

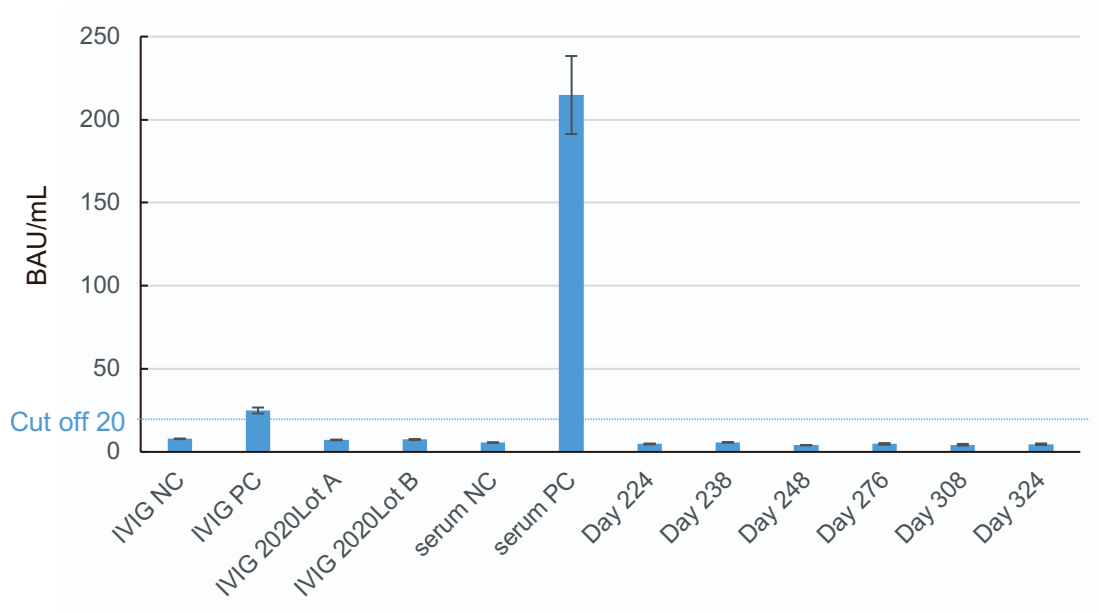
**Supplemental information**

**COVID-19 relapse associated with SARS-CoV-2**

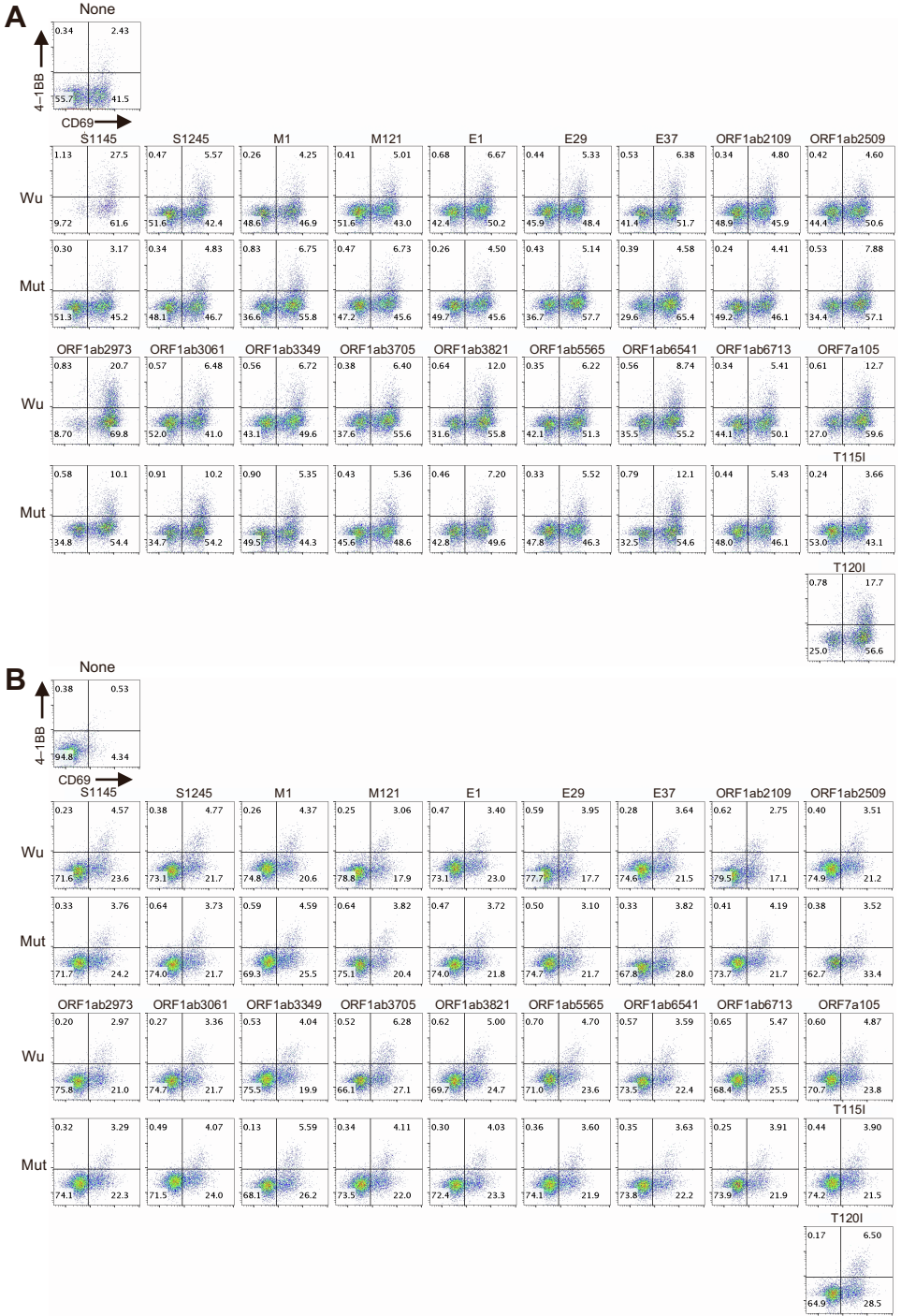
**evasion from CD4<sup>+</sup> T-cell recognition**

