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Review article

SARS-CoV-2 variant evasion of monoclonal antibodies based on in vitro studies

In the format provided by the authors and unedited

Methods

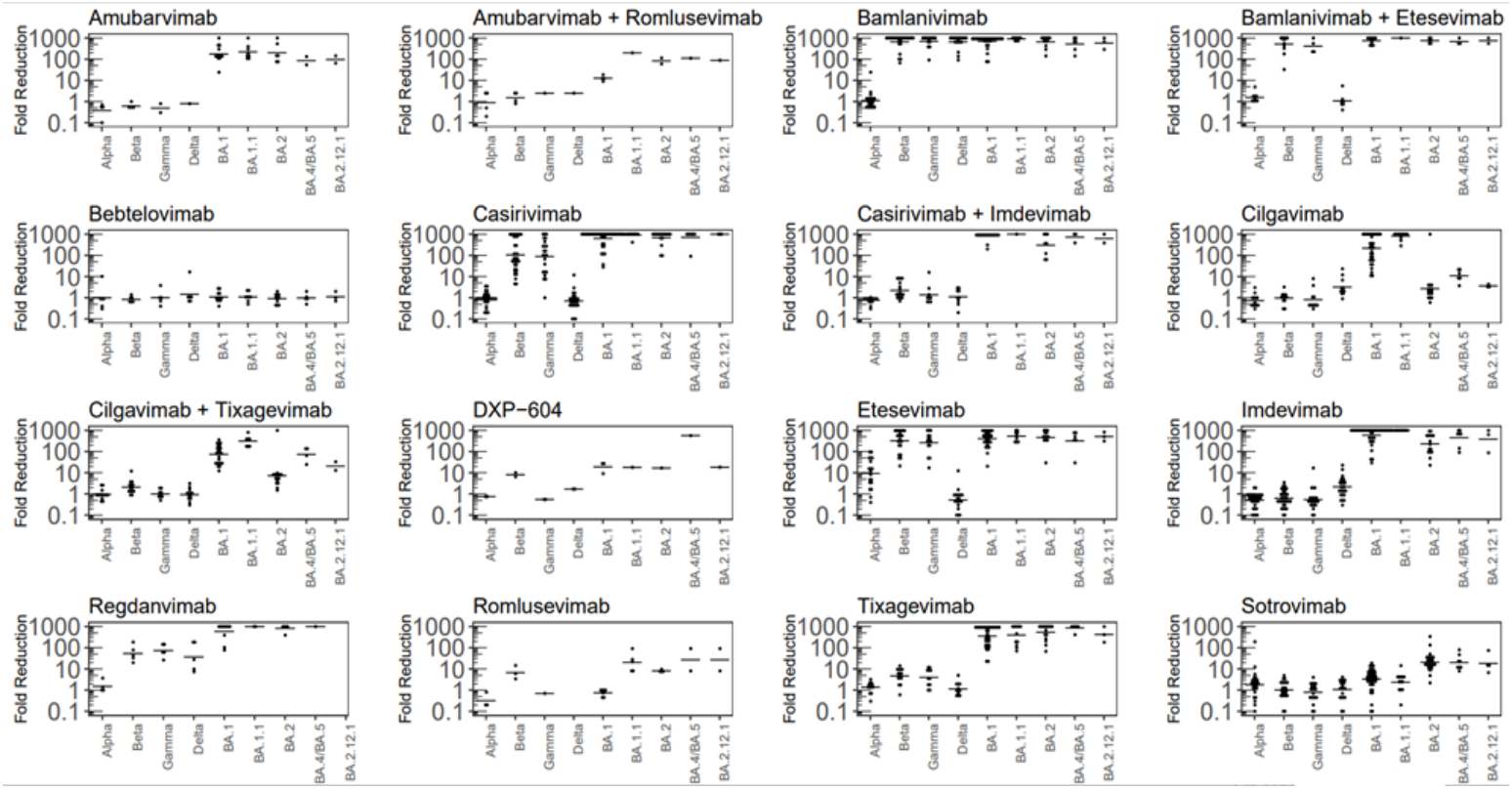
We scanned LitCovid, BioRxiv, MedRixv, and Google between September 2021 and March 2022 using search terms relevant to SARS-CoV-2, Monoclonal antibodies, Neutralisation assays, and antigenic change. e.g. "SARS-CoV-2", "Covid-19", "Variant", "Alpha", "Delta", "Omicron", "Monoclonal Antibodies", "Bamlanivimab", "Ronapreve", "Sotrovimab", "Neutralisation", "Resistance", "Escape", and "Evasion". We included studies if they reported neutralisation assays on the major VOC's (Alpha, Beta, Gamma, Delta, Omicron/BA.1, Omicron/BA.2), or their constituent single mutations, against mAb that have clinical approval somewhere in the world. Data were extracted from each study and combined to give mean Fold Reduction Neutralisation values for each virus-antibody pair. Data from variants with the same name were combined, unless they contained differences at known antigenic sites. e.g. results from Alpha and Alpha/E484K were separated. Data on antibodies and their precursors were combined. e.g. Data on Sotrovimab is combined with data on S309, its parental antibody. Summary data was periodically published on the COG Mutational Explorer Dashboard. Studies and data identified were checked against and contributed to the Stanford CoVDB.

