

Supplemental Information

Longitudinal Isolation of Potent Near-Germline

SARS-CoV-2-Neutralizing Antibodies

from COVID-19 Patients

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Table S1: Clinical data of SARS-CoV-2-infected study patients, related to Figure 1 and Figure 2

Patient ID	Sex	Age	Symptoms	Radiological findings	Detection of viral RNA	Days from onset of symptoms to diagnosis	Days from diagnosis to blood draw 1	Days from diagnosis to blood draw 2	Days from diagnosis to blood draw 3	Days from diagnosis to last negative PCR
IDCnC2	M	54	dry cough, fever, arthralgia, hyposmia	N/A	NP swabs	3	17	N/A	N/A	23
IDFnC2	M	59	asymptomatic	no findings	NP swabs, stool	No Symptoms	8	N/A	N/A	9
IDHbnC1	F	52	dry cough, fever	N/A	NP swabs	2	35	N/A	N/A	19
IDHbnC2	F	44	dry cough, fever, arthralgia, hyposmia	N/A	NP swabs	2	36	N/A	N/A	18
IDHbnC3	F	38	asymptomatic	N/A	NP swabs	N/A	35	N/A	N/A	17
IDHbnC4	F	50	dry cough, fever, dyspnea	N/A	NP swabs	N/A	36	N/A	N/A	16
IDHbnC5	M	56	dry cough, fever, dyspnea, hyposmia, ageusia, hepatitis, diarrhea	N/A	NP swabs	2	36	N/A	N/A	26
IDFnC1	F	45	dry cough, rash, pharyngitis, otitis	no findings	NP swabs, stool	13	8	36	63	8
IDMnC1 (#10)*	M	58	dry cough, fever, hyposmia, ageusia	interstitial pneumonia of the left lower lobe	NP swabs, sputum, stool	2	9	16	36	26
IDMnC2 (#3)*	M	28	dry cough, fever, sinusitis, dysosmia, ageusia, athralgia	N/A	NP swabs, sputum, stool	3	15	42	69	19
IDMnC4 (#14)*	F	49	dry cough, fever, diarrhea	N/A	NP swabs, sputum, stool	2	14	34	61	12
IDMnC5 (#7)*	M	52	dry cough, fever, hyposmia, hypogeusia, dyspnea	bipulmonal, interstitial pneumonia, minimal pleural effusion	NP swabs, sputum, stool	4	19	39	66	23

*Clinical data partially taken from Wölfel R (2020) Virological assessment of hospitalized patients with COVID-2019. Nature; ID in brackets corresponds to ID in this reference.

M, F : male, female

N/A : not available

NP : nasopharyngeal

Table S2: Poly-IgG of SARS-CoV-2-infected study patients, related to Figure 1 and 2

poly-IgG		Binding data ¹		Neutralization
Name	Time point	SARS-CoV-2 (spike protein)		
		EC ₅₀ (µg/mL)	Commercial ELISA*	IC ₁₀₀ (µg/mL)
IDCnC2	1	15,65	0,75	187,50
IDFnC1	1	106,44	0,16	n.n.
	2	92,19	0,27	1500,00
	3	100,81	0,26	1500,00
IDFnC2	1	76,37	0,17	n.n.
IDHnC1	1	96,14	0,27	1500,00
IDHnC2	1	58,05	0,20	891,91
IDHnC3	1	14,82	1,84	157,67
IDHnC4	1	61,14	<0,15	n.n.
IDHnC5	1	3,10	5,75	78,83
IDMnC1	1	129,18	<0,15	n.n.
	2	61,94	0,16	n.n.
	3	41,74	0,33	891,91
IDMnC2	1	41,47	0,43	750,00
	2	36,56	0,73	530,33
	3	45,60	0,60	445,95
IDMnC3	1	47,48	0,30	891,91
IDMnC4	1	5,97	3,87	265,17
	2	8,29	3,90	111,49
	3	10,83	3,03	157,67
IDMnC5	1	1,54	7,75	78,83
	2	2,04	6,77	78,80
	3	4,10	5,01	78,83

1) Signal intensity of an OD ≥ 0.25 (not shown) and EC₅₀ below 30 µg/mL was defined as binding

* Euroimmun IgG detection kit

n.n. not neutralizing (IC₁₀₀ > 1500 µg/mL)

