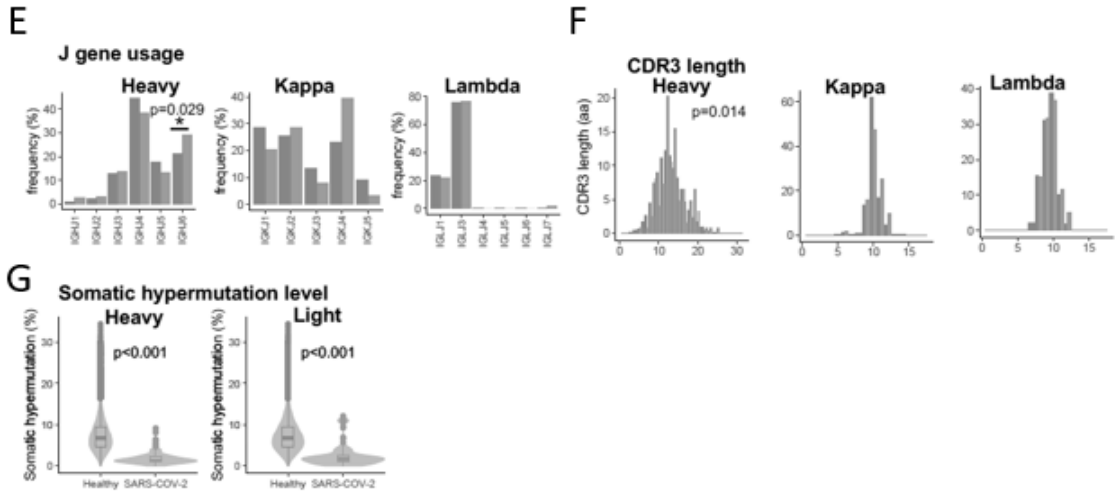

C
Healthy donor
Patient 1
Patient 2
Patient 3
Patient 4
Patient 5
0.2%
-
1.1%
602
0.8%
325
1.4%
14
0.4%
147
1.0%
145
SSC-A
S trimer+

FIG. 22C


A
Isotype
frequency (%)
IgM
IgG1
IgG2
IgG3
IgA1
IgA2
IgK
IgL
B
Heavy
Healthy
SARS-COV-2
**
p<0.001
frequency (%)
C
Kappa
*
p=0.038
frequency (%)
D
Lambda
frequency (%)

FIGS. 23A-D



FIGS. 23E-G

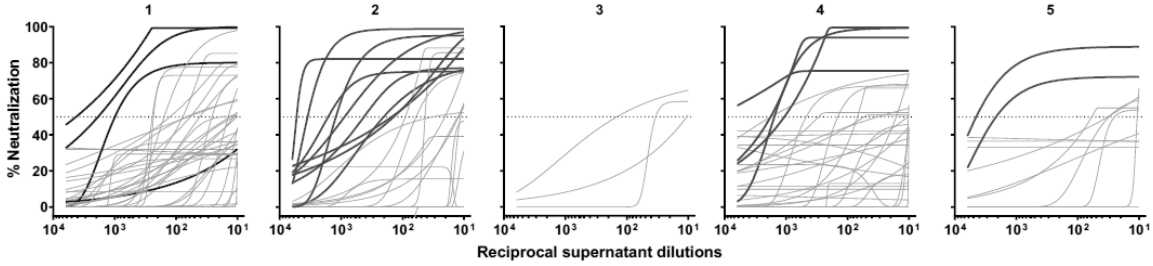


FIG. 24

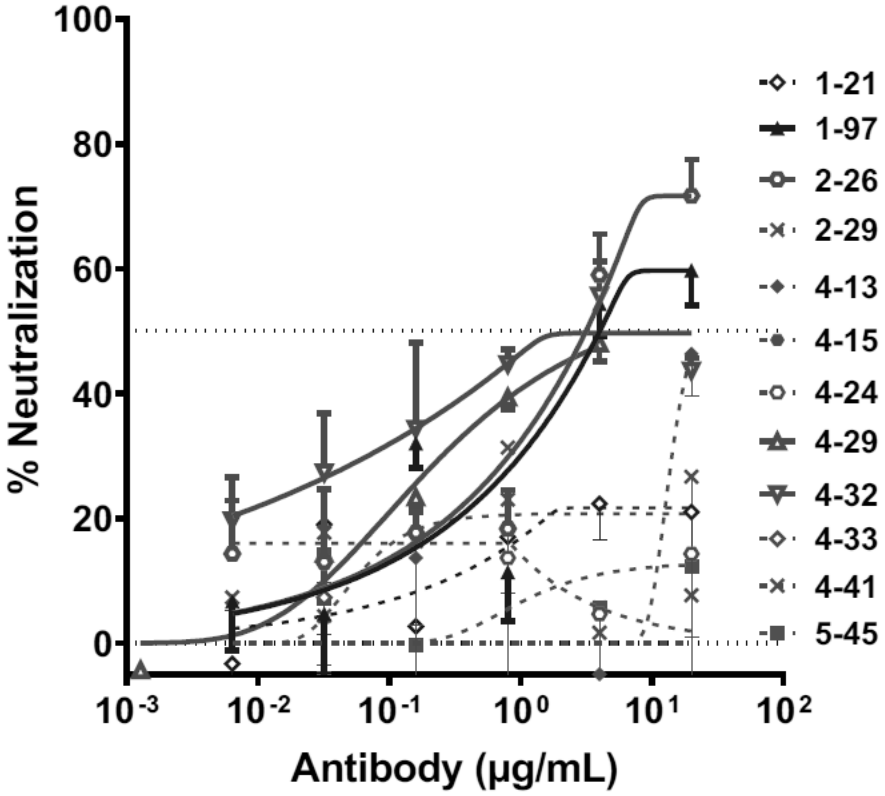
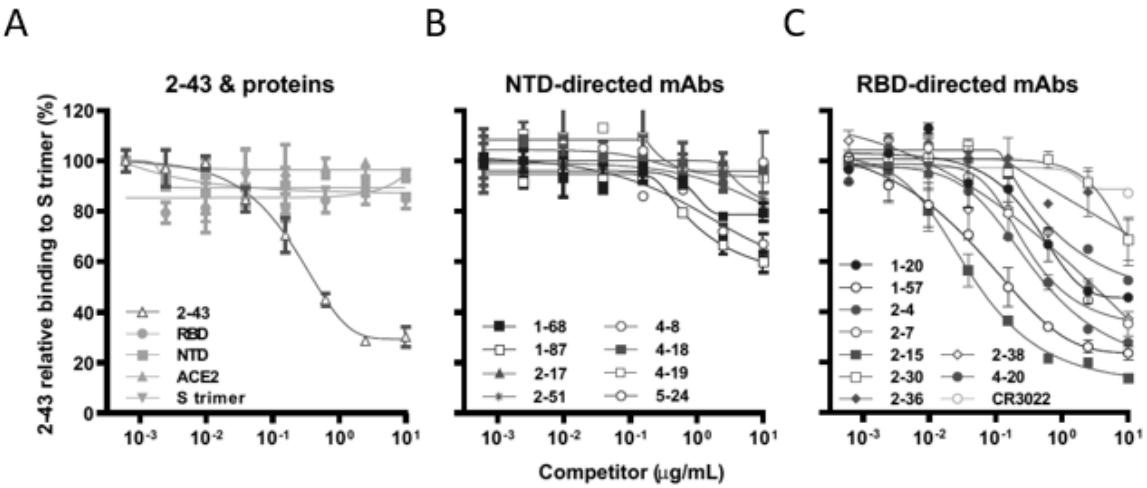
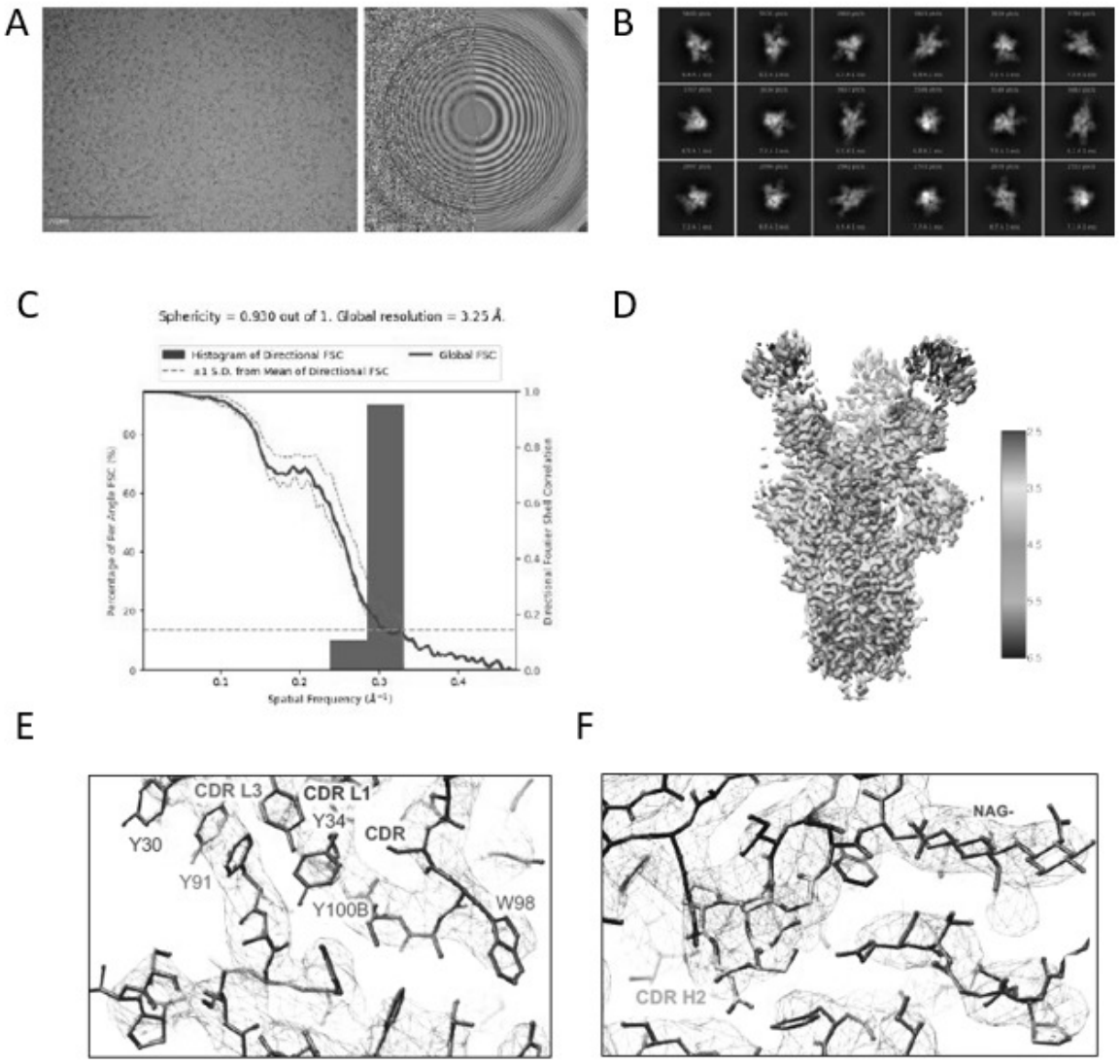

100
80
60
40
20
0
% Neutralization
10-3
10-2
10-1
100
101
102
Antibody (µg/mL)
1-21
1-97
2-26
2-29
4-13
4-15
4-24
4-29
4-32
4-33
4-41
5-45

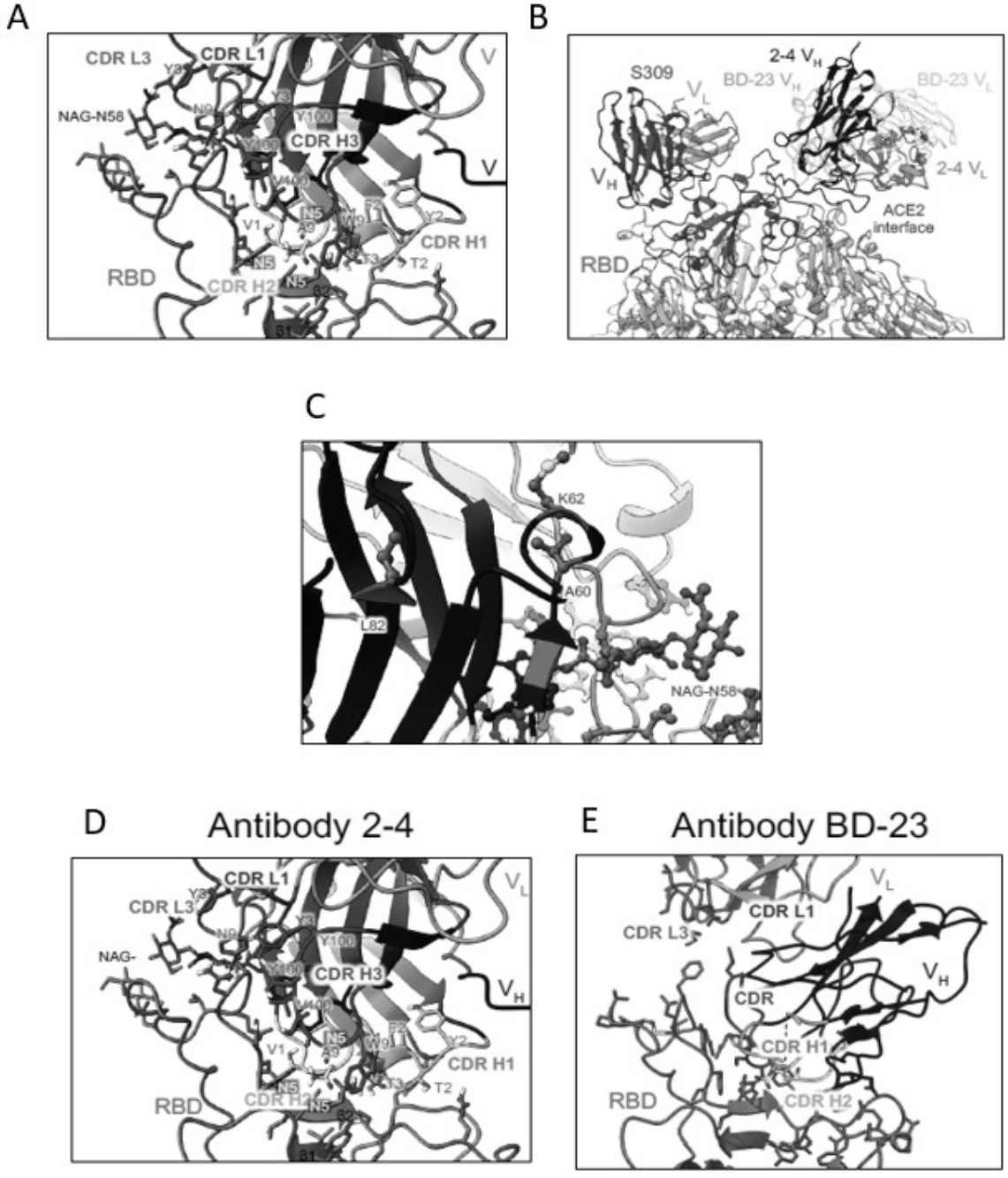
FIG. 25


A
B
C
2-43 & proteins
NTD-directed mAbs
RBD-directed mAbs
2-43 relative binding to S trimer (%)
120
100
80
60
40
20
0
2-43
RBD
NTD
ACE2
S trimer
1-68
1-87
2-17
2-51
4-8
4-18
4-19
5-24
1-20
1-57
2-4
2-7
2-15
2-30
2-36
2-38
4-20
CR3022
10-3
10-2
10-1
100
101
Competitor (μg/mL)

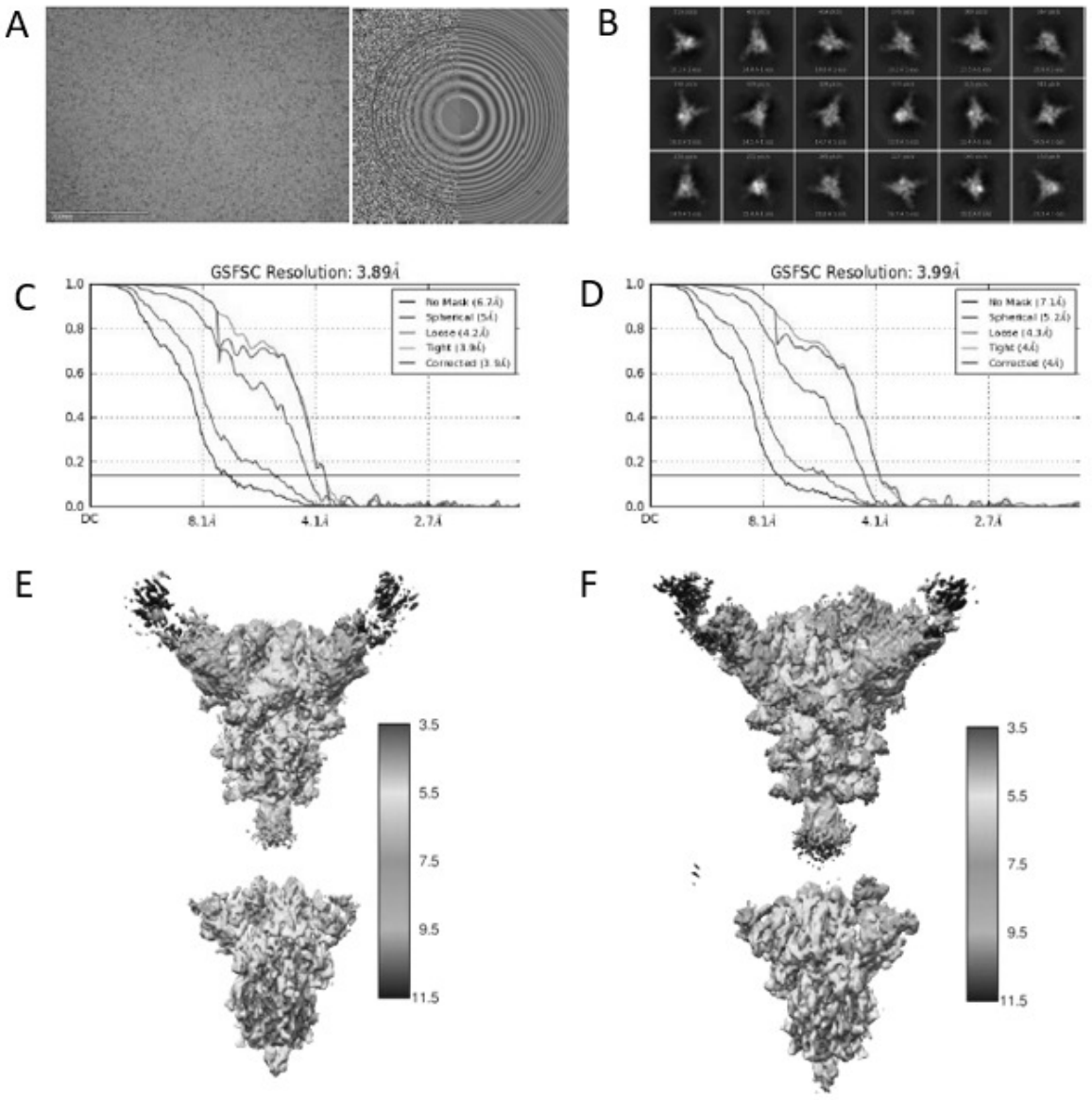
FIGS. 26A-C


A
B
C
Sphericity = 0.930 out of 1. Global resolution = 3.25 Å.
Histogram of Directional FSC
Global FSC
±1 S.D. from Mean of Directional FSC
Percentage of Ewr Angle FSC (%)
Directional Fourier Shell Correlation
Spatial Frequency (Å⁻¹)
D
E
CDR L3
CDR L1
Y34
CDR
Y30
Y91
Y100B
W98
F
NAG-
CDR H2

FIGS. 27A-F


A
CDR L3
CDR L1
V
NAG-N58
CDR H3
V
RBD
CDR H2
CDR H1
B
S309
2-4 V_H
BD-23 V_H
V_L
BD-23 V_L
2-4 V_L
V_H
ACE2
interface
RBD
C
K62
A60
L82
NAG-N58
D
Antibody 2-4
CDR L1
CDR L3
V_L
NAG-
CDR H3
V_H
CDR H1
RBD
CDR H2
E
Antibody BD-23
CDR L1
CDR L3
V_L
V_H
CDR
CDR H1
RBD
CDR H2

FIGS. 28A-E


A
B
C
GSFSC Resolution: 3.89Å
No Mask (6.2Å)
Spherical (5Å)
Loose (4.2Å)
Tight (3.9Å)
Corrected (3.9Å)
1.0
0.8
0.6
0.4
0.2
0.0
DC
8.1Å
4.1Å
2.7Å
D
GSFSC Resolution: 3.99Å
No Mask (7.1Å)
Spherical (5.2Å)
Loose (4.3Å)
Tight (4Å)
Corrected (4Å)
E
3.5
5.5
7.5
9.5
11.5
F

FIGS. 29A-F

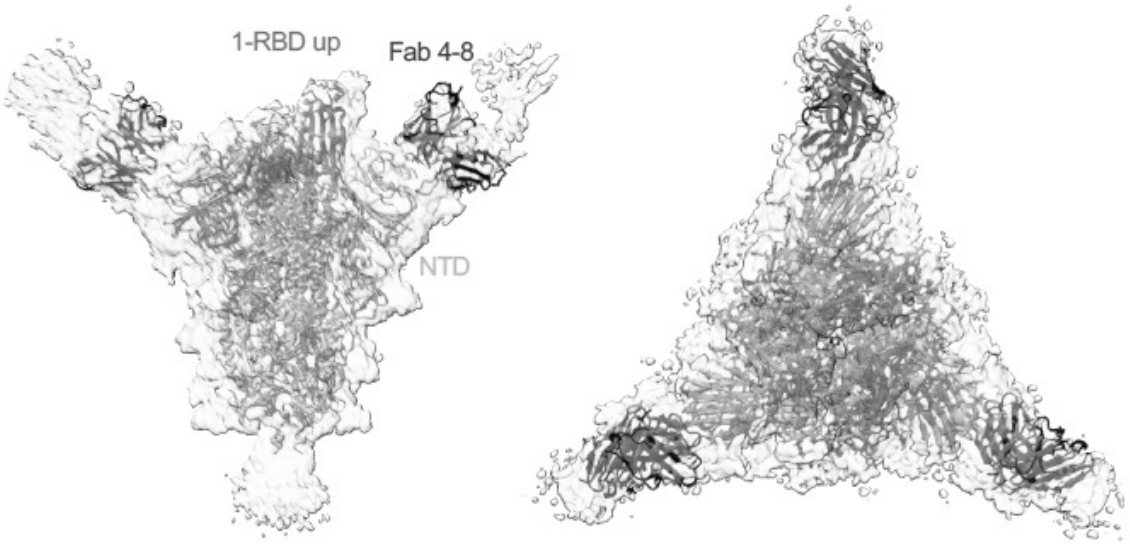
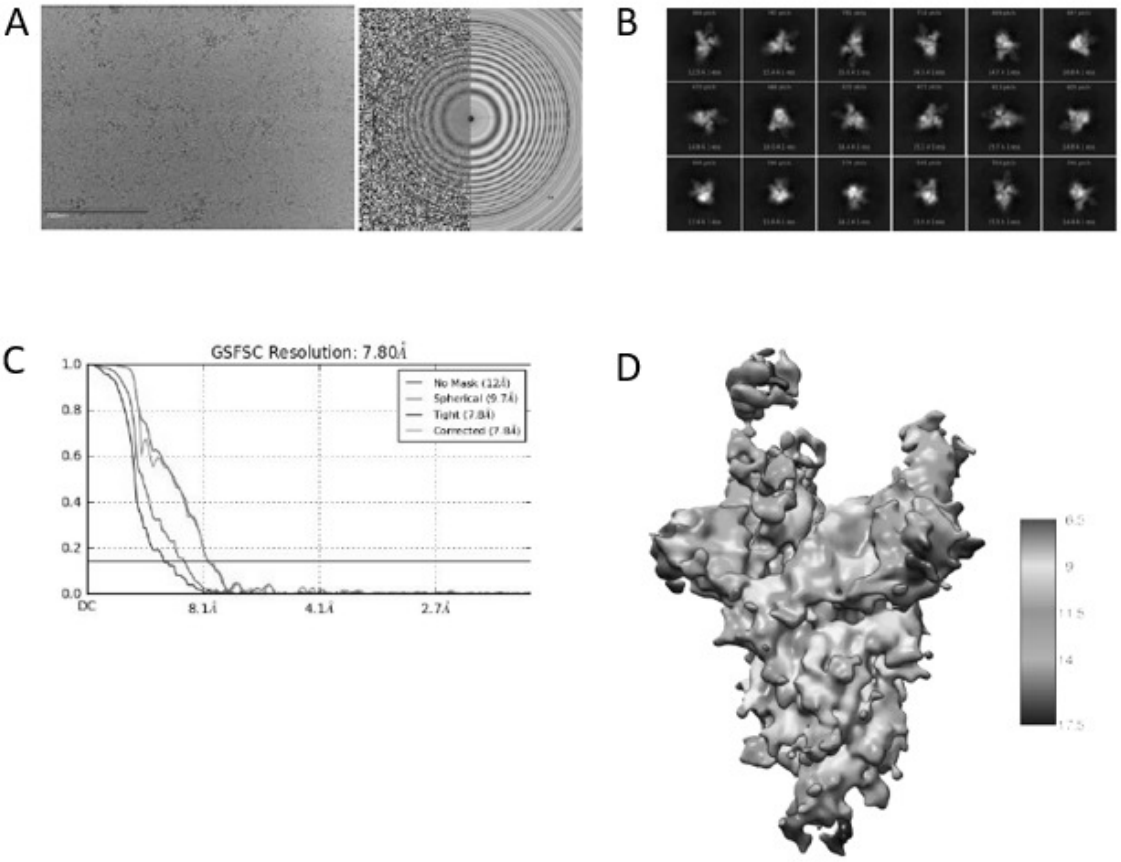
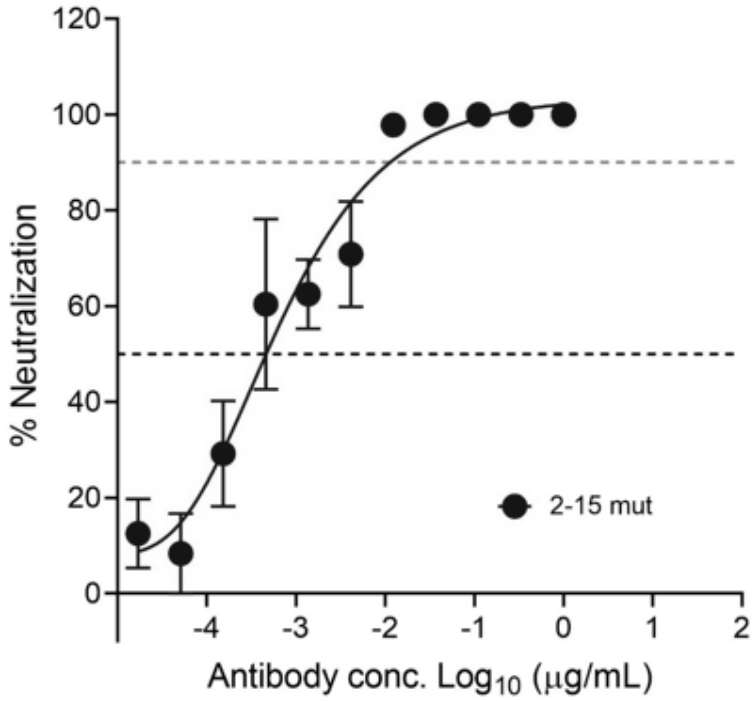


FIG. 30


A
B
C
GSFSC Resolution: 7.80Å
No Mask (12Å)
Spherical (9.7Å)
Tight (7.8Å)
Corrected (7.8Å)
1.0
0.8
0.6
0.4
0.2
0.0
DC
8.1Å
4.1Å
2.7Å
D
6.5
9
11.5
14
17.5

