Supplemental Methods, Data Figures, and Tables for Fortmann and Patton *et al.* "Circulating SARS-CoV-2+ Megakaryocytes Associate with Severe Viral Infection in COVID-19"

Single-Cell RNA-Sequencing Analysis

FASTQ files from 69 single-cell RNA-sequencing (scRNA-seq) samples were downloaded from the European Nucleotide Archive or Gene Expression Omnibus. The samples were derived from 4 separate studies (1-4), all of which used the droplet-based 10X Genomics platform. Two of the datasets used 3' RNA sequencing (1,3) and the other two used 5' sequencing (2,4). Severity of infection for each patient was determined by the original authors. Transcriptomic alignment, barcode demultiplexing, and gene count quantification were done using Cell Ranger (version 3.1.0) with the force-cells option set to 15,000. The reference transcriptome was GRCh38 and was downloaded from 10X Genomics. All downstream analyses were done using Scanpy (version 1.6.0), a Python-based suite of packages for scRNA-seq analysis. For quality control filtering, cells were removed that contained >50,000 or <500 reads and >4,500 or <500 genes. Additionally, mitochondrial and ribosomal gene percentage cutoffs of 20% and 50%, respectively, were used to further eliminate low quality cells. Lastly, Scrublet (version 0.2.1) was used to remove potential doublets. After quality control filtering, the 69 samples were concatenated and 321,035 cells were recovered in total. Normalization was performed using Scran (version 1.10.2), and Scanpy was then used to perform complete cell cycle regression using the cell cycle genes identified by Tirosh *et al* (*5*). Scanpy was used to select the top 2,000 highly variable genes, which were then used to calculate the top 20

principal components (PCs). Batch correction was performed using Harmony with the Scanpy external application programming interface (**Figure S1**). Two categorical covariates were used for Harmony integration, one designating individual samples and the other designating one of four different datasets that each sample originated from. Final dimensionality reduction was done using uniform manifold approximation and projection (UMAP) with default settings. Clustering was performed using the Leiden algorithm with a resolution of 0.8, and 14 clusters were identified. The assignment of cluster identities was guided by the expression of lineage-specific marker genes (**Figure S2**). One cluster composed of 12 total cells was identified as damaged red blood cells and removed. The megakaryocyte (MK) cluster was identified by specific expression of Integrin Subunit Beta 3 (ITGB3; CD61), Integrin Subunit Alpha 2b (ITGA2B; CD41), and Platelet Glycoprotein Ib Alpha Chain (GP1BA; CD42b) and other MK/platelet marker genes (**Figure S2**). Subclustering of the MKs revealed two populations, one of which was contaminated with CD3+ T cells and was removed. The final dataset was composed of 317,574 total cells with 13 distinct clusters, including MKs (4,180 cells; **Figure S2**). Upon publication, a GitHub repository will be posted containing all scRNA-seq data and notebooks.

MK frequencies for each donor were calculated as the proportion of MKs compared to all cells for a given sample. Median values for each group were used for Kruskal–Wallis nonparametric one-way ANOVA with Dunn's post-hoc multiple comparisons test (GraphPad Prism, version 6.01). All groups were compared to uninfected controls.

Differential gene expression analysis was performed on normalized expression data using MAST (version 1.8.2). MKs from severe COVID-19 patients were compared

to MKs from uninfected donors and the following covariates were included: number of genes expressed per cell and the dataset that each cell originated from.

Mean MK-derived S100A8 and S100A9 gene expression was determined for each donor. These individual donor values were then used to calculate the mean expression of S100A8 and S100A9 per group. Statistical analyses of mean S100A8 and S100A9 gene expression per group were done using two-way ANOVA with Dunnett's post-hoc multiple comparisons test (GraphPad Prism, version 6.01). All groups were compared to uninfected controls.

Flow Cytometry

Cryopreserved cell suspensions were rapidly thawed in a 37^{o}C water bath for 3 minutes and filtered through a 100µm strainer. 1mL of fresh FBS was added to each sample followed by centrifugation at 1000xg for 5 minutes at 4^{o}C. The samples were resuspended in 1mL of flow cytometry staining buffer (FACS; phosphate-buffered saline with 5% FBS, 2mM EDTA, and 0.1% sodium azide). 10µL of each sample was stained with anti-CD61 (VI-PL2; AF647) and the concentration of CD61+ cells were determined using flow cytometry. Ten million CD61+ cells were used to standardize each sample for the final flow cytometry panel. Cell suspensions were surface stained at room temperature for 30 minutes in 100µL of staining buffer (50µL of Brilliant Stain Buffer (Becton Dickinson) and 50µL of FACS) with the following antibody cocktail: anti-CD61 (VI-PL2; BV605), anti-CD41 (HIP8; APC/Cy7), anti-CD45 (HI30; BV510), viability dye (violet; Invitrogen), and Human TruStain FcX (BioLegend). Cells were fixed and permeabilized with BD Cytofix/Cytoperm (Becton Dickinson) for 30 minutes on ice. Cells were intracellularly stained with anti-S100A8/A9 (27E10; Santa Cruz) and anti-spike

protein (P05DHuRb; Invitrogen) for 30 minutes on ice in 100µL of Perm/Wash Buffer (Becton Dickinson). Finally, cells were incubated with 200µL RNase and propidium iodide (PI/RNase Staining Buffer; Becton Dickinson) for 15 minutes at room temperature, per the manufacturer's instruction. Each sample was resuspended in 300µL of FACS buffer and analyzed with a three-laser FACSCelesta flow cytometer (Becton Dickinson). All 220 peripheral blood samples were analyzed in 6 batches during a 1 week period. FCS files were analyzed using FlowJo (version 10.7). The gating scheme (**Figure S3**),fluorescence minus one (FMO; **Figure S4**) controls, and isotype control stains for S100A8/A9 and spike protein (**Figure S5**) are provided.

