

Supplemental Table 1 Demographic and clinical data of the COVID-19 patients in multiple analyses.

N	All patients			Transcriptomic and Systemic cytokine profiling			T cell restimulation analysis			Antibody profiling (S-flow and peptide ELISA)		
	WT (n=36)	66 Δ382 (n=30)	*p value	WT (n=14)	25 Δ382 (n=11)	*p value	WT (n=14)	28 Δ382(n=14)	*p value	WT (n=20)	50 Δ382 (n=30)	*p value
Demographics												
Mean age, years	45 (13)	40 (12)	0.0925	48 (16)	41 (11)	0.2207	42 (12)	43 (13)	0.8834	42 (11)	41 (12)	0.7885
Sex, male	19 (42.9%)	18 (72.7%)	0.6233	6 (42.9%)	8 (72.7%)	0.2270	9 (64.3%)	9 (64.3%)	> 0.999	10 (50.0%)	19 (63.3%)	0.3927
Ethnicity												
Chinese	31 (86.1%)	23 (76.7%)	0.355	13 (92.9%)	10 (90.9%)	> 0.999	11 (78.6%)	12 (85.7%)	> 0.999	18 (90.0%)	23 (76.7%)	0.2847
Malay	1 (2.8%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		1 (7.1%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Indian	0 (0.0%)	1 (3.3%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	1 (0.0%)	
Others	4 (11.1%)	6 (20.0%)		1 (7.1%)	1 (9.1%)		2 (14.3%)	2 (14.3%)		2 (10.0%)	6 (20.0%)	
Comorbidities												
Diabetes	4 (11.1%)	0 (0.0%)	0.1196	3 (21.4%)	0 (0.0%)	0.2300	0 (0.0%)	0 (0.0%)	> 0.999	1 (5.0%)	0 (0.0%)	0.4118
Hypertension	8 (22.2%)	1 (3.3%)	0.0331	6 (42.9%)	1 (9.1%)	0.0900	0 (0.0%)	2 (14.3%)	0.4815	2 (10.0%)	2 (6.7%)	> 0.999
Laboratory findings												
Platelets, x 10 ⁹ /L	183.7 (59.9)	212.1 (56.4)	0.0688	-	-	-	-	-	-	-	-	-
White blood cells, x 10 ⁹ /L	4.8 (1.9)	4.7 (1.6)	0.8467	-	-	-	-	-	-	-	-	-
Lymphocytes, x 10 ⁹ /L	1.2 (0.6)	1.4 (0.6)	0.2256	-	-	-	-	-	-	-	-	-
Neutrophils, x 10 ⁹ /L	3.0 (1.5)	2.7 (1.6)	0.4870	-	-	-	-	-	-	-	-	-
Monocytes, x 10 ⁹ /L	0.5 (0.3)	0.5 (0.2)	0.3675	-	-	-	-	-	-	-	-	-
Clinical manifestation												
Pneumonia	20 (55.6%)	15 (50.0%)	0.6232	10 (71.4%)	6 (54.6%)	0.4341	6 (42.9%)	8 (57.1%)	0.7064	9 (45.0%)	15 (50.0%)	0.779
Hypoxia	6 (16.7%)	1 (3.3%)	0.1158	6 (42.9%)	1 (9.1%)	0.0900	0 (0.0%)	0 (0.0%)	> 0.999	0 (0.0%)	0 (0.0%)	> 0.999
Clinical severity												
No pneumonia (mild)	16 (44.4%)	15 (50.0%)		-	-	-	-	-	-	-	-	-
Pneumonia, without hypoxia (moderate)	14 (38.9%)	14 (46.7%)	0.214	-	-	-	-	-	-	-	-	-
Pneumonia, with hypoxia (severe)	6 (16.7%)	1 (3.3%)		-	-	-	-	-	-	-	-	-
Length of hospitalization (days)	13.0 (6.1)	13.8 (5.6)	0.571	-	-	-	-	-	-	-	-	-
Interval between symptom onset and sample collection, median days (IQR)	-	-	-	9.5 (6.5-12.3)	6.0 (4.0-9.0)	0.2090	18.5 (16.8-27.8)	19.5 (15.0-25.0)	0.3595	-	-	-
RNA integrity value of acute sample	-	-	-	7.6 (0.8)	7.7 (0.7)	0.6490	-	-	-	-	-	-

