
Supplementary information

Broad sarbecovirus neutralization by a human monoclonal antibody

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SUPPLEMENTARY TABLES

Table S1. Characteristics of S2X259. VH and VL % identity refers to V gene identity compared to germline (IMGT).

Donor Gender	Male
Donor Age	52
Donor Status	Symptomatic
Days after symptoms onset	75
VH gene usage	VH1-69
VH % identity	94.1
HCDR3	ARGFNGNYYGWGDDDAFDI
VL gene usage	VL1-40
VL % identity	98.26
LCDR3	QSYDSSLSGPNWV

Table S2. S2X259-mediated neutralization (IC₅₀) of VSV pseudotypes harbouring SARS-CoV-2 S representing VOC, single mutants and different sarbecovirus clades related to Fig. 1.

Clade	Strain/VOC/RBD mutant	IC₅₀ (ng/ml)
1a	SARS-CoV	90.8
	RsSHC014	7.3
	WIV1	581.1
	WIV16	196.5
1b	SARS-CoV-2	213.2
	B.1.1.7	205.0
	B.1.351	357.9
	B.1.429	114.2
	P.1	458.3
	N439K	281.3
	Y453F	221.5
	RaTG13	38.3
	P-GX	4857.0
	P-GD	106.1

Table S3. CryoEM data collection and refinement statistics.

	SARS-CoV-2 S/S2X259 PDB 7RA8 EMD-24347	SARS-CoV-2 S/S2X259 (local refinement) PDB 7RAL EMD-24365
Data collection and processing		
Magnification	130,000	130,000
Voltage	300	300
Electron exposure (e ⁻ /Å ²)	70	70
Defocus range (μm)	0.8-2.0	0.8-2.0
Pixel size (Å)	0.525	0.525
Symmetry imposed	C3	C1
Final particle images (no.)	251,102	223,152
Map resolution (Å)	3.2	3.6
FSC threshold	0.143	0.143
Validation		
MolProbity score	0.82	0.94
Clash score	0.56	0.56
Poor rotamers (%)	0.75	0.39
Ramachandran plot		
Favored (%)	97.29	96.25
Allowed (%)	2.62	3.22
Disallowed (%)	0.09	0.54
EMRinger score	3.45	3.85

Table S4. X-ray data collection and refinement statistics.

RBD/S2X259/S2H97 PDB ID: 7M7W	
Data collection	
Space group	P2 ₁
Cell dimensions	
<i>a</i> , <i>b</i> , <i>c</i> (Å)	86.19, 66.40, 237.66
α , β , γ (°)	90.00, 94.34, 90.00
Resolution (Å)	63.94-2.65 (2.70-2.65)
<i>R</i> _{merge}	0.149 (2.494)
<i>I</i> / σI	10.9 (0.8)
Completeness (%)	98.6 (98.3)
Redundancy	6.9 (6.8)
Refinement	
Resolution (Å)	2.65
No. reflections	73,189
<i>R</i> _{work} / <i>R</i> _{free}	0.221/0.271
No. atoms	
Protein	16,162
Ligand/ion	28
Water	95
<i>B</i> -factors	
Protein	75.86
Ligand	84.00
Water	50.09
R.m.s. deviations	
Bond lengths (Å)	0.002
Bond angles (°)	0.817

Values for the highest-resolution shell are shown in parentheses.

Table S5. Summary of nucleotide and amino acid mutations found in 18 neutralization-resistant VSV-SARS-CoV-2-S chimera plaques.

	S2X259		S2X35	
Plaque	Nt mutation	Aa Mutant	Nt mutation	Aa Mutant
1	G1511A	G504D	A1106C	Y369S
2	G1511A	G504D	G1511A	G504D
3	G1511A	G504D	T1508G	V503G
4	G1511A	G504D	G1213A	D405N
5	G1511A	G504D	G1511A	G504D
6	G1511A	G504D	A1132G	K378E
7	G1511A	G504D	G1511A	G504D
8	G1511A	G504D	G1213A	D405N
9	G1511A	G504D	T1508G	V503G
10	G1511A	G504D	T1508G	V503G
11	G1511A	G504D	G1511A	G504D
12	G1511A	G504D	G1511A	G504D
13	G1511A	G504D	G1511A	G504D
14	G1511A	G504D	T1508A	V503D
15	G1511A	G504D	G1213A	D405N
16	G1511A	G504D	T1508G	V503G
17	G1511A	G504D	G1511A	G504D
18	G1511A	G504D	G1511A	G504D
19			G1511A	G504D
20			G1510A	G504S
21			G1511A	G504D
22			G1511A	G504D
23			G1510A	G504S
24			A1132G	K378E
25			G1213A	D405N
26			G1510A	G504S
27			G1511A	G504D
28			G1511A	G504D
29			G1511A	G504D
30			A1132G	K378E
31			T1508G	V503G