

**SUPPLEMENTARY MATERIAL**

to the article “Transcriptomics of severe COVID-19”

by A.A. Gusarova, E.A. Trifonova, A.A. Babovskaya, M.M. Gavrilenko, V.A. Stepanov

**Table S1.** Studies of the severe form of COVID-19 using a single-cell RNA-seq

Material and time of collecting	Severity of COVID-19 (number of patients)	Features of gene expression and cellular composition in severe COVID-19
Hadjadj et al., 2020		
Peripheral blood leukocytes; during hospitalization (median = 10 days after the onset of symptoms)	Mild or moderate form ( <i>n</i> = 15), severe form ( <i>n</i> = 17) and critical form ( <i>n</i> = 18)	↑ <i>BATF</i> , <i>IRF4</i> and <i>CD274</i> ; genes associated with apoptosis; genes involved in the type I interferon signaling ( <i>IFNAR1</i> , <i>JAK1</i> and <i>TYK2</i> ); IL-6-induced genes ( <i>IL6R</i> , <i>SOCS3</i> and <i>STAT3</i> ); <i>TNFSF10</i> ; <i>IL1B</i> ; genes of the NF-κB signaling pathway; <i>CXCR2</i> ; ↓ IFN-stimulated genes (ISG) ( <i>MX1</i> , <i>IFITM1</i> and <i>IFIT2</i> )
Arunachalam et al., 2020		
Peripheral blood mononuclear cells (PBMCs); at different points in time	1 cohort ( <i>n</i> = 36, mild – 75 %, severe – 14 %, critical – 11 %); 2 cohort ( <i>n</i> = 40, mild – 18 %, severe – 60 %, critical – 18 %)	↑ <i>S100A12</i> in myeloid cells; ↓ genes encoding TNFSF14 and OSM in monocytes; type I interferons; CD86 and HLA-DR proteins on monocytes and myeloid dendritic cells; temporary expression of IFN-stimulated genes
Silvin et al., 2020		
Peripheral blood samples; at different points in time	Mild course of the disease ( <i>n</i> = 27), moderate ( <i>n</i> = 16), severe ( <i>n</i> = 43)	↑ classical monocytes expressing CD141 (THBD); immature neutrophils; ↑ <i>S100A8</i> and <i>S100A9</i> ; genes involved in the production of reactive oxygen species (ROS) and nitric oxide (NO); genes involved in the induced NOS pathway, IL-1 signaling, and NF-κB activation; transcription factor RelA/p65 (P-p65) in classical monocytes; ↓ classical monocytes expressing CD169; HLA-DR protein on the surface of monocytes; nonclassical monocytes
Schulte-Schrepping et al., 2020		
Peripheral blood samples and peripheral blood mononuclear cells (PBMCs); at different points in time between the 3rd and 20th days after the onset of symptoms	1 cohort ( <i>n</i> = 8 mild and <i>n</i> = 10 severe), 2 cohort ( <i>n</i> = 8 mild and <i>n</i> = 9 severe)	↑ white blood cells, neutrophils; ↓ total number of lymphocytes and T cells, non-classical monocytes; ↑ expression of CD226 and CD69, <i>SELL</i> (CD62L), <i>MAFB</i> , <i>PLBD1</i> , <i>CD163</i> , <i>MPO</i> , <i>PLAC8</i> in monocytes; <i>CD24</i> , <i>PGLYRP1</i> , <i>DEFA3</i> and <i>DEFA4</i> in immature neutrophils; <i>FCGR3B</i> (CD16b), <i>CXCL8</i> and <i>LCN2</i> in neutrophils; <i>PADI4</i> , <i>CD24</i> , <i>OLFM4</i> , <i>LCN2</i> , <i>BPI</i> , <i>S100A8</i> , <i>S100A9</i> , <i>ISG15</i> , <i>IFITM1/3</i> , <i>RSAD2</i> , <i>FCGR1A</i> (CD64), <i>CD274</i> (PD-L1) and <i>ARG1</i> in low-density neutrophils (LDN); <i>MPO</i> , <i>ELANE</i> and <i>PRTN3</i> in the pro-neutrophils; <i>CD177</i> on mature activated neutrophils; ↓ expression of <i>HLA-DR</i> ; <i>ISG15</i> and <i>IFI6</i> in monocytes
Lee J.S. et al., 2020		
Peripheral blood mononuclear cells (PBMCs); during hospitalization	Severe form, mild form and asymptomatic form ( <i>n</i> = 8)	↑ proportion of classical monocytes; ↓ proportion of dendritic cells, non-classical monocytes, intermediate monocytes, NK cells, EM-like CD8 <sup>+</sup> T cells and EM-like CD4 <sup>+</sup> T cells; ↑ IFN-stimulated genes (ISG), including <i>ISG15</i> , <i>IFITM1/2/3</i> and <i>ISG20</i> ; <i>TNF</i> , <i>IL1B</i> , <i>CCL3</i> , <i>CCL4</i> and <i>CXCL2</i> in monocytes