Data represented as Mean (S.D), Median (IQR) or n (%). COVID-19, Coronavirus Disease-19; WT, wildtype; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2. *Continuous variables were compared using unpaired t test and categorical variables were compared using Fisher's exact test. Patients in this cohort were classified into three groups based on clinical severity: mild (no pneumonia on chest radiographs [CXR] at baseline and during hospital admission), moderate (pneumonia on CXR without hypoxia), and severe (pneumonia on CXR with hypoxia [desaturation to ≤94%]).

Supplemental Table 2 Demographics of healthy controls.

Variable	Transcriptomic profiling (n=6)	Systemic cytokine profiling (n=23)	S-flow and peptide ELISA (n=22)
Demographics			
Mean age, years	39 (11)	51 (17)	45 (13)
Sex			
Male	4 (66.7%)	9 (39.1%)	9 (40.9%)
Female	2 (33.3%)	14 (60.9%)	12 (54.5%)

*Values reported as number (percentage) for categorical variables and mean (SD) for continuous variables.

Supplemental Table 3 Summary statistics of RNA-seq data and mapping results

Sample Name	Total Sequences (millions)	% Assigned reads	Assigned reads (millions)	% Uniquely mapped reads	Uniquely mapped reads (millions)	Average % GC Content
R10830	22.2	50.30%	27.5	85.80%	19	48%
R10831_R	17	53.70%	22.2	86.10%	14.7	49%
R10832	20	49.30%	25.8	86.00%	17.2	49%
R10833	19.8	48.90%	26.5	84.70%	16.8	49%
R10834	20.1	48.20%	23.8	85.90%	17.3	48%
R10835_R	16.7	55.50%	22.7	85.50%	14.3	49%
R10836	22.6	40.10%	27	81.60%	18.4	50%
R10837	20.1	45.20%	23.7	84.10%	16.9	49%
R10838	23.9	51.20%	30.3	86.80%	20.7	48%
R10839_R	18.6	47.60%	20.9	85.90%	16	48%
R10840_R	20.6	58.20%	28.2	86.90%	17.9	49%
R10841	22.5	37.60%	28.1	77.30%	17.4	51%
R10842	21.9	37.80%	27.1	76.60%	16.7	51%
R10843	20.2	40.10%	24.9	77.30%	15.6	51%
R10844	21.8	48.20%	27.8	84.70%	18.5	50%
R10845	22.3	49.90%	29	84.70%	18.8	50%
R10846	22.2	56.00%	30.8	86.30%	19.2	49%
R10847	20.6	43.80%	24.4	82.90%	17.1	49%
R10848	20.1	55.20%	26.4	87.20%	17.5	48%
R10849	21.7	50.50%	23.8	86.30%	19.2	48%
R10852_R	21.9	24.20%	10.3	87.00%	19.1	44%
R10853_R	21.3	53.90%	28.6	85.10%	18.1	49%
R10854_R	20	50.20%	26.4	84.10%	16.8	47%
R10855	20.5	34.10%	23.2	74.10%	15.2	51%
R10856	21.5	58.40%	29.4	87.10%	18.7	49%
R10857	22.1	48.30%	27.3	84.90%	18.8	50%
R10858	17.3	35.50%	21.3	76.70%	13.2	51%
R10859	20.5	47.80%	26	84.90%	17.4	49%
R10860	19.5	56.90%	27	86.60%	16.9	50%
R10861	20.4	46.00%	26.5	83.20%	17	50%
R10862	21.3	59.20%	27.9	88.90%	18.9	47%
R10863_R	22.8	59.50%	31.2	88.00%	20.1	49%
R10864_R	21.6	62.90%	30.9	87.00%	18.8	51%
R10865	23.7	44.80%	30.4	81.50%	19.3	51%
R10866_R	24.2	59.60%	31.2	88.60%	21.4	49%
R10867	21.1	41.60%	21.2	84.00%	17.7	48%
R10868	21.1	52.00%	27.7	85.00%	17.9	50%
R10869	24.9	35.70%	26.5	76.10%	19	51%
R10870	18.8	56.80%	25.3	87.10%	16.3	49%
R10871_R	14.4	41.60%	18.1	77.70%	11.2	51%
R10872_R	14	48.20%	16.9	84.30%	11.8	49%
R10873	21.4	41.80%	24.6	80.10%	17.2	50%
R10874	18.4	54.40%	24	85.80%	15.8	48%
R10875	17.6	34.90%	17.9	74.60%	13.1	50%
R10876_2	17.6	35.80%	19.9	73.50%	12.9	53%
R10877_2	21.2	43.30%	25.1	81.30%	17.2	51%
R10878	23.6	50.20%	29.1	86.90%	20.5	47%
R10879	23.5	51.20%	28.5	86.90%	20.4	47%
R10880	24	47.90%	29	85.50%	20.5	48%
R10881_R	24.7	52.70%	31	87.10%	21.5	48%
R10882	21	43.00%	27.2	77.20%	16.2	47%
R10883	24.1	50.00%	31.1	85.20%	20.5	49%
R10884_R	19.6	56.50%	27.4	86.10%	16.9	49%
R10885	26.6	44.70%	30.5	83.40%	22.2	49%
R10886_2	22.9	40.20%	28.3	74.00%	16.9	53%
R10887	22.3	42.20%	28	79.00%	17.6	50%