For quantification of specific proteins, the following antibodies were used: anti-ACE2 (FAB933G[Novus]; AF488), anti-TMPRSS2 (H-4; AF488), anti-FURIN (B-6; AF488), anti-p52/p100 (C-5; AF488), anti-p65 (F-6; AF488), anti-TLR2 (W15145C; AF488), anti-TLR3 (TLR3.7; biotin), anti-TLR4 (HTA125; biotin), anti-ICAM1 (HA58; APC/Fire750), anti-HLA-DR (G46-6; BV510), anit-CD62p (AK4; BV510), anti-activated GPII/IIIa (PAC-1; FITC), anti-P2Y12 (S16001E; FITC), anti-PAR1 (ATAP2; AF488), anti-CD66b (QA17A51; APC/Fire750), and anti-CD14 (M5E2; BV605). For PrimeFlow, predesigned oligonucleotide probes against S100A8, S100A9, IFITM3, IFI27, SARS-CoV-2, IL-6, IL-1β, and TNF-α were purchased from Thermo Fisher and used according to the manufacturer's instructions. For antibody stains, isotype controls were used for calculating MFIs and percent positive quantifications. For PrimeFlow stains, the target oligonucleotide was omitted for negative controls used in percent positive quantifications. All other steps, including amplifications and fluorophore staining, for PrimeFlow were identical across negative controls and experimental samples.

FACS Sorting and Imaging Flow Cytometry

Residual samples that were stained for the 218 patient cohort were pooled together and used for fluorescence activated cell sorting (FACS) and imaging flow cytometry experiments. The three megakaryocyte subpopulations, S100A8/A9- virus-, S100A8/A9+ virus-, and S100A8/A9+ virus+, were FACS sorted using a FACSAria II (Becton Dickinson). The cells were then pelleted with centrifugation and 3,000 cells per subpopulation were resuspended in 20μL of FACS buffer (phosphate buffered saline with 5% FBS, 2mM EDTA, and 0.1% sodium azide). The samples were run on an Amnis ImageStream^X Mk II System and were analyzed using the IDEAS software (version 6.2). Mouse splenocytes were used for compensation controls. Identical image display mapping values (X range: min & max and midpoint: x & y) for each specific channel were uniformly applied to the three megakaryocyte samples before the final images were exported.

Immunofluorescence Staining of Lung and Brain Tissues

Lungs from a deceased COVID-19 donor with acute respiratory distress syndrome (ARDS) were inflated isobarically with 10% formalin. Brains from 8 deceased COVID-19 donors were fixed in 10% formalin and dissected to obtain sections from the frontal cortex, pons, and medulla. Both lung and brain specimens were processed using standard tissue processing techniques (dehydration, clearing, and infiltration), embedded in paraffin blocks, sequential 5 μm tissue sections were cut, and transferred on to positively charged glass slides. The slides were incubated for 2 hours at 60^{o}C. Deparaffinization and rehydration of the slides was performed with three sequential 5 minute incubations in xylene, two sequential 5 minute incubations in 100% ethanol, two sequential 5 minute

incubations in 95% ethanol, and washed in distilled water in three sequential 5 minute incubations with gentle agitation. Citrate buffer (Vector Laboratories) prewarmed to 70^{o}C was used for antigen retrieval and was incubated in a heated steamer for 20 minutes, followed by three washes in distilled water with gentle agitation. Sections were incubated with 1X phosphate buffered saline (PBS) for 10 minutes and were then blocked with Trident Universal Protein Blocking Reagent (GeneTex; GTX30963) and Human TruStain FcX (Biolegend) at room temperature for 45 minutes. Sections were then stained overnight in Trident Universal Protein Blocking Reagent at 4^{o}C with the following conjugated antibodies: anti-CD61 (FITC; VI-PL2), anti-S100A8/A9 (PE; 27E10; Santa Cruz), and anti-spike protein (AF647; P05DHuRb; Invitrogen). Sections were washed with gentle agitation at room temperature using excess 1X Tris-Buffered Saline with 0.01% Triton x-100. Nuclear staining was done using Hoechst. Lastly, the sections were treated with TrueVIEW Autofluorescence Quencher (Vector Laboratories) following the manufacturer's instructions and were mounted using ProLong Gold Antifade Mountant (Invitrogen). Images were collected using a Zeiss Axio Imager Z2 upright microscope. Negative control stains were done using a mouse isotype antibody conjugated to AF488 (Invitrogen).

