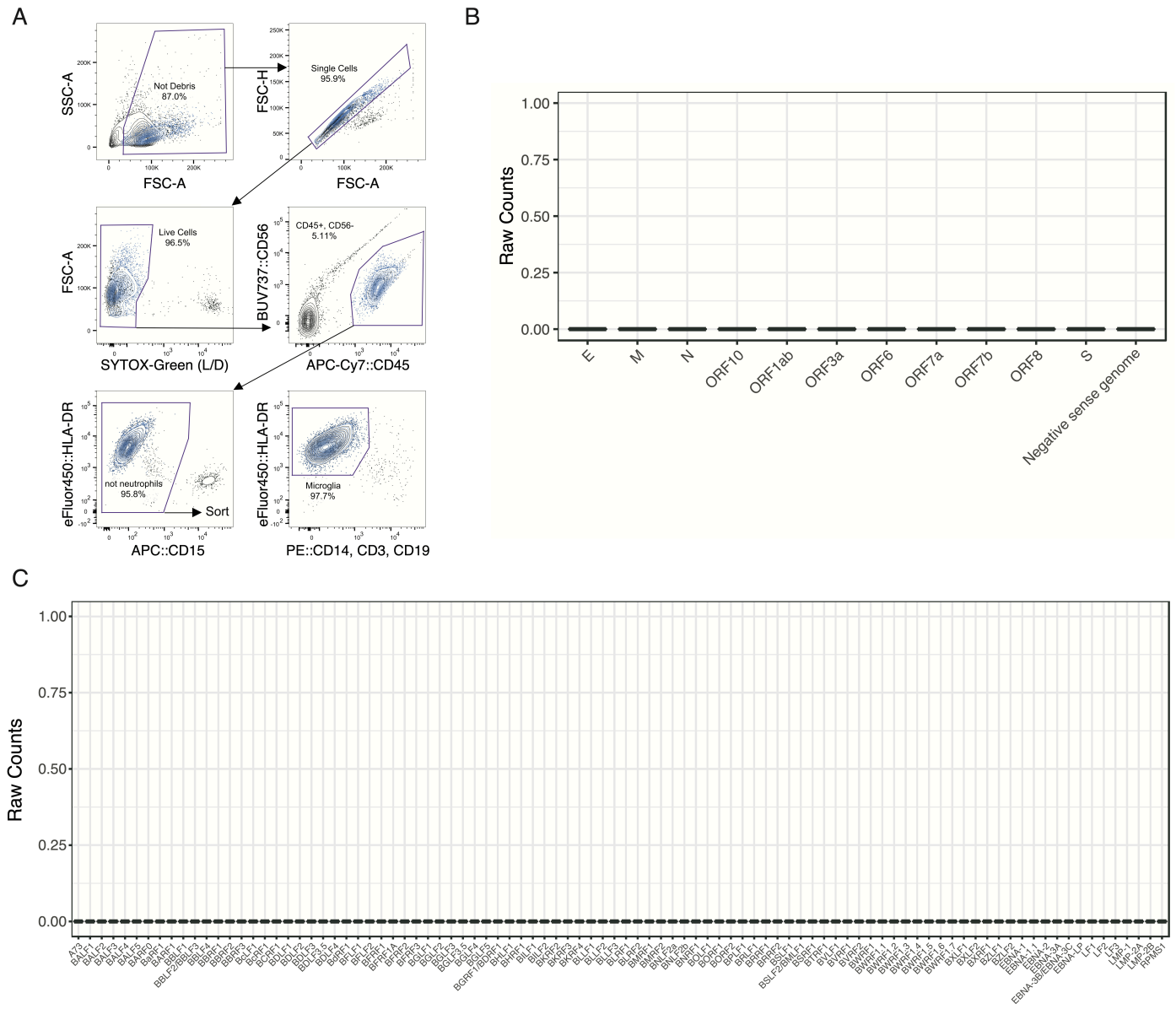
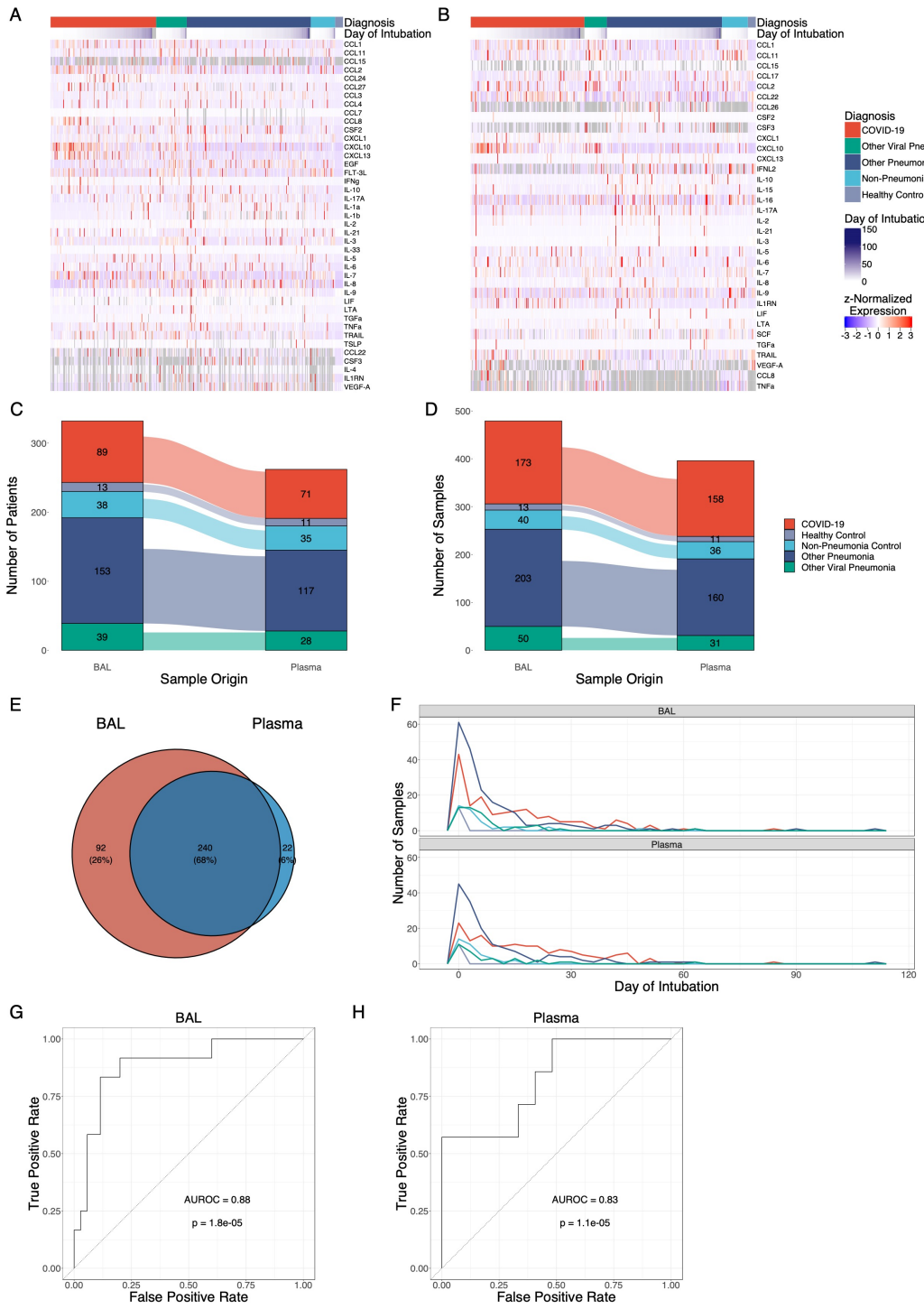