Supplemental Table 4 Flow cytometry antibodies for T cell Intracellular Panel (1 million PBMCs)

No.	Marker	Colour	Volume (µL)	Clone	Cat. No.	Vendor
1	CD66B	BV421	2	G10F5	562940	BD Biosciences
2	CD45RA	SB436	2	H100	62-0458-42	Thermo Fisher
3	CD27	PB	1	O323	302822	Biolegend
4	NKG2C	BV480	2	134591	748168	BD Biosciences
5	CD8	BV605	1	SK1	564116	BD Biosciences
6	CD19	BV605	1	H1B19	740394	BD Biosciences
7	VD2	BV711	1	B6	331412	Biolegend
8	CD107A	BV785	2	H4A3	563869	BD Biosciences
9	NKP46	BB515	2	9-e2	564536	BD Biosciences
10	CD3	SB550	1	SK7	344852	Biolegend
11	CD169	PERCP5.5	5	7-239	346020	Biolegend
12	HLADR	APCR700	2	L243	307626	Biolegend
13	CD4	SN685	1	SK3	344658	Biolegend
14	CD14	APC CY7	1	M0P9	557831	BD Biosciences
15	VD1	APC Vio770	1	REA173	130-120-578	Miltenyi Biotec
16	L/D	ZOMBIE NIR	0.5		423105	Biolegend
17	CXCR5	PE VIO615	1	J252D4	356928	Biolegend
18	CD154	PE CY5	5	TRAP-1	555701	BD Biosciences
19	CD56	PE CY5.5	2	NCAM16.2	35-0567-42	Thermo Fisher
20	CD16	PEAF700	1	3G8	MHCD1624	Thermo Fisher
21	CD45	BUV805	2	H130	612891	BD Biosciences
22	Granzyme B	BV510	2.5	GB11	563388	BD Biosciences
23	IFN-γ	BV570	2.5	4S.B3	502534	Biolegend
24	IL-2	BV650	5	MQ1-17H12	564166	BD Biosciences
25	TNF-α	BV750	2.5	MAB11	566359	BD Biosciences
26	IL-6	FITC	2.5	MQ2-13A5	11-7069-82	Thermo Fisher
27	IL-17a	AF647	10	N49-653	560490	BD Biosciences
28	IL-10	PE	2.5	JES-9D7	501404	Biolegend
29	IL-4	PECY7	2.5	8D4-8	560672	BD Biosciences

