# Supplementary Material for

## Distinguishing Incubation and Acute Disease Stages of Mild-to-Moderate COVID-19

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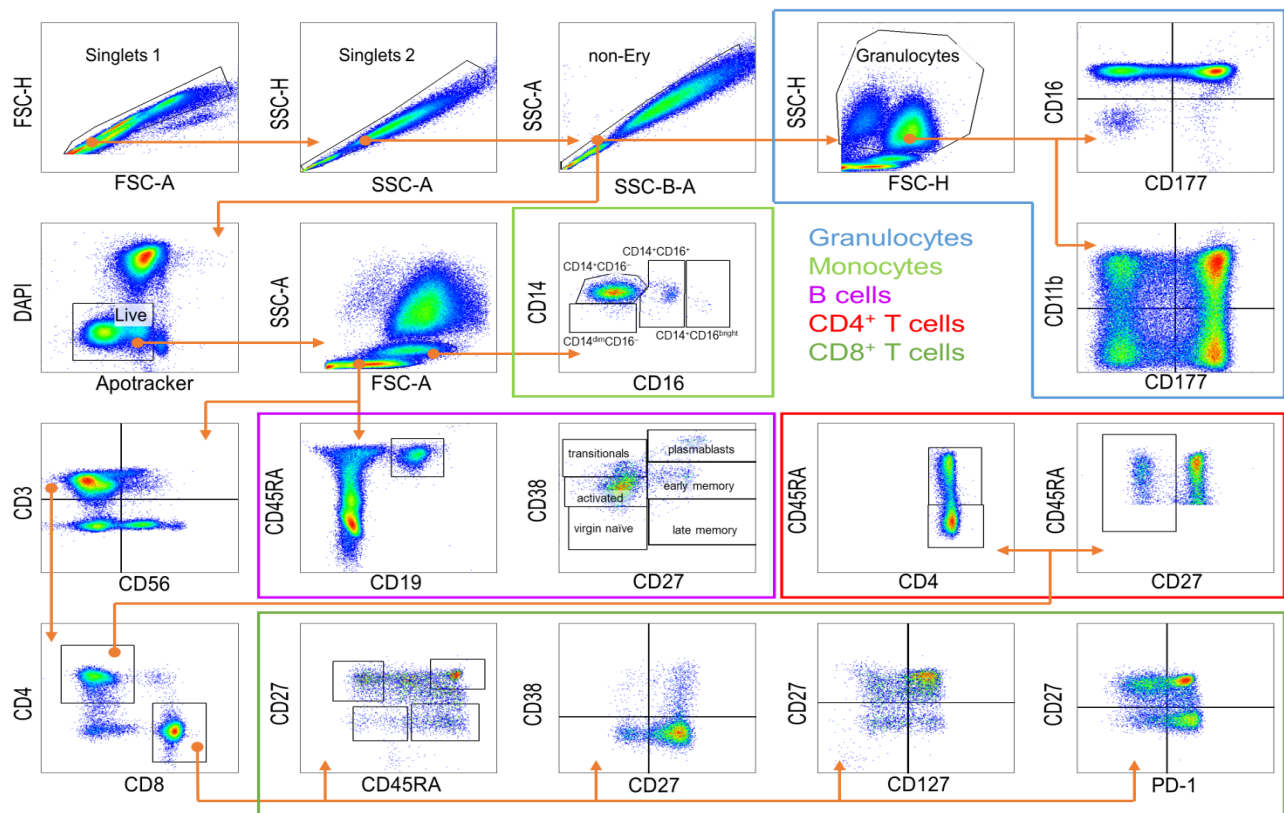
**The file includes:**

Figure S1

Tables S1 to S17

**Table S1.** CD14^{+} Multi-Pathway Signaling.

| Protein [1/µg] | Controls (n = 12) Median (IQR) | COVID-19 (n = 11) Median (IQR) | MWW p-value | p-Protein/Protein | Controls (n = 12) Median (IQR) | COVID-19 (n = 11) Median (IQR) | MWW p-value |
|---|---|---|---|---|---|---|---|
| CREB | 35.8 (26.0 – 53.6) | 8.0 (3.87 – 36.3) | 0.0792 | p-CREB/CREB | 0.0013 (0.0006 – 0.0108) | 0.0108 (0.0019 – 0.0340) | 0.212 |
| JNK | 15.0 (12.5 – 23.3) | 10.0 (6.89 – 13.6) | 0.051 | p-JNK/JNK | 0.0294 (0.0113 – 0.0621) | 0.0483 (0.0259 – 0.0670) | 0.566 |
| NF-κB | 0.10 (0.10 – 0.20) | 0.09 (0.06 – 0.15) | 0.288 | p-NF-κB/NF-κB | 1.9189 (0.0412 – 7.6768) | 2.4977 (1.7329 – 5.5697) | 0.695 |
| p38 | 3.74 (3.32 – 10.9) | 2.21 (1.47 – 12.2) | 0.091 | p-p38/p38 | 0.0193 (0.0075 – 0.0730) | 0.1469 (0.0696 – 0.1703) | 0.060 |
| ERK1/2 | 0.18 (0.14 – 0.21) | 0.14 (0.08 – 0.20) | 0.260 | p-ERK1/2/ERK1/2 | 0.0145 (0.0008 – 0.1724) | 0.1881 (0.0683 – 0.2638) | 0.151 |
| Akt | 13.8 (11.2 – 16.3) | 8.57 (5.90 – 16.3) | 0.260 | p-Akt/Akt | 0.0107 (0.0048 – 0.0166) | 0.0099 (0.0071 – 0.0113) | 0.786 |
| p70S6k | 27.1 (20.7 – 29.3) | 9.97 (5.72 – 15.6) | **0.0036** | p-p70S6K/p70S6k | 0.3323 (0.1159 – 0.5749) | 0.4024 (0.1059 – 0.7781) | 0.786 |
| STAT3 | 157 (112 – 240) | 58.9 (33.8 – 137) | **0.023** | p-STAT3/STAT3 | 0.0429 (0.0217 – 0.1226) | 0.1209 (0.0274 – 0.5245) | 0.316 |
| STAT5 | 33.2 (28.4 – 51.7) | 27.4 (15.5 – 54.5) | 0.449 | p-STAT5/STAT5 | 0.0444 (0.0107 – 0.0580) | 0.0357 (0.0092 – 0.0882) | 0.740 |

