**Supplementary Table S1** 108 specific target genes for Microfluidic qPCR

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ABCC4 | FOS | MAP2K7 | PARP2 | PYCARD | TGM2 |
| AHR | FOXP3 | MAPK14 | PIAS1 | RANBP10 | TMEM57 |
| AKR1C4 | GRB2 | MAPK8 | PIAS2 | RIPK2 | TNF |
| ATG13 | HSPA8 | MCL1 | PIAS4 | RPS21 | TNFRSF10A |
| B3GAT1 | HSPBAP1 | MRPL13 | PIK3R3 | RPS6 | TNFRSF10B |
| CALM3 | IL17F | MYT1 | PPIA | RXRB | TNFRSF1A |
| CARM1 | IL2RA | NAIP | PPP3CA | S100A7A | TNFRSF1B |
| CBL | IL2RB | NBAS | PPP3CB | SCP2 | TNFRSF25 |
| CD86 | IL6ST | NDUFA2 | PRKAA1 | SELL | TNFRSF8 |
| CEBPB | IRGM | NDUFS1 | PRKAB1 | SNX5 | TNFRSF9 |
| CFLAR | JAK1 | NFATC1 | PRKCH | SOAT1 | TNFSF10 |
| COMMD4 | JUNB | NFATC2 | PRKCQ | SOCS3 | TRADD |
| DENND4A | JUND | NFATC3 | PTEN | SOS1 | TRAF2 |
| E2F2 | LCK | NFATC4 | PTPN11 | SRC | TRAF3 |
| E2F7 | LCP2 | NMI | PTPN6 | STAT3 | TRAP1 |
| E2F8 | LTA | NOD1 | PTPRC | STAT5A | TYK2 |
| EGF | LTBR | NPC1 | PTPRF | SYK | UBXN1 |
| FKBP1A | M6PR | PARP1 | PUS1 | TGFB1 | VDR |

**Supplementary Table S2**

Table 2. Clinical characteristics after initial treatment of COVID-19 patients

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Group A (n=6) | | | Group B (n=3) | | |
| A1 | A2 | *p* value | B1 | B2 | *p* value |
| Leucocytes (×10⁹/L, normal range 3.5-9.5) a |  |  | 1.00 |  |  | 1.00 |
| Increased | 1 (16.7) | 1 (16.7) |  | 0 (0) | 0 (0) |  |
| Decreased | 1 (16.7) | 0 (0) |  | 1 (33.3) | 0 (0) |  |
| Neutrophils (×10⁹/L, normal range 1.8-6.3) a |  |  | 1.00 |  |  | / |
| Increased | 3 (50) | 2 (33.3) |  | 0 (0) | 0 (0) |  |
| Lymphocytes (×10⁹/L, normal range 1.1-3·2) a |  |  | 1.00 |  |  | 1.00 |
| Decreased | 4 (66.7) | 4 (66.7) |  | 1 (33.3) | 0 (0) |  |
| Platelets (×10⁹/L, normal range 125.0-350.0) a |  |  | 1.00 |  |  | / |
| Increased | 1 (16.7) | 1 (16.7) |  | 0 (0) | 0 (0) |  |
| Haemoglobin (g/L, normal range 130.0-175.0) a |  |  | 1.00 |  |  | / |
| Decreased | 4 (66.7) | 5 (83.3) |  | 0 (0) | 0 (0) |  |
| Prothrombin time (s, normal range 10.5-13.5) a |  |  | 1.00 |  |  | / |
| Increased | 0 (0) | 1 (16.7) |  | 0 (0) | 0 (0) |  |
| Albumin (g/L, normal range 40.0-55.0) a |  |  | / |  |  | 1.00 |
| Decreased | 6 (100) | 6 (100) |  | 2 (66.67) | 3 (1) |  |
| Alanine aminotransferase (U/L, normal range 9.0-50.0) a |  |  | 1.00 |  |  | 1.00 |
| Increased | 2 (33.3) | 3 (50) |  | 0 (0) | 0 (0) |  |
| Decreased | 1 (16.7) | 0 (0) |  | 1 (33.3) | 0 (0) |  |
| Aspartate aminotransferase (U/L, normal range 51.0-310.0) a |  |  | 1.00 |  |  | / |
| Increased | 3 (50) | 3 (50) |  | 0 (0) | 0 (0) |  |
| Creatine kinase (U/L, normal range 50.0-310.0) a |  |  | 0.740 |  |  | 1.00 |
| Increased | 1 (16.7) | 1 (16.7) |  | 1 (33.3) | 0 (0) |  |
| Decreased | 1 (16.7) | 3 (50) |  | 2 (66.7) | 2 (66.7) |  |
| Lactic acid (mmol/L, normal range 0.4-2.0) a |  |  | 0.545 |  |  | / |
| Increased | 3 (50) | 1 (16.7) |  | 0 (0) | 0 (0) |  |
| Creatinine (μmol/L, normal range 57.0-111.0) a |  |  | 1.000 |  |  | 1.00 |
| Increased | 1 (16.7) | 1 (16.7) |  | 0 (0) | 0 (0) |  |
| Decreased | 2 (33.3) | 3 (50) |  | 0 (0) | 1 (33.3) |  |
| Procalcitonin (ng/mL, normal range 0.0-5.0) a |  |  | 1.000 |  |  | / |
| Decreased | 0 (0) | 1 (16.7) |  | 0 (0) | 0 (0) |  |
| C-reactive protein (mg/L, normal range <3) a |  |  | 1.000 |  |  | 1.00 |
| Increased | 6 (100) | 5 (83.3) |  | 2 (66.7) | 2 (66.7) |  |