FIGS. 31A-D

A

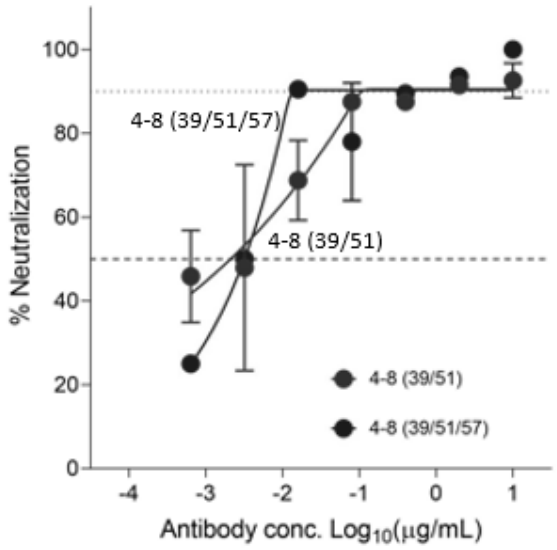


B

	Potency (µg/mL)	
mAb	**IC_{50}**	**IC_{90}**
2-15mut	**<0.00064**	**0.011**

FIGS. 32A-B

A



B

	Potency (μg/mL)	
mAb	IC_{50}	IC_{80}
4-8 (39/51)	0.002	0.108
4-8 (39/51/57)	0.003	0.014

FIGS. 33A-B

	Potency (μg/mL)	
mAb	**IC_{50}**	**IC_{90}**
2-15mut	<0.00064	0.011
4-8 (39/51)	0.002	0.108
4-8 (39/51/57)	0.003	0.014

FIG. 34

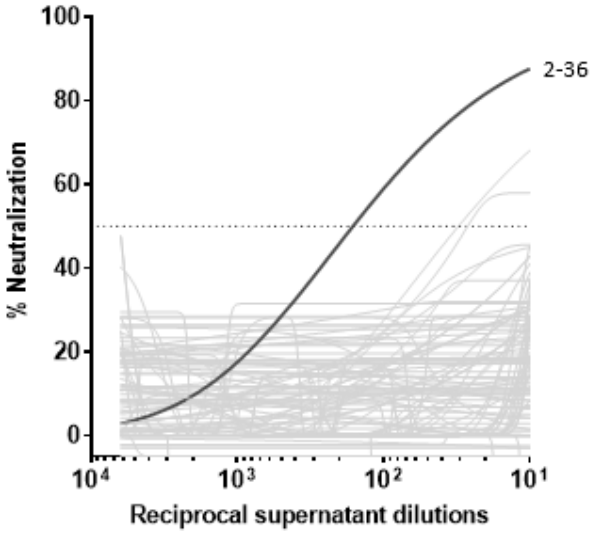
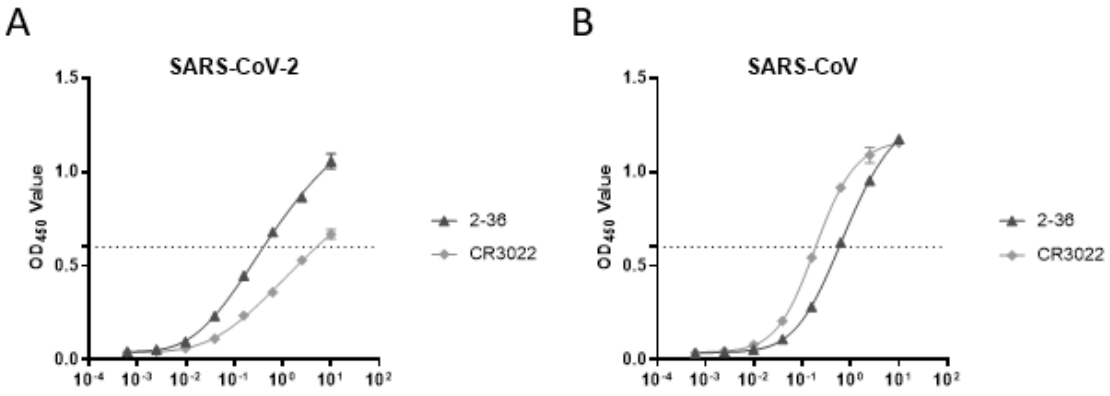
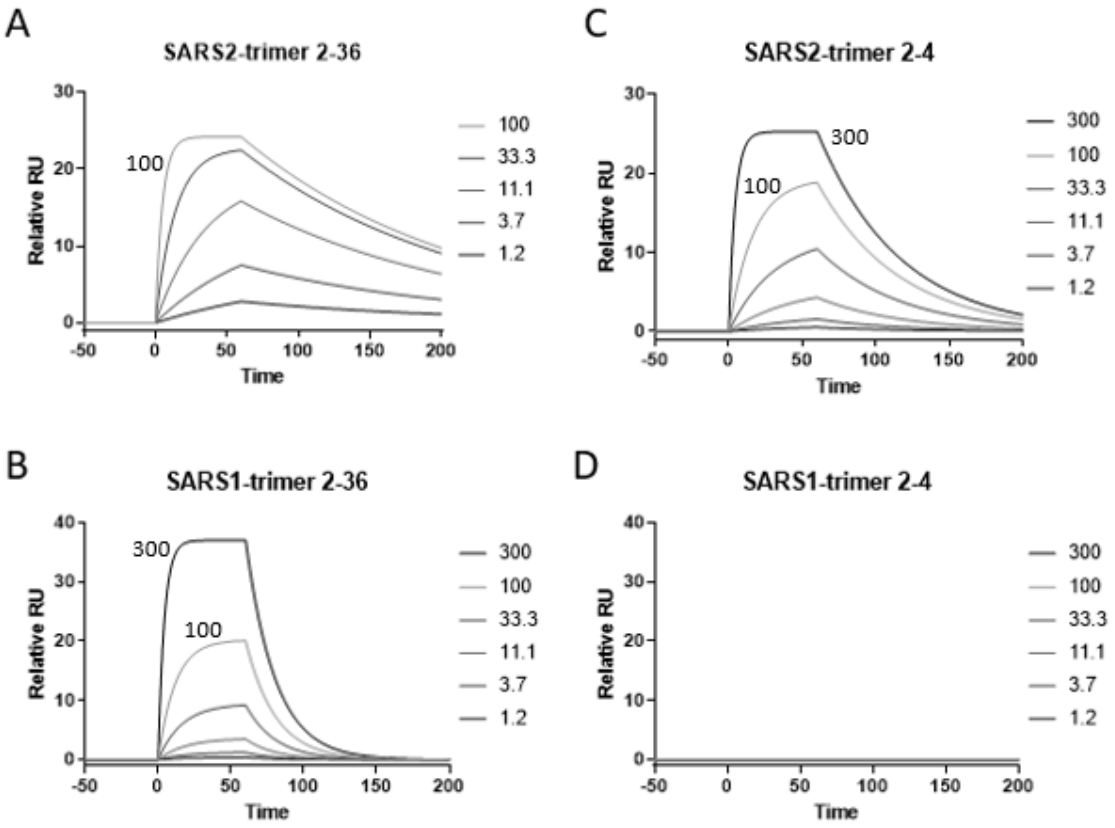

100
80
60
40
20
0
% Neutralization
2-36
10^4
10^3
10^2
10^1
Reciprocal supernatant dilutions

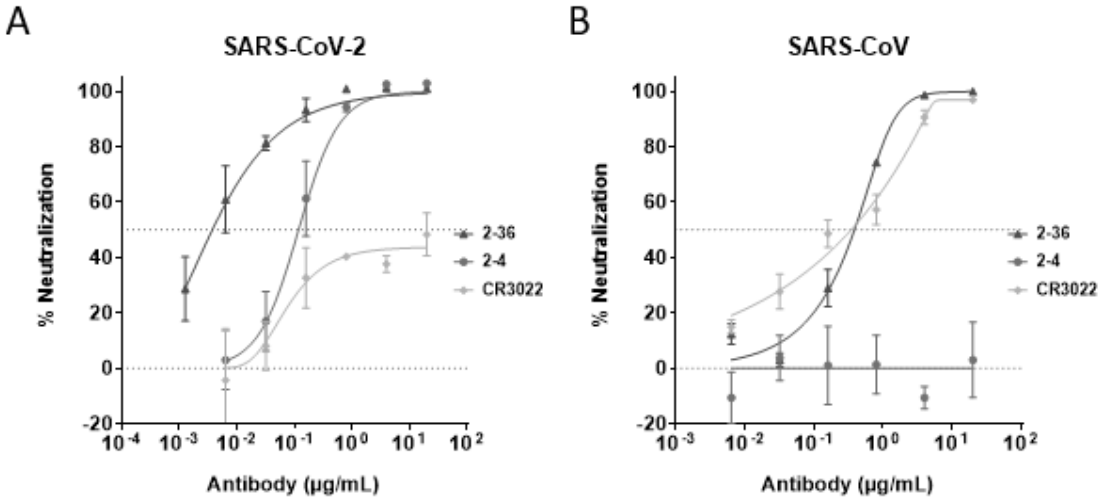
FIG. 35


A
SARS-CoV-2
OD450 Value
1.5
1.0
0.5
0.0
10-4 10-3 10-2 10-1 100 101 102
2-38
CR3022
B
SARS-CoV
OD450 Value
1.5
1.0
0.5
0.0
10-4 10-3 10-2 10-1 100 101 102
2-38
CR3022

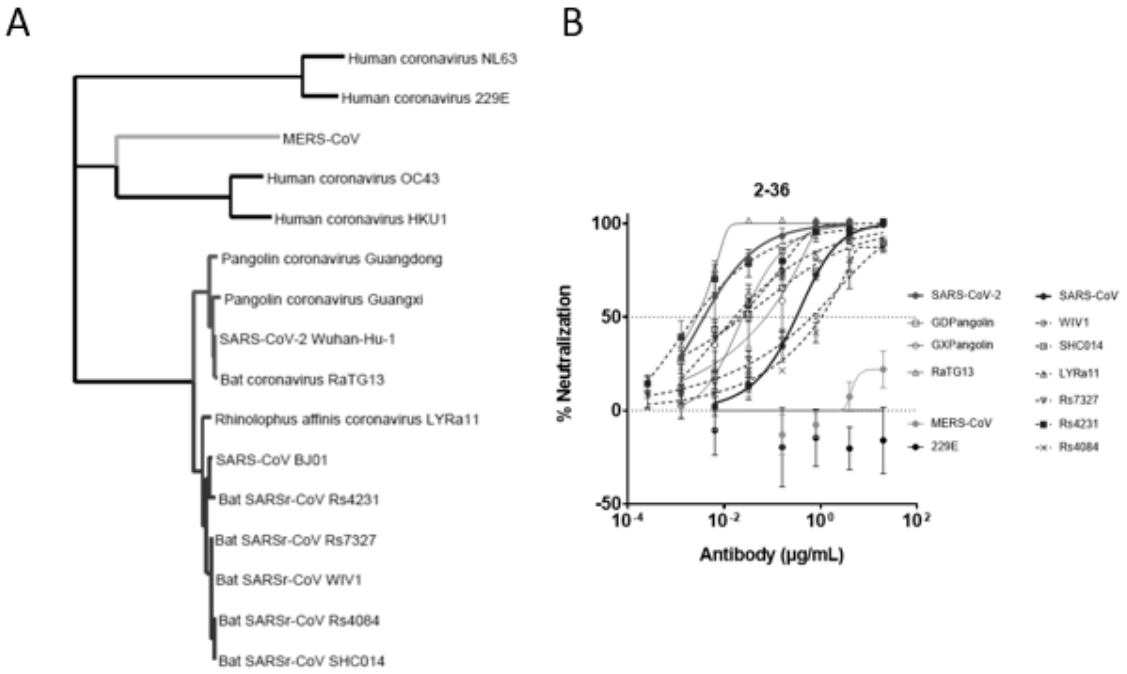
FIGS. 36A-B


A
SARS2-trimer 2-36
Relative RU
Time
100
100
33.3
11.1
3.7
1.2
C
SARS2-trimer 2-4
300
100
B
SARS1-trimer 2-36
D
SARS1-trimer 2-4

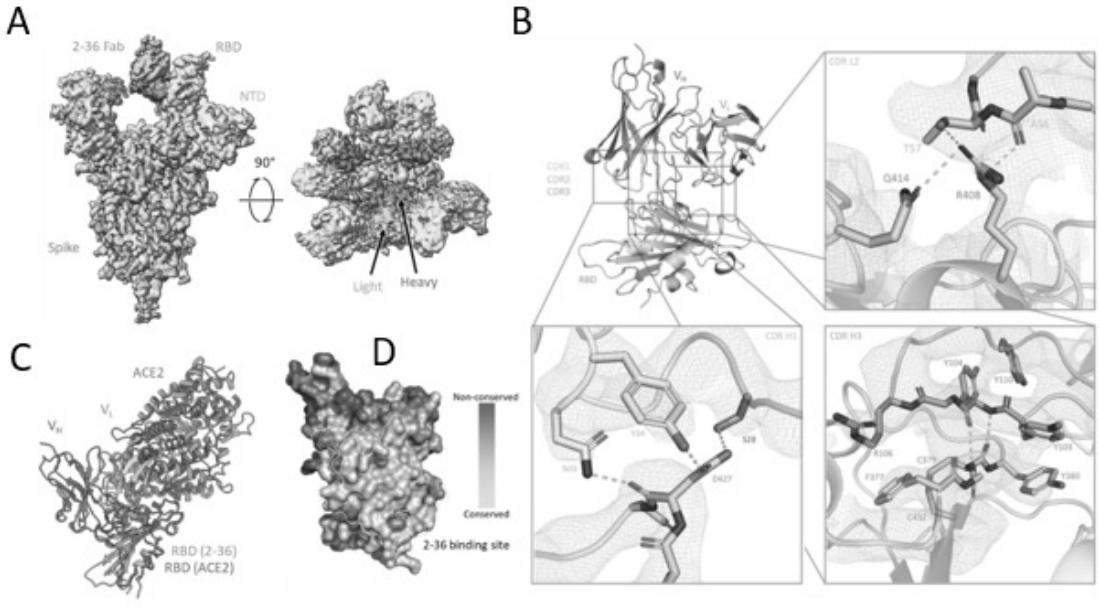
FIGS. 37A-D


A
SARS-CoV-2
% Neutralization
Antibody (µg/mL)
2-36
2-4
CR3022
B
SARS-CoV
% Neutralization
Antibody (µg/mL)
2-36
2-4
CR3022

FIGS. 38A-B


A
Human coronavirus NL63
Human coronavirus 229E
MERS-CoV
Human coronavirus OC43
Human coronavirus HKU1
Pangolin coronavirus Guangdong
Pangolin coronavirus Guangxi
SARS-CoV-2 Wuhan-Hu-1
Bat coronavirus RaTG13
Rhinolophus affinis coronavirus LYRa11
SARS-CoV BJ01
Bat SARSr-CoV Rs4231
Bat SARSr-CoV Rs7327
Bat SARSr-CoV WIV1
Bat SARSr-CoV Rs4084
Bat SARSr-CoV SHC014
B
2-36
% Neutralization
100
50
0
-50
10-4
10-2
100
102
Antibody (µg/mL)
SARS-CoV-2
GDPangolin
GXPangolin
RaTG13
MERS-CoV
229E
SARS-CoV
WIV1
SHC014
LYRa11
Rs7327
Rs4231
Rs4084

FIGS. 39A-B


A
2-36 Fab
RBD
NTD
Spike
90°
Light
Heavy
B
C
ACE2
RBD (2-36)
RBD (ACE2)
D
Non-conserved
Conserved
2-36 binding site

FIGS. 40A-D

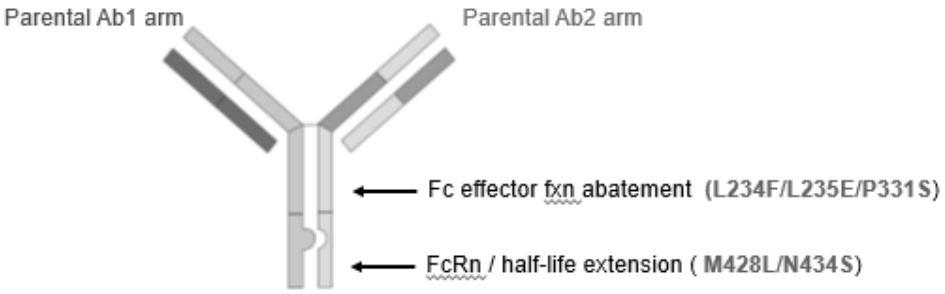

Parental Ab1 arm
Parental Ab2 arm
Fc effector fxn abatement (L234F/L235E/P331S)
FcRn / half-life extension (M428L/N434S)

FIG. 41

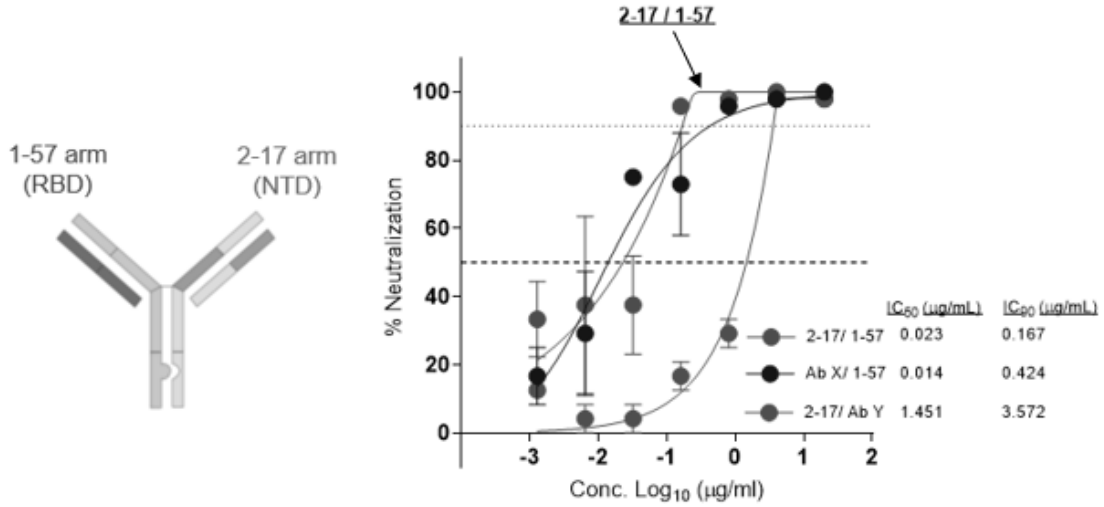

1-57 arm
(RBD)
2-17 arm
(NTD)
2-17 / 1-57
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
2-17/ 1-57 0.023 0.167
Ab X/ 1-57 0.014 0.424
2-17/ Ab Y 1.451 3.572

FIG. 42

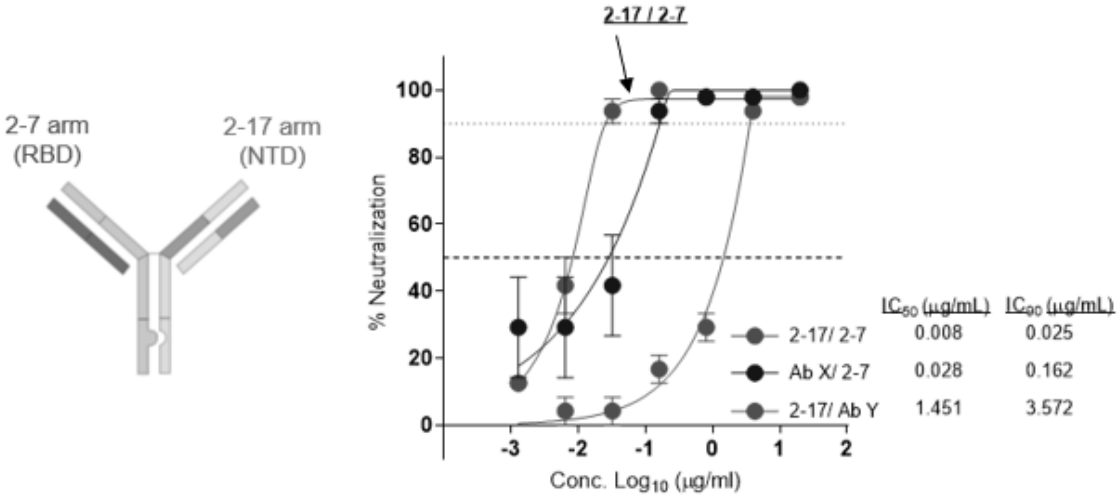

2-7 arm
(RBD)
2-17 arm
(NTD)
2-17 / 2-7
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
2-17/ 2-7
0.008
0.025
Ab X/ 2-7
0.028
0.162
2-17/ Ab Y
1.451
3.572

FIG. 43

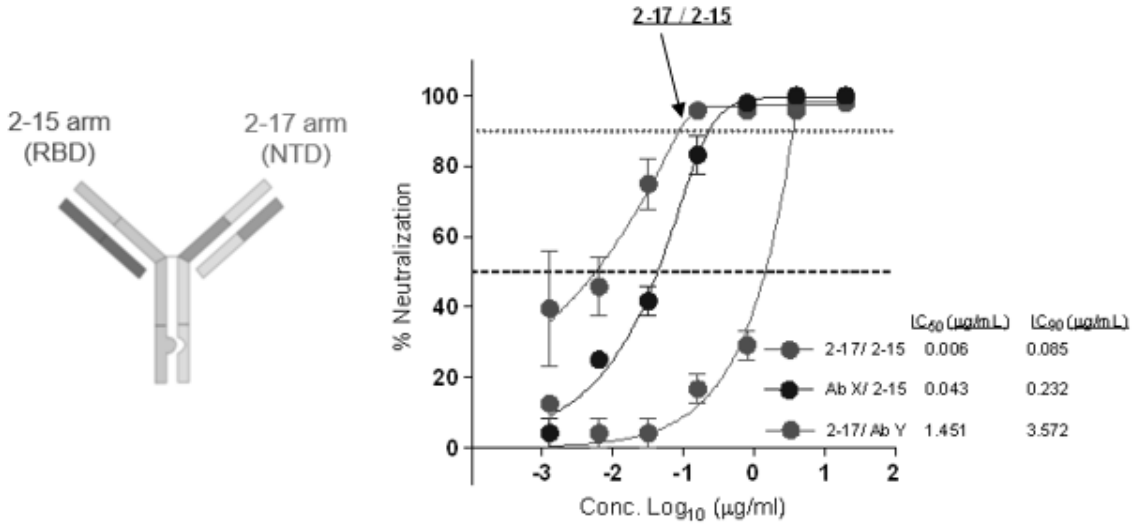

2-15 arm
(RBD)
2-17 arm
(NTD)
2-17 / 2-15
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
2-17/ 2-15 0.006 0.085
Ab X/ 2-15 0.043 0.232
2-17/ Ab Y 1.451 3.572

FIG. 44

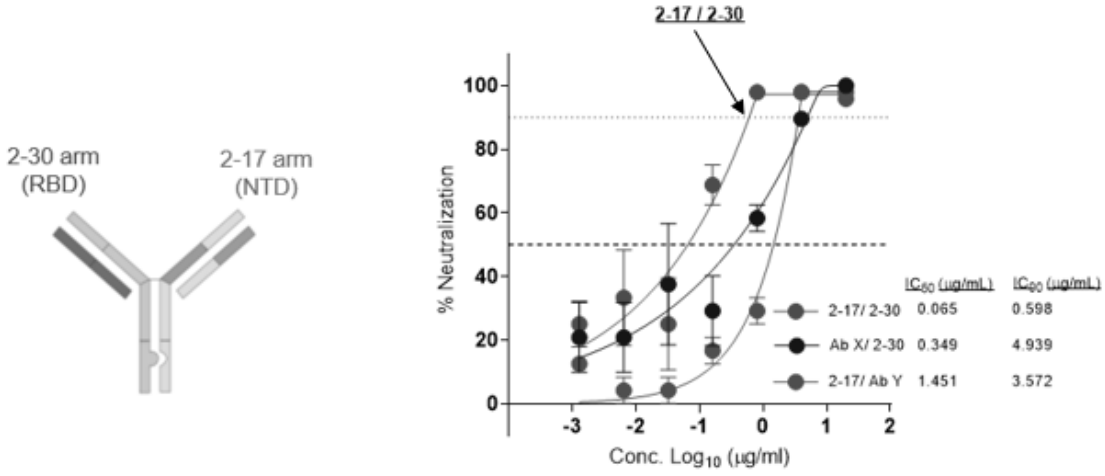

2-30 arm
(RBD)
2-17 arm
(NTD)
2-17 / 2-30
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
2-17/ 2-30 0.065 0.598
Ab X/ 2-30 0.349 4.939
2-17/ Ab Y 1.451 3.572

FIG. 45

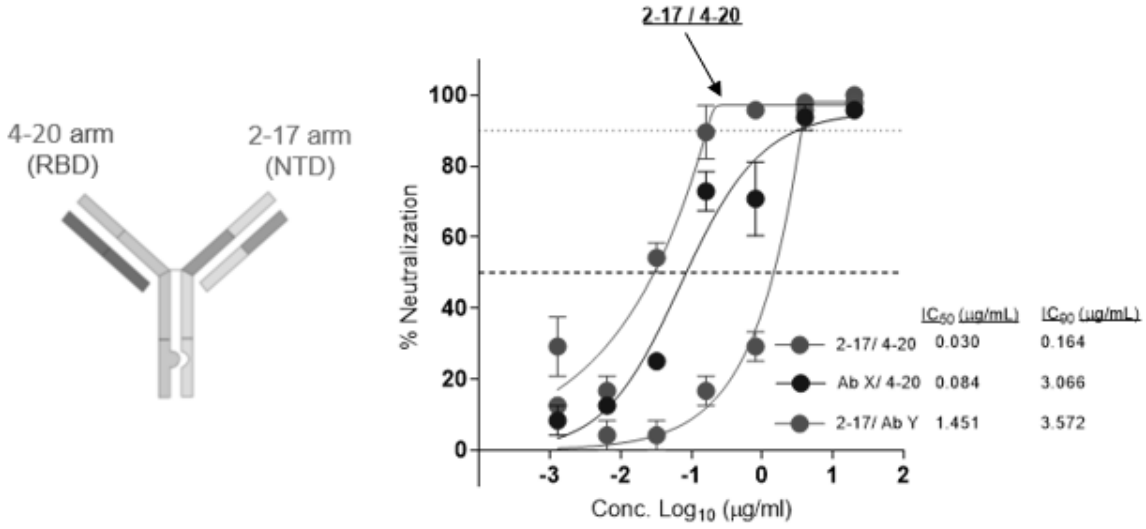

4-20 arm
(RBD)
2-17 arm
(NTD)
2-17 / 4-20
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC80 (µg/mL)
2-17/ 4-20 0.030 0.164
Ab X/ 4-20 0.084 3.066
2-17/ Ab Y 1.451 3.572

FIG. 46

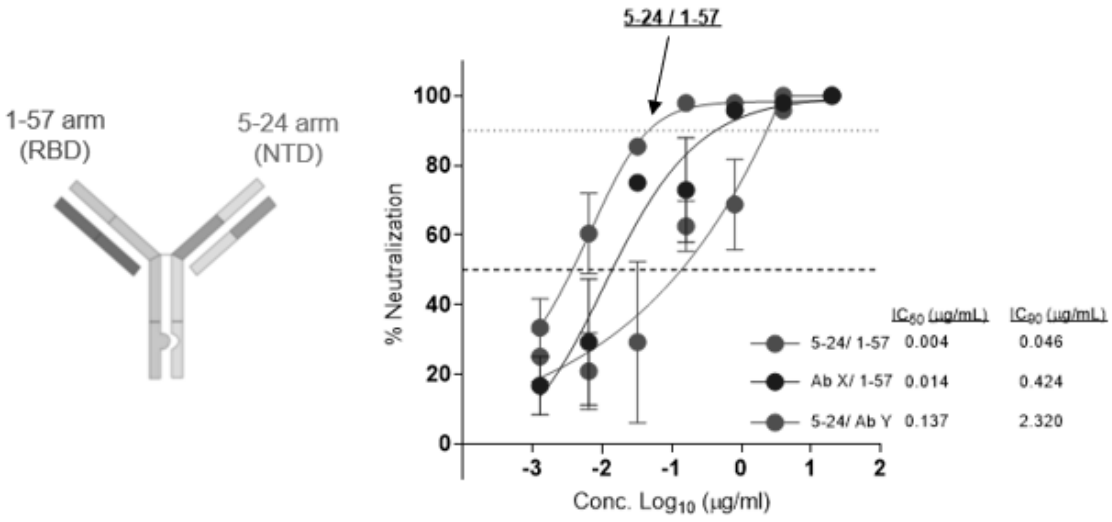

1-57 arm
(RBD)
5-24 arm
(NTD)
5-24 / 1-57
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
5-24/ 1-57 0.004 0.046
Ab X/ 1-57 0.014 0.424
5-24/ Ab Y 0.137 2.320

