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Supplemental Information

PPARγ Cistrome Repression during Activation of Lung Monocyte-Macrophages in Severe COVID-19

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Transparent Methods

Transcriptomes from public datasets

We obtained transcriptomes from COVID-19 lung biopsies from dataset GSE147507 in the Gene Expression Omnibus database (**https://www.biorxiv.org/content/10.1101/2020.03.24.004655v1**) and now published in Cell on 28th May 2020 (https://www.sciencedirect.com/science/article/pii/S009286742030489X?via%3Dihub) (Blanco-Melo et al., 2020, p.).

This dataset comprised human biological samples: lung biopsies from one male (age 72) and one female (age 60), used as biological replicates. Additionally, lung samples from a single male (COVID-19 deceased, age 74) patient were processed in technical replicates. These experiments had been performed with the approval of the institutional review board at the Icahn School of Medicine at Mount Sinai under protocol HS#12-00145. Samples were sequenced on NextSeq 500 technology (Illumina , CA) after the selection of a polyA RNA library using the TruSeq RNA Library Prep Kit v2 (Illumina, CA); the library was prepared from total RNA extracted using the RNeasy Mini Kit (Qiagen). Raw sequencing reads were aligned to the human genome (hg19) using the RNA-Seq Alignment App (v2.0.1). We then used the matrix of raw count data to perform the bioinformatics analyses described below.

The GSE150316 dataset had been prepared from distinct tissues from 5 COVID-19 patients and 5 healthy donors via RNAseq sequencing; samples from COVID-19 patients were processed in triplicate. Sequencing was performed on an Illumina NextSeq500 instrument after library preparation with the Smarter Stranded Total RNA-Seq kit v2 (634413, Illumina) starting from 10 ng of RNA (FFPE slides) extracted with the FormaPure Total nucleic acid extraction kit (C16675, Beckman Coulter).

Transcriptome of human tissues with immune cell sub-populations

Normalized transcriptomes from different human tissues were retrieved from the dataset GSE76340 on the GEO website. Samples in this dataset had been processed with different versions of the HumanHT-12 beadchip (Illumina, CA): versions V3 & V4 were annotated with the transcriptome platforms gpl6947 & gpl10558. These experiments comprised 166 human samples which were representative of hematopoietic and non-hematopoietic tissues present in the human body and were compatible with immune deconvolution analysis (Pont et al., 2016).

CHIP-sequencing from THP-1 cell line

Data from CHIP-sequencing experiments conducted using the THP-1 cell line were downloaded from the Cistrome Project website, in Bed and Bigwig format and aligned on version HG38 of the human genome. Promoter mapping was performed with BETA cistrome with a prediction +/-100 kb around transcription starting sites; promoter heatmaps were drawn with the deeptools application +/- 5 kb around transcription starting sites. CHIP-seq signals were visualized in the Integrative Genomics Viewer (IGV) standalone software after uploading the corresponding BigWig files.

Bioinformatics analyses

Bioinformatics analyses were performed in R software environment version 3.5.3. Functional network analysis was carried out using an immune gene-set enrichment analysis with the standalone software Cytoscape version 3.4.0. Raw counts of next-generation sequencing data were normalized with the algorithm 'variance stabilization transformation' (VST) from EdgeR. The cross-matrix between datasets, which comprised 170 transcriptome samples (Supplemental Table 3), was constructed by merging experiment sets based on their unique gene symbol identifiers. Cross-batch normalization was applied to the resulting matrix with the algorithm 'Combat' of the SVA R-package. Unsupervised principal component analyses were performed with FactoMineR. Transcriptome expression heatmaps were created with the Made4 and pheatmap R-packages, with default Pearson distances for small heatmaps and Euclidean distances for large ones. Immune landscape transcriptome analysis was performed with the xcell R-package and multi-testing linear model fit correction was applied to immune scores with the limma R-package. Gene-set enrichment analysis was performed on human lung biopsy samples with the standalone software GSEA version 4.0.3 using the MSigDB database, version 7.1.

Single-cell analysis of lung samples from healthy donors and patients with mild and severe COVID-19

In order to validate, at the single-cell level, the disruption observed in immune molecules in the transcriptome analysis of lung cells from COVID-19 patients, single-cell transcriptome (10x Genomics) data from bronchoalveolar lavage fluid samples were downloaded in H5 format from the dataset GSE145926. From this dataset, we created a merged matrix by aggregating a total of 90696 transcriptomes. This included six healthy donor samples—GSM4475048, GSM4475049, GSM4475050, GSM4475051, GSM4475052, GSM4475053—comprising 39900 transcriptomes, three mild COVID-19 samples—GSM4339769, GSM4339770, GSM4339772—comprising 9710 transcriptomes, and three severe COVID-19 samples—GSM4339771, GSM4339773, GSM4339774—comprising 41086 transcriptomes.

After canonical correlation and scaling, a total of 23742 features were analyzed, with 38738 anchors identified between samples. After variable feature selection with the VST algorithm, dimensionality reduction was carried out by principal component analysis on 2000 variable features (30 components) and UMAP dimensionality reduction of the 20 best components of the PCA. Single-cell analyses on the CD14+/CD16+ subset of cells were performed in Seurat and PPARγ gamma-dependent trajectories were constructed for the CD14+/CD16+ subset with the monocle2 R-package. The transparent bioinformatics code for all single-cell analyses in R software is provided in the supplemental data (supplemental bioinformatics code).

References

Blanco-Melo, D., Nilsson-Payant, B.E., Liu, W.-C., Uhl, S., Hoagland, D., Møller, R., Jordan, T.X., Oishi, K., Panis, M., Sachs, D., Wang, T.T., Schwartz, R.E., Lim, J.K., Albrecht, R.A., tenOever, B.R., 2020. Imbalanced Host Response to SARS-CoV-2 Drives Development of COVID-19. Cell 181, 1036-1045.e9. https://doi.org/10.1016/j.cell.2020.04.026

Pont, M.J., Honders, M.W., Kremer, A.N., van Kooten, C., Out, C., Hiemstra, P.S., de Boer, H.C., Jager, M.J., Schmelzer, E., Vries, R.G., Al Hinai, A.S., Kroes, W.G., Monajemi, R., Goeman, J.J., Böhringer, S., Marijt, W. a. F., Falkenburg, J.H.F., Griffioen, M., 2016. Microarray Gene Expression Analysis to Evaluate Cell Type Specific Expression of Targets Relevant for

Immunotherapy of Hematological Malignancies. PloS One 11, e0155165.
https://doi.org/10.1371/journal.pone.0155165

Supplemental figure legends

Supplemental Figure 1. Transcriptomic view of the immune response in lungs of COVID-19 patients compared to those of healthy donors, related to figure 1:

A. Genes highlighed by the gene-set enrichment analysis that are associated with the innate immune response; **B.** Genes highlighted by the gene-set enrichment analysis that are implicated both in the innate and adaptive immune responses; **C.** Genes highlighted by the gene-set enrichment analysis that are implicated in the adaptive immune response (for A to C: NES: normalized enrichment score, FDR: false discovery rate); **D.** Expression heatmap of immune-related genes that were upregulated in COVID-19 lung biopsy samples (Euclidean distances).

Supplemental Figure 2: **Single cell expression of T and NK lymphocyte markers in lung of COVID-19 patients as compared to Healthy donors, related to figure 1:**

UMAP projection of single cell expression split on lung from Healthy donors (control), from patient with COVID-19 mild and from patient with COVID-19 severe: respective expression of CD3E, CD8A (T lymphocyte) and NKG7 (Natural Killers)

Supplemental Figure 3. **Single cell expression of B lymphocyte and epthelial markers in lung of COVID-19 patients as compared to Healthy donors, related to figure 1:**

UMAP projection of single cell expression split on lung from Healthy donors (control), from patient with COVID-19 mild and from patient with COVID-19 severe: respective expression of MS4A1 alias CD20 (B lymphocyte) and KRT8 (epithelial cells)

Supplemental Figure 4. Immune score and immune characterization of COVID-19 lung samples, related to figure 2:

A. Volcanoplot of differentially expressed genes (DEG) in COVID-19 lung biopsies compared to healthy donor tissues; **B.** Expression heatmap of DEGs between COVID-19 lung biopsies and healthy tissues; **C.** Expression of the most upregulated marker, IFI6, in single cells from healthy donors, patients with mild COVID-19, and patients with severe COVID-19; **D.** Volcanoplot and heatmap of significant immune scores found in the immune infiltration of COVID-19 lung biopsies compared to those healthy donors; **E.** Immune deconvolution of the transcriptomes of COVID-19 and healthy donor lung biopsies via unsupervised principal component analysis (p-value: group stratification by Pearson correlation along the first principal axis**)**

Supplemental Figure 5: Repression of mitosis/cell cycle, stem cell and heme metabolism in COVID-19 lung biopsy as compared to healthy donor ones, related to figure 1:

(NES: normalized enrichment score, FDR: false discovery rate)