**in an agammaglobulinemia patient**

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**Figure S1. The anti-SARS-CoV-2 spike (S) protein in the patient plasma (related to Figure 1).** Binding antibody titers against the SARS-CoV-2 S protein in the patient plasma and intravenous immunoglobulin (IVIG) lots administered to the patient during the study. BAU, binding antibody unit; NC, negative control; PC, positive control. Values over 20 BAU/mL were considered positive. Error bars indicate mean  $\pm$  SD of triplicate measurements.



**Figure S2. Responses of CD4<sup>+</sup> and CD8<sup>+</sup> T cells to the Wuhan and mutant peptides of SARS-CoV-2 (related to Figure 3).**

PBMCs collected from the donor on day 308 were stimulated with 19 pooled Wuhan peptides that covered the mutations detected in the donor for 13 days. CD4<sup>+</sup> and CD8<sup>+</sup> T cells were then sorted separately and re-stimulated with nothing (None), individual Wuhan peptides (Wu), or corresponding mutant peptides (Mut) in the presence of autologous monocyte-derived dendritic cells for 20 h. CD69<sup>+</sup>4-1BB<sup>+</sup> populations within the CD4<sup>+</sup> T-cell gate (A) and CD69<sup>+</sup>4-1BB<sup>+</sup> populations within the CD8<sup>+</sup> T-cell gate (B) are shown.

**Table S1. HLA type, lymphocyte subsets, and activity of neutrophils and natural killer cells in the patient (related to Figure 1 and Figure 5).**

Lymphocyte subset	% lymphocytes	Activity of neutrophils, and natural killer cells	%	
	Day 276		Day 276	Day 790
CD3	92.6	Neutrophil phagocytosis function	44.9	40.8
CD4	39.2			
CD8	46.1	Neutrophil sterilizing function	99.8	99.9
CD13	0.5			
CD19	0.0	Natural killer cell activity	33.1	47.4
<b>HLA type</b>				
	<b>Allele 1</b>	<b>Allele 2</b>		
<b>A</b>	11:01:01	31:01:02		
<b>B</b>	15:01:01	48:01:01		
<b>C</b>	04:01:01	–		
<b>DRB1</b>	04:06:01	09:01:02		
<b>DRB345</b>	01:03:01	–		
<b>DQA1</b>	03:01:01	–		
<b>DQB1</b>	03:02:01	03:03:02		
<b>DPA1</b>	02:02:02	–		
<b>DPB1</b>	05:01:01	–		

**Table S2. Results of the multiplex PCR testing of sputum samples for 19 respiratory tract infections (BioFire® FilmArray Respiratory Panel 2.1) (related to Figure 1).**

