



Research article

Unveiling common markers in COVID-19: ADAMTS2, PCSK9, and OLAH emerged as key differential gene expression profiles in PBMCs across diverse disease conditions

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Abstract: Diverse COVID-19 severity levels and a spectrum of clinical manifestations underscore the need to comprehend the underlying genetic mechanisms. Such knowledge is essential for improving disease management and therapeutic approaches. This study aims to explore and uncover pivotal genes and pathways linked to distinct COVID-19 conditions, providing insights into potential therapeutic avenues. Gene expression data from COVID-19 patients across different conditions were analyzed using differential gene expression analysis. Significant genes were subjected to pathway analysis and protein–protein interaction network analysis. Gene ontology was used to identify the functions of these genes. The genes *ADAMTS2*, *PCSK9*, and *OLAH* were upregulated across all disease conditions including SARS-CoV-2 bacterial coinfection, potentially serving as therapeutic targets. The proteins, including RPL and CEACAM, could serve as a potential therapeutic target. The deregulated genes were majorly involved in inflammation, lipid metabolism, and immune regulation. The study's findings reveal significant gene expression differences among COVID-19 disease conditions. These insights guide future research toward targeted therapies and an improved understanding of disease progression and long-term consequences.

Keywords: COVID-19; Asymptomatic COVID-19; Severe COVID-19; Gene regulation; Disease severity

Supplementary

Supplementary Table 1. Differentially expressed genes in asymptomatic COVID-19 and mild COVID-19.

Gene ID	Symbol	log ₂ (FC)	P-value	Gene ID	Symbol	log ₂ (FC)	P-value
Upregulated genes asymptomatic COVID-19				Downregulated genes asymptomatic COVID-19			
100287083	DEFT1P2	9.786	5.561	28706	TRAJ49	-4.618	2.354
170949	DEFT1P	9.613	5.745	399940	TRIM51EP	-4.321	1.343
1670	DEFA5	9.11	2.113	200772	UICLM	-3.582	1.738
9509	ADAMTS2	6.953	9.172	137797	LYPD2	-3.535	1.551
449491	DEFA8P	6.682	3.842	28785	IGLV4-60	-3.263	1.948
255738	PCSK9	6.627	4.561	28520	TRDJ3	-3.076	1.771
55301	OLAH	6.623	5.42	149345	SHISA4	-2.997	3.617
5657	PRTN3	6.526	6.316	28518	TRDV1	-2.773	2.783
1511	CTSG	6.153	7.152	28745	TRAJ10	-2.766	1.327
1991	ELANE	5.957	6.436	28722	TRAJ33	-2.706	1.336
Upregulated genes mild COVID-19				Downregulated genes mild COVID-19			
170949	DEFT1P	7.53	3.055	81796	SLCO5A1	-5.261	3.15
57126	CD177	6.242	5.666	106635683	SNORD141A	-3.804	5.666
55301	OLAH	6.228	4.118	80312	TET1	-2.665	2.516
9509	ADAMTS2	5.65	5.356	56241	SUSD2	-2.544	1.545
113452	TMEM54	4.844	1.925	339318	ZNF181	-2.337	1.541
7401	CLRN1	4.785	2.215	3820	KLRB1	-2.316	2.088
5657	PRTN3	4.74	2.889	414196	CELF2-AS1	-2.27	1.316
1991	ELANE	4.283	2.883	101929355	CFAP97D2	-2.204	1.496
255738	PCSK9	4.281	1.677	65065	NBEAL1	-2.187	5.071
731779	LINC01300	4.265	1.725	101243545	LINC02067	-1.993	3.448

Supplementary Table 2. Differentially expressed genes in moderate COVID-19 and severe COVID-19.

