Table S1. Antibodies used for APC staining

fluorochrome	Antigen	Vendor	Cat#
BUV395	HLA-DR	BD biosciences	564040
L/D blue	L/D		
BUV496	CD56	BD biosciences	750479
BUV563	CD27	BD biosciences	748705
BUV615	CD206	BD biosciences	751638
BUV661	CD10	BD biosciences	741600
BUV737	CD69	BD biosciences	612817
BUV805	CXCR4	BD biosciences	742043
BV421	CD303	BioLegend	354212
BV480	Siglec 6	BD biosciences	747914
BV510	CD3	BioLegend	344828
BV570	CD11b	BioLegend	301325
BV605	CD1c	BioLegend	331538
BV650	CCR7	BioLegend	353234
BV711	CD25	BioLegend	356138
BV750	CD163	BD biosciences	747185
BV785	CD16	BioLegend	302046
BB515	CD141	BioLegend	565084
PerCP	CXCR3	BioLegend	353740
PerCP Cy5.5	CD83	BioLegend	305320
PE	CLEC9A	BioLegend	353804
PE-Dazzle 594	CD11c	BioLegend	337228
PE-Cy5	CD86	BioLegend	305408
PE-Cy7	CD80	BioLegend	375408
AF700	CD19	BioLegend	302226
APC Cy7	CD14	BioLegend	301820
APC fire 810	CD38	BioLegend	303550

Table S2. The information of peptide pools used in the study

Viral protein	Peptide pool name	Cat #	Vendor
SARS-CoV2-N	PepMix™ SARS-CoV-2 (NCAP)	PM-WCPV-NCAP	JPT
SARS-CoV2-VME	PepMix™ SARS-CoV-2 (VME1)	PM-WCPV-VME	JPT
SARS-CoV2-S	PepMix™ SARS-CoV-2 (Spike Glycoprotein SUB1)	PM-WCPV-S-SU1-1	JPT
	PepMix™ SARS-CoV-2 (Spike Glycoprotein SUB2)	PM-WCPV-S-SU2-1	JPT
SARS-CoV2-VEMP	PepMix™ SARS-CoV-2 (VEMP)	PM-WCPV-VEMP-1	JPT
HKU1-S	PepMix™ HCoV- HKU1 (Spike Glycoprotein)	PM-HKU1-S	JPT
229E-S	PepMix™ HCoV-229E (Spike Glycoprotein)	PM-229E-S	JPT
NL63-S	PepMix™ HCoV-NL63 (Spike Glycoprotein)	PM-NL63-S-1	JPT
OC43-S	PepMix™ HCoV-OC43 (Spike Glycoprotein)	PM-OC43-S	JPT
CMV	CMV peptide pool for human CD4 and CD8 T cells	3619-1	Mabtech