Supplementary Figures

	G339D	R346K	S371L	S371F	S373P	S375F	T376A	D405N	R408S	K417N	K417T	N440K	G446S	L452R	L452Q	S477N	T478K	E484K	E484A	F486V	Q493R	G496S	Q498R	N501Y	Y505H
Alpha																								X	
Beta										X								X						X	
Gamma											X							X						X	
Delta														X			X								
BA.1	X		X		X	X				X		X	X			X	X		X		X	X	X	X	X
BA.1.1	X	X	X		X	X				X		X	X			X	X		X		X	X	X	X	X
BA.2	X			X	X	X	X	X	X	X		X				X	X		X		X		X	X	X
BA.4/5	X			X	X	X	X	X	X	X		X		X		X	X		X	X			X	X	X
BA.2.12.1	X			X	X	X	X	X	X	X		X			X	X	X		X		X		X	X	X

Supplementary Fig. 1. Receptor binding domain (RBD) mutations across VOCs

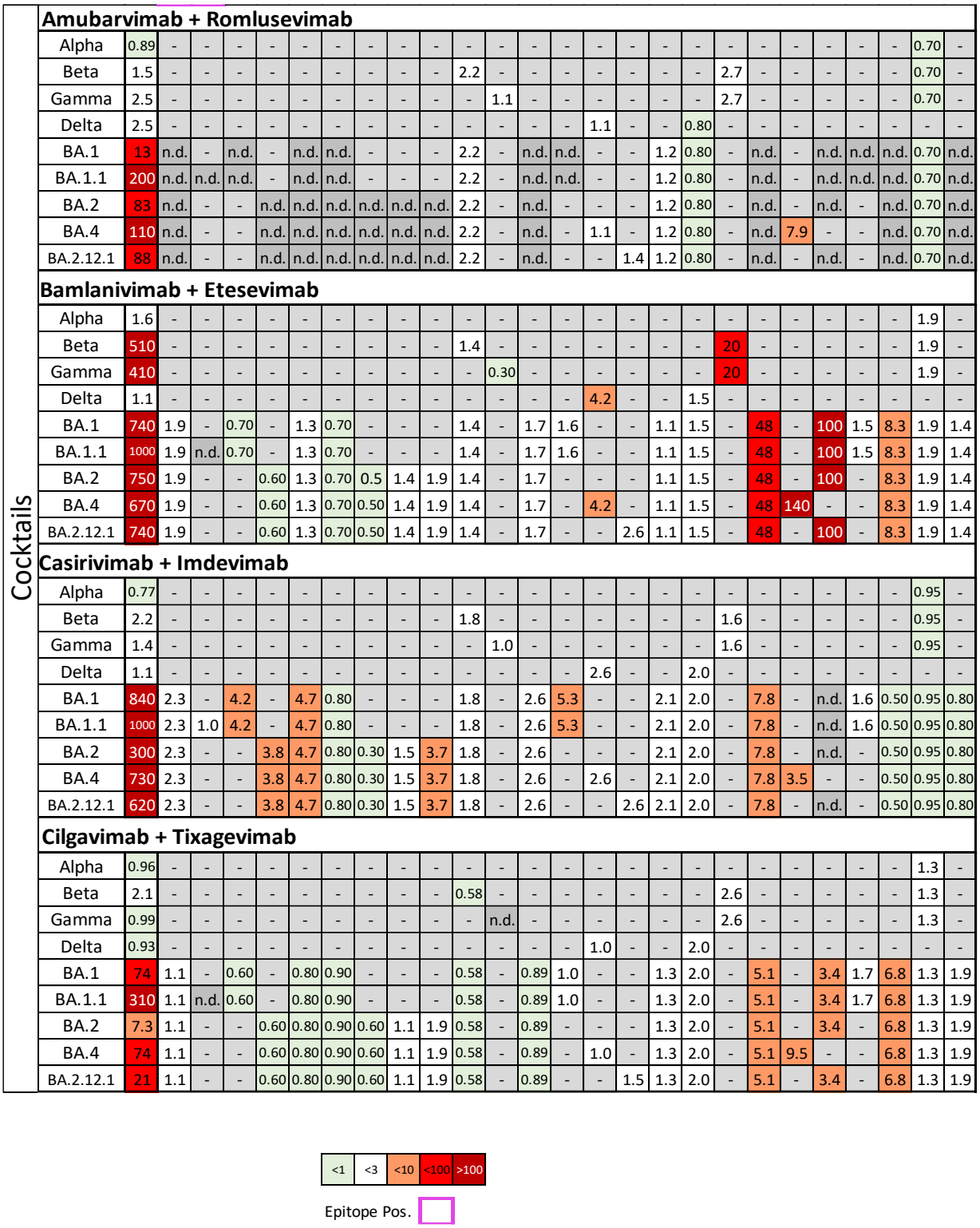
Supplementary Fig. 2. FRN results from individual studies.



Supplementary Fig. 2. FRN results from individual studies.

