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Supplemental information

Cell-Type-Specific Immune Dysregulation in Severely Ill COVID-19 Patients

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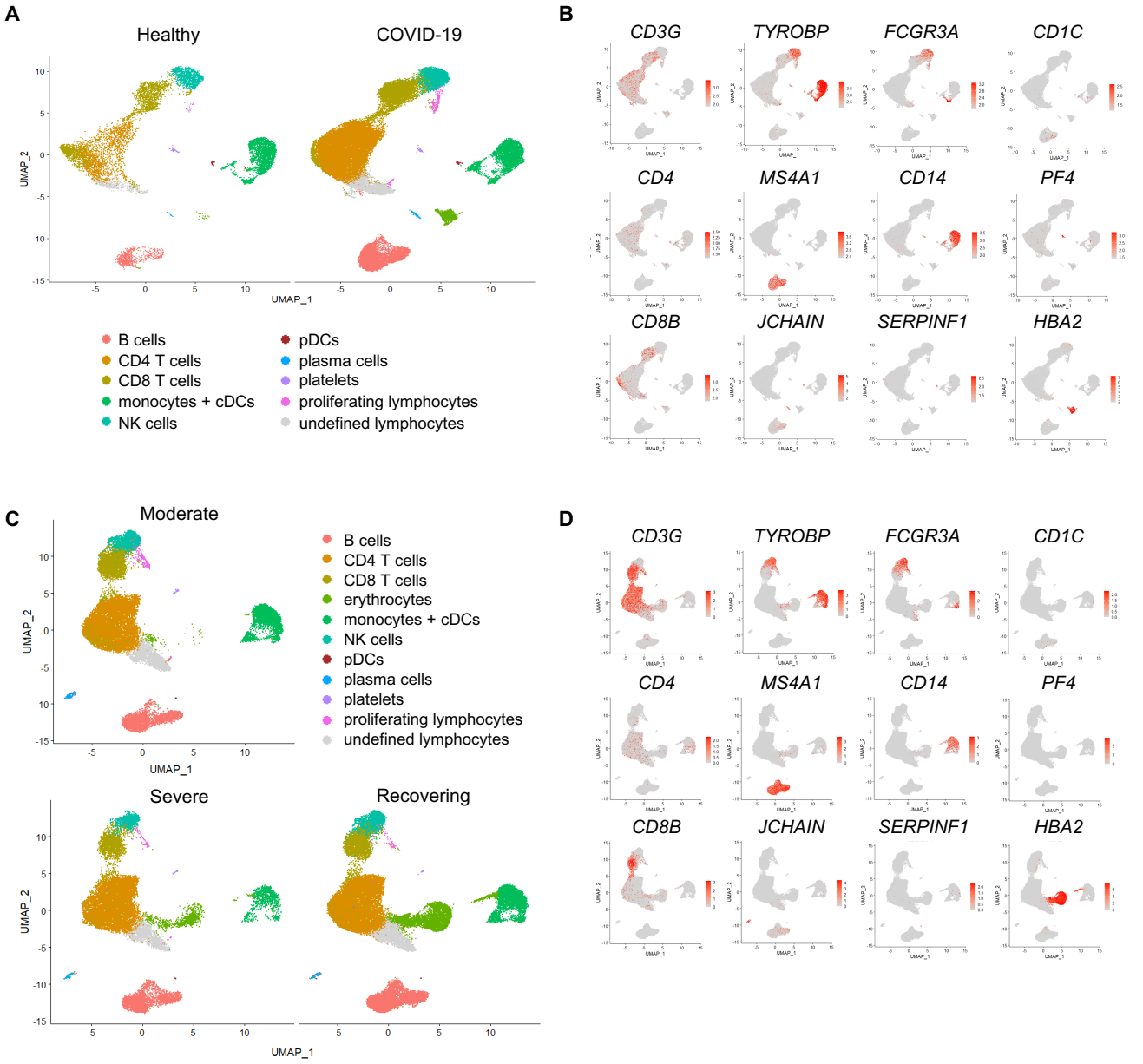
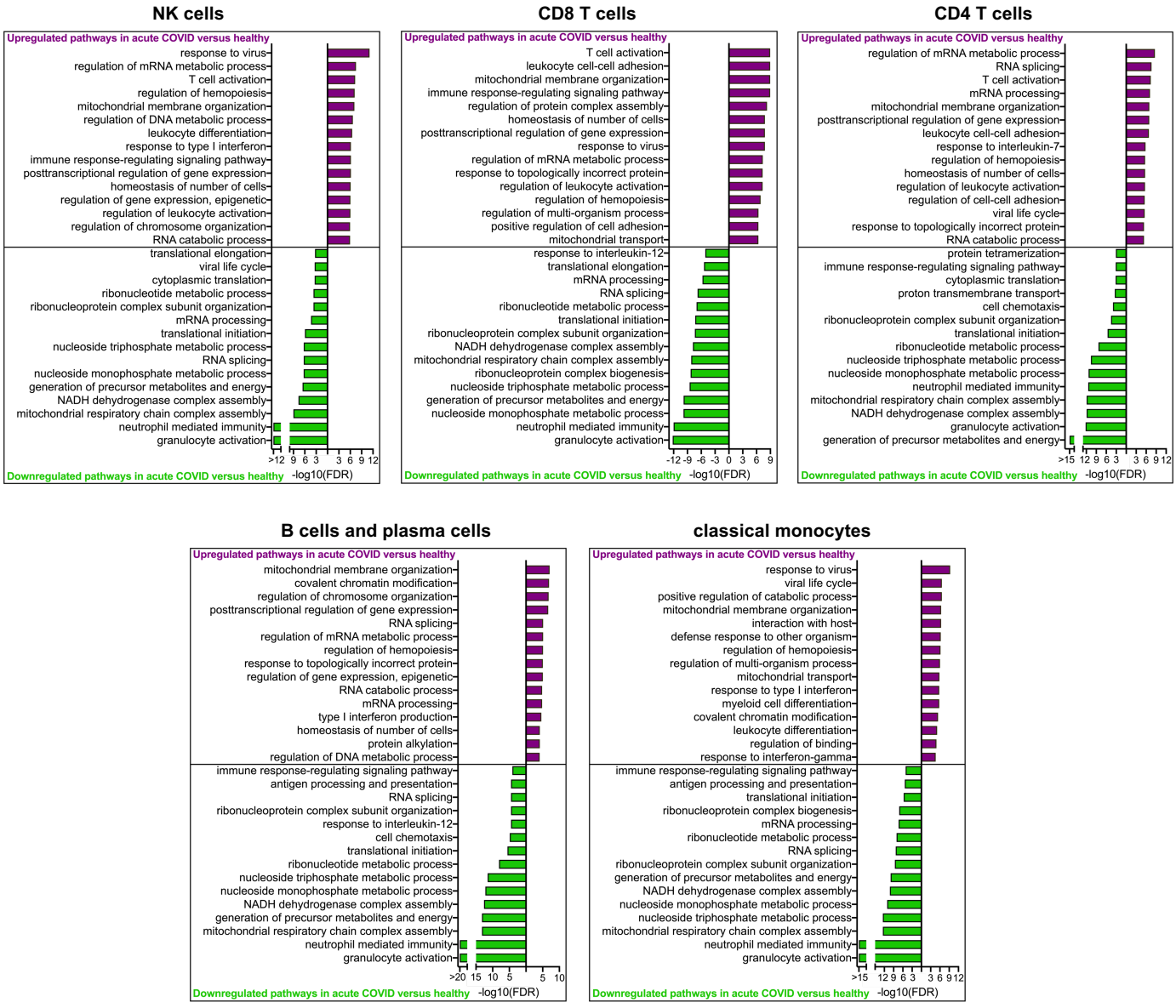
Supplemental Figure 1



