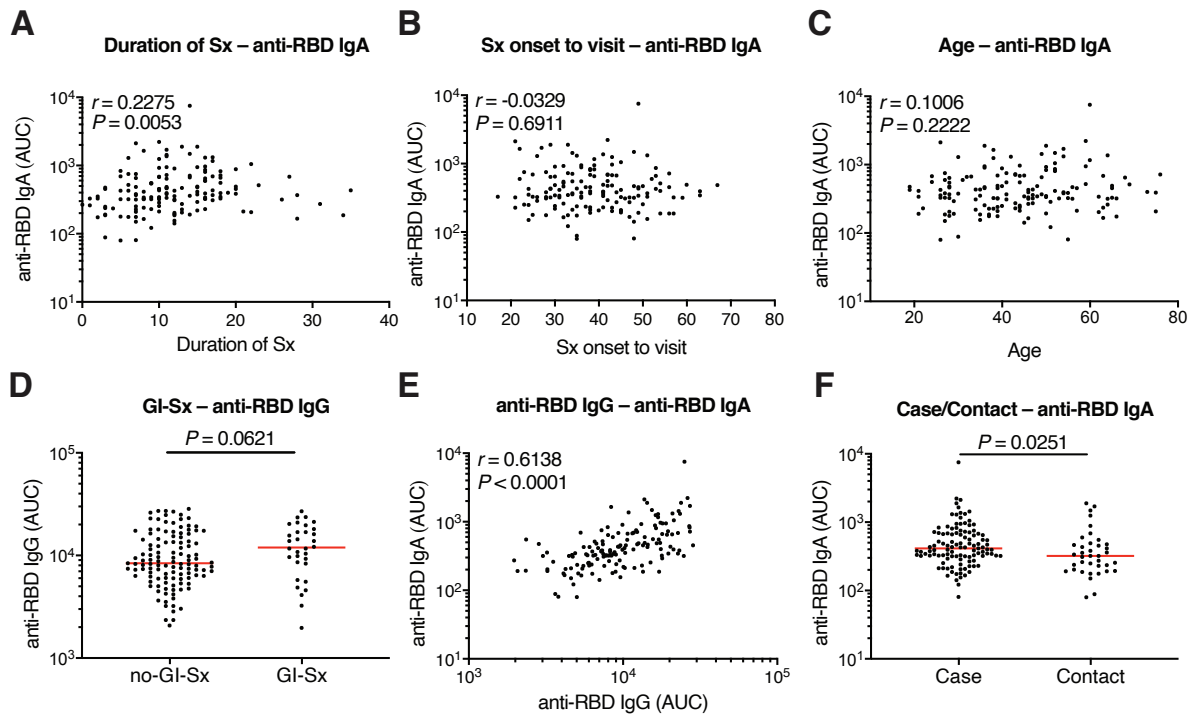
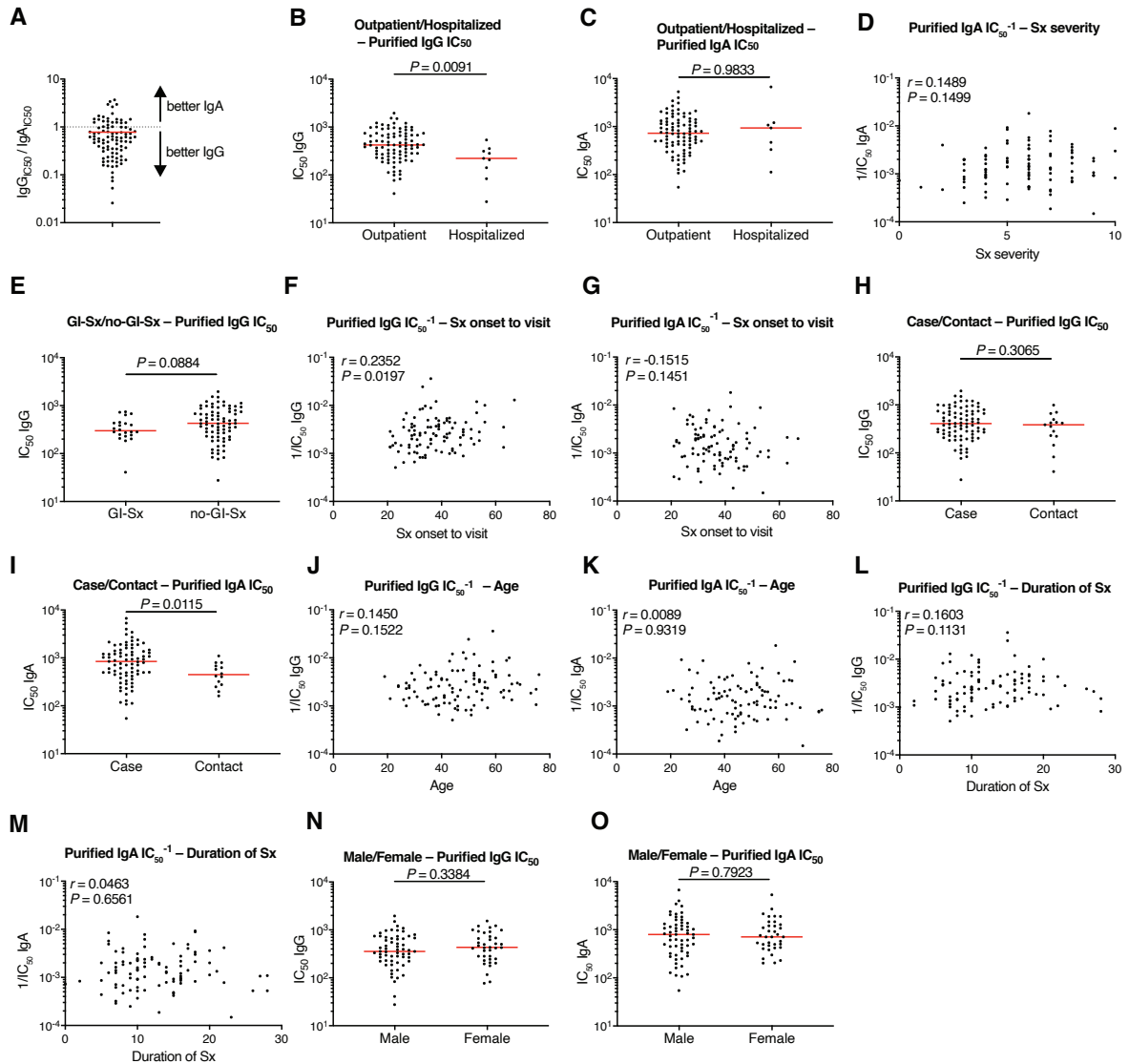


