Supplementary Table 1. 17 Prioritized genes located in GWAS suggestive loci (p-value < 1 x 10-6)

Cytoband	Lead SNP	Target gene	Types of gene prioritization methods			Phenotypes of COVID-19			
	Lead SNP		TWAS	POPS			TWAS	POPS	
1p13.2	rs7535387	TRIM33				V			V
6p21.32	rs9501257	HLA-DPB1				V	V		
10q24.1	rs117098321	SORBS1				V	V		
1p13.1	rs188398686	VANGL1		V					V
17p13.1	rs149399480	GAS7	V				V		
6p24.3	rs2299036	DSP				V	V		
11q23.3	rs75256341	GRIK4		V				V	
22q11.21	rs150868259	CLDN5			V	V		V	
5q13.2	rs139478596	ZNF366				V		V	
8q23.1	rs189378134	TRHR				V		V	
4q21.1	rs185675098	G3BP2		V		V			V
6p21.1	rs9462875	CUL9			V	V			V
1q21.1	rs28381173	FMO5		V					V
21q22.12	rs77619227	RUNX1		V		V			V
4q35.1	rs72691535	ING2				V			V
5q34	rs75309214	MAT2B				V			V

Supplementary Table 2. Protein-Protein Interactions between 42 prioritized genes and 332 Viral-Host PPIs

Protein has PPI indirectly with viral protein	Protein has PPI directly with viral protein	SARS-CoV-2 proteins
	TLE1*	nsp13
TLE1*	GOLGA2	nsp13
	TLE3	nsp13
	TLE5	nsp13
	FYCO1*	nsp13
XCR1*	PLEKHF2	Orf8
CCHCR1*	GOLGA2	nsp13
	GRIPAP1	nsp13
	HSBP1	nsp13
	NINL	nsp13
	NUP54	nsp9
	NUP62	nsp9
	PKP2	nsp1
	RBM41	nsp12
IGF1*	IDE	nsp4
DPP9*	CSNK2A2	N
	TRMT1	nsp5(C145A)
HDGFL2*	CSNK2A2	N
OAS3*	EXOSC3	nsp8
	G3BP2	N
	PABPC4	N
OAS1*	GOLGA2	nsp13
IFNAR1*	AP2M1	nsp10
	PRKACA	nsp13
LZTFL1*	CEP250	nsp13
	SEPSECS	nsp8
TCF19*	GOLGA2	nsp13

Supplementary Table 3. Gene Set Enrichment Analysis with WikiPathways Human

Term	Category	P-value	Adjusted P-value	Odds Ratio	Combined Score	Genes
Type I interferon induction and signaling during SARS-CoV-2 infection WP4868	antiviral	4.18E-11	2.51E-09	132.89	3175.66	IFNAR2;OAS1;OAS2;OAS3;TYK2;IFNAR1
Host-pathogen interaction of human coronaviruses - interferon induction WP4880	antiviral	6.27E-11	2.51E-09	123.030864	2890.27593	IFNAR2;OAS1;OAS2;OAS3;TYK2;IFNAR1
Immune response to tuberculosis WP4197	antibacteria	1.44E-07	3.85E-06	110.465374	1739.85736	IFNAR2;OAS1;TYK2;IFNAR1
Type III interferon signaling WP2113	immunosuppressant	1.92E-04	1.98E-03	124.6875	1067.29086	IL10RB;TYK2
Overview of interferons-mediated signaling pathway WP4558	immunosuppressant	1.05E-06	2.11E-05	63.5566188	874.676203	IFNAR2;IL10RB;TYK2;IFNAR1

SARS coronavirus and innate immunity WP4912	antiviral	3.72E-05	4.95E-04	54.7527473	558.504028	IFNAR2;TYK2;IFNAR1

Supplementary Table 4. Gene Set Enrichment Analysis with Elsevier Pathway Collection

Term	Category	P-value	Adjusted P-value	Odds Ratio	Combined Score	Genes
IL22R -> STAT3 Signaling	immunosuppressant	6.42E-05	4.88E-03	249.43	2407.70	IL10RB;TYK2
IL10R -> STAT Signaling	immunosuppressant	1.20E-04	4.88E-03	166.27	1501.64	IL10RB;TYK2
SOCS in Negative Feedback Regulation in Myocarditis	anti-inflammatory immunosuppressant	8.15E-06	2.00E-03	95.875	1123.40605	IFNAR2;TYK2;IFNAR1
STAT3 Facilitates the Function of Treg Cells and Cancer Progression	antineoplastic	3.31E-04	7.01E-03	90.6681818	726.585254	IL10RB;TYK2
STAT3 Inhibits Maturation of Dendritic Cells and Facilitates Cancer Progression	antineoplastic	5.07E-04	9.56E-03	71.2285714	540.402969	IL10RB;TYK2