FIG. 47

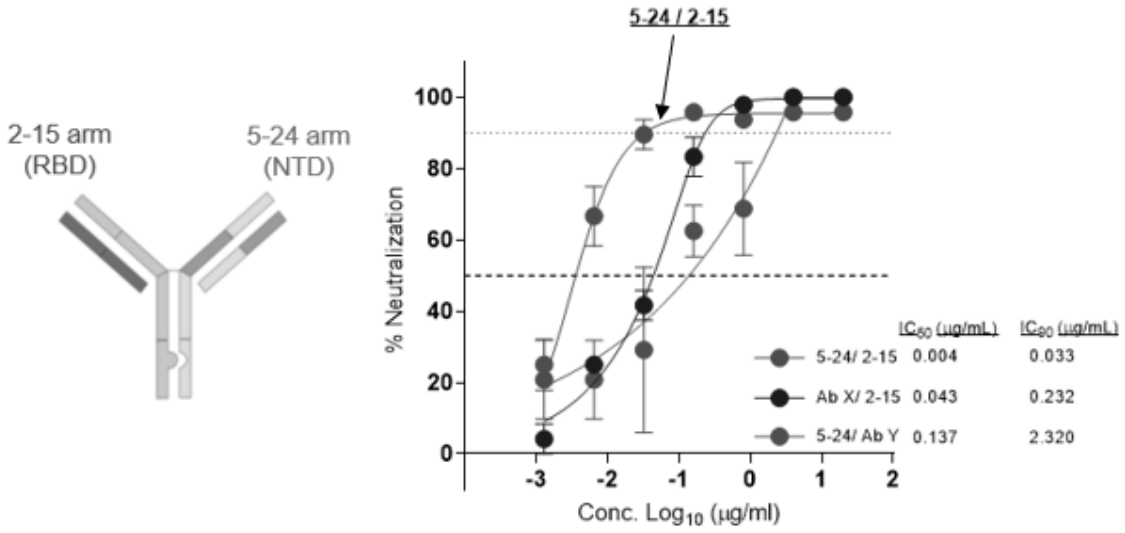

2-15 arm
(RBD)
5-24 arm
(NTD)
5-24 / 2-15
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC80 (µg/mL)
5-24/ 2-15 0.004 0.033
Ab X/ 2-15 0.043 0.232
5-24/ Ab Y 0.137 2.320

FIG. 48

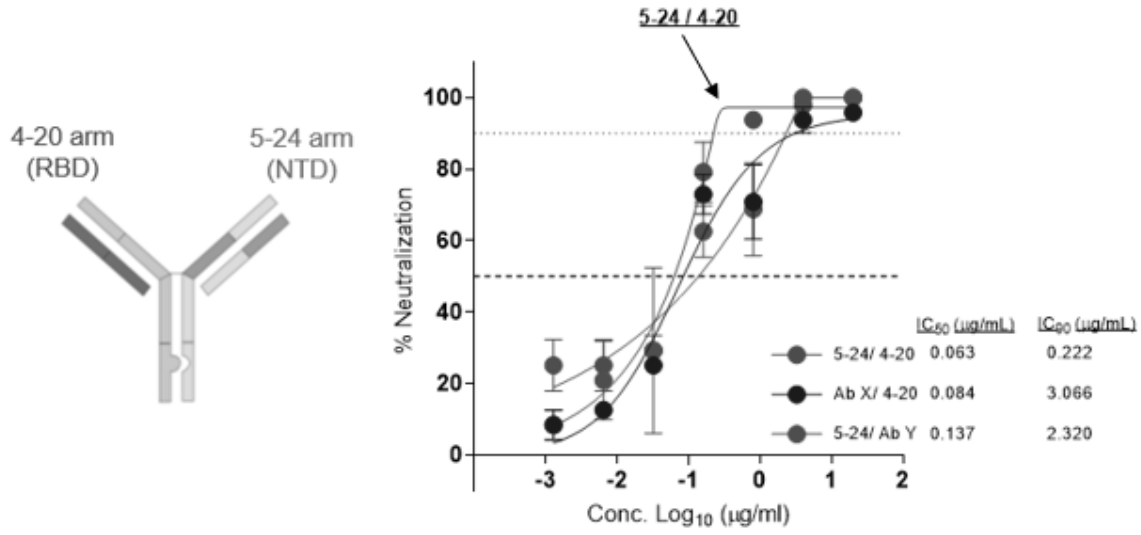

4-20 arm
(RBD)
5-24 arm
(NTD)
5-24 / 4-20
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
5-24/ 4-20 0.063 0.222
Ab X/ 4-20 0.084 3.066
5-24/ Ab Y 0.137 2.320

FIG. 49

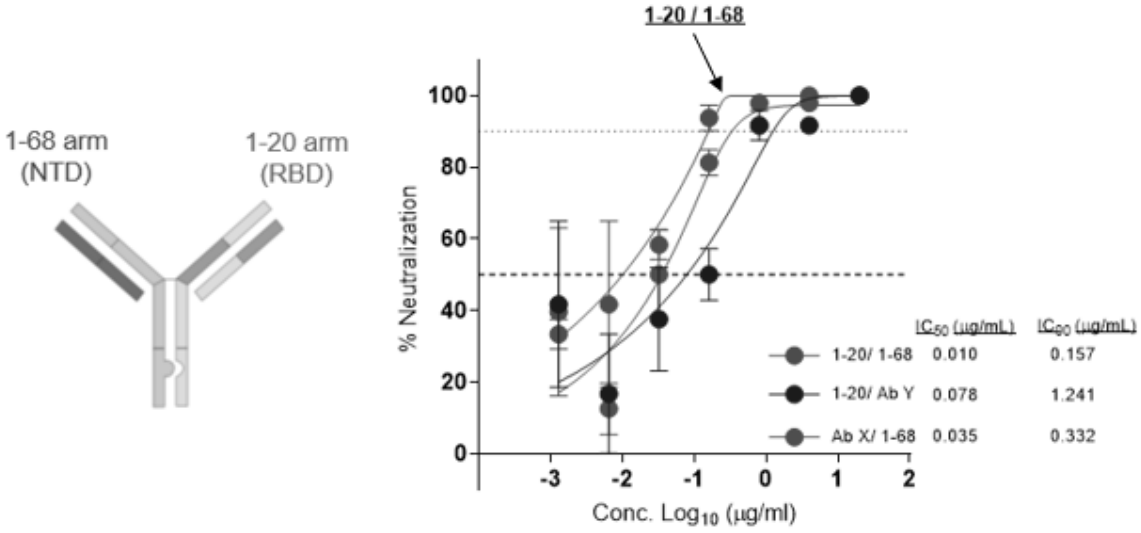

1-68 arm
(NTD)
1-20 arm
(RBD)
1-20 / 1-68
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
1-20/ 1-68 0.010 0.157
1-20/ Ab Y 0.078 1.241
Ab X/ 1-68 0.035 0.332

FIG. 50

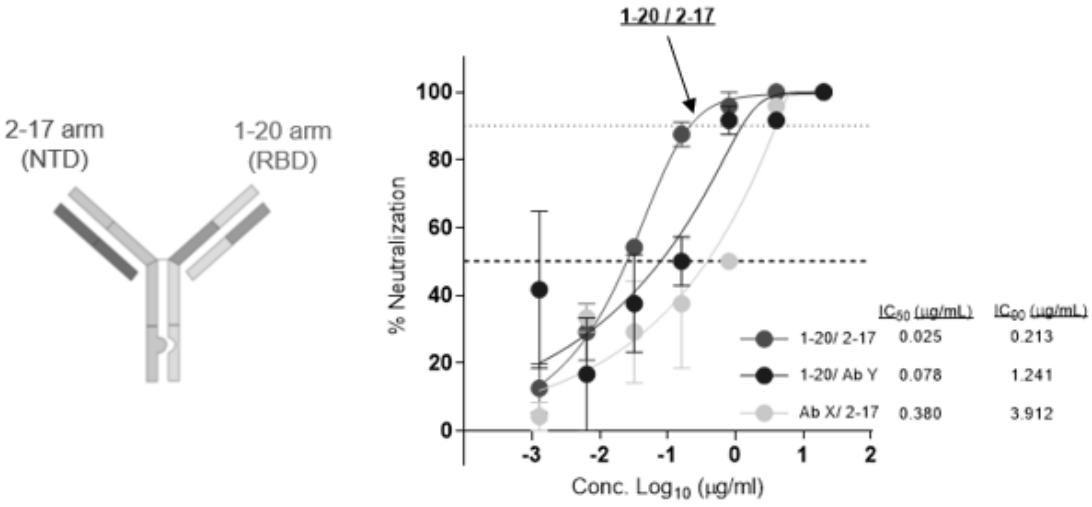

2-17 arm
(NTD)
1-20 arm
(RBD)
1-20 / 2-17
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
1-20/ 2-17 0.025 0.213
1-20/ Ab Y 0.078 1.241
Ab X/ 2-17 0.380 3.912

FIG. 51

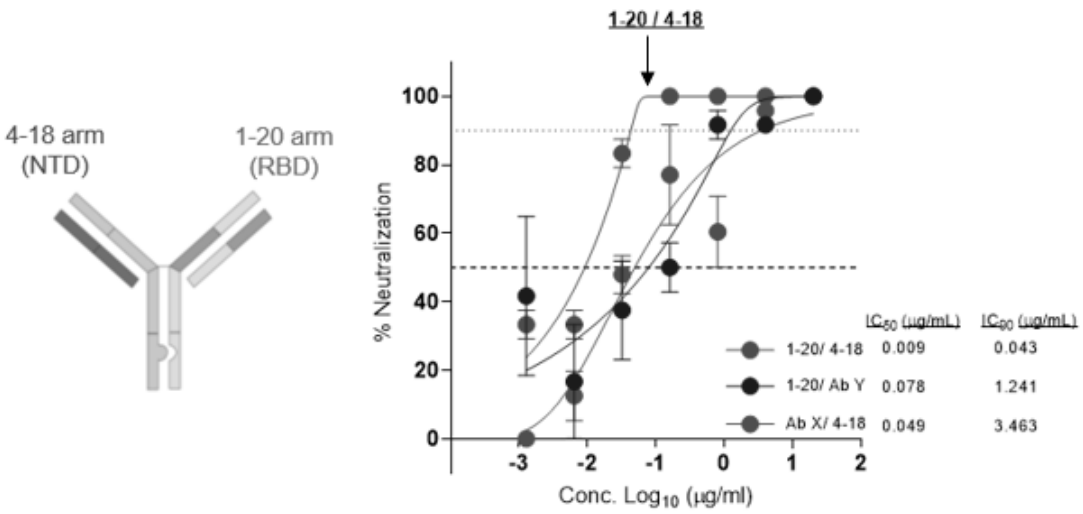

4-18 arm
(NTD)
1-20 arm
(RBD)
1-20 / 4-18
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
1-20/ 4-18 0.009 0.043
1-20/ Ab Y 0.078 1.241
Ab X/ 4-18 0.049 3.463

FIG. 52

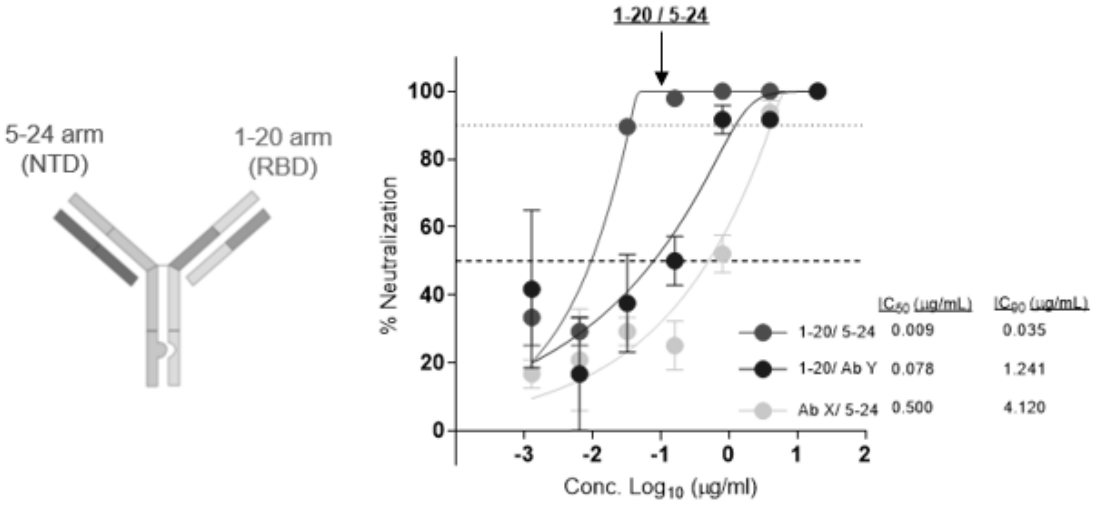

5-24 arm
(NTD)
1-20 arm
(RBD)
1-20 / 5-24
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
1-20/ 5-24 0.009 0.035
1-20/ Ab Y 0.078 1.241
Ab X/ 5-24 0.500 4.120

FIG. 53

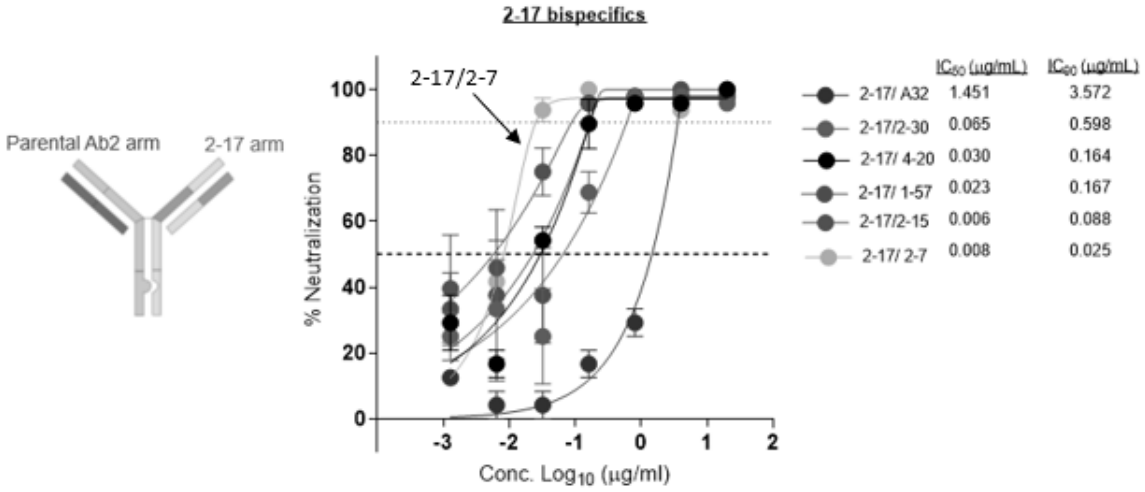

2-17 bispecifics
Parental Ab2 arm
2-17 arm
2-17/2-7
% Neutralization
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
2-17/ A32 1.451 3.572
2-17/2-30 0.065 0.598
2-17/ 4-20 0.030 0.164
2-17/ 1-57 0.023 0.167
2-17/2-15 0.006 0.088
2-17/ 2-7 0.008 0.025

FIG. 54

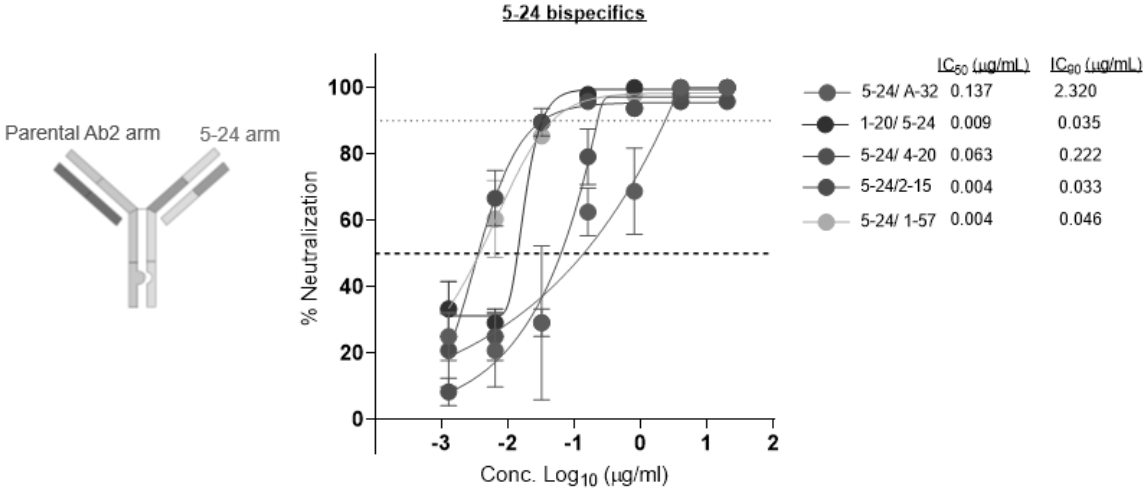

5-24 bispecifics
Parental Ab2 arm
5-24 arm
% Neutralization
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
5-24/ A-32 0.137 2.320
1-20/ 5-24 0.009 0.035
5-24/ 4-20 0.063 0.222
5-24/2-15 0.004 0.033
5-24/ 1-57 0.004 0.046

FIG. 55

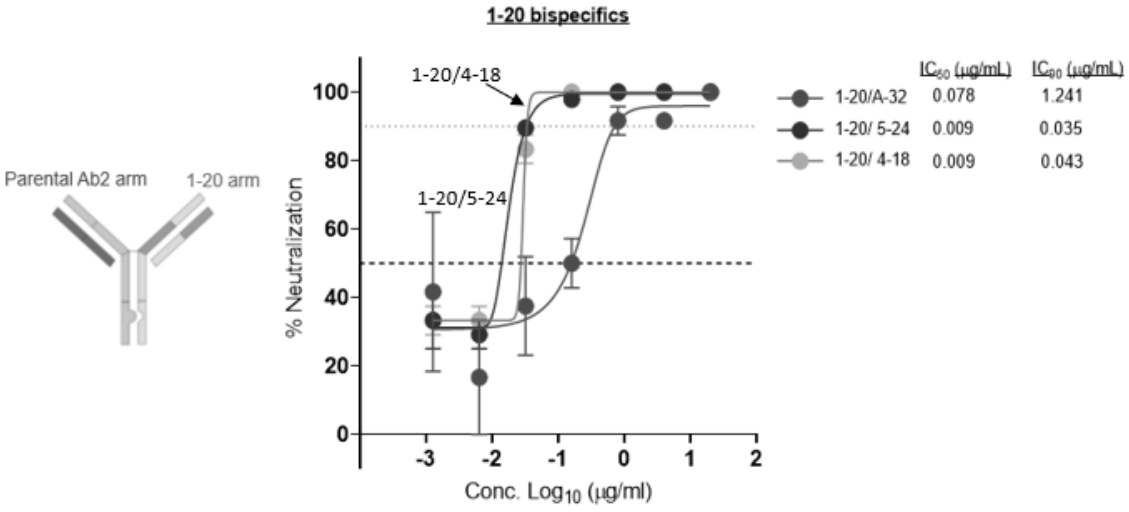

1-20 bispecifics
Parental Ab2 arm
1-20 arm
1-20/4-18
1-20/5-24
% Neutralization
Conc. Log10 (µg/ml)
IC50 (µg/mL)
IC90 (µg/mL)
1-20/A-32 0.078 1.241
1-20/ 5-24 0.009 0.035
1-20/ 4-18 0.009 0.043

FIG. 56

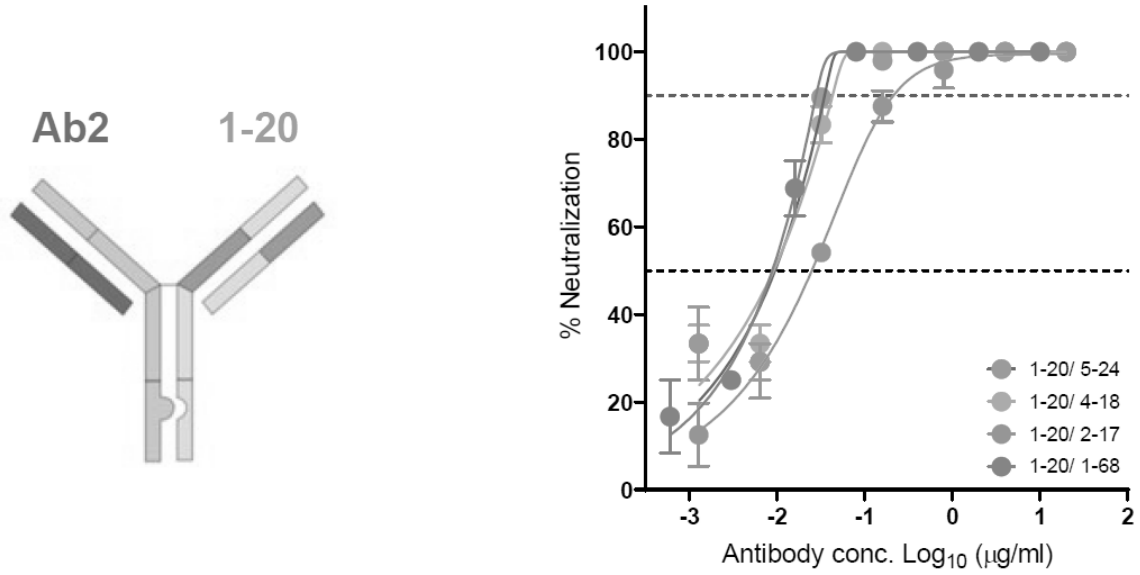
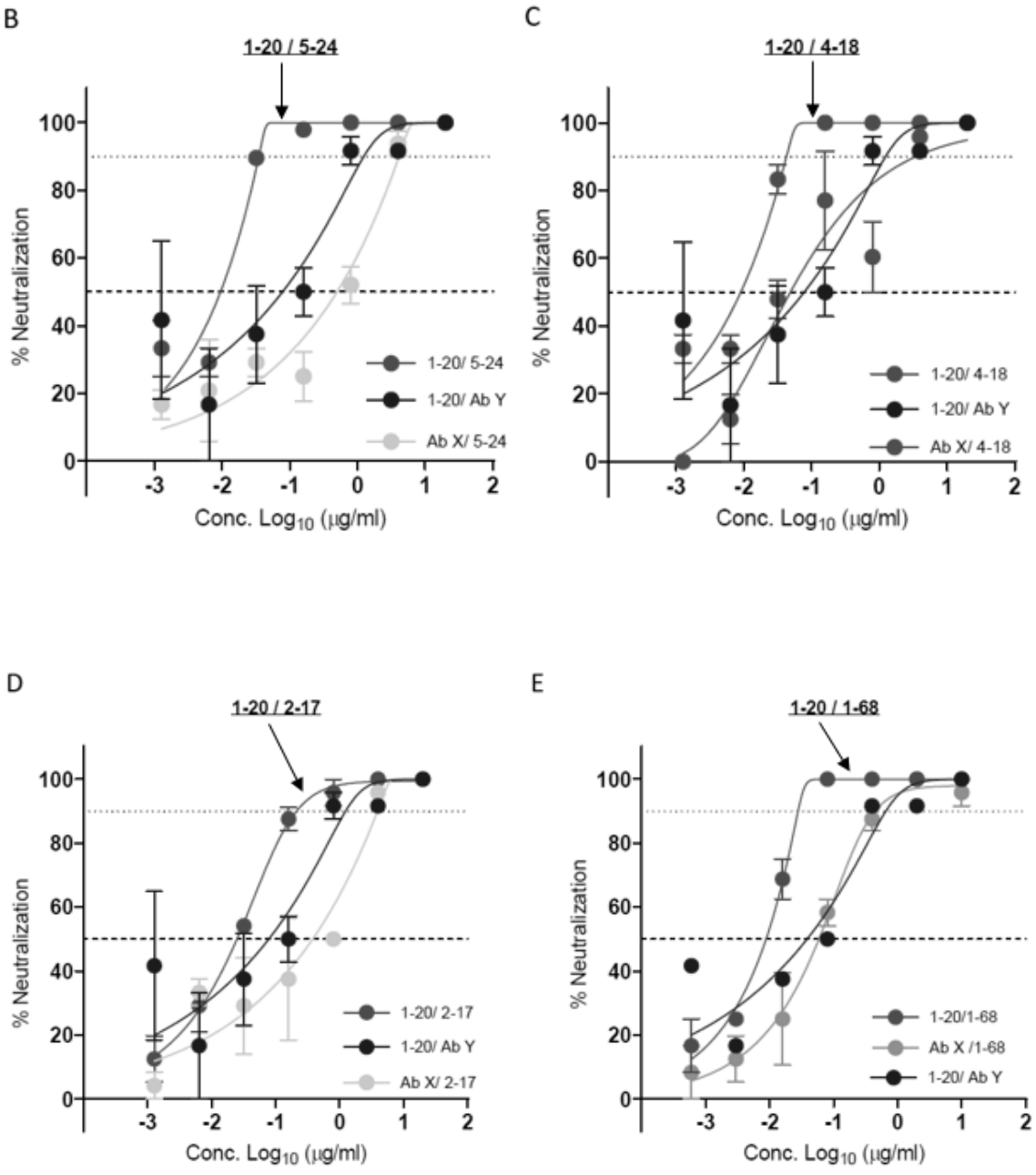

Ab2
1-20
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Antibody conc. Log10 (μg/ml)
1-20/ 5-24
1-20/ 4-18
1-20/ 2-17
1-20/ 1-68

FIG. 57A

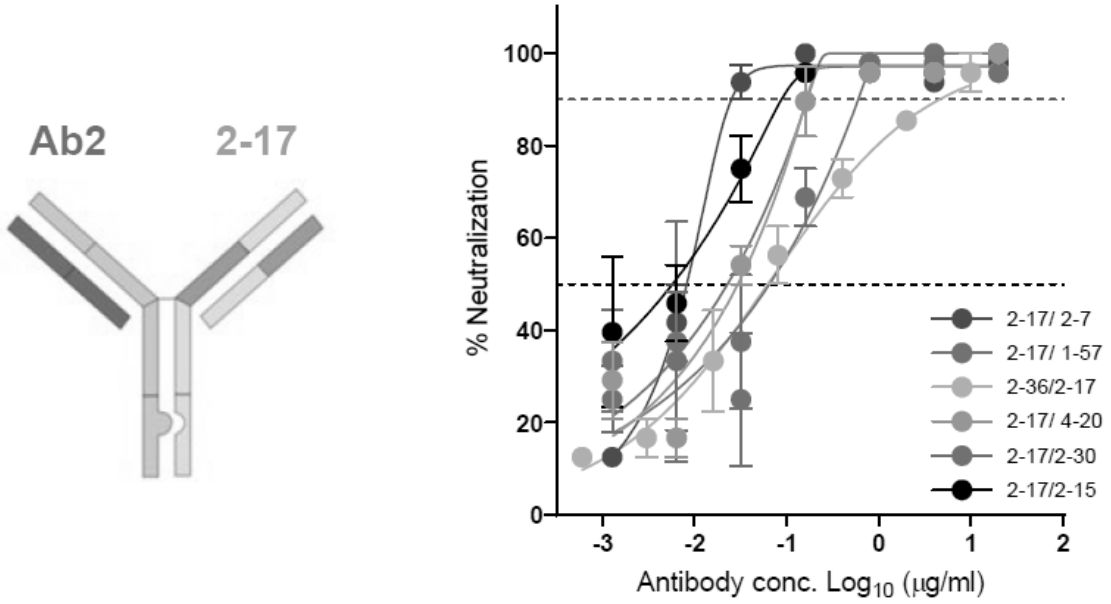

B
1-20 / 5-24
% Neutralization
Conc. Log10 (µg/ml)
1-20/ 5-24
1-20/ Ab Y
Ab X/ 5-24
C
1-20 / 4-18
% Neutralization
Conc. Log10 (µg/ml)
1-20/ 4-18
1-20/ Ab Y
Ab X/ 4-18
D
1-20 / 2-17
% Neutralization
Conc. Log10 (µg/ml)
1-20/ 2-17
1-20/ Ab Y
Ab X/ 2-17
E
1-20 / 1-68
% Neutralization
Conc. Log10 (µg/ml)
1-20/1-68
Ab X /1-68
1-20/ Ab Y