<b>Viruses and Bacteria</b>	<b>Result</b>
<b>Adenovirus</b>	not detected
<b>Coronavirus 229E</b>	not detected
<b>Coronavirus HKU1</b>	not detected
<b>Coronavirus NL63</b>	not detected
<b>Coronavirus OC43</b>	not detected
<b>SARS-CoV-2</b>	detected
<b>Human Metapneumovirus</b>	not detected
<b>Human Rhinovirus/Enterovirus</b>	not detected
<b>Influenza A</b>	not detected
<b>Influenza B</b>	not detected
<b>Parainfluenza Virus 1</b>	not detected
<b>Parainfluenza Virus 2</b>	not detected
<b>Parainfluenza Virus 3</b>	not detected
<b>Parainfluenza Virus 4</b>	not detected
<b>Respiratory Syncytial Virus</b>	not detected
<b><i>Bordetella parapertussis</i> (IS1001)</b>	not detected
<b><i>Bordetella pertussis</i> (ptxP)</b>	not detected
<b><i>Chlamydia pneumoniae</i></b>	not detected
<b><i>Mycoplasma pneumoniae</i></b>	not detected

**Table S3. Data from the blood test results obtained during the observation period, particularly data related to the severity of COVID-19 (related to Figure 1).**

Days since first PCR(+)	0	1	3	7	21	35	63	92	140	175	181	209	216	224	230	235
WBC( $\mu$ L)	8,680	8,620	6,830	6,790	9,050	8,580	7,360	10,740	9,420	9,340	8,850	9,930	9,530	8,090	9,090	8,170
Lymph ( $\mu$ L)	930	1,030	1,340	2,170	1,340	1,170	1,320	1,180	890	650	1,120	960	1,040	1,150	1,140	1,450
Hb (g/dL)	14.7	14.0	14.3	15.5	14.9	13.9	13.9	13.0	12.5	12.9	13.4	13.4	13.2	12.6	12.4	
Plt ( $\mu$ L)	127,000	151,000	170,000	198,000	130,000	131,000	128,000	165,000	197,000	171,000	185,000	219,000	195,000	173,000	208,000	154,000
Alb (g/dL)	..	3.6	3.5	4.0	4.1	3.5	..	3.8	..	3.4	3.7	3.9	3.9	3.9	3.7	3.4
ALT (IU/L)	20	17	14	27	22	25	25	35	18	13	14	16	18	14	15	11
LDH (IU/L)	157	155	126	138	149	145	147	152	177	138	137	145	159	160	159	149
CK (IU/L)	30	32	23	24	30	25	28	24	21	19	20	22	22	23	23	18
Cre (mg/dL)	0.55	0.56	0.58	0.65	0.58	0.61	0.62	0.49	0.47	0.42	0.47	0.50	0.48	0.50	0.52	0.54
Troponin (pg/mL)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	<0.003	..
PT (s)	..	11.2	11.4	11.1	11.4	10.9	..	..	..	12.1	..	..	11.6	11.4	..	12.0
D-dimer ( $\mu$ g/mL)	..	0.6	0.6	0.5	0.5	..	..	..	..	..	..	..	..	..	<0.5	..
CRP (mg/dL)	2.37	1.95	1.77	1.55	2.71	3.06	4.15	3.61	3.38	5.06	3.69	3.67	4.85	5.08	4.73	7.01
Ferritin ( $\mu$ g/L)	135	251	258	247	141	319	346	..	254	221	208	183	164	163	156	..
IL-6 (pg/mL)	..	..	..	..	..	..	..	..	..	..	..	21.9	21.5	18.9	17.3	..
Procalcitonin (ng/mL)	..	0.06	..	..	..	..	..	..	..	0.06	..	..	..	0.03	..	0.06
KL-6 (IU/mL)	..	185	188	225	236	..	..	..	..	430	..	..	..	522	..	..
IgG (mg/dL) <sup>a</sup>	964	2,183	..	..	1,137	1,349	1,192	..	954	1,695	1,425	1,478	1,248	978	1,899	..