aFisher’s Exact Test

**Supplementary Table S3**

The 34 DEGs both occurred in A1 and B1 were involved in the significant dysregulated pathways

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| GroupID | Category | Term | Description | LogP | Log(q-value) | InTerm\_InList | Symbols |
| 1\_Summary | KEGG Pathway | hsa04659 | Th17 cell differentiation | -13.6521 | -9.33454522 | 9/107 | AHR,IL2RB,JAK1,NFATC2,NFATC3,PPP3CA,PPP3CB,RXRB,STAT5A,FKBP1A,JUNB,TNF,TNFRSF1A,LCP2,PTPRC,PRKAA1,JUND,PTEN,PTPN11,SELL,PYCARD,PIAS1 |
| 2\_Summary | GO Biological Processes | GO:0019221 | cytokine-mediated signaling pathway | -13.2567 | -9.24019767 | 15/798 | TNFRSF8,HSPA8,IL2RB,JAK1,JUNB,MCL1,PTPN11,PTPRC,STAT5A,TNF,TNFRSF1A,TNFRSF1B,PIAS1,TRADD,PYCARD |
| 3\_Summary | KEGG Pathway | hsa04380 | Osteoclast differentiation | -12.8732 | -9.03279961 | 9/130 | JAK1,JUNB,JUND,LCP2,NFATC2,PPP3CA,PPP3CB,TNF,TNFRSF1A,HSPA8,NFATC3,NDUFA2,NDUFS1,TRADD |
| 4\_Summary | KEGG Pathway | hsa04920 | Adipocytokine signaling pathway | -11.2409 | -7.76843983 | 7/69 | PRKAA1,PTPN11,RXRB,TNF,TNFRSF1A,TNFRSF1B,TRADD,JAK1,PTPRC,PIAS1,PYCARD,HSPA8,TNFRSF10B,PTEN,NDUFA2,NDUFS1,RPS6,STAT5A,MCL1,UBXN1 |
| 5\_Summary | Canonical Pathways | M11736 | SA MMP CYTOKINE CONNECTION | -10.918 | -7.50357149 | 5/15 | TNFRSF8,SELL,TNF,TNFRSF1A,TNFRSF1B,PPP3CA,PPP3CB,IL2RB,TNFRSF10B,FKBP1A,PTEN,PTPN11,HSPA8,JUND |
| 6\_Summary | GO Biological Processes | GO:0097191 | extrinsic apoptotic signaling pathway | -10.7324 | -7.3691382 | 9/224 | MCL1,PTEN,PTPRC,TNF,TNFRSF1A,TNFRSF1B,TRADD,TNFRSF10B,PYCARD,TNFRSF8,RPS6,JUNB,FKBP1A,PPP3CA,JUND,STAT5A,LCP2,UBXN1 |
| 7\_Summary | KEGG Pathway | hsa04650 | Natural killer cell mediated cytotoxicity | -9.20631 | -6.09288869 | 7/133 | LCP2,NFATC2,PPP3CA,PPP3CB,PTPN11,TNF,TNFRSF10B,FKBP1A,PTEN,PTPRC,HSPA8,PRKAA1,TNFRSF1B,PYCARD,AHR,PIAS2,RPS6,TNFRSF1A,RPS21,JAK1,STAT5A |
| 8\_Summary | KEGG Pathway | hsa04630 | Jak-STAT signaling pathway | -8.72078 | -5.72545682 | 7/156 | IL2RB,JAK1,MCL1,PTPN11,STAT5A,PIAS1,PIAS2,JUNB,RPS6,HSPA8,TNFRSF10B,TNF,TRADD,PYCARD |
