

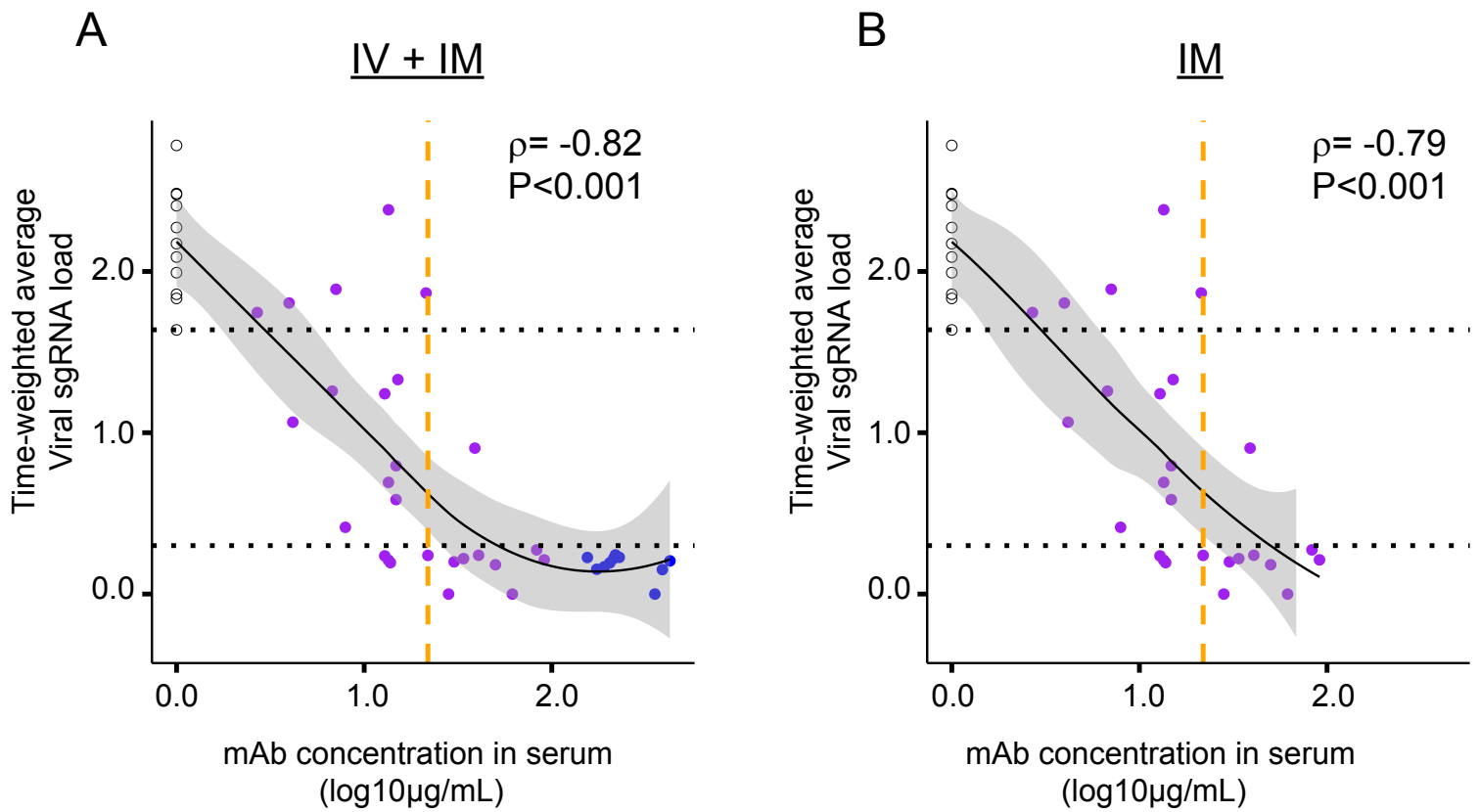
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Supplemental information

A combination of two human neutralizing antibodies prevents SARS-CoV-2 infection in cynomolgus macaques

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Figure S1



<u>Treatment</u>		<u>Threshold</u>
Blue – IV (Bottom) – TWA threshold for full protection	Cut-off for protective mAb concentration or titer in serum
Violet – IM (Top) – TWA threshold for partial protection	
Open – sham	

Figure S1. Correlation analysis between the change of sgRNA viral load in NP swabs and human antibody concentration in NHP serum. Related to **Figure 5**.