Days since first PCR(+)	237	238	239	240	241	242	243	244	246	248	252	258	265	276	308	336
WBC( $\mu$ L)	8,720	7,400	6,420	3,940	2,860	3,800	5,010	5,430	6,670	6,560	13,580	9,300	7,680	9,180	5,650	4,990
Lymph ( $\mu$ L)	920	1,030	920	1,080	1,290	1,240	1,060	1,860	2,160	1,770	2,340	1,570	1,660	1,520	1,040	1,220
Hb (g/dL)	12.2	12.0	11.6	11.2	11.6	11.3	11.2	11.5	12.0	12.4	12.0	11.5	11.5	10.9	10.6	10.4
Plt ( $\mu$ L)	151,000	147,000	157,000	162,000	144,000	161,000	168,000	175,000	204,000	209,000	211,000	152,000	145,000	185,000	134,000	134,000
Alb (g/dL)	3.5	3.6	3.4	3.3	3.4	3.3	3.2	3.4	3.5	3.8	3.9	4.1	4.4	4.5	4.6	4.8
ALT (IU/L)	11	12	14	13	14	25	47	50	62	63	39	52	35	27	17	17
LDH (IU/L)	157	164	179	164	158	167	179	162	166	161	233	151	156	164	141	163
CK (IU/L)	20	19	17	18	18	18	22	23	24	24	41	50	95	79	56	70
Cre (mg/dL)	0.51	0.48	0.49	0.48	0.48	0.44	0.49	0.44	0.48	0.53	0.60	0.59	0.55	0.54	0.68	0.69
Troponin (pg/mL)	..	0.003	..	..	..	..	..	..	0.003	..	..	..	..	..	..	..
PT (s)	..	11.7	11.6	11.9	12.1	12.5	12.5	12.5	12.4	12.2	11.3	11.0	11.2	11.3	11.7	11.3
D-dimer ( $\mu$ g/mL)	..	0.5	0.5	<0.5	0.5	0.5	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5	..
CRP (mg/dL)	7.49	7.01	7.25	5.88	2.70	1.29	0.64	0.48	0.25	0.33	0.34	0.27	0.13	0.16	0.06	0.09
Ferritin ( $\mu$ g/L)	193	207	204	208	237	212	191	169	133	96	57	32	17	11	6	9
IL-6 (pg/mL)	..	20.8	31.5	9.1	4.9	6.2	6.0	2.0	3.9	3.3	4.1	3.8	1.8	2.3	<1.5	1.9
Procalcitonin (ng/mL)	..	0.05	..	..	..	..	..	..	0.05	..	..	..	..	0.06	..	..
KL-6 (IU/mL)	..	510	476	480	516	508	516	550	567	594	494	398	358	266	170	156
IgG (mg/dL) <sup>a</sup>	1,371	1,372	1,229	1,199	1,227	1,141	1,148	1,131	1,108	1,134	1,021	1,909	1,557	1,146	1,150	1,197

The green shaded area indicates remdesivir administration.

<sup>a</sup>The patient received regular intravenous immunoglobulin transfusions.

**Table S4. Detection of infectious viruses and viral RNA in clinical specimens (related to Figure 2).**

Sample	Collection day	Virus titers (FFUs/mL)	Virus isolation	qRT-PCR (Ct value)	Viral RNA (copies/ $\mu$ L)
Saliva	Day 0	not done	not done	31.9	2.6E+01
Nasopharyngeal swab	Day 1	not done	not done	21.3	1.1E+05
<u>Nasopharyngeal swab</u> <sup>a</sup>	Day 1	2,160	+	23.0	4.4E+04
Saliva	Day 63	not done	not done	34.7	3.3E+00
Saliva	Day 77	not done	not done	33.8	6.4E+00
Saliva	Day 77	<5	–	–	NA <sup>b</sup>
Saliva	Day 92	not done	not done	–	NA
Saliva	Day 92	not done	not done	–	NA
Sputum	Day 175	not done	not done	35.9	1.0E+01
<u>Sputum</u>	Day 175	not done	–	38.8	6.5E–01
Sputum	Day 176	not done	not done	36.5	8.7E+00
<u>Sputum</u>	Day 176	not done	–	37.0	2.2E+00
Sputum	Day 181	not done	not done	35.3	3.9E+01
<u>Sputum</u>	Day 196	<2.5	–	37.6	1.8E+00
<u>Sputum</u>	Day 204	<2.5	–	not done	NA
<u>Sputum</u>	Day 209	<2.5	–	31.2	1.1E+00
<u>Bronchoalveolar lavage fluid–1</u>	Day 218	10	+	–	NA
<u>Bronchoalveolar lavage fluid–2</u>	Day 218	15	+	31.5	9.1E+01
<u>Bronchoalveolar lavage fluid–3</u> <sup>a</sup>	Day 218	17.5	+	32.1	6.2E+01
<u>Lung tissue (by biopsy)</u> <sup>a</sup>	Day 218	15	+	not done	NA
<u>Suction phlegm</u>	Day 218	<2.5	–	35.6	6.5E+00
<u>Sputum</u> <sup>a</sup>	Day 224	5	+	35.0	9.6E+00
Saliva	Day 224	<5	–	39.8	4.3E–01
Nasopharyngeal swab	Day 237	not done	–	–	NA
<u>Sputum</u>	Day 237	not done	–	37.0	3.0E+00
Sputum	Day 238	not done	–	34.4	1.8E+01
Urine	Day 238	not done	–	–	NA
Whole blood	Day 238	not done	–	–	NA
Sputum–1	Day 239	10	+	31.0	1.9E+02
Sputum–2 <sup>a</sup>	Day 239	130	+	33.4	3.6E+01
Sputum	Day 240	<5	–	–	NA
Sputum	Day 241	<5	–	43.7	2.9E–02
Sputum–1	Day 242	<5	–	42.0	9.5E–02
Sputum–2	Day 242	<5	–	–	NA
Sputum	Day 243	<5	–	–	NA
Sputum	Day 244	<5	–	–	NA
Sputum	Day 245	<5	–	–	NA
Sputum	Day 246	<5	–	–	NA
Sputum	Day 247	<5	–	–	NA
Sputum	Day 248	<5	–	–	NA
Sputum	Day 251	<5	–	–	NA
Sputum	Day 252	<5	–	–	NA
Sputum	Day 253	<5	–	–	NA
Sputum	Day 255	<5	–	–	NA
Nasopharyngeal swab	Day 255	<5	–	–	NA
Sputum	Day 258	<5	–	–	NA
Nasopharyngeal swab	Day 258	<5	–	–	NA
Sputum	Day 260	<5	–	–	NA
Sputum	Day 262	<5	–	–	NA
Sputum	Day 265	<5	–	–	NA
Sputum	Day 267	<5	–	–	NA
Sputum	Day 269	<5	–	–	NA
Sputum	Day 273	<5	–	–	NA
Sputum	Day 276	<5	–	–	NA
Sputum	Day 308	not done	–	–	NA