N/A not available

Table S3: B cell analysis summary, related to Figure 1, Figure 2, and Figure 3

Patient ID	% IgG+ B cells [†]	% bait positive [†]	Isolated B cells	Productive heavy chains	% clonal	Total clones	Median clone size	Largest clone size	Cloned mAbs	S-binding mAbs	Neutralizing mAbs
IDCnC2	10.63 ± 0.12	0.67 ± 0.16	210	181	34	23	2	7	51	15	6
IDFnC2	10.42 ± 1.1	0.04 ± 0.06	176	119	43	12	2	29	14	1	0
IDHbnC1	6.74 ± 0.41	0.23 ± 0.06	311	280	30	36	2	7	24	1	0
IDHbnC2	11.87 ± 0.5	0.21 ± 0.07	213	178	33	24	2	7	12	1	1
IDHbnC3	5.98 ± 0.13	1.02 ± 0.11	372	324	20	27	2	10	15	5	5
IDHbnC4	9.46 ± 0.22	0.25 ± 0.03	223	144	42	27	2	13	14	5	1
IDHbnC5	15.83 ± 0.5	0.22 ± 0.02	246	208	45	38	2	6	6	3	0
IDFnC1 [‡]	17.1 ± 0.82	0.05 ± 0.03	652	562	47	95	2	23	39	6	3
IDMnC1 (#10) ^{*‡}	6.06 ± 1.24	0.27 ± 0.16	245	199	34	20	2	22	19	6	1
IDMnC2 (#3) ^{*‡}	10.75 ± 0.69	0.07 ± 0.07	732	570	22	49	2	13	30	10	3
IDMnC4 (#14) ^{*‡}	7.12 ± 0.65	0.52 ± 0.15	348	297	51	40	2	18	19	15	7
IDMnC5 (#7) ^{*‡}	7.32 ± 0.72	0.44 ± 0.28	585	513	21	50	2	5	12	11	1
mean	9.94 ± 3.66	0.33 ± 0.29	359	298	35	37	2	13	21	7	2
sum	-	-	4313	3575	-	441	-	-	255	79	28

* ID in brackets corresponds to IDs in Wölfel R (2020) Virological assessment of hospitalized patients with COVID-2019. Nature.

† % IgG+ and bait positive cells show mean ± SD over all sorted plates

‡ For longitudinal data % IgG and % bait positives are given as mean values and clonal analysis was performed over all time points. See to Figure 2 for time-resolved analyses.