TWA values for the change of sgRNA viral load for IM and IV administration routes (**A**) or IM and administration route (**B**) were compared to antibody concentration in serum using Spearman's rank correlation analysis. Spearman's rank correlation coefficient (ρ) and P-values are indicated. The fitting curves were estimated using Lowess curve smoothing method and are shown in black, and grey shading indicates the confidence interval. Shapes indicate individual animals and colors indicate route of antibody treatment as detailed in the figure. Horizontal black dotted lines indicate designated TWA thresholds for full (bottom line) and partial (top line) protection. Vertical dotted orange dashed line in the graphs indicates designated estimated optimal cut-off for protective antibody concentration or titer in NHP serum as detailed in **Figure 5**.

Table S1. Measurements to determine thresholds for antibody-mediated protection against viral challenge in BAL or NP sites in NHP. Related to Figure 5.

Study	Treatment	NHP ID	Day 0 Ab concentration (log ₁₀ µg/mL)*	Day 0 Ab log ₁₀ NT50**	BAL			NP swab		
					Day 0-10 area under the curve (AUC) sgRNA level	Day 0-10 area under the curve (AUC) sgRNA level minus AUC of LOD***	Time-weighted average (TWA) viral sgRNA load	Day 0-10 area under the curve (AUC) sgRNA level	Day 0-10 area under the curve (AUC) sgRNA level minus AUC of LOD***	Time-weighted average (TWA) viral sgRNA load
2	Sham	V293	-2.00	1.30	22.1	5.10	0.51	39.72	22.70	2.27
		V294	-2.00	1.30	34.75	17.80	1.78	41.83	24.80	2.48
		V280	-2.00	1.30	25.75	8.80	0.88	35.58	18.60	1.86
		V284	-2.00	1.30	27.01	10.00	1.00	38.72	21.70	2.17
	3.9 mg/kg I.M.	V313	1.18	4.33	16.99	0.00	0.00	30.29	13.30	1.33
		V318	1.48	4.31	16.99	0.00	0.00	18.99	2.00	0.20
		V286	1.13	3.92	18.2	1.20	0.12	19.09	2.10	0.21
		V290	1.34	3.92	16.99	0.00	0.00	19.39	2.40	0.24
	11.7 mg/kg I.M.	V324	1.70	4.21	16.99	0.00	0.00	18.81	1.80	0.18
		V291	1.79	5.02	17.83	0.80	0.08	16.99	0.00	0.00
		V299	1.92	5.35	18.15	1.20	0.12	19.73	2.70	0.27
		V303	1.96	4.59	16.99	0.00	0.00	19.11	2.10	0.21
	31.3 mg/kg I.V.	V331	2.63	5.69	16.99	0.00	0.00	19.05	2.10	0.21
		V308	2.36	5.64	16.99	0.00	0.00	19.27	2.30	0.23
		V314	2.59	5.74	16.99	0.00	0.00	18.51	1.50	0.15
		V315	2.55	5.27	16.99	0.00	0.00	16.99	0.00	0.00
3	Sham	V298	-2.00	1.30	34.76	17.80	1.78	41.77	24.80	2.48
		V302	-2.00	1.30	27.36	10.40	1.04	35.32	18.30	1.83
		V319	-2.00	1.30	38.39	21.40	2.14	41.07	24.10	2.41
		V326	-2.00	1.30	31.51	14.50	1.45	44.81	27.80	2.78
	1.95 mg/kg I.M.	V306	1.17	3.50	18.37	1.40	0.14	24.95	8.0	0.80
		V307	1.33	4.0	16.99	0.00	0.00	35.66	18.70	1.87
		V296	1.45	4.30	18.83	1.80	0.18	16.99	0.00	0.00
	15.65 mg/kg I.V.	V309	2.33	4.60	18.53	1.50	0.15	19.2	2.20	0.22
		V311	2.24	4.40	17.99	1.00	0.10	18.53	1.50	0.15
		V300	2.34	4.70	18.93	1.90	0.19	19.42	2.40	0.24
	1.95 mg/kg I.M.	V316	1.11	2.50	16.99	0.00	0.00	19.36	2.40	0.24
		V301	1.13	2.60	24.89	7.90	0.79	40.82	23.80	2.38
		V304	1.17	2.30	18.96	2.00	0.20	22.85	5.90	0.59
	15.65 mg/kg I.V.	V317	2.19	3.80	16.99	0.00	0.00	19.26	2.30	0.23
		V310	2.31	3.80	18.68	1.70	0.17	18.93	1.90	0.19
		V312	2.28	3.40	18.65	1.70	0.17	18.68	1.70	0.17