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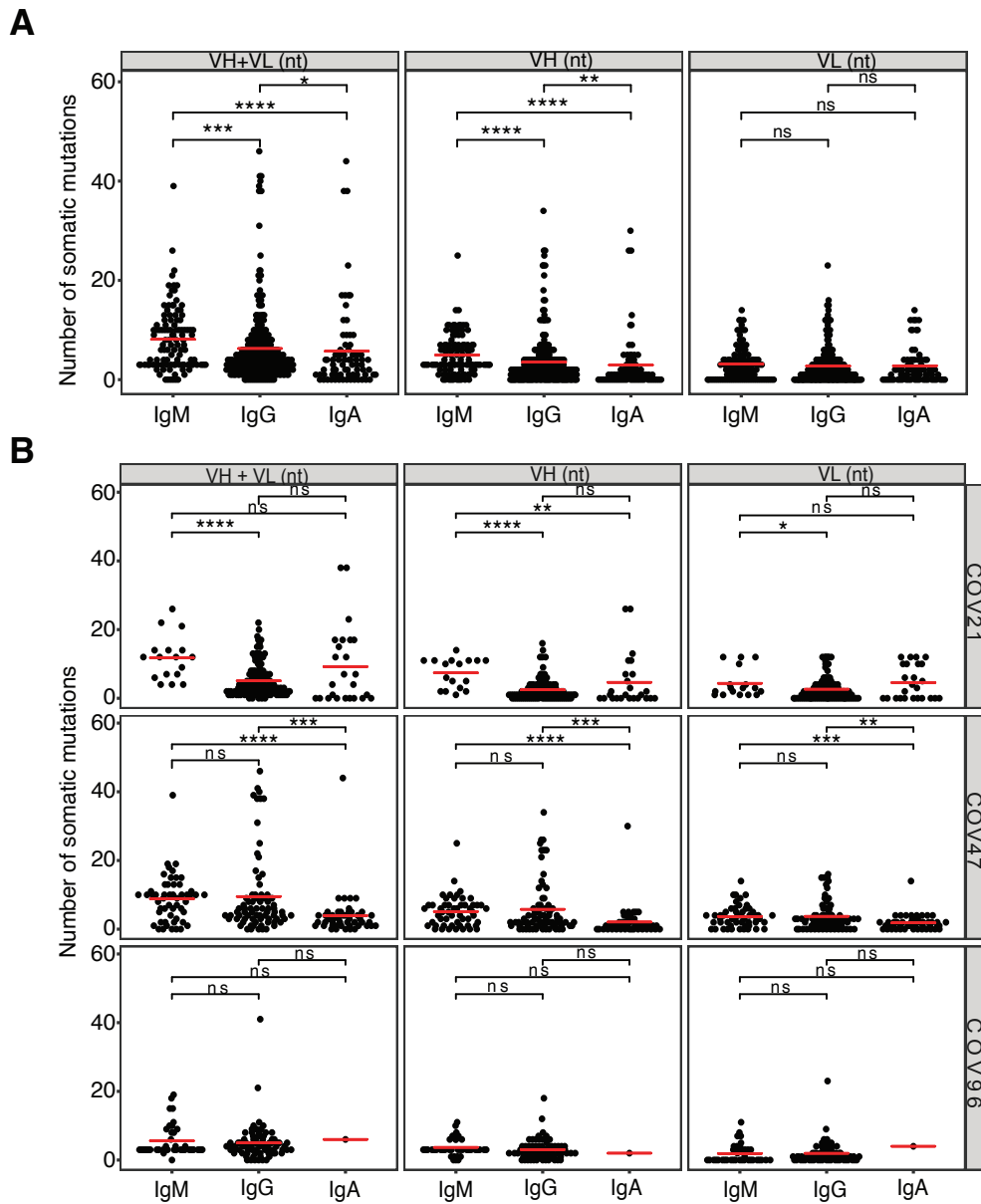
538 **Fig. S1 Clinical correlates of plasma IgA antibody titers** (A) Duration of Symptom (Sx) in days (X axis) plotted  
539 against normalized AUC for plasma IgA binding to RBD (Y axis).  $r = 0.2275$ ,  $P = 0.0053$ . (B) Sx onset to time of  
540 sample collection in days plotted against normalized AUC for plasma IgA anti-RBD.  $r = -0.0329$  and  $P = 0.6911$ .  
541 (C) Age plotted against normalized AUC for plasma IgA anti-RBD.  $r = 0.1006$ ,  $P = 0.2222$ . (D) Normalized AUC  
542 of plasma anti-RBD IgG ELISA for patients with gastrointestinal (GI) symptoms (n=32) and without GI symptoms  
543 (n=117);  $P = 0.0621$ . (E) Normalized AUC of plasma anti-RBD IgG ELISA plotted against normalized AUC for  
544 plasma IgA anti-RBD.  $r = 0.6138$ ,  $P < 0.0001$ . (F) Normalized AUC of plasma anti-RBD IgA ELISA for all cases (n  
545 = 111) and contacts (n = 38) in the cohort;  $P = 0.0251$ . For (A-C, E) the correlations were analyzed by two-tailed  
546 Spearman's tests; For (D and F), Horizontal bars indicate median values. Statistical significance was determined  
547 using two-tailed Mann-Whitney U-tests.