MWW: Mann-Whitney-Wilcoxon test.

**Table S2.** CD3+ Multi-Pathway Signaling.

| Protein [1/μg] | Controls (n =10) Median (IQR) | COVID-19 (n = 14) Median (IQR) | MWW p-value | p-Protein/Protein | Controls (n = 10) Median (IQR) | COVID-19 (n = 14) Median (IQR) | MWW p-value |
|---|---|---|---|---|---|---|---|
| CREB | 210 (131 – 347) | 242 (61.4 – 412) | 0.977 | p-CREB/CREB | 1.576 (0.738 – 4.597) | 1.428 (0.023 – 29.87) | 0.886 |
| JNK | 396 (321 – 609) | 332 (174 – 528) | 0.667 | p-JNK/JNK | 0.098 (0.036 – 0.353) | 0.130 (0.043 – 0.174) | 0.886 |
| NF-κB | 95.2 (63.8 – 110) | 44.7 (1.13 – 108) | 0.341 | p-NF-κB/NF-κB | 3.024 (0.352 – 20.42) | 4.258 (3.591 – 6.356) | 0.886 |
| p38 | 144 (120 – 180) | 146 (47.4 – 183) | 0.796 | p-p38/p38 | 0.983 (0.322 – 8.661) | 0.850 (0.207 – 3.785) | 0.508 |
| ERK1/2 | 136 (95.8 – 182) | 85.4 (1.93 – 156) | 0.235 | p-ERK1/2/ERK1/2 | 0.034 (0.002 – 0.283) | 0.125 (0.074 – 0.354) | 0.437 |
| Akt | 5461 (2263 – 10271) | 697 (33 – 6049) | 0.096 | p-Akt/Akt | 0.611 (0.092 – 3.065) | 0.023 (0.008 – 0.149) | **0.036** |
| p70S6k | 202 (150 – 257) | 183 (101 – 257) | 0.709 | p-p70S6K/p70S6k | 0.251 (0.105 – 0.566) | 0.350 (0.096 – 0.648) | 0.752 |
| STAT3 | 42640 (17715 – 62047) | 3656 (690 – 26623) | **0.013** | p-STAT3/STAT3 | 0.024 (0.004 – 0.110) | 0.107 (0.041 – 0.340) | 0.138 |
| STAT5 | 7070 (4494 – 10922) | 630 (106 – 3715) | **0.011** | p-STAT5/STAT5 | 0.044 (0.009 – 0.056) | 0.077 (0.016 – 0.206) | 0.172 |