Supplemental Figure 6: Single cell expression of macrophages M1 and M2 markers in lung of COVID-19 patients as compared to Healthy donors, related to figure 3:

UMAP projection of single cell expression split on lung from Healthy donors (control), from patient with COVID-19 mild and from patient with COVID-19 severe: respective expression of CD68 for M1 macrophages and CD163 for M2 macrophages

Supplemental Figure 7: **Workflow procedure of Batch cross normalization between transcriptome datasets used for immune deconvolution of COVID-19 lung biopsy, related to figure 3:**

Cross transcriptome matrix from two datasets with three platforms was built on unique gene symbol, ComBat batch normalization was applied to the matrix to correct batch error

Supplemental Figure 8: **Unsupervised principal component analysis performed with immune induced signature according to the batches used to build the transcriptome cross dataset matrix, related to figure 3**

(respective batches merged during microarray analysis B1: batch1, B2: batch2, B3: batch3)

Supplemental Figure 9: Deregulation of inhibitory immune checkpoints in COVID-19 lung samples, related to figure 1:

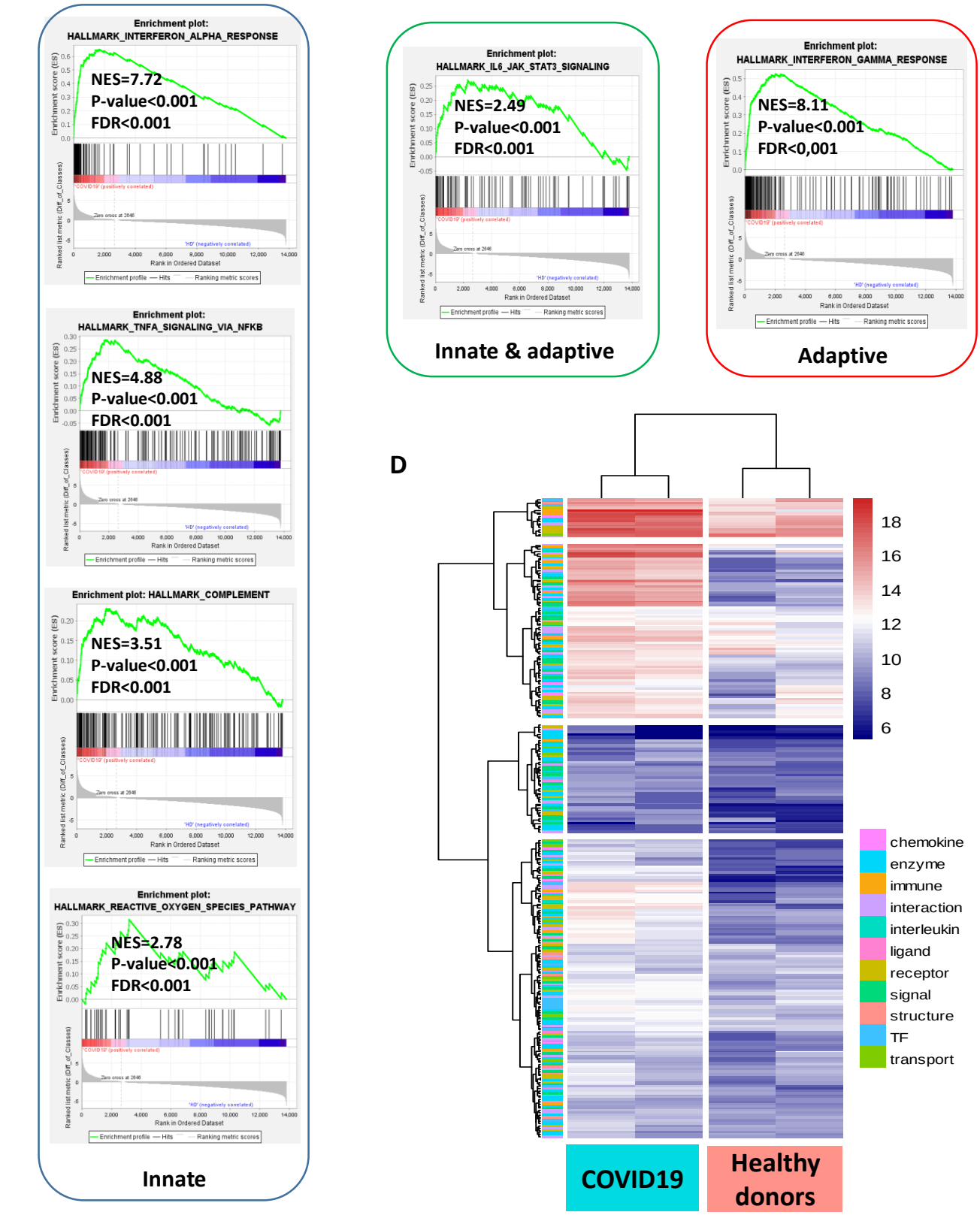
A. Transcriptome expression heatmap of inhibitory immune checkpoints expressed in COVID-19 lung samples compared to those from healthy donors; **B-D.** Single-cell expression (bronchoalveolar lavage fluid) dotplots of inhibitory immune checkpoint markers by patient of origin: HD, mild COVID-19, and severe COVID-19 (percent: percent of cells expressing each marker, expression level: color intensity), **C**. UMAP representation of single-cell transcriptome (bronchoalveolar lavage fluid) expression data from HDs and patients with mild or severe COVID-19 for CD47 and **D**. LGALS9; **E**. Expression heatmap of stimulatory immune checkpoints expressed in COVID-19 lung samples compared to healthy donors; **F.** Single-cell expression (bronchoalveolar lavage fluid) dotplots of stimulatory immune checkpoints markers by patient of origin: HD, mild COVID-19, and severe COVID-19 (percent: percent of cells expressing each marker, expression level: color intensity), **G.** UMAP representation of single-cell transcriptome (bronchoalveolar lavage fluid) expression data for CD48 from HDs and patients with mild or severe COVID-19.

Supplemental Figure 10: Single cell expression of inhibitory immune checkpoints in lung of COVID-19 patients as compared to Healthy donors, related to figure 1:

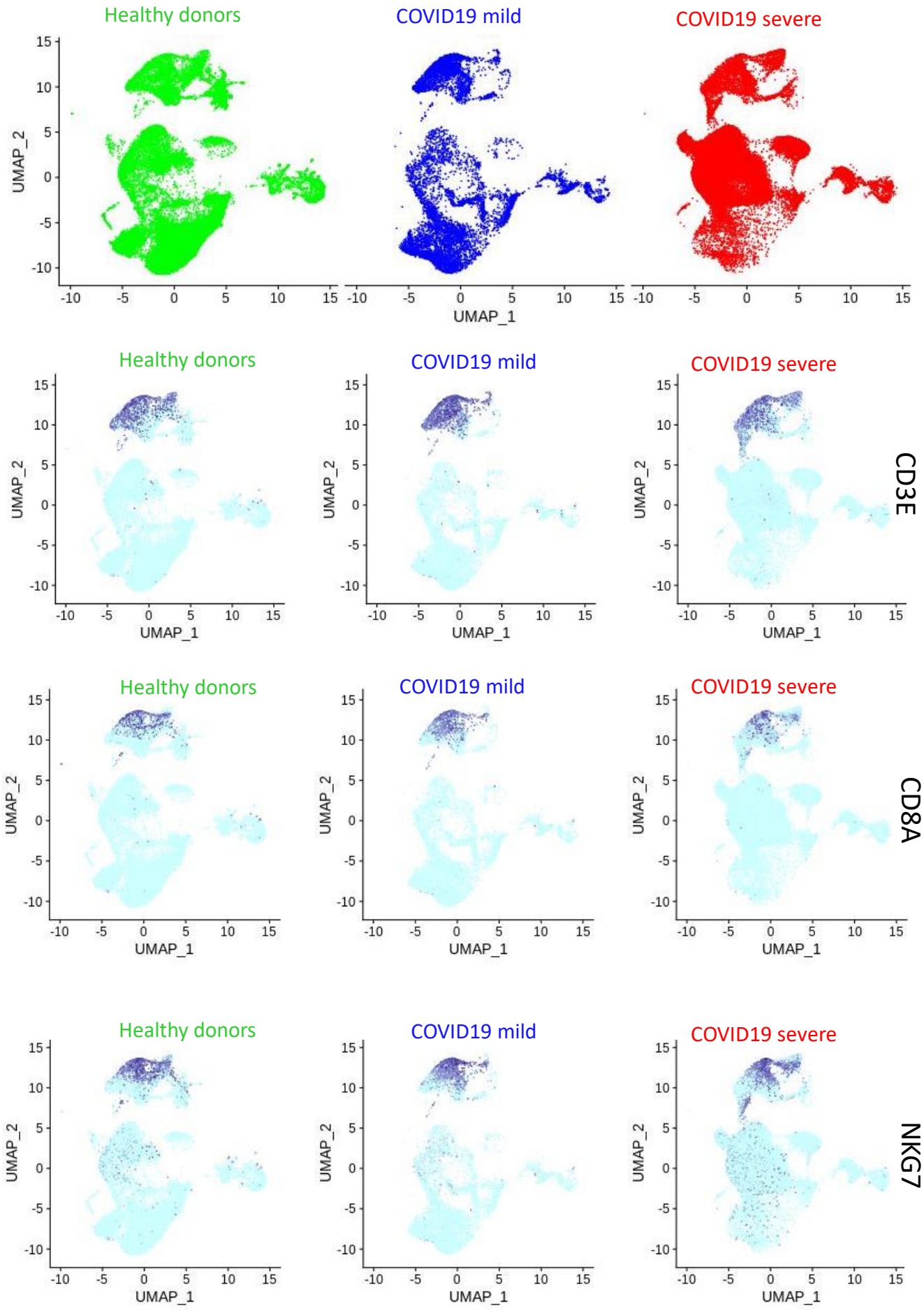
UMAP projection of single cell expression split on lung from Healthy donors (control), from patient with COVID-19 mild and from patient with COVID-19 severe: respective expression of HAVCR2, IDO1, CD274