548

549 **Fig. S2 Clinical correlates of plasma IgA/IgG neutralization** (A) Ratio of pseudovirus neutralization IC<sub>50</sub> values  
 550 of purified IgG to IgA (n=95). (B, C) Purified plasma IgG (B) and IgA(C) pseudovirus neutralizing IC<sub>50</sub> values for  
 551 all outpatient (n = 90) and hospitalized (n = 9) participants in the cohort. (Fig. S2B,  $P = 0.0091$ ) and (Fig. S2C,  $P =$   
 552  $0.9833$ ). (D) Purified plasma IgA  $1/IC_{50}$  values plotted against symptom severity.  $r = 0.1489$ ,  $P=0.1499$ . (E) Purified  
 553 plasma IgG IC<sub>50</sub> values for patients with GI symptoms (n=22) and without GI symptoms (n=77);  $p=0.0884$ . (F, G)  
 554 Sx onset to time of sample collection in days plotted against purified plasma IgG (F) and IgA(G) pseudovirus  
 555 neutralization  $1/IC_{50}$  values. (Fig. S2F,  $r = 0.2352$ ,  $P = 0.0197$ ) and (Fig. S2G,  $r = -0.1515$ ,  $P = 0.1451$ ). (H, I)  
 556 Purified plasma IgG (H) and IgA(I) pseudovirus neutralization IC<sub>50</sub> values for all cases (n = 84) and contacts (n =  
 557 15) in the cohort. (Fig. S2H,  $P = 0.3065$ ) and (Fig. S2I,  $P = 0.0115$ ). (J, K) Age plotted against purified plasma IgG

558 (J) and IgA(K) pseudovirus neutralization  $1/IC_{50}$  values. (Fig. S2J,  $r = 0.1450$ ,  $P = 0.1522$ ) and (Fig. S2K,  $r =$   
559  $0.0089$ ,  $P = 0.9319$ ). (L, M) Duration of Symptom (Sx) in days (X axis) plotted against purified plasma IgG (L) and  
560 IgA(M) pseudovirus neutralization  $1/IC_{50}$  values. (Fig. S2L,  $r = 0.1603$ ,  $P = 0.1131$ ) and (Fig. S2M,  $r = 0.0463$ ,  $P =$   
561  $0.6561$ ). (N, O) Purified plasma IgG (N) and IgA(O) pseudovirus neutralization  $IC_{50}$  values for males ( $n=61$ ) and  
562 females ( $n=38$ ). (Fig. S2N,  $P=0.3384$ ) and (Fig.S2O,  $P=0.7923$ ). For (A), horizontal bars indicate mean value. For  
563 (B, C, E, H, I, N, O), horizontal bars indicate median values. Statistical significance was determined using two-tailed  
564 Mann–Whitney U-tests; For (D, F, G, J-M), the correlations were analyzed by two-tailed Spearman’s tests.  
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**Fig. S3 Analysis of antibody somatic hypermutation**

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(A) The number of somatic nucleotide mutations (Y axis) at the IGVH and IGVL for IgM, IgG and IgA antibodies

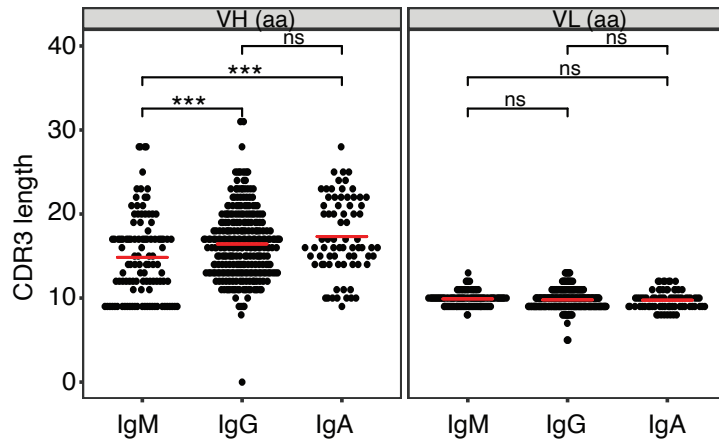
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(X axis), the horizontal bars indicate the mean. The number of antibody sequences was evaluated for both IGVH and