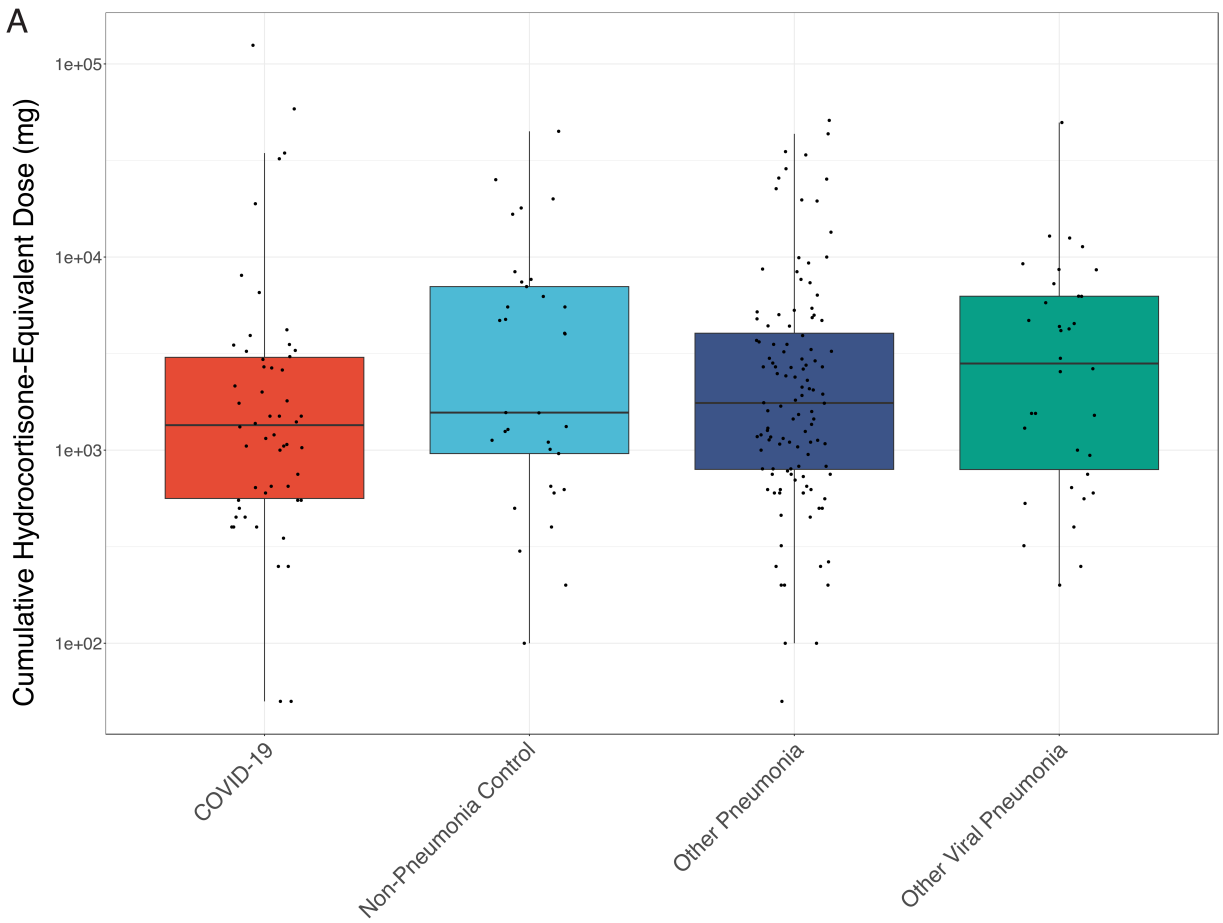
## Supplemental Figures