**Table S3.** CD19+ Multi-Pathway Signaling.

| Protein [1/μg] | Controls (n = 12) Median (IQR) | COVID-19 (n = 11) Median (IQR) | MWW p-value | p-Protein/Protein | Controls (n = 12) Median (IQR) | COVID-19 (n = 11) Median (IQR) | MWW p-value |
|---|---|---|---|---|---|---|---|
| CREB | 309 (144 – 576) | 216 (6.30 – 642) | 0.950 | p-CREB/CREB | 0.0615 (0.0228 – 1.6268) | 0.0647 (0.0038 – 10.281) | 0.950 |
| JNK | 120 (66.6 – 273) | 59.3 (19.7 – 158) | 0.345 | p-JNK/JNK | 0.0519 (0.0221 – 0.1445) | 0.0231 (0.0041 – 0.1370) | 0.414 |
| NF-κB | 9.51 (1.02 – 64.2) | 22.2 (0.31 – 56.0) | 0.662 | p-NF-κB/NF-κB | 2.1005 (1.3766 – 2.8504) | 1.4228 (0.0477 – 3.4136) | 0.950 |
| p38 | 117 (56 – 174) | 43.7 (7.04 – 149) | 0.491 | p-p38/p38 | 0.2374 (0.0764 – 2.7023) | 0.0956 (0.0159 – 2.2763) | 0.573 |
| ERK1/2 | 25.7 (1.19 – 162) | 20.8 (0.20 – 68.4) | 0.345 | p-ERK1/2/ERK1/2 | 0.0982 (0.0342 – 0.2211) | 0.0635 (0.0019 – 0.1417) | 0.491 |
| Akt | 44.7 (32.6 – 103) | 57.7 (24.9 – 67.5) | 0.950 | p-Akt/Akt | 0.0159 (0.0090 – 0.0342) | 0.0096 (0.0024 – 0.0150) | 0.282 |
| p70S6k | 73.1 (62.1 – 92.5) | 69.1 (25.1 – 123) | 0.852 | p-p70S6K/p70S6k | 0.2391 (0.1140 – 0.7140) | 0.4369 (0.0945 – 1.0544) | 1.00 |
| STAT3 | 437 (169 – 1249) | 154 (32.5 – 653) | 0.282 | p-STAT3/STAT3 | 0.0551 (0.0431 – 0.3685) | 0.0305 (0.0052 – 0.1297) | 0.414 |
| STAT5 | 124 (19.6 – 281) | 46.8 (22.4 – 109) | 0.414 | p-STAT5/STAT5 | 0.0449 (0.0370 – 0.0745) | 0.0148 (0.0035 – 0.0278) | 0.059 |

**Table S4.** CD11b+ Multi-Pathway Signaling.

| Protein [1/µg] | Controls (n = 11) Median (IQR) | COVID-19 (n = 9) Median (IQR) | MWW p-value | p-Protein/Protein | Controls (n = 11) Median (IQR) | COVID-19 (n = 9) Median (IQR) | MWW p-value |
|---|---|---|---|---|---|---|---|
| CREB | 1.40 (1.31 – 2.24) | 2.28 (0.69 – 2.87) | 0.766 | p-CREB/CREB | 0.0005 (0.0003 – 0.0114) | 0.0009 (0.0001 – 0.0345) | 0.456 |
| JNK | 12.8 (11.9 – 24.7) | 14.2 (7.40 – 21.2) | 0.552 | p-JNK/JNK | 0.0058 (0.0021 – 0.0362) | 0.0475 (0.0210 – 0.0494) | 0.112 |
| NF-κB | 0.33 (0.29 – 0.47) | 0.22 (0.14 – 0.56) | 0.456 | p-NF-κB/NF-κB | 0.0746 (0.0106 – 2.2910) | 2.0574 (0.0322 – 4.547) | 0.331 |
| p38 | 2.76 (1.96 – 6.34) | 3.52 (1.09 – 6.75) | 0.552 | p-p38/p38 | 0.0138 (0.0033 – 0.0930) | 0.0737 (0.0069 – 0.1237) | 0.370 |
| ERK1/2 | 0.11 (0.07 – 0.25) | 0.13 (0.04 – 0.20) | 0.412 | p-ERK1/2/ERK1/2 | 0.0022 (0.0002 – 0.1471) | 0.0793 (0.0007 – 0.1605) | 0.552 |
| Akt | 13.1 (10.5 – 26.0) | 18.0 (5.71 – 25.9) | 0.603 | p-Akt/Akt | $0.0050 (2.1 \times 10^{-5} – 0.0077)$ | 0.0051 (0.0038 – 0.0099) | 0.456 |
| p70S6k | 4.74 (2.89 – 12.4) | 4.66 (1.37 – 14.9) | 0.656 | p-p70S6K/p70S6k | 0.0789 (0.0312 – 0.3158) | 0.1912 (0.0826 – 0.2617) | 0.503 |
| STAT3 | 9.89 (6.71 – 22.9) | 18.3 (4.65 – 26.5) | 0.824 | p-STAT3/STAT3 | 0.0143 (0.0002 – 0.0855) | 0.0821 (0.0343 – 0.3226) | 0.261 |
| STAT5 | 11.8 (11.4 – 22.2) | 18.9 (6.84 – 19.5) | 0.456 | p-STAT5/STAT5 | 0.0050 (0.0005 – 0.0291) | 0.0125 (0.0071 – 0.0361) | 0.370 |

**Table S5.** Percentages of B cell Subpopulations.

| among gated CD19⁺CD45RA⁺ lymphocytes [%] | healthy controls (n=19) mean ± SEM | incubation phase (n=7) mean ± SEM | early acute infection (n=11) mean ± SEM | late acute infection (n=15) mean ± SEM | ANOVA p-value | ANCOVA p-value |
|---|---|---|---|---|---|---|
| age | 60.00 ± 4.9 | 61.00 ± 6.5 | 64.73 ± 4.1 | 41.43 ± 4.6 | 0.01 | – |
| activated naive | 47.95 ± 3.8 | 56.56 ± 2.1 | 48.63 ± 6.9 | 45.97 ± 3.7 | 0.571 | 0.561 |
| early memory | 11.26 ± 1.3 | 8.25 ± 1.2 | 6.76 ± 0.8 | 12.82 ± 1.1 | **6.50E-03** | **0.035** |
| late memory | 17.63 ± 2.4 | 10.70 ± 1.4 | 10.07 ± 2.3 | 13.60 ± 1.9 | 0.085 | 0.09 |
| plasmablasts | 1.10 ± 0.2 | 2.88 ± 0.8 | 11.47 ± 2.6 | 4.43 ± 1.1 | **6.00E-06** | **5.00E-06** |
| transitionals | 7.07 ± 0.9 | 10.45 ± 1.3 | 6.01 ± 1.2 | 7.48 ± 1.2 | 0.151 | 0.169 |
| virgin naive | 13.42 ± 1.5 | 9.43 ± 0.9 | 14.98 ± 4.3 | 12.92 ± 1.4 | 0.577 | 0.586 |