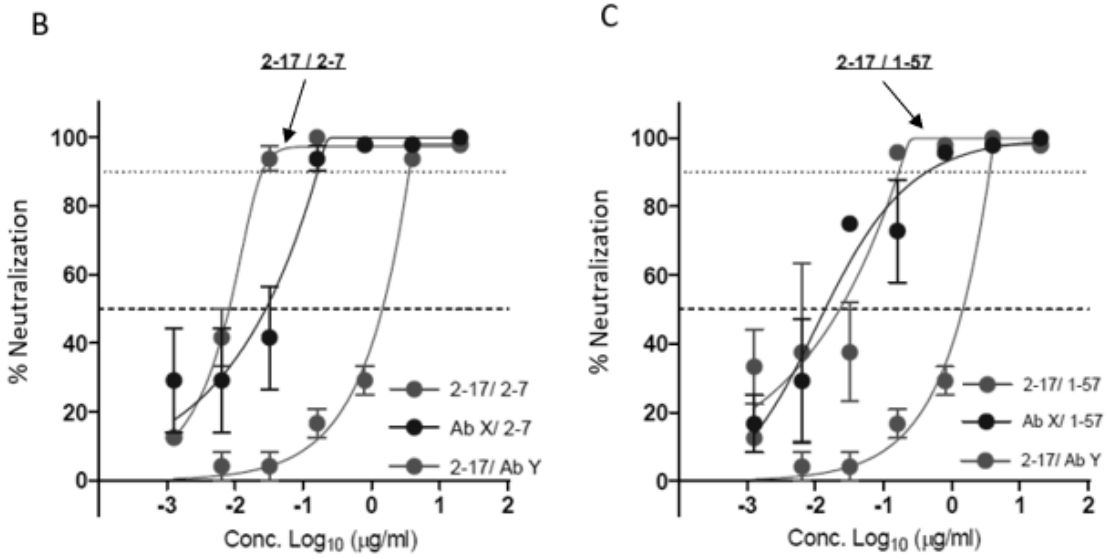
FIGS. 57B-E

	μg/mL	
Bispecific Ab	IC_{50}	IC_{90}
1-20 / 5-24	0.009	0.035
1-20 / 4-18	0.009	0.043
1-20 / 2-17	0.025	0.212
1-20 / 1-68	0.009	0.028

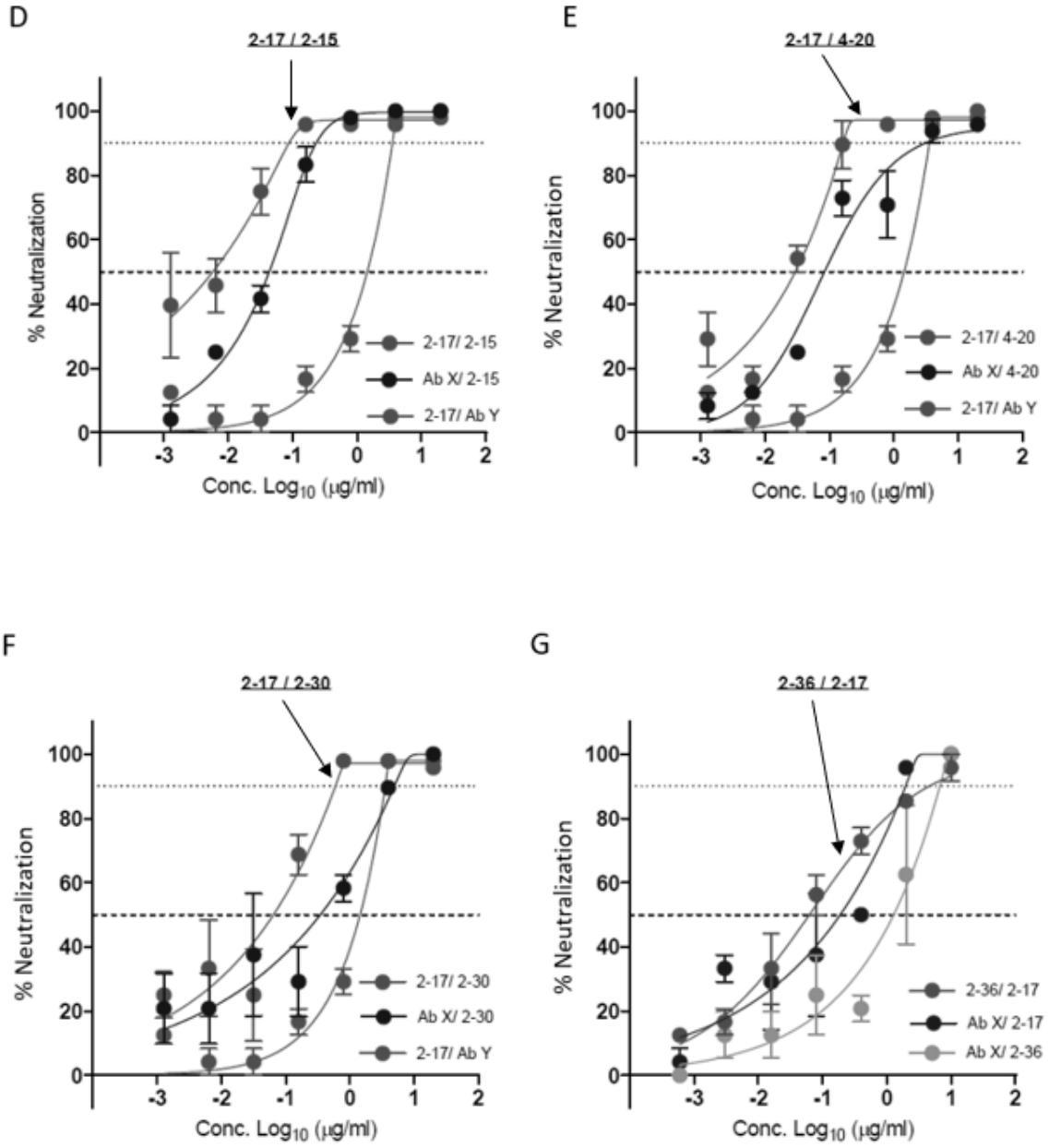
FIG. 58

A


Ab2
2-17
% Neutralization
Antibody conc. Log10 (μg/ml)
2-17/ 2-7
2-17/ 1-57
2-36/2-17
2-17/ 4-20
2-17/2-30
2-17/2-15


B
2-17 / 2-7
% Neutralization
Conc. Log10 (μg/ml)
2-17/ 2-7
Ab X/ 2-7
2-17/ Ab Y
C
2-17 / 1-57
% Neutralization
Conc. Log10 (μg/ml)
2-17/ 1-57
Ab X/ 1-57
2-17/ Ab Y

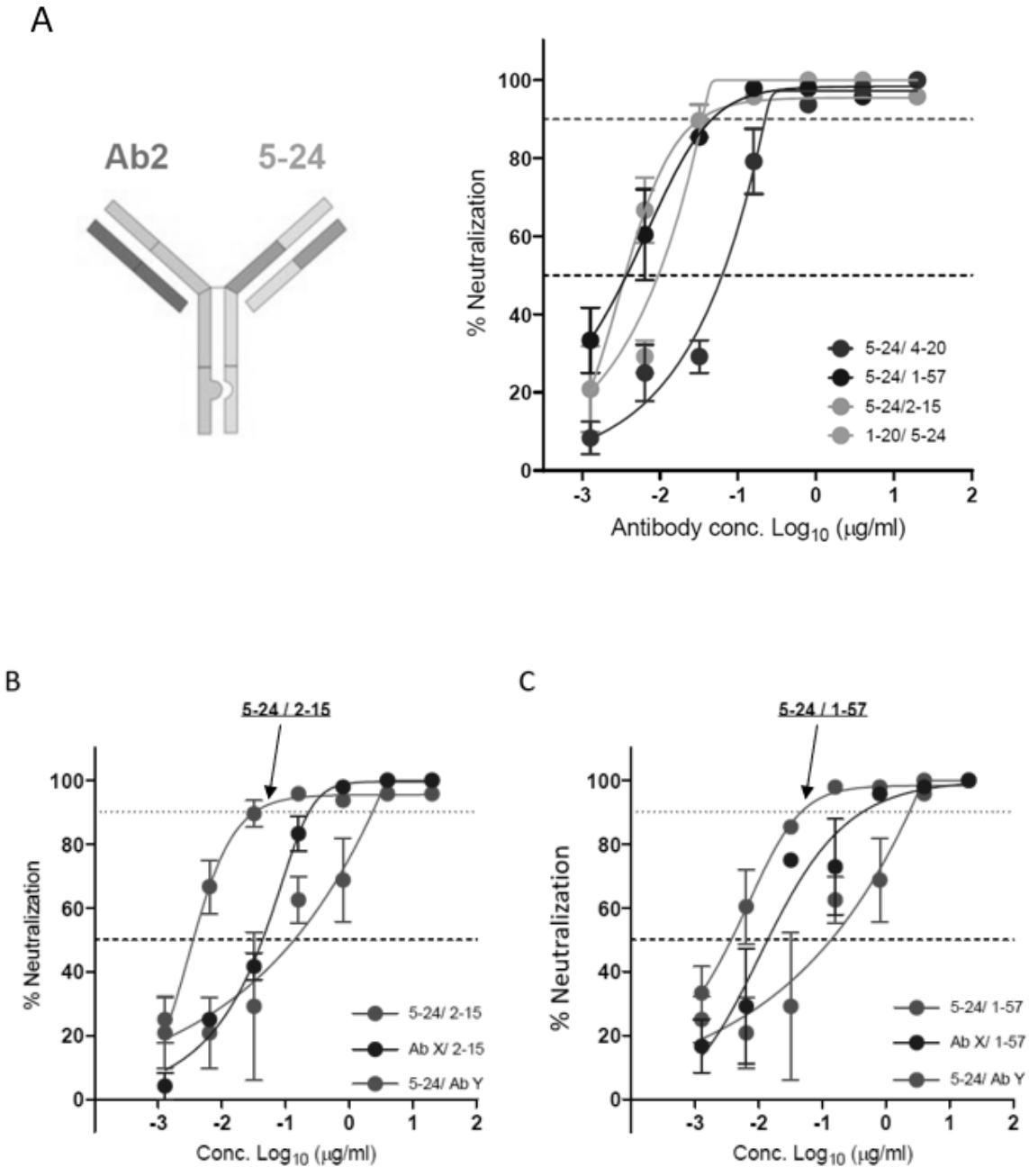
FIGS. 59A-C


D
2-17 / 2-15
% Neutralization
Conc. Log10 (µg/ml)
2-17/ 2-15
Ab X/ 2-15
2-17/ Ab Y
E
2-17 / 4-20
% Neutralization
Conc. Log10 (µg/ml)
2-17/ 4-20
Ab X/ 4-20
2-17/ Ab Y
F
2-17 / 2-30
% Neutralization
Conc. Log10 (µg/ml)
2-17/ 2-30
Ab X/ 2-30
2-17/ Ab Y
G
2-36 / 2-17
% Neutralization
Conc. Log10 (µg/ml)
2-36/ 2-17
Ab X/ 2-17
Ab X/ 2-36

FIGS. 59D-G

	μg/mL	
Bispecific Ab	IC50	IC90
2-17 / 1-57	0.075	0.144
2-17 / 2-7	0.009	0.027
2-17 / 2-15	0.005	0.087
2-17 / 2-30	0.065	0.598
2-17 / 4-20	0.029	0.164
2-36 / 2-17	0.063	4.55

FIG. 60


A
Ab2
5-24
% Neutralization
Antibody conc. Log10 (µg/ml)
5-24/ 4-20
5-24/ 1-57
5-24/2-15
1-20/ 5-24
B
5-24 / 2-15
% Neutralization
Conc. Log10 (µg/ml)
5-24/ 2-15
Ab X/ 2-15
5-24/ Ab Y
C
5-24 / 1-57
% Neutralization
Conc. Log10 (µg/ml)
5-24/ 1-57
Ab X/ 1-57
5-24/ Ab Y

FIGS. 61A-C

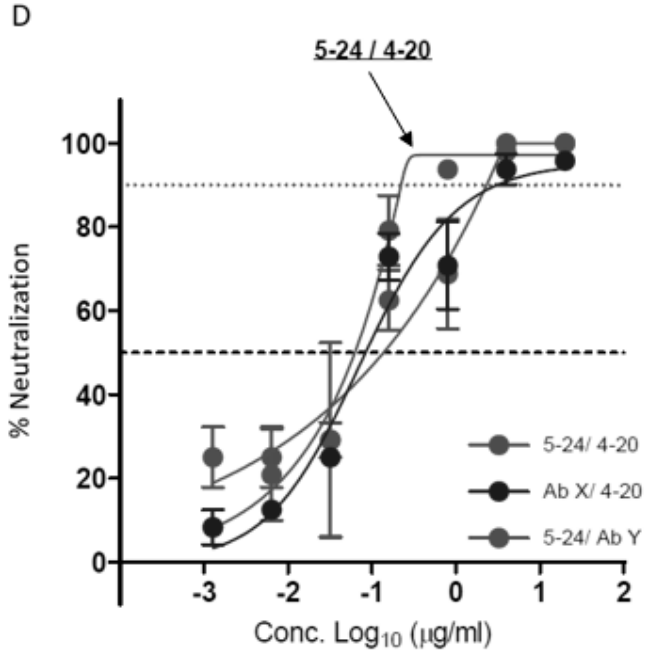
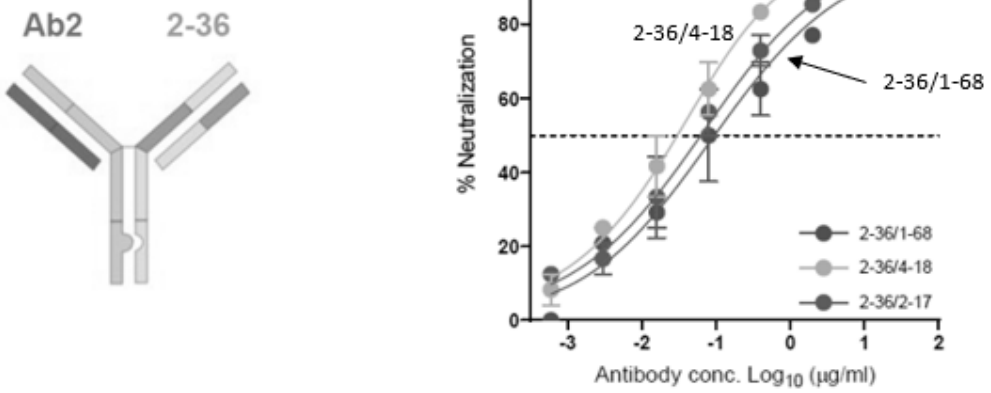

D
5-24 / 4-20
100
80
60
40
20
0
% Neutralization
-3
-2
-1
0
1
2
Conc. Log10 (μg/ml)
5-24/ 4-20
Ab X/ 4-20
5-24/ Ab Y

FIG. 61D

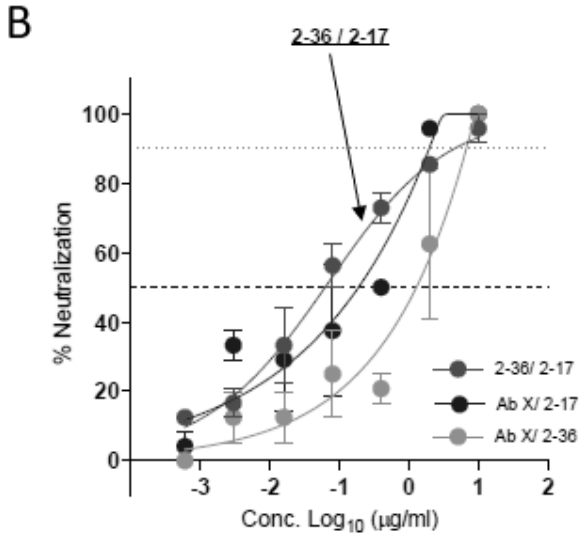
	μg/mL	
Bispecific Ab	IC_{50}	IC_{90}
1-20 / 5-24	0.009	0.035
5-24 / 2-15	0.003	0.033
5-24 / 1-57	0.004	0.045
5-24 / 4-20	0.062	0.222

FIG. 62

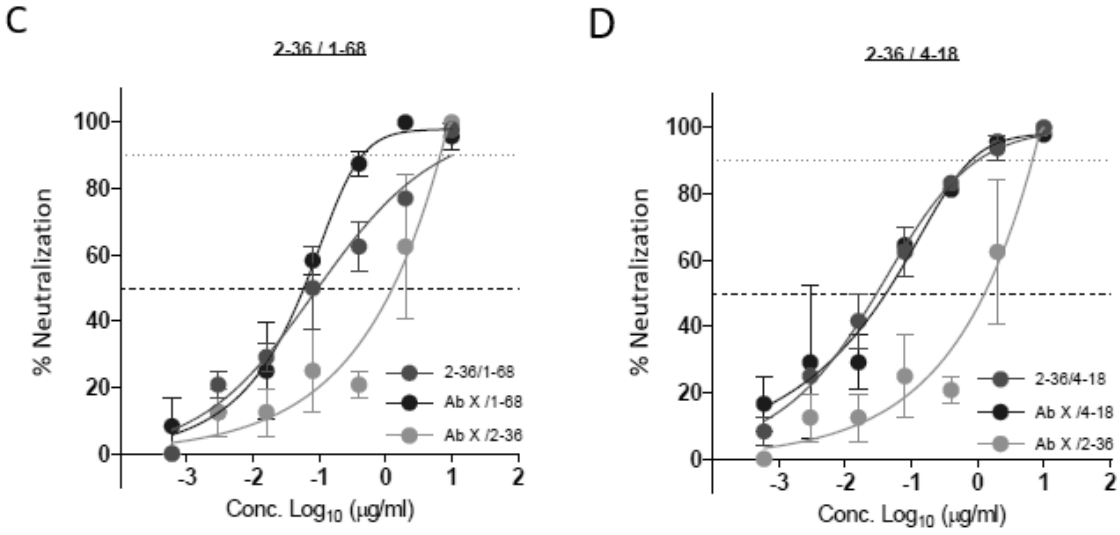
A


Ab2
2-36
% Neutralization
2-36/4-18
2-36/1-68
2-36/1-68
2-36/4-18
2-36/2-17
Antibody conc. Log10 (µg/ml)

B


2-36 / 2-17
% Neutralization
2-36/ 2-17
Ab X/ 2-17
Ab X/ 2-36
Conc. Log10 (µg/ml)

FIGS. 63A-B


C
2-36 / 1-68
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
2-36/1-68
Ab X /1-68
Ab X /2-36
D
2-36 / 4-18
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
2-36/4-18
Ab X /4-18
Ab X /2-36

FIGS. 63C-D

	μg/mL	
Bispecific Ab	IC50	IC90
2-36/1-68	0.096	9.948
2-36/4-18	0.03	0.982
2-36/2-17	0.063	4.55

FIG. 64

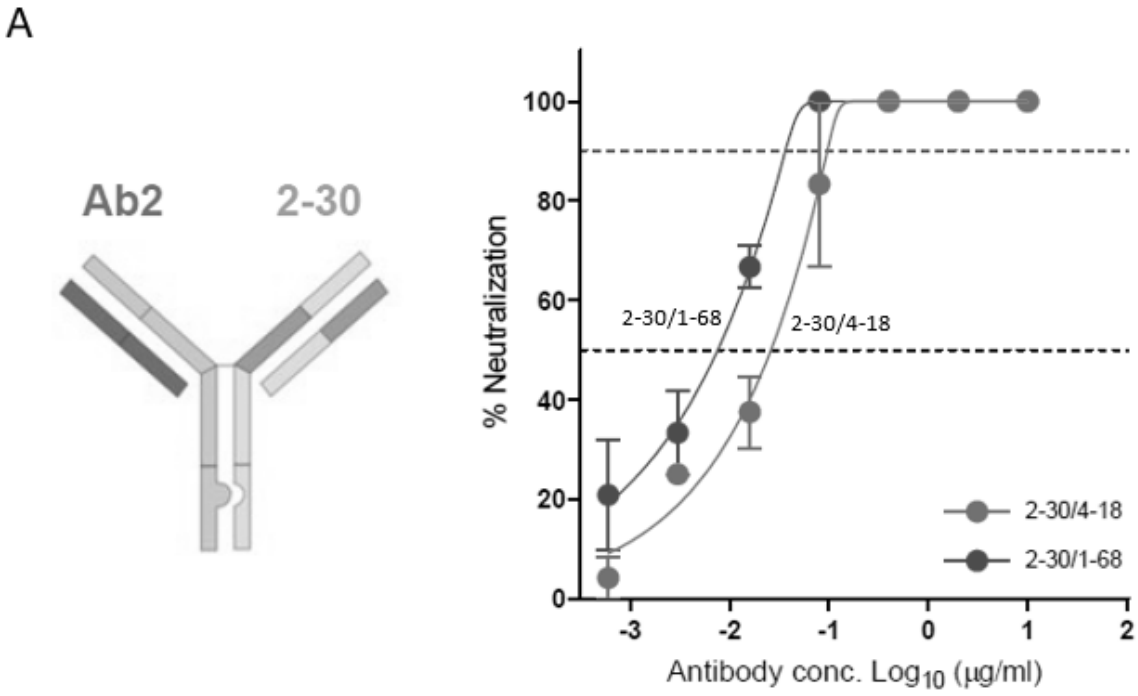
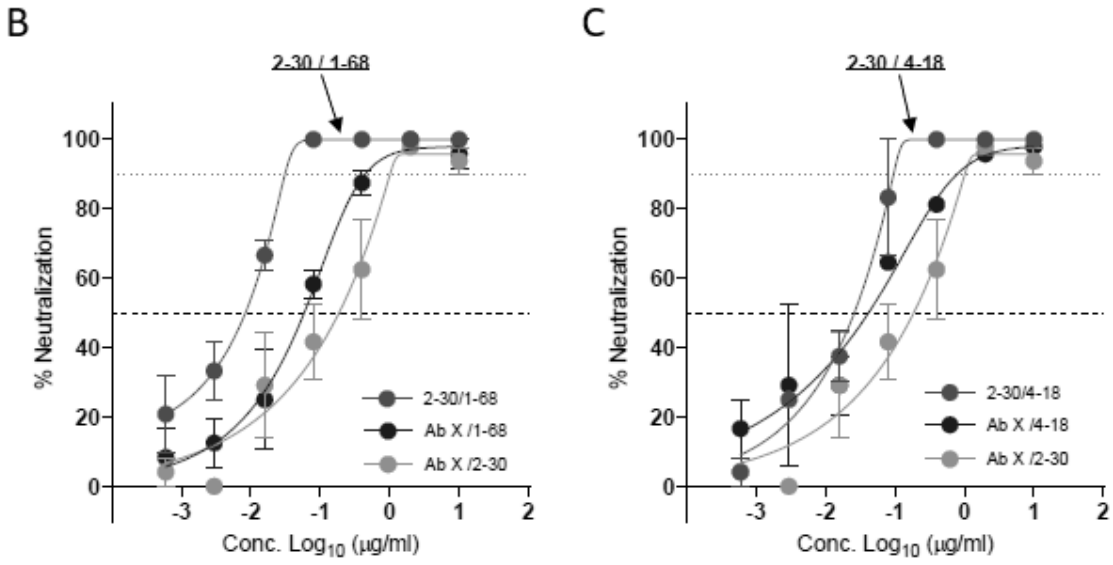

A
Ab2
2-30
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Antibody conc. Log10 (µg/ml)
2-30/1-68
2-30/4-18
2-30/4-18
2-30/1-68

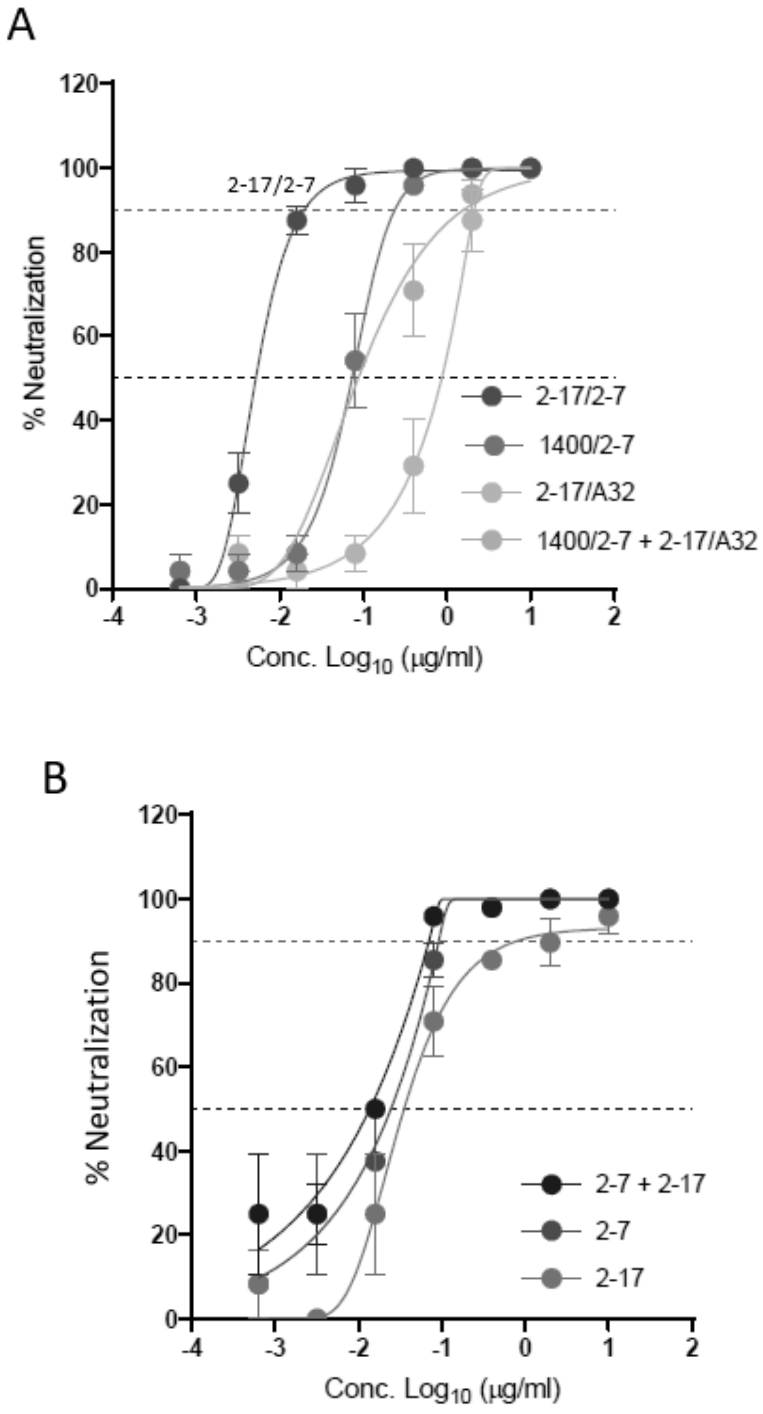
FIG. 65A


B
2-30 / 1-68
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
2-30/1-68
Ab X /1-68
Ab X /2-30
C
2-30 / 4-18
% Neutralization
100
80
60
40
20
0
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
2-30/4-18
Ab X /4-18
Ab X /2-30

FIGS. 65B-C

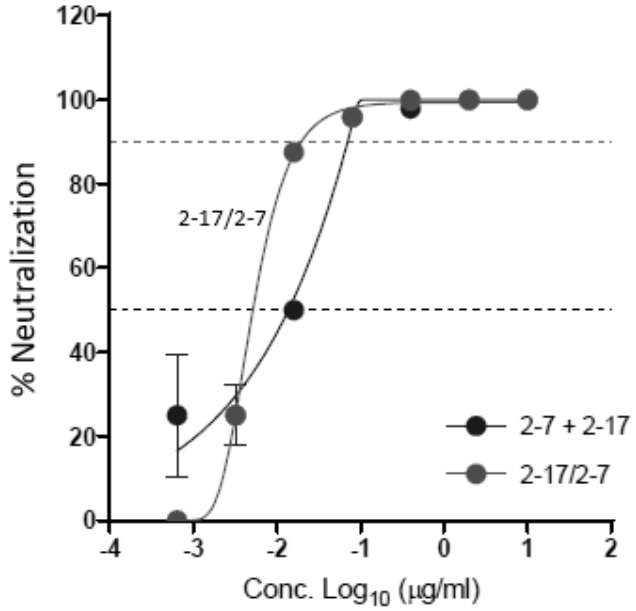
	μg/mL	
Bispecific Ab	IC50	IC90
2-30/ 4-18	0.026	0.096
2-30/ 1-68	0.008	0.036

FIG. 66


A
120
100
80
60
40
20
0
% Neutralization
2-17/2-7
2-17/2-7
1400/2-7
2-17/A32
1400/2-7 + 2-17/A32
-4
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
B
120
100
80
60
40
20
0
% Neutralization
2-7 + 2-17
2-7
2-17
-4
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)