4	Sham	GA94 5H	-2.00	1.30	27.37	10.40	1.04	33.37	16.40	1.64
		V320	-2.00	1.30	28.36	11.4	1.14	36.92	19.90	1.99
		V305	-2.00	1.30	32.52	15.50	1.55	37.89	20.90	2.09
	3.91 mg/kg I.M.	V328	1.59	3.86	21.56	4.60	0.46	26.04	9.10	0.91
		V289	1.53	3.82	18.85	1.90	0.19	19.19	2.20	0.22
		V295	1.61	4.30	21.2	4.20	0.42	19.4	2.40	0.24
	1.95 mg/kg I.M.	V281	1.13	3.75	20.27	3.30	0.33	23.92	6.90	0.69
		V321	1.11	4.03	22.67	5.70	0.57	29.41	12.40	1.24
		V288	1.14	3.96	20.72	3.70	0.37	18.94	2.00	0.20
	0.98 mg/kg I.M.	V329	0.85	3.31	16.99	0.00	0.00	35.89	18.90	1.89
		V330	0.90	2.90	18.24	1.30	0.13	21.13	4.10	0.41
		V285	0.83	3.01	21.02	4.00	0.40	29.58	12.60	1.26
	0.49 mg/kg I.M.	V323	0.43	2.58	23.46	6.50	0.65	34.45	17.50	1.75
		V327	0.60	3.40	20.59	3.60	0.36	35.04	18.10	1.81
		V282	0.62	3.01	21.12	4.10	0.41	27.65	10.70	1.07

* Indicates LOD of antibody concentration measurement in serum with the value that is equal to 10 ng/mL (designated to zero in **Figure 8A**); ** indicates LOD of antibody neutralizing titer measurement in serum with the value that is equal to $1.3\log_{10} NT_{50}$ (designated to zero in **Figure 8A**); ***AUC LOD value was estimated for the curve from day 0 to 10 with viral sgRNA load below the detection limit on each timepoint and was equal to 16.99.

Table S2. Estimated specificity, sensitivity, and cut-off values for protective mAb concentration or titer in NHP serum. Related to Figure 5.

Site	BAL			NP swap		
	Sensitivity	Specificity	Cut-off*	Sensitivity	Specificity	Cut-off*
Antibody concentration	0.85	0.90	1.17	0.86	0.96	1.34
Antibody neutralizing titer	0.76	0.81	3.8	0.91	0.84	3.8

* $\log_{10}\mu\text{g/mL}$ for mAb concentration and $\log_{10} \text{NT}_{50}$ for neutralizing titer measurements.