ENSG00000278875.1	1802	AC025809.2	TEC	5.2466078	-0.47932121	10.22409279	0.004710844	0.218311104
ENSG00000283384.1	3376	AL138694.1	lncRNA	5.281720086	-0.994466553	10.11385888	0.004897294	0.222659797
ENSG00000162062.15	2848	TEDC2	protein_coding	5.310436248	-0.377134713	8.566506191	0.009355856	0.28078551
ENSG00000128965.13	2051	CHAC1	protein_coding	5.346045166	-0.0012451	11.60455763	0.003330456	0.187179665
ENSG00000227502.3	2755	LINC01268	lncRNA	5.357834031	-0.000272502	11.14204186	0.004450259	0.214458329
ENSG00000227181.1	1745	AC107067.2	lncRNA	5.491399264	-1.136050444	13.92543986	0.004570067	0.215773794
ENSG00000205837.7	2202	LINC00487	lncRNA	5.515300304	0.064881937	29.80943744	4.12661E-05	0.063559168
ENSG00000183722.9	4564	LHFPL6	protein_coding	5.5277603	-0.168637275	11.89025074	0.002844192	0.177002596
ENSG00000115884.11	3613	SDC1	protein_coding	5.568853488	1.910942087	26.14848851	0.00010162	0.065041535
ENSG00000227742.2	2704	CALR4P	transcribed_unitary_pseudogene	5.61580431	-1.373983182	20.89378783	0.000266502	0.077698735
ENSG00000104067.16	11265	TJP1	protein_coding	5.617993763	-0.846885133	15.9458766	0.001157383	0.129462221
ENSG00000259319.1	4059	AF111167.2	lncRNA	5.656386322	0.406713563	17.65701507	0.000433436	0.083493325
ENSG00000246375.3	2591	PPM1K-DT	lncRNA	5.695589778	-1.170099	24.15138111	9.45102E-05	0.065041535
ENSG00000185585.20	6771	OLFML2A	protein_coding	5.767212688	-0.714704927	21.8780796	0.000291228	0.080341116
ENSG00000115155.17	7885	OTOF	protein_coding	6.288569642	3.703149031	24.17855822	8.17335E-05	0.065041535
ENSG00000049130.16	6205	KITLG	protein_coding	6.339772383	-1.02651118	18.70698841	0.001856105	0.15097794
ENSG00000233975.1	441	LINC02574	lncRNA	6.497385309	-1.153826693	18.70004483	0.001858307	0.15097794
ENSG00000151364.17	1899	KCTD14	protein_coding	7.001026545	0.04032819	24.7517518	0.000162089	0.065041535