virgin naïve: CD27⁻CD38⁻; activated naïve: CD27⁻CD38⁺; transitionals: CD27⁻CD38$^{bright}$; late memory: CD27⁺CD38⁻; early memory: CD27⁺CD38$^{dim}$, plasmablasts: CD27⁺CD38$^{very\ bright.}$

**Table S6.** Serum Antibodies.

| Analyte | healthy controls (n=19) mean ± SEM | incubation phase (n=7) mean ± SEM | early acute infection (n=11) mean ± SEM | late acute infection (n=15) mean ± SEM | ANOVA p-value | ANCOVA p-value |
|---|---|---|---|---|---|---|
| Anti-S1_IgM* | 171.76 ± 131.5 | 131.46 ± 65.4 | 4735.23 ± 1193.8 | 5390.80 ± 962.2 | **1.5269E-07** | **1.53E-07** |
| Anti-S1_IgG* | 18.17 ± 2.1 | 19.89 ± 2.5 | 6100.32 ± 2078.9 | 9863.68 ± 1569.5 | **2.9686E-07** | **7.23E-09** |
| Anti-S2_IgM* | 443.58 ± 167.7 | 316.86 ± 96.9 | 3979.75 ± 898.7 | 4161.82 ± 726.6 | **2.0E-06** | **3.93E-07** |
| Anti-S2_IgG* | 1541.97 ± 539.1 | 1227.86 ± 406.5 | 15312.57 ± 1667.5 | 19179.20 ± 1569.7 | **3.3328E-16** | **1.37E-16** |
| Anti-RBD_IgM* | 1383.63 ± 453.2 | 1190.46 ± 435.7 | 8381.55 ± 1496.8 | 8646.05 ± 1089.8 | **3.3099E-08** | **2.59E-09** |
| Anti-RBD_IgG* | 134.55 ± 19.9 | 180.11 ± 42.3 | 9625.34 ± 2391.9 | 14700.11 ± 1288.4 | **3.2145E-12** | **2.68E-13** |
| Anti-N_IgM* | 417.88 ± 153.4 | 238.11 ± 40.0 | 7109.66 ± 1438.3 | 4292.18 ± 964.4 | **7.4512E-07** | **5.32E-07** |
| Anti-N_IgG* | 289.08 ± 36.8 | 503.86 ± 149.2 | 12357.75 ± 1567.5 | 14931.00 ± 1386.9 | **7.3522E-16** | **1.65E-14** |
| Anti-S_IgA# | 0.34 ± 0.0 | 0.38 ± 0.0 | 4.72 ± 1.1 | 6.64 ± 0.7 | **2.5591E-10** | **1.24E-10** |

*[MFI]; #[$A_{450}$].

**Table S7.** Percentages of Monocyte Subpopulations.

| among gated monocytes | healthy controls (n=19) mean ± SEM | incubation phase (n=7) mean ± SEM | early acute infection (n=11) mean ± SEM | late acute infection (n=15) mean ± SEM | ANOVA p-value | ANCOVA p-value |
|---|---|---|---|---|---|---|
| CD14$^+$CD16$^-$ | 0.43 ± 0.1 | 2.31 ± 1.0 | 3.11 ± 1.7 | 2.19 ± 1.2 | 0.254 | 0.251 |
| CD14$^+$CD16$^+$ | 70.69 ± 2.7 | 67.06 ± 3.1 | 68.95 ± 3.6 | 73.35 ± 2.7 | 0.596 | 0.805 |
| CD14$^{dim}$CD16$^-$ | 13.04 ± 1.5 | 9.56 ± 1.5 | 11.24 ± 2.1 | 12.24 ± 1.6 | 0.616 | 0.626 |
| CD14$^+$CD16$^{bright}$ | 11.12 ± 1.0 | 15.29 ± 2.5 | 9.91 ± 1.5 | 7.19 ± 1.0 | **4.0E-03** | **0.026** |