Supplemental Figure 11. Single cell expression of stimulatory immune checkpoints in lung of COVID-19 patients as compared to Healthy donors, related to figure 1:

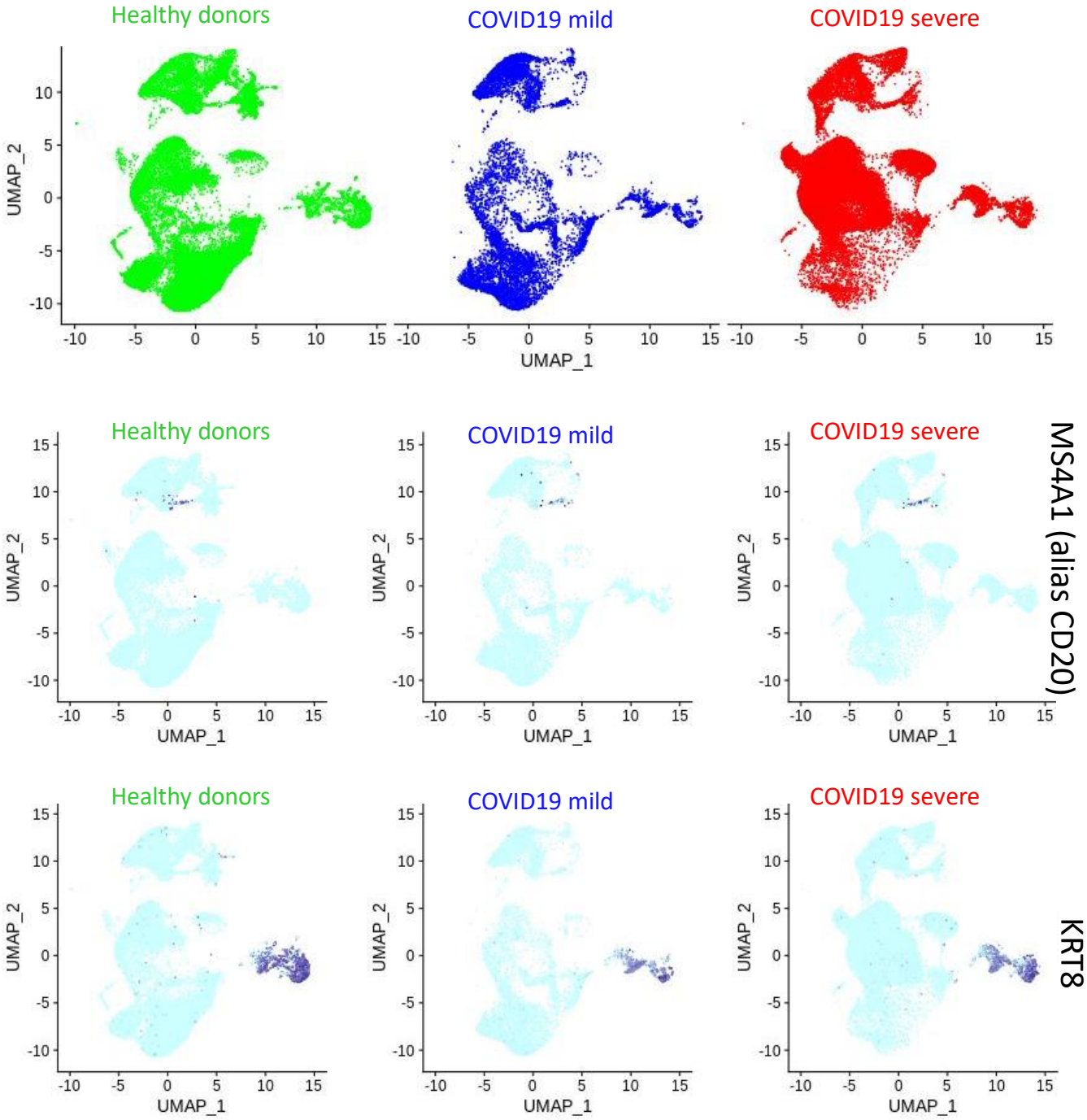
UMAP projection of single cell expression split on lung from Healthy donors (control), from patient with COVID-19 mild and from patient with COVID-19 severe: respective expression of CD40.