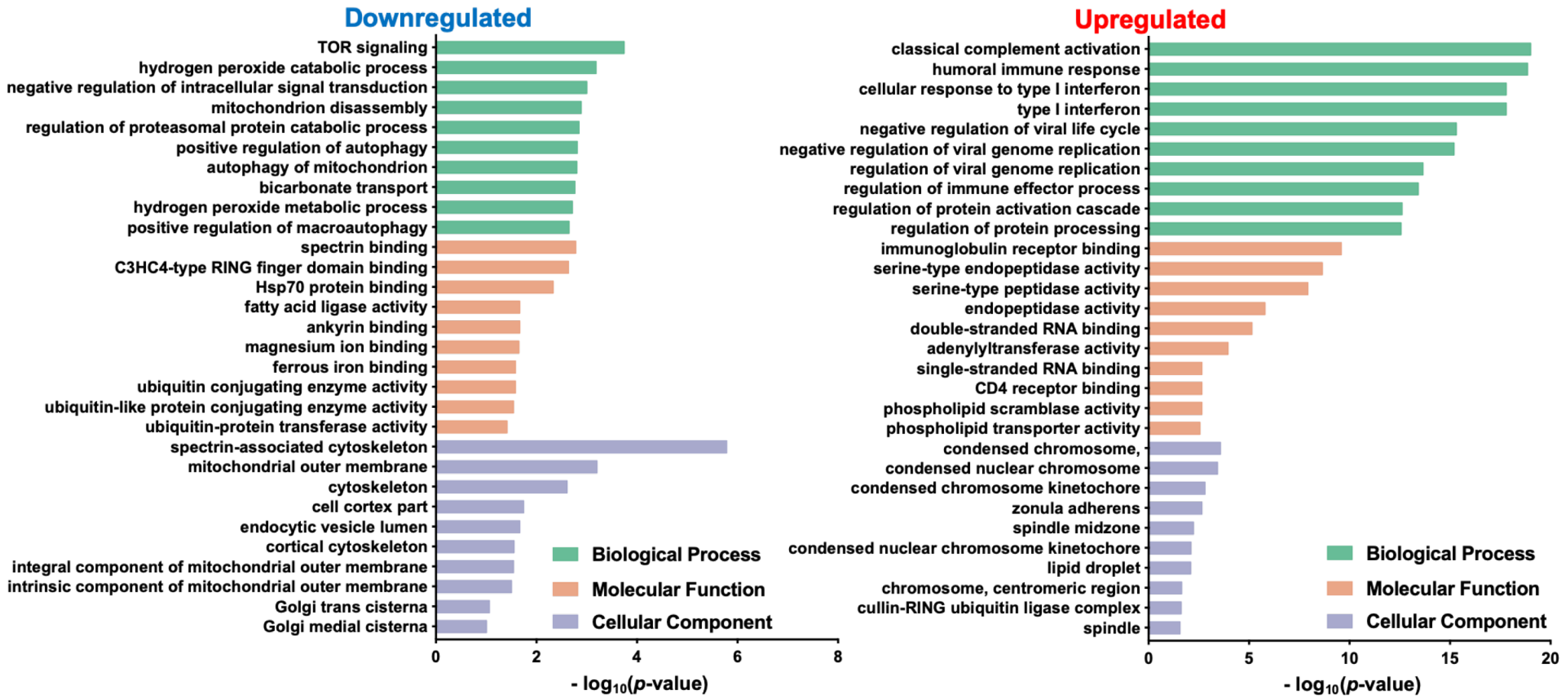
DEGs, differentially expressed genes; WT, wildtype; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; FC, fold change.

Supplemental Table 7 Plasma immune mediators of COVID-19 patients at the acute phase of infection (median 8 days PIO; n=25).