| 9\_Summary | GO Biological Processes | GO:0042110 | T cell activation | -7.93116 | -5.10498147 | 9/466 | FKBP1A,NFATC2,PPP3CA,PPP3CB,PTPN11,PTPRC,RPS6,TNFRSF1B,PYCARD,AHR,IL2RB,PTEN,TNF,PRKAA1,TNFRSF8,LCP2,TNFRSF10B,UBXN1,HSPA8,SELL,JUNB,TNFRSF1A,MCL1 |
| 10\_Summary | GO Biological Processes | GO:0032870 | cellular response to hormone stimulus | -6.41011 | -3.88207091 | 9/703 | JUNB,JUND,PRKAA1,PTEN,PTPN11,RXRB,STAT5A,PIAS1,PIAS2,LCP2,PTPRC,TNF,AHR,TNFRSF1B,TRADD,FKBP1A,RPS6 |
| 12\_Summary | GO Biological Processes | GO:0045862 | positive regulation of proteolysis | -6.19974 | -3.7484617 | 7/364 | PTEN,TNF,TNFRSF1B,PIAS1,TRADD,TNFRSF10B,PYCARD,PRKAA1,UBXN1,FKBP1A,PPP3CA,RPS6,PPP3CB,PTPRC |
| 13\_Summary | GO Biological Processes | GO:0001816 | cytokine production | -5.97845 | -3.59437963 | 9/792 | TNFRSF8,LCP2,NFATC2,NFATC3,PTPN11,PTPRC,TNF,TNFRSF1B,PYCARD |
| 14\_Summary | GO Biological Processes | GO:0071396 | cellular response to lipid | -5.79413 | -3.46615823 | 8/610 | AHR,PRKAA1,RXRB,TNF,TNFRSF1B,PIAS1,PIAS2,PYCARD,JAK1,PTEN,STAT5A,PTPN11 |
| 15\_Summary | GO Biological Processes | GO:0014074 | response to purine-containing compound | -5.68228 | -3.38062744 | 5/150 | AHR,JUNB,JUND,PRKAA1,PTEN,PPP3CA,TNF,PTPRC,PIAS1,STAT5A,JAK1 |
| 16\_Summary | KEGG Pathway | hsa04151 | PI3K-Akt signaling pathway | -5.12953 | -2.93584331 | 6/342 | IL2RB,JAK1,MCL1,PRKAA1,PTEN,RPS6 |
| 17\_Summary | GO Biological Processes | GO:0080135 | regulation of cellular response to stress | -3.25344 | -1.43832503 | 6/749 | HSPA8,MCL1,PTEN,TNF,PYCARD,UBXN1,PRKAA1 |
| 18\_Summary | GO Biological Processes | GO:0046034 | ATP metabolic process | -3.06681 | -1.28959938 | 4/305 | HSPA8,NDUFA2,NDUFS1,PRKAA1,PTPRC,PYCARD,PTEN |
| 19\_Summary | GO Biological Processes | GO:0072594 | establishment of protein localization to organelle | -3.01736 | -1.25369794 | 5/549 | HSPA8,PPP3CA,PRKAA1,RPS6,RPS21,TNFRSF1B,TNF,PPP3CB,PTEN |
| 20\_Summary | GO Biological Processes | GO:0006457 | protein folding | -2.39236 | -0.74320579 | 3/229 | FKBP1A,HSPA8,UBXN1 |