Gene ID	Symbol	log2(FC)	P-value	Gene ID	Symbol	log2(FC)	P-value
Upregulated genes Moderate COVID-19				Downregulated genes Moderate COVID-19			
170949	DEFT1P	7.463	3.493	81796	SLCO5A1	-4.958	3.368
55301	OLAH	6.636	5.678	106635683	SNORD141A	-3.969	6.912
255738	PCSK9	6.508	4.372	101929355	CFAP97D2	-3.222	3.361
23500	DAAM2	6.425	6.815	4897	NRCAM	-3.105	2.241
9509	ADAMTS2	6.194	6.996	9241	NOG	-3.052	3.013
100505635	DAAM2-AS1	5.856	4.302	80312	TET1	-2.73	3.287
100287083	DEFT1P2	5.317	1.852	256691	MAMDC2	-2.582	5.927
116933	CLRN1-AS1	4.878	2.409	284013	VMO1	-2.495	1.763
170949	DEFT1P	7.463	3.493	101929010	SIRPG-AS1	-2.48	1.787
55301	OLAH	6.636	5.678	81796	SLCO5A1	-4.958	3.368
Upregulated genes Severe COVID-19				Downregulated genes Severe COVID-19			
170949	DEFT1P	8.571	4.288	2205	FCER1A	-4.608	3.344
55301	OLAH	8.334	7.837	93979	CPA5	-4.502	2.353
1670	DEFA5	8.288	2.03	54674	LRRN3	-4.424	4.851
9509	ADAMTS2	7.16	8.53	28634	TRBJ1-2	-3.962	3.553
10028	DEFT1P7083	6.9112	2.723	100506178	STEAP1B-AS1	-3.933	3.112
57126	CD177	6.812	6.943	9241	NOG	-3.881	4.018
255738	PCSK9	6.522	4.288	28706	TRAJ49	-3.856	1.994
84985	FAM83A	6.517	3.031	28701	TRAJ54	-3.77	1.788
4128	MAOA	6.455	4.695	7539	ZFP37	-3.745	2.528
10562	OLFM4	6.241	7.837	28617	TRBV4-1	-3.686	4.594

Supplementary Table 3. Differentially expressed genes in COVID-bacterial coinfection.

Gene ID	Symbol	log2(FC)	P-value	Gene ID	Symbol	log2(FC)	P-value
Upregulated genes				Downregulated genes			
55301	OLAH	7.8	4.921	165530	CLEC4F	-5.878	2.077
9509	ADAMTS2	7.728	8.279	3429	IFI27	-4.493	1.973
23500	DAAM2	6.821	4.724	284013	VMO1	-4.446	2.254
100505635	DAAM2-AS1	6.546	3.56	3116	HLA-DPB2	-4.4	1.411
4128	MAOA	6.12	2.856	81796	SLCO5A1	-4.303	1.696
57126	CD177	6.069	3.871	57801	HES4	-4.238	2.099
255738	PCSK9	5.975	2.558	137797	LYPD2	-4.128	1.509
116933	CLRN1-AS1	5.7	2.153	106635683	SNORD141A	-4.067	4.536
7079	TIMP4	5.641	2.117	105371809	LINC02086	-3.922	1.631
11326	VSIG4	5.6177.8	5.287	165530	CLEC4F	-5.878	2.077

Supplementary Table 4. Commonly regulated genes across COVID-19 disease severity.

Disease	Genes	Regulation
Asymptomatic and mild	PRTN3 and ELANE	Upregulation
Mild and moderate	TET1 and CFAP97D2	Downregulation
Moderate and severe	NOG	Downregulation
Severe and coinfection	MAOA	Upregulation
Coinfection and asymptomatic	LYPD2	Downregulation
Asymptomatic and severe	DEFA5	Upregulation
	TRAJ49	Downregulation
Asymptomatic, mild and moderate	DEFT1P	Upregulation
Asymptomatic, mild, and severe	DEFT1P	Upregulation
Mild, moderate, and coinfection	SLCO5A1 and SNORD141A	Downregulation
Mild, severe, and coinfection	CD177	Upregulation
Asymptomatic, mild, moderate, severe, and coinfection	ADAMTS2, PCSK9 and OLAH	Upregulation

Supplementary Table 5. Top five protein–host interactions using IntAct.

Molecule A	Molecule B	Host organism	Detection method	Interaction type
FKBP5	STK11	<i>Homo sapiens</i> HEK293T embryonic kidney cell	lumier	Physical association
STK11	FKBP5	<i>Homo sapiens</i> HEK293 embryonic kidney cell	Anti-tag co-immunoprecipitation	Direct association
STK11	FKBP5	<i>Homo sapiens</i> HEK293T embryonic kidney cell	Anti-tag co-immunoprecipitation	Direct association
FKBP5	HSP90AB1	in vitro	Solution sedimentation	Physical association
CDK9	FKBP5	<i>Homo sapiens</i> HEK293 embryonic kidney cell	Tandem affinity purification	Direct association



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