Supplemental Figure 1. Identification of immune cell subsets in healthy control and COVID-19 patient samples. (related to Figures 1-7)

A) UMAP plot of all cells from healthy controls (n=3) and acutely ill COVID-19 patients with moderate and severe disease (n=11). B) UMAP plots identify T cells (CD3G), NK cells (TYROBP, FCGR3A), B cells (MS4A1), plasma cells (JCHAIN), proliferating lymphocytes (MKI67 and CD3G or FCGR3A), monocytes (CD14 or FCGR3A), cDCs (CD1C), pDCs (SERPINF1), platelets (PF4) and erythrocytes (HBA2). Erythrocytes, platelets and undefined lymphocytes were excluded from further analysis. C) UMAP plot of all cells from moderate (n=5), severe (n=6) and recovering (n=6) COVID-19 patients. D) UMAP plots identify T cells (CD3G), NK cells (TYROBP, FCGR3A), B cells (MS4A1), plasma cells (JCHAIN), proliferating lymphocytes (MKI67 and CD3G or FCGR3A), monocytes (CD14 or FCGR3A), cDCs (CD1C), pDCs (SERPINF1), platelets (PF4) and erythrocytes (HBA2). Erythrocytes, platelets and undefined lymphocytes were excluded from further analysis.

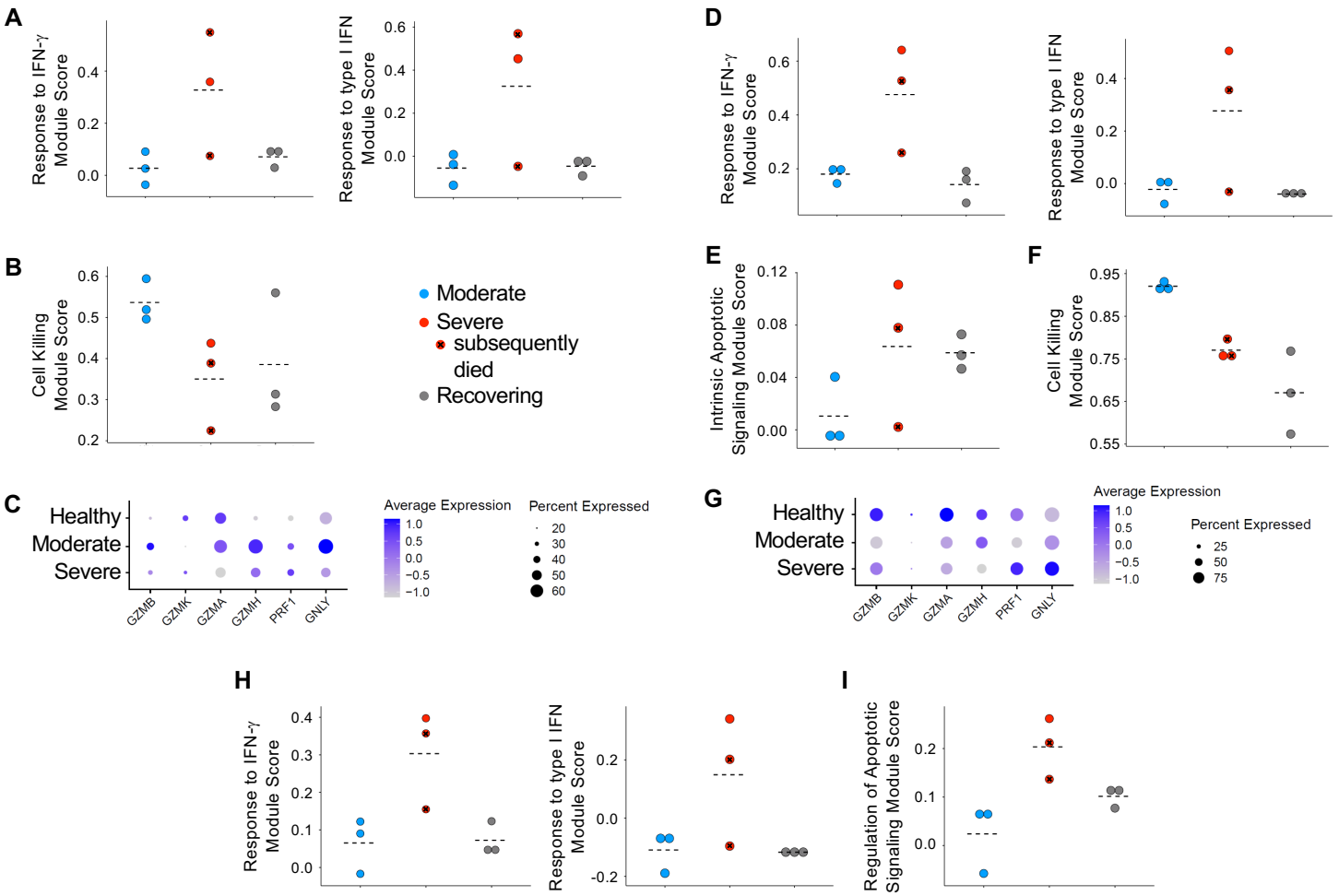
Supplemental Figure 2



Supplemental Figure 2. Healthy control versus acutely ill COVID-19 patient samples. (related to Figure 1)

Global transcriptome differences between healthy control and acutely ill COVID-19 patient NK cells, CD8 T cells, CD4 T cells, B cells and monocytes were defined by over representation analysis of up- and downregulated biological processes.