**Supplementary Table S4** The 29 genes that specific to A1 group were involved in the significant dysregulated pathways

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| GroupID | Category | Term | Description | LogP | Log(q-value) | InTerm\_InList | Symbols |
| 1\_Summary | Canonical Pathways | M88 | PID CD8 TCR PATHWAY | -12.7322 | -8.41463 | 7/53 | CBL,CD86,GRB2,LCK,PRKCQ,PTPN6,SOS1,MAP2K7,CEBPB,STAT3,PPIA,SOCS3,TRAF3,CFLAR,SOAT1 |
| 2\_Summary | Canonical Pathways | M233 | PID EPO PATHWAY | -11.7452 | -7.90479 | 6/34 | CBL,GRB2,MAPK8,PTPN6,SOS1,SOCS3,LCK,STAT3,MAP2K7,CEBPB,TRAF3,PPIA,TNFRSF10A,PRKCQ,NPC1,CFLAR,CARM1,CD86 |
| 3\_Summary | Reactome Gene Sets | R-HSA-449147 | Signaling by Interleukins | -10.2716 | -6.90832 | 11/634 | CBL,CD86,GRB2,LCK,PPIA,MAPK8,MAP2K7,PTPN6,SOS1,STAT3,SOCS3,TRAF3,PIAS4 |
| 4\_Summary | KEGG Pathway | hsa04668 | TNF signaling pathway | -8.6172 | -5.4136 | 6/108 | CEBPB,MAPK8,MAP2K7,TRAF3,CFLAR,SOCS3,GRB2,LCK,CBL,CD86,TNFRSF10A,PIAS4,NAIP,PTPN6 |
| 5\_Summary | Canonical Pathways | M28 | PID IL4 2PATHWAY | -7.94693 | -4.88466 | 5/65 | CBL,CEBPB,GRB2,PTPN6,SOCS3,M6PR,NBAS |
| 6\_Summary | KEGG Pathway | hsa04064 | NF-kappa B signaling pathway | -7.11128 | -4.2251 | 5/95 | LCK,PRKCQ,TRAF3,CFLAR,PIAS4,CEBPB,MAPK8,TNFRSF10A,PARP2,SOS1,STAT3,NAIP |
| 7\_Summary | Canonical Pathways | M161 | PID IFNG PATHWAY | -6.89202 | -4.02164 | 4/40 | CBL,CEBPB,STAT3,PIAS4,NAIP,PARP2 |
| 8\_Summary | GO Biological Processes | GO:0030260 | entry into host cell | -6.34812 | -3.64336 | 5/135 | CBL,CD86,GRB2,NPC1,PPIA,PTPN6,STAT3 |
| 9\_Summary | GO Biological Processes | GO:0051090 | regulation of DNA-binding transcription factor activity | -6.32137 | -3.63865 | 7/432 | PRKCQ,MAPK8,STAT3,TRAF3,CFLAR,CARM1,PIAS4,SOCS3,TNFRSF10A,LCK,ATG13,GRB2,MAP2K7 |
| 10\_Summary | GO Biological Processes | GO:0042129 | regulation of T cell proliferation | -6.03699 | -3.43768 | 5/156 | CD86,CEBPB,PRKCQ,PTPN6,SOS1,STAT3,LCK,NPC1,MAPK8,CFLAR,CARM1,TRAF3 |
| 11\_Summary | Canonical Pathways | M290 | PID IL12 STAT4 PATHWAY | -5.12871 | -2.87563 | 3/33 | CD86,MAPK8,STAT3,MAP2K7,CEBPB,TRAF3,ATG13,NPC1,PTPN6,M6PR |
| 12\_Summary | Reactome Gene Sets | R-HSA-5663205 | Infectious disease | -4.14842 | -2.09095 | 5/383 | CBL,GRB2,LCK,PPIA,MAP2K7,PRKCQ |
| 13\_Summary | GO Biological Processes | GO:0045859 | regulation of protein kinase activity | -3.59449 | -1.63489 | 6/796 | CBL,MAP2K7,PTPN6,TNFRSF10A,SOCS3,ATG13,PRKCQ |
| 14\_Summary | GO Biological Processes | GO:0071407 | cellular response to organic cyclic compound | -3.44618 | -1.49786 | 5/542 | CEBPB,NPC1,STAT3,CFLAR,CARM1,SOS1,PARP2,PRKCQ,SOCS3 |
| 15\_Summary | Reactome Gene Sets | R-HSA-5693532 | DNA Double-Strand Break Repair | -3.03608 | -1.12678 | 3/166 | MAPK8,PARP2,PIAS4,PRKCQ |
| 16\_Summary | GO Biological Processes | GO:0031330 | negative regulation of cellular catabolic process | -2.45237 | -0.62338 | 3/266 | NPC1,STAT3,NBAS |
| 17\_Summary | GO Biological Processes | GO:0008202 | steroid metabolic process | -2.18835 | -0.39715 | 3/331 | NPC1,SOAT1,PIAS4 |