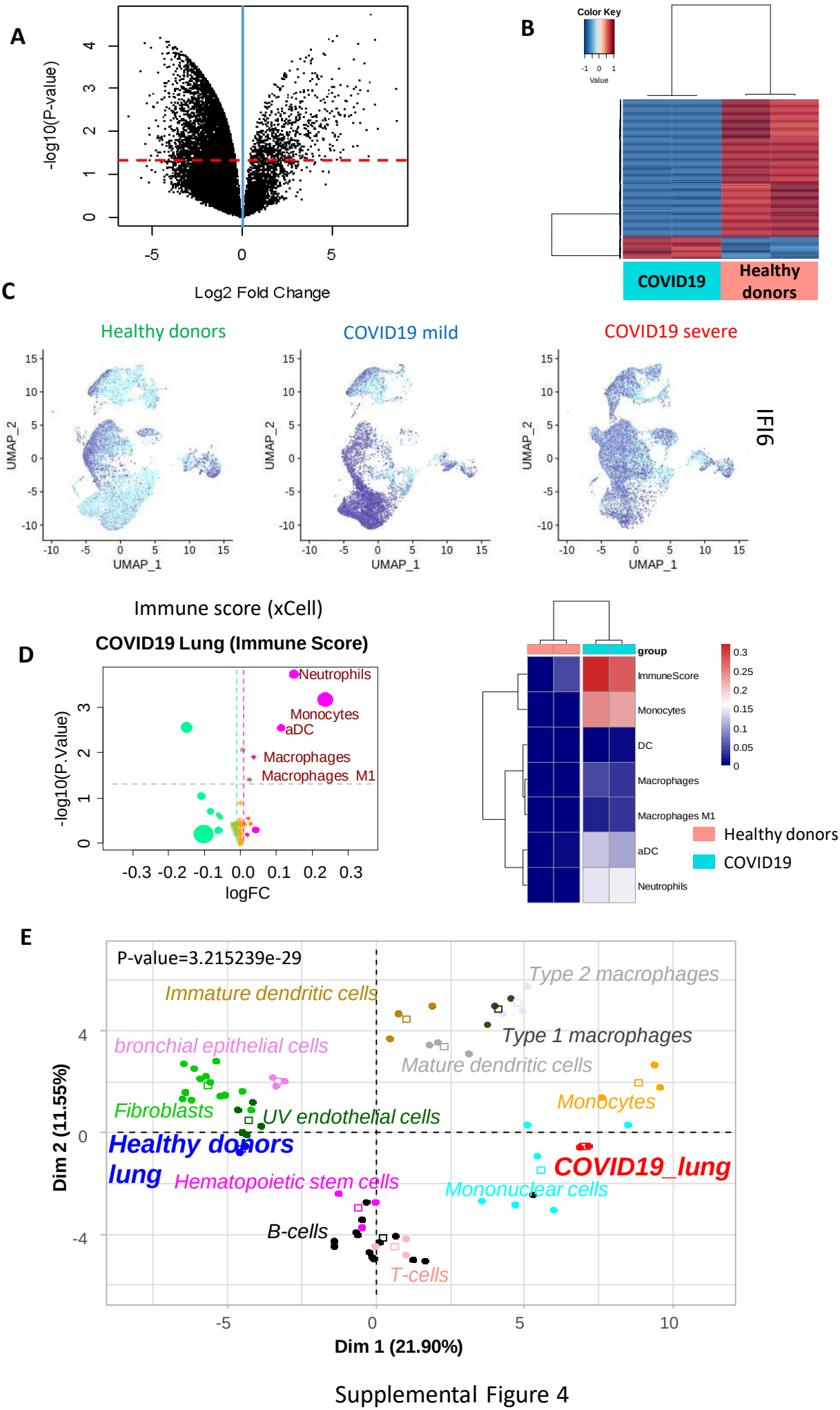
Supplemental Figure 1



Supplemental Figure 2

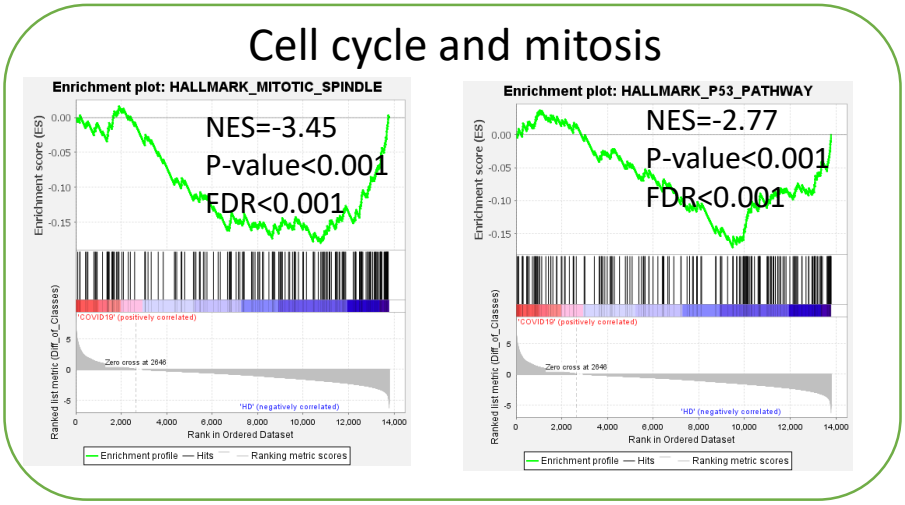


Supplemental Figure 3



Supplemental Figure 4

A



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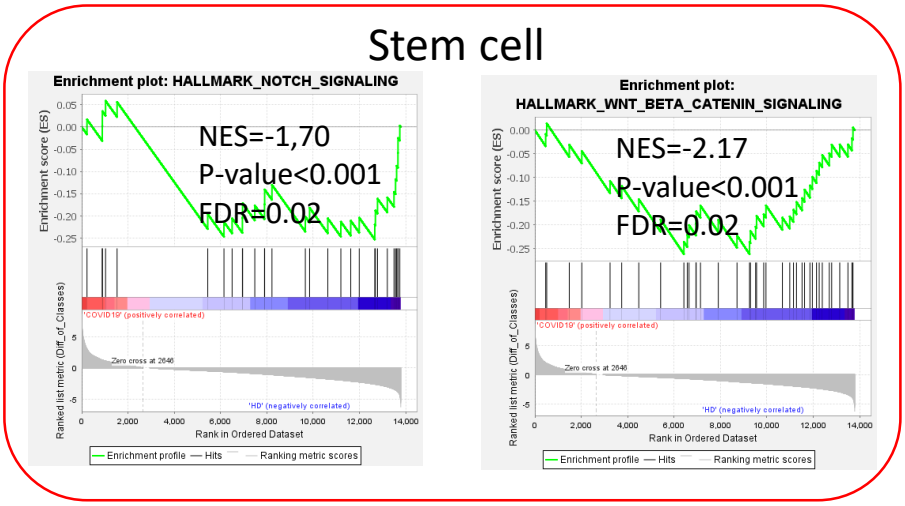

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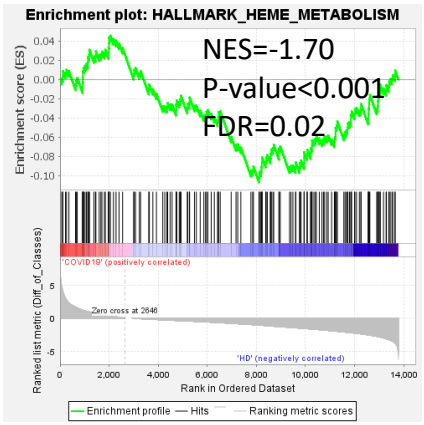
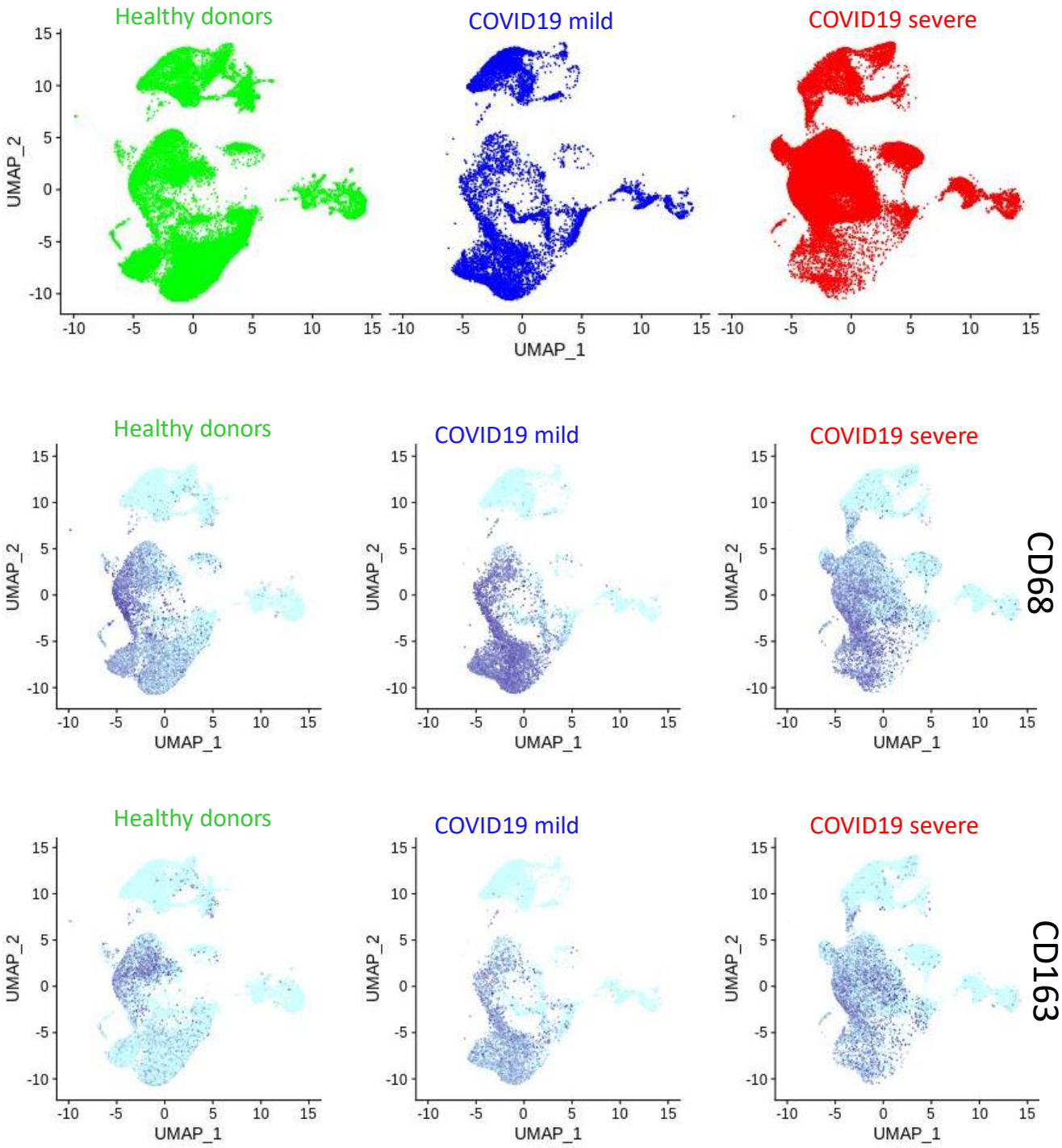
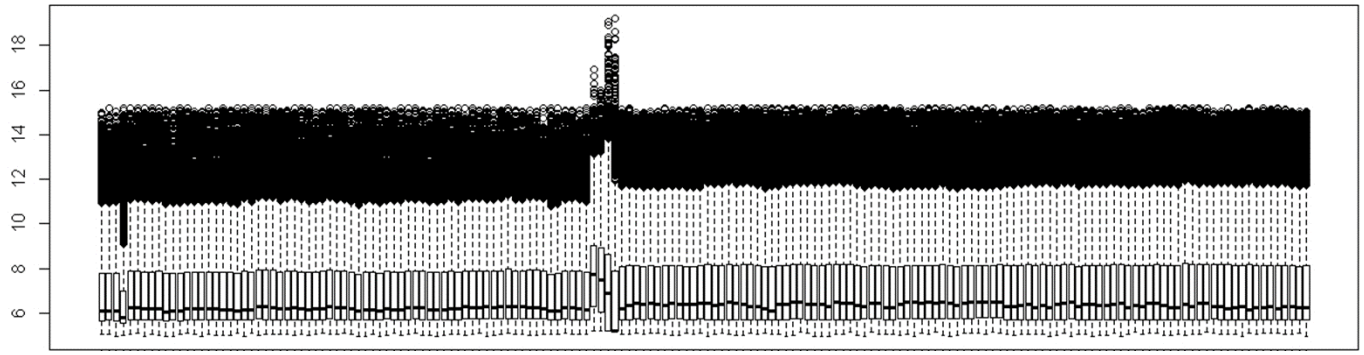