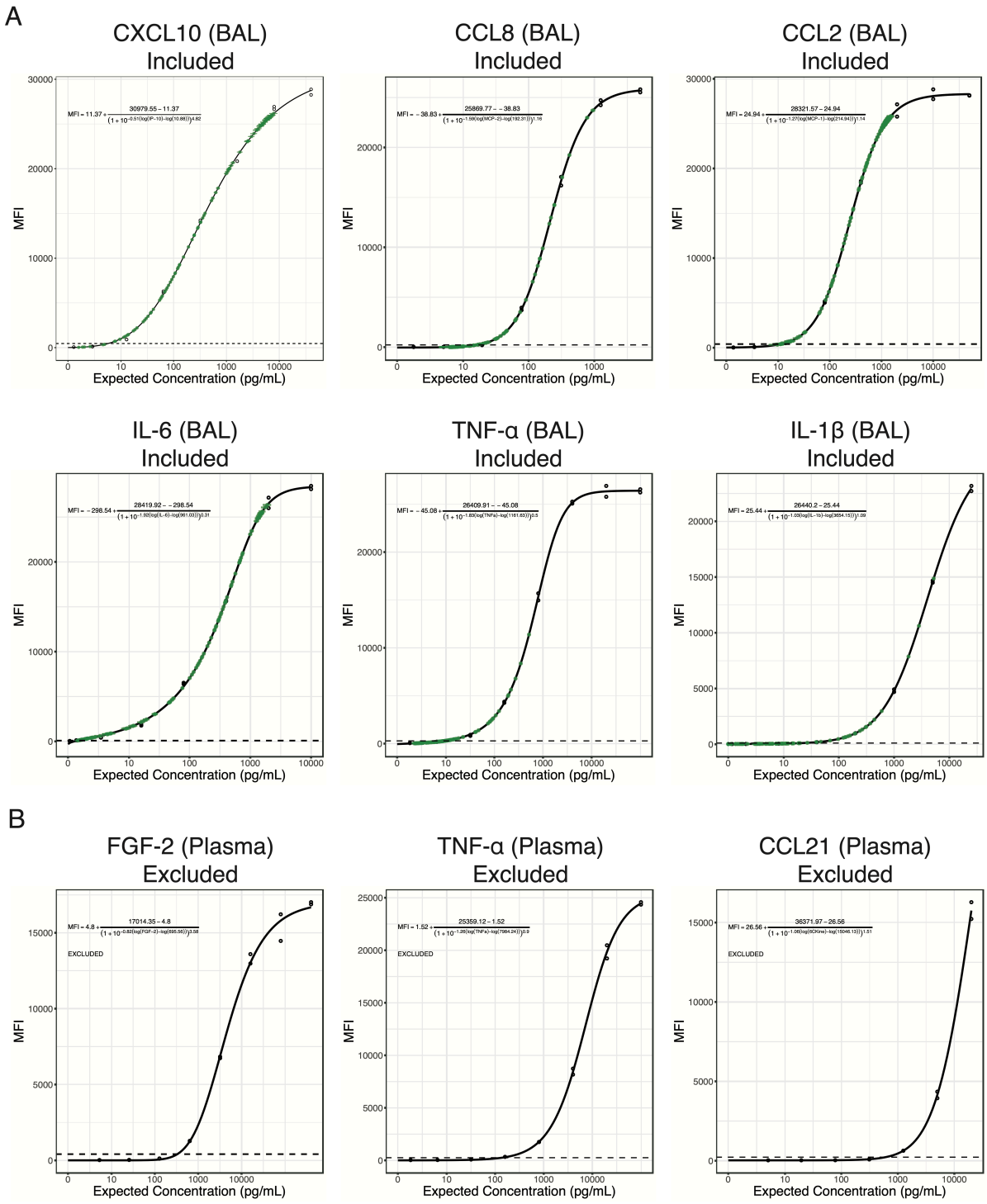

**Supplemental Figure S1.** Related to figure 1**. (A)** Representative flow cytometry sorting scheme for isolating neuro-immune cells from human postmortem brain tissue from a frontal lobe sample. **(B)** Boxplots of raw gene counts for all genes in the SARS-CoV-2 (NC045512.2) genome from human neuro-immune cell scRNA-seq. Zero counts are detected for all genes. **(C)** Boxplots of raw gene counts for all genes in the EBV1 genome (NC007605.1) from human neuro-immune cell scRNA-seq. Zero counts are detected for all genes.




**Supplemental Figure S2.** Related to figure 2**. (A)** Heatmap of 41 cytokines showing significant variability by diagnosis (q < 0.05, Kruskal–Wallis) from 479 BAL samples collected throughout the entire ICU stay from 332 patients. **(B)** Heatmap of 31 cytokines showing significant variability by diagnosis (q < 0.05, Kruskal–Wallis) from 396 plasma samples collected throughout the entire ICU stay from 262 patients. **(C,D)** Alluvial plot of total numbers of patients included in the BAL fluid (c) and plasma (d) datasets. **(E)** Venn diagram of patients with BAL and plasma samples. **(F)** Frequency polygon plot of BAL and plasma sampling distributions throughout patient stay by group. **(G)** AUROC of prediction of a diagnosis of COVID-19 as compared to all other diagnoses from CXCL10 measurement on initial BAL using a logistic-regression-based machine learning model. **(H)** AUROC of prediction of a diagnosis of COVID-19 as compared to all other diagnoses from CXCL10 measurement on initial plasma draw using a logistic-regression-based machine learning model.




**Supplemental Figure S3. Cumulative equivalent steroid dosing by cohort.** Cumulative hydrocortisone-equivalent corticosteroid doses were calculated over the course of each patient's ICU stay as previously defined in (1). Patients not receiving a single dose of corticosteroids throughout their ICU stay were discarded for this analysis. No significant differences were observed between cohorts of critically ill patients.




**Supplemental Figure S4. Representative standard curve fitting plots for cytokine data exclusion. (A)** Representative standard curves and fitted cytokine expression values for analytes included in this study. From left to right, top to bottom: CXCL10 (IP-10), CCL8 (MCP-2), CCL2 (MCP-1) IL-6, TNF-α, IL-1b. **(B)** Representative standard curves for analytes excluded for poor sensitivity in this study. From left to right: FGF-2, TNF-α, and CCL21. For all plots, empty points represent standards of known concentration used for curve-fitting. Black curves and associated formulae represent the function fitted to these points. Green points represent experimental values, and green whiskers are the standard error of prediction. Dotted lines are the upper limit of the 95% confidence interval of lower asymptote prediction.