**Supplementary Table S5** The top DEGs of A1 ranked by degree (>20) and significantly FC (|log2 FC| > 1) involved in the pathways through PPI analysis

|  |  |  |  |
| --- | --- | --- | --- |
| A1\_Label | Degree | Betweenness | Expression |
| CBL | 181 | 192782.8 | -1.93228 |
| HSPA8 | 129 | 196558.8 | -1.94818 |
| TNFRSF1B | 120 | 111922.2 | -1.07704 |
| TNFRSF1A | 114 | 124687.9 | -1.19104 |
| LCK | 94 | 77297.98 | -3.07017 |
| PTPN11 | 82 | 78407.59 | -1.26595 |
| PTEN | 78 | 91890.88 | -1.29593 |
| MAPK8 | 72 | 87660.32 | -1.19076 |
| CEBPB | 70 | 81454.75 | -1.21814 |
| PTPN6 | 68 | 55654.25 | -1.02874 |
| PIAS1 | 65 | 66120.44 | -1.7528 |
| SOCS3 | 61 | 55991.13 | -1.70761 |
| RPS6 | 52 | 49634.01 | -4.34778 |
| STAT5A | 51 | 40731.6 | -2.1158 |
| JAK1 | 49 | 45962.87 | -1.84876 |
| TRADD | 46 | 20636.43 | -2.66783 |
| TRAF3 | 45 | 48733.56 | -1.81163 |
| CFLAR | 45 | 39096.84 | -1.58937 |
| TNF | 44 | 36379.07 | -2.79356 |
| PRKAA1 | 41 | 49220.33 | -1.5301 |
| PIAS4 | 41 | 42400.12 | -1.52085 |
| PPIA | 34 | 30454.93 | -1.09238 |
| LCP2 | 33 | 28531.6 | -1.93431 |
| PIAS2 | 32 | 33946.83 | -2.38271 |
| SOS1 | 31 | 22897.2 | -1.85018 |
| JUNB | 28 | 23729.24 | -3.30264 |
| PRKCQ | 28 | 23640.17 | -2.2003 |
| MCL1 | 25 | 24162.43 | -1.75095 |
| NFATC2 | 24 | 17536.86 | -3.16357 |
| IL2RB | 22 | 17898.34 | -3.07834 |
| UBXN1 | 21 | 23068.16 | -1.61258 |
| PTPRC | 20 | 19966.89 | -2.385 |
| CD86 | 20 | 5937.56 | -1.48543 |
| CARM1 | 18 | 18981.86 | -2.42769 |
| JUND | 17 | 9885.8 | -1.82418 |
| TNFRSF10A | 17 | 8361.54 | -1.00943 |
| MAP2K7 | 13 | 10535.28 | -2.31535 |
| TNFRSF10B | 13 | 2037.5 | -1.54604 |
| AHR | 13 | 11059.89 | -1.35261 |
| SELL | 12 | 14588.11 | -1.63141 |
| FKBP1A | 12 | 13735.48 | -1.26562 |
| RPS21 | 11 | 1950.7 | -2.33341 |
| RXRB | 11 | 15297.31 | -2.03817 |
| PARP2 | 10 | 9144.88 | -1.49388 |
| NAIP | 10 | 10958.53 | -1.24764 |