Table S3. Antibodies used for T cell staining

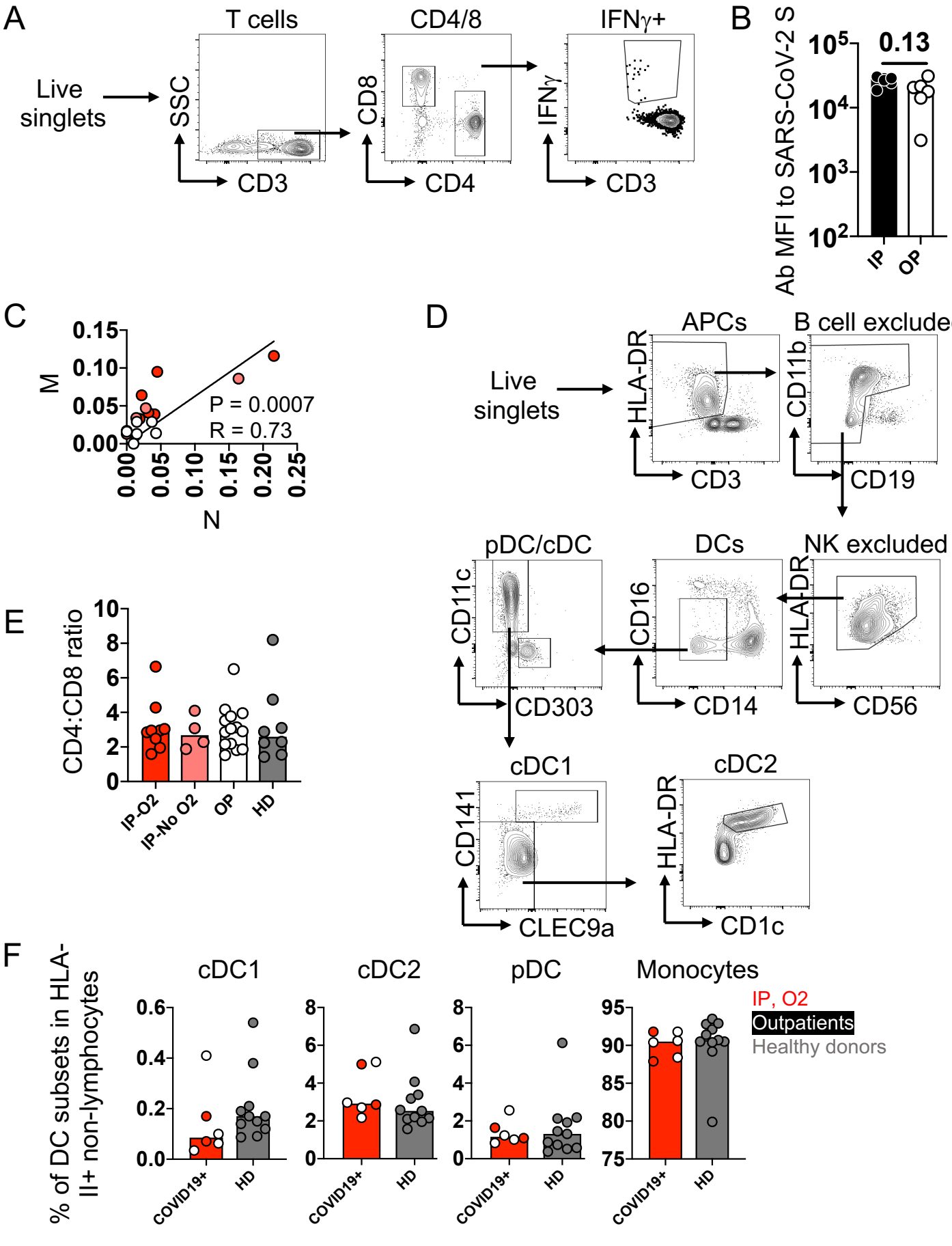
fluorochrome	Antigen	Vendor	Cat#
Surface			
BUV395	HLA-DR	BD biosciences	564040
L/D blue		ThermoFisher	L23105
BUV563	CD27	BD biosciences	748705
BUV661	PD1	BD biosciences	750260
BUV737	CD69	BD biosciences	612817
BUV805	CD28	BD biosciences	742037
BV421	CD3	BD biosciences	562877
BV510	CD62L	BioLegend	304844
BV650	CCR7	BioLegend	353234
BV750	CXCR3	BD biosciences	746895
BV785	CD107a	BioLegend	328644
Spark Blue 550	CD4	BioLegend	344656
PerCP	CD8a	BioLegend	301030
PE Cy5	CTLA4	BD biosciences	555854
PE Cy5.5	CD45RA	ThermoFisher	MHCD45RA18
APC Fire 810	CD38	BioLegend	303550
Intracellular			
BUV615	CD154	BD biosciences	751177
BV480	Ki67	BD biosciences	566109
BV711	IL13	BD biosciences	564288
BB700	FoxP3	BD biosciences	566526
PE	IL21	BioLegend	513004
PE Dazzle 594	IL4	BioLegend	500832
PE Cy7	IFNγ	BioLegend	506518
APC	Granzyme B	ThermoFisher	MHGB05
APC-R700	IL17A	BD biosciences	565163
APC Fire750	IL2	BioLegend	500352