## Supplemental Tables

| | COVID-19 (N = 5) | Control (N = 3) | Total (N = 8) |
|---|---|---|---|
| **Age (years)** | | | |
| Minimum | 35 | 44 | 35 |
| Median (IQR) | 61.0 (61.0, 72.0) | 51.0 (47.5, 63.5) | 61.0 (49.2, 73.0) |
| Mean (SD) | 61.4 ± 16.5 | 57.0 ± 16.8 | 59.8 ± 15.5 |
| Maximum | 78 | 76 | 78 |
| **Sex** | | | |
| Female | 0 (0.0%) | 1 (33.3%) | 1 (12.5%) |
| Male | 5 (100.0%) | 2 (66.7%) | 7 (87.5%) |
| **Race** | | | |
| Asian | 1 (20.0%) | 0 (0.0%) | 1 (12.5%) |
| Black or African-American | 1 (20.0%) | 1 (33.3%) | 2 (25.0%) |
| Other | 0 (0.0%) | 1 (33.3%) | 1 (12.5%) |
| White | 3 (60.0%) | 1 (33.3%) | 4 (50.0%) |
| **Ethnicity** | | | |
| Hispanic or Latino | 1 (20.0%) | 0 (0.0%) | 1 (12.5%) |
| Not Hispanic or Latino | 4 (80.0%) | 3 (100.0%) | 7 (87.5%) |
| **SOFA** | | | |
| Minimum | 12 | 10 | 10 |
| Median (IQR) | 15.0 (13.5, 16.5) | 14.5 (12.2, 16.8) | 15.0 (12.5, 17.5) |
| Mean (SD) | 15.0 ± 2.6 | 14.5 ± 6.4 | 14.8 ± 3.5 |
| Maximum | 18 | 19 | 19 |
| Unknown/Missing | 1 (20.0%) | 1 (33.3%) | 2 (25.0%) |
| **Discharge Status** | | | |
| Deceased | 5 (100.0%) | 3 (100.0%) | 8 (100.0%) |
| **Duration of Intubation (days)** | | | |
| Minimum | 0.8 | 0.9 | 0.8 |
| Median (IQR) | 7.0 (1.2, 18.0) | 1.7 (1.3, 8.8) | 4.3 (1.1, 16.5) |
| Mean (SD) | 9.3 ± 9.0 | 6.2 ± 8.5 | 8.1 ± 8.3 |
| Maximum | 19.4 | 16 | 19.4 |
| **Length of ICU Stay (days)** | | | |
| Minimum | 0.8 | 0 | 0 |
| Median (IQR) | 7.9 (1.2, 15.4) | 1.7 (0.8, 8.8) | 4.8 (1.1, 15.6) |
| Mean (SD) | 8.3 ± 7.4 | 5.9 ± 8.8 | 7.4 ± 7.4 |
| Maximum | 16 | 16 | 16 |
| **BMI (kg/m2)** | | | |
| Minimum | 23.8 | 20.7 | 20.7 |
| Median (IQR) | 26.4 (24.6, 29.4) | 21.3 (21.0, 28.1) | 24.9 (22.6, 30.8) |
| Mean (SD) | 27.6 ± 4.4 | 25.7 ± 8.1 | 26.8 ± 5.7 |
| Maximum | 33.6470588235294 | 35 | 35 |
| Unknown/Missing | 1 (20.0%) | 0 (0.0%) | 1 (12.5%) |
| **Smoking Status** | | | |
| Current Smoker | 1 (20.0%) | 0 (0.0%) | 1 (12.5%) |
| Never Smoker | 4 (80.0%) | 2 (66.7%) | 6 (75.0%) |
| Past Smoker | 0 (0.0%) | 1 (33.3%) | 1 (12.5%) |
| **Postmortem Interval (hours)** | | | |
| Minimum | 15.2 | 16.7 | 15.2 |
| Median (IQR) | 38.4 (18.9, 45.5) | 24.3 (20.5, 36.4) | 31.4 (18.3, 46.2) |
| Mean (SD) | 35.1 ± 17.9 | 29.8 ± 16.6 | 33.1 ± 16.4 |
| Maximum | 57.5 | 48.5 | 57.5 |
| **Immunosuppressed** | | | |
| Immunosuppressed | 2 (40.0%) | 0 (0.0%) | 2 (25.0%) |
| Not Immunosuppressed | 3 (60.0%) | 3 (100.0%) | 6 (75.0%) |
| **Cancer** | | | |
| Diagnosed | 0 (0.0%) | 1 (33.3%) | 1 (12.5%) |
| Not Diagnosed | 5 (100.0%) | 2 (66.7%) | 7 (87.5%) |
| **Cardiac Arrest** | | | |
| Cardiac Arrest with ROSC | 2 (40.0%) | 2 (66.7%) | 4 (50.0%) |
| No Cardiac Arrest with ROSC | 3 (60.0%) | 1 (33.3%) | 4 (50.0%) |
| **Cognitive Impairment** | | | |
| Diagnosed | 1 (20.0%) | 1 (33.3%) | 2 (25.0%) |
| Not Diagnosed | 4 (80.0%) | 2 (66.7%) | 6 (75.0%) |
| **Diabetes** | | | |
| Diagnosed | 1 (20.0%) | 0 (0.0%) | 1 (12.5%) |
| Not Diagnosed | 4 (80.0%) | 3 (100.0%) | 7 (87.5%) |
| **Renal Disease** | | | |
| Diagnosed | 3 (60.0%) | 1 (33.3%) | 4 (50.0%) |
| Not Diagnosed | 2 (40.0%) | 2 (66.7%) | 4 (50.0%) |
| **Substance Use Disorder** | | | |
| Not Diagnosed | 5 (100.0%) | 3 (100.0%) | 8 (100.0%) |
| **Venous Thromboembolism** | | | |
| Diagnosed | 0 (0.0%) | 1 (33.3%) | 1 (12.5%) |

**Supplemental Table S1.** Demographics of the postmortem brain scRNA-seq cohort. Frontal lobe samples were collected in the course of autopsy at Northwestern Memorial Hospital.

| | COVID-19 (N = 5) | Control (N = 3) | Total (N = 8) |
|---|---|---|---|
| Not Diagnosed | 5 (100.0%) | 2 (66.7%) | 7 (87.5%) |
| **Convalescent Plasma** | | | |
| Received Treatment | 1 (20.0%) | 0 (0.0%) | 1 (12.5%) |
| Did Not Receive Treatment | 4 (80.0%) | 3 (100.0%) | 7 (87.5%) |
| **Dexamethasone** | | | |
| Received Treatment | 2 (40.0%) | 0 (0.0%) | 2 (25.0%) |
| Did Not Receive Treatment | 3 (60.0%) | 3 (100.0%) | 6 (75.0%) |
| **IL-6 Blockers** | | | |
| Received Treatment | 1 (20.0%) | 0 (0.0%) | 1 (12.5%) |
| Did Not Receive Treatment | 4 (80.0%) | 3 (100.0%) | 7 (87.5%) |
| **Remdesivir** | | | |
| Received Treatment | 1 (20.0%) | 0 (0.0%) | 1 (12.5%) |
| Did Not Receive Treatment | 4 (80.0%) | 3 (100.0%) | 7 (87.5%) |
| **CRP (mg/L)** | | | |
| Minimum | 137.3 | Inf | 137.3 |
| Median (IQR) | 283.6 (210.5, 356.8) | NA (NA, NA) | 283.6 (210.5, 356.8) |
| Mean (SD) | 283.6 ± 207.0 | NaN ± NA | 283.6 ± 207.0 |
| Maximum | 430 | -Inf | 430 |
| Unknown/Missing | 3 (60.0%) | 3 (100.0%) | 6 (75.0%) |
| **D-Dimer (ng/mL)** | | | |
| Minimum | 1135 | 6226 | 1135 |
| Median (IQR) | 3,078.5 (2,106.8, 4,050.2) | 6,226.0 (6,226.0, 6,226.0) | 5,022.0 (3,078.5, 5,624.0) |
| Mean (SD) | 3,078.5 ± 2,748.5 | 6,226.0 ± NA | 4,127.7 ± 2,660.7 |
| Maximum | 5022 | 6226 | 6226 |
| Unknown/Missing | 3 (60.0%) | 2 (66.7%) | 5 (62.5%) |