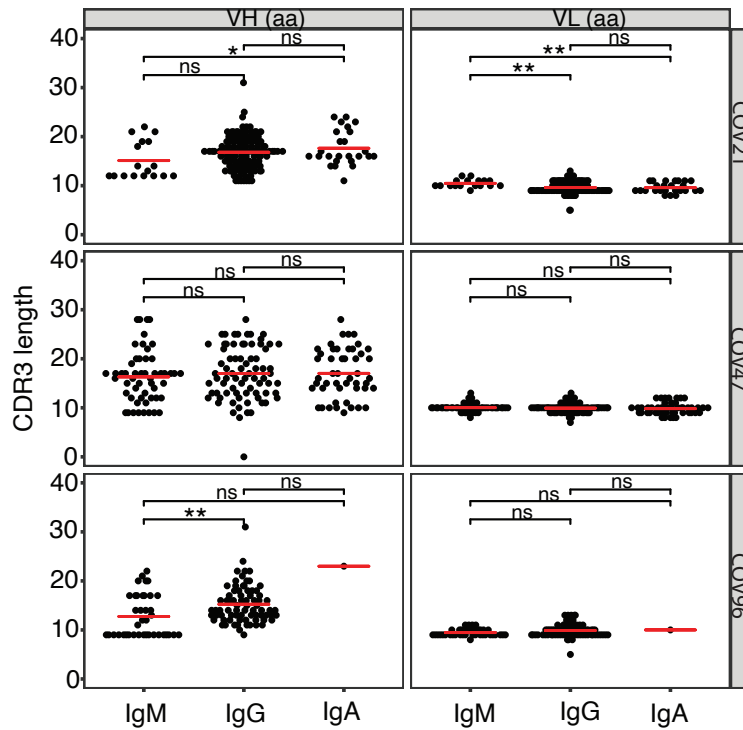
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IGVL. (n=455). (B) Same as (A) but for each individual.

**A**



**B**



571

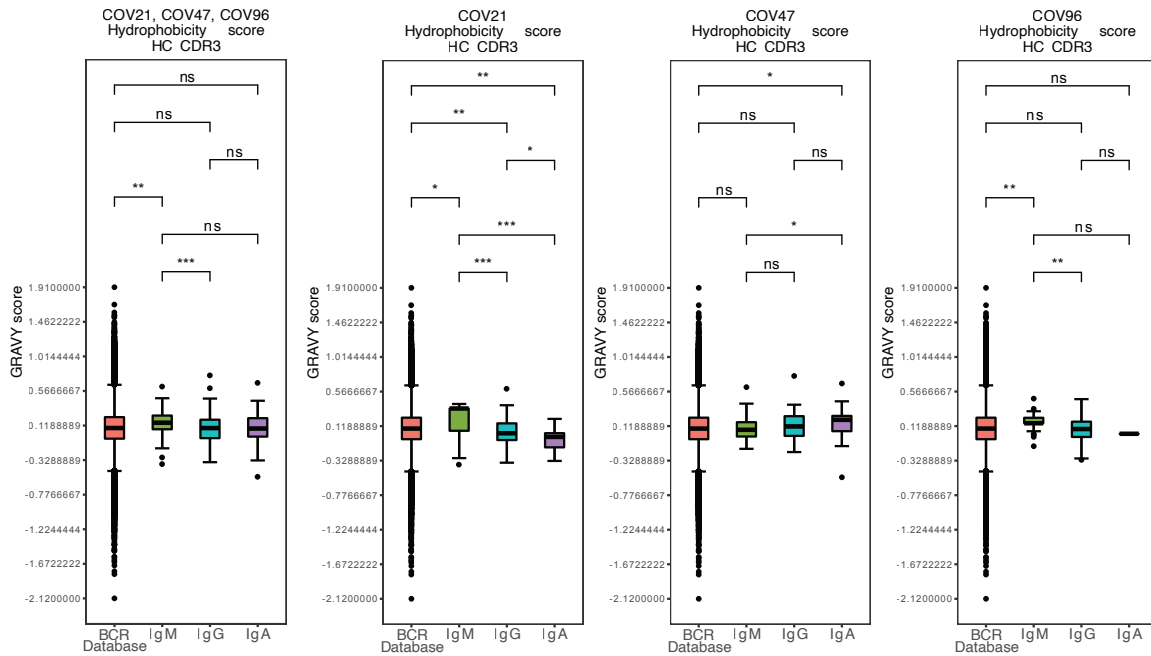
572 **Fig. S4 Analysis of antibody CDR3 length**

573 (A) IGHV and IGLV CDR3s length (Y axis) for IgM, IgG and IgA (X axis). (B) Same as (A) but for each

574 individual. The horizontal bars indicate the mean.