	Full Variants	G339D	R346K	S371L	S371F	S373P	S375F	T376A	D405N	R408S	K417N	K417T	N440K	G446S	L452R	L452Q	S477N	T478K	E484K	E484A	F486V	Q493R	G496S	Q498R	N501Y	Y505H
Class 1	**Amubarvimab**																									
	Alpha	0.38	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.96	-
	Beta	0.62	-	-	-	-	-	-	-	-	1.8	-	-	-	-	-	-	-	1.4	-	-	-	-	-	0.96	-
	Gamma	0.49	-	-	-	-	-	-	-	-	-	0.88	-	-	-	-	-	-	1.4	-	-	-	-	-	0.96	-
	Delta	0.80	-	-	-	-	-	-	-	-	-	-	-	-	1.2	-	-	0.85	-	-	-	-	-	-	-	-
	BA.1	180	2.0	-	17	-	1.4	0.69	-	-	1.8	-	2.0	2.1	-	-	1.0	0.85	-	4.8	-	11	1.8	2.8	0.96	0.89
	BA.1.1	220	2.0	0.60	17	-	1.4	0.69	-	-	1.8	-	2.0	2.1	-	-	1.0	0.85	-	4.8	-	11	1.8	2.8	0.96	0.89
	BA.2	200	2.0	-	-	120	1.4	0.69	1.8	1.9	0.47	1.8	-	2.0	-	-	-	1.0	0.85	-	4.8	-	11	-	2.8	0.96	0.89
	BA.4/5	85	2.0	-	-	120	1.4	0.69	1.8	1.9	0.47	1.8	-	2.0	-	1.2	-	1.0	0.85	-	4.8	12	-	-	2.8	0.96	0.89
	BA.2.12.1	97	2.0	-	-	120	1.4	0.69	1.8	1.9	0.47	1.8	-	2.0	-	-	1.3	1.0	0.85	-	4.8	-	11	-	2.8	0.96	0.89
	Casirivimab																									
	Alpha	0.91	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.1	-
	Beta	110	-	-	-	-	-	-	-	-	17	-	-	-	-	-	-	-	15	-	-	-	-	-	1.1	-
	Gamma	89	-	-	-	-	-	-	-	-	-	7.1	-	-	-	-	-	-	15	-	-	-	-	-	1.1	-
	Delta	0.71	-	-	-	-	-	-	-	-	-	-	-	-	1.4	-	-	1.0	-	-	-	-	-	-	-	-
	BA.1	630	1.9	-	3.6	-	2.3	0.53	-	-	17	-	1.1	1.2	-	-	2.1	1.0	-	9.8	-	38	1.0	1.8	1.1	0.74
	BA.1.1	910	1.9	0.95	3.6	-	2.3	0.53	-	-	17	-	1.1	1.2	-	-	2.1	1.0	-	9.8	-	38	1.0	1.8	1.1	0.74
	BA.2	670	1.9	-	-	11	2.3	0.53	1.6	7.6	1.7	17	-	1.1	-	-	-	2.1	1.0	-	9.8	-	38	-	1.8	1.1	0.74
	BA.4/5	710	1.9	-	-	11	2.3	0.53	1.6	7.6	1.7	17	-	1.1	-	1.4	-	2.1	1.0	-	9.8	660	-	-	1.8	1.1	0.74
	BA.2.12.1	1000	1.9	-	-	11	2.3	0.53	1.6	7.6	1.7	17	-	1.1	-	-	1.5	2.1	1.0	-	9.8	-	38	-	1.8	1.1	0.74
	DXP-604																									
	Alpha	0.75	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	n.d.	-
	Beta	8.1	-	-	-	-	-	-	-	-	n.d.	-	-	-	-	-	-	-	n.d.	-	-	-	-	-	n.d.	-
	Gamma	0.55	-	-	-	-	-	-	-	-	-	n.d.	-	-	-	-	-	-	n.d.	-	-	-	-	-	n.d.	-
	Delta	1.7	-	-	-	-	-	-	-	-	-	-	-	-	n.d.	-	-	n.d.	-	-	-	-	-	-	-	-
	BA.1	19	n.d.	-	n.d.	-	n.d.	n.d.	-	-	n.d.	-	n.d.	n.d.	-	-	n.d.	n.d.	-	n.d.	-	n.d.	n.d.	n.d.	n.d.	n.d.
	BA.1.1	18	n.d.	n.d.	n.d.	-	n.d.	n.d.	-	-	n.d.	-	n.d.	n.d.	-	-	n.d.	n.d.	-	n.d.	-	n.d.	n.d.	n.d.	n.d.	n.d.
	BA.2	17	n.d.	-	-	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	-	n.d.	-	-	-	n.d.	n.d.	-	n.d.	-	n.d.	-	n.d.	n.d.	n.d.
	BA.4/5	570	n.d.	-	-	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	-	n.d.	-	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-	-	n.d.	n.d.	n.d.
	BA.2.12.1	18	n.d.	-	-	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	-	n.d.	-	-	n.d.	n.d.	n.d.	-	n.d.	-	n.d.	-	n.d.	n.d.	n.d.
	Etesevimab																									
	Alpha	9.3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5.7	-
	Beta	330	-	-	-	-	-	-	-	-	210	-	-	-	-	-	-	-	3.1	-	-	-	-	-	5.7	-
	Gamma	270	-	-	-	-	-	-	-	-	-	32	-	-	-	-	-	-	3.1	-	-	-	-	-	5.7	-
	Delta	0.52	-	-	-	-	-	-	-	-	-	-	-	-	1.2	-	-	0.77	-	-	-	-	-	-	-	-
	BA.1	410	1.7	-	15	-	1.3	1.1	-	-	210	-	1.1	1.0	-	-	0.90	0.77	-	3.8	-	55	1.2	4.3	5.7	2.9
	BA.1.1	540	1.7	2.2	15	-	1.3	1.1	-	-	210	-	1.1	1.0	-	-	0.90	0.77	-	3.8	-	55	1.2	4.3	5.7	2.9
	BA.2	460	1.7	-	-	36	1.3	1.1	2.0	20	0.58	210	-	1.1	-	-	-	0.90	0.77	-	3.8	-	55	-	4.3	5.7	2.9
	BA.4/5	320	1.7	-	-	36	1.3	1.1	2.0	20	0.58	210	-	1.1	-	1.2	-	0.90	0.77	-	3.8	11	-	-	4.3	5.7	2.9
	BA.2.12.1	510	1.7	-	-	36	1.3	1.1	2.0	20	0.58	210	-	1.1	-	-	1.7	0.90	0.77	-	3.8	-	55	-	4.3	5.7	2.9
	Regdanvimab																									
	Alpha	1.5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3.3	-
	Beta	53	-	-	-	-	-	-	-	-	0.60	-	-	-	-	-	-	-	8.7	-	-	-	-	-	3.3	-
	Gamma	73	-	-	-	-	-	-	-	-	-	0.70	-	-	-	-	-	-	8.7	-	-	-	-	-	3.3	-
	Delta	37	-	-	-	-	-	-	-	-	-	-	-	-	35	-	-	1.0	-	-	-	-	-	-	-	-
	BA.1	590	1.0	-	1.1	-	0.30	1.4	-	-	0.60	-	0.30	1.1	-	-	n.d.	1.0	-	1.1	-	950	0.60	0.30	3.3	0.50
	BA.1.1	1000	1.0	0.30	1.1	-	0.30	1.4	-	-	0.60	-	0.30	1.1	-	-	n.d.	1.0	-	1.1	-	950	0.60	0.30	3.3	0.50
	BA.2	830	1.0	-	-	21	0.30	1.4	1.0	1.0	0.60	0.60	-	0.30	-	-	-	n.d.	1.0	-	1.1	-	950	-	0.30	3.3	0.50
	BA.4/5	1000	1.0	-	-	21	0.30	1.4	1.0	1.0	0.60	0.60	-	0.30	-	35	-	n.d.	1.0	-	1.1	n.d.	-	-	0.30	3.3	0.50
	BA.2.12.1	n.d.	1.0	-	-	21	0.30	1.4	1.0	1.0	0.60	0.60	-	0.30	-	-	n.d.	n.d.	1.0	-	1.1	-	950	-	0.30	3.3	0.50
	Tixagevimab																									
	Alpha	1.4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.7	-
	Beta	4.7	-	-	-	-	-	-	-	-	0.61	-	-	-	-	-	-	-	6.8	-	-	-	-	-	1.7	-
	Gamma	4.0	-	-	-	-	-	-	-	-	-	n.d.	-	-	-	-	-	-	6.8	-	-	-	-	-	1.7	-
	Delta	1.1	-	-	-	-	-	-	-	-	-	-	-	-	0.50	-	-	1.9	-	-	-	-	-	-	-	-
	BA.1	360	2.1	-	3.5	-	1.2	0.77	-	-	0.61	-	0.94	1.4	-	-	2.0	1.9	-	7.6	-	6.0	1.0	2.0	1.7	1.2
	BA.1.1	400	2.1	2.0	3.5	-	1.2	0.77	-	-	0.61	-	0.94	1.4	-	-	2.0	1.9	-	7.6	-	6.0	1.0	2.0	1.7	1.2
	BA.2	540	2.1	-	-	17	1.2	0.77	1.4	2.0	1.2	0.61	-	0.94	-	-	-	2.0	1.9	-	7.6	-	6.0	-	2.0	1.7	1.2
	BA.4/5	860	2.1	-	-	17	1.2	0.77	1.4	2.0	1.2	0.61	-	0.94	-	0.50	-	2.0	1.9	-	7.6	140	-	-	2.0	1.7	1.2
	BA.2.12.1	420	2.1	-	-	17	1.2	0.77	1.4	2.0	1.2	0.61	-	0.94	-	-	0.50	2.0	1.9	-	7.6	-	6.0	-	2.0	1.7	1.2