**Table S1 (continued)**

Material and time of collecting	Severity of COVID-19 (number of patients)	Features of gene expression and cellular composition in severe COVID-19
Zhang J.Y. et al., 2020		
Peripheral blood mononuclear cells (PBMCs); during hospitalization	Moderate ( $n = 7$ ), severe ( $n = 4$ ) and convalescent ( $n = 6$ , of which 4 were combined with cases of moderate severity)	<p>↓ relative % of naive T cells, mucosal-associated invariant T cells (MAIT), and dendritic cells;</p> <p>↑ relative % of pro-T cells, plasma B cells, CD14<sup>+</sup> monocytes and platelets;</p> <p>↑ response to IFN-<math>\alpha</math> in all major cell types, with the exception of plasma B cells; metabolic and catabolic processes, cytokine secretion in monocytes; signaling NF-<math>\kappa</math>B pathway and cytotoxicity in NK cells; <i>ITGB2</i>, <i>CCL5</i> and <i>CXCR2</i> in NK cells; pathways of cell death and migration; <i>TRAJ39</i> and <i>TRAJ43</i>; genes associated with IFN-<math>\alpha</math> response, protein synthesis, maturation, and biological processes related to transport in B cells</p>
Yao et al., 2021		
Peripheral blood mononuclear cells (PBMCs); at different time points	Moderate ( $n = 5$ ), acute respiratory distress syndrome ( $n = 6$ ) and convalescents ( $n = 6$ )	<p>↑ biological processes “response to type I IFN”, “response to virus”, “response to IFN-<math>\gamma</math>” and “response to IFN-<math>\beta</math>” in NK cells, CD8<sup>+</sup> T cells, CD4<sup>+</sup> T cells; apoptosis genes in CD8<sup>+</sup> T cells, classical monocytes, and B cells; genes of metabolic and apoptotic pathways in CD4<sup>+</sup> T cells; IFN-mediated response and apoptotic signals in B cells; oxidative phosphorylation pathways in all cellular compartments; the PD-1 signaling pathway in monocytes; IRF7 in lymphocytes;</p> <p>↓ genes associated with cytotoxic function in NK cells, CD8<sup>+</sup> T cells; activation genes of B cells, classical monocytes; major histocompatibility complex (MHC) class I and MHC class II in monocytes; IFN type I pathways in monocytes; signaling of sirtuins in all cellular compartments; the signaling pathway of eukaryotic translation initiation factor 2 (eIF2) in all cells except monocytes; impaired phagocytosis and altered differentiation of classical monocytes</p>
Wilk et al., 2021		
Peripheral blood samples and peripheral blood mononuclear cells (PBMCs); at different time points	Mild form ( $n = 8$ ), moderate form ( $n = 11$ ), severe form ( $n = 8$ ), critical form ( $n = 6$ )	<p>Depletion of CD16 monocytes, dendritic cells, and NK cells;</p> <p>↑ plasmoblasts; the emergence of a population of developing neutrophils;</p> <p>↑ genes associated with anti-inflammatory reactions (<i>PKM</i> and <i>CD163</i>); <i>PADI4</i>, <i>CXCR1</i>, <i>S100A8</i>, <i>S100A9</i>, <i>CD274</i>, <i>CXCL16</i>, <i>TNFSF10</i>, genes associated with neutrophil phagocytosis and degranulation; <i>DEFA1B</i>, <i>LCN2</i> and <i>MMP8</i> in immature neutrophils; IFN-stimulated genes (ISG), <i>CD163</i>, <i>PLAC8</i>, <i>MPO</i>, <i>ARG1</i>, <i>C19orf59</i>, <i>IRAK3</i>, <i>ANXA3</i>, <i>RBM47</i> and <i>TLR5</i> in monocytes;</p> <p>↓ <i>FCER1A</i>, <i>CD83</i>, <i>CTSS</i> in type 2 dendritic cells; <i>CD4</i>, <i>HLA-DR</i>, <i>IL1B</i>, <i>TNF</i>, NF-<math>\kappa</math>B pathway, level of proinflammatory cytokines in monocytes</p>