FIGS. 67A-B

C

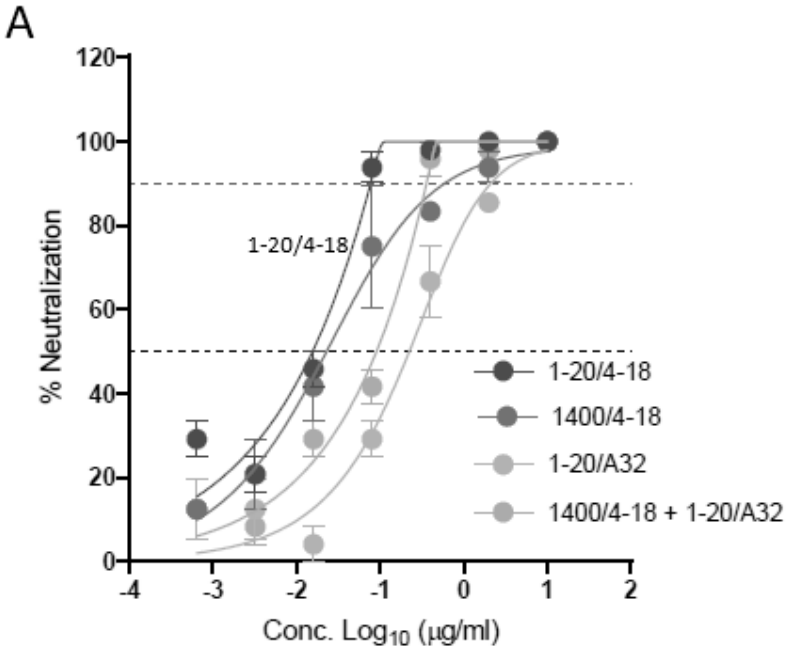


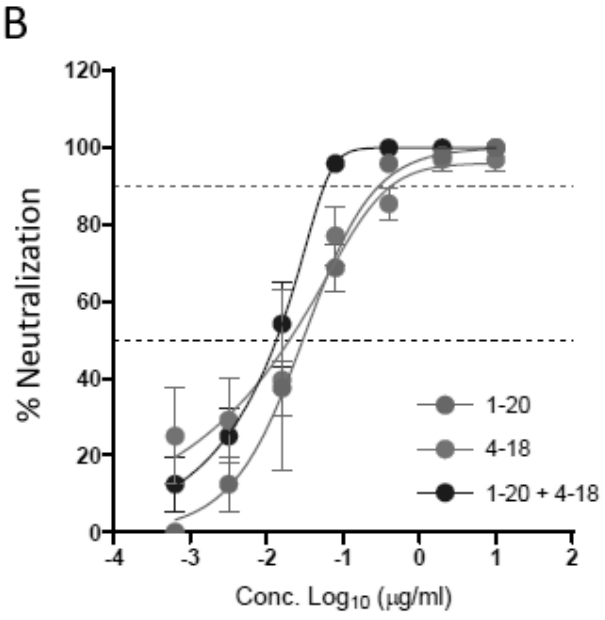
D

	IC_{50} (µg/mL)	IC_{90} (µg/mL)
2-17/2-7	0.005	0.020
2-7 + 2-17	0.014	0.070

*Combination mAbs tested each at half of the amount of the corresponding bispecific Ab

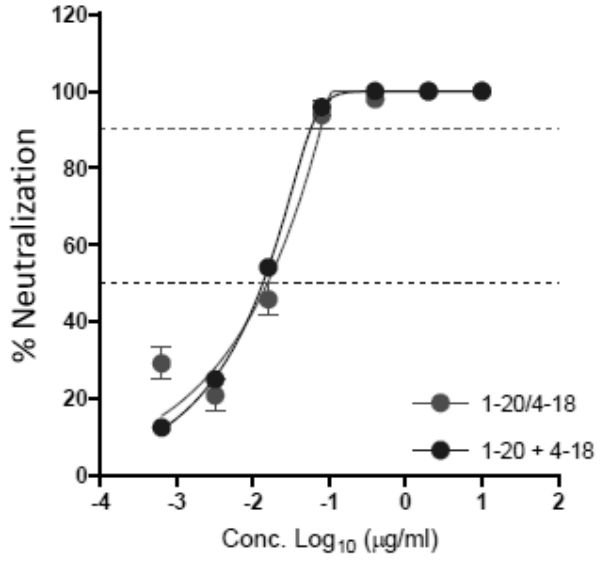
FIGS. 67C-D


A
% Neutralization
Conc. Log10 (µg/ml)
1-20/4-18
1-20/4-18
1400/4-18
1-20/A32
1400/4-18 + 1-20/A32


B
% Neutralization
Conc. Log10 (µg/ml)
1-20
4-18
1-20 + 4-18

FIGS. 68A-B

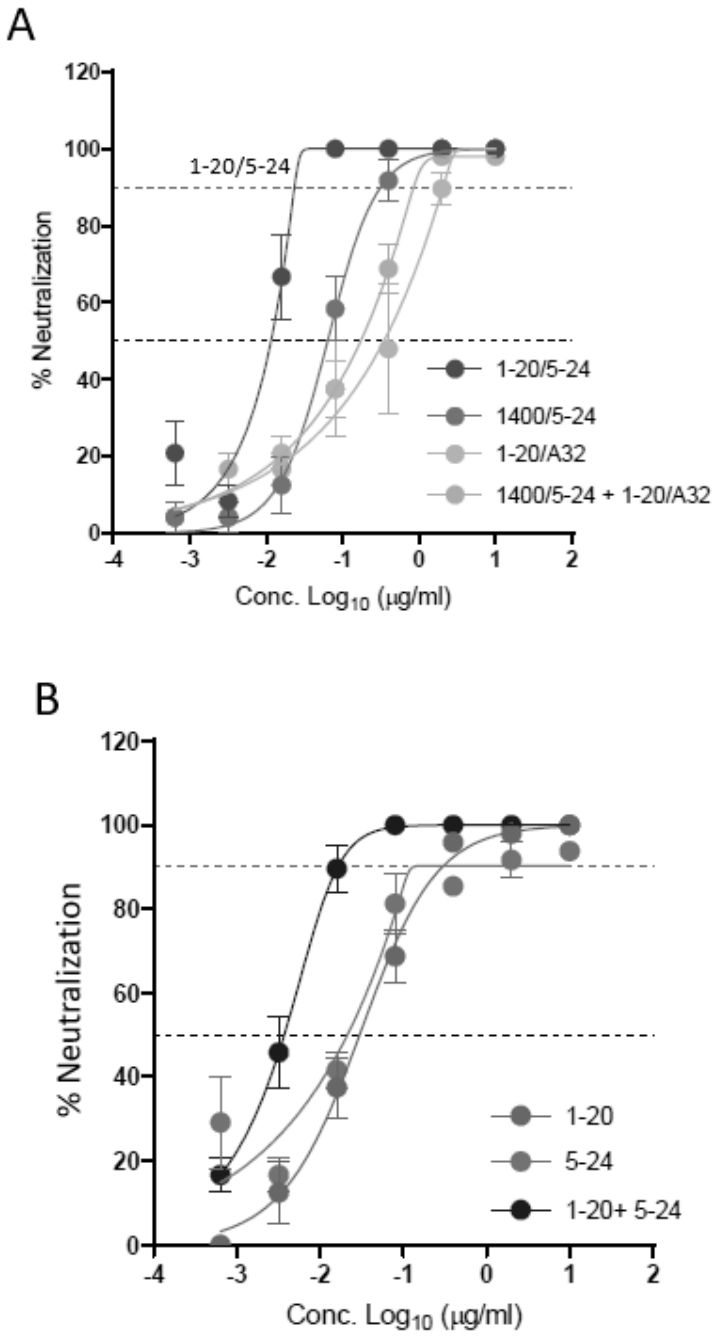
C



D

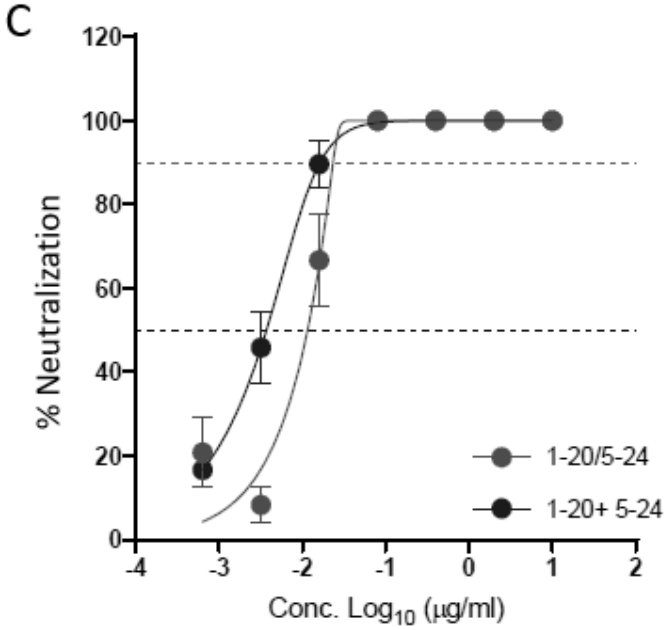
	IC_{50} (µg/mL)	IC_{90} (µg/mL)
1-20/4-18	0.016	0.076
1-20 + 4-18	0.014	0.057

FIGS. 68C-D


A
120
100
80
60
40
20
0
% Neutralization
1-20/5-24
1-20/5-24
1400/5-24
1-20/A32
1400/5-24 + 1-20/A32
-4
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)
B
120
100
80
60
40
20
0
% Neutralization
1-20
5-24
1-20+ 5-24
-4
-3
-2
-1
0
1
2
Conc. Log10 (µg/ml)

FIGS. 69A-B

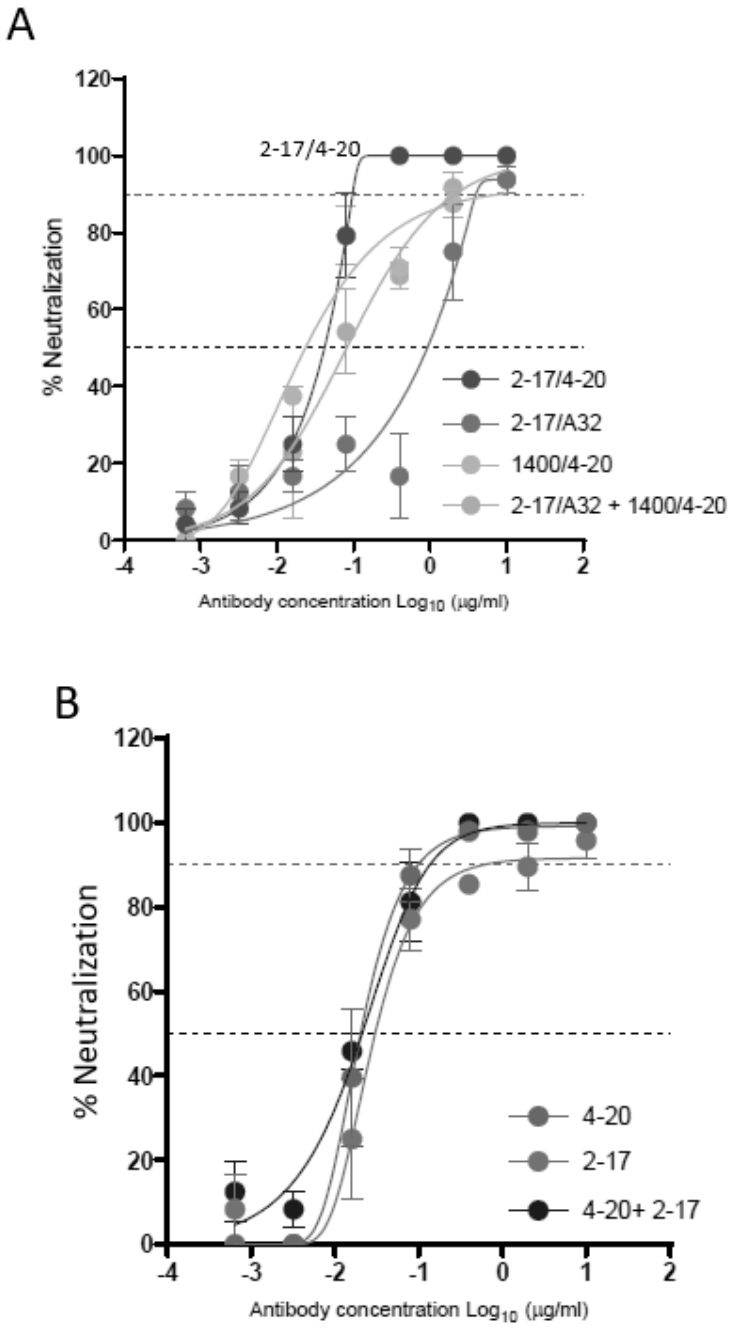
C



D

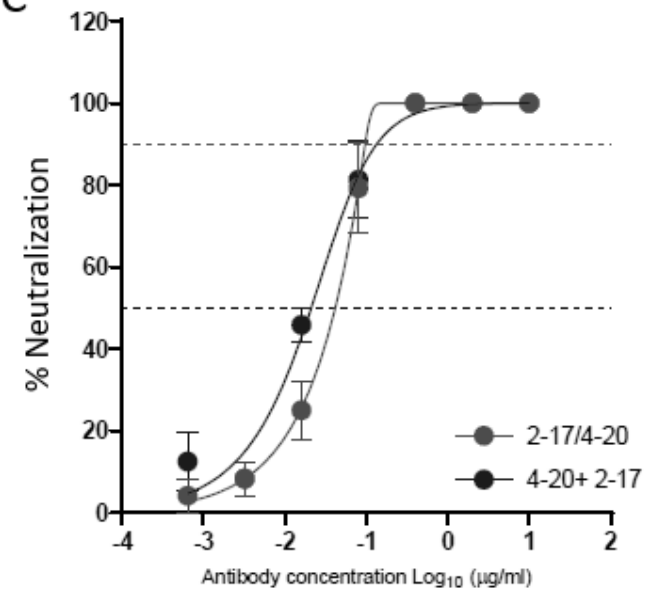
	IC_{50} (µg/mL)	IC_{90} (µg/mL)
1-20/5-24	0.012	0.023
1-20 + 5-24	0.004	0.016

FIGS. 69C-D


A
120
100
80
60
40
20
0
% Neutralization
2-17/4-20
2-17/4-20
2-17/A32
1400/4-20
2-17/A32 + 1400/4-20
-4
-3
-2
-1
0
1
2
Antibody concentration Log10 (µg/ml)
B
120
100
80
60
40
20
0
% Neutralization
4-20
2-17
4-20+ 2-17
-4
-3
-2
-1
0
1
2
Antibody concentration Log10 (µg/ml)

FIGS. 70A-B

C



D

	IC_{50} (µg/mL)	IC_{90} (µg/mL)
2-17/4-20	0.042	0.097
2-17 + 4-20	0.021	0.135

FIGS. 70C-D

A

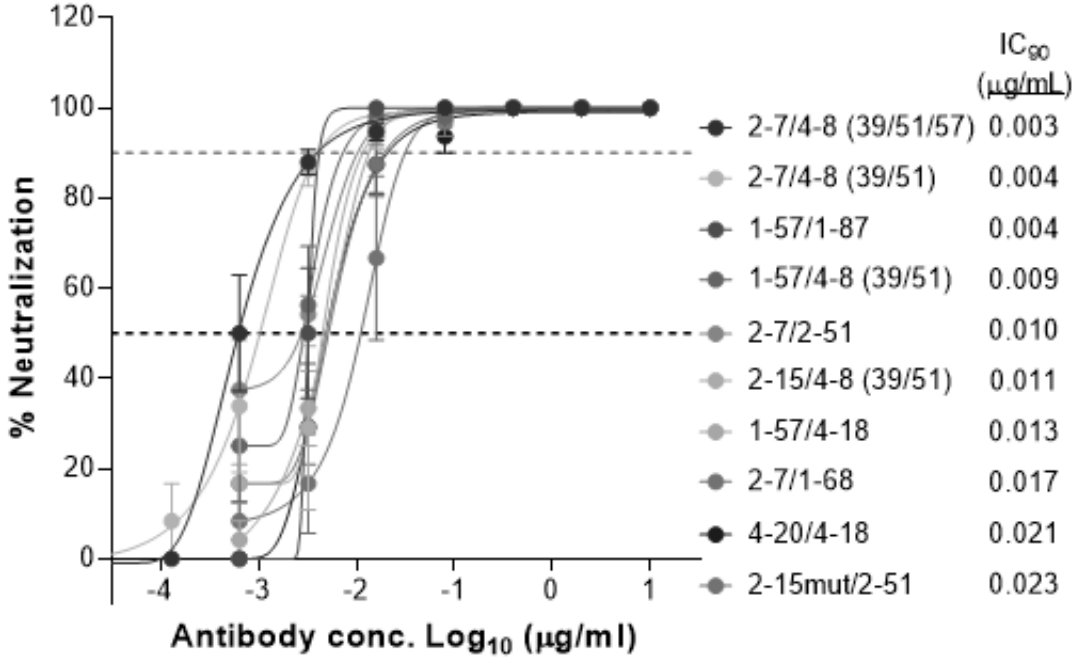

120
100
80
60
40
20
0
% Neutralization
-4
-3
-2
-1
0
1
Antibody conc. Log10 (µg/ml)
IC90 (µg/mL)
2-7/4-8 (39/51/57) 0.003
2-7/4-8 (39/51) 0.004
1-57/1-87 0.004
1-57/4-8 (39/51) 0.009
2-7/2-51 0.010
2-15/4-8 (39/51) 0.011
1-57/4-18 0.013
2-7/1-68 0.017
4-20/4-18 0.021
2-15mut/2-51 0.023

FIG. 71A

B

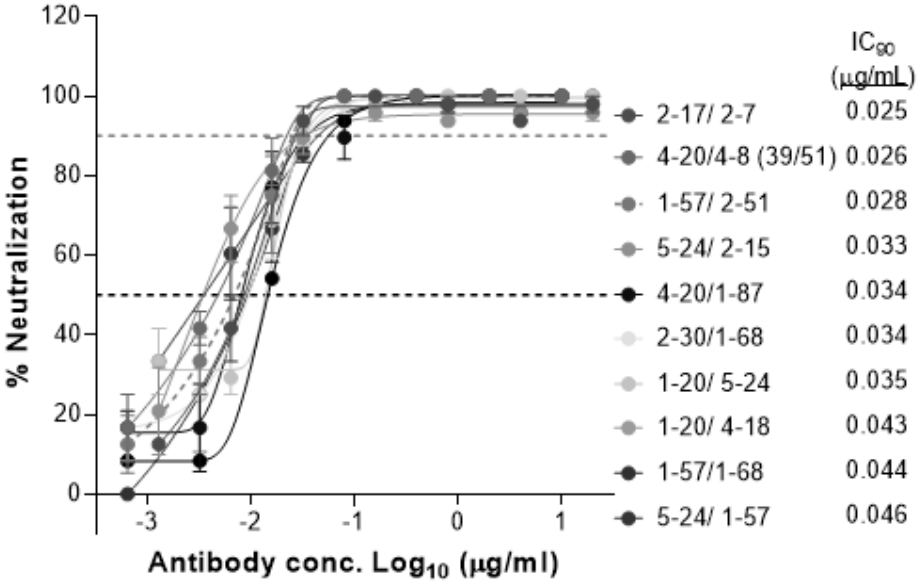
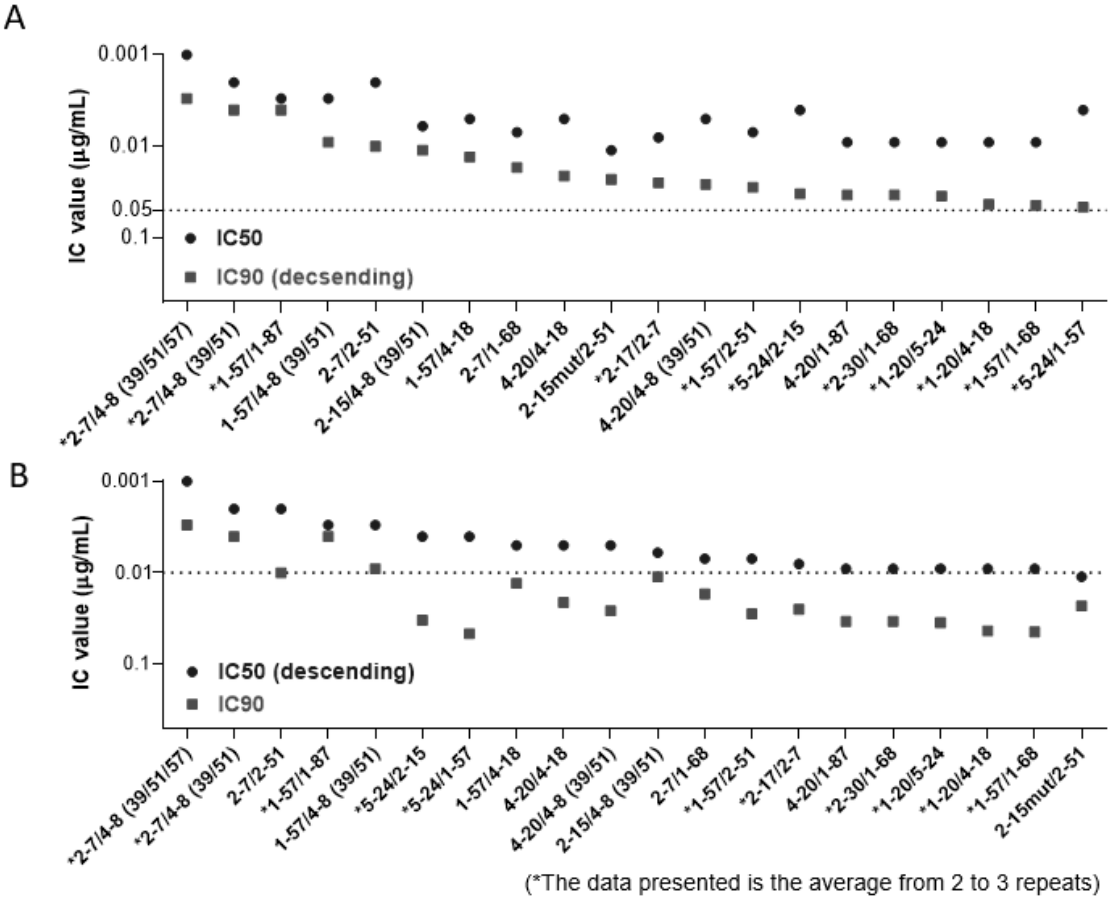

120
100
80
60
40
20
0
% Neutralization
-3
-2
-1
0
1
Antibody conc. Log10 (µg/ml)
IC90 (µg/mL)
2-17/ 2-7 0.025
4-20/4-8 (39/51) 0.026
1-57/ 2-51 0.028
5-24/ 2-15 0.033
4-20/1-87 0.034
2-30/1-68 0.034
1-20/ 5-24 0.035
1-20/ 4-18 0.043
1-57/1-68 0.044
5-24/ 1-57 0.046

FIG. 71B

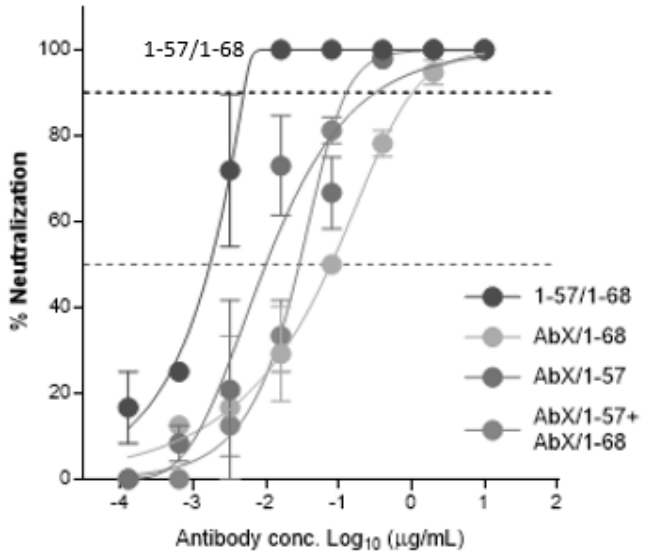
Bispecific	Potency (μg/mL)	
	IC_{50}	IC_{90}
2-7/4-8 (39/51/57)	0.001	0.003
2-7/4-8 (39/51)	0.002	0.004
1-57/1-87	0.003	0.004
1-57/4-8 (39/51)	0.003	0.009
2-7/2-51	0.002	0.01
2-15/4-8 (39/51)	0.006	0.011
1-57/4-18	0.005	0.013
2-7/1-68	0.007	0.017
4-20/4-18	0.005	0.021
2-15mut/2-51	0.011	0.023
2-17/2-7	0.008	0.025
4-20/4-8 (39/51)	0.005	0.026
1-57/2-51	0.007	0.028
5-24/2-15	0.004	0.033
4-20/1-87	0.009	0.034
2-30/1-68	0.009	0.034
1-20/5-24	0.009	0.035
1-20/4-18	0.009	0.043
1-57/1-68	0.009	0.044
5-24/1-57	0.004	0.046

FIG. 72

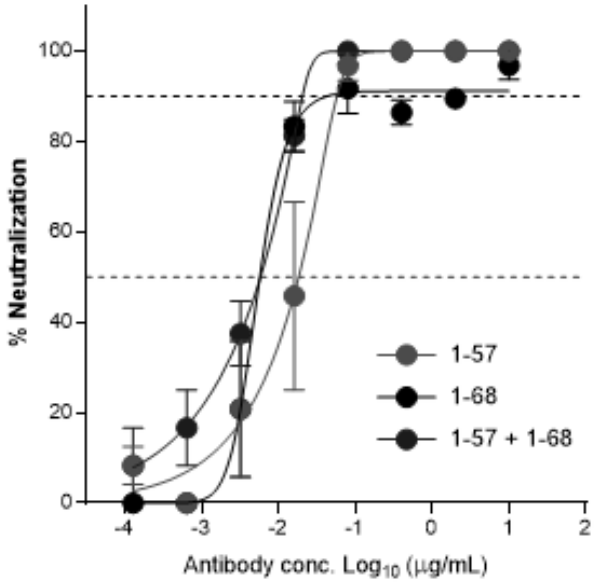

A
0.001
0.01
0.05
0.1
IC value (µg/mL)
IC50
IC90 (decsending)
*2-7/4-8 (39/51/57)
*2-7/4-8 (39/51)
*1-57/1-87
1-57/4-8 (39/51)
2-7/2-51
2-15/4-8 (39/51)
1-57/4-18
2-7/1-68
4-20/4-18
2-15mut/2-51
*2-17/2-7
4-20/4-8 (39/51)
*1-57/2-51
*5-24/2-15
4-20/1-87
*2-30/1-68
*1-20/5-24
*1-20/4-18
*1-57/1-68
*5-24/1-57
B
0.001
0.01
0.1
IC value (µg/mL)
IC50 (descending)
IC90
*2-7/4-8 (39/51/57)
*2-7/4-8 (39/51)
2-7/2-51
*1-57/1-87
1-57/4-8 (39/51)
*5-24/2-15
*5-24/1-57
1-57/4-18
4-20/4-18
4-20/4-8 (39/51)
2-15/4-8 (39/51)
2-7/1-68
*1-57/2-51
*2-17/2-7
4-20/1-87
*2-30/1-68
*1-20/5-24
*1-20/4-18
*1-57/1-68
2-15mut/2-51
(*The data presented is the average from 2 to 3 repeats)

FIGS. 73A-B

A

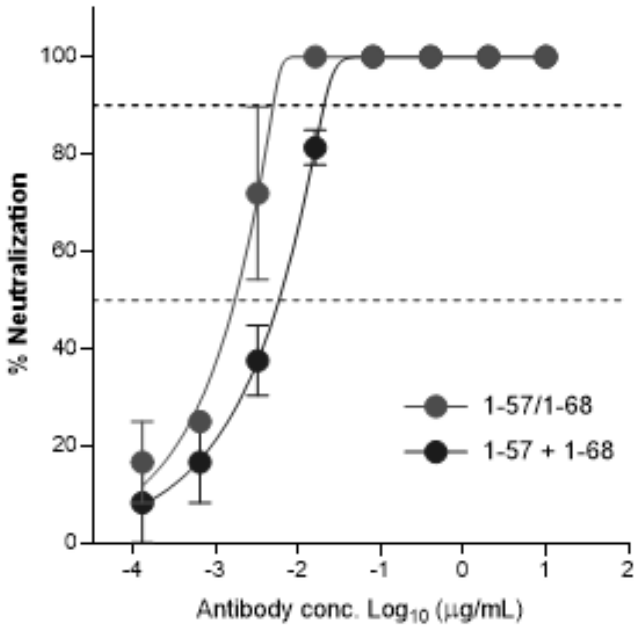

1-57/1-68
% Neutralization
100
80
60
40
20
0
-4
-3
-2
-1
0
1
2
Antibody conc. Log10 (µg/mL)
1-57/1-68
AbX/1-68
AbX/1-57
AbX/1-57+
AbX/1-68