Primary Human Megakaryocyte Experiments

Primary human megakaryocytes were produced from CD34+ cord blood using the Stem Cell Technologies StemSpan™ Megakaryocyte Expansion Supplement, according to the manufacturer's instructions. Briefly, highly enriched CD34+ cord blood was purchased from Stem Cell Technologies. 6 separate cultures were initiated in StemSpan™ SFEM II media with Megakaryocyte Expansion Supplement and were

differentiated for 1 month. Cultures were assessed for morphologic and surface expression changes (CD41, CD61, CD42b) consistent with MK phenotype. At 1 month, MKs were enriched using anti-CD61 beads (Miltenyi Biotec), with an average purity of ~95% MKs. The cultures were then inoculated with SARS-CoV-2 (MOI=2) for 24h. The inoculant was removed, and the cells were then chemically induced to produce platelets using phorbol ester myristate acetate (PMA; 10ng/mL) for 96h. Platelets were identified with flow cytometry, using a similar gating scheme to that described earlier (**Figure S7**), and were assessed for expression of spike protein. For immunofluorescence, infected primary human megakaryocytes and non-infected controls, were moved to glass slides coated with Attachment Factor (Cell Systems) following removal of inoculant and were subsequently cultured for 96h in the presence of 10ng/mL PMA. Cells were stained with anti-CD61 (FITC), anti-spike protein (AF647), anti-acetylated tubulin (6-11B-1; unconjugated), and DAPI. Acetylated tubulin was counterstained with an anti-mouse secondary antibody conjugated to AF594, prior to staining with the conjugated antibodies.

Statistics

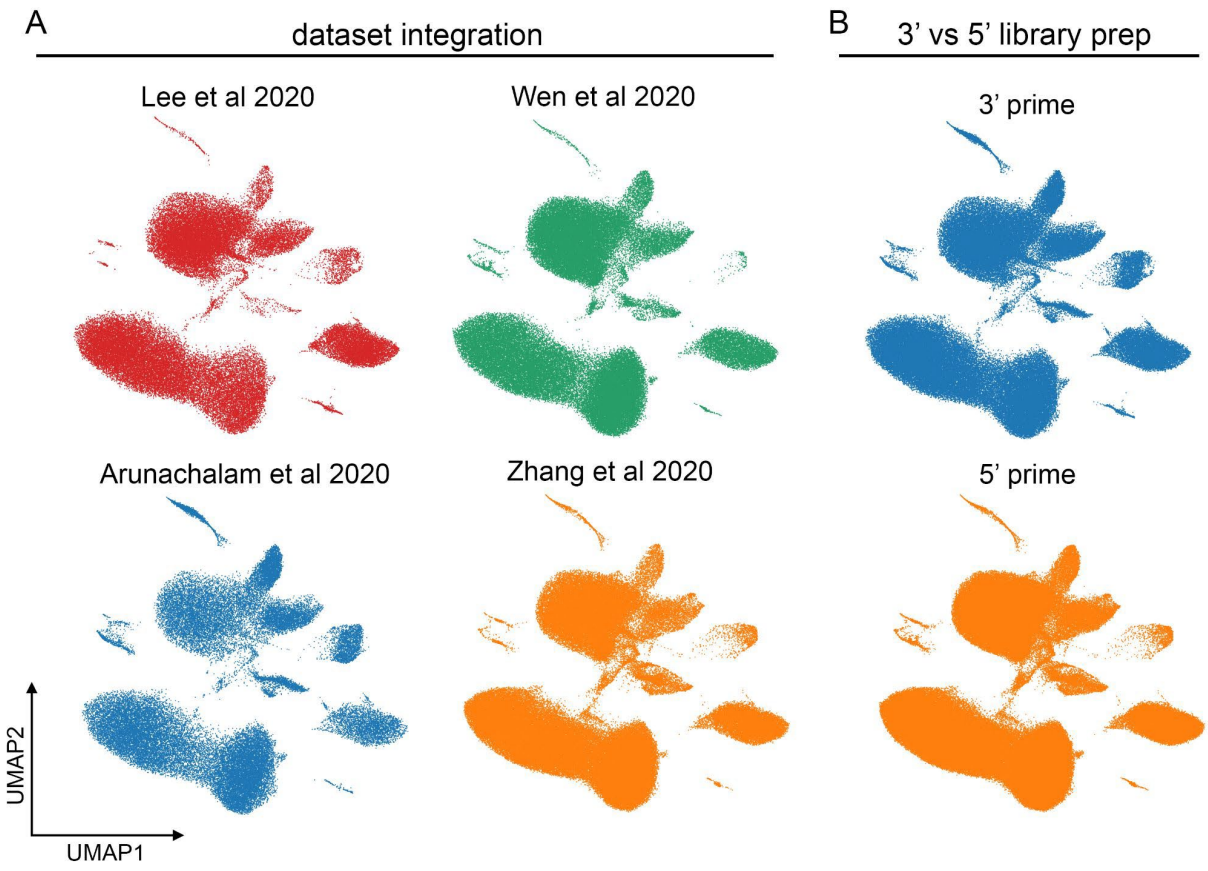
Flow Cytometry

Student's t-test was used when two groups were being compared. ANOVA was used when more than two groups were being compared. GraphPad Prism (version 6.01) was used for statistical analyses.