Supplementary Table 5. Gene Set Enrichment Analysis with GO Molecular Function

Term	Category	P-value	Adjusted P-value	Odds Ratio	Combined Score	Genes
interferon receptor activity (GO:0004904)	immunosuppressant	4.29E-05	4.59E-04	332.58	3344.84	IFNAR2;IFNAR1
adenylyltransferase activity (GO:0070566)	other	1.29E-05	3.17E-04	80.72	908.84	OAS1;OAS2;OAS3
C-C chemokine receptor activity (GO:0016493)	anti-inflammatory	1.48E-05	3.17E-04	76.68	852.75	XCR1;CCR9;CXCR6
C-C chemokine binding (GO:0019957)	anti-inflammatory	1.69E-05	3.17E-04	73.03	802.46	XCR1;CCR9;CXCR6
chemokine receptor activity (GO:0004950)	anti-inflammatory immunosuppressant antiviral	2.16E-05	3.25E-04	66.67	716.10	XCR1;CCR9;CXCR6

Supplementary Table 6. Gene Set Enrichment Analysis with GO Biological Process

Term	Category	P-value	Adjusted P-value	Odds Ratio	Combined Score	Genes
regulation of ribonuclease activity (GO:0060700)	antineoplastic	8.59E-08	1.53E-05	767.54	12488.3576	OAS1;OAS2;OAS3
regulation of nuclease activity (GO:0032069)	antineoplastic	1.71E-07	2.29E-05	511.67	7971.23775	OAS1;OAS2;OAS3
interleukin-27-mediated signaling	immunosuppressant	3.85E-06	4.12E-04	127.86	1594.08542	OAS1;OAS2;TYK2

pathway (GO:0070106)						
positive regulation of monocyte chemotactic protein-1 production (GO:0071639)	anti-inflammatory	1.20E-04	5.40E-03	166.27	1501.641	OAS1;OAS3
cellular response to type I interferon (GO:0071357)	immunosuppressant	4.45E-09	1.19E-06	56.21	1080.9438	IFNAR2;OAS1;OAS2;OAS3;TYK2;IFNAR1
type I interferon signaling pathway (GO:0060337)	immunosuppressant	4.45E-09	1.19E-06	56.21	1080.9438	IFNAR2;OAS1;OAS2;OAS3;TYK2;IFNAR1
positive regulation of cellular respiration (GO:1901857)	other	2.34E-04	6.95E-03	110.83	926.563103	IL10RB;IFNAR1
regulation of monocyte chemotactic protein-1 production (GO:0071637)	immunosuppressant	2.34E-04	6.95E-03	110.83	926.563103	OAS1;OAS3
regulation of chemokine (C-X-C motif) ligand 2 production (GO:2000341)	immunosuppressant	3.31E-04	9.19E-03	90.67	726.585254	OAS1;OAS3

positive regulation of glycogen biosynthetic process (GO:0045725)	other	3.86E-04	9.38E-03	83.11	653.30253	IGF1;SORBS1
positive regulation of glycogen metabolic process (GO:0070875)	other	4.44E-04	9.51E-03	76.71	592.142891	IGF1;SORBS1
regulation of type I interferon-mediated signaling pathway (GO:0060338)	immunosuppressant	3.36E-05	2.56E-03	56.78	584.915066	IFNAR2;OAS1;OAS3

Supplementary Table 7. Functional Characterization on druggable targets

Gene	Differentially expressed Gene	TOP10 Enriched Pathways	TOP10 Enriched Gene Ontology	Meet functioal requirment (Number of condition)
SLC6A20	Transcriptional and proteomic insights into the host response in fatal COVID-19 cases(PMID:33082228)	NA	NA	No (1)
CCR9	1. TWAS Whole blood (FDR:9.68E-07) 2. Mock v SARS-CoV-2 Lung GSE150847 up	NA	1. C-C chemokine receptor activity (GO:0016493) 2. C-C chemokine receptor activity (GO:0016493) 3. chemokine receptor activity (GO:0004950)	Yes (2)
CXCR6	TWAS Lung (FDR:2.23E-13)	NA	1. C-C chemokine receptor activity (GO:0016493) 2. C-C chemokine binding (GO:0019957) 3. chemokine receptor activity (GO:0004950)	Yes (2)
XCR1	Transcriptional and proteomic insights into the host response in fatal COVID-19 cases(PMID:33082228)	NA	1. C-C chemokine receptor activity (GO:0016493) 2. C-C chemokine binding (GO:0019957) 3. chemokine receptor activity (GO:0004950)	Yes (2)