B


% Neutralization
100
80
60
40
20
0
-4
-3
-2
-1
0
1
2
Antibody conc. Log10 (µg/mL)
1-57
1-68
1-57 + 1-68

FIGS. 74A-B

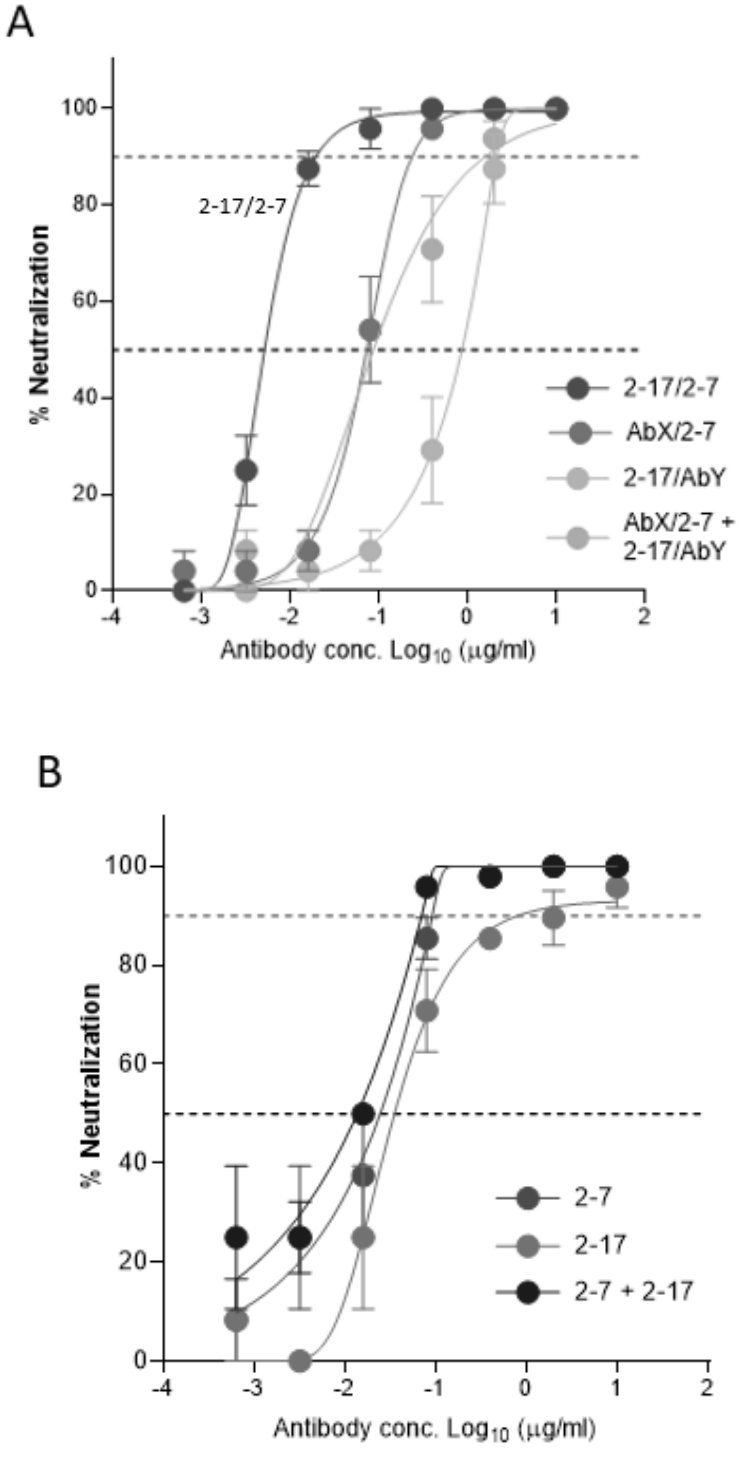
C



D

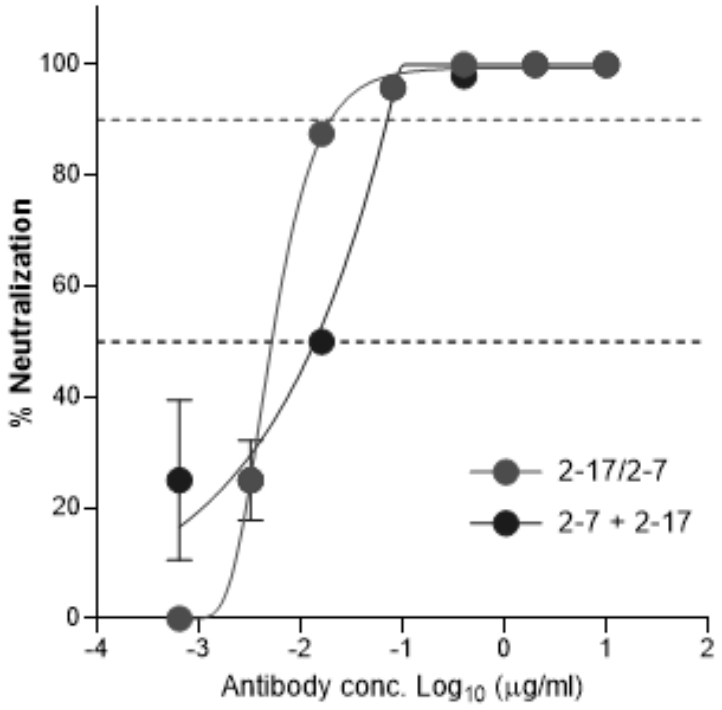
	IC_{50} (µg/mL)	IC_{90} (µg/mL)
1-57/1-68	0.002	0.005
1-57 + 1-68	0.006	0.020

FIGS. 74C-D


A
100
80
60
40
20
0
% Neutralization
2-17/2-7
2-17/2-7
AbX/2-7
2-17/AbY
AbX/2-7 +
2-17/AbY
-4
-3
-2
-1
0
1
2
Antibody conc. Log10 (μg/ml)
B
100
80
60
40
20
0
% Neutralization
2-7
2-17
2-7 + 2-17
-4
-3
-2
-1
0
1
2
Antibody conc. Log10 (μg/ml)

FIGS. 75A-B

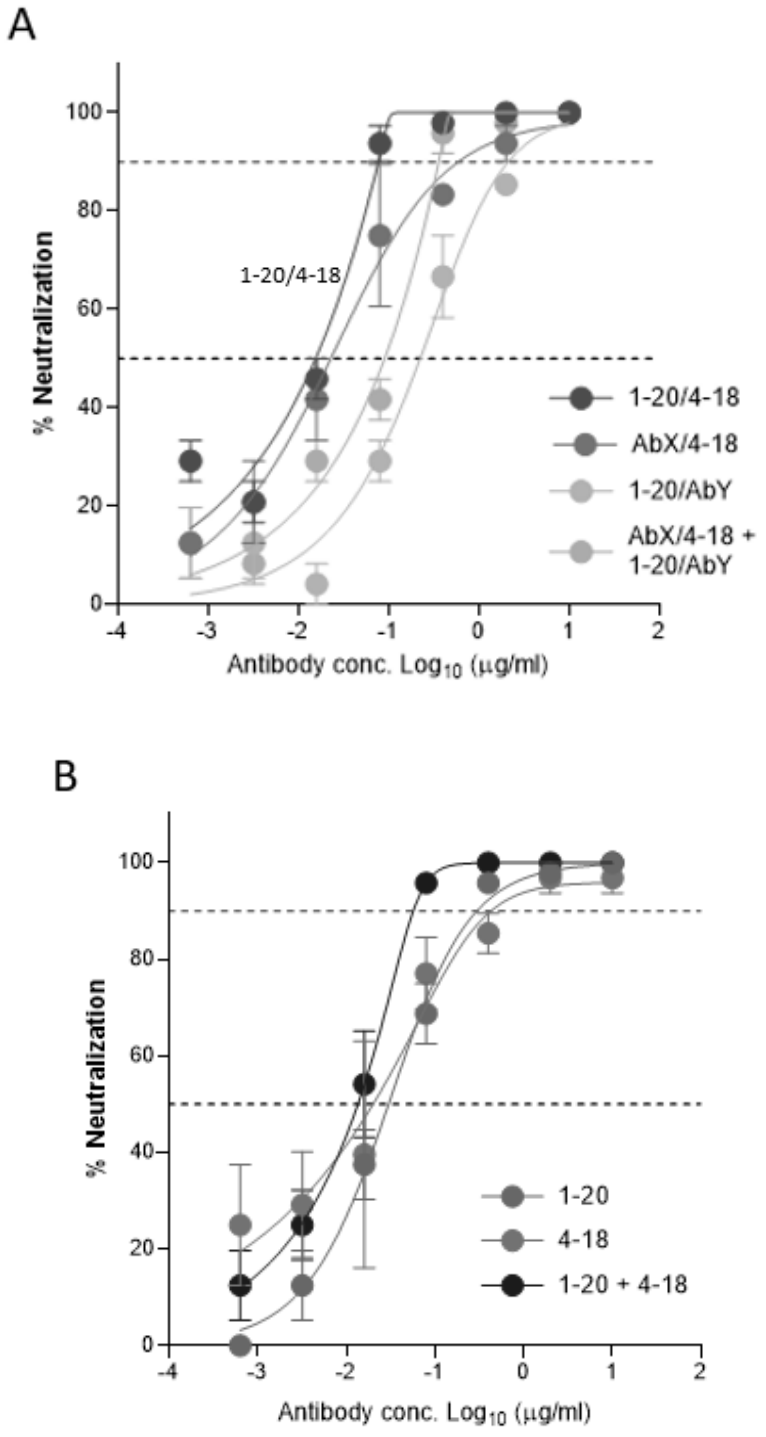
C



D

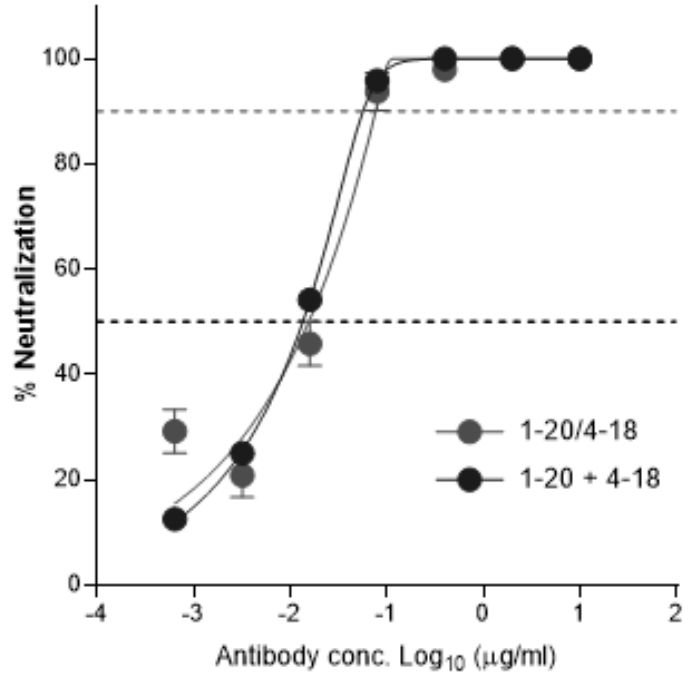
	IC_{50} (µg/mL)	IC_{90} (µg/mL)
2-17/2-7	0.005	0.020
2-7 + 2-17	0.014	0.070

FIGS. 75C-D


A
% Neutralization
100
80
60
40
20
0
-4
-3
-2
-1
0
1
2
Antibody conc. Log10 (μg/ml)
1-20/4-18
1-20/4-18
AbX/4-18
1-20/AbY
AbX/4-18 +
1-20/AbY
B
% Neutralization
100
80
60
40
20
0
-4
-3
-2
-1
0
1
2
Antibody conc. Log10 (μg/ml)
1-20
4-18
1-20 + 4-18

FIGS. 76A-B

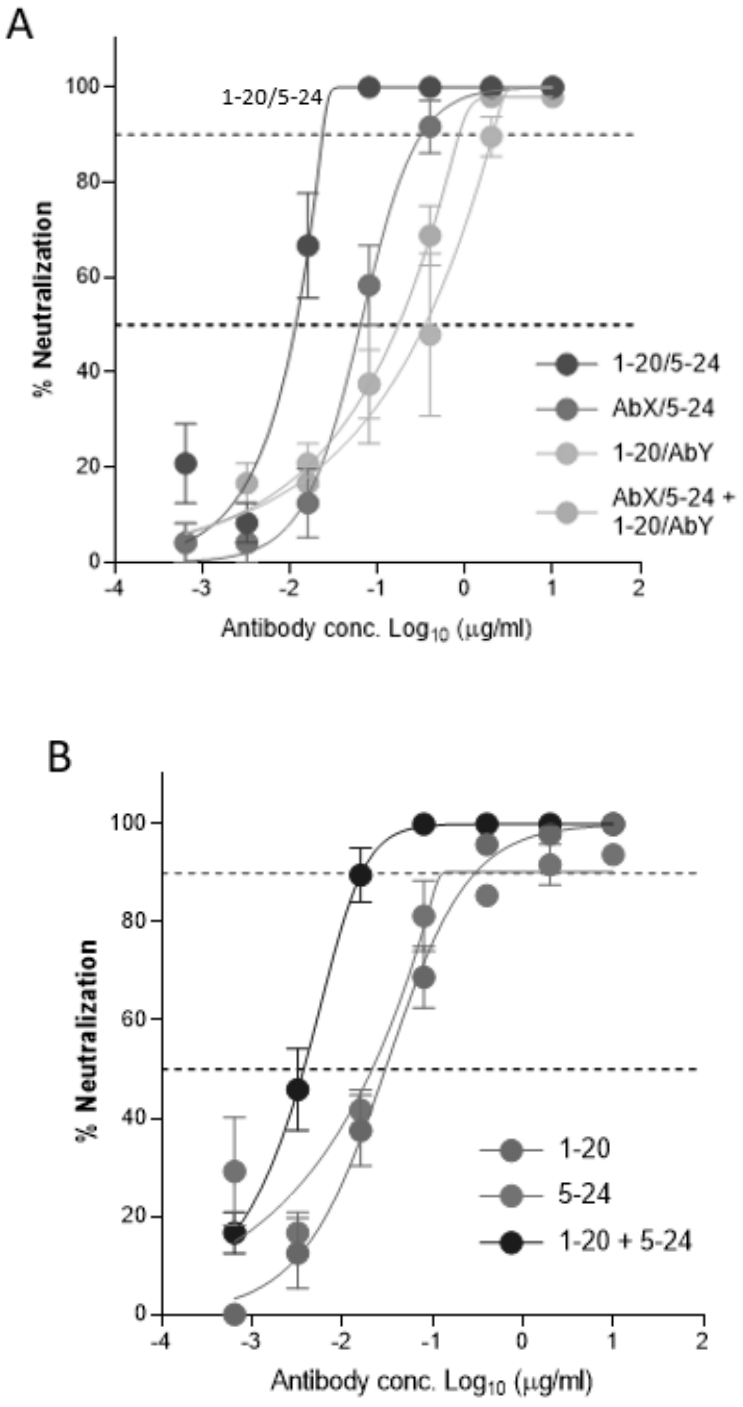
C



D

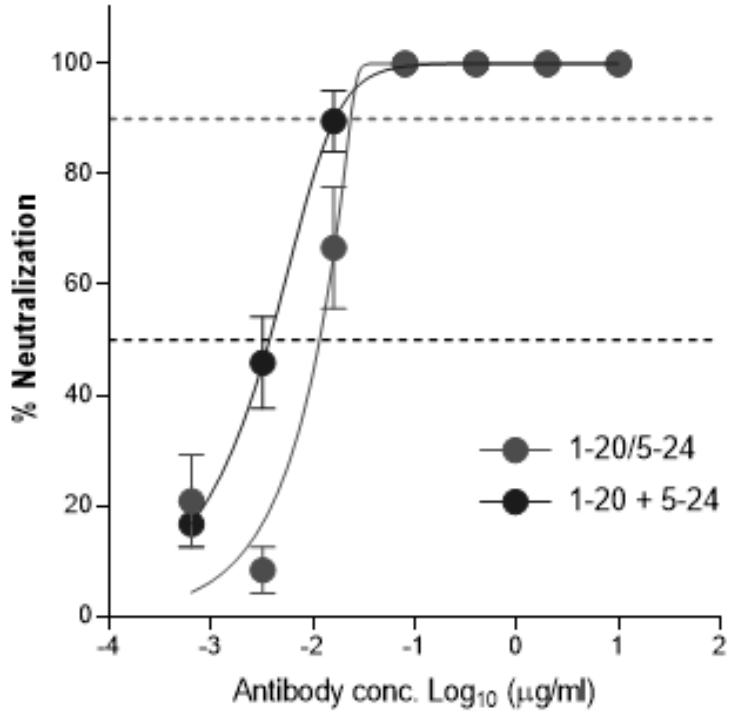
	IC_{50} (µg/mL)	IC_{90} (µg/mL)
1-20/4-18	0.016	0.077
1-20 + 4-18	0.014	0.057

FIGS. 76C-D


A
1-20/5-24
% Neutralization
Antibody conc. Log10 (μg/ml)
1-20/5-24
AbX/5-24
1-20/AbY
AbX/5-24 +
1-20/AbY
B
% Neutralization
Antibody conc. Log10 (μg/ml)
1-20
5-24
1-20 + 5-24

FIGS. 77A-B

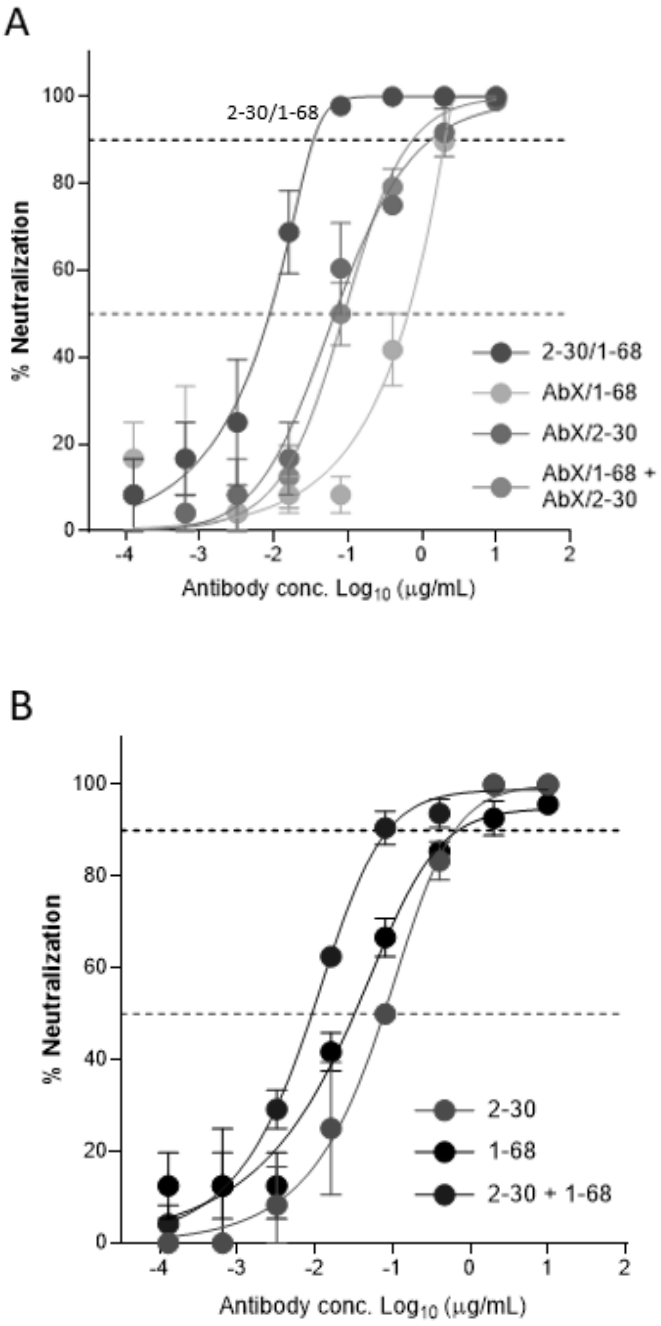
C



D

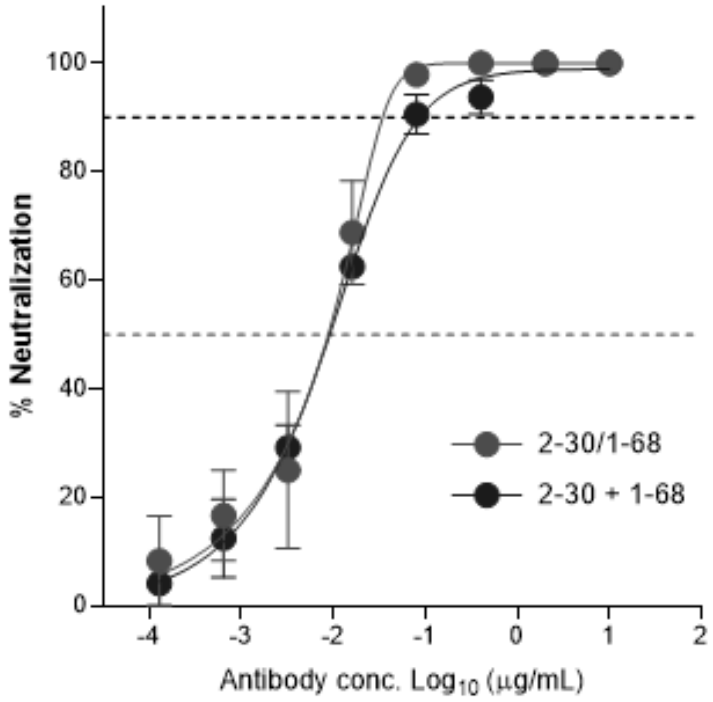
	IC_{50} (μg/mL)	IC_{90} (μg/mL)
1-20 / 5-24	0.012	0.023
1-20 + 5-24	0.004	0.016

FIGS. 77C-D


A
100
80
60
40
20
0
% Neutralization
2-30/1-68
-4
-3
-2
-1
0
1
2
Antibody conc. Log10 (μg/mL)
2-30/1-68
AbX/1-68
AbX/2-30
AbX/1-68 +
AbX/2-30
B
100
80
60
40
20
0
% Neutralization
-4
-3
-2
-1
0
1
2
Antibody conc. Log10 (μg/mL)
2-30
1-68
2-30 + 1-68

FIGS. 78A-B

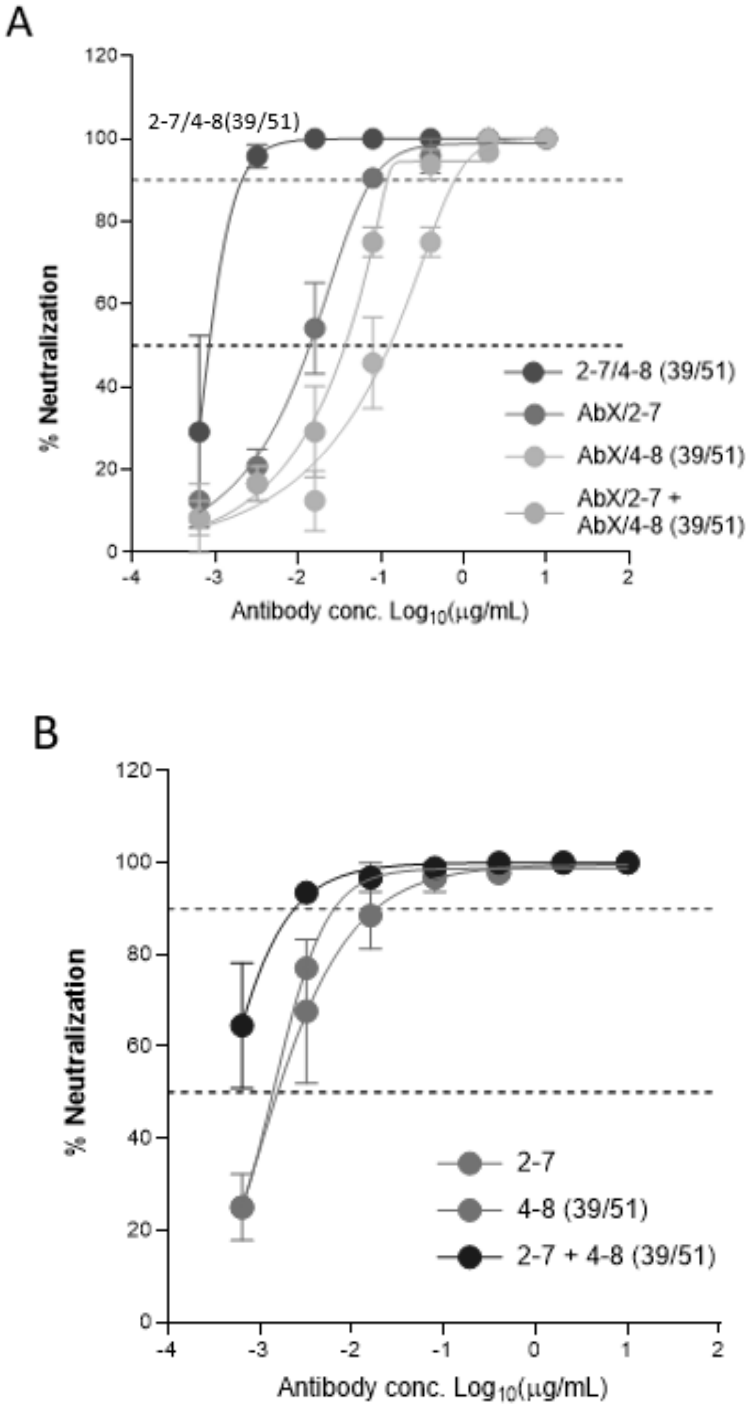
C



D

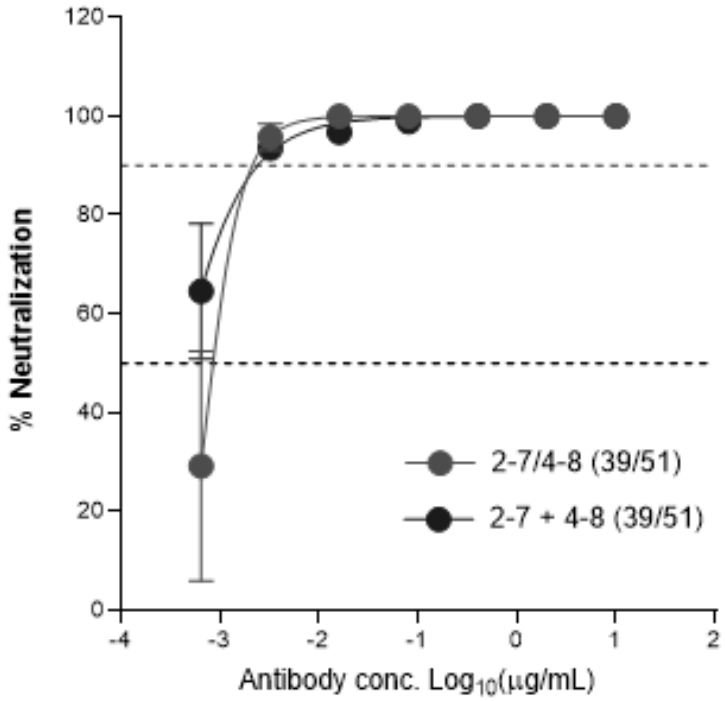
	IC_{50} (µg/mL)	IC_{90} (µg/mL)
2-30/ 1-68	0.009	0.034
2-30 + 1-68	0.009	0.086

FIGS. 78C-D


A
2-7/4-8(39/51)
% Neutralization
Antibody conc. Log10(μg/mL)
2-7/4-8 (39/51)
AbX/2-7
AbX/4-8 (39/51)
AbX/2-7 +
AbX/4-8 (39/51)
B
% Neutralization
Antibody conc. Log10(μg/mL)
2-7
4-8 (39/51)
2-7 + 4-8 (39/51)