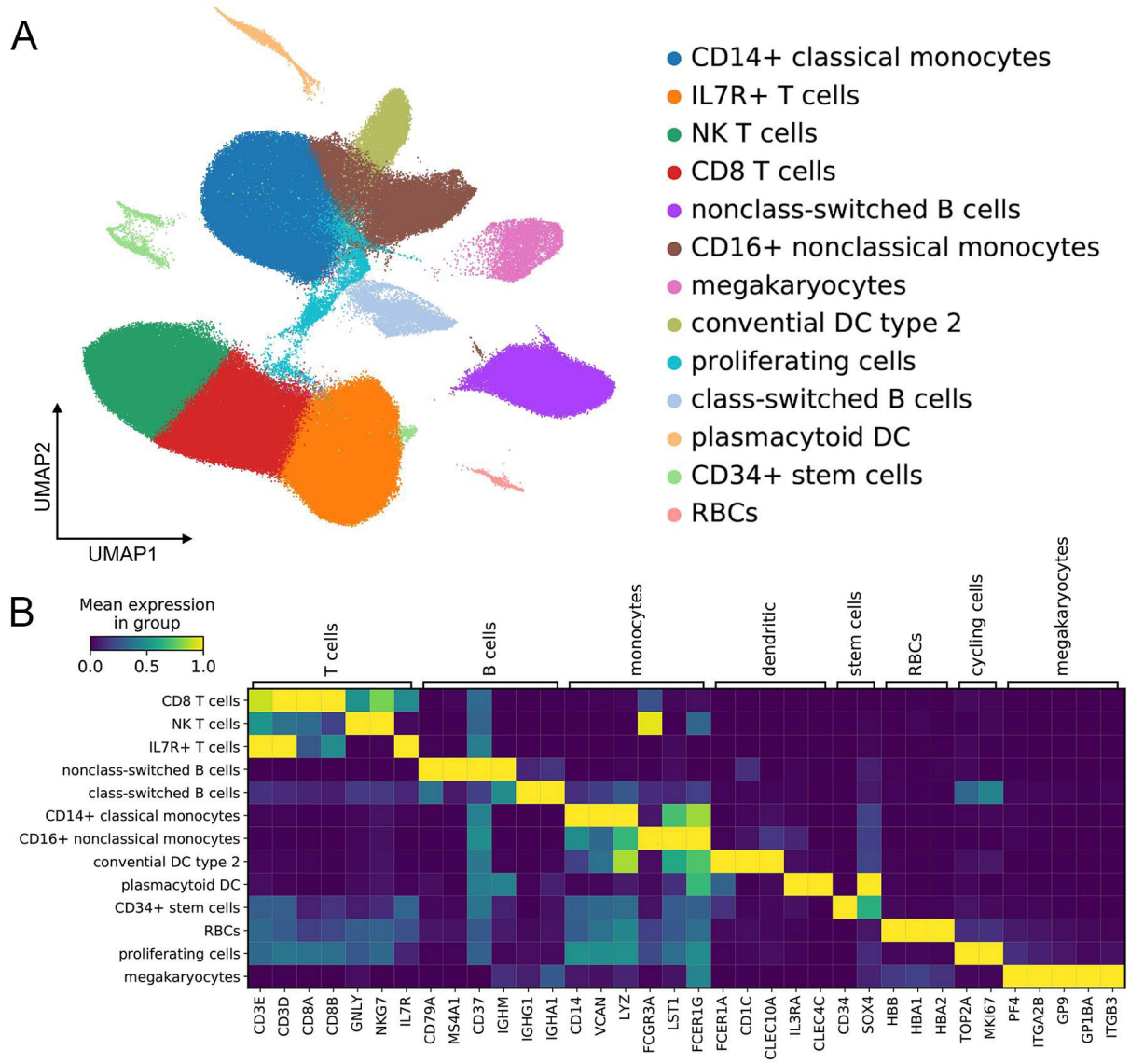
Clinical Correlations and Outcomes

Statistically significant correlations between continuous patient variables, cumulative 60-day outcomes, and patient MK proportions were determined using

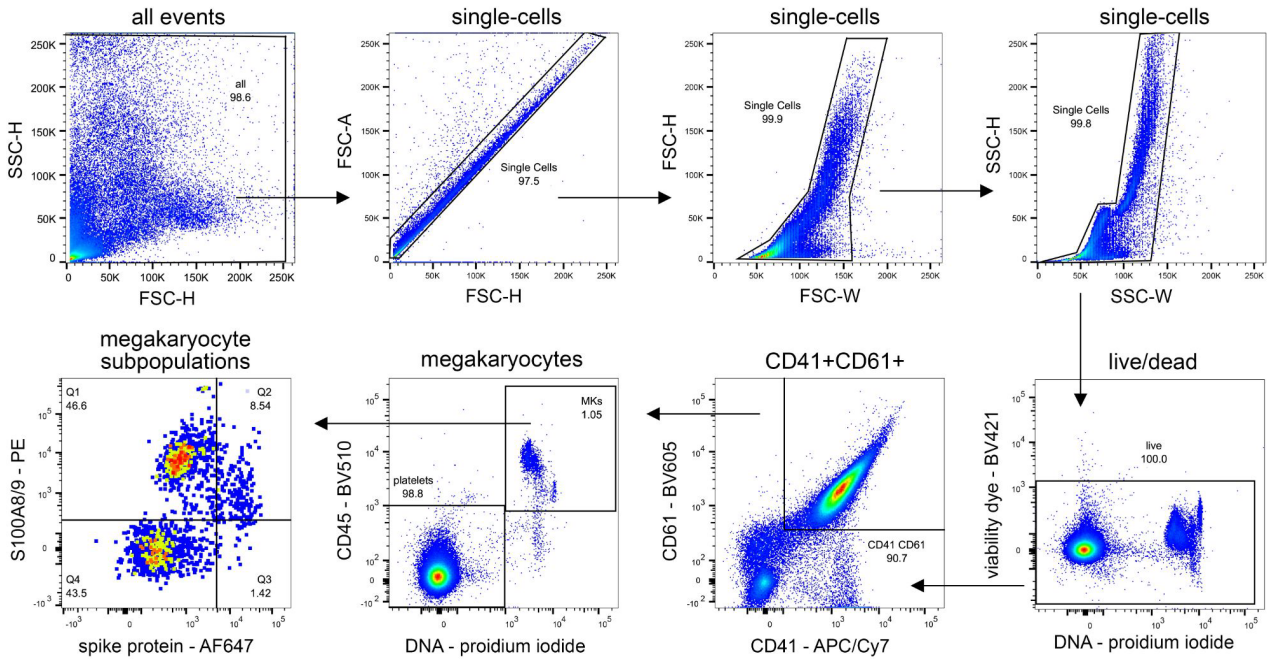
Spearman correlation analysis. For analyses comparing MK frequencies with COVID-19 severity, statistical significance was assessed using the Dunn and Durbin-Conover tests with median values from each nonparametric distribution and adjusted for multiple comparisons with the Bonferroni method. Multivariate logistic regression models were used to determine the associations between MK frequencies and the likelihood of 30-day clinical outcomes. Adjusted odds ratios represent the predicted change in likelihood for a 20% increase in MK subpopulation frequencies (see **Tables S2-S4**, for model details). Statistical significance for the multivariate logistic regression was assessed with the Wald test and bootstrapped 95% confidence intervals were generated using 1000 iterations. All figures, tables, modeling, and correlation analyses were performed and generated using R version 4.2. Corresponding code will be openly available online at time of publication.