The underlined samples were stored at –80°C and tested retrospectively.

<sup>a</sup>Samples tested for the viral genome analysis.

<sup>b</sup>Not applicable.

**Table S5. List of intravenous immunoglobulin (IVIG) products administered to the patient (related to Figure 1).**

Day	Product	Company	Period of blood collection	Dosage (g)
-112	GAMMAGARD Solvent/Detergent Treated Intravenous 5g	Baxalta US Inc.	-2019 May	40
	Venoglobulin IH 10% I.V.10g/100mL	Japan Blood Products Organization	2017 Oct	10
-84	GAMMAGARD Solvent/Detergent Treated Intravenous 5g	Baxalta US Inc.	-2019 May	40
	Venoglobulin IH 10% I.V.10g/100mL	Japan Blood Products Organization	2018 Jan	10
-56	GAMMAGARD Solvent/Detergent Treated Intravenous 5g	Baxalta US Inc.	-2019 Aug	40
	Venoglobulin IH 10% I.V.10g/100mL	Japan Blood Products Organization	2018 Jan	10
-28	GAMMAGARD Solvent/Detergent Treated Intravenous 5g	Baxalta US Inc.	-2019 Aug	40
	Venoglobulin IH 10% I.V.10g/100mL	Japan Blood Products Organization	2018 Jan	10
0	GAMMAGARD Solvent/Detergent Treated Intravenous 5g	Baxalta US Inc.	-2019 Aug	40
	Venoglobulin IH 10% I.V.10g/100mL	Japan Blood Products Organization	2018 Jan	10
21	GAMMAGARD Solvent/Detergent Treated Intravenous 5g	Baxalta US Inc.	-2019 Aug	50
	Venoglobulin IH 10% I.V.10g/100mL	Japan Blood Products Organization	2018 Jun	10
42	GAMMAGARD Solvent/Detergent Treated Intravenous 5g	Baxalta US Inc.	-2019 Aug	50
	Venoglobulin IH 10% I.V.10g/100mL	Japan Blood Products Organization	2018 Jun	10
63	GAMMAGARD Solvent/Detergent Treated Intravenous 5g	Baxalta US Inc.	-2019 Aug	50
	Venoglobulin IH 10% I.V.10g/100mL	Japan Blood Products Organization	2018 Jun	10
	Venoglobulin IH 10% I.V.5g/50mL	Japan Blood Products Organization	2018 Aug	10
84	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Apr-2019 Mar	60
112	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
140	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
168	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
196	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
224	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
262	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
280	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
308	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
336	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
364	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
392	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
420	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2018 Sep-2019 May <sup>a</sup>	70
448	Privigen 10% I.V.Drip Infusion 10g/100mL	CSL Behring	2019 Apr-2019 Jul <sup>b</sup>	70

<sup>a</sup>IVIG 2020Lot A was tested for anti-SARS-CoV-2 spike protein antibodies using ELISA (Figure S1).

<sup>b</sup>IVIG 2020Lot B was tested for anti-SARS-CoV-2 spike protein antibodies using ELISA (Figure S1).