**Supplementary Table S6** The top DEGs of B1 ranked by degree (>20) and significantly FC (|log2 FC| > 1) involved in the pathways through PPI analysis

|  |  |  |  |
| --- | --- | --- | --- |
| B1\_Label | Degree | Betweenness | Expression |
| RPS6 | 52 | 39343.71 | -3.95987 |
| TNF | 44 | 32595.07 | -3.50587 |
| JUNB | 28 | 21049.64 | -2.82229 |
| RPS21 | 11 | 1387.16 | -2.32529 |
| TRADD | 46 | 18924.72 | -2.32069 |
| PIAS2 | 32 | 24811.08 | -2.29114 |
| STAT5A | 51 | 43898.78 | -2.22307 |
| AHR | 13 | 9888.96 | -2.21396 |
| IL2RB | 22 | 10788.21 | -1.89278 |
| JUND | 17 | 10012.73 | -1.84332 |
| RXRB | 11 | 10086.96 | -1.8043 |
| TNFRSF1A | 114 | 96405.47 | -1.69855 |
| NFATC2 | 24 | 17532.97 | -1.63171 |
| PTPRC | 20 | 17031.17 | -1.62054 |
| FKBP1A | 12 | 9700.55 | -1.55267 |
| TNFRSF10B | 13 | 5289.46 | -1.40777 |
| JAK1 | 49 | 41657.42 | -1.32924 |
| PIAS1 | 65 | 59952.28 | -1.29143 |
| MCL1 | 25 | 20363.13 | -1.27261 |
| TNFRSF1B | 120 | 110077.5 | -1.24562 |
| LCP2 | 33 | 33216.19 | -1.22276 |
| HSPA8 | 129 | 140170.8 | -1.17403 |
| PTEN | 78 | 74899.31 | -1.15863 |
| PRKAA1 | 41 | 37981.67 | -1.06613 |
| PYCARD | 31 | 26356.01 | -1.05434 |
| NOD1 | 19 | 14694.01 | -1.02841 |
| UBXN1 | 21 | 16934.62 | -1.01984 |
| CALM3 | 206 | 197022.8 | -1.01457 |

**Supplementary FigureS1 Correlation between IL-10 level of COVID-19 cases and IL-2 levels (1A), IL-4 (1B), IL-17 (1C), TNFα (1D) and IFNγ (1E). P values (two-sided) and r values are based on Spearman’s rank test.**

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