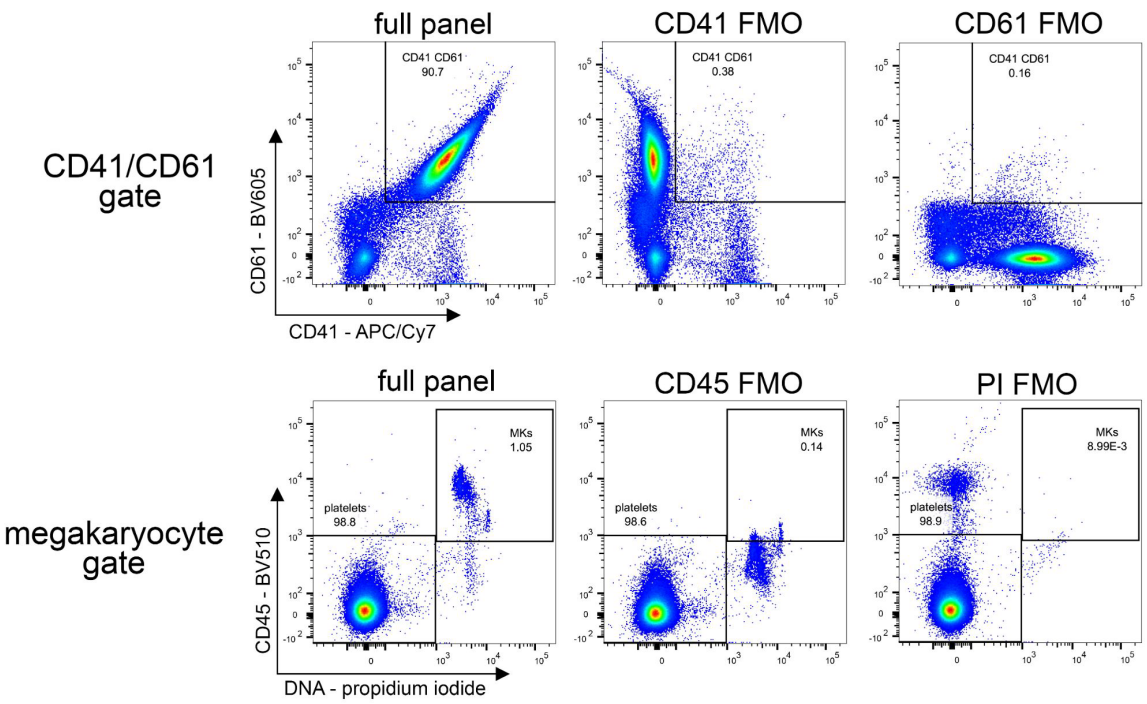
Supplemental Figure 1. Single-cell RNA-sequencing batch correction. Harmony integration successfully resolves batch effect by (**A**) dataset and (**B**) 3'/5' library preparation.



Supplemental Figure 2. Single-cell RNA-sequencing of peripheral blood in COVID-19. (**A**) UMAP projection of 317,574 cells showing 13 distinct cell populations. (**B**) Marker gene expression for each cluster.



Supplemental Figure 3. Flow cytometry gating scheme for circulating megakaryocytes.