IGF1	NA	NA	1. positive regulation of glycogen biosynthetic process (GO:0045725) 2. positive regulation of glycogen metabolic process (GO:0070875)	No (1)
IL10RB	1. Mock v SARS-CoV-2 24h liver-organoid GSE151803 up 2. Untreated v SARS-CoV-2 IntestinalOrganoid 60h Expansion GSE149312 down	1. Type III interferon signaling WP2113 2. Overview of interferons-mediated signaling pathway WP4558 3. IL22R -> STAT3 Signaling 4. IL10R -> STAT Signaling 5. STAT3 Facilitates the Function of Treg Cells and Cancer Progression 6. STAT3 Inhibits Maturation of Dendritic Cells and Facilitates Cancer Progression	1. positive regulation of cellular respiration (GO:1901857)	Yes (3)
OAS1	1. Healthy v SARS-CoV-2 lung GSE147507 up	1. Type I interferon induction and signaling during SARS-	1. adenylyltransferase activity (GO:0070566)	Yes (3)

	2. Mock v SARS-CoV-2 24h hiPSC-CMs GSE150392 up 3. Mock v SARS-CoV-2 A549 Series2 GSE147507 up 4. Mock v SARS-CoV-2 Calu-3 24h totalRNA GSE148729 up 5. Mock v SARS-CoV-2 Calu-3 4h totalRNA GSE148729 down 6. Mock v SARS-CoV-2 Calu-3 s1 24h polyA GSE148729 up 7. Mock v SARS-CoV-2 Calu-3 s1 4h polyA GSE148729 down 8. Mock v SARS-CoV-2 Calu-3 s2 12h polyA GSE148729 up 9. Mock v SARS-CoV-2 Calu3 GSE147507 up 10. Mock v SARS-CoV-2 NHBE GSE147507 up 11. SARS-CoV-2 Mock v DMSO Organoids GSE154613 up 12. Untreated v SARS-CoV-2 Calu-3 4h	CoV-2 infection WP4868 2. Host-pathogen interaction of human coronaviruses - interferon induction WP4880 3. Immune response to tuberculosis WP4197	2. regulation of ribonuclease activity (GO:0060700) 3. regulation of nuclease activity (GO:0032069) 4. interleukin-27-mediated signaling pathway (GO:0070106) 5. positive regulation of monocyte chemotactic protein-1 production (GO:0071639) 6. cellular response to type I interferon (GO:0071357) 7. type I interferon signaling pathway (GO:0060337) 8. regulation of monocyte chemotactic protein-1 production (GO:0071637) 9. regulation of chemokine (C-X-C motif) ligand 2 production (GO:2000341)	

	totalRNA GSE148729 down Untreated v SARS-CoV-2 Calu-3 s1 4h polyA GSE148729 down Untreated v SARS-CoV-2 IntestinalOrganoid 24h Expansion GSE149312 up Untreated v SARS-CoV-2 IntestinalOrganoid 60h Expansion GSE149312 up			
OAS2	1. Healthy v SARS-CoV-2 lung GSE147507 up 2. Mock v SARS-CoV-2 24h hiPSC-CMs GSE150392 up 3. Mock v SARS-CoV-2 24h liver-organoid GSE151803 up 4. Mock v SARS-CoV-2 A549 Series2 GSE147507 up 5. Mock v SARS-CoV-2 Calu-3 24h totalRNA GSE148729 up 6. Mock v SARS-CoV-2 Calu-3 s1 24h polyA GSE148729 up 7. Mock v SARS-CoV-2 Calu-3 s2 12h polyA GSE148729 up	1. Type I interferon induction and signaling during SARS-CoV-2 infection WP4868 2. Host-pathogen interaction of human coronaviruses - interferon induction WP4880	1. adenylyltransferase activity (GO:0070566) 2. regulation of ribonuclease activity (GO:0060700) 3. regulation of nuclease activity (GO:0032069) 4. interleukin-27-mediated signaling pathway (GO:0070106) 5. cellular response to type I interferon (GO:0071357) 6. type I interferon signaling pathway (GO:0060337)	Yes (3)