**Table S8.** Percentages of Granulocyte Subpopulations.

| among gated granulocytes [%] | healthy controls (n=19) mean ± SEM | incubation phase (n=7) mean ± SEM | early acute infection (n=11) mean ± SEM | late acute infection (n=15) mean ± SEM | ANOVA p-value | ANCOVA p-value |
|---|---|---|---|---|---|---|
| CD177$^-$CD11b$^+$ | 19.35 ± 4.0 | 16.32 ± 4.2 | 16.24 ± 4.5 | 13.55 ± 2.2 | 0.696 | 0.18 |
| CD177$^+$CD11b$^+$ | 32.56 ± 4.9 | 29.77 ± 8.2 | 33.64 ± 9.0 | 35.03 ± 6.2 | 0.97 | 0.691 |
| CD177$^+$CD11b$^-$ | 28.33 ± 5.1 | 32.27 ± 8.1 | 28.15 ± 5.6 | 29.35 ± 3.5 | 0.969 | 0.969 |
| CD177$^-$CD11b$^-$ | 19.77 ± 3.7 | 21.66 ± 5.8 | 21.96 ± 4.8 | 22.08 ± 4.9 | 0.976 | 0.987 |
| CD177$^-$CD16$^+$ | 36.57 ± 5.5 | 31.93 ± 7.9 | 34.65 ± 8.0 | 26.76 ± 5.2 | 0.664 | 0.536 |
| CD177$^+$CD16$^+$ | 60.01 ± 5.3 | 63.46 ± 9.1 | 63.35 ± 8.0 | 65.68 ± 5.8 | 0.938 | 0.558 |
| CD177$^+$CD16$^-$ | 0.04 ± 0.0 | 0.17 ± 0.1 | 0.29 ± 0.1 | 0.45 ± 0.1 | **0.02** | **0.012** |
| CD177$^-$CD16$^-$ | 2.98 ± 1.5 | 4.43 ± 3.7 | 1.72 ± 0.6 | 7.12 ± 4.6 | 0.42 | 0.782 |

**Table S9.** Percentages of CD8$^+$ T Cell Subpopulations.

| among CD8$^+$ [%] | healthy controls (n=19) mean ± SEM | incubation phase (n=7) mean ± SEM | early acute infection (n=11) mean ± SEM | late acute infection (n=15) mean ± SEM | ANOVA p-value | ANCOVA p-value |
|---|---|---|---|---|---|---|
| PD-1$^-$CD27$^+$ | 58.14 ± 6.1 | 55.16 ± 8.1 | 47.13 ± 7.2 | 66.63 ± 5.4 | 0.237 | 0.799 |
| PD-1$^+$CD27$^+$ | 3.97 ± 1.8 | 1.29 ± 0.5 | 13.19 ± 3.6 | 7.84 ± 3.2 | **0.049** | **0.048** |
| PD-1$^+$CD27$^-$ | 3.87 ± 1.8 | 0.86 ± 0.6 | 14.51 ± 4.7 | 5.02 ± 2.4 | **0.021** | **0.031** |
| PD-1$^-$CD27$^-$ | 34.02 ± 5.7 | 42.70 ± 8.5 | 25.17 ± 6.7 | 20.52 ± 3.8 | 0.101 | 0.23 |
| PD-1$^+$ | 7.84 ± 3.5 | 2.14 ± 0.8 | 27.70 ± 7.6 | 12.86 ± 5.6 | **0.023** | **0.027** |
| | | | | | | |
| CD127$^-$CD27$^+$ | 11.81 ± 1.6 | 12.07 ± 2.4 | 14.17 ± 3.6 | 21.37 ± 2.4 | 0.178 | **0.003** |
| CD127$^+$CD27$^+$ | 51.54 ± 5.6 | 46.51 ± 8.4 | 48.34 ± 6.5 | 54.48 ± 3.8 | 0.645 | 0.816 |
| CD127$^+$CD27$^-$ | 12.91 ± 2.6 | 11.86 ± 3.3 | 11.43 ± 2.3 | 5.55 ± 1.4 | 0.207 | 0.598 |
| CD127$^-$CD27$^-$ | 23.75 ± 4.9 | 29.55 ± 7.8 | 26.06 ± 6.7 | 18.60 ± 3.6 | 0.491 | 0.941 |
| | | | | | | |
| CD38$^-$CD27$^+$ | 56.32 ± 4.7 | 47.11 ± 8.0 | 45.28 ± 3.9 | 54.90 ± 3.7 | 0.315 | 0.14 |
| CD38$^+$CD27$^+$ | 7.23 ± 1.2 | 11.63 ± 1.8 | 15.15 ± 3.5 | 21.08 ± 3.4 | **1.39E-03** | **0.002** |
| CD38$^+$CD27$^-$ | 6.35 ± 1.3 | 26.41 ± 6.5 | 14.09 ± 1.3 | 5.44 ± 0.8 | **2.73E-07** | **6.31E-07** |
| CD38$^-$CD27$^-$ | 30.10 ± 4.8 | 14.88 ± 4.2 | 25.49 ± 6.0 | 18.58 ± 3.2 | 0.138 | 0.211 |

