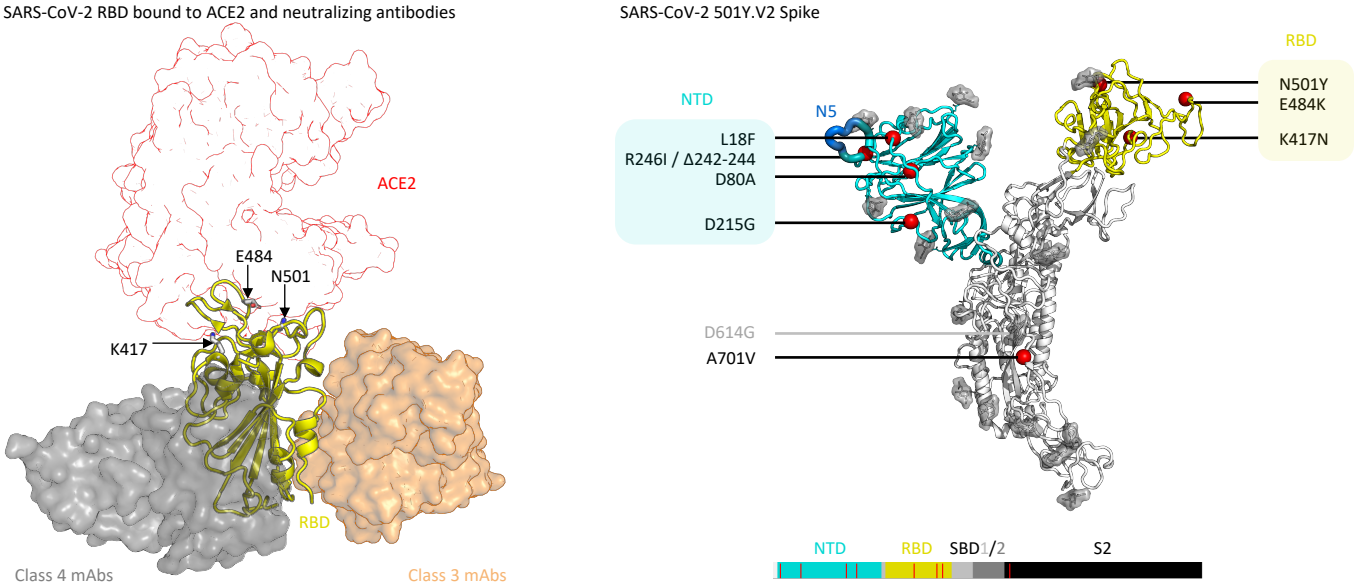
a

b



Supplementary Fig.1|Location of 501Y.V2 defining mutations. a. The SARS-CoV-2 RBD is shown in yellow cartoon view, bound to human ACE2 (red outline, surface view), as well as a class 3 (translucent orange) or class 4 (translucent grey) neutralizing antibodies that are not affected by 501Y.V2 changes. The location of 501Y.V2 associated changes 417N, 484K, and 501Y are indicated. B. Cartoon schematic of a single SARS-CoV-2 spike protomer, with NTD and RBD coloured cyan and yellow, respectively. A single N-acetylglucosamine is shown at each glycosylation site, and the location of 501Y.V2 changes are shown with the red spheres and labelled. A linear schematic is also shown.