Table S4. COVID-19 study participant characteristics

Code	Acute illness status	Sex	Race/ Ethnicity	Age (years)	Days hospitalized for COVID19	Scale	Comorbidities	**Treatment**/ Routine medications/ Other	Vaccinated before collection
P01	Inpatient	Male	Black	52	5	Conventional O2	Obesity		Yes
P03		Female	Black	45.4	7		Borderline HTN		No
P05		Male	Black	47.5	4		Diabetes, asthma, obesity	ICS/LABA	No
P06		Male	White	49.2	6		Chronic neurologic disorder	Ocrelizumab, InCS	No
P30		Male	White	28.8	15		Leukemia, asthma, surgical asplenia	**Dexamethasone**, **remdesivir**, ICS	Yes
P17		Female	Black	61.7	12	High flow O2	Chronic cardiac, pulmonary, and kidney disease, obesity	Dialysis	No
P20		Female	Asian	52.7	8		Asthma	**convalescent plasma**, **prednisone**, ICS	Yes
P38		Male	Hispanic	40.5	13			**remdesivir**	No
P09		Female	Black	56.2	13	Invasive O2	Graves disease, obesity	InCS	No
P41		Male	Asian	21.4	4		Chronic hematologic disease	**Ionotropes, remdesivir**, renal replacement therapy, lisinopril	Yes
P02		Male	Black	54.5	8	No O2	Obesity		No
P04		Female	Black	45.3	4		Obesity	Ibuprofen, Smoker	No
P07		Male	White	57.6	2		HIV	Bictegravir/FTC/TAF, ICS	Yes
P08		Female	Black	72.4	5		Diabetes	lisinopril	Yes
P11	Outpatient	Female	White	42		Minimal symptoms	Chronic neurologic disorder		No
P14		Male	White	54.4			Cancer, HIV	valacyclovir, ABC/3TC/ dolutegravir, vape	Yes
P28		Male	White	52.6			Asthma	InCS	Yes
P32		Female	Hispanic	40			Obesity		Yes
P13		Female	White	56.3		Limited activity	Cancer		Yes
P23		Female	Black	46.4					Yes
P25		Male	White	60.2					No
P33		Male	Asian	36.2					No
P34		Male	White	39.3					No
P35		Male	Native Hawaiian	49.1				losartan	Yes
P36		Female	Hispanic	40.3			Diabetes	losartan	Yes
P37		Male	Hispanic	32.9					No
P39		Female	Multiple	44.6					Yes
P40		Female	Hispanic	46			Mild liver disease, cancer, obesity		Yes
P42		Male	Hispanic	20.1					No

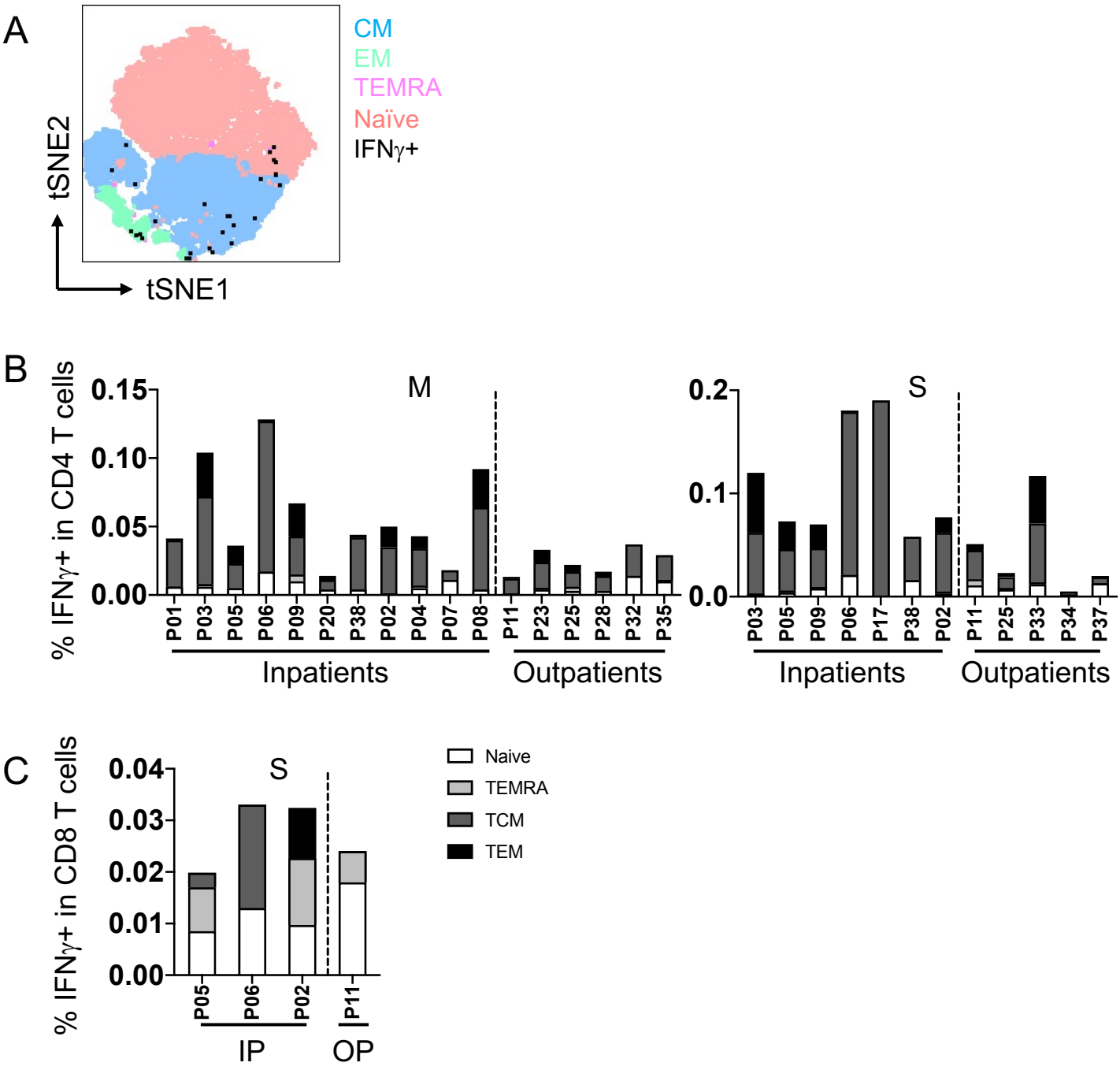
Abbreviations:
ICS= inhaled corticosteroid,
LABA=long acting beta2-adrenergic agonist,
InCS=intranasal corticosteroids
HTN=hypertension
ACE=angiotensin converting enzyme
ABC=abacavir
3TC=lamivudine
FTC=emtricitabine
TAF=tenofovir alafenamide