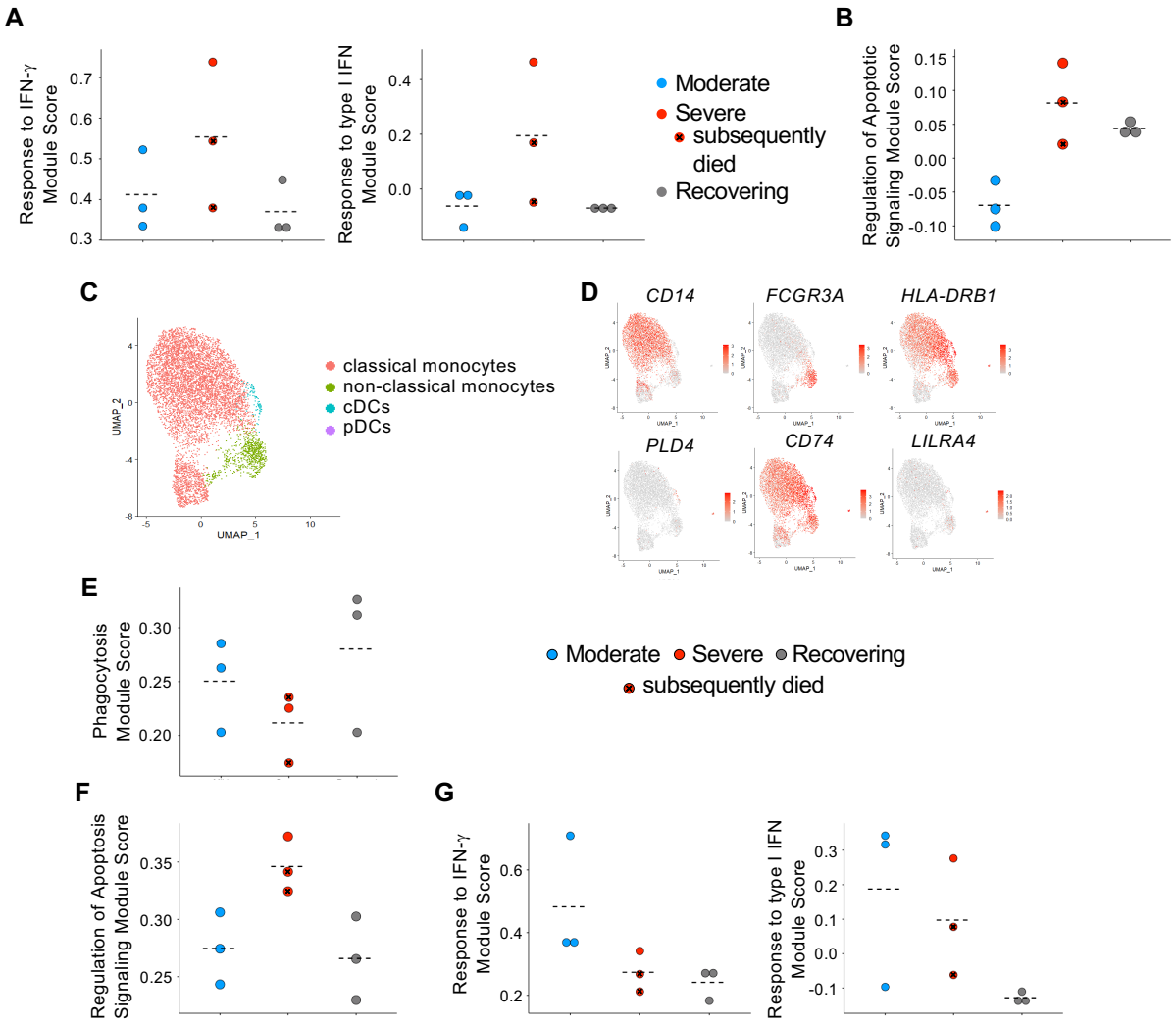
Supplemental Figure 3



Supplemental Figure 3. Comparison of NK and CD8 and CD4 T cell gene expression. (related to Figures 2-4)