Class 2	**Bamlanivimab**																												
	Alpha	1.1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.3	-
	Beta	660	-	-	-	-	-	-	-	-	-	0.50	-	-	-	-	-	-	-	750	-	-	-	-	-	-	1.3	-
	Gamma	700	-	-	-	-	-	-	-	-	-	-	0.10	-	-	-	-	-	-	750	-	-	-	-	-	-	1.3	-
	Delta	650	-	-	-	-	-	-	-	-	-	-	-	-	-	1000	-	-	1.4	-	-	-	-	-	-	-	-	-
	BA.1	700	1.4	-	1.2	-	0.95	0.67	-	-	-	0.50	-	1.1	1.4	-	-	1.1	1.4	-	570	-	760	0.75	2.2	1.3	0.86
	BA.1.1	910	1.4	1.1	1.2	-	0.95	0.67	-	-	-	0.50	-	1.1	1.4	-	-	1.1	1.4	-	570	-	760	0.75	2.2	1.3	0.86
	BA.2	660	1.4	-	-	1.2	0.95	0.67	1.5	1.5	1.0	0.50	-	1.1	-	-	-	1.1	1.4	-	570	-	760	-	2.2	1.3	0.86
	BA.4	520	1.4	-	-	1.2	0.95	0.67	1.5	1.5	1.0	0.50	-	1.1	-	1000	-	1.1	1.4	-	570	490	-	-	2.2	1.3	0.86
	BA.2.12.1	580	1.4	-	-	1.2	0.95	0.67	1.5	1.5	1.0	0.50	-	1.1	-	-	3.0	1.1	1.4	-	570	-	760	-	2.2	1.3	0.86
	Cilgavimab																												
	Alpha	0.73	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.5	-
	Beta	0.97	-	-	-	-	-	-	-	-	-	0.73	-	-	-	-	-	-	-	1.2	-	-	-	-	-	-	1.5	-
	Gamma	0.82	-	-	-	-	-	-	-	-	-	-	n.d.	-	-	-	-	-	-	1.2	-	-	-	-	-	-	1.5	-
	Delta	3.2	-	-	-	-	-	-	-	-	-	-	-	-	-	2.9	-	-	1.4	-	-	-	-	-	-	-	-	-
	BA.1	220	1.6	-	0.99	-	0.94	0.78	-	-	-	0.73	-	1.3	5.0	-	-	1.4	1.4	-	1.8	-	0.95	1.5	1.7	1.5	1.4
	BA.1.1	820	1.6	2.5	0.99	-	0.94	0.78	-	-	-	0.73	-	1.3	5.0	-	-	1.4	1.4	-	1.8	-	0.95	1.5	1.7	1.5	1.4
	BA.2	2.7	1.6	-	-	1.5	0.94	0.78	1.4	1.2	1.3	0.73	-	1.3	-	-	-	1.4	1.4	-	1.8	-	0.95	-	1.7	1.5	1.4
	BA.4	11	1.6	-	-	1.5	0.94	0.78	1.4	1.2	1.3	0.73	-	1.3	-	2.9	-	1.4	1.4	-	1.8	0.80	-	-	1.7	1.5	1.4
	BA.2.12.1	3.6	1.6	-	-	1.5	0.94	0.78	1.4	1.2	1.3	0.73	-	1.3	-	-	2.2	1.4	1.4	-	1.8	-	0.95	-	1.7	1.5	1.4
Class 3	**Bebtelovimab**																												
	Alpha	1.0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.85	-
	Beta	0.84	-	-	-	-	-	-	-	-	-	0.84	-	-	-	-	-	-	-	0.70	-	-	-	-	-	0.85	-
	Gamma	1.0	-	-	-	-	-	-	-	-	-	-	0.70	-	-	-	-	-	-	0.70	-	-	-	-	-	0.85	-
	Delta	1.5	-	-	-	-	-	-	-	-	-	-	-	-	-	0.74	-	-	0.75	-	-	-	-	-	-	-	-
	BA.1	1.1	2.4	-	1.4	-	1.0	0.53	-	-	-	0.84	-	0.91	1.8	-	-	1.6	0.75	-	1.3	-	0.99	1.5	1.0	0.85	1.4
	BA.1.1	1.1	2.4	0.61	1.4	-	1.0	0.53	-	-	-	0.84	-	0.91	1.8	-	-	1.6	0.75	-	1.3	-	0.99	1.5	1.0	0.85	1.4
	BA.2	0.91	2.4	-	-	2.5	1.0	0.53	1.1	0.57	0.65	0.84	-	0.91	-	-	-	1.6	0.75	-	1.3	-	0.99	-	1.0	0.85	1.4
	BA.4	0.97	2.4	-	-	2.5	1.0	0.53	1.1	0.57	0.65	0.84	-	0.91	-	0.74	-	1.6	0.75	-	1.3	1.4	-	-	1.0	0.85	1.4
	BA.2.12.1	1.1	2.4	-	-	2.5	1.0	0.53	1.1	0.57	0.65	0.84	-	0.91	-	-	1.2	1.6	0.75	-	1.3	-	0.99	-	1.0	0.85	1.4
	Imdevimab																												
	Alpha	0.52	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.0	-
	Beta	0.62	-	-	-	-	-	-	-	-	-	0.67	-	-	-	-	-	-	-	0.92	-	-	-	-	-	1.0	-
	Gamma	0.54	-	-	-	-	-	-	-	-	-	-	1.1	-	-	-	-	-	-	0.92	-	-	-	-	-	1.0	-
	Delta	2.2	-	-	-	-	-	-	-	-	-	-	-	-	-	2.1	-	-	1.3	-	-	-	-	-	-	-	-
	BA.1	600	1.2	-	22	-	4.5	3.9	-	-	-	0.67	-	92	390	-	-	1.2	1.3	-	1.6	-	1.7	3.9	2.6	1.0	0.49
	BA.1.1	1000	1.2	2.6	22	-	4.5	3.9	-	-	-	0.67	-	92	390	-	-	1.2	1.3	-	1.6	-	1.7	3.9	2.6	1.0	0.49
	BA.2	230	1.2	-	-	50	4.5	3.9	2.4	2.6	1.9	0.67	-	92	-	-	-	1.2	1.3	-	1.6	-	1.7	-	2.6	1.0	0.49
	BA.4	450	1.2	-	-	50	4.5	3.9	2.4	2.6	1.9	0.67	-	92	-	2.1	-	1.2	1.3	-	1.6	0.90	-	-	2.6	1.0	0.49
	BA.2.12.1	380	1.2	-	-	50	4.5	3.9	2.4	2.6	1.9	0.67	-	92	-	-	4.2	1.2	1.3	-	1.6	-	1.7	-	2.6	1.0	0.49
	Romlusevimab																												
	Alpha	0.32	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.9	-
	Beta	6.7	-	-	-	-	-	-	-	-	-	0.45	-	-	-	-	-	-	-	2.7	-	-	-	-	-	1.9	-
	Gamma	0.70	-	-	-	-	-	-	-	-	-	-	0.57	-	-	-	-	-	-	2.7	-	-	-	-	-	1.9	-
	Delta	n.d.	-	-	-	-	-	-	-	-	-	-	-	-	-	80	-	-	1.2	-	-	-	-	-	-	-	-
	BA.1	0.74	3.9	-	17	-	2.5	0.90	-	-	-	0.45	-	1.6	1.4	-	-	1.6	1.2	-	1.9	-	2.0	1.2	1.2	1.9	0.90
	BA.1.1	21	3.9	21	17	-	2.5	0.90	-	-	-	0.45	-	1.6	1.4	-	-	1.6	1.2	-	1.9	-	2.0	1.2	1.2	1.9	0.90
	BA.2	8.1	3.9	-	-	22	2.5	0.90	0.50	1.6	0.70	0.45	-	1.6	-	-	-	1.6	1.2	-	1.9	-	2.0	-	1.2	1.9	0.90
	BA.4	27	3.9	-	-	22	2.5	0.90	0.50	1.6	0.70	0.45	-	1.6	-	80	-	1.6	1.2	-	1.9	1.6	-	-	1.2	1.9	0.90
	BA.2.12.1	27	3.9	-	-	22	2.5	0.90	0.50	1.6	0.70	0.45	-	1.6	-	-	21	1.6	1.2	-	1.9	-	2.0	-	1.2	1.9	0.90
	Sotrovimab																												
	Alpha	1.8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.3	-
	Beta	1.0	-	-	-	-	-	-	-	-	-	0.94	-	-	-	-	-	-	-	0.43	-	-	-	-	-	1.3	-
	Gamma	0.79	-	-	-	-	-	-	-	-	-	-	0.70	-	-	-	-	-	-	0.43	-	-	-	-	-	1.3	-
	Delta	1.1	-	-	-	-	-	-	-	-	-	-	-	-	-	0.98	-	-	1.4	-	-	-	-	-	-	-	-
	BA.1	3.3	2.2	-	20	-	1.5	1.1	-	-	-	0.94	-	1.4	1.8	-	-	1.4	1.4	-	0.73	-	0.88	1.0	1.1	1.3	0.82
	BA.1.1	2.4	2.2	1.3	20	-	1.5	1.1	-	-	-	0.94	-	1.4	1.8	-	-	1.4	1.4	-	0.73	-	0.88	1.0	1.1	1.3	0.82
	BA.2	21	2.2	-	-	12	1.5	1.1	1.2	0.97	1.3	0.94	-	1.4	-	-	-	1.4	1.4	-	0.73	-	0.88	-	1.1	1.3	0.82
	BA.4	20	2.2	-	-	12	1.5	1.1	1.2	0.97	1.3	0.94	-	1.4	-	0.98	-	1.4	1.4	-	0.73	1.05	-	-	1.1	1.3	0.82
	BA.2.12.1	18	2.2	-	-	12	1.5	1.1	1.2	0.97	1.3	0.94	-	1.4	-	-	2.7	1.4	1.4	-	0.73	-	0.88	-	1.1	1.3	0.82