**Supplemental Table S1.** Demographics of the postmortem brain scRNA-seq cohort. Frontal lobe samples were collected in the course of autopsy at Northwestern Memorial Hospital.

| | COVID-19 (N = 93) | Healthy Control (N = 13) | Non-Pneumonia Control (N = 45) | Other Pneumonia (N = 162) | Other Viral Pneumonia (N = 41) | Total (N = 354) |
|---|---|---|---|---|---|---|
| **Age (years)** | | | | | | |
| Minimum | 21 | 21 | 19 | 22 | 34 | 19 |
| Median (IQR) | 59.0 (46.0, 68.2) | 25.0 (23.0, 33.0) | 62.0 (49.0, 72.0) | 66.0 (51.2, 73.0) | 59.0 (52.0, 69.0) | 62.0 (48.0, 72.0) |
| Mean (SD) | 57.1 ± 14.3 | 27.8 ± 6.7 | 59.2 ± 17.6 | 61.8 ± 16.3 | 60.3 ± 13.1 | 58.9 ± 16.6 |
| Maximum | 86 | 40 | 90 | 99 | 88 | 99 |
| Unknown/Missing | 5 (5.4%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 5 (1.4%) |
| **Sex** | | | | | | |
| Female | 31 (33.3%) | 7 (53.8%) | 20 (44.4%) | 63 (38.9%) | 18 (43.9%) | 139 (39.3%) |
| Male | 60 (64.5%) | 6 (46.2%) | 25 (55.6%) | 99 (61.1%) | 23 (56.1%) | 213 (60.2%) |
| Unknown or Not Reported | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Race** | | | | | | |
| White | 36 (38.7%) | 8 (61.5%) | 28 (62.2%) | 109 (67.3%) | 26 (63.4%) | 207 (58.5%) |
| Black/African American | 19 (20.4%) | 1 (7.7%) | 8 (17.8%) | 34 (21.0%) | 8 (19.5%) | 70 (19.8%) |
| Unknown or Not Reported | 37 (39.8%) | 0 (0.0%) | 6 (13.3%) | 13 (8.0%) | 5 (12.2%) | 61 (17.2%) |
| Asian | <=5 | <=5 | <=5 | <=5 | <=5 | 14 (4.0%) |
| American Indian/Alaska Native | <=5 | <=5 | <=5 | <=5 | <=5 | <=5 |
| **Ethnicity** | | | | | | |
| Hispanic or Latino | 40 (43.0%) | 2 (15.4%) | 7 (15.6%) | 13 (8.0%) | 8 (19.5%) | 70 (19.8%) |
| Not Hispanic or Latino | 39 (41.9%) | 11 (84.6%) | 35 (77.8%) | 137 (84.6%) | 30 (73.2%) | 252 (71.2%) |
| Unknown or Not Reported | 14 (15.1%) | 0 (0.0%) | 3 (6.7%) | 12 (7.4%) | 3 (7.3%) | 32 (9.0%) |
| **SOFA** | | | | | | |
| Minimum | 4 | Inf | 3 | 4 | 2 | 2 |
| Median (IQR) | 9.0 (7.6, 11.2) | NA (NA, NA) | 10.8 (8.2, 13.2) | 11.0 (9.0, 13.9) | 9.5 (8.2, 12.5) | 10.1 (8.1, 13.0) |
| Mean (SD) | 9.7 ± 2.8 | NaN ± NA | 10.8 ± 3.6 | 11.4 ± 3.6 | 10.2 ± 3.0 | 10.7 ± 3.4 |
| Maximum | 18.5 | -Inf | 20.3 | 21.2 | 15.3 | 21.2 |
| Unknown/Missing | 2 (2.2%) | 13 (100.0%) | 5 (11.1%) | 15 (9.3%) | 7 (17.1%) | 42 (11.9%) |
| **APS** | | | | | | |
| Minimum | 39.2 | Inf | 35.2 | 23 | 23.8 | 23 |
| Median (IQR) | 72.3 (61.5, 86.4) | NA (NA, NA) | 66.6 (51.0, 78.6) | 66.2 (53.6, 80.4) | 63.3 (56.4, 77.3) | 68.4 (56.0, 81.1) |
| Mean (SD) | 73.6 ± 17.7 | NaN ± NA | 67.5 ± 19.1 | 68.2 ± 21.3 | 66.0 ± 19.0 | 69.3 ± 20.0 |
| Maximum | 108.6 | -Inf | 109.8 | 161 | 105 | 161 |
| Unknown/Missing | 2 (2.2%) | 13 (100.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 15 (4.2%) |
| **Discharge Status** | | | | | | |