**Table S10.** Expression of CD38 among CD8+ T Cell Subpopulations.

| CD38 Expression [MFI] | healthy controls (n=19) | | | incubation phase (n=7) | | | early acute infection (n=11) | | | late acute infection (n=15) | | | ANOVA | ANCOVA |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | mean | ± | SEM | mean | ± | SEM | mean | ± | SEM | mean | ± | SEM | p-value | p-value |
| CD8+ | 2038.3 | ± | 150.5 | 4304.9 | ± | 697.8 | 3739.0 | ± | 467.9 | 3847.7 | ± | 398.5 | **1.72E-04** | **5.5E-05** |
| CD38+CD27− | 11940.0 | ± | 540.8 | 16399.7 | ± | 1172.6 | 21154.0 | ± | 6389.5 | 14559.1 | ± | 1684.6 | 0.150 | 0.187 |
| CD27+CD45RA+ | 17.13 | ± | 4.8 | 19.34 | ± | 6.0 | 18.37 | ± | 3.6 | 33.05 | ± | 4.1 | 0.052 | 0.674 |
| CD27+CD45RA− | 17.00 | ± | 2.4 | 12.77 | ± | 2.3 | 12.33 | ± | 2.2 | 10.38 | ± | 1.5 | 0.131 | 0.216 |
| CD27−CD45RA− | 5.99 | ± | 1.2 | 5.28 | ± | 1.6 | 2.96 | ± | 0.4 | 2.26 | ± | 0.3 | **0.016** | **0.043** |
| CD27−CD45RA+ | 29.74 | ± | 5.5 | 35.77 | ± | 7.8 | 35.02 | ± | 6.1 | 22.24 | ± | 3.6 | 0.342 | 0.915 |
| CD25−CD127+ | 54.58 | ± | 4.9 | 46.59 | ± | 6.3 | 45.05 | ± | 5.2 | 54.20 | ± | 4.1 | 0.679 | 0.293 |
| CD25+CD127+ | 7.42 | ± | 0.8 | 8.06 | ± | 1.5 | 13.87 | ± | 6.2 | 6.92 | ± | 2.1 | 0.546 | 0.665 |
| CD25+CD127− | 0.88 | ± | 0.2 | 2.49 | ± | 0.4 | 2.49 | ± | 0.4 | 2.28 | ± | 0.4 | 0.115 | 0.066 |
| CD25−CD127− | 37.11 | ± | 5.0 | 42.87 | ± | 7.5 | 38.59 | ± | 6.6 | 36.61 | ± | 4.0 | 0.908 | 0.35 |

**Table S11.** Percantages of CD4+ T Cell Subpopulations.

| | healthy controls (n=19) | incubation phase (n=7) | early acute infection (n=11) | late acute infection (n=15) | ANOVA | ANCOVA |
|---|---|---|---|---|---|---|

| among CD4$^+$CD45RA$^+$ [%] | mean ± SEM | mean ± SEM | mean ± SEM | mean ± SEM | p-value | p-value |
|---|---|---|---|---|---|---|
| CD27$^-$CD127$^+$ | 9.08 ± 2.49 | 4.55 ± 1.95 | 7.12 ± 3.98 | 6.10 ± 2.40 | 0.746 | 0.765 |
| CD27$^+$CD127$^+$ | 72.56 ± 4.13 | 74.00 ± 4.02 | 78.70 ± 7.05 | 74.60 ± 3.49 | 0.83 | 0.72 |
| CD27$^+$CD127$^+$CD38$^+$ | 78.99 ± 3.26 | 78.86 ± 2.12 | 80.63 ± 2.25 | 78.69 ± 2.61 | 0.972 | 0.77 |
| CD27$^+$CD127$^+$CD38$^-$ | 20.95 ± 3.24 | 21.10 ± 2.11 | 19.33 ± 2.25 | 21.26 ± 2.61 | 0.972 | 0.77 |
| CD27$^+$CD127$^-$ | 11.09 ± 1.43 | 17.47 ± 2.94 | 9.23 ± 1.70 | 16.13 ± 1.73 | **0.012** | **0.042** |
| CD27$^-$CD127$^-$ | 7.27 ± 2.30 | 3.96 ± 1.31 | 4.93 ± 3.38 | 3.18 ± 1.76 | 0.586 | 0.732 |
| **among CD4$^+$CD45RA$^-$ [%]** | | | | | | |
| CD27$^-$CD127$^+$ | 16.92 ± 2.18 | 13.89 ± 4.24 | 10.71 ± 1.54 | 11.08 ± 0.83 | 0.091 | 0.114 |
| CD27$^+$CD127$^+$ | 63.43 ± 2.02 | 63.89 ± 5.84 | 72.18 ± 3.52 | 66.45 ± 1.63 | 0.135 | 0.125 |
| CD27$^+$CD127$^-$ | 15.18 ± 1.29 | 18.43 ± 2.48 | 14.89 ± 2.13 | 20.29 ± 1.32 | 0.054 | 0.147 |
| CD27$^-$CD127$^-$ | 4.48 ± 1.01 | 3.77 ± 2.06 | 2.22 ± 0.76 | 2.20 ± 0.50 | 0.238 | 0.183 |
| CD27$^+$CD38$^-$ | 69.86 ± 2.2 | 71.49 ± 5.6 | 73.38 ± 1.8 | 66.05 ± 2.5 | 0.288 | 0.057 |
| CD27$^-$CD38$^-$ | 19.47 ± 2.5 | 14.52 ± 5.0 | 11.31 ± 1.9 | 11.38 ± 0.9 | **0.035** | 0.059 |
| CD25$^+$CD127$^-$ Tregs | 8.95 ± 0.6 | 11.43 ± 0.8 | 9.47 ± 1.2 | 9.76 ± 0.5 | 0.257 | 0.242 |