Supplementary Figure 3. Effect of single mutations on mAbs. Values show mean fold reduction of neutralisation. Fill colours depict the strength of resistance: Dark Red - strong (mFRN > 100), Red - moderate (mFRN 10-100), Light Red - mild (mFRN 3-10), White - no resistance (mFRN 1-3), Light Green (mFRN <1) - increased sensitivity. "-" mutation not present

in the variant. “n.d.” mutation present in variant but no neutralisation data available. All definitive VOC mutations at RBD positions are included. The RBD is defined as spike positions 331-524 (Tai et al., 2020).

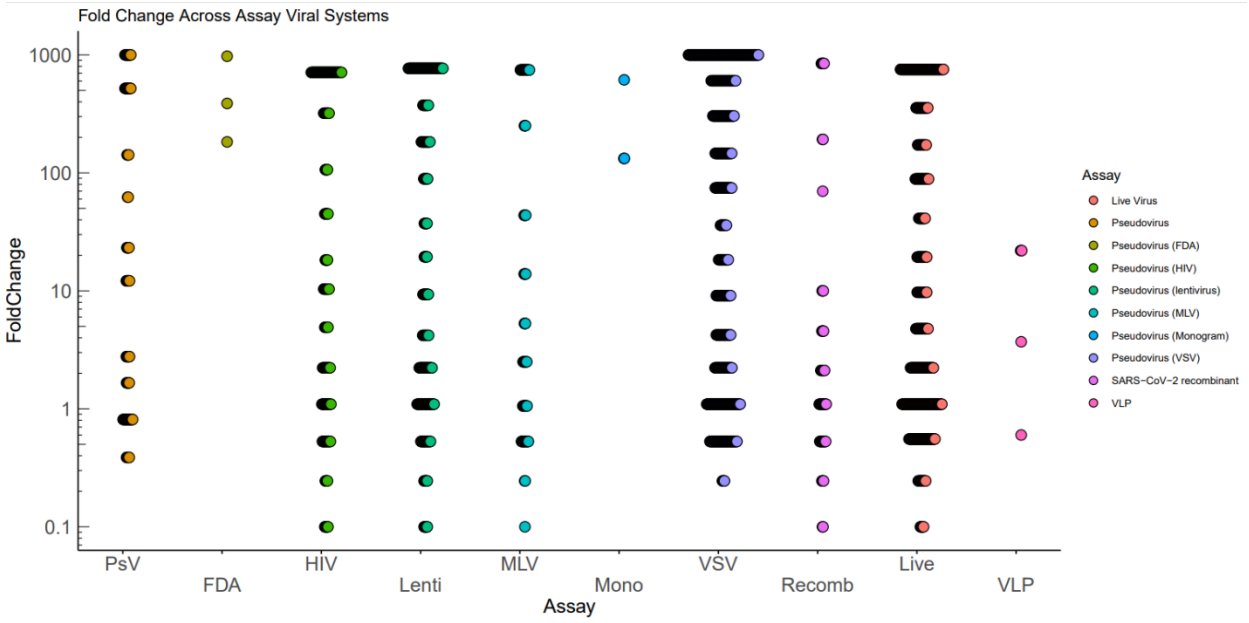
		Variant IC50 (ng/ml)								
	Antibody	Alpha	Beta	Delta	Gamma	BA.1	BA.2	BA.1.1	BA.4	BA.2.12.1
Class 1	Amubarvimab	18	14	42	13	3600	4300	4900	2600	3000
	Casirivimab	5.2	780	3.5	790	6800	6800	9900	9400	17000
	DXP-604	9.5	110	22	7.4	230	180	200	6300	200
	Etesevimab	200	8500	8.9	10000	9000	8500	10000	5500	8500
	Regdanvimab	3.9	95	67	53	8000	8200	10000	4000	NaN
	Tixagevimab	5.4	17	3.7	9.6	1800	2700	1500	7000	1800
Class 2	Bamlanivimab	5.9	9400	5000	8900	8500	8200	10000	5100	7200
	Cilgavimab	6.6	12	20	5.7	2000	20	12000	67	25
Class 3	Bebtelovimab	4.7	3.6	3.6	3.6	2.6	2.1	1.9	2	2.1
	Imdevimab	5.2	6.3	21	6.6	8500	1200	10000	3400	3800
	Romlusevimab	14	110	NaN	12	240	5000	10000	10000	10000
	Sotrovimab	94	64	95	31	290	1400	180	790	860
Cocktails	Amu + Rom	NaN	NaN	NaN	NaN	280	2800	4400	2400	1900
	Bam + Ete	9.4	4400	5.6	5000	8100	7400	10000	5500	6100
	Cas + Imd	1.5	7.5	3.1	6.6	6700	1600	10000	2900	2400
	Cil + Tix	5.4	14	3.5	4.5	270	37	810	180	59