Fig S1


A
T cells
CD4/8
IFNγ+
Live singlets
SSC
CD3
CD8
CD4
IFNγ
CD3
B
Ab MFI to SARS-CoV-2 S
0.13
IP
OP
C
M
N
P = 0.0007
R = 0.73
D
APCs
B cell excluded
Live singlets
HLA-DR
CD3
CD11b
CD19
pDC/cDC
DCs
NK excluded
CD11c
CD303
CD16
CD14
HLA-DR
CD56
cDC1
cDC2
CD141
CLEC9a
HLA-DR
CD1c
E
CD4:CD8 ratio
IP-O2
IP-No O2
OP
HD
F
% of DC subsets in HLA-II+ non-lymphocytes
cDC1
cDC2
pDC
Monocytes
COVID19+
HD
IP, O2
Outpatients
Healthy donors

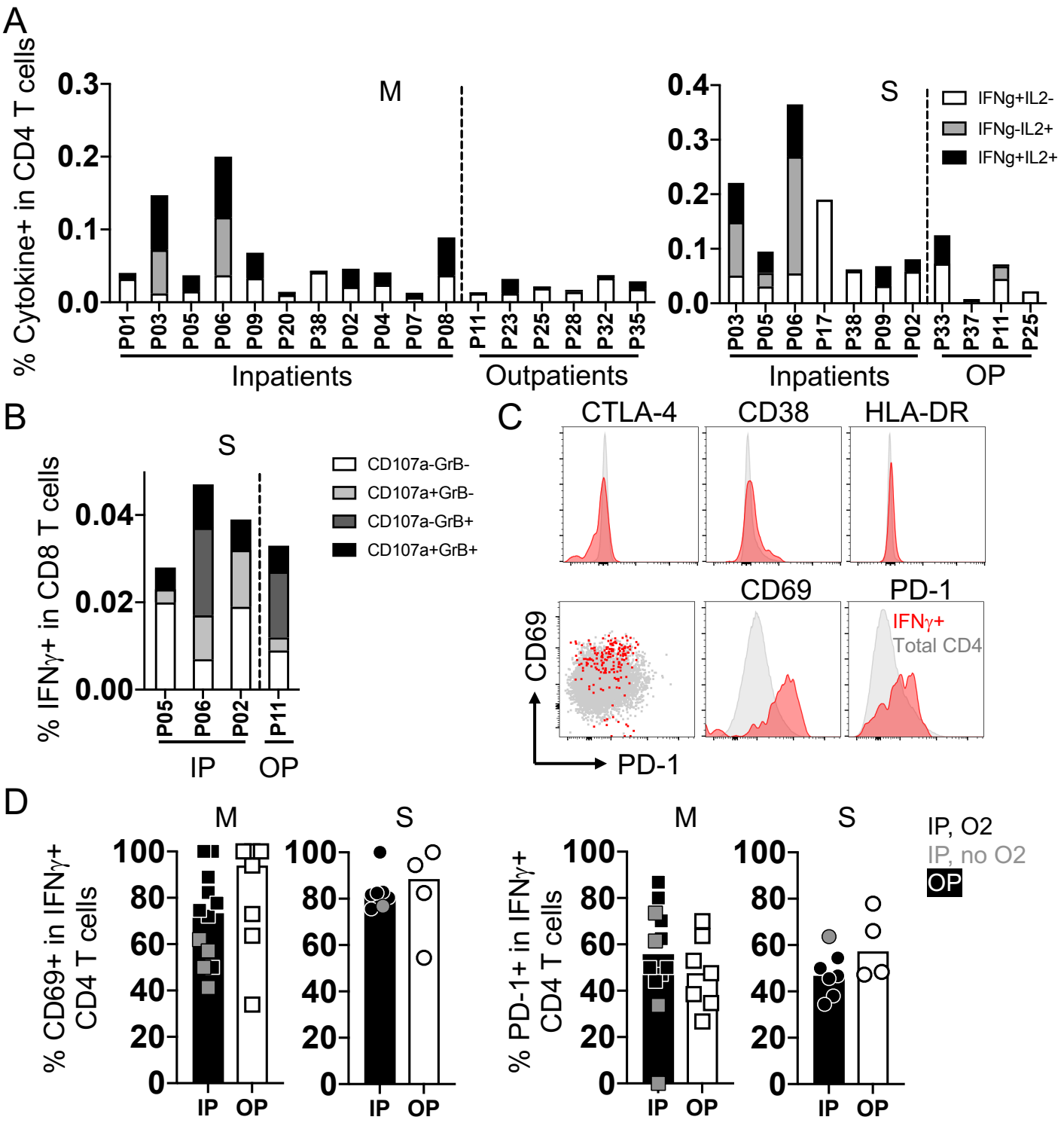
Supplemental Figure 1. Investigation of antigen presenting cells (APCs) and major T cell subsets. A. Gating strategy to characterize CD4 and CD8 T cells and antigen-specific T cells by expression of IFNγ. **B.** Antibodies to SARS-CoV-2 spike glycoprotein at 12-months post-infection. Participants vaccinated before blood collection were excluded. **C**. Correlation of T cell responses to SARS-CoV-2 N and M. P value in the plot indicates significance by Spearman rank correlation. R value in the plot indicates coefficient. **D.** Gating strategy to characterize the classical APCs in PBMCs. **E.** CD4:CD8 ratio among groups were similar. Red dots represent inpatients with oxygen supplementation, pink dots represent inpatients without oxygen supplementation, open dots represent outpatients, grey dots represent healthy donors, respectively. **F.** Frequencies of APC subsets including cDC1 and 2, plasmacytoid DCs, and monocytes in HLA-II+CD19- non-lymphocytes between COVID-19 patients and healthy donors.