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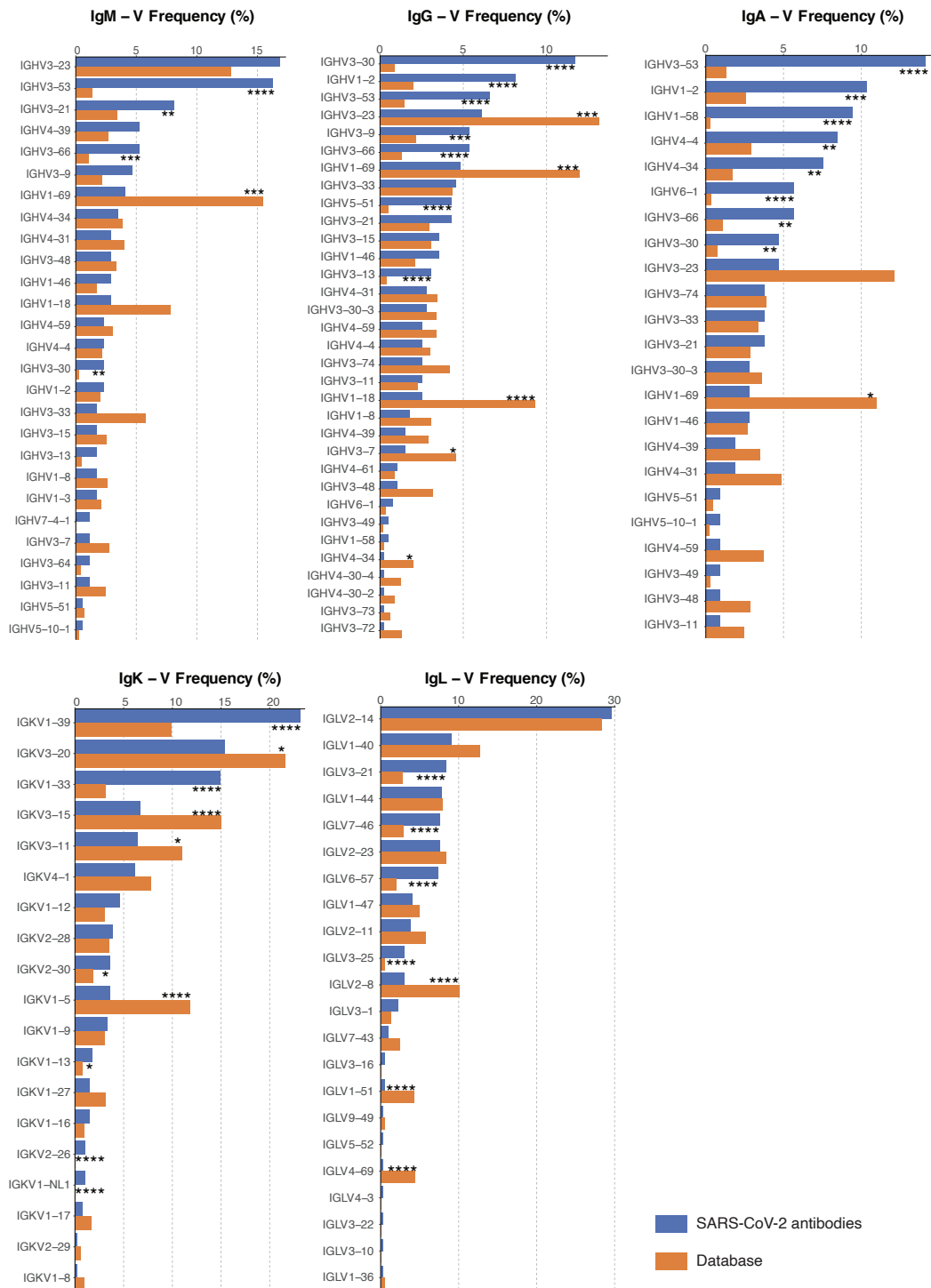


577

### 578 Fig. S5 Analysis of antibody CDR3 hydrophobicity

579 Distribution of the hydrophobicity GRAVY scores at the IGH CDR3 in antibody sequences from this study  
580 compared to a public database (see Methods for statistical analysis). The box limits are at the lower and upper  
581 quartiles, the center line indicates the median, the whiskers are 1.5x interquartile range and the dots represent  
582 outliers.

583



584

585 **Fig. S6 Frequency distributions of human V genes.**

586 Comparison of the frequency distributions of human V genes for heavy chain (IgM, IgG and IgA) and light chains

587 of anti-SARS-CoV-2 antibodies from this study and from a database of shared clonotypes of human B cell receptor

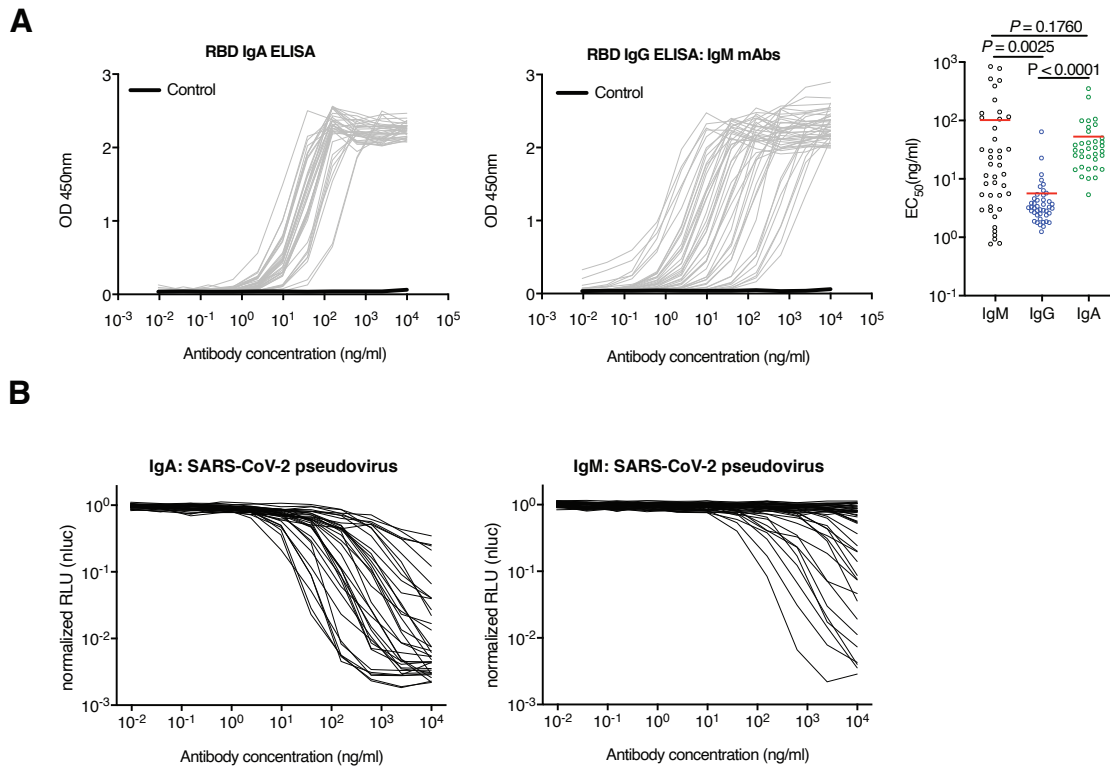
588 generated by Cinque Soto et al. (44). Statistical significance was determined using the two-sided binomial test.