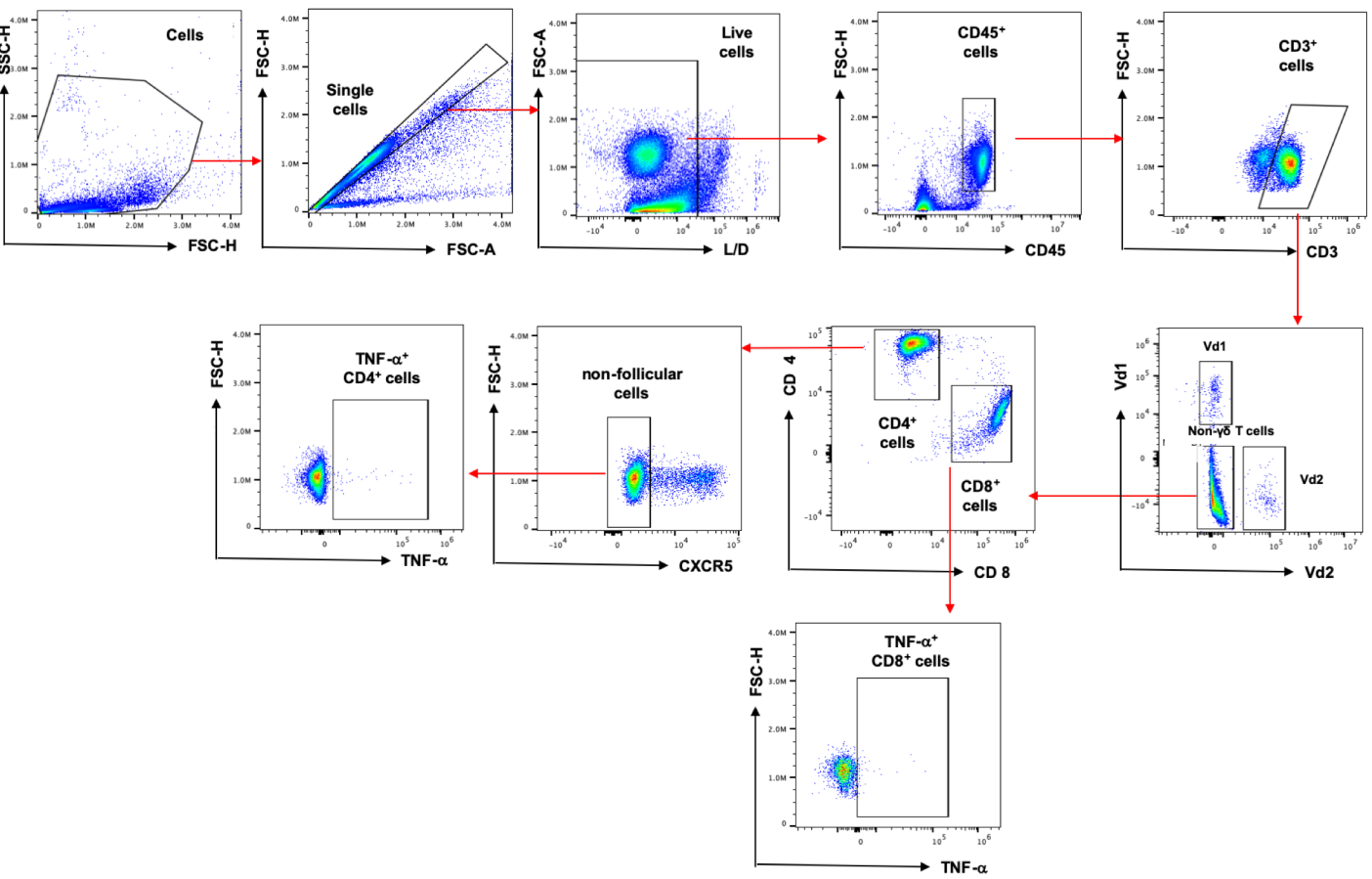
Log₁₀ concentration (pg/ml)