A-B) Mean NK cell module scores for pairs of individual patients sequenced together. C) Average NK cell expression of differentially expressed genes involved in cytotoxicity in patient groups compared to healthy controls. D-F) Mean CD8 T cell module scores for pairs of individual patients sequenced together. G) Average CD8 T cell expression of differentially expressed genes involved in cytotoxicity in patient groups compared to healthy controls. H-I) Mean CD4 T cell module scores for pairs of individual patients sequenced together.

Supplemental Figure 4



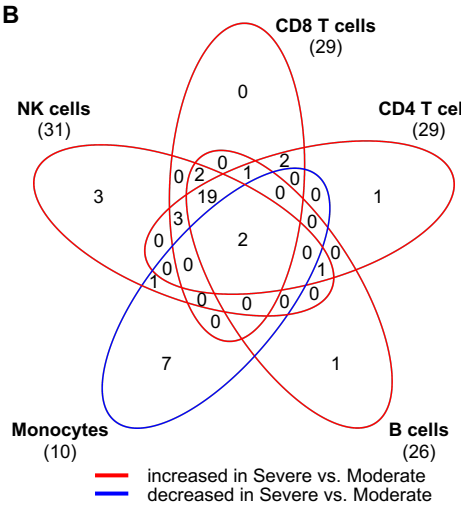
Supplemental Figure 4. Comparison of B and plasma cell and monocyte gene expression. (related to Figures 5 and 6)

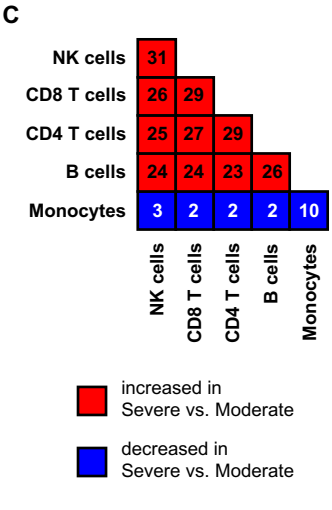
A-B) Mean B and plasma cell module scores for pairs of individual patients sequenced together. C) UMAP of monocytes and DCs from all patients. D) Monocyte and DC clusters were identified as classical monocytes (CD14), non-classical monocytes (FCGR3A), cDCs (HLA-DRB1, CD74) and pDCs (PLD4, LILRA4) cells. E-G) Mean classical monocyte module scores for pairs of individual patients sequenced together.