Table S4: Isolated SARS-CoV-2-interacting antibodies, related to Figure 3 and 4

Antibody							Binding data ¹					Epitope			HEp2 autoreactivity	Neutralization IC ₁₀₀ (µg/mL)
Name	Clone #	Number of clonal members	VH-gene	VH-gene germline identity (% nt)	VL-gene	VL-gene germline identity (% nt)	SARS-CoV-2 (spike protein)			EBOVΔTM	HIV gp140	RBD ³	S1 ⁴	Monomeric ⁵		
							EC ₅₀ (µg/mL)	K _D (nM) ²	Commercial ELISA*	EC ₅₀	EC ₅₀	EC ₅₀	EC ₅₀	EC ₅₀	EC ₅₀	
CnC2t1p1_A2	C2_5	4	IGHV1-46	99.7	IGKV3-20	100	0.03	N/A	2.40	-	-	+	++	++	N/A	n.n.
CnC2t1p1_A6	C2_17	2	IGHV3-30	99.3	IGKV3-11	100	3.90	N/A	N/A	-	-	-	-	++	N/A	N/A
CnC2t1p1_B10	C2_8	2	IGHV1-69	100	IGKV3-11	100	0.32	8.10	N/A	-	-	+++	++	+	-	12.50
CnC2t1p1_B4	C2_2	2	IGHV1-18	100	IGLV2-23	100	0.03	80	7.57	-	-	+++	+++	+++	-	0.78
CnC2t1p1_D6	C2_23	2	IGHV3-49	100	IGKV2-28	99.7	0.03	37	9.26	-	-	+++	+	+++	-	3.72
CnC2t1p1_E11	single	-	IGHV3-30	100	IGLV2-14	99.3	5.20	N/A	<0.15	-	-	-	-	-	N/A	n.n.
CnC2t1p1_E12	C2_23	2	IGHV3-49	99.7	IGKV2-28	100	0.03	38	9.03	-	-	+++	+++	+++	-	3.13
CnC2t1p1_E7	C2_5	4	IGHV1-46	100	IGKV3-20	99	0.04	N/A	N/A	-	-	-	++	+	N/A	n.n.
CnC2t1p1_E8	C2_3	6	IGHV1-2	91.5	IGLV2-23	95.6	0.13	3.20	6.88	-	-	+++	+	+++	-	4.42
CnC2t1p1_F5	single	-	IGHV3-30	99	IGLV5-45	99.7	0.05	N/A	N/A	-	-	+	+	+	++	N/A
CnC2t1p1_G6	C2_3	6	IGHV1-2	90.1	IGLV2-23	94.6	0.31	7.30	4.72	-	-	+++	+	++	-	12.50
CnC2t1p2_E4	C2_11	3	IGHV3-15	100	IGKV3-20	100	0.26	N/A	<0.15	-	-	-	-	-	N/A	n.n.
CnC2t1p2_F12	C2_10	2	IGHV3-15	100	IGKV3-20	100	0.06	N/A	<0.15	-	-	-	-	-	N/A	n.n.
CnC2t1p2_F4	C2_15	3	IGHV3-30	96.3	IGKV6-21	97.9	3.04	N/A	<0.15	-	-	-	-	-	N/A	n.n.
CnC2t1p2_G4	C2_11	3	IGHV3-15	100	IGKV3-20	100	0.25	N/A	<0.15	-	-	-	+++	-	N/A	n.n.
FnC1t1p1_B6	F1_77	11	IGHV3-53	93.8	IGLV2-8	98.6	0.96	N/A	<0.15	-	-	+++	++	+	N/A	n.n.
FnC1t1p1_C11	F1_76	4	IGHV3-53	93.8	IGLV2-8	99.7	2.91	N/A	<0.15	+	+	+	+	+	-	n.n.
FnC1t1p2_A5	single	-	IGHV1-8	100	IGKV3-20	100	1.36	N/A	<0.15	+	++	-	-	-	++	16.00
FnC1t2p1_A12	F1_89	2	IGHV4-4	97.9	IGLV2-14	97.6	2.81	N/A	<0.15	+	+	-	-	+	+	n.n.
FnC1t2p1_D4	F1_95	2	IGHV7-4-1	96.6	IGKV1-33	99	0.02	0.20	9.00	-	-	+++	+++	+++	-	0.28
FnC1t2p1_G5	F1_95	2	IGHV7-4-1	96.6	IGKV1-33	99	0.02	0.10	9.00	-	-	+++	+++	+++	-	0.33
FnC2t1p1_B1	F2_12	3	IGHV4-34	92.2	IGLV1-44	92.7	0.78	N/A	<0.15	-	-	++	++	+	N/A	n.n.
HbnC1t1p3_H8	H1_6	2	IGHV3-21	100	IGKV1-5	99.6	0.08	N/A	<0.15	-	-	-	+++	+++	N/A	n.n.
HbnC2t1p2_D9	H2_20	2	IGHV3-33	98.6	IGKV3-11	99	0.04	72	N/A	-	-	++	++	++	-	0.93
HbnC3t1p1_C6	H3_3	2	IGHV1-58	99.7	IGKV3-20	99.7	0.06	0.19	9.00	-	-	+++	+++	+++	-	0.04
HbnC3t1p1_F4	H3_10	10	IGHV3-30	93.2	IGKV1-5	96.1	0.04	0.26	8.78	-	-	++	+++	++	+	0.78
HbnC3t1p1_G4	single	-	IGHV3-66	99.7	IGKV3-20	98.3	0.02	1.50	N/A	-	-	+++	+++	+++	++	0.12
HbnC3t1p2_B10	single	-	IGHV3-66	99	IGKV3-20	97.9	0.22	1.00	9.00	-	-	+++	+++	+++	-	0.25
HbnC3t1p2_C6	H3_3	2	IGHV1-58	98.3	IGKV3-20	99.7	0.04	16	10.00	-	-	+++	+++	+++	-	0.33
HbnC4t1p1_A1	H4_5	9	IGHV3-23	100	IGKV1-33	100	0.12	N/A	2.98	-	-	+++	+++	+++	N/A	n.n.
HbnC4t1p1_A6	H4_23	2	IGHV3-30-3	98	IGKV4-1	98.4	3.36	N/A	<0.15	-	-	-	-	+	N/A	N/A
HbnC4t1p1_C11	H4_5	9	IGHV3-23	100	IGKV1-33	100	0.25	N/A	8.04	-	-	+++	+++	+++	N/A	n.n.
HbnC4t1p1_D5	H4_27	4	IGHV3-9	99.7	IGKV1-39	98.2	0.25	153	<0.15	++	+++	++	++	+	-	10.51
HbnC4t1p1_G2	single	-	IGHV3-30	98.3	IGKV1-39	99.7	0.09	N/A	<0.15	-	-	-	-	+++	N/A	N/A
HbnC5t1p1_B6	H5_2	6	IGHV1-46	87.6	IGKV2-24	97.0	0.07	N/A	9.86	-	-	-	+++	+++	N/A	N/A
HbnC5t1p1_C11	H5_4	2	IGHV1-46	93.9	IGKV2-24	96.4	0.46	N/A	N/A	-	-	-	-	+	N/A	N/A
HbnC5t1p1_D4	H5_26	2	IGHV3-53	98.6	IGKV1-9	100	0.04	N/A	<0.15	-	-	-	-	+++	N/A	n.n.
MnC1t2p1_A5	M1_19	22	IGHV3-49	89.3	IGKV4-1	96.4	0.03	N/A	<0.15	-	-	+++	-	+++	N/A	N/A
MnC1t2p1_B11	M1_19	22	IGHV3-49	93.3	IGKV4-1	97.7	0.03	N/A	<0.15	-	-	-	-	+++	N/A	n.n.
MnC1t3p1_B7	M1_19	22	IGHV3-49	90.1	IGKV4-1	94.7	0.04	N/A	N/A	-	-	N/A	N/A	N/A	N/A	N/A