<10 <100 <1000 >1000

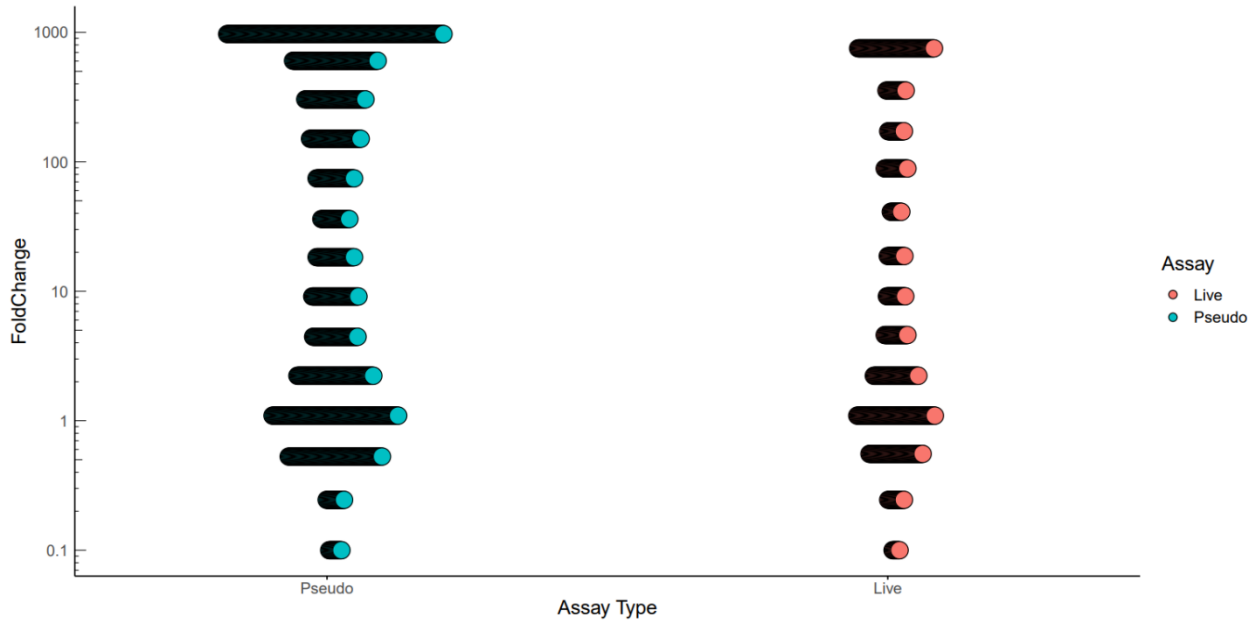
<10 <100 <1000 >1000

Supplementary Fig. 4. Geometric mean IC50 values for each mAb against VoCs. IC50 data were reported for 1358 assays out of the 1551 assays included in the analysis of fold change values.

A


Fold Change Across Assay Viral Systems
FoldChange
1000
100
10
1
0.1
PsV
FDA
HIV
Lenti
MLV
Mono
VSV
Recomb
Live
VLP