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211 **Supplemental Figure 4. Fluorescence minus one (FMO) flow cytometry controls.**

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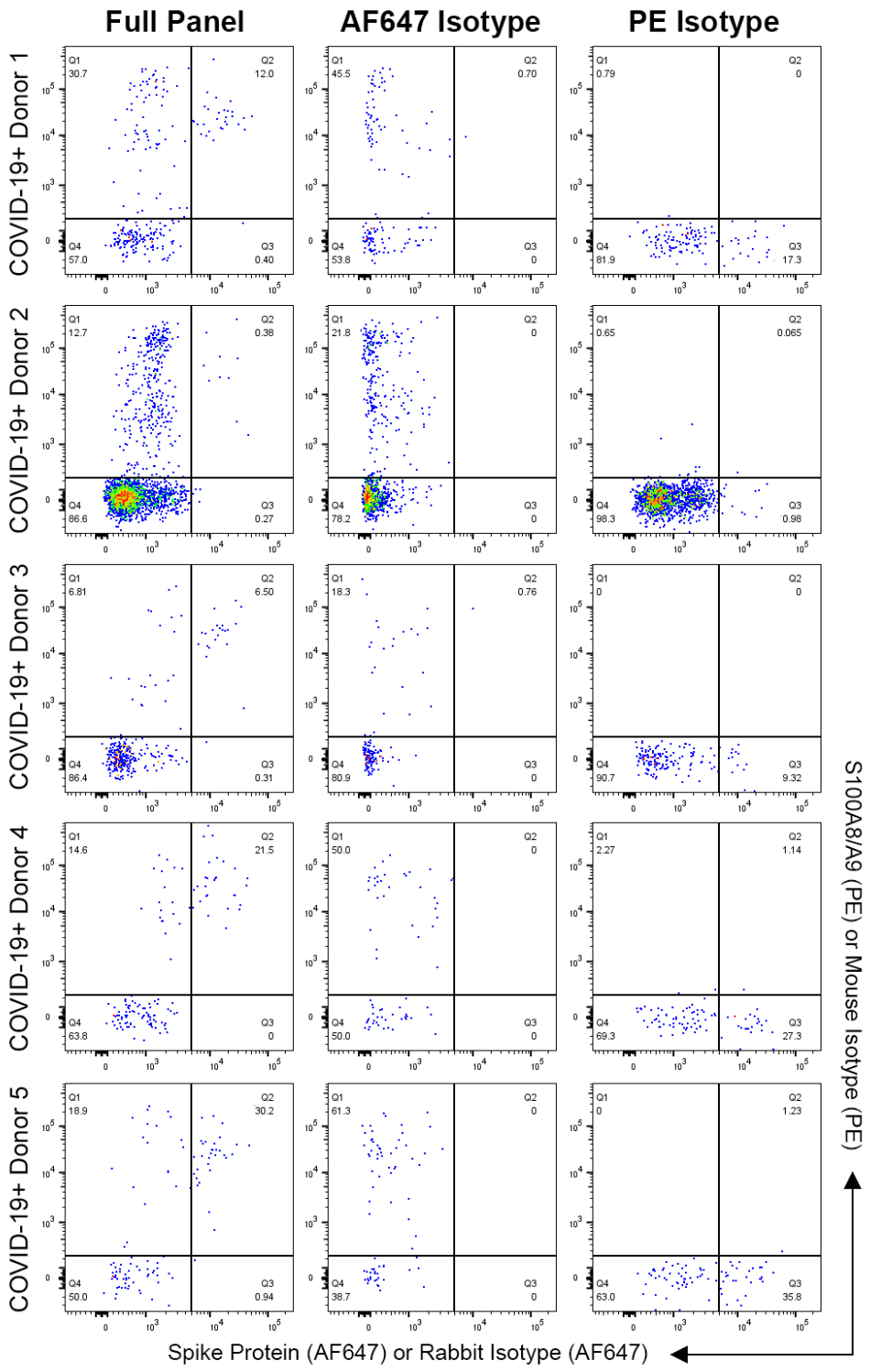