589 Significant differences are denoted with stars.

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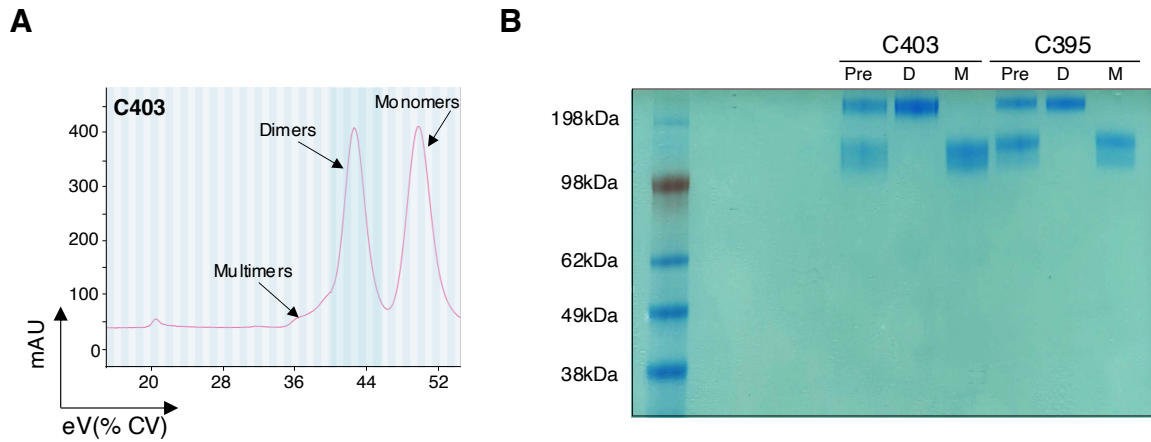


592

593 **Fig. S7 Binding and neutralizing activity of anti-SARS-CoV-2 RBD IgA and IgM monomers.**

594 (A) Binding profiles of 35 IgA and 46 IgM monoclonals against RBD. Comparisons of IgM, published IgG (11) and  
595 IgA  $EC_{50}$  values shown as in right panel. Red lines indicate mean value. (B) The normalized relative luminescence  
596 values for cell lysates of 293T<sub>ACE2</sub> cells 48 h after infection with SARS-CoV-2 pseudovirus in the presence of  
597 increasing concentrations of monoclonal IgA and IgM antibodies. Statistical analysis was performed using the  
598 student's *t* test.