Assay
Assay
Live Virus
Pseudovirus
Pseudovirus (FDA)
Pseudovirus (HIV)
Pseudovirus (lentivirus)
Pseudovirus (MLV)
Pseudovirus (Monogram)
Pseudovirus (VSV)
SARS−CoV−2 recombinant
VLP

B


FoldChange
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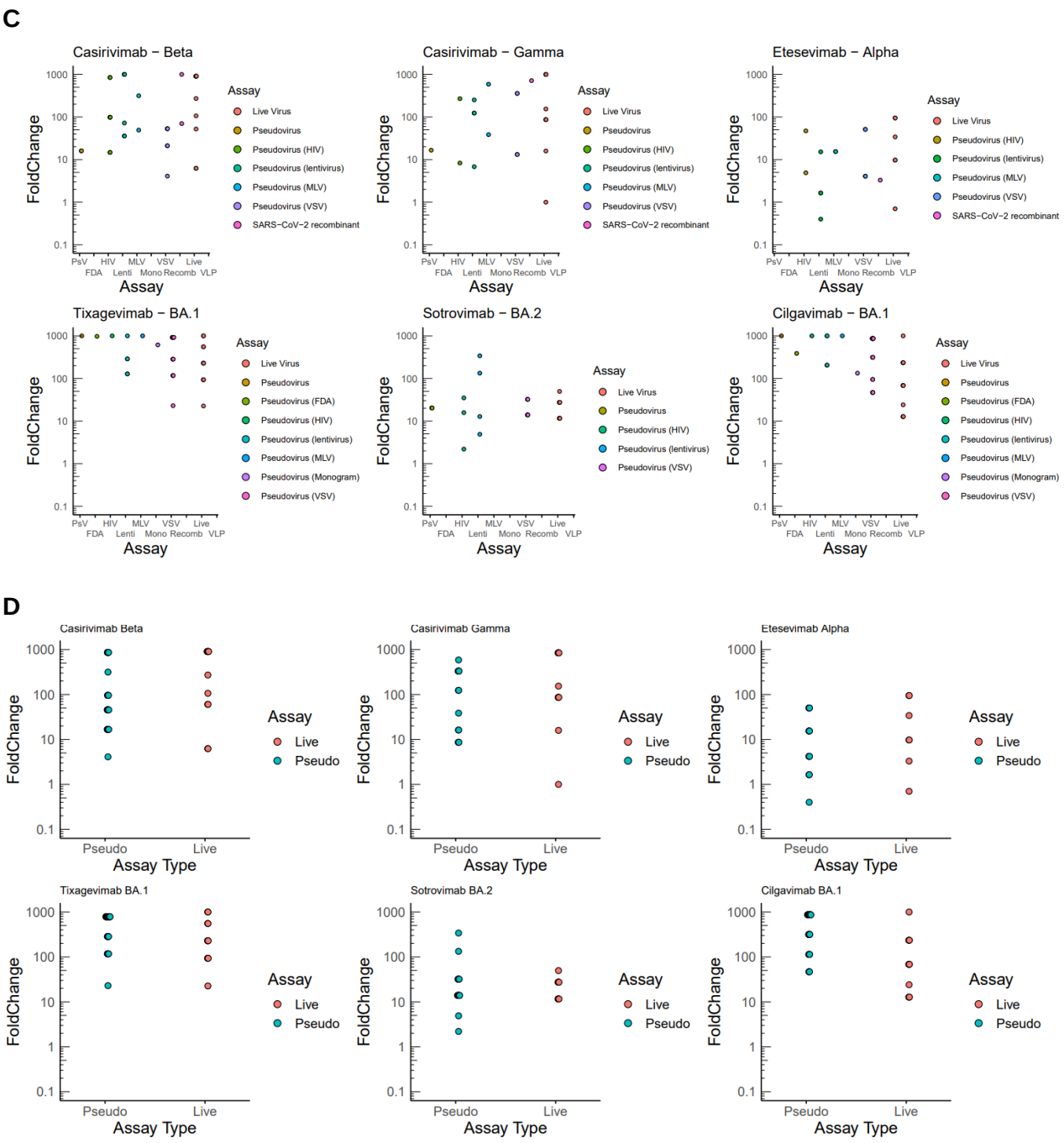
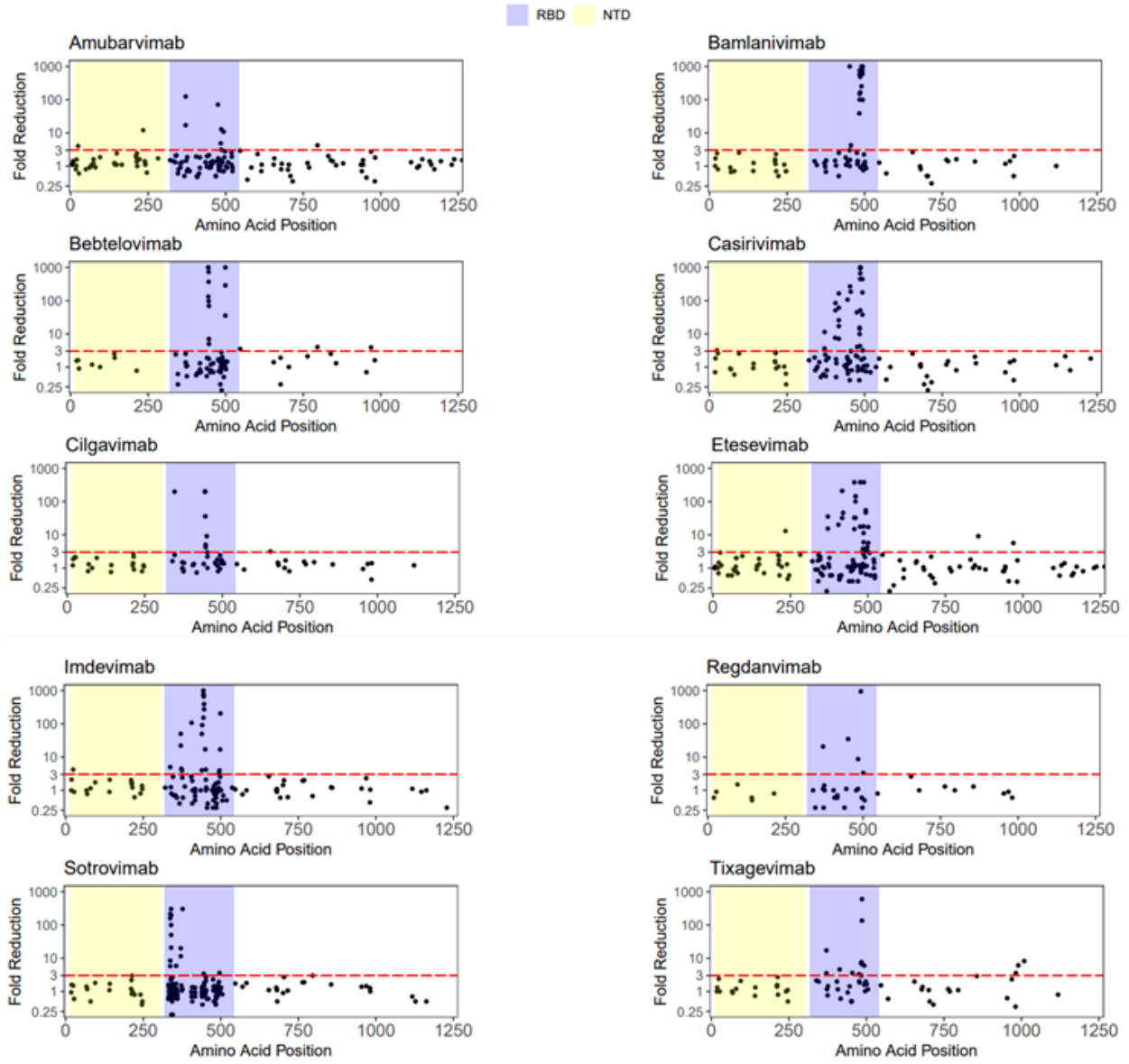
100
10
1
0.1
Pseudo
Live
Assay Type
Assay
Live
Pseudo