1) Signal intensity of an OD ≥0.25 (not shown) and EC₅₀ below 30 µg/mL was defined as binding

2) Interaction with the receptor-binding domain

3) Receptor-binding domain

4) Truncated S1 subunit

5) Interaction with a non-trimerized spike protein

* Euroimmun IgG detection kit

+ EC₅₀ >1 µg/µl

++ 0.1 µg/µL < EC₅₀ ≤1 µg/µL

+++ EC₅₀ ≤0.1 µg/µL

n.n. not neutralizing (IC₁₀₀ >100 µg/mL)

nt. nucleotide

N/A not available

Table S4 (continued): Isolated SARS-CoV-2-interacting antibodies, related to Figure 3 and Figure 4

Antibody							Binding data ¹					Epitope			HEp2 autoreactivity	Neutralization IC ₁₀₀ (µg/mL)
Name	Clone #	Number of clonal members	VH-gene	VH-gene germline identity (% nt)	VL-gene	VL-gene germline identity (% nt)	SARS-CoV-2 (spike protein)			EBOVΔTM	HIV gp140	RBD ³	S1 ⁴	Monomeric ⁵		
							EC ₅₀ (µg/mL)	K _D (nM) ²	Commercial ELISA*	EC ₅₀	EC ₅₀	EC ₅₀	EC ₅₀	EC ₅₀		
MnC1t3p1_E3	M1_19	22	IGHV3-49	93.9	IGKV4-1	98.7	0.03	N/A	N/A	-	-	-	-	+++	N/A	N/A
MnC1t3p1_F3	single	-	IGHV3-30	97.3	IGLV2-23	98.3	2.82	N/A	N/A	+	+	-	-	+++	-	N/A
MnC1t3p1_G9	M1_2	3	IGHV3-23	94.5	IGLV7-46	97.6	0.33	34	5.42	-	-	+++	+++	+++	++	8.84
MnC2t1p1_A12	single	-	IGHV1-2	99.7	IGLV2-14	99	4.03	N/A	<0.15	-	+	-	-	+	-	n.n.
MnC2t1p1_A3	M2_25	3	IGHV3-66	99	IGKV1D-12	100	0.05	0.70	6.44	-	-	+++	+++	+++	-	0.78
MnC2t1p1_C1	single	-	IGHV3-21	99.7	IGKV3-15	99	0.18	N/A	<0.15	++	-	-	++	+++	-	n.n.
MnC2t1p1_C12	single	-	IGHV4-31	97.3	IGKV3-20	96.8	0.02	N/A	<0.15	-	-	-	-	+++	N/A	n.n.
MnC2t1p1_C5	M2_25	3	IGHV3-66	100	IGKV1D-12	100	0.07	N/A	5.85	-	-	+++	+++	+++	-	3.72
MnC2t2p1_C11	single	-	IGHV1-69	98.6	IGKV1-39	98.9	0.02	0.02	6.79	-	-	+++	+++	+++	-	0.25
MnC2t2p1_D7	M2_29	3	IGHV3-7	95.9	IGLV2-8	98.3	1.41	N/A	<0.15	+	+	-	-	-	N/A	n.n.
MnC2t2p1_E1	single	-	IGHV4-61	98.3	IGKV1-9	98.6	0.50	N/A	<0.15	-	-	-	-	+	N/A	n.n.
MnC2t2p1_E4	M2_42	3	IGHV4-4	95.9	IGLV2-14	95.9	0.70	N/A	<0.15	-	-	-	-	++	N/A	n.n.
MnC2t2p1_G7	M2_33	2	IGHV3-73	91.4	IGLV2-14	93.8	4.48	N/A	<0.15	+	+	-	-	-	-	n.n.
MnC4t1p1_A10	M4_27	18	IGHV4-39	94.6	IGKV1-17	96.8	0.07	520	4.87	-	-	+++	+++	+++	-	42.04