**Table S6. List of viruses used in the phylogenetic analysis (related to Figure 2 and the STAR Methods).**

	Accession ID		Virus name	Pango lineage	Clade
	GISAD	NCBI			
Day_218_BALF	EPI_ISL_4935777	..	hCoV-19/Japan/RIMD-DVI-C10B/2021	B.1.1.284	GR
Day_218_Lung	EPI_ISL_4935949	..	hCoV-19/Japan/RIMD-DVI-C10L/2021	B.1.1.284	GR
Day_224_Sputum	EPI_ISL_4936095	..	hCoV-19/Japan/RIMD-DVI-C16/2021	B.1.1.284	GR
Day_1_NPS	EPI_ISL_4936243	..	hCoV-19/Japan/RIMD-DVI-H06/2020	B.1.1.284	GR
Day_239_Sputum	EPI_ISL_4936533	..	hCoV-19/Japan/RIMD-DVI-C31/2021	B.1.1.284	GR
OCGH_P2_2021	EPI_ISL_4929525	..	hCoV-19/Japan/RIMD-DVI-C26H/2021	R.1	..
OCGH_P3_2021	EPI_ISL_4930839	..	hCoV-19/Japan/RIMD-DVI-C26W/2021	R.1	..
OCGH_P4_2021	EPI_ISL_4931056	..	hCoV-19/Japan/RIMD-DVI-D09/2021	B.1.1.7	GRY
OCGH_P6_2021	EPI_ISL_4931846	..	hCoV-19/Japan/RIMD-DVI-D21/2021	B.1.1.7	GRY
OIPH_1_2020	EPI_ISL_4932136	..	hCoV-19/Japan/OIPH14/2020	A	S
OIPH_2_2020	EPI_ISL_4932550	..	hCoV-19/Japan/OIPH16/2020	B.1.1.284	GR
OIPH_3_2020	EPI_ISL_4932712	..	hCoV-19/Japan/OIPH21/2020	B.1.1.284	GR
OIPH_24_2020	EPI_ISL_4932860	..	hCoV-19/Japan/OIPH29/2020	B.1.1.284	GR
OIPH_35_2020	EPI_ISL_4933015	..	hCoV-19/Japan/OIPH34/2020	B.1.1.284	GR
OIPH_43_2020	EPI_ISL_4933271	..	hCoV-19/Japan/OIPH6/2020	B.1.1.285	GR
OIPH_71_2020	EPI_ISL_4933542	..	hCoV-19/Japan/OIPH51/2020	B.1.1.284	GR
OIPH_76_2020	EPI_ISL_4933741	..	hCoV-19/Japan/OIPH54/2020	B.1.1.284	GR
OIPH_92_2020	EPI_ISL_4933859	..	hCoV-19/Japan/OIPH61/2020	B.1.1.284	GR
OIPH_123_2021	EPI_ISL_4933990	..	hCoV-19/Japan/OIPH1/2021	B.1.1.28	..
OIPH11_2020	EPI_ISL_4934247	..	hCoV-19/Japan/OIPH25/2020	B.1.1.284	GR
OIPH19_2020	EPI_ISL_4934751	..	hCoV-19/Japan/OIPH28/2020	B.1.1.284	GR
OIPH127_2021	EPI_ISL_4934873	..	hCoV-19/Japan/OIPH5/2021	B.1.1.214	GR
OIPH128_2021	EPI_ISL_4934996	..	hCoV-19/Japan/OIPH6/2021	B.1.1.214	GR
OIPH133_2021	EPI_ISL_4935185	..	hCoV-19/Japan/OIPH10/2021	B.1.1.214	GR
OIPH135_2021	EPI_ISL_4935429	..	hCoV-19/Japan/OIPH12/2021	B.1.1.214	GR
Japan_TKYE626993_2020	.. <sup>a</sup>	LC606017	hCoV-19/Japan/TKYE626993/2020	B.1.1.284	GR
Japan_TKYET29933_2020	EPI_ISL_649137	LC593812	hCoV-19/Japan/TKYET29933/2020	B.1.1.284	GR
Japan_TKYE618937_2020	.. <sup>a</sup>	LC573279	hCoV-19/Japan/TKYE618937/2020	..	..
Japan_TKYT22395_2020	EPI_ISL_649132	LC593807	hCoV-19/Japan/TKYT22395/2020	B.1.1.284	GR
Japan_TKYE630074_2020	EPI_ISL_649138	LC593813	hCoV-19/Japan/TKYE630074/2020	B.1.1.284	GR
Japan_TKYE624705_2020	EPI_ISL_649135	LC593810	hCoV-19/Japan/TKYE624705/2020	B.1.1.284	GR
Japan_TK-Y17873_2020	EPI_ISL_486909	LC567857	hCoV-19/Japan/TK-Y17873/2020	B.1.1.284	GR
Japan_TKYE618779_2020	..	LC573283	hCoV-19/Japan/TKYE618779/2020	..	..
Japan_TKYE627000_2020	EPI_ISL_649136	LC593811	hCoV-19/Japan/TKYE627000/2020	B.1.1.284	GR
Japan_TKYE618749_2020	..	LC573282	hCoV-19/Japan/TKYE618749/2020	..	..
Japan_TKYT22355_2020	EPI_ISL_649127	LC593802	hCoV-19/Japan/TKYT22355/2020	B.1.1.284	GR
Japan_TKYT22342_2020	EPI_ISL_649126	LC593801	hCoV-19/Japan/TKYT22342/2020	B.1.1.284	GR
Japan_TKYE618930_2020	..	LC573278	hCoV-19/Japan/TKYE618930/2020	..	..
Japan_TKYE630094_2020	EPI_ISL_649139	LC593814	hCoV-19/Japan/TKYE630094/2020	B.1.1.284	GR
Japan_TKYT30095_2020	EPI_ISL_649140	LC593815	hCoV-19/Japan/TKYT30095/2020	B.1.1.284	GR
Japan_TKYE618928_2020	..	LC573276	hCoV-19/Japan/TKYE618928/2020	..	..
Japan_TKYE618929_2020	..	LC573277	hCoV-19/Japan/TKYE618929/2020	..	..
England_MILK-9E05B3_2020	EPI_ISL_601443	..	hCoV-19/England/MILK-9E05B3/2020	B.1.1.7	GRY
England_20168037604_2020	EPI_ISL_466615	..	hCoV-19/England/20168037604/2020	B.1.1	GR
Spain_CT-ISCIII-2013597_2020	EPI_ISL_539548	..	hCoV-19/Spain/CT-ISCIII-2013597/2020	B.1.177	GV
Canada_ON-PHL-8751_2020	EPI_ISL_418345	..	hCoV-19/Canada/ON-PHL-8751/2020	B.1	GH
Germany_BY-ChVir-929_2020	EPI_ISL_406862	..	hCoV-19/Germany/BY-ChVir-929/2020	B.1.153	G
Wuhan_WIV04_2019	EPI_ISL_402124	MN996528	hCoV-19/Wuhan/WIV04/2019	B	L
Italy_LAZ-INMI-SPL1_2020	EPI_ISL_412974	..	hCoV-19/Italy/LAZ-INMI-SPL1/2020	B	V
Guangdong_20SF012_2020	EPI_ISL_403932	..	hCoV-19/Guangdong/20SF012/2020	A	S