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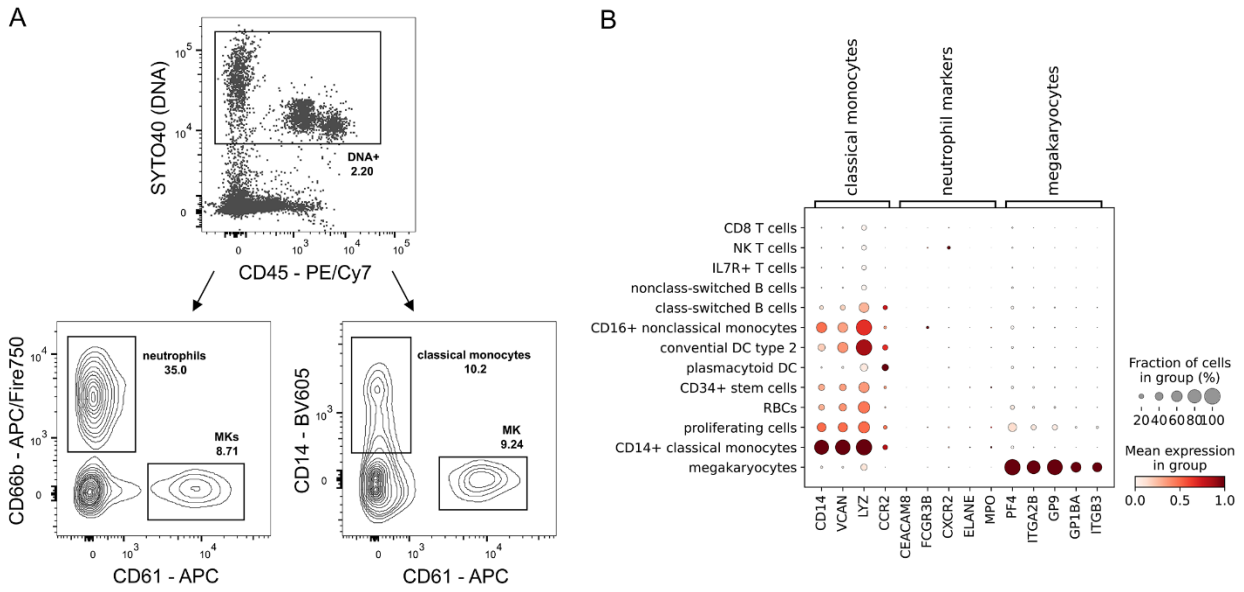
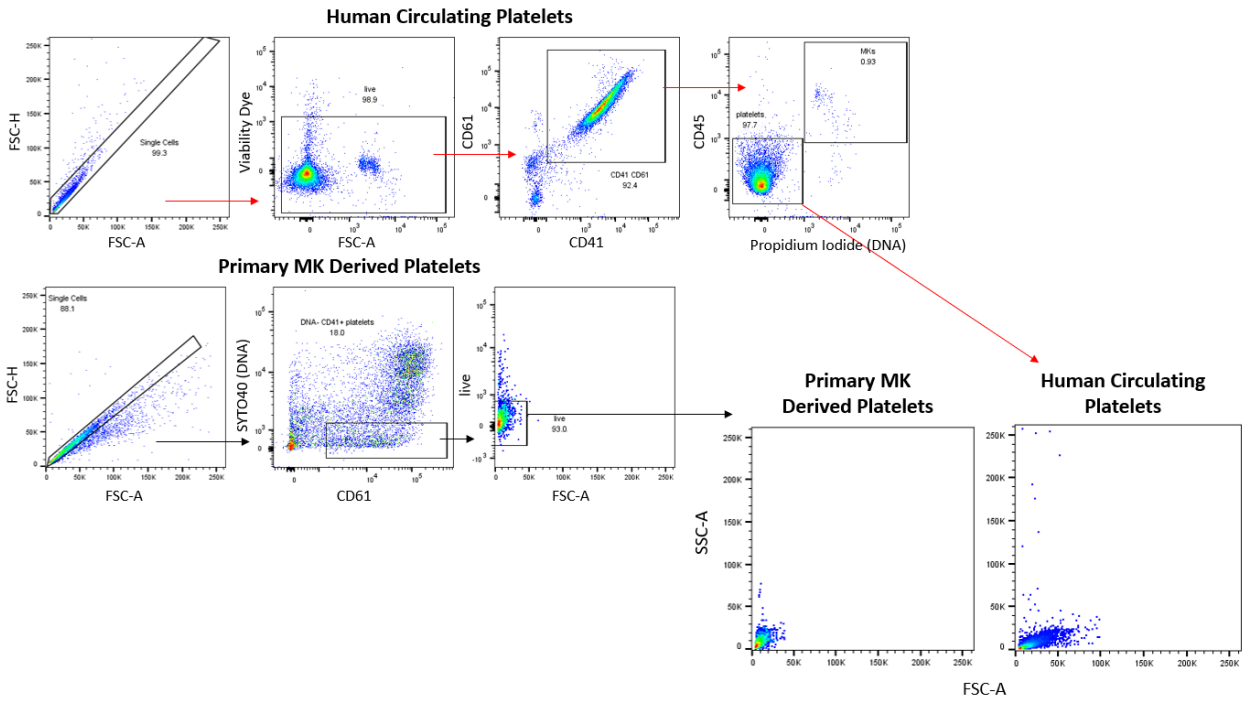
218 **Supplemental Figure 5. Isotype control stains for S100A8/A9 and spike protein from**

219 **five COVID-19+ donors.**



Supplemental Figure 6. Circulating megakaryocytes lack expression of neutrophil and classical monocyte markers. (**A**) Representative flow cytometry staining for neutrophil (CD66b) and classical monocyte (CD14) markers versus CD61 in DNA+ live cells. (**B**) Single-cell RNA-sequencing (scRNA-seq) data showing gene expression per cluster for markers associated with classical monocytes, neutrophils, and megakaryocytes. Note that neutrophils are not present in this scRNA-seq dataset, consistent with original publications of the data (1-4).