MnC4t1p1_A11	M4_22	5	IGHV3-48	96.9	IGKV3-20	97.9	0.05	2000	4.52	-	-	+++	+++	+++	-	100.00
MnC4t1p1_A6	M4_25	15	IGHV3-9	95.3	IGKV1-12	97.5	0.07	N/A	10.24	-	-	+++	+++	+++	N/A	n.n.
MnC4t1p1_A7	M4_38	7	IGHV4-61	93.6	IGKV1-39	92.3	2.81	N/A	<0.15	-	-	-	-	-	N/A	N/A
MnC4t2p1_A8	M4_40	3	IGHV7-4-1	96.6	IGKV3-20	96.8	1.60	N/A	0.24	-	-	+++	++	++	N/A	n.n.
MnC4t2p1_B3	M4_25	15	IGHV3-9	94.6	IGKV1-12	96.8	0.06	0.09	N/A	-	-	+++	+++	+++	-	0.66
MnC4t2p1_C5	M4_3	7	IGHV1-2	95.9	IGLV2-8	98.6	0.79	N/A	<0.15	++	++	+	+	+	-	n.n.
MnC4t2p1_D1	single	-	IGHV1-69	99	IGKV1-5	98.9	3.86	N/A	<0.15	+	+	-	-	++	-	n.n.
MnC4t2p1_D10	M4_27	18	IGHV4-39	94.6	IGKV1-17	96.8	0.18	440	5.30	-	-	+++	+++	+++	-	21.02
MnC4t2p1_E6	M4_25	15	IGHV3-9	95.3	IGKV1-12	97.5	0.03	40	8.08	-	-	+++	+++	+++	-	50.00
MnC4t2p1_F5	M4_27	18	IGHV4-39	94.6	IGKV1-17	96.8	0.07	89	5.19	-	-	+++	+++	+++	-	100.00
MnC4t2p1_F8	M4_25	15	IGHV3-9	95.3	IGKV1-12	97.5	0.03	N/A	10.08	-	-	+++	+++	+++	N/A	n.n.
MnC4t2p1_G3	M4_40	3	IGHV7-4-1	95.2	IGKV3-20	95.8	0.03	N/A	7.60	-	-	+++	+++	+++	N/A	n.n.
MnC4t2p2_A4	M4_39	5	IGHV7-4-1	96.6	IGKV3-20	95.8	0.02	14	10.17	-	-	+++	+++	+++	-	21.02
MnC4t2p2_A7	M4_35	2	IGHV4-59	95.6	IGKV4-1	98.0	0.11	N/A	<0.15	-	-	-	-	++	N/A	N/A
MnC5t1p1_C12	single	-	IGHV3-30	99.3	IGKV1-9	99.7	1.40	N/A	<0.15	-	-	-	-	+++	N/A	n.n.
MnC5t1p1_C4	M5_30	2	IGHV3-30-3	99.3	IGKV3-20	99.3	1.31	N/A	<0.15	-	-	-	-	+++	N/A	n.n.
MnC5t1p1_C6	single	-	IGHV3-30-3	99.7	IGKV3-20	100	4.23	N/A	<0.15	+	-	-	-	++	-	n.n.
MnC5t1p1_C7	single	-	IGHV3-30-3	99	IGKV1-5	99.6	4.62	N/A	<0.15	-	-	-	-	-	N/A	n.n.
MnC5t2p1_B5	single	-	IGHV3-30-3	97.6	IGKV3-20	99.3	3.69	N/A	<0.15	-	-	-	-	+++	N/A	n.n.
MnC5t2p1_C2	single	-	IGHV3-30-3	100	IGLV4-69	100	4.17	N/A	<0.15	-	-	-	-	-	N/A	n.n.
MnC5t2p1_C5	single	-	IGHV3-30-3	100	IGKV4-1	100	3.76	N/A	<0.15	-	-	-	-	++	N/A	n.n.
MnC5t2p1_E12	single	-	IGHV3-30-3	97.6	IGKV6-21	99.3	3.87	N/A	<0.15	-	-	-	-	+++	N/A	n.n.
MnC5t2p1_E9	M5_1	4	IGHV1-18	85.3	IGKV3-15	97.6	3.01	N/A	<0.15	+	-	-	-	++	-	n.n.
MnC5t2p1_G1	M5_4	2	IGHV1-58	98.6	IGKV3-20	99	0.03	17	10.48	-	-	+++	+++	+++	-	2.63
MnC5t2p1_G6	M5_1	4	IGHV1-18	87.7	IGKV3-15	96.2	3.71	N/A	<0.15	-	-	-	-	++	N/A	n.n.