Supplemental Figure 5

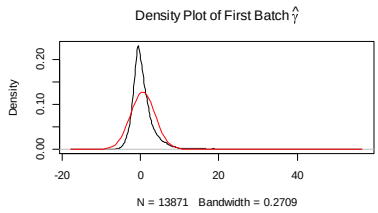


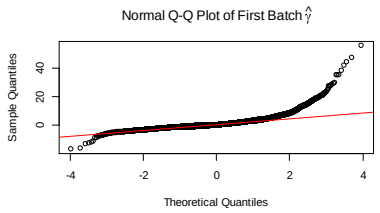
Supplemental Figure 6

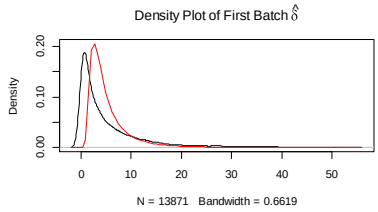
Three dataset expression matrix before batch normalization

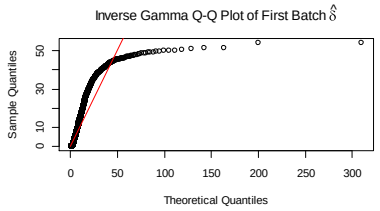


Combat
Cross
Normalization

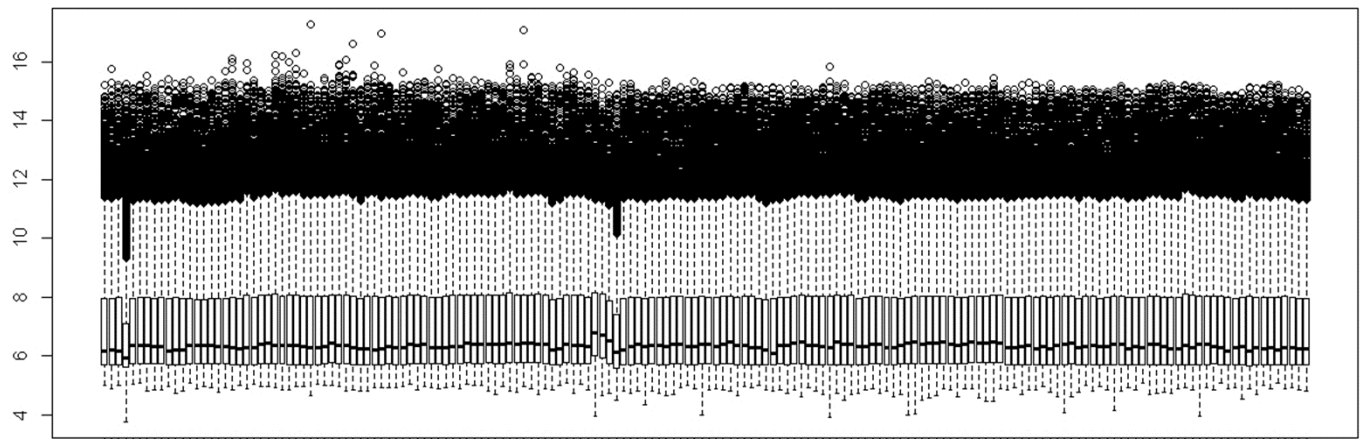