	8. Mock v SARS-CoV-2 Calu3 GSE147507 up 9. Mock v SARS-CoV-2 Lung GSE150847 up 10. Mock v SARS-CoV-2 NHBE GSE147507 up 11. SARS-CoV-2 Mock v DMSO Organoids GSE154613 up 12. Untreated v SARS-CoV-2 Calu-3 s1 4h polyA GSE148729 down 13. Untreated v SARS-CoV-2 IntestinalOrganoid 60h Differentiation GSE149312 up 14. Untreated v SARS-CoV-2 IntestinalOrganoid 60h Expansion GSE149312 up			
OAS3	1. Healthy v SARS-CoV-2 lung GSE147507 up 2. Mock v SARS-CoV-2 24h hiPSC-CMs GSE150392 up 3. Mock v SARS-CoV-2 A549 Series2 GSE147507 up	1. Type I interferon induction and signaling during SARS-CoV-2 infection WP4868 2. Host-pathogen interaction of human coronaviruses -	1. adenylyltransferase activity (GO:0070566) 2. regulation of ribonuclease activity (GO:0060700) 3. regulation of nuclease activity (GO:0032069)	Yes (3)

	4. Mock v SARS-CoV-2 Calu-3 24h totalRNA GSE148729 up 5. Mock v SARS-CoV-2 Calu-3 s1 24h polyA GSE148729 up 6. Mock v SARS-CoV-2 Calu-3 s2 12h polyA GSE148729 up 7. Mock v SARS-CoV-2 Calu3 GSE147507 up 8. Mock v SARS-CoV-2 Lung GSE150847 up 9. Mock v SARS-CoV-2 NHBE GSE147507 up 10. SARS-CoV-2 Mock v DMSO Organoids GSE154613 up 11. Untreated v SARS-CoV-2 IntestinalOrganoid 60h Expansion GSE149312 up	interferon induction WP4880	4. positive regulation of monocyte chemotactic protein-1 production (GO:0071639) 5. cellular response to type I interferon (GO:0071357) 6. type I interferon signaling pathway (GO:0060337) 7. regulation of monocyte chemotactic protein-1 production (GO:0071637) 8. regulation of chemokine (C-X-C motif) ligand 2 production (GO:2000341) 9. regulation of type I interferon-mediated signaling pathway (GO:0060338)	
GRIK4	Mock v SARS-CoV-2 Lung GSE150847 down	NA	NA	No (1)
FMO5	1. Mock v SARS-CoV-2 24h liver-organoid GSE151803 down	NA	NA	No (1)

	2. Mock v SARS-CoV-2 Lung GSE150847 down 3. Mock v SARS-CoV-2 NHBE GSE147507 down 4. Untreated v SARS-CoV-2 IntestinalOrganoid 24h Differentiation GSE149312 down 5. Untreated v SARS-CoV-2 IntestinalOrganoid 60h Expansion GSE149312 down			
ST3GAL1	1. Mock v SARS-CoV-2 A549 Series5 GSE147507 up 2. Mock v SARS-CoV-2 Calu-3 s1 4h polyA GSE148729 up 3. Mock v SARS-CoV-2 Calu3 GSE147507 up 4. Untreated v SARS-CoV-2 Caco2 4h polyA GSE148729 up 5. Untreated v SARS-CoV-2 Calu-3 4h totalRNA GSE148729 up	NA	NA	No (2)

	6. Untreated v SARS-CoV-2 Calu-3 s1 4h polyA GSE148729 up 7. Untreated v SARS-CoV-2 IntestinalOrganoid 60h Differentiation GSE149312 down			
GAS7	1. Mock v SARS-CoV-2 Calu-3 s2 12h polyA GSE148729 down 2. Mock v SARS-CoV-2 Lung GSE150847 down 3. Untreated v SARS-CoV-2 IntestinalOrganoid 60h Expansion GSE149312 up	NA	NA	No (1)
TRIM33	1. Mock v SARS-CoV-2 Caco2 4h polyA GSE148729 up 2. Mock v SARS-CoV-2 Calu-3 s2 4h polyA GSE148729 up	NA	NA	No (1)
DPP9	Untreated v SARS-CoV-2 IntestinalOrganoid 60h Differentiation GSE149312 up	NA	NA	No (1)

MAT2B	1. Mock v SARS-CoV-2 Calu-3 4h totalRNA GSE148729 down 2. Mock v SARS-CoV-2 Calu-3 s1 4h polyA GSE148729 down 3. Mock v SARS-CoV-2 VeroE6 24h GSE153940 down 4. Untreated v SARS-CoV-2 Calu-3 4h totalRNA GSE148729 down 5. Untreated v SARS-CoV-2 Calu-3 s1 4h polyA GSE148729 down	NA	NA	No (1)
ICAM4	NA	NA	NA	No (0)
OBP2B	NA	NA	NA	No (0)
TRHR	NA	NA	NA	No (0)