Fig S2



Supplemental Figure 2. Memory phenotype characterization of SARS-CoV-2-specific T cell responses. **A.** tSNE using memory markers CCR7, CD45RA, CD62L, CD27, and CD28 to show that IFNγ+ CD4 T cells were mainly CCR7+CD45RA-CD28+CD27+, indicating central memory phenotype. **B.** Similar to N-specific CD4 T cell memory phenotypes, M and S-specific CD4 T cells were mainly central memory. **C.** Similar to N-specific CD8 T cell memory phenotypes, S-specific CD8 T cells exhibited diverse memory phenotypes.

Fig S3



Supplemental Figure 3. Polyfunctionality, cytotoxicity, and activation of SARS-CoV-2-specific CD4 or CD8 T cells. A. Polyfunctionality of CD4 T cell responses to SARS-CoV-2 M and S proteins measured by IL2 and IFNγ. **B.** Cytotoxicity of IFNγ+ CD8 T cells to SARS-CoV-2 S protein measured by expression of intracellular Granzyme B and membrane CD107a. **C.** Histograms of the expression of T cell activation markers CTLA-4, CD38, HLA-DR, CD69, and PD-1, and a dot plot of expression of CD69 and PD-1 in parent and IFNγ+ CD4 T cells. Red indicates IFNγ+ CD4 T cells; grey indicates parent CD4 T cells. **D.** The frequencies of CD69 and PD-1 in SARS-CoV-2 M and S-specific IFNγ+ CD4 T cells in each patient group. Grey dots in the inpatient group represent inpatients without oxygen supplementation.