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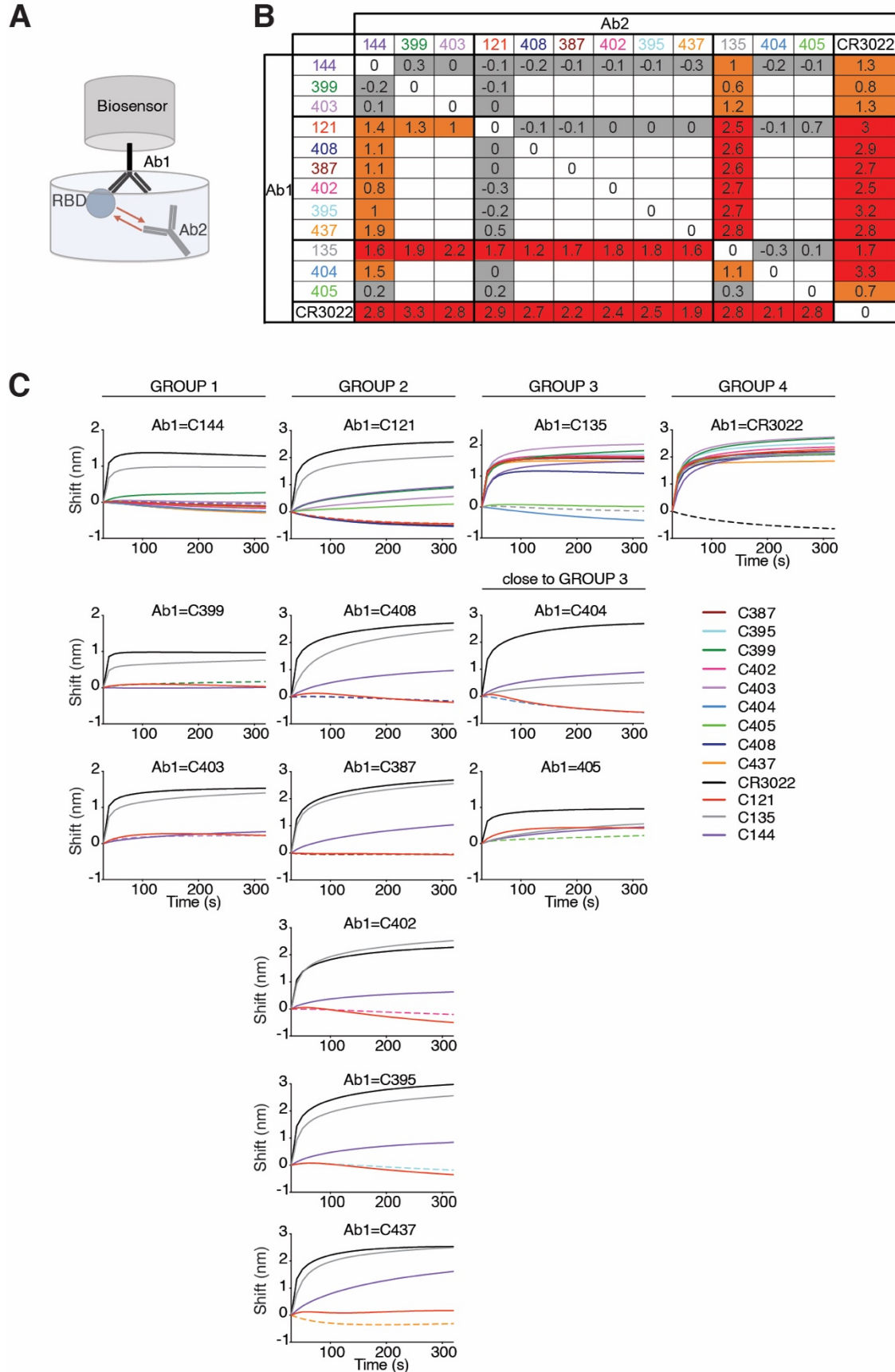
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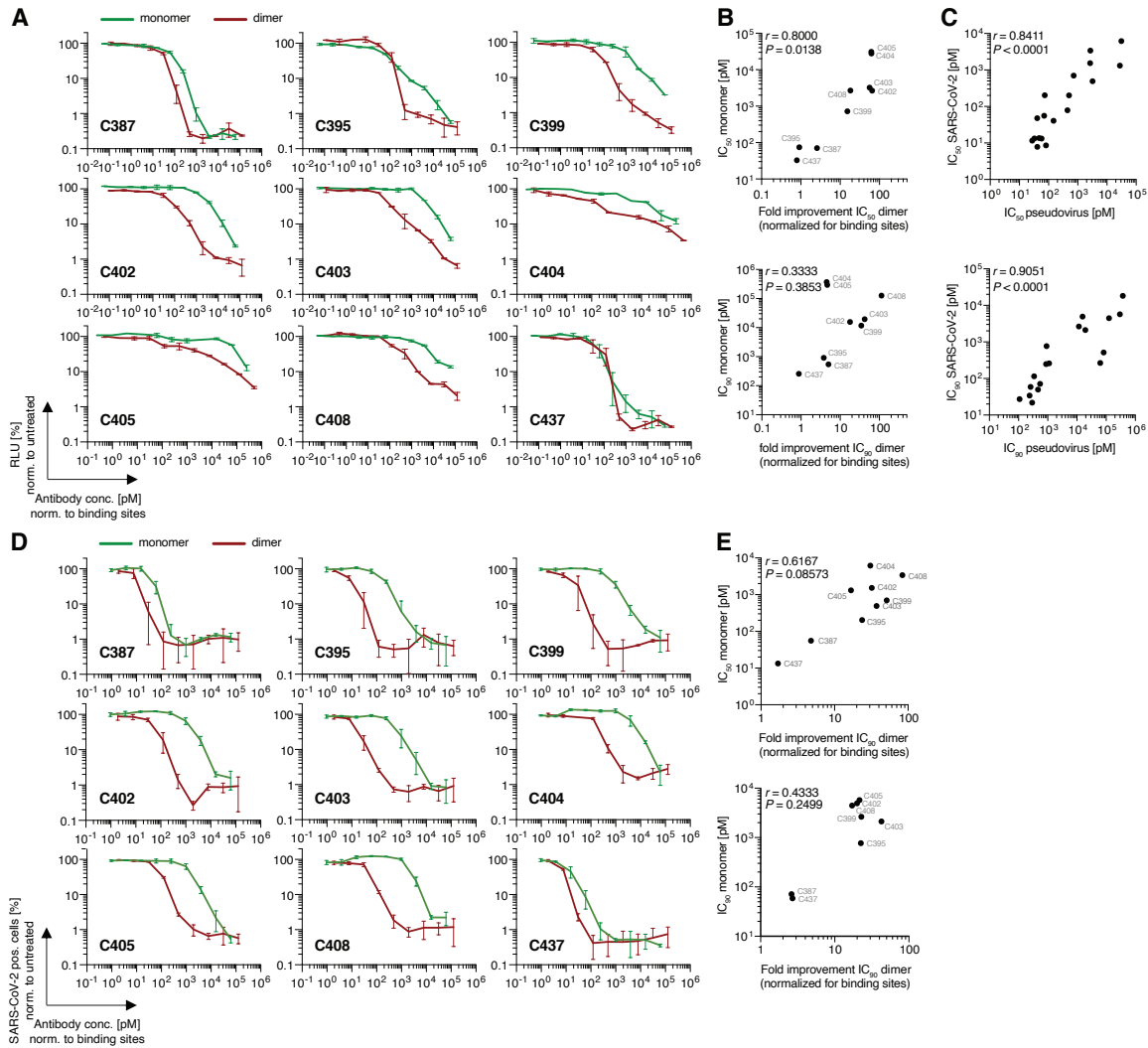
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**Fig. S8 Purification of Dimeric IgA by Size Exclusion Chromatography.** (A) Monomers and dimers of IgA1 or IgA2 were separated using a Superdex 200 (Cytiva) with PBS at a flow rate of 0.5 ml/min. Representative example: C403. The X axis is elution volume (eV) as a percent of Column volume. The Y axis is absorption at 280nm (mAU). (B) Coomassie Blue stained non-reducing SDS-PAGE gel of pre-separation antibody mixture (Pre), isolated dimers (D) and monomers (M).