| Deceased | 26 (28.6%) | 0 (NaN%) | 15 (33.3%) | 59 (36.4%) | 14 (34.1%) | 114 (33.6%) |
| Home | 36 (39.6%) | 0 (NaN%) | 20 (44.4%) | 36 (22.2%) | 10 (24.4%) | 102 (30.1%) |
| Inpatient Facility | 17 (18.7%) | 0 (NaN%) | 7 (15.6%) | 48 (29.6%) | 14 (34.1%) | 86 (25.4%) |
| LTAC | 12 (13.2%) | 0 (NaN%) | 3 (6.7%) | 18 (11.1%) | 3 (7.3%) | 36 (10.6%) |
| Other | 0 (0.0%) | 0 (NaN%) | 0 (0.0%) | 1 (0.6%) | 0 (0.0%) | 1 (0.3%) |
| Unknown/Missing | 2 (2.2%) | 13 (100.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 15 (4.2%) |
| **Duration of Intubation (days)** | | | | | | |
| Minimum | 0 | 0 | 0 | 0 | 1 | 0 |
| Median (IQR) | 20.0 (10.0, 32.0) | 0.0 (0.0, 0.0) | 4.0 (2.0, 9.0) | 8.0 (3.0, 17.0) | 9.0 (3.0, 14.0) | 9.0 (3.0, 19.0) |
| Mean (SD) | 23.9 ± 21.6 | 0.0 ± 0.0 | 8.4 ± 11.6 | 11.7 ± 11.6 | 10.4 ± 8.9 | 13.9 ± 15.8 |
| Maximum | 153 | 0 | 58 | 68 | 34 | 153 |
| **Length of ICU Stay (days)** | | | | | | |
| Minimum | 3 | 0 | 1 | 1 | 2 | 0 |
| Median (IQR) | 22.0 (13.5, 35.0) | 0.0 (0.0, 0.0) | 7.0 (4.0, 12.0) | 10.0 (5.0, 19.0) | 11.0 (7.0, 20.0) | 12.0 (5.0, 22.0) |
| Mean (SD) | 26.6 ± 21.2 | 0.0 ± 0.0 | 11.3 ± 13.9 | 14.7 ± 14.2 | 13.4 ± 8.9 | 16.6 ± 16.8 |
| Maximum | 153 | 0 | 80 | 86 | 34 | 153 |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **BMI (kg/m2)** | | | | | | |
| Minimum | 19.22 | 18.4 | 16.56 | 12.46 | 17.34 | 12.46 |
| Median (IQR) | 31.8 (27.9, 38.9) | 24.1 (22.3, 26.0) | 27.2 (24.5, 33.5) | 26.6 (21.9, 31.6) | 26.8 (23.2, 31.3) | 28.1 (23.9, 33.8) |
| Mean (SD) | 34.1 ± 9.1 | 24.8 ± 4.2 | 30.7 ± 9.9 | 27.5 ± 8.3 | 29.0 ± 9.3 | 29.7 ± 9.1 |
| Maximum | 81.81 | 35.1 | 70.6 | 70.25 | 64.18 | 81.81 |
| Unknown/Missing | 3 (3.2%) | 0 (0.0%) | 1 (2.2%) | 1 (0.6%) | 0 (0.0%) | 5 (1.4%) |
| **Smoking Status** | | | | | | |
| Current Smoker | 0 (0.0%) | 0 (0.0%) | 6 (13.3%) | 21 (13.0%) | 5 (12.2%) | 32 (9.0%) |
| Never Smoker | 36 (38.7%) | 13 (100.0%) | 25 (55.6%) | 65 (40.1%) | 20 (48.8%) | 159 (44.9%) |
| Past Smoker | 13 (14.0%) | 0 (0.0%) | 10 (22.2%) | 59 (36.4%) | 15 (36.6%) | 97 (27.4%) |
| Unknown or Not Reported | 44 (47.3%) | 0 (0.0%) | 4 (8.9%) | 17 (10.5%) | 1 (2.4%) | 66 (18.6%) |
| **Immunocompromised** | | | | | | |
| Immunocompromised | 9 (9.9%) | 0 (0.0%) | 10 (22.2%) | 49 (30.2%) | 18 (43.9%) | 86 (24.4%) |
| Not Immunocompromised | 82 (90.1%) | 13 (100.0%) | 35 (77.8%) | 113 (69.8%) | 23 (56.1%) | 266 (75.6%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **AIDS/HIV** | | | | | | |
| Diagnosed | 1 (1.1%) | 0 (0.0%) | 0 (0.0%) | 2 (1.2%) | 3 (7.3%) | 6 (1.7%) |
| Not Diagnosed | 90 (98.9%) | 13 (100.0%) | 45 (100.0%) | 160 (98.8%) | 38 (92.7%) | 346 (98.3%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Cancer** | | | | | | |
| Diagnosed | 14 (15.4%) | 0 (0.0%) | 15 (33.3%) | 58 (35.8%) | 21 (51.2%) | 108 (30.7%) |