<sup>a</sup>Not applicable.

**Table S7. SARS-CoV-2 mutations observed in the patient (related to Figure 2).**

Nucleotide position	ORF	Day 1 reference	Allele	Amino acid substitution	Protein	Amino acid position in protein	Samples with mutation	Frequency in Cov-Glue data base <sup>g</sup>
6617	<i>ORF1ab</i>	G	T	G2118C	NSP3	G1300C	A <sup>b</sup>	102
7814	<i>ORF1ab</i>	T	C	S2517P	NSP3	S1699P	224 <sup>c</sup>	80
9202	<i>ORF1ab</i>	T	A	F2979L	NSP4	F216L	224	19
9316	<i>ORF1ab</i>	T	C	V3017V	NSP4	– <sup>a</sup>	A	
9474	<i>ORF1ab</i>	C	T	A3070V	NSP4	A307V	A	828
10323	<i>ORF1ab</i>	A	G	K3353R	NSP5	K90R	A	19588
11266	<i>ORF1ab</i>	G	A	L3667L	NSP6	–	224	
11388	<i>ORF1ab</i>	T	C	V3708A	NSP6	V139A	239 <sup>d</sup>	4
11750	<i>ORF1ab</i>	C	T	L3829F	NSP6	L260F	A	5,611
15654	<i>ORF1ab</i>	C	T	D5130D		–	218L <sup>e</sup>	
16993	<i>ORF1ab</i>	T	C	Y5577H	NSP13	Y253H	224	545
19906	<i>ORF1ab</i>	A	G	I6548V	NSP15	I96V	218B <sup>f</sup> , 239	19
20421	<i>ORF1ab</i>	T	G	D6719E	NSP15	D267E	A	148
21132	<i>ORF1ab</i>	A	G	Q6956Q		–	218L	
21637	<i>S</i>	C	T	P25P	<i>S</i>	–	218L	
22987	<i>S</i>	C	T	A475A	<i>S</i>	–	A	
25008	<i>S</i>	A	C	K1149T	<i>S</i>	K1149T	A	0
25313	<i>S</i>	G	A	G1251R	<i>S</i>	G1251R	218B, 239	51
25487	<i>ORF3a</i>	C	T	T32I	<i>ORF3a</i>	T32I	239	1115
26270	<i>E</i>	C	T	T9I	<i>E</i>	T9I	239	1448
26333	<i>E</i>	C	T	T30I	<i>E</i>	T30I	218L	298
26369	<i>E</i>	A	G	Y42C	<i>E</i>	Y42C	A	5
26550	<i>M</i>	G	T	V10F	<i>M</i>	V10F	A	9
26895	<i>M</i>	C	T	H125Y	<i>M</i>	H125Y	A	2030
27696	<i>ORF7a</i>	T	C	F101F	<i>ORF7a</i>	–	218B, 239	
27737	<i>ORF7a</i>	C	T	T115I	<i>ORF7a</i>	T115I	A	507
27752	<i>ORF7a</i>	C	T	T120I	<i>ORF7a</i>	T120I	A	2335