Supplementary Figure 5. FRN data from individual assays plotted against the viral system used in the assay. a) All FRN data for specific viral assay types b) All FRN data pooled into live virus or pseudovirus categories c) FRN data from the 6 mAb variant pairs with the most variable

FRN results for specific viral assay types. d) FRN data from the 6 mAb variant pairs with the most variable FRN results pooled into live virus or pseudovirus categories

A



B

mAb Class	Antibody	All Positions	Non Epitope	Epitope	Epitope +/- 1	RBD Non Epitope	RBD Epitope
1	Amubarvimab	1.3(211)	1.3(188)	2.1(23)	0.95(20)	1.4(81)	2.1(23)
	Casirivimab	3.4(290)	1.3(212)	46(78)	1.5(27)	1.5(122)	46(78)
	Etesevimab	2.5(339)	1.2(203)	7.7(136)	1.1(28)	1.3(86)	7.7(136)
	Regdanvimab	1.3(38)	1.0(28)	2.6(10)	n.d.	1.1(13)	2.6(10)
	Tixagevimab	1.8(142)	1.4(118)	6.9(24)	n.d.	1.5(60)	6.9(24)
2	Bamlanivimab	3.3(215)	1.2(171)	210(44)	1.5(2)	1.2(107)	210(44)
	Cilgavimab	1.6(155)	1.3(120)	3.7(35)	1.7(4)	1.2(64)	3.7(35)
3	Bebtelovimab	1.9(130)	1.1(92)	7.6(38)	1.5(2)	0.99(69)	7.6(38)
	Imdevimab	2.1(323)	1.3(283)	84(40)	1.4(16)	1.4(175)	84(40)
	Romlusevimab	1.6(97)	1.6(97)	n.d.	n.d.	2.2(48)	
	Sotrovimab	1.8(335)	1.1(223)	3.8(112)	0.94(21)	1.2(146)	3.8(112)

<1
<3
<10
<100
>100

Supplementary Fig 6. a) Single mutant mFRN data for each mAb. The dotted red line shows the mFRN = 3 threshold. Alternative substitutions at the same amino acid position are shown as separate points at the same x coordinate. Spike domains indicated by shading; Blue - RBD, Yellow - NTD; b) Pooled mFRN comparison between epitope, non-epitope mutations, epitope proximal, and RBD positions. "(#)" indicates the number of assays contributing to each geometric mean value. (*) epitope unknown for Romlusevimab.

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