FIGS. 79A-B

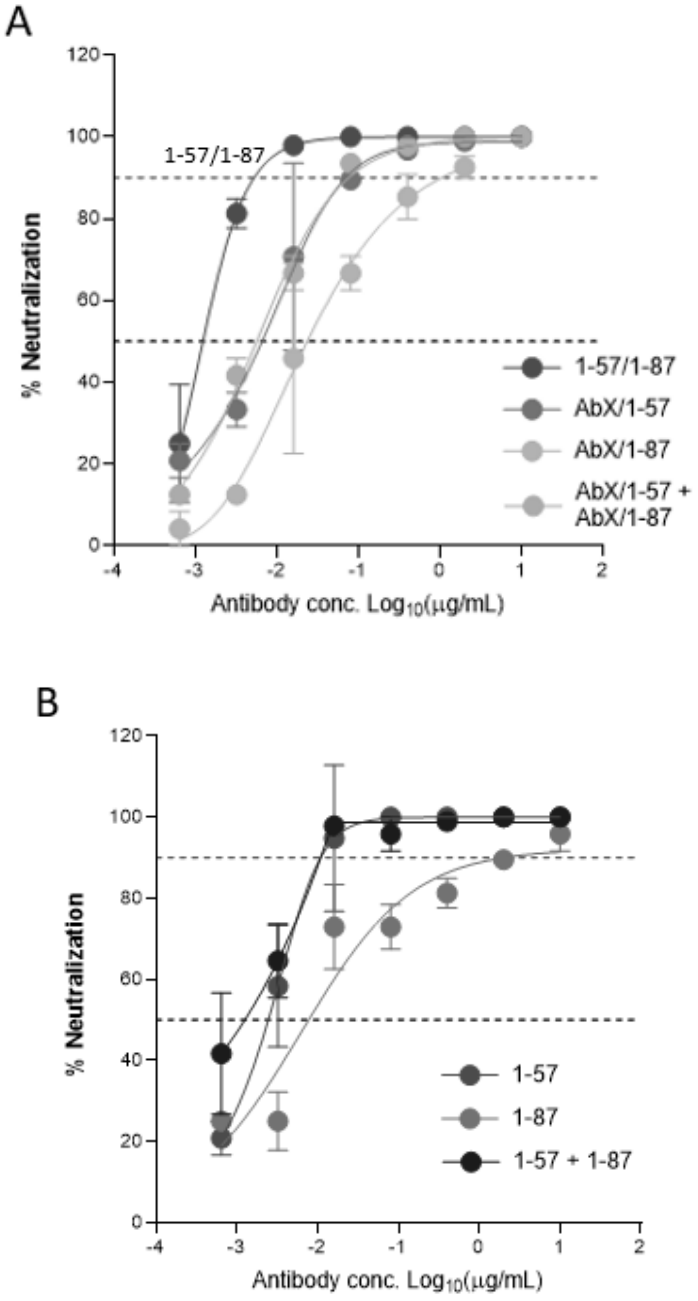
C



D

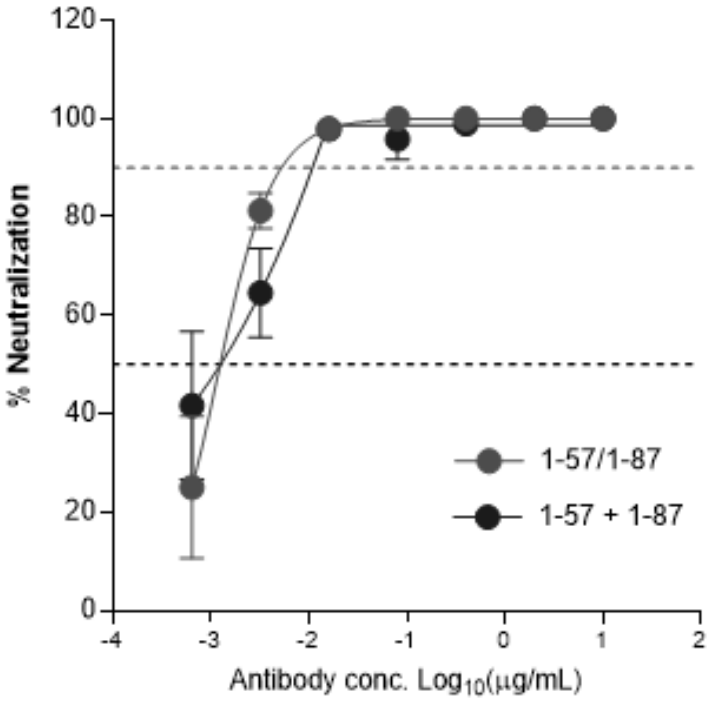
	IC_{50} (µg/mL)	IC_{90} (µg/mL)
2-7/4-8 (39/51)	0.0008	0.002
2-7 + 4-8 (39/51)	0.0004	0.002

FIGS. 79C-D


A
% Neutralization
120
100
80
60
40
20
0
-4
-3
-2
-1
0
1
2
Antibody conc. Log10(µg/mL)
1-57/1-87
1-57/1-87
AbX/1-57
AbX/1-87
AbX/1-57 +
AbX/1-87
B
% Neutralization
Antibody conc. Log10(µg/mL)
1-57
1-87
1-57 + 1-87

FIGS. 80A-B

C



D

	IC_{50} (µg/mL)	IC_{90} (µg/mL)
1-57/1-87	0.0012	0.002
1-57 + 1-87	0.0012	0.010

FIGS. 80C-D

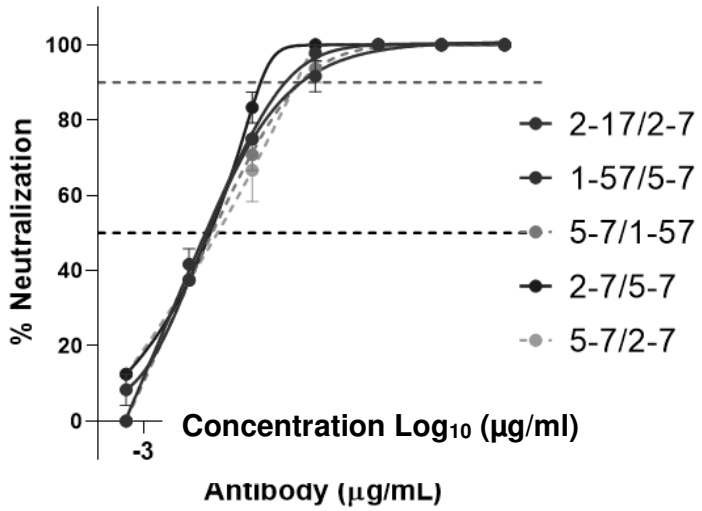
Bispecific	Potency (μg/mL)	
	IC_{50}	IC_{90}
2-36/2-15	0.023	0.054
1-20/1-68	0.015	0.055
2-43/2-51	0.011	0.069
2-15/1-87	0.008	0.072
2-30/1-87	0.014	0.075
2-43/2-51	0.004	0.076
1-20/2-51	0.029	0.081
2-17/2-15	0.006	0.088
2-17/2-43	0.007	0.088
2-15mut/4-18	0.057	0.091
4-20/4-19	0.035	0.103
2-43/1-68	0.007	0.124
2-17/4-20	0.03	0.164
2-17/1-57	0.023	0.167
2-36/1-57	0.066	0.175
1-20/4-8 (39/51)	0.036	0.191
2-15mut/1-87	0.007	0.193
1-20/2-17	0.025	0.213
5-24/4-20	0.063	0.222

FIG. 81

Bispecific	Potency (μg/mL)	
	IC_{50}	IC_{90}
1-57/4-19	0.072	0.367
2-36/4-20	0.188	0.418
2-15mut/5-24	0.083	0.421
2-15mut/2-17	0.266	0.476
2-36/1-20	0.174	0.549
2-17/2-30	0.065	0.598
2-36/2-7	0.084	0.712
2-15mut/1-68	0.072	0.756
1-20/1-87	0.027	0.87
2-36/4-18	0.03	0.982
2-30/4-19	0.529	1.747
2-36/2-17	0.063	4.55
2-15mut/4-19	2.549	5.718
1-20/4-19	1.579	6.096
2-36/1-68	0.096	9.948
2-15/4-19	4.857	18.883
2-30/4-18	0.108	>10
5-24/2-43	0.01	>10

FIG. 81 CONT.

A

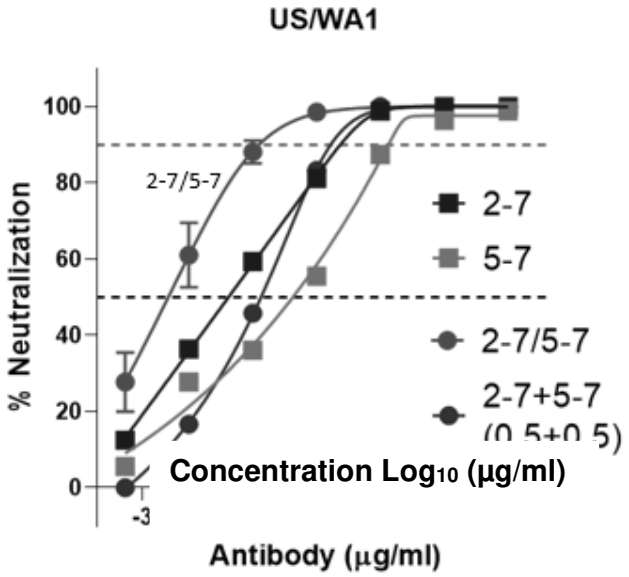


B

Bispecific antibodies	Potency against wild-type virus (WA1)	
	IC50 (µg/mL)	IC90 (µg/mL)
2-17/2-7 (control)	0.005~0.008	0.025~0.055
1-57/5-7	0.005	0.037
5-7/1-57	0.006	0.054
2-7/5-7	0.005	0.020
5-7/2-7	0.007	0.049

FIGS. 82A-B

A

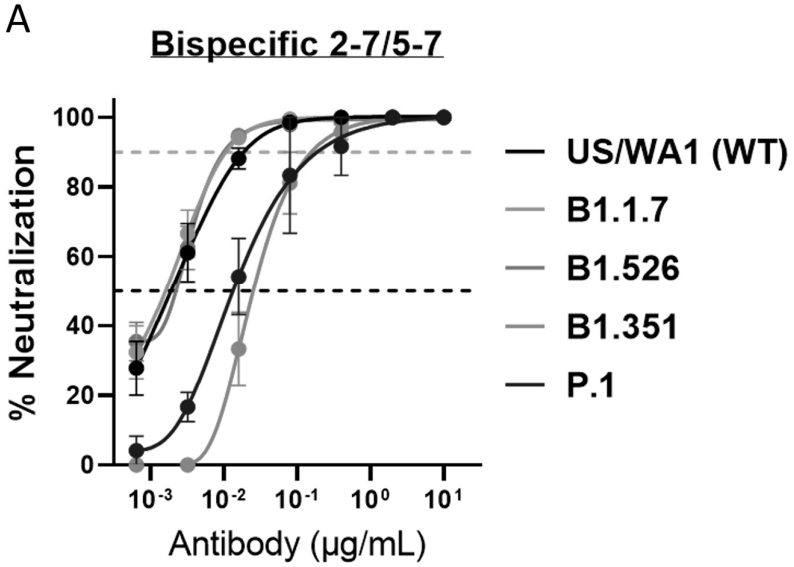


B

Antibodies	IC50 (µg/mL)
2-7	0.009
5-7	0.044
2-7/5-7	0.002
2-7+5-7	0.020

FIGS. 83A-B

A

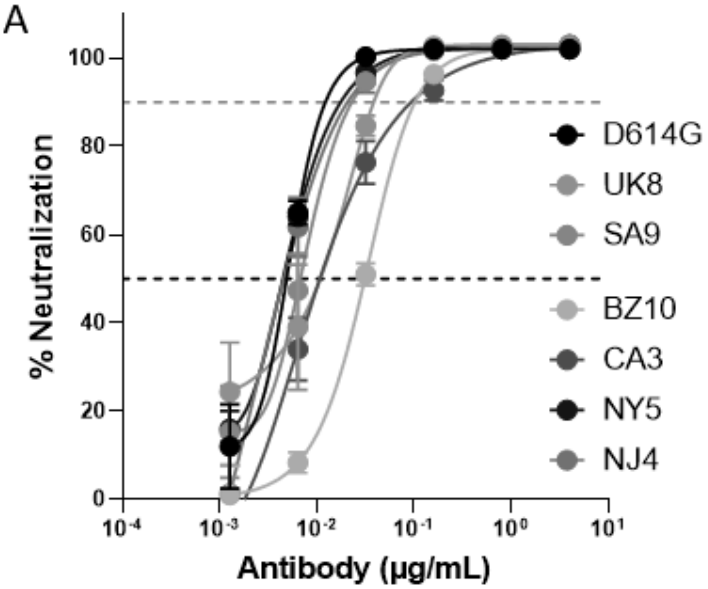


B

Virus	IC50 (µg/mL)	IC90 (µg/mL)
WA1 (WT)	0.002	0.019
B1.1.7	0.002	0.011
B1.526	0.002	0.01
B1.351	0.025	0.156
P.1	0.013	0.188

FIGS. 84A-B

A

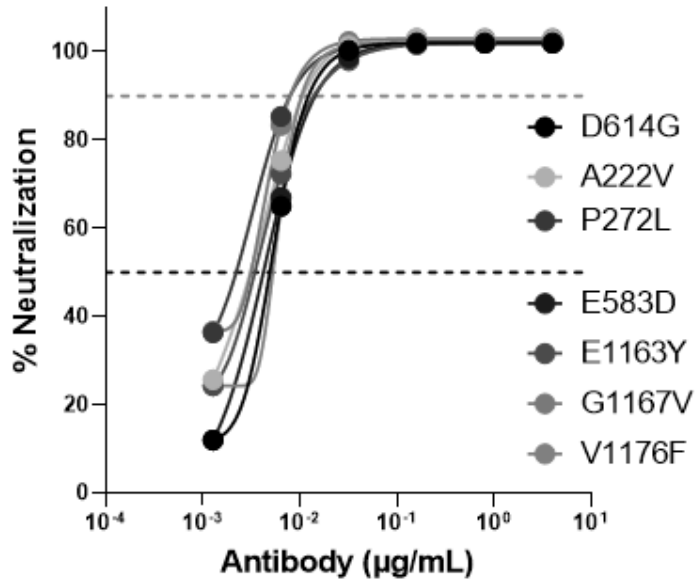


B

Variants	Potency (µg/mL)	
	IC50	IC90
D614G	0.005	0.012
UK8	0.011	0.039
SA9	0.007	0.023
BZ10	0.031	0.102
CA3	0.011	0.094
NY5	0.004	0.018
NJ4	0.005	0.021

FIGS. 85A-B

C

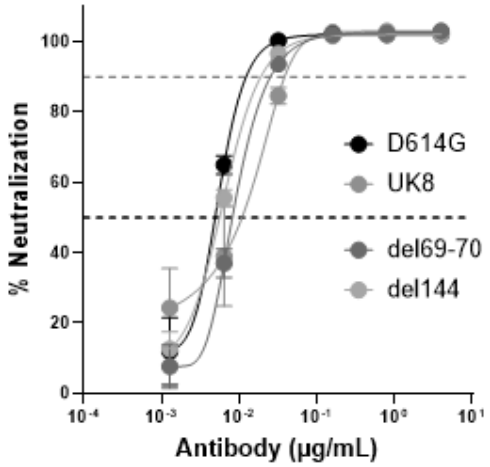


D

Mutations	Potency (µg/mL)	
	IC50	IC90
D614G	0.005	0.012
A222V	0.003	0.011
P272L	0.002	0.008
E583D	0.004	0.014
E1163Y	0.003	0.014
G1167V	0.003	0.008
V1176F	0.005	0.010

FIGS. 85C-D

A

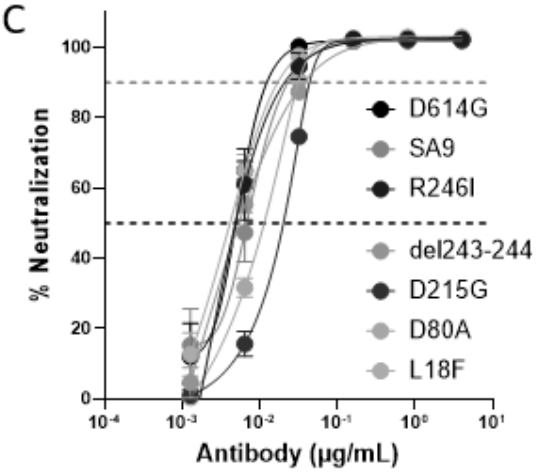


B

Mutations	Potency (µg/mL)	
	IC50	IC90
D614G	0.005	0.012
UK8	0.011	0.039
del69-70	0.008	0.025
del144	0.006	0.019

FIGS. 86A-B

C

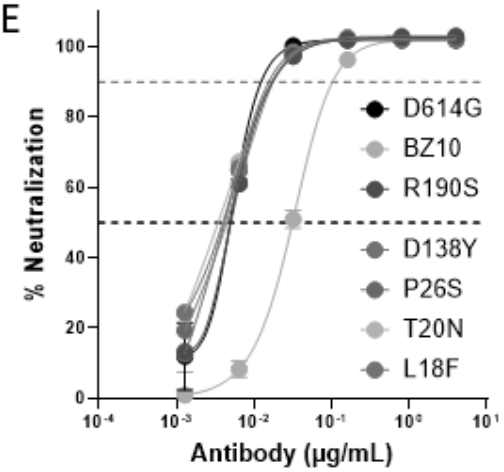


D

Mutations	Potency (µg/mL)	
	IC50	IC90
D614G	0.005	0.012
SA9	0.007	0.023
R246I	0.005	0.021
del243-244	0.005	0.037
D215G	0.020	0.044
D80A	0.011	0.031
L18F	0.004	0.017

FIGS. 86C-D

E

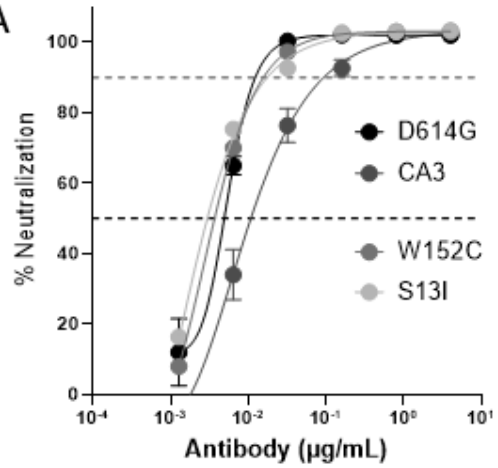


F

Mutations	Potency (µg/mL)	
	IC50	IC90
D614G	0.005	0.012
BZ10	0.031	0.102
R190S	0.005	0.017
D138Y	0.004	0.015
P26S	0.004	0.018
T20N	0.003	0.017
L18F	0.004	0.017

FIGS. 86E-F

A

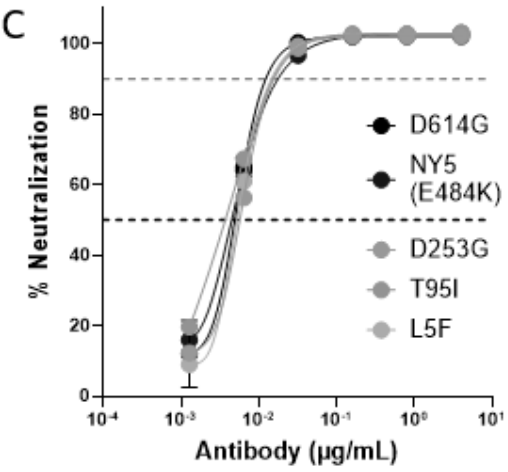


B

Mutations	Potency (µg/mL)	
	IC50	IC90
D614G	0.005	0.012
CA3	0.011	0.094
W152C	0.004	0.016
S13I	0.003	0.017

FIGS. 87A-B

C

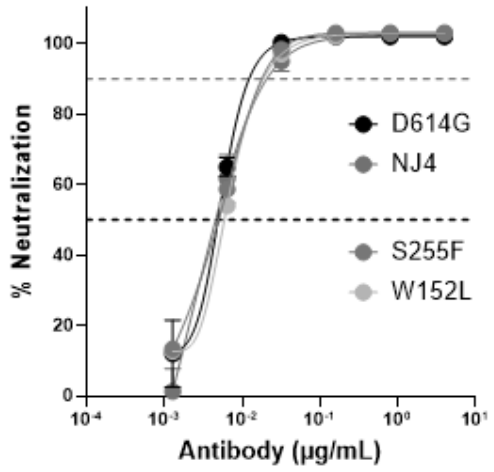


D

Mutation	Potency (µg/mL)	
	IC50	IC90
D614G	0.005	0.012
NY5	0.004	0.018
D253G	0.006	0.015
T95I	0.004	0.015
L5F	0.005	0.015

FIGS. 87C-D

E



F

Mutation	Potency (µg/mL)	
	IC50	IC90
D614G	0.005	0.012
NJ4	0.005	0.021
S255F	0.005	0.018
W152L	0.006	0.019

FIGS. 87E-F

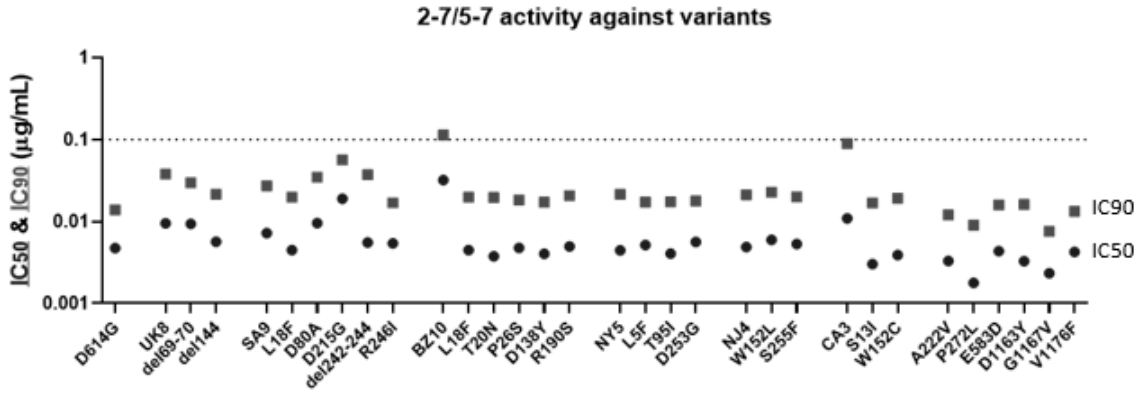
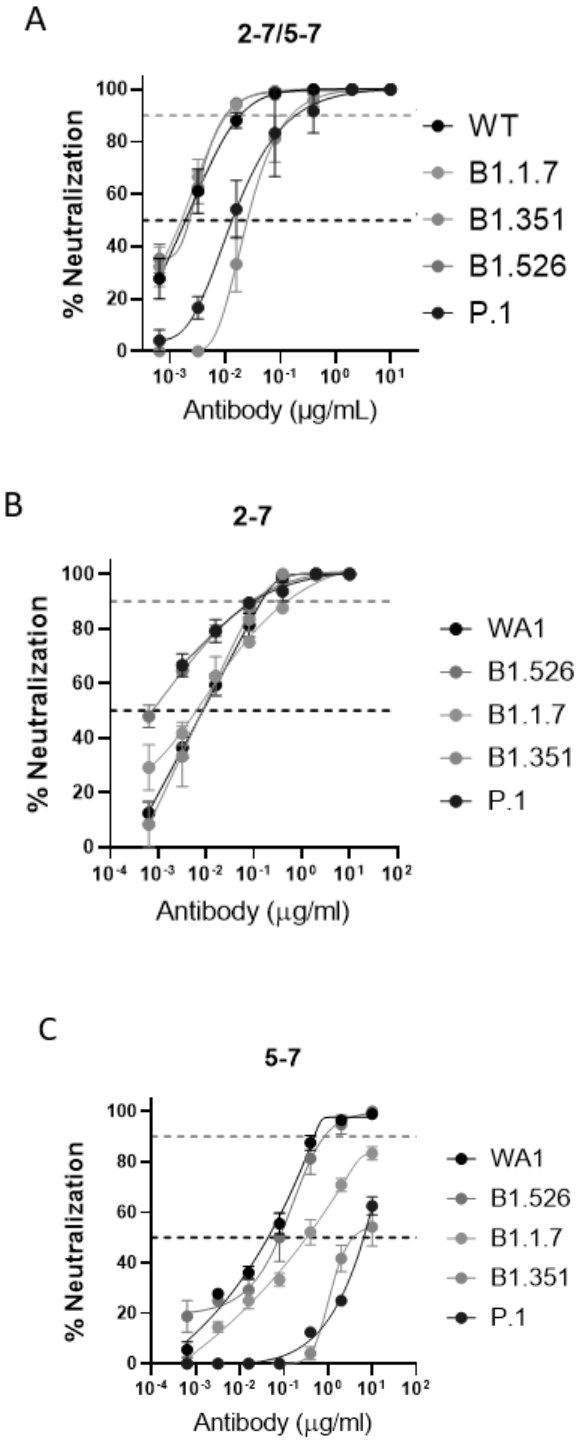
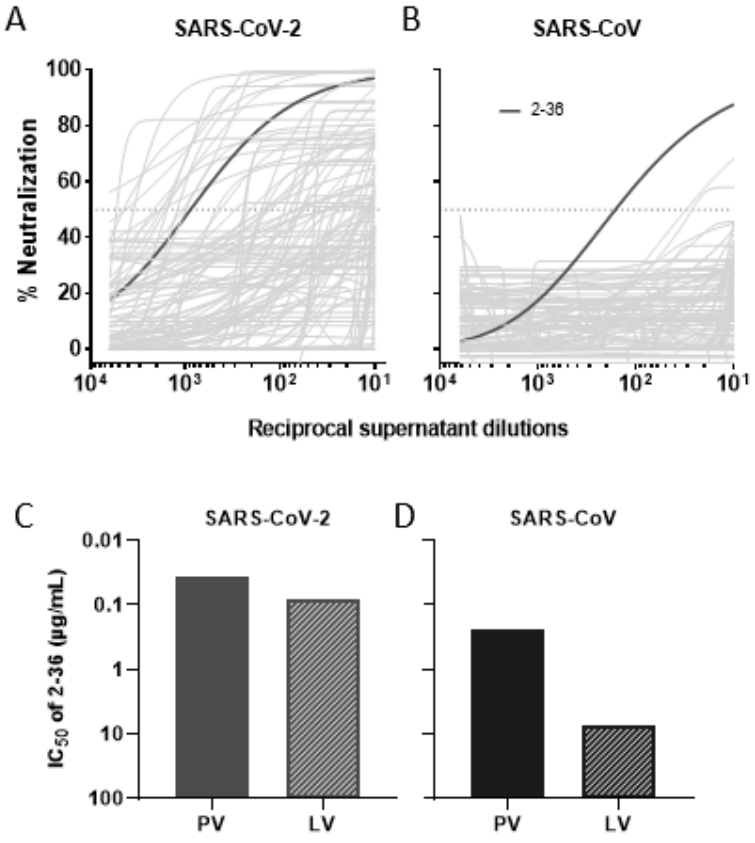

2-7/5-7 activity against variants
IC50 & IC90 (µg/mL)
1
0.1
0.01
0.001
IC90
IC50
D614G
UK8
del69-70
del144
SA9
L18F
D80A
D215G
del242-244
R246I
BZ10
L18F
T20N
P26S
D138Y
R190S
NY5
L5F
T95I
D253G
NJ4
W152L
S255F
CA3
S13I
W152C
A222V
P272L
E583D
D1163Y
G1167V
V1176F

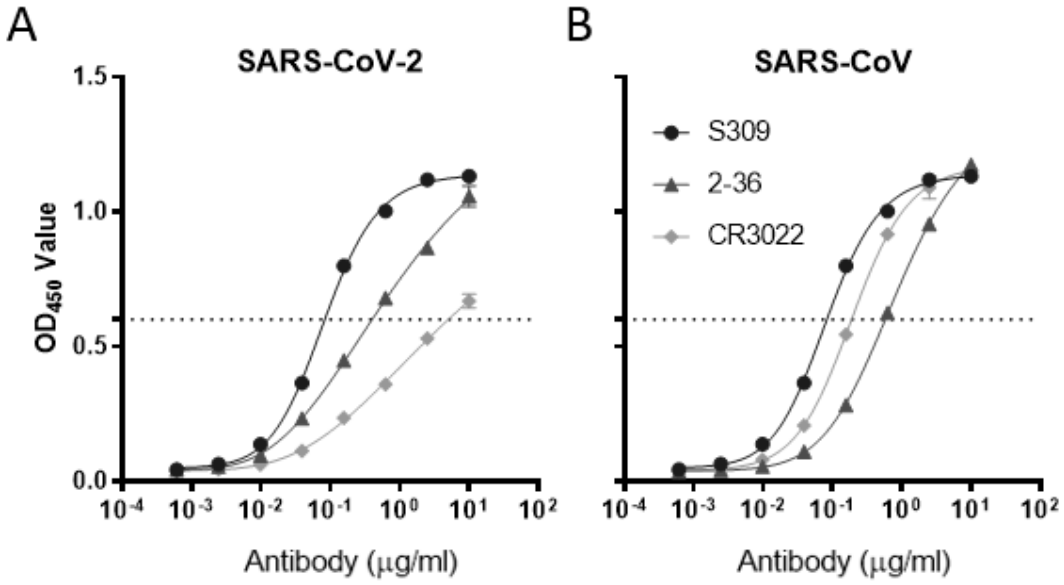
FIG. 88


A
2-7/5-7
% Neutralization
Antibody (µg/mL)
WT
B1.1.7
B1.351
B1.526
P.1
B
2-7
% Neutralization
Antibody (µg/ml)
WA1
B1.526
B1.1.7
B1.351
P.1
C
5-7
% Neutralization
Antibody (µg/ml)
WA1
B1.526
B1.1.7
B1.351
P.1