**Supplemental Table S2.** Demographics of the SCRIPT cytokines cohort.

| | COVID-19 (N = 93) | Healthy Control (N = 13) | Non-Pneumonia Control (N = 45) | Other Pneumonia (N = 162) | Other Viral Pneumonia (N = 41) | Total (N = 354) |
|---|---|---|---|---|---|---|
| Not Diagnosed | 77 (84.6%) | 13 (100.0%) | 30 (66.7%) | 104 (64.2%) | 20 (48.8%) | 244 (69.3%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Cerebrovascular Disease** | | | | | | |
| Diagnosed | 9 (9.9%) | 0 (0.0%) | 9 (20.0%) | 39 (24.1%) | 10 (24.4%) | 67 (19.0%) |
| Not Diagnosed | 82 (90.1%) | 13 (100.0%) | 36 (80.0%) | 123 (75.9%) | 31 (75.6%) | 285 (81.0%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Chronic Pulmonary Disease** | | | | | | |
| Diagnosed | 21 (23.1%) | 0 (0.0%) | 16 (35.6%) | 68 (42.0%) | 17 (41.5%) | 122 (34.7%) |
| Not Diagnosed | 70 (76.9%) | 13 (100.0%) | 29 (64.4%) | 94 (58.0%) | 24 (58.5%) | 230 (65.3%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Congestive Heart Failure** | | | | | | |
| Diagnosed | 14 (15.4%) | 0 (0.0%) | 19 (42.2%) | 58 (35.8%) | 7 (17.1%) | 98 (27.8%) |
| Not Diagnosed | 77 (84.6%) | 13 (100.0%) | 26 (57.8%) | 104 (64.2%) | 34 (82.9%) | 254 (72.2%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Dementia** | | | | | | |
| Diagnosed | 3 (3.3%) | 0 (0.0%) | 4 (8.9%) | 4 (2.5%) | 3 (7.3%) | 14 (4.0%) |
| Not Diagnosed | 88 (96.7%) | 13 (100.0%) | 41 (91.1%) | 158 (97.5%) | 38 (92.7%) | 338 (96.0%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Diabetes** | | | | | | |
| Diagnosed | 41 (45.1%) | 0 (0.0%) | 14 (31.1%) | 44 (27.2%) | 21 (51.2%) | 120 (34.1%) |
| Not Diagnosed | 50 (54.9%) | 13 (100.0%) | 31 (68.9%) | 118 (72.8%) | 20 (48.8%) | 232 (65.9%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Hemiplagia or Paraplegia** | | | | | | |
| Diagnosed | 2 (2.2%) | 0 (0.0%) | 5 (11.1%) | 17 (10.5%) | 3 (7.3%) | 27 (7.7%) |
| Not Diagnosed | 89 (97.8%) | 13 (100.0%) | 40 (88.9%) | 145 (89.5%) | 38 (92.7%) | 325 (92.3%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Myocardial Infarction** | | | | | | |
| Diagnosed | 2 (2.2%) | 0 (0.0%) | 8 (17.8%) | 15 (9.3%) | 2 (4.9%) | 27 (7.7%) |
| Not Diagnosed | 89 (97.8%) | 13 (100.0%) | 37 (82.2%) | 147 (90.7%) | 39 (95.1%) | 325 (92.3%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Peripheral Vascular Disease** | | | | | | |
| Diagnosed | 12 (13.2%) | 0 (0.0%) | 10 (22.2%) | 44 (27.2%) | 8 (19.5%) | 74 (21.0%) |
| Not Diagnosed | 79 (86.8%) | 13 (100.0%) | 35 (77.8%) | 118 (72.8%) | 33 (80.5%) | 278 (79.0%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Renal Disease** | | | | | | |
| Diagnosed | 13 (14.3%) | 0 (0.0%) | 20 (44.4%) | 50 (30.9%) | 12 (29.3%) | 95 (27.0%) |
| Not Diagnosed | 78 (85.7%) | 13 (100.0%) | 25 (55.6%) | 112 (69.1%) | 29 (70.7%) | 257 (73.0%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Rheumatic Disease** | | | | | | |
| Diagnosed | 4 (4.4%) | 0 (0.0%) | 5 (11.1%) | 15 (9.3%) | 4 (9.8%) | 28 (8.0%) |
| Not Diagnosed | 87 (95.6%) | 13 (100.0%) | 40 (88.9%) | 147 (90.7%) | 37 (90.2%) | 324 (92.0%) |
| Unknown/Missing | 2 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.6%) |
| **Charlson Comorbidity Index** | | | | | | |
| Minimum | 1 | Inf | 1 | 1 | 1 | 1 |
| Median (IQR) | 3 (1.0, 5.0) | NA (NA, NA) | 6 (4.0, 9.0) | 5 (3.0, 8.0) | 5 (3.0, 8.0) | 5.0 (2.0, 8.0) |
| Mean (SD) | 3.9 ± 3.7 | NaN ± NA | 6.3 ± 3.4 | 5.7 ± 3.5 | 6.1 ± 4.0 | 5.4 ± 3.7 |
| Maximum | 18 | -Inf | 14 | 17 | 21 | 21 |
| Unknown/Missing | 36 (38.7%) | 13 (100.0%) | 8 (17.8%) | 25 (15.4%) | 4 (9.8%) | 86 (24.3%) |
| **Steroids** | | | | | | |
| Treated | 54 (58.1%) | 0 (0.0%) | 33 (73.3%) | 116 (71.6%) | 34 (82.9%) | 237 (66.9%) |
| Untreated | 39 (41.9%) | 13 (100.0%) | 12 (26.7%) | 46 (28.4%) | 7 (17.1%) | 117 (33.1%) |
| **CRP (mg/L)** | | | | | | |
| Minimum | 0 | Inf | 0 | 0 | 16.8 | 0 |
| Median (IQR) | 17.1 (10.7, 28.8) | NA (NA, NA) | 2.8 (1.2, 8.2) | 8.6 (2.8, 15.3) | 29.5 (23.1, 32.8) | 15.3 (6.0, 27.1) |
| Mean (SD) | 22.9 ± 25.7 | NaN ± NA | 8.8 ± 15.2 | 10.3 ± 9.4 | 27.4 ± 9.8 | 19.4 ± 23.0 |
| Maximum | 197.3 | -Inf | 48.3 | 32.2 | 36 | 197.3 |
| Unknown/Missing | 4 (4.3%) | 13 (100.0%) | 36 (80.0%) | 136 (84.0%) | 38 (92.7%) | 227 (64.1%) |
| **D-Dimer (ng/mL)** | | | | | | |
| Minimum | 0 | Inf | 187 | 0 | 181 | 0 |
| Median (IQR) | 1,069.0 (512.0, 3,573.0) | NA (NA, NA) | 3,507.0 (2,734.2, 4,712.2) | 2,237.0 (733.0, 6,360.0) | 2,398.0 (876.0, 3,315.0) | 1,905.0 (610.0, 4,622.0) |
| Mean (SD) | 2,777.3 ± 3,680.2 | NaN ± NA | 10,501.4 ± 18,742.0 | 5,482.0 ± 9,262.9 | 3,229.5 ± 3,327.0 | 4,328.7 ± 8,142.1 |
| Maximum | 18329 | -Inf | 55024 | 48657 | 11692 | 55024 |
| Unknown/Missing | 4 (4.3%) | 13 (100.0%) | 31 (68.9%) | 101 (62.3%) | 24 (58.5%) | 173 (48.9%) |
| **Ferritin (ng/mL)** | | | | | | |
| Minimum | 66.5 | Inf | 21.6 | 33.3 | 184.9 | 21.6 |
| Median (IQR) | 798.5 (380.6, 1,394.2) | NA (NA, NA) | 250.5 (92.4, 290.1) | 376.7 (135.9, 1,257.8) | 938.1 (599.2, 1,166.8) | 677.9 (257.4, 1,361.5) |
| Mean (SD) | 1,671.3 ± 3,383.9 | NaN ± NA | 298.8 ± 321.8 | 1,367.2 ± 4,169.4 | 1,095.3 ± 904.7 | 1,498.1 ± 3,456.3 |
| Maximum | 25815 | -Inf | 839.5 | 23599.7 | 2781.7 | 25815 |
| Unknown/Missing | 21 (22.6%) | 13 (100.0%) | 40 (88.9%) | 131 (80.9%) | 35 (85.4%) | 240 (67.8%) |
| **WBC Count, BAL (cells/µL)** | | | | | | |
| Minimum | 31 | Inf | 0 | 3 | 0 | 0 |