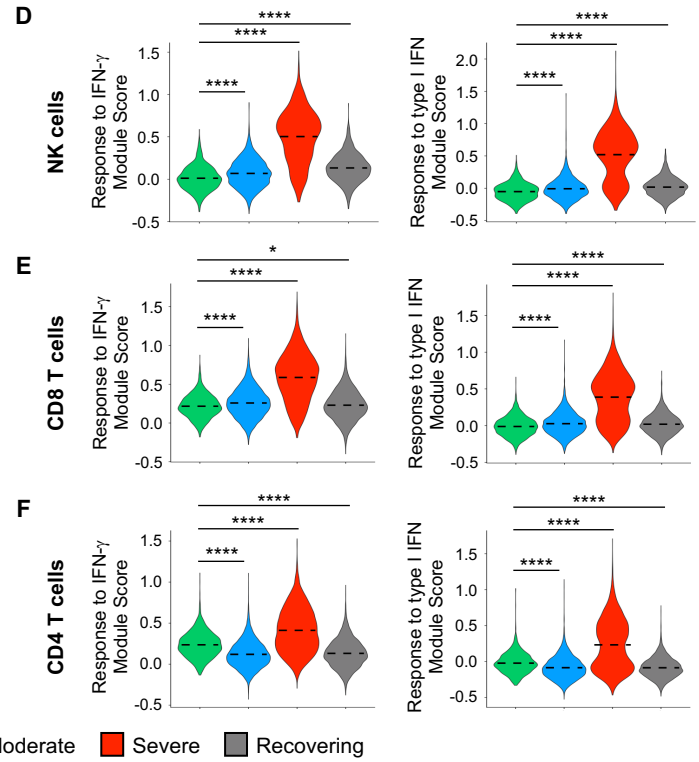
Supplemental Figure 5

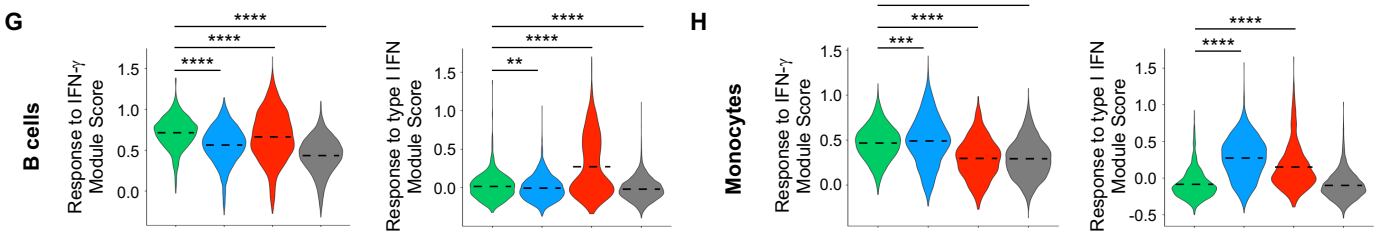
A

NK cells	CD8 T cells	CD4 T cells	B cells	Monocytes
ADAR	ADAR	ADAR	ADAR	-
BST2	BST2	BST2	BST2	-
-	C19orf66	C19orf66	-	-
-	-	CDC37	-	-
-	-	-	-	EGR1
-	-	-	-	GBP2
-	-	-	-	HLA-E
-	-	-	-	HLA-F
HSP90AB1	HSP90AB1	-	HSP90AB1	-
-	-	-	-	IFI27
IFI35	IFI35	-	IFI35	-
IFI6	IFI6	IFI6	IFI6	IFI6
IFIT1	IFIT1	IFIT1	IFIT1	-
IFIT3	IFIT3	IFIT3	IFIT3	-
IFITM1	IFITM1	IFITM1	IFITM1	-
-	IFITM2	IFITM2	IFITM2	-
IFITM3	-	-	-	IFITM3
-	IFNAR1	IFNAR1	-	-
-	-	-	-	IRF1
IRF7	IRF7	IRF7	IRF7	-
-	-	-	-	IRF9
ISG15	ISG15	ISG15	ISG15	-
ISG20	ISG20	ISG20	ISG20	-
JAK1	-	-	-	-
MX1	MX1	MX1	MX1	-
MX2	MX2	MX2	MX2	-
OAS1	OAS1	OAS1	OAS1	OAS1
OAS2	OAS2	OAS2	-	-
OAS3	-	-	-	-
OASL	OASL	OASL	-	-
PSMB8	-	PSMB8	PSMB8	-
PTPN11	PTPN11	PTPN11	PTPN11	-
RSAD2	-	-	-	-
SAMHD1	SAMHD1	SAMHD1	-	-
SETD2	SETD2	SETD2	SETD2	-
SP100	SP100	SP100	SP100	-
STAT1	STAT1	STAT1	STAT1	-
STAT2	STAT2	STAT2	STAT2	-
XAF1	XAF1	XAF1	XAF1	-
EIF2AK2	EIF2AK2	EIF2AK2	EIF2AK2	-
-	-	-	AIM2	-
NDUFA13	NDUFA13	NDUFA13	NDUFA13	-
PLSCR1	PLSCR1	PLSCR1	PLSCR1	-









Supplemental Figure 5. Comparison of IFN responses in immune cell subsets. (related to Figure 7)
A) List of type I IFN response genes increased (red) or decreased (blue) in the severe group compared to the moderate group. B) Venn diagram showing overlapping gene targets in the immune cell subsets. C) Total number of DEG overlapping between immune cell subsets. D-H) Mean module scores for COVID-19 patients compared to healthy controls. Kruskal-Wallis test was used to test overall significance in module scores, $P<2.2 \times 10^{-16}$. Wilcoxon test was used for pairwise comparisons, *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001