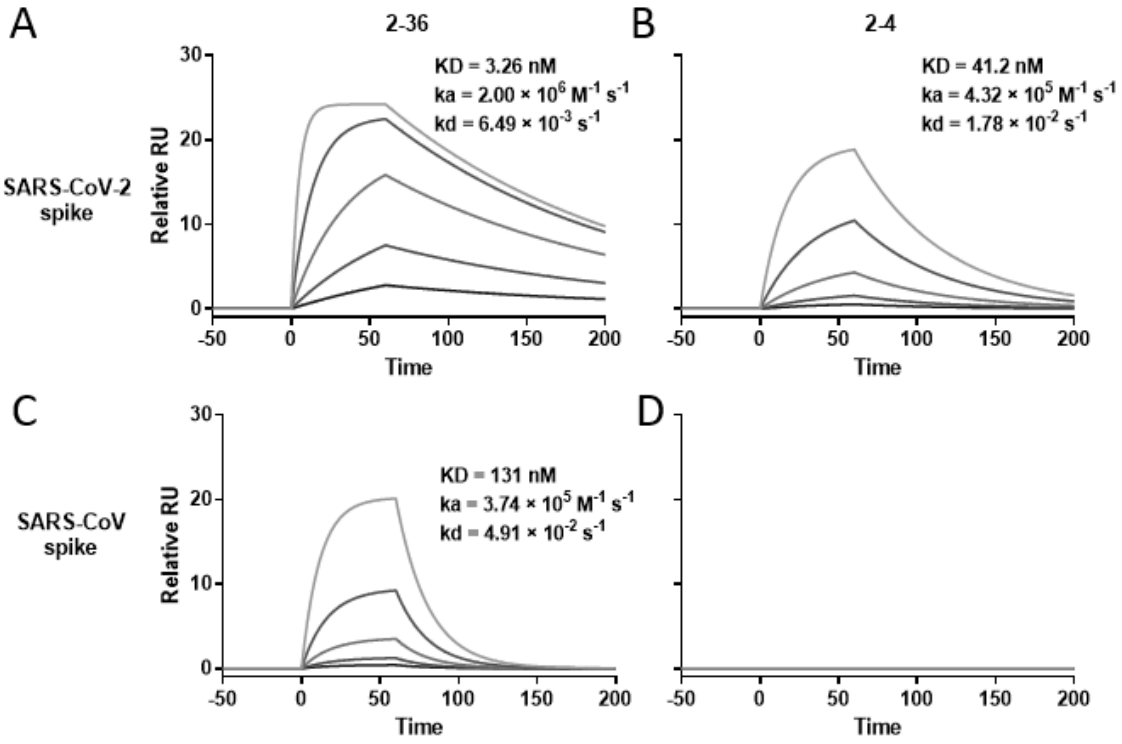
FIGS. 89A-C


A
SARS-CoV-2
B
SARS-CoV
2-36
% Neutralization
100
80
60
40
20
0
10^4
10^3
10^2
10^1
Reciprocal supernatant dilutions
C
SARS-CoV-2
D
SARS-CoV
IC_{50} of 2-36 (µg/mL)
0.01
0.1
1
10
100
PV
LV
PV
LV

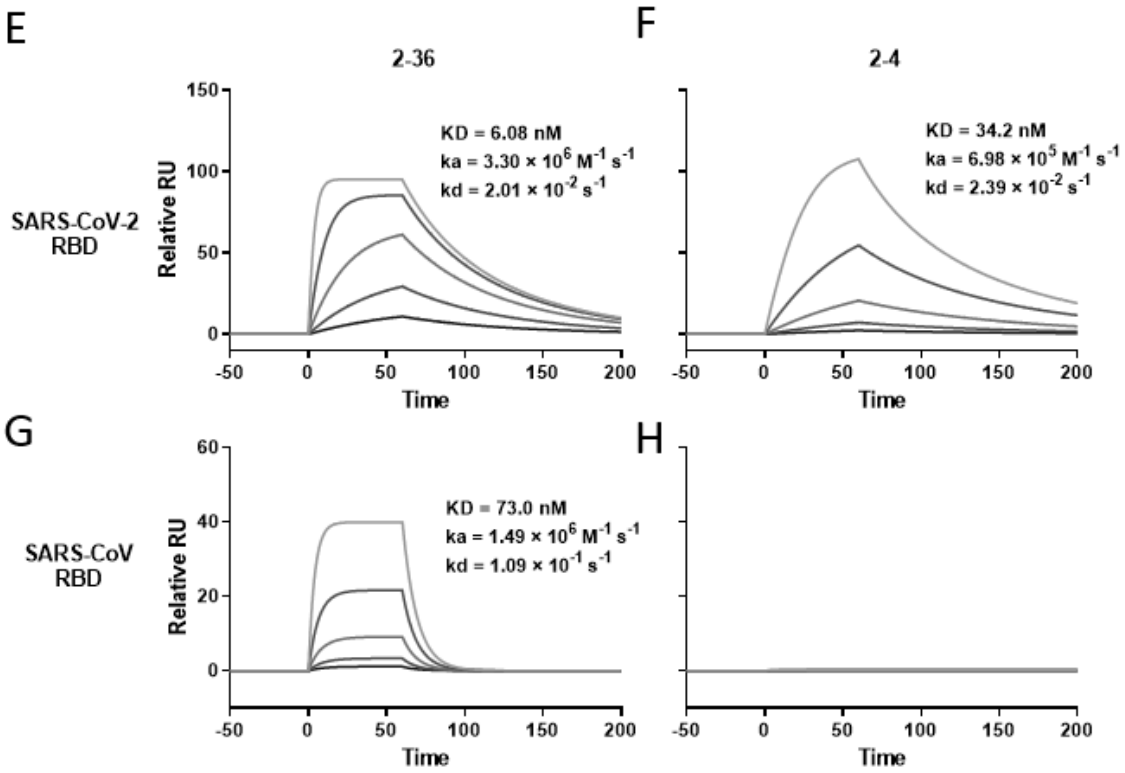
FIGS. 90A-D


A
SARS-CoV-2
1.5
1.0
0.5
0.0
OD450 Value
10-4 10-3 10-2 10-1 100 101 102
Antibody (μg/ml)
B
SARS-CoV
S309
2-36
CR3022
10-4 10-3 10-2 10-1 100 101 102
Antibody (μg/ml)

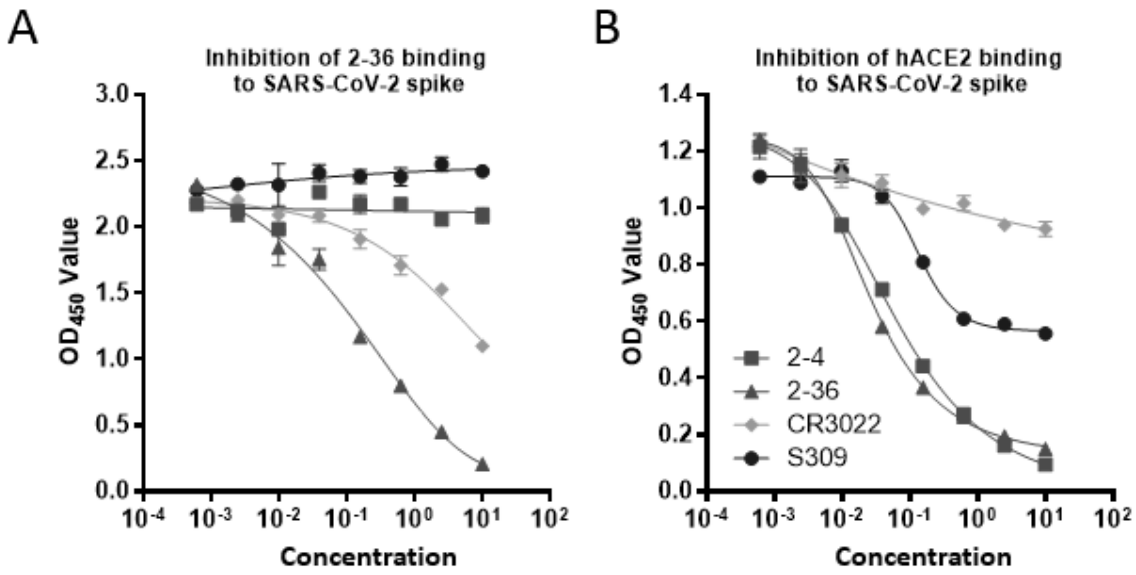
FIGS. 91A-B


A
2-36
KD = 3.26 nM
ka = 2.00 × 10^6 M^-1 s^-1
kd = 6.49 × 10^-3 s^-1
SARS-CoV-2 spike
Relative RU
Time
B
2-4
KD = 41.2 nM
ka = 4.32 × 10^5 M^-1 s^-1
kd = 1.78 × 10^-2 s^-1
Time
C
KD = 131 nM
ka = 3.74 × 10^5 M^-1 s^-1
kd = 4.91 × 10^-2 s^-1
SARS-CoV spike
Relative RU
Time
D
Time

FIGS. 92A-D


E
2-36
SARS-CoV-2 RBD
Relative RU
KD = 6.08 nM
ka = 3.30 × 10^6 M^-1 s^-1
kd = 2.01 × 10^-2 s^-1
Time
F
2-4
KD = 34.2 nM
ka = 6.98 × 10^5 M^-1 s^-1
kd = 2.39 × 10^-2 s^-1
Time
G
SARS-CoV RBD
Relative RU
KD = 73.0 nM
ka = 1.49 × 10^6 M^-1 s^-1
kd = 1.09 × 10^-1 s^-1
Time
H
Time

FIGS. 92E-H


A
Inhibition of 2-36 binding to SARS-CoV-2 spike
OD450 Value
Concentration
B
Inhibition of hACE2 binding to SARS-CoV-2 spike
OD450 Value
Concentration
2-4
2-36
CR3022
S309

FIGS. 93A-B

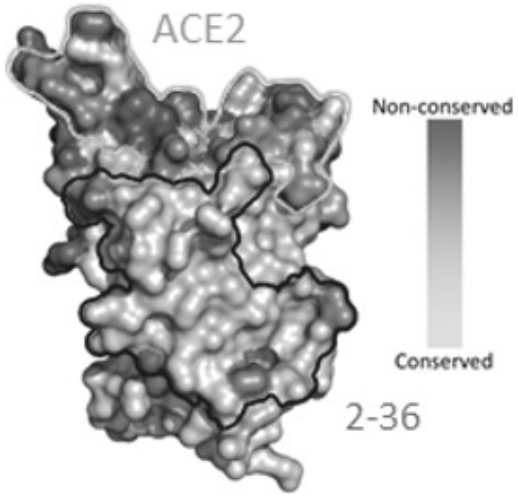


FIG. 94

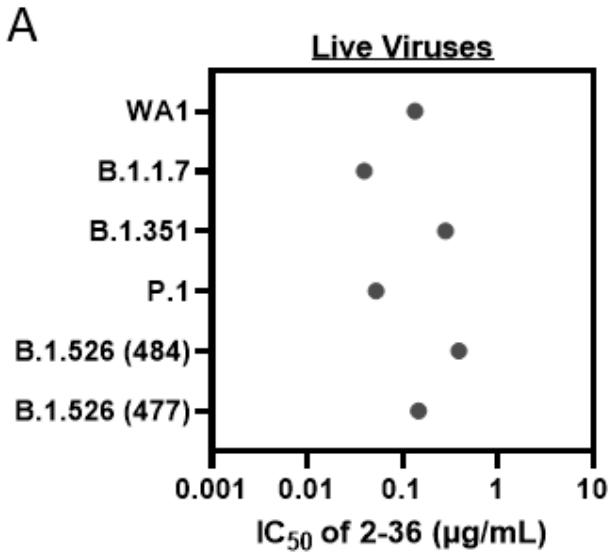

A
Live Viruses
WA1
B.1.1.7
B.1.351
P.1
B.1.526 (484)
B.1.526 (477)
0.001
0.01
0.1
1
10
IC50 of 2-36 (µg/mL)

FIG. 95A

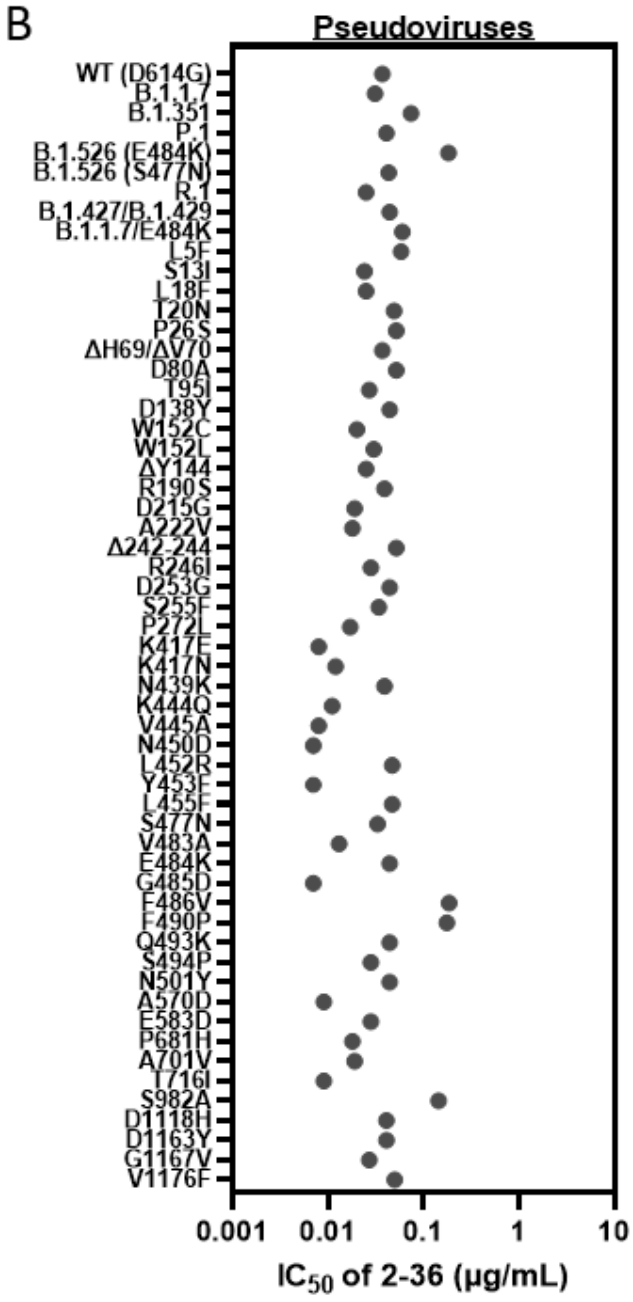

B
Pseudoviruses
WT (D614G)
B.1.1.7
B.1.351
P.1
B.1.526 (E484K)
B.1.526 (S477N)
R.1
B.1.427/B.1.429
B.1.1.7/E484K
L5F
S13I
L18F
T20N
P26S
ΔH69/ΔV70
D80A
T95I
D138Y
W152C
W152L
ΔY144
R190S
D215G
A222V
Δ242-244
R246I
D253G
S255F
P272L
K417E
K417N
N439K
K444Q
V445A
N450D
L452R
Y453F
L455F
S477N
V483A
E484K
G485D
F486V
F490P
Q493K
S494P
N501Y
A570D
E583D
P681H
A701V
T716I
S982A
D1118H
D1163Y
G1167V
V1176F
0.001
0.01
0.1
1
10
IC50 of 2-36 (μg/mL)

FIG. 95B

C

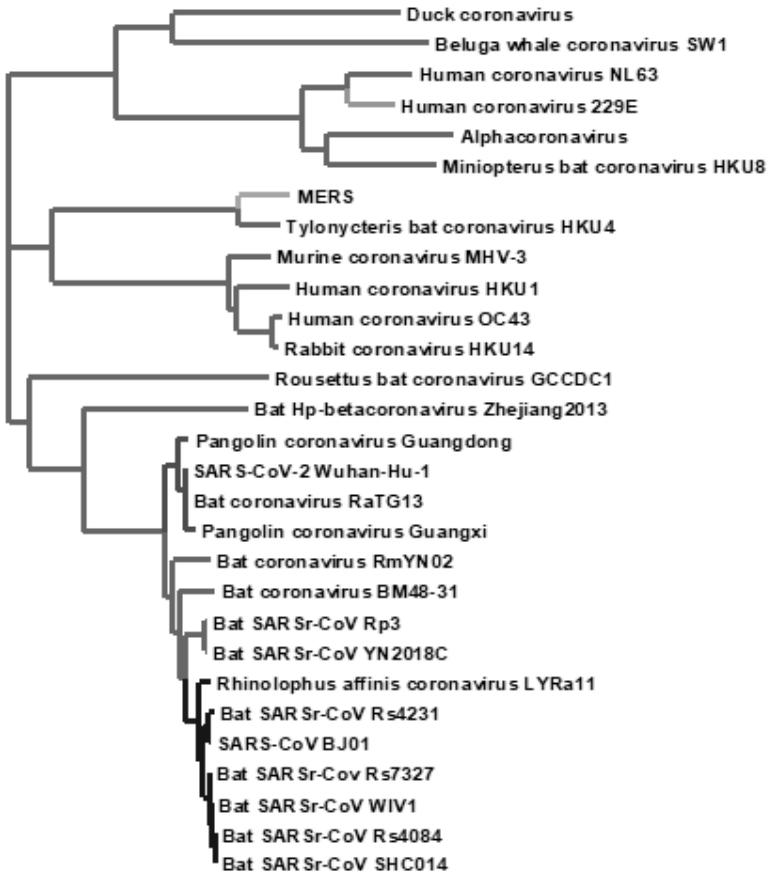

Duck coronavirus
Beluga whale coronavirus SW1
Human coronavirus NL63
Human coronavirus 229E
Alphacoronavirus
Miniopterus bat coronavirus HKU8
MERS
Tylonycteris bat coronavirus HKU4
Murine coronavirus MHV-3
Human coronavirus HKU1
Human coronavirus OC43
Rabbit coronavirus HKU14
Rousettus bat coronavirus GCCDC1
Bat Hp-betacoronavirus Zhejiang2013
Pangolin coronavirus Guangdong
SARS-CoV-2 Wuhan-Hu-1
Bat coronavirus RaTG13
Pangolin coronavirus Guangxi
Bat coronavirus RmYN02
Bat coronavirus BM48-31
Bat SARSr-CoV Rp3
Bat SARSr-CoV YN2018C
Rhinolophus affinis coronavirus LYRa11
Bat SARSr-CoV Rs4231
SARS-CoV BJ01
Bat SARSr-Cov Rs7327
Bat SARSr-CoV WIV1
Bat SARSr-CoV Rs4084
Bat SARSr-CoV SHC014

FIG. 95C

D

	2-36	COVA1-16	S309	CR3022
229E	>20	>20	>20	>20
MERS-CoV	>20	>20	>20	>20
SARS-CoV-2	0.029	0.178	0.007	>20
GDPangolin	0.025	0.040	0.024	>20
GXPangolin	0.073	0.053	>20	>20
RaTG13	0.003	0.007	>20	0.604
SARS-CoV	0.224	15.116	0.020	1.494
WIV1	0.020	1.888	0.047	0.668
SHC014	0.025	1.062	>20	>20
LYRa11	0.016	1.275	0.011	>20
Rs7327	0.658	>20	>20	>20
Rs4231	0.002	1.179	0.141	>20
Rs4084	1.041	1.183	>20	>20

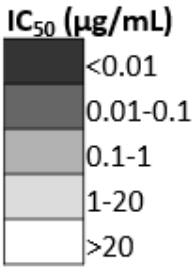
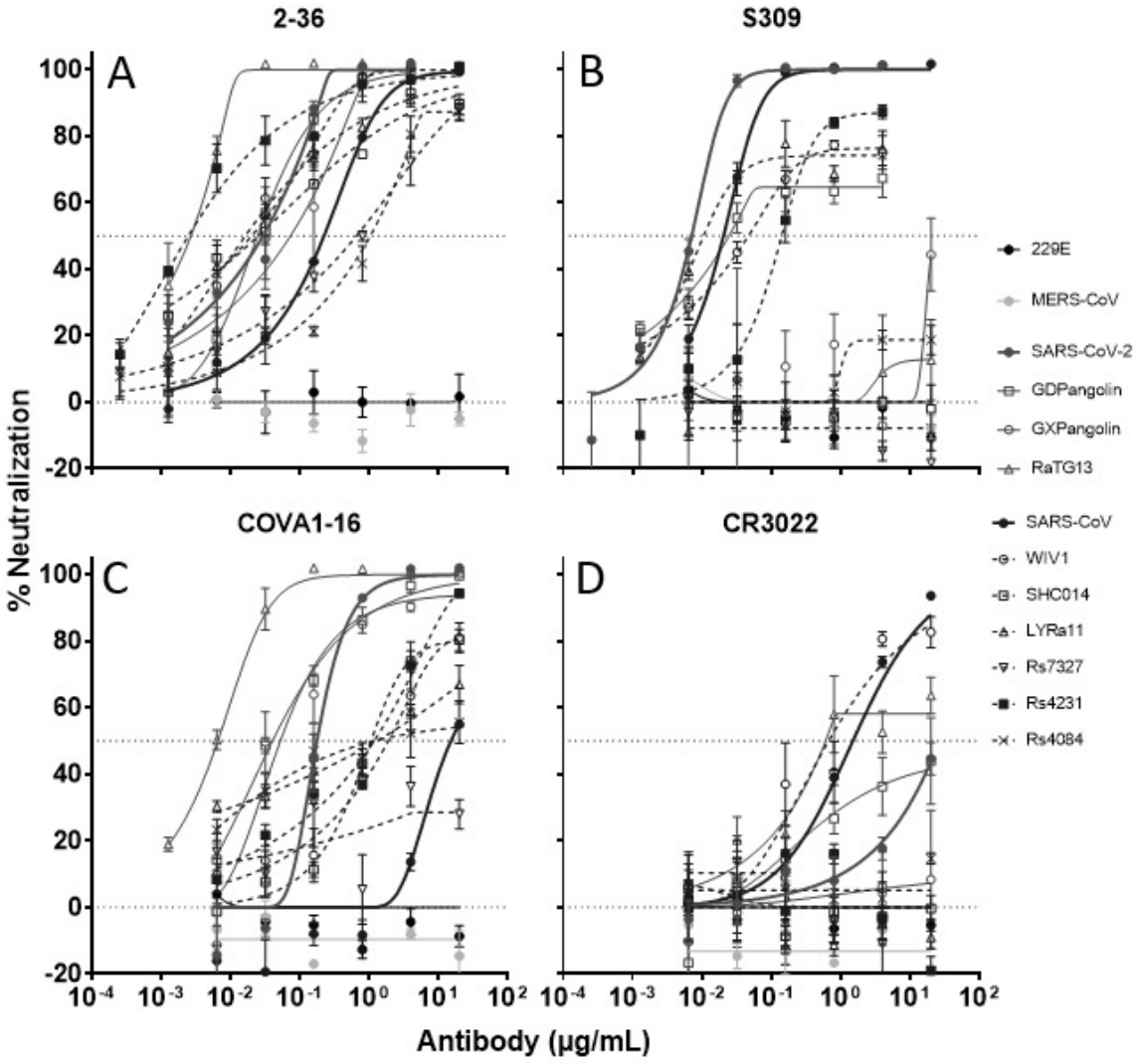


FIG. 95D


2-36
S309
A
B
C
D
% Neutralization
Antibody (µg/mL)
229E
MERS-CoV
SARS-CoV-2
GDPangolin
GXPangolin
RaTG13
SARS-CoV
WIV1
SHC014
LYRa11
Rs7327
Rs4231
Rs4084

FIGS. 96A-D

A

Passage	P0	P4	P9	P12
IC50 (µg/ml)	0.148	0.327	0.587	>50
H655Y		100%	100%	100%
T284I				100%
K378T				100%
V1128A		9%	94%	100%

B

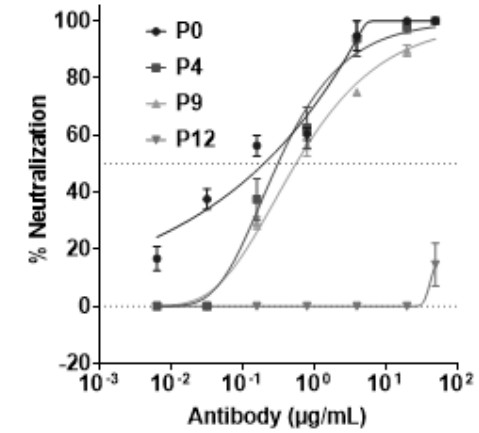


FIG. 97A-B

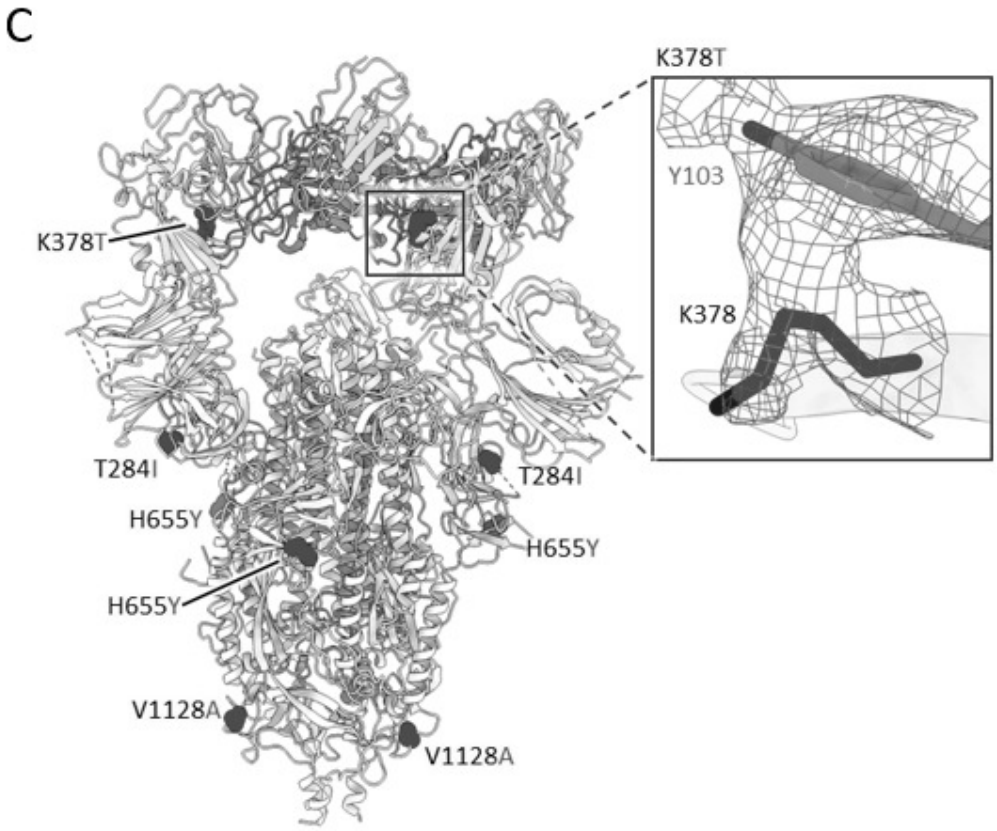

C
K378T
Y103
K378
K378T
T284I
T284I
H655Y
H655Y
H655Y
V1128A
V1128A

FIG. 97C

D

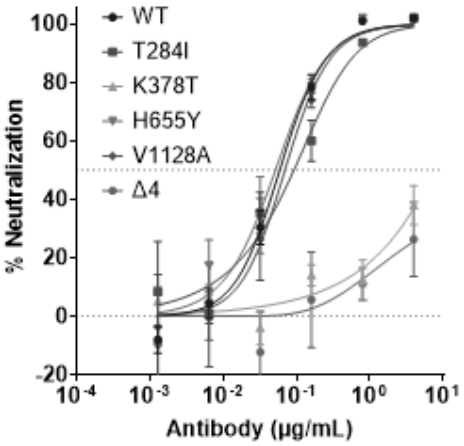

WT
T284I
K378T
H655Y
V1128A
Δ4
% Neutralization
100
80
60
40
20
0
-20
10-4
10-3
10-2
10-1
100
101
Antibody (µg/mL)

FIG. 97D