**Table S12.** Percantages of NK Cell Subpopulations.

| | healthy controls (n=19) | incubation phase (n=7) | early acute infection (n=11) | late acute infection (n=15) | ANOVA | ANCOVA |
|---|---|---|---|---|---|---|

| among gated lymphocytes [%] | mean | ± | SEM | mean | ± | SEM | mean | ± | SEM | mean | ± | SEM | p-value | p-value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CD56$^-$CD3$^+$ | 59.36 | ± | 1.9 | 49.24 | ± | 3.9 | 48.88 | ± | 3.9 | 53.57 | ± | 2.6 | 0.031 | 0.014 |
| CD56$^+$CD3$^+$ | 5.88 | ± | 1.1 | 3.97 | ± | 1.7 | 5.01 | ± | 2.1 | 5.79 | ± | 1.5 | 0.865 | 0.89 |
| CD56$^+$CD3$^-$ | 10.31 | ± | 1.1 | 13.61 | ± | 2.6 | 10.60 | ± | 1.1 | 9.22 | ± | 0.9 | 0.215 | 0.38 |

**Table S13.** Serum Cytokines.

| Analyte [pg/ml] | healthy controls (n=19) mean ± SEM | incubation phase (n=7) mean ± SEM | early acute infection (n=11) mean ± SEM | late acute infection (n=15) mean ± SEM | ANOVA p-value | ANCOVA p-value |
|---|---|---|---|---|---|---|
| IL-1β | 18.18 ± 15.6 | 2.09 ± 0.0 | 99.14 ± 49.7 | 33.23 ± 20.3 | 0.112 | 0.109 |
| IL-6 | 9.81 ± 7.5 | 21.20 ± 11.7 | 102.84 ± 48.6 | 47.02 ± 25.8 | 0.079 | 0.045 |
| TNFα | 12.76 ± 11.1 | 1.44 ± 0.0 | 30.46 ± 18.1 | 19.43 ± 10.6 | 0.591 | 0.566 |
| IP-10 | 91.13 ± 14.8 | 402.04 ± 104.2 | 423.90 ± 75.4 | 157.12 ± 74.8 | **3.97E-04** | **6.12E-04** |
| IFNλ1 | 8.67 ± 2.1 | 5.82 ± 1.0 | 19.93 ± 8.6 | 13.52 ± 3.8 | 0.224 | 0.239 |
| IL-8 | 5.66 ± 2.5 | 12.15 ± 5.5 | 42.84 ± 20.4 | 12.12 ± 6.5 | 0.048 | 0.05 |
| IL-12p70 | 2.15 ± 1.4 | 0.67 ± 0.0 | 21.23 ± 12.1 | 6.47 ± 4.4 | 0.092 | 0.05 |
| IFNα2 | 8.34 ± 5.4 | 12.01 ± 4.9 | 75.63 ± 43.8 | 28.07 ± 16.9 | 0.137 | 0.074 |
| IFNλ2/3 | 55.07 ± 28.8 | 11.13 ± 0.0 | 79.37 ± 44.1 | 110.40 ± 57.2 | 0.54 | 0.367 |
| GM-CSF | 5.12 ± 4.0 | 1.14 ± 0.0 | 134.71 ± 82.9 | 32.68 ± 26.2 | 0.084 | **0.046** |
| IFNβ | 4.41 ± 0.0 | 5.66 ± 1.2 | 129.01 ± 84.3 | 37.34 ± 32.9 | 0.143 | 0.057 |
| IL-10 | 3.98 ± 1.9 | 3.45 ± 1.2 | 45.92 ± 23.9 | 13.37 ± 7.1 | 0.042 | 0.032 |
| IFNγ | 18.41 ± 17.1 | 11.93 ± 7.0 | 70.25 ± 40.3 | 27.50 ± 20.7 | 0.409 | 0.466 |

**Table S14.** Absolute Numbers of Live Leukocytes.

| cell count/μL | healthy controls (n=19) mean ± SEM | incubation phase (n=7) mean ± SEM | early acute infection (n=11) mean ± SEM | late acute infection (n=15) mean ± SEM | ANOVA p-value | ANCOVA p-value |
|---|---|---|---|---|---|---|
| granulocytes | 2241 ± 279 | 2025 ± 504 | 2256 ± 377 | 2739 ± 709 | 0.799 | 0.407 |
| lymphocytes | 1788 ± 137 | 1275 ± 145 | 943 ± 116 | 1493 ± 128 | **6.3E-04** | **9.4E-04** |
| CD3 | 1195 ± 97 | 740 ± 87 | 543 ± 82 | 919 ± 88 | **1.02E-04** | **1.04E-04** |
| CD8 | 357 ± 43 | 223 ± 42 | 132 ± 39 | 293 ± 46 | **6,4E-03** | **9.8E-03** |
| CD4 | 693 ± 47 | 418 ± 46 | 344 ± 53 | 531 ± 52 | **8.3E-05** | **3.7E-05** |
| CD19 | 302 ± 61 | 103 ± 25 | 160 ± 28 | 205 ± 35 | 0.066 | 0.074 |
| CD56 | 205 ± 25 | 159 ± 39 | 106 ± 18 | 136 ± 17 | **0.030** | **0.038** |
| monocytes | 388 ± 29 | 361 ± 36 | 414 ± 78 | 368 ± 60 | 0.923 | 0.859 |