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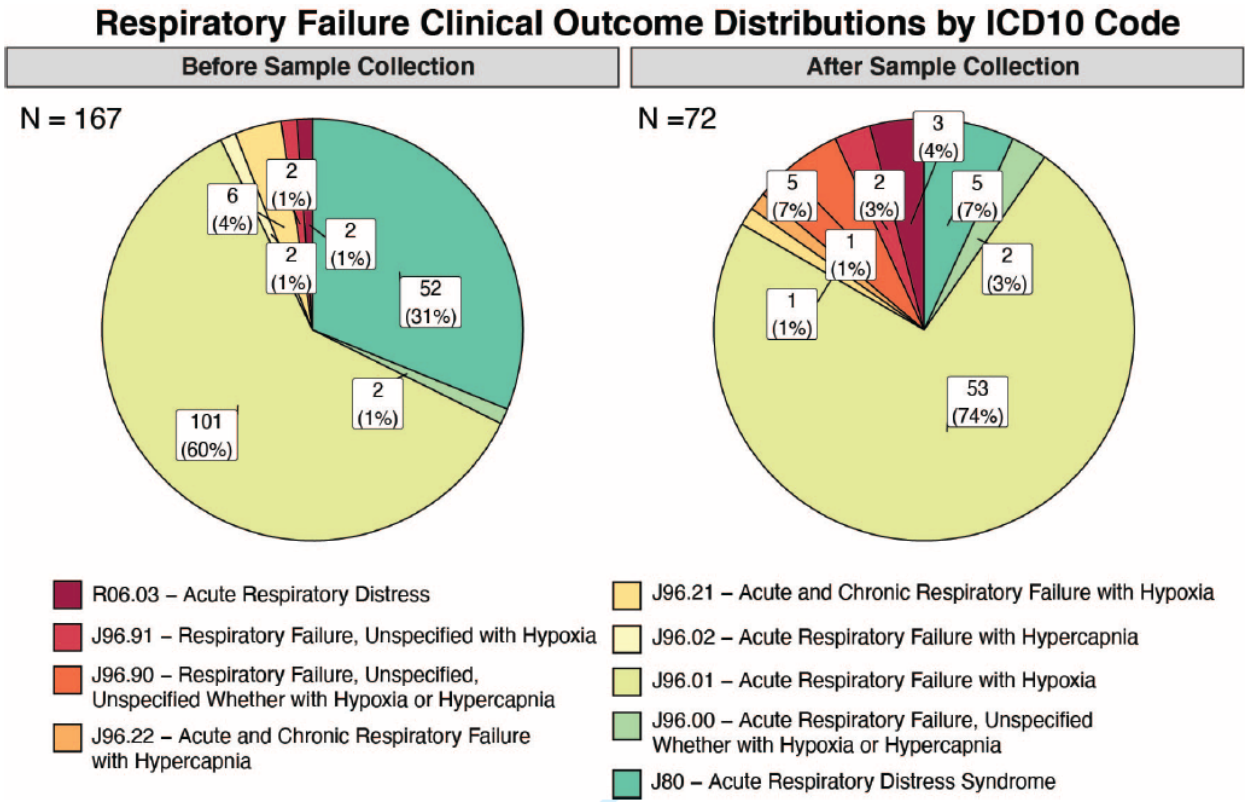
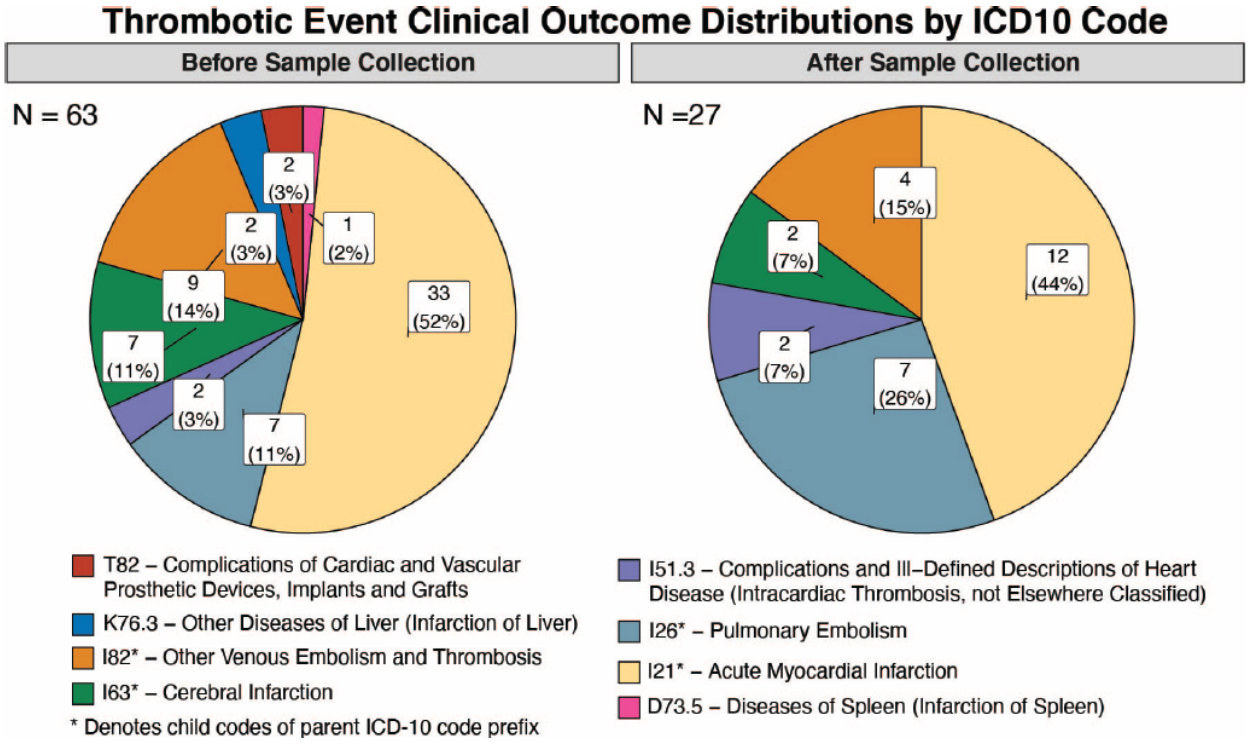
229 **Supplemental Figure 7. Flow cytometry gating scheme for primary megakaryocyte-**