**Table S1 (end)**

Material and time of collecting	Severity of COVID-19 (number of patients)	Features of gene expression and cellular composition in severe COVID-19
Saichi et al., 2021		
APC-enriched peripheral blood mononuclear cells (PBMCs); on the first and fourth days of hospitalization	Moderate form ( <i>n</i> = 5) and severe form ( <i>n</i> = 10)	<p>↑ <i>IL1B</i>, <i>CXCR4</i>, <i>CD36</i>, <i>CD83</i>, <i>AREG</i>, <i>ITGAM</i>, <i>CTSD</i>, <i>CTSB</i> and <i>RETN</i>, <i>EREG</i>, <i>ANXA2</i>; hypoxia and TNF-<math>\alpha</math> signaling; <i>AREG</i>, <i>IL1R2</i>, <i>NRGN</i> and <i>S100A12</i>; <i>CXCL8</i>, <i>NAMPT</i> and <i>GOS2</i> in APC; signaling pathways "TNF-<math>\alpha</math>", "IL2 STAT5", "hypoxia", "IL6 JAK STAT3", "P53" and "MTORC" in plasmacytoid dendritic cells (pDC); complement system (C1GC and C1GB), VSIG4 and CD163 in monocytes; signaling pathways "complement system", "TNF-<math>\alpha</math>", "KRAS" and "hypoxia" in monocytes; complement-related genes (<i>C1QA</i>, <i>C1QB</i> and <i>C1GC</i>) in CD16<sup>+</sup> monocytes; signaling pathways NFKB/STAT; ↓ <i>TGFB1</i> and <i>IL10RA</i>; IFN, MX2, ISG15, IRF7, BST2, IFITM2 and ADAR; genes in modules "innate perception", "antiviral effector molecules" and "cytotoxicity"; TLR7, DHX9, DHX36, TNFSF10 and IRF7; antiviral ISG, <i>BST2</i> and <i>PYCARD</i> in pDC; signaling "IFN-<math>\alpha</math>" and "IFN-<math>\gamma</math>" in monocytes; IL10, CCL5 and TGFb, <i>IFNAR1</i> and <i>IFNAR2</i> in APC</p>
Ren et al., 2021		
Peripheral blood mononuclear cells (PBMCs) with further sorting into B and T cells; –	Mild and moderate forms ( <i>n</i> = 22), severe form ( <i>n</i> = 54), convalescents ( <i>n</i> = 95), mild and moderate forms ( <i>n</i> = 57), severe form ( <i>n</i> = 38)	<p>↑ B cells, plasma cells, macrophages, megakaryocytes and CD14<sup>+</sup> monocytes; plasmoblastic cells <i>MKI67</i>; hyperinflammatory megakaryocytes; CD4<sup>+</sup> T cells; ↓ T cells, dendritic cells, <math>\gamma\delta</math>T cells and MAIT cells; ↑ genes encoding constant regions IgA1, IgA2, IgG1 and IgG2 in plasma cells; <i>MKI67</i> in plasmoblastic cells; <i>TNF</i>, <i>CCL3</i>, <i>IL1B</i>, <i>CXCL8</i>, <i>IL6</i>, <i>TGFB1</i>, <i>LTB</i> and <i>IFNG</i>; <i>ANXA1</i>, <i>FPR1</i>, <i>S100A9</i>, <i>S100A8</i> in T, B, NK and dendritic cells; cytokines in monocyte subtypes, T cell subtypes (CD4<sup>+</sup> and CD8<sup>+</sup>) and in one subtype of megakaryocytes; <i>CCL3</i>, <i>IL1RN</i> and <i>TNF</i> in monocytes; proinflammatory cytokines (IL1B, TNF, IL-6, CCL3); <i>IFNG</i> in subtype of CD8<sup>+</sup> T cells</p>
Liu C. et al., 2021		
Peripheral blood mononuclear cells (PBMCs); material collected during hospitalization (median = 11 days after onset of symptoms)	Moderate form ( <i>n</i> = 3), severe form ( <i>n</i> = 5) and critical form ( <i>n</i> = 25, 4 of whom died during hospitalization)	<p>↑ adaptive NK cells; signs of NK cell depletion; ↓ plasmacytoid dendritic cells; ↑ signatures of apoptotic genes (<i>BRCA2</i>, <i>CASP3</i>, <i>CASP8</i>, <i>BID</i>, <i>BAK1</i> and <i>XBP1</i>) in pDC; oxidative stress genes (<i>FOS</i>, <i>PHC3</i>, <i>MDM4</i>, <i>CBX6</i> and <i>CDKN2D</i>), genes of fatty acid biosynthesis and oxidation in NK cells; NF-<math>\kappa</math>B pathway in nonclassical monocytes, subgroups of NK cells, MAIT cells, memory cells and naive B cells; signals of cellular activation and proliferation (cell cycle genes) in CD8<sup>+</sup> memory T cells; IL-6, TNFRSF1B, IL-17, IL-18; cytokine-mediated signaling pathways (IL-4/13 and IL-17) in classical monocytes; ↓ TNF-<math>\beta</math>; IFN-I gene signatures; <i>RELA</i>, <i>NFKB1B</i>, <i>STAT1</i> and <i>IL8</i>, NF-<math>\kappa</math>B pathway in NK cells and classical monocytes; chemokine signaling; IL-1 response; mTORC1 pathway; <i>IFNG</i> in NK cells</p>

Note. ↑ – increase in proportion or expression. ↓ – decreased proportion or expression. "–" – the time of collection is not specified. IL – Interleukin. APC – Antigen-presenting cells.