**Supplemental Table S2.** Demographics of the SCRIPT cytokines cohort.

| | COVID-19 (N = 93) | Healthy Control (N = 13) | Non-Pneumonia Control (N = 45) | Other Pneumonia (N = 162) | Other Viral Pneumonia (N = 41) | Total (N = 354) |
|---|---|---|---|---|---|---|
| Median (IQR) | 207.5 (127.2, 434.0) | NA (NA, NA) | 146.5 (33.2, 251.0) | 423.5 (193.8, 1,612.2) | 781.5 (177.0, 2,147.0) | 273.5 (143.8, 863.2) |
| Mean (SD) | 848.3 ± 3,873.2 | NaN ± NA | 495.5 ± 1,403.1 | 2,434.8 ± 5,691.9 | 2,038.4 ± 4,215.8 | 1,661.5 ± 4,674.0 |
| Maximum | 34300 | -Inf | 7800 | 43375 | 24500 | 43375 |
| Unknown/Missing | 11 (11.8%) | 13 (100.0%) | 3 (6.7%) | 30 (18.5%) | 5 (12.2%) | 62 (17.5%) |
| **Neutrophils, BAL (%)** | | | | | | |
| Minimum | 2 | Inf | 0 | 0 | 0 | 0 |
| Median (IQR) | 41.5 (22.5, 69.0) | NA (NA, NA) | 26.0 (6.0, 56.8) | 82.0 (63.8, 91.2) | 84.0 (57.5, 90.0) | 69.0 (32.0, 87.0) |
| Mean (SD) | 45.4 ± 27.2 | NaN ± NA | 34.4 ± 30.3 | 72.9 ± 25.0 | 66.8 ± 32.8 | 59.7 ± 31.2 |
| Maximum | 95 | -Inf | 97 | 100 | 96 | 100 |
| Unknown/Missing | 11 (11.8%) | 13 (100.0%) | 3 (6.7%) | 14 (8.6%) | 3 (7.3%) | 44 (12.4%) |
| **Lymphocytes, BAL (%)** | | | | | | |
| Minimum | 1 | Inf | 1 | 1 | 1 | 1 |
| Median (IQR) | 14.0 (6.5, 29.5) | NA (NA, NA) | 5.0 (3.0, 8.8) | 3.0 (1.0, 6.0) | 2.0 (1.0, 5.2) | 5.0 (2.0, 12.0) |
| Mean (SD) | 20.5 ± 18.7 | NaN ± NA | 8.8 ± 15.1 | 5.7 ± 8.2 | 5.8 ± 10.5 | 10.7 ± 14.9 |
| Maximum | 85 | -Inf | 88 | 51 | 55 | 88 |
| Unknown/Missing | 14 (15.1%) | 13 (100.0%) | 11 (24.4%) | 48 (29.6%) | 9 (22.0%) | 95 (26.8%) |
| **WBC Count, Blood (10e3 cells/µL)** | | | | | | |
| Minimum | 3.4 | Inf | 4.8 | 0.1 | 5.2 | 0.1 |
| Median (IQR) | 10.2 (7.2, 14.2) | NA (NA, NA) | 9.2 (6.9, 11.5) | 11.9 (9.1, 15.8) | 8.7 (7.7, 10.2) | 10.4 (7.6, 14.5) |
| Mean (SD) | 12.5 ± 10.8 | NaN ± NA | 9.9 ± 4.8 | 13.9 ± 8.7 | 9.2 ± 3.8 | 12.6 ± 9.9 |
| Maximum | 98.6 | -Inf | 20.4 | 43.6 | 14.4 | 98.6 |
| Unknown/Missing | 4 (4.3%) | 13 (100.0%) | 36 (80.0%) | 128 (79.0%) | 37 (90.2%) | 218 (61.6%) |
| **Absolute Neutrophils, Blood (10e3 cells/µL)** | | | | | | |
| Minimum | 2.3 | Inf | 0.6 | 0.1 | 0 | 0 |
| Median (IQR) | 8.1 (5.4, 10.7) | NA (NA, NA) | 11.2 (5.7, 17.9) | 10.0 (5.8, 15.6) | 7.4 (4.9, 13.0) | 9.0 (5.4, 14.1) |
| Mean (SD) | 8.9 ± 4.6 | NaN ± NA | 12.3 ± 8.5 | 11.7 ± 8.5 | 9.3 ± 7.3 | 10.7 ± 7.5 |
| Maximum | 25.4 | -Inf | 32.3 | 48.3 | 27.1 | 48.3 |
| Unknown/Missing | 9 (9.7%) | 13 (100.0%) | 11 (24.4%) | 25 (15.4%) | 8 (19.5%) | 66 (18.6%) |
| **Absolute Lymphocytes, Blood (10e3 cells/µL)** | | | | | | |
| Minimum | 0 | Inf | 0 | 0 | 0 | 0 |
| Median (IQR) | 1.0 (0.6, 1.4) | NA (NA, NA) | 0.6 (0.4, 1.4) | 0.9 (0.5, 1.8) | 0.8 (0.3, 1.6) | 0.9 (0.5, 1.6) |
| Mean (SD) | 2.3 ± 10.1 | NaN ± NA | 1.4 ± 2.1 | 1.6 ± 2.3 | 1.1 ± 0.9 | 1.7 ± 5.7 |
| Maximum | 93.7 | -Inf | 11.2 | 18.2 | 3.8 | 93.7 |
| Unknown/Missing | 9 (9.7%) | 13 (100.0%) | 11 (24.4%) | 24 (14.8%) | 8 (19.5%) | 65 (18.4%) |

**Supplemental Table S2.** Demographics of the SCRIPT cytokines cohort.

| Laser | Filter | Dye | Antigen | Clone | Dilution | Catalog Number | RR ID |
|---|---|---|---|---|---|---|---|
| 305 | 750/50 | BUV737 | CD56 | NCAM16.2 | 1:10 | BD 612766 | AB_2813880 |
| 405 | 450/50 | eFluor450 | HLA-DR | L243 | 1:20 | Thermo-Fisher 48-9952-42 | AB_1603291 |
| 552 | 575/25 | PE | CD14 | MΦP9 | 1:10 | BD 562691 | AB_2737725 |
| 552 | 575/25 | PE | CD3 | SK7 | 1:20 | Thermo-Fisher 12-0036-42 | AB_10805512 |
| 552 | 575/25 | PE | CD19 | J3-119 | 1:10 | Beckman Coulter IM1285U | AB_10640419 |
| 488 | 530/30 | SYTOX Green | | | 1:500-1:1000 | Thermo-Fisher S7020 | |
| 640 | 670/39 | APC | CD15 | W6D3 | 1:10 | BioLegend 323008 | AB_756014 |
| 640 | 780/60 | APC-Cy7 | CD45 | HI30 | 1:10 | CST 77322 | AB_2799894 |

**Supplemental Table S3.** List of reagents used for FACS sorting of human neuroimmune cells.

## References

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