1) Signal intensity of an OD ≥0.25 (not shown) and EC₅₀ below 30 µg/mL was defined as binding

2) Interaction with the receptor-binding domain

3) Receptor-binding domain

4) TruncatedS1 subunit

5) Interaction with a non-trimerized spike protein

* Euroimmun IgG detection kit

+ EC₅₀ >1 µg/µl

++ 0.1 µg/µL < EC₅₀ ≤1 µg/µL

+++ EC₅₀ ≤0.1 µg/µL

n.n. not neutralizing (IC₁₀₀ >100 µg/mL)

nt. nucleotide

N/A not available

Table S5: Healthy individuals, related to Figure 2 and Figure 5

Patient ID	Sex	Age	Date of blood draw
75	F	47	27.12.16
76	F	51	27.12.16
84	M	47	28.12.16
85	M	23	28.12.16
86	M	47	28.12.16
90	F	25	02.01.17
91	M	55	02.01.17
92	F	54	02.01.17
93	M	34	02.01.17
94	M	31	02.01.17
95	M	19	03.01.17
96	M	55	03.01.17
97	F	22	03.01.17
98	M	34	03.01.17
99	M	51	03.01.17
100	M	46	03.01.17
101	M	46	04.01.17
102	M	31	04.01.17
103	M	25	04.01.17
104	M	21	04.01.17
105	M	20	04.01.17
106	F	48	04.01.17
117	F	24	10.01.17
118	M	30	10.01.17
119	F	28	10.01.17
120	M	21	10.01.17
121	F	21	10.01.17
126	F	24	11.01.17
127	M	42	11.01.17
128	F	67	11.01.17
130	M	37	12.01.17
131	F	67	12.01.17
132	M	39	12.01.17
133	M	35	12.01.17
134	M	36	12.01.17
135	F	22	18.01.17
136	F	20	18.01.17
137	F	21	18.01.17
138	F	26	18.01.17
139	F	36	18.01.17
140	M	23	18.01.17
141	M	21	24.01.17
145	F	21	24.01.17
146	F	21	24.01.17
147	F	50	01.02.17
148	F	24	01.02.17
151	F	49	14.02.17
176	F	20	09.10.17

M, F : male, female