608 **Fig. S9 Biolayer interferometry experiment.** (A) Diagrammatic representation of biolayer interferometry  
609 experiment. (B) The table displays the shift in nanometers after second antibody (Ab2) binding to the antigen in the  
610 presence of the first antibody (Ab1). Values are normalized by the subtraction of the autologous antibody control.  
611 (C) Second antibody (Ab2) binding to preformed first antibody (Ab1)–RBD complexes. Dotted line denotes when  
612 Ab1 and Ab2 are the same, and Ab2 is according to the colour-coding in Fig. 4B (right panel).  
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617 **Fig. S10 Neutralizing activity of monoclonal monomeric and dimeric IgAs**

618 (A) The normalized relative luminescence values for cell lysates of 293T<sub>ACE2</sub> cells 48 h after infection with SARS-  
619 CoV-2 pseudovirus in the presence of increasing concentrations of monoclonal antibodies C387, C395, C399, C402,  
620 C403, C404, C405, C408, C437 in their monomeric (green curves) and dimeric (red curves) form. (B) Fold  
621 improvement of the  $IC_{50}$  (upper panel) and  $IC_{90}$  (lower panel) values of dimeric IgA to monomeric IgA (X axis)  
622 plotted against  $IC_{50}$  ( $r = 0.8000$ ,  $P = 0.0138$ ),  $IC_{90}$  ( $r = 0.3333$ ,  $P = 0.3853$ ) values of monomeric IgAs. (C)  $IC_{50}$   
623 (upper panel) and  $IC_{90}$  (lower panel) values of dimeric and monomeric IgAs determined by pseudovirus  
624 neutralization assay (x axis) plotted against  $IC_{50}$  ( $r = 0.8411$ ,  $P < 0.0001$ ) and  $IC_{90}$  ( $r = 0.9051$ ,  $P < 0.0001$ ) values

625 determined by authentic SARS-CoV-2 neutralization assay (y axis). (D) SARS-CoV-2 neutralization assay. The  
 626 normalized percentage of SARS-CoV-2 positive VeroE6 cells 48 h after infection with SARS-CoV-2 authentic virus  
 627 in the presence of increasing concentrations of abovementioned antibodies in their dimeric and monomeric form. (E)  
 628 Fold improvement of the IC<sub>50</sub> (upper panel) and IC<sub>90</sub> (lower panel) values of dimeric IgA to monomeric IgA (X axis)  
 629 plotted against IC<sub>50</sub> ( $r = 0.6167$ ,  $P = 0.08573$ ), IC<sub>90</sub> ( $r = 0.4333$ ,  $P = 0.2499$ ) values of monomeric IgAs. Correlations  
 630 were analyzed by two-tailed Spearman's tests.

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634 **Table S1. Sequences of anti-SARS-CoV-2 antibodies**

635 Auxiliary Supplementary Material.

636

637 **Table S2. Sequences of antibodies from isotype shared clones**

638 Auxiliary Supplementary Material.

639

640 **Table S3. Inhibitory concentrations of monoclonal antibodies from isotype shared clones**

Patient ID	IgM	IC50(ng/ml)	IC90(ng/ml)	IgG	IC50(ng/ml)*	IC90(ng/ml)*	IgA	IC50(ng/ml)	IC90(ng/ml)
COV21	-			CG002	8.88	37.61	CA386	5.76	123.33
	-			CG005	60.49	205.20	CA387	9.68	129.87
COV47	-			CG144	6.91	29.66	CA394	13.06	371.86
	CM169	UD	UD	CG148	>1000	>1000	-		
	CM170	5806	37082	CG171	5250	17156	CA457	1721.6	298325.6
	-			CG379	126.98	2368.18	CA403	23.88	126.05
	CM381	UD	UD	CG160	>1000	>1000	-		
	CM349	844.59	26446.73	CG380	2.94	35.96	-		
	CM311	126.85	846.13	CG151	31.79	>1000	CA390	417.42	46597.44
COV96	CM194	UD	UD	CG382	42.92	122.33	-		
	CM365	1226.09	8268.46	CG202	>1000	>1000	-		

UD=Undetectable  
 \*(Robbiani et al. 2020)

641

642 **Table S4. Sequences of cloned recombinant antibodies**

643 Auxiliary Supplementary Material.

644

645 **Table S5. Effective and inhibitory concentrations of monoclonal antibodies**

646 Auxiliary Supplementary Material.

647

648 **Table S6. Inhibitory concentrations of monoclonal IgA monomers and dimers**

**Table S6. Inhibitory concentrations of monoclonal IgA monomers and dimers**

Antibody ID	SARS-CoV-2 pseudovirus				SARS-CoV-2			
	IC50 (pM)		IC90 (pM)		IC50 (pM)		IC90 (pM)	
	monomer	dimer	monomer	dimer	monomer	dimer	monomer	dimer
C387	70.68	27.46	543.91	108.06	55.74	11.64	71.46	27.37
C395	74.15	81.64	909.67	239.03	203.72	8.59	769.49	34.10
C399	722.84	47.48	11692.05	339.46	700.38	13.67	2636.98	114.74
C402	2652.52	40.86	15603.86	874.99	1536.24	47.90	4939.53	247.79
C403	3222.29	57.62	19499.80	461.45	491.11	13.18	2115.67	49.85
C404	31112.25	502.11	371134.20	82318.65	6182.08	201.78	18271.60	514.05
C405	27801.09	444.36	294918.48	62867.98	1312.88	78.57	5725.29	266.04
C408	2691.09	147.89	126130.74	1114.44	3392.62	40.51	4458.13	259.84
C437	32.67	41.18	258.08	292.35	13.32	7.84	58.85	21.82

*IC50/90 values for dimers were adjusted for number of binding sites*

649

650 **Table S7. Primers**

651 Auxiliary Supplementary Material.

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