Cytokine	Difference			Healthy Controls (n=23)
	WT (n=14)	Δ382 (n=11)	(WT vs. Δ382)	
BDNF	34.92	21.85	-13.07	11.10
EGF	0.17	3.63	3.46	0.40
Eotaxin	16.84	14.25	-2.59	26.90
FGF-2	0.18	0.18	0.00	0.20
GM-CSF	0.82	0.82	0.00	1.10
GRO-α	0.05	0.05	0.00	2.50
HGF*	190.00	49.13	-140.90	55.50
IFN-α	0.02	0.02	0.00	0.10
IFN-γ***	6.84	36.14	29.30	17.20
IL-1α	0.19	0.01	-0.18	0.30
IL-1β	1.90	2.21	0.31	0.80
IL-1RA*	497.60	116.40	-381.30	5.00
IL-2**	12.36	24.20	11.85	12.10
IL-4	0.21	0.21	0.00	5.30
IL-5*	0.04	2.25	2.21	0.10
IL-6	5.99	1.54	-4.45	0.40
IL-7	0.66	0.41	-0.25	0.30
IL-8	0.15	0.15	0.00	0.20
IL-9	2.35	2.35	0.00	2.35
IL-10	0.04	0.04	0.00	0.10
IL-12p70*	0.22	1.06	0.84	0.10
IL-13	0.20	0.20	0.00	0.60
IL-15**	9.14	1.07	-8.07	1.90
IL-17A*	0.08	0.08	0.00	0.20
IL-18	34.35	66.66	32.31	29.20
IL-21	0.38	0.38	0.00	1.20
IL-22	0.36	0.36	0.00	9.60
IL-23	0.32	0.32	0.00	0.40
IL-27	0.99	0.99	0.00	2.00
IL-31	2.69	2.69	0.00	2.70
IP-10	26.52	19.34	-7.18	29.00
LIF	5.61	3.48	-2.13	3.10
MCP-1	55.24	44.96	-10.28	43.60
MIP-1α	5.38	0.47	-4.91	2.00
MIP-1β*	35.81	4.38	-31.43	2.80
PDGF-BB	38.96	45.43	6.48	91.40
PIGF-1	0.76	8.90	8.15	4.70
RANTES	42.51	66.21	23.70	100.90
SCF	4.39	4.53	0.14	4.00
SDF-1α	551.90	586.50	34.60	645.90
TNF-α	6.91	9.23	2.32	1.30
TNF-β	2.98	2.98	0.00	2.98
VEGF-A*	94.71	37.23	-57.48	1.90
VEGF-D	0.10	0.10	0.00	1.40
β-NGF	0.01	0.58	0.57	2.52

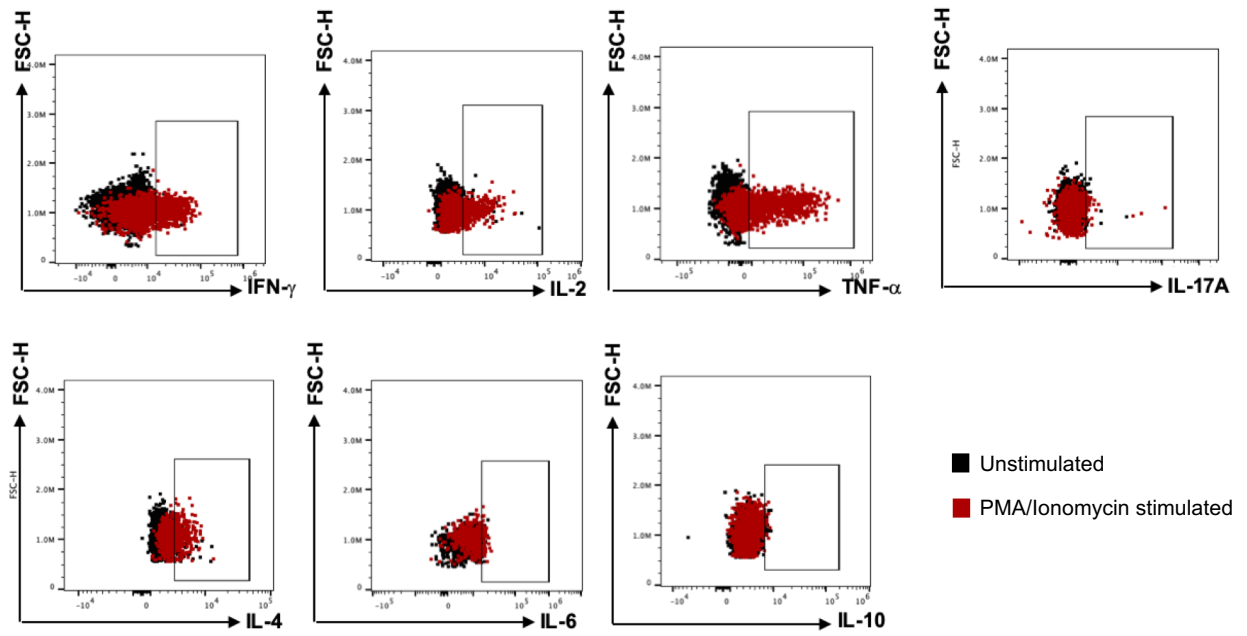
Data presented as median. COVID-19, Coronavirus Disease-19; WT, wild-type; PIO, post-illness onset; BDNF, brain-derived neurotropic factor; EGF, epidermal growth factor; FGF-2, basic fibroblast growth factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; GRO-α, chemokine (C-X-C motif) ligand (CXCL) 1; HGF, hepatocyte growth factor; IFN, interferon; IL, interleukin, IL-1RA, IL-1 receptor antagonist; IP-10, IFN-γ-induced protein 10; LIF, leukemia inhibitory factor; MCP-1, monocyte chemoattractant protein 1; MIP-1α, macrophage inflammatory protein 1α; PDGF-BB, platelet-derived growth factor; PIGF-1, placental growth factor; RANTES, regulated on activation, normal T cell expressed and secreted; SCF, stem cell factor; SDF-1α, stromal cell-derived factor 1α; TNF, tumor necrosis factor; VEGF, vascular endothelial growth factor; β-NGF, beta-nerve growth factor. (*p < 0.05; **p < 0.01; ***p < 0.001). ^Majority of the samples have readings below limit of quantitation (LOQ).