**Table S15.** Apoptotic among Live Leukocytes.

| [%] | healthy controls (n=19) mean ± SEM | incubation phase (n=7) mean ± SEM | early acute infection (n=11) mean ± SEM | late acute infection (n=15) mean ± SEM | ANOVA p-value | ANCOVA p-value |
|---|---|---|---|---|---|---|
| granulocytes | 3.14 ± 2.56 | 22.93 ± 22.71 | 2.51 ± 1.72 | 5.21 ± 3.66 | 0.266 | 0.217 |
| lymphocytes | 0.57 ± 0.30 | 0.11 ± 0.03 | 3.48 ± 2.12 | 0.48 ± 0.18 | 0.078 | 0.117 |
| CD3 | 0.75 ± 0.41 | 0.14 ± 0.05 | 5.33 ± 3.02 | 0.81 ± 0.36 | 0.05 | 0.076 |
| CD8 | 0.11 ± 0.05 | 0.03 ± 0.01 | 2.90 ± 2.25 | 0.51 ± 0.30 | 0.17 | 0.219 |
| CD4 | 0.06 ± 0.02 | 0.02 ± 0.01 | 1.65 ± 1.45 | 0.25 ± 0.16 | 0.252 | 0.314 |
| CD19 | 4.19 ± 3.62 | 0.22 ± 0.08 | 5.96 ± 4.33 | 0.91 ± 0.46 | 0.625 | 0.744 |
| CD56 | 0.22 ± 0.06 | 0.08 ± 0.01 | 2.12 ± 1.60 | 0.21 ± 0.06 | 0.153 | 0.221 |
| monocytes | 0.45 ± 0.11 | 0.32 ± 0.14 | 6.83 ± 5.66 | 0.75 ± 0.34 | 0.214 | 0.228 |

**Table S16.** Correlations among Humoral and Cellular Immune Parameters in Healthy Controls.

| | monocytes CD14+CD16bright | granulocytes CD177+CD16- | serum conc. IP-10 | plasmablasts | anti-S1 IgM | anti-S1 IgG | anti-S IgA | cytotoxic T CD38+CD27- | cytotoxic T PD-1+ | mfi CD38 on cytotoxic T |
|---|---|---|---|---|---|---|---|---|---|---|
| monocytes CD14+CD16bright | 1 | | | | | | | | | |
| granulocytes CD177+CD16- | | 1 | | | | | | | | |
| IP-10 serum conc. | r = 0.746 p = 0.001 | | 1 | | | | | | | |
| plasmablasts | | | | 1 | | | | | | |
| anti-S1 IgM | | | | | 1 | | | | | |
| anti-S1 IgG | | | | | | 1 | | | | |
| anti-S1 IgA | | | | | | | 1 | | | |
| cytotoxic T CD38+CD27- | | | | | | | | 1 | | |
| cytotoxic T cells PD-1+ | | | | | | | | | 1 | |
| MFI CD38 on cytotoxic T cells | | | | | | | | | | 1 |

Spearman rank correlation analysis. The table only contains results that withstand Bonferroni correction.

**Table S17.** Correlations among Humoral and Cellular Immune Parameters in COVID-19 Patients.

| | monocytes CD14+CD16 bright | granulocytes CD177+CD16- | serum conc. IP-10 | plasmablasts | anti-S1 IgM | anti-S1 IgG | anti-S IgA | cytotoxic T CD38+CD27- | cytotoxic T PD-1+ | mfi CD38 on cytotoxic T |
|---|---|---|---|---|---|---|---|---|---|---|
| monocytes CD14+CD16bright | 1 | | | | | | | | | |
| granulocytes CD177+CD16- | | 1 | | | | | | | | |
| IP-10 serum conc. | | | 1 | | | | | | | |
| plasmablasts | | | | 1 | | | | | | |
| anti-S1 IgM | | r=0.594 p<0.0001 | | | 1 | | | | | |
| anti-S1 IgG | | r=0.594 p<0.0001 | | | r=0.810 p< 0.0001 | 1 | | | | |
| anti-S1 IgA | | r=0.609 p<0.0001 | | | r=0.882 p< 0.0001 | r=0.926 p< 0.0001 | 1 | | | |
| cytotoxic T cells CD38+/CD27- | | | r=0.667 p<0.0001 | | | | | 1 | | |
| cytotoxic T cells PD-1+ | | | | | | | | | 1 | |
| MFI CD38 on cytotoxic T cells | | | | | | | | | | 1 |