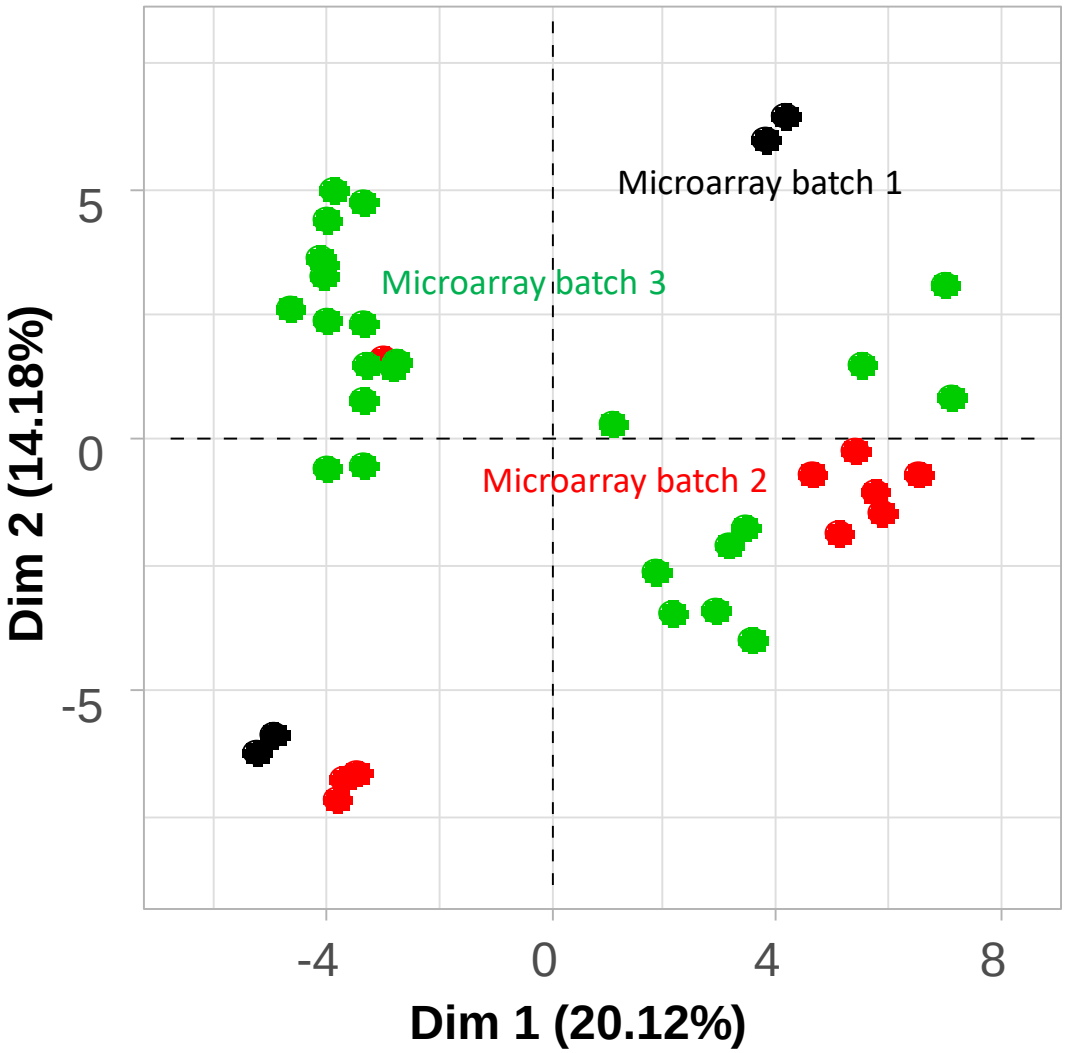




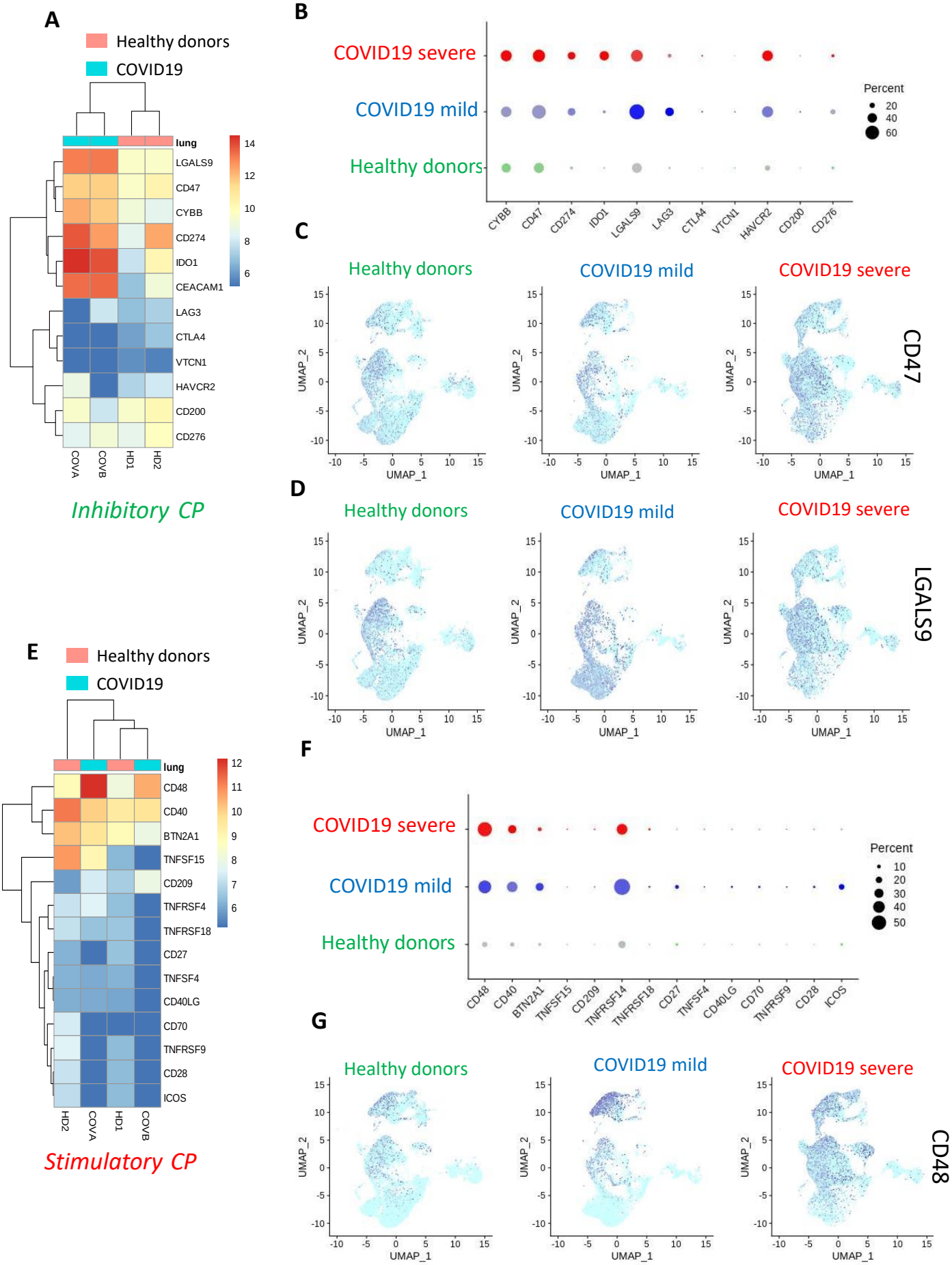
Three dataset expression matrix after batch normalization



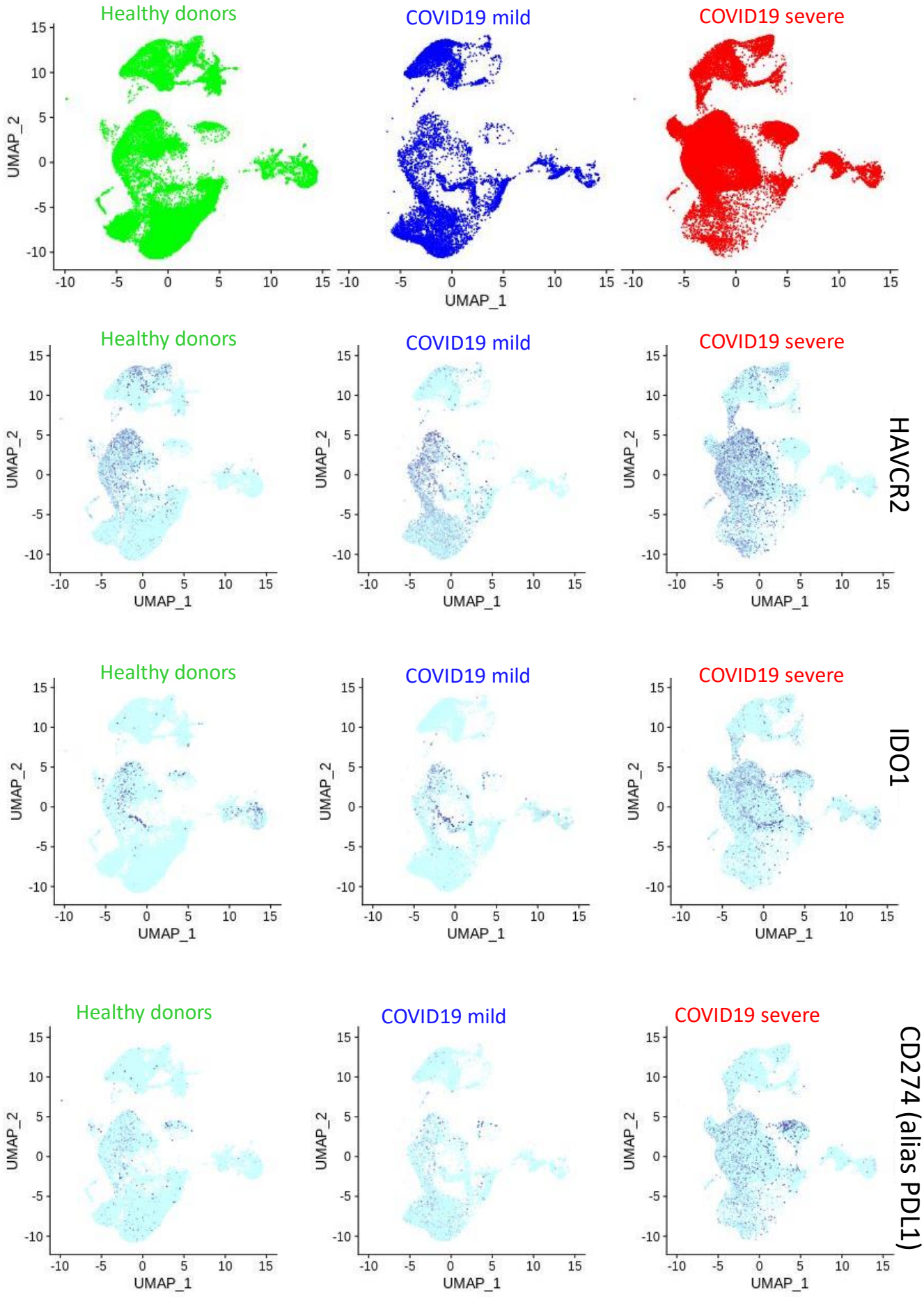
Supplemental Figure 7



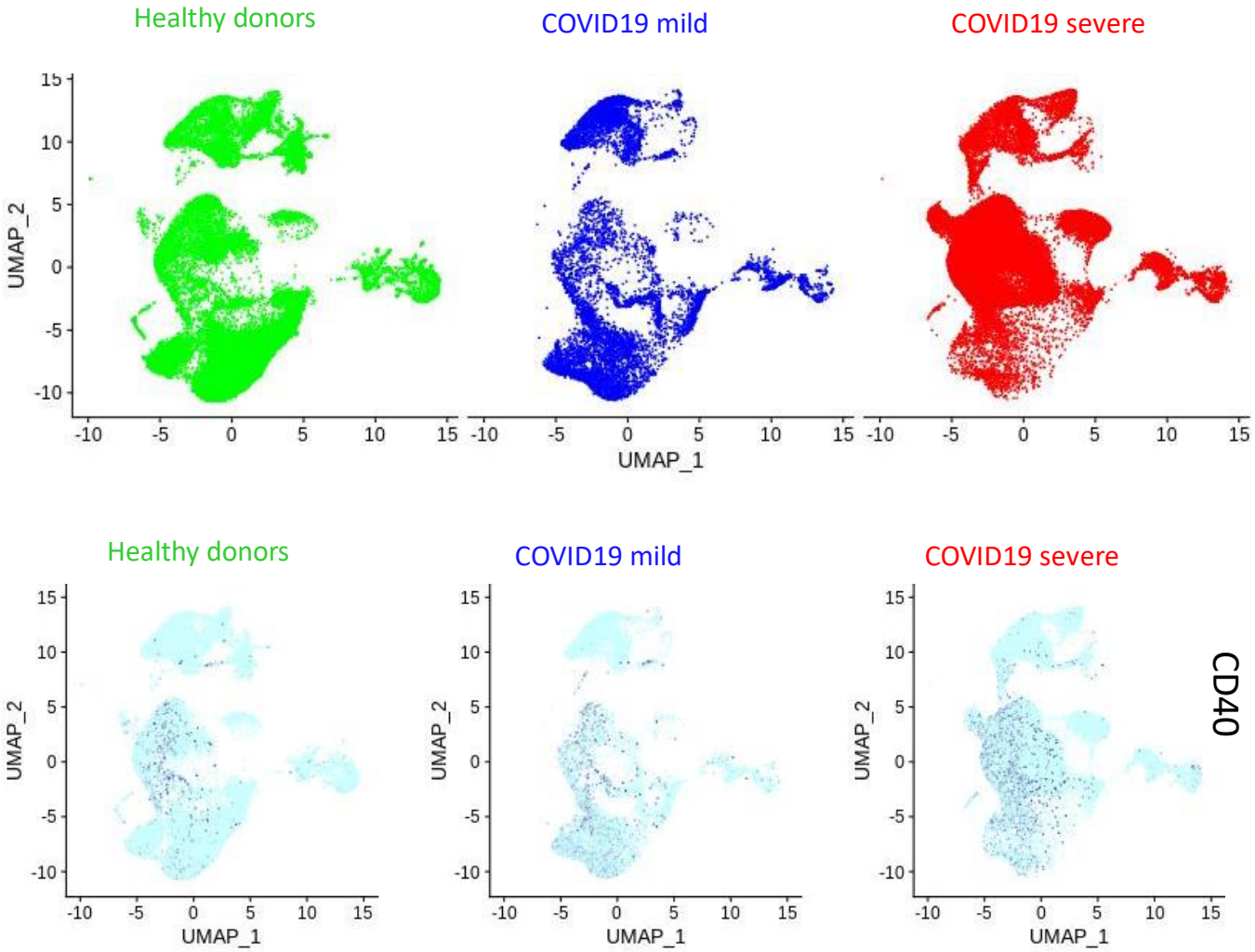
Supplemental Figure 8



Supplemental Figure 9



Supplemental Figure 10



Supplemental Figure 11

Supplemental Tables:

Supplemental Table 1: list of differential expressed genes found to be up regulated in COVID-19 lung biopsy transcriptome as compared to healthy donor ones, related to figure 1

gene symbol	logFC	AveExpr	t	P.Value	adj.P.Val	B
IFI6	7.1776	13.6855	62.6608	0.0000	0.0416	2.8234
DAPP1	5.3198	9.5271	40.7539	0.0001	0.0416	2.4574
MX1	4.8482	12.2353	38.6539	0.0001	0.0416	2.3942
CLEC4E	7.4028	11.3749	37.9561	0.0001	0.0416	2.3713
CASP5	5.0590	8.6360	37.1177	0.0001	0.0416	2.3426
FFAR2	6.4971	10.1686	35.2980	0.0001	0.0416	2.2748
RAC2	3.8602	11.8497	31.1533	0.0001	0.0416	2.0869
TREM1	4.5248	11.1755	28.9204	0.0002	0.0416	1.9616
TNFSF10	4.5746	12.1425	28.7743	0.0002	0.0416	1.9527
TREML3P	3.7333	7.7467	27.8337	0.0002	0.0416	1.8931
LGALS9	3.5443	11.3215	26.9698	0.0002	0.0416	1.8346
CXCL16	3.2593	11.6221	26.7020	0.0002	0.0416	1.8157
CYP19A1	3.9088	7.3177	26.6198	0.0002	0.0416	1.8099
ALOX5AP	6.2144	12.7068	26.0076	0.0002	0.0416	1.7650
PTK2B	3.8377	11.0414	25.2922	0.0002	0.0416	1.7098
HCK	2.7985	10.7928	24.9444	0.0002	0.0416	1.6819
ZC3HAV1	3.4884	11.5295	24.8897	0.0002	0.0416	1.6775
PLAC8	3.8467	9.6419	24.1251	0.0003	0.0416	1.6132
ST20	6.8379	9.7565	23.9457	0.0003	0.0416	1.5975
FDCSP	5.4337	8.0010	21.9213	0.0003	0.0416	1.4047
TRIM21	3.0901	10.4027	21.6234	0.0004	0.0416	1.3736
TLE4	2.6830	9.6468	21.1623	0.0004	0.0416	1.3240
BASP1	4.0718	11.5338	20.1227	0.0004	0.0416	1.2048
ZBP1	3.4269	7.9723	20.0985	0.0004	0.0416	1.2019
KLK10	3.9032	8.8989	20.0770	0.0004	0.0416	1.1993
WIPF1	2.3939	10.4371	19.7917	0.0005	0.0416	1.1646
METTL7B	2.3545	6.6711	19.6145	0.0005	0.0416	1.1426
CERS6	2.4488	8.0154	19.2357	0.0005	0.0416	1.0945
HSH2D	4.2234	8.9230	19.0770	0.0005	0.0416	1.0739
S100A11	4.4486	14.6746	18.8674	0.0005	0.0416	1.0462
STAT2	2.3554	10.8830	18.7197	0.0005	0.0416	1.0264
TAOK3	3.1629	10.2652	18.5327	0.0005	0.0416	1.0010
TRIM38	4.2132	10.8972	18.4762	0.0005	0.0416	0.9932
PLP2	2.4331	11.3802	18.4719	0.0005	0.0416	0.9926
MSMO1	2.1889	9.7341	18.1669	0.0006	0.0416	0.9500
C19ORF66	3.8901	10.8223	17.9042	0.0006	0.0416	0.9123
MXD1	4.9895	11.6460	17.9034	0.0006	0.0416	0.9122
PADI2	4.2443	8.9215	17.8949	0.0006	0.0416	0.9109
CD38	2.2730	7.4678	17.7960	0.0006	0.0416	0.8965

TET2	2.3199	9.0819	17.6588	0.0006	0.0416	0.8763
P2RY13	6.5491	9.5865	17.5438	0.0006	0.0416	0.8592
TMEM71	3.8052	8.8363	17.1109	0.0007	0.0416	0.7931
FCER1G	7.1125	14.1999	16.9234	0.0007	0.0416	0.7636
SH3BGRL3	2.9494	13.5637	16.7161	0.0007	0.0416	0.7305
LCP1	4.1459	12.8424	16.2003	0.0008	0.0416	0.6452
YIPF1	1.8240	8.9549	16.0496	0.0008	0.0416	0.6195
HP	1.8822	7.6909	15.8171	0.0008	0.0416	0.5792
LILRA6	5.4992	9.7715	15.7799	0.0008	0.0416	0.5726
EIF2AK2	5.8701	10.5396	15.7027	0.0009	0.0416	0.5590
TNFSF8	2.2703	7.9982	15.5407	0.0009	0.0416	0.5300
STAP1	5.0370	8.4880	15.3400	0.0009	0.0416	0.4936
HPGDS	1.9920	8.2100	15.2378	0.0009	0.0416	0.4747
BCL2A1	6.3646	12.8711	15.1775	0.0009	0.0416	0.4635
SP140	5.1011	9.3682	15.1710	0.0009	0.0416	0.4623
GSK3A	2.0767	9.9251	15.0107	0.0010	0.0416	0.4321
OAS1	6.2611	11.2966	14.7159	0.0010	0.0416	0.3755
SELL	8.5898	12.3057	14.6870	0.0010	0.0416	0.3699
SLC9B2	2.1402	9.2398	14.6463	0.0010	0.0416	0.3619
PLEK	6.5675	12.6105	14.5396	0.0011	0.0418	0.3408
DHRS9	2.0806	7.6688	14.5022	0.0011	0.0418	0.3334
S100P	3.9222	9.9067	14.5012	0.0011	0.0418	0.3332
MMP8	4.8508	8.4352	14.4707	0.0011	0.0419	0.3271
SERPINA1	3.6621	13.6439	14.3424	0.0011	0.0420	0.3014
RTP4	3.4262	8.7756	14.3371	0.0011	0.0420	0.3003
KCNH7	3.8933	7.7884	14.2806	0.0011	0.0421	0.2888
CCL8	7.0072	11.9994	14.0218	0.0012	0.0428	0.2355
UBE2L6	3.2563	11.7618	13.9081	0.0012	0.0430	0.2117
CASP4	3.4312	12.2297	13.8508	0.0012	0.0430	0.1995
GBP1P1	3.0089	8.5281	13.6575	0.0013	0.0433	0.1581
IFITM1	5.0111	13.7490	13.6058	0.0013	0.0433	0.1469
ANXA3	1.6882	10.8230	13.4706	0.0013	0.0436	0.1173
SERF2	2.8845	12.6592	13.3953	0.0013	0.0437	0.1006
IFIT1	6.4460	11.5361	13.3266	0.0013	0.0437	0.0853
RNASE2	4.8415	7.6583	13.3042	0.0014	0.0438	0.0803
CXORF21	3.7354	7.9206	13.1232	0.0014	0.0442	0.0393
PFN1	2.5686	14.7434	13.1121	0.0014	0.0442	0.0367
IFIT3	6.0584	12.4936	12.9875	0.0014	0.0445	0.0080
FAM49A	1.8188	9.4999	12.9724	0.0014	0.0445	0.0045
POGLUT1	1.5187	8.4467	12.9673	0.0014	0.0445	0.0034
DOK3	4.0627	9.5715	12.8563	0.0015	0.0451	-0.0226
CCL11	6.0886	10.9454	12.8467	0.0015	0.0451	-0.0248
ISG15	5.3753	12.6734	12.8325	0.0015	0.0451	-0.0282
C1ORF194	2.0250	6.9651	12.7017	0.0015	0.0457	-0.0592
LYRM1	2.0250	9.9753	12.5245	0.0016	0.0457	-0.1019