Supplemental Fig. 1

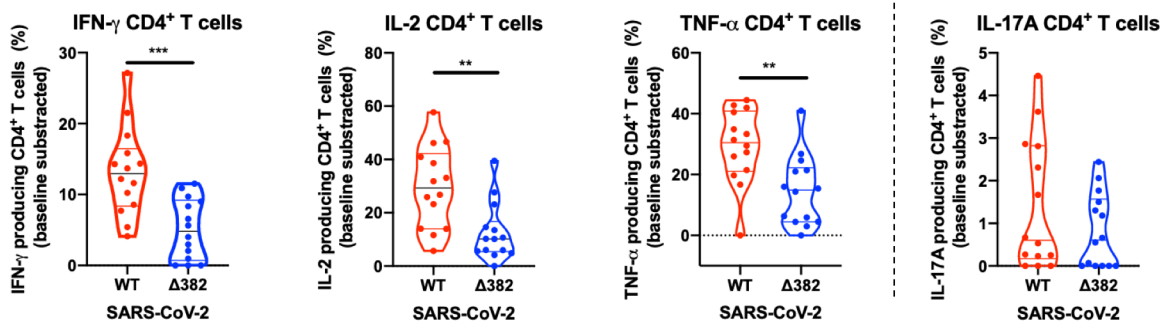


Supplemental Fig. 2

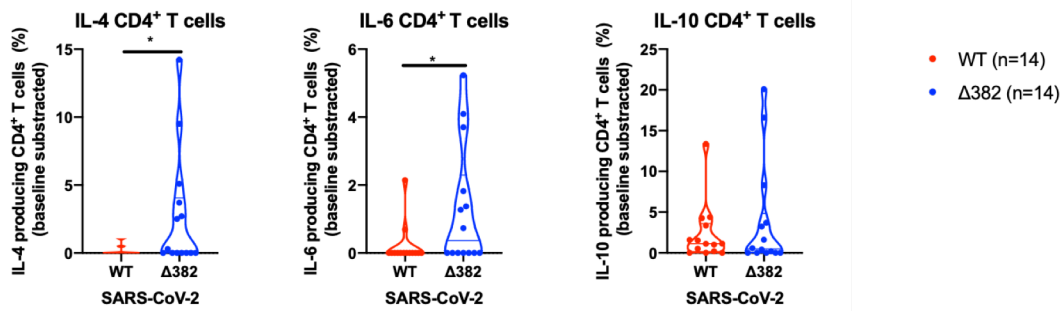


Th₁

Th₁₇



Th₂



Supplemental Fig. 3