a

SARS-CoV-2 Neutralization

	Titre	Titre	Fold reduction	Titre	Fold reduction
	42	43	1	41	1
	42	42	1	40	1
	43	39	1	36	1
Ⓗ	47	84	1	50	1
	49	76	1	20	KO
	51	20	KO	20	KO
	132	28	5	20	KO
	140	20	KO	20	KO
	154	20	KO	20	KO
	164	20	KO	20	KO
	174	20	KO	20	KO
	174	28	6	20	KO
	177	26	7	20	KO
	216	26	8	20	KO
	216	20	KO	20	KO
Ⓗ	226	67	3	72	3
	237	20	KO	20	KO
	245	20	KO	20	KO
	251	20	KO	20	KO
	255	24	11	20	KO
	308	33	9	44	9
	326	20	KO	20	KO
	401	39	10	20	KO
	614	765	1	291	2
	695	56	12	20	KO
	728	46	16	20	KO
	790	337	2	198	4
Ⓗ	897	146	6	72	12
	1286	44	29	40	32
	1448	53	27	20	KO
Ⓗ	1511	267	6	100	15
Ⓗ	1764	381	5	204	9
	1767	24	74	20	KO
Ⓗ	1936	936	2	233	8
Ⓗ	2235	1227	2	302	7
	2283	1245	2	303	8
Ⓗ	4984	232	21	66	75
Ⓗ	5189	2079	2	1217	4
Ⓗ	7288	2210	3	912	8
Ⓗ	7363	562	13	109	67
Ⓗ	8966	359	25	116	77
Ⓗ	15312	2163	7	177	86
	>1245	822	>5	258	>10
Ⓗ	>1245	950	>5	401	>10
+ve	25μg/mL	25μg/mL	1	25μg/mL	1
-ve	No neut	No neut	N/A	No neut	N/A

Titre
- < 25
- 25 - 400
- >400

Fold reduction
- <10
- >10
- Knock out

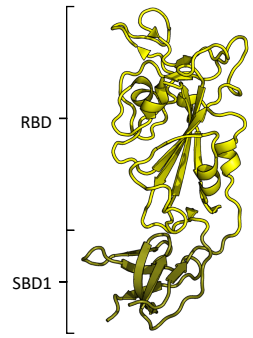
b

ELISA

	AUC D614G | 501Y.V2		Fold reduction
	1870	706	3
	1801	957	2
	1261	1186	1
	1362	111	12
	1047	1027	1
	2009	677	3
	1782	455	4
	755	114	7
	1411	479	3
	1311	213	6
	878	56	16
	1245	971	1
	861	233	4
	974	274	4
	402	74	5
	6197	1339	5
	783	114	7
	2141	198	11
	991	236	4
	1788	342	5
	451	328	1
	7415	1488	5
	3291	1180	3
	11993	6044	2
	48219	24642	2
	4435	1319	3
	15902	6184	3
	5576	2623	2
	87179	24146	4
	1699	401	4
	19232	7528	3
	20750	8219	3
	1203	145	8
	30184	6034	5
	85451	10432	8
	8289	3072	3
	8376	2864	3
	22833	4235	5
	94067	35985	3
	21756	11972	2
	14527	5764	3
	56158	14519	4
	27868	8109	3
	19028	4995	4
+ve	608438	416285	1
-ve	0	0	N/A

Ⓗ Hospitalised, <10d symptom onset
Ⓗ Hospitalised, moderate illness
Ⓗ Hospitalised, severe illness
Ⓗ Hospitalised, unknown severity

Fold reduction
- <5
- >5



Supplementary Fig.2|SARS-CoV-2 501Y.V2 shows increased resistance to neutralization but not binding by convalescent plasma/serum. a. Plasma/serum samples collected from SARS-CoV-2 infected individuals who were (n=14) or were not (n=30) hospitalized with COVID-19, ranked by titre against the original SARS-CoV-2 D614G lineage (column 1). Neutralization titre is coloured according to magnitude, where titres greater or lesser than 1:400 are coloured dark or light blue, respectively. Neutralization titre and fold decrease relative to the original lineage are shown for an RBD-only chimeric virus containing the K417N, E484K, and N501Y substitutions (columns 2 and 3), and the 501Y.V2 lineage virus (column 4 and 5). Neutralization titres <1:25 are coloured red, while a complete knock out of neutralization activity is highlighted in black. b. Binding of plasma samples (from Fig.2a) against the Receptor Binding Domain + Sub-Domain 1 (shown in yellow and olive cartoon view) from the original virus (column 1) or the 501Y.V2 lineage (column 2) and plotted as area under the curve. The fold reduction in AUC is shown in column 3. All experiments were performed in duplicate. In all instances, monoclonal antibodies CC12.23 or palivizumab were used as positive and negative controls, respectively.