CPNE8	1.5333	9.2754	12.5214	0.0016	0.0457	-0.1026
DDX60L	5.1716	10.7959	12.5189	0.0016	0.0457	-0.1032
WAS	4.7416	9.4159	12.5157	0.0016	0.0457	-0.1040
BCL2L14	3.4702	7.6795	12.4910	0.0016	0.0457	-0.1100
PSME3	2.5692	11.4849	12.4163	0.0016	0.0460	-0.1283
CCL19	4.1790	9.5531	12.4143	0.0016	0.0460	-0.1288
TIMM23	2.8022	10.1641	12.3870	0.0016	0.0461	-0.1355
CISD2	1.9337	8.6465	12.3203	0.0017	0.0464	-0.1521
NFKBID	3.0303	9.3245	12.0344	0.0018	0.0479	-0.2242
CCL7	4.5305	8.3294	12.0065	0.0018	0.0479	-0.2313
GPR84	5.7629	10.1132	11.7846	0.0019	0.0486	-0.2890
CACNA1A	4.3593	8.1171	11.7675	0.0019	0.0486	-0.2936
EIF1B	2.5061	11.4329	11.5612	0.0020	0.0495	-0.3485
C2CD4B	1.6818	9.4010	11.5384	0.0020	0.0495	-0.3547
NME1	2.4402	9.5301	11.5345	0.0020	0.0495	-0.3557
GAPT	5.0651	8.6691	11.4180	0.0021	0.0496	-0.3875
MX2	5.8224	11.3090	11.4094	0.0021	0.0496	-0.3898
CYSTM1	3.2616	12.3467	11.4046	0.0021	0.0496	-0.3911
HESX1	3.3577	7.3091	11.3742	0.0021	0.0496	-0.3995
ABHD16A	1.2973	9.4706	11.3154	0.0021	0.0496	-0.4157
NBN	4.5922	10.9019	11.2639	0.0021	0.0497	-0.4300
RGL4	3.2771	8.8751	11.2201	0.0022	0.0498	-0.4423
U2AF2	1.3388	10.9096	11.2121	0.0022	0.0498	-0.4445
PAK2	1.4921	10.7463	11.1938	0.0022	0.0498	-0.4496

Supplemental Table 2: limma score performed on immune score cell subpopulations of COVID-19 lung biopsy as compared to healthy donor ones, related to figure 3

cell populations	logFC	AveExpr	t	P.Value	adj.P.Val	B
Neutrophils	0.1488	0.0744	41.9348	0.0002	0.0121	1.1275
Monocytes	0.2360	0.1180	24.2226	0.0007	0.0223	-0.7054
Osteoblast	-0.1505	0.0865	-13.2767	0.0028	0.0475	-2.7148
aDC	0.1128	0.0599	13.1170	0.0028	0.0475	-2.7550
ImmuneScore	0.2760	0.1617	9.7578	0.0057	0.0761	-3.7348
DC	0.0064	0.0032	8.1319	0.0087	0.0969	-4.3321
Macrophages	0.0378	0.0213	6.9778	0.0123	0.1181	-4.8279
MicroenvironmentScore	0.2182	0.2119	5.2521	0.0235	0.1966	-5.7282
MacrophagesM1	0.0243	0.0146	4.1635	0.0391	0.2911	-6.4352
Pericytes	-0.1096	0.0603	-2.7570	0.0912	0.6108	-7.5848
Melanocytes	-0.0004	0.0002	-2.0301	0.1588	0.7562	-8.3090
mv Endothelial cells	-0.0837	0.0491	-1.7636	0.1994	0.7562	-8.5945
MSC	-0.0613	0.0307	-1.5870	0.2336	0.7562	-8.7872
Endothelial cells	-0.0548	0.0383	-1.4402	0.2675	0.7562	-8.9479
Plasma cells	0.0209	0.0152	1.3946	0.2791	0.7562	-8.9976
Neurons	-0.0016	0.0012	-1.2885	0.3086	0.7562	-9.1127
Smooth muscle	0.0283	0.0142	1.0903	0.3736	0.7562	-9.3223
CD8+ T-cells	-0.0193	0.0097	-1.0903	0.3736	0.7562	-9.3224
CD4+ T-cells	-0.0133	0.0067	-1.0903	0.3736	0.7562	-9.3224
CD4+ Tcm	-0.0112	0.0056	-1.0902	0.3737	0.7562	-9.3225
Basophils	0.0080	0.0040	1.0900	0.3737	0.7562	-9.3227
Megakaryocytes	-0.0061	0.0030	-1.0898	0.3738	0.7562	-9.3229
MacrophagesM2	-0.0047	0.0024	-1.0895	0.3739	0.7562	-9.3233
naive B-cells	-0.0033	0.0017	-1.0885	0.3743	0.7562	-9.3242
Tgd cells	0.0027	0.0014	1.0877	0.3746	0.7562	-9.3251
Keratinocytes	-0.0022	0.0011	-1.0863	0.3751	0.7562	-9.3265
CD4+ memory T-cells	-0.0022	0.0011	-1.0860	0.3752	0.7562	-9.3269
CD8+ Tem	-0.0016	0.0008	-1.0821	0.3766	0.7562	-9.3308
Adipocytes	0.0015	0.0007	1.0812	0.3770	0.7562	-9.3318
B-cells	0.0114	0.0059	1.0679	0.3819	0.7562	-9.3455
Mesangial cells	0.0009	0.0005	1.0677	0.3819	0.7562	-9.3456
Hepatocytes	0.0007	0.0004	1.0540	0.3871	0.7562	-9.3597
CD8+ naive T-cells	-0.0187	0.0172	-1.0419	0.3916	0.7562	-9.3720
Memory B-cells	0.0006	0.0003	1.0350	0.3943	0.7562	-9.3790
Mast cells	0.0063	0.0035	1.0331	0.3950	0.7562	-9.3809
Th2 cells	-0.0206	0.0120	-1.0030	0.4068	0.7571	-9.4112
StromaScore	-0.0578	0.0502	-0.9484	0.4291	0.7770	-9.4653
ly endothelial cells	-0.0113	0.0089	-0.8289	0.4821	0.8295	-9.5784

Chondrocytes	-0.0177	0.0142	-0.8273	0.4828	0.8295	-9.5799
iDC	0.0420	0.0531	0.7703	0.5103	0.8442	-9.6308
Myocytes	-0.0098	0.0088	-0.7577	0.5166	0.8442	-9.6418
Fibroblasts	-0.0622	0.0614	-0.7328	0.5292	0.8442	-9.6632
Platelets	-0.0002	0.0001	-0.6848	0.5542	0.8583	-9.7031
Epithelial cells	-0.0144	0.0157	-0.6670	0.5637	0.8583	-9.7174
Sebocytes	-0.0044	0.0053	-0.6383	0.5793	0.8625	-9.7400
HSC	-0.1026	0.1514	-0.5509	0.6291	0.8848	-9.8042
CD8+ Tcm	0.0032	0.0079	0.5413	0.6348	0.8848	-9.8108
Tregs	-0.0114	0.0172	-0.5206	0.6471	0.8848	-9.8248
CLP	-0.0023	0.0036	-0.5048	0.6567	0.8848	-9.8352
GMP	0.0198	0.0289	0.4988	0.6603	0.8848	-9.8390
Th1 cells	-0.0026	0.0091	-0.3123	0.7801	1.0000	-9.9392
pDC	0.0001	0.0003	0.2239	0.8406	1.0000	-9.9719
Class-switched memory B-cells	0.0002	0.0009	0.2108	0.8498	1.0000	-9.9758
MEP	0.0003	0.0027	0.0719	0.9483	1.0000	-10.0034
pro B-cells	0.0000	0.0000	-0.0107	0.9923	1.0000	-10.0070
Astrocytes	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071
CD4+ naive T-cells	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071
CD4+ Tem	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071
cDC	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071
CMP	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071
Eosinophils	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071
Erythrocytes	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071
MPP	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071
NK cells	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071
NKT	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071
Preadipocytes	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071
Skeletal muscle	0.0000	0.0000	0.0000	1.0000	1.0000	-10.0071

Supplemental Table 3: list of Gene expression omnibus (GEO) transcriptome samples included to performed integrative immune deconvolution of COVID-19 lung biopsy, related to figure 3: DOI: http://dx.doi.org/10.17632/3xnypzvcf7.1#file-39267130-458c-41d8-8bf7-26ae18b717d1

Supplemental Table 4: PPARγ integrative repressed program in COVID-19 lung transcriptome, related to the figure 8: DOI: http://dx.doi.org/10.17632/3xnypzvcf7.1#file-03b71cec-f317-439c-9176-170edd6ac7e0

Supplemental Table 5 : Human and SARS virus interactome connections in VirusHostNet database, related to figure 8: DOI: http://dx.doi.org/10.17632/3xnypzvcf7.1#file-71c195a0-6834-4a0a-8719-826bae172b31