<sup>a</sup>Synonymous substitution.

<sup>b</sup>All four virus isolates.

<sup>c</sup>224, virus isolated from sputum on day 224.

<sup>d</sup>239, virus isolated from sputum on day 239.

<sup>e</sup>218L, virus isolated from lung tissue on day 218.

<sup>f</sup>218B, virus isolated from bronchoalveolar lavage fluid on day 218.

<sup>g</sup>Accessed on Sept 13, 2021. In the database, 867,980 sequences with D614G and 257,333 sequences with N501Y were found.

**Table S8. List of peptides used to stimulate T cells (related to Figure 3, 4, and 5).**

Peptide name	Sequence	
	Wuhan	Mutant
<b>E1</b>	MYSFVSEETGLIVN	MYSFVSEE <u>I</u> GLIVN
<b>E29</b>	VTLAILTALRLCAYC	V <u>I</u> LAILTALRLCAYC
<b>E37</b>	LRLCAYCCNIVNVSL	LRLC <u>A</u> CCNIVNVSL
<b>M1</b>	MADSNGTITVEELKK	MADSNGTIT <u>E</u> EELKK
<b>M121</b>	NVPLHGTILTRP <u>L</u> LE	NVPLY <u>G</u> TILTRP <u>L</u> LE
<b>ORF1ab 2109</b>	KPNELSRVLGLKTLA	KPNELSRVL <u>Q</u> LKTLA
<b>ORF1ab 2509</b>	GQKTYERHSLSHFVN	GQKTYERH <u>P</u> LSHFVN
<b>ORF1ab 2973</b>	VRVVTTFDSEYCRHG	VRVVT <u>T</u> DSEYCRHG
<b>ORF1ab 3061</b>	AYYFMRFRRAFGEYS	AYYFMRFR <u>R</u> VFGEYS
<b>ORF1ab 3349</b>	VLKLVDTANPKTPK	VLK <u>L</u> RVDANPKTPK
<b>ORF1ab 3705</b>	ARRVWTLMNVLTLVY	ARR <u>A</u> WTLMNVLTLVY
<b>ORF1ab 3821</b>	RYMNSQGLLPKNSI	RYMNSQGL <u>F</u> PKNSI
<b>ORF1ab 5565</b>	VPQEHYVRITGLYPT	VPQEHYVRITGL <u>H</u> PT
<b>ORF1ab 6541</b>	KRDAPAHISTIGVCS	KRDAPAH <u>V</u> STIGVCS
<b>ORF1ab 6713</b>	SPFELED <u>F</u> IPMDSTV	SPFELE <u>E</u> FIPMDSTV
<b>ORF3a 25</b>	PSDFVRATATIPIQA	PSDFVRA <u>I</u> ATIPIQA
<b>ORF7a 105</b>	AAIVFITLCFTLKRKTE	AAIVFITLCF <u>I</u> LKRKTE (T115I) AAIVFITLCFTLKRK <u>E</u> (T120I)
<b>S1145</b>	LDSFKEELD <u>K</u> YFKNH	LDSF <u>I</u> EELD <u>K</u> YFKNH
<b>S1245</b>	KGCCSCGSCCKFDED	KGCCSC <u>R</u> SCCKFDED

Underlined amino acid sequences in the mutant peptides indicate the amino acids that differed from those in the Wuhan peptides.

**Table S9. V(D)J usages of clone-111 (related to Figure 4 and 5).**

<b>Clone ID</b>	<b>TRAV</b>	<b>CDR3a</b>	<b>TRAJ</b>	<b>TRBV</b>	<b>CDR3b</b>	<b>TRBJ</b>
111	13-2	CAENPRFSGGYNKLIF	4	6-1	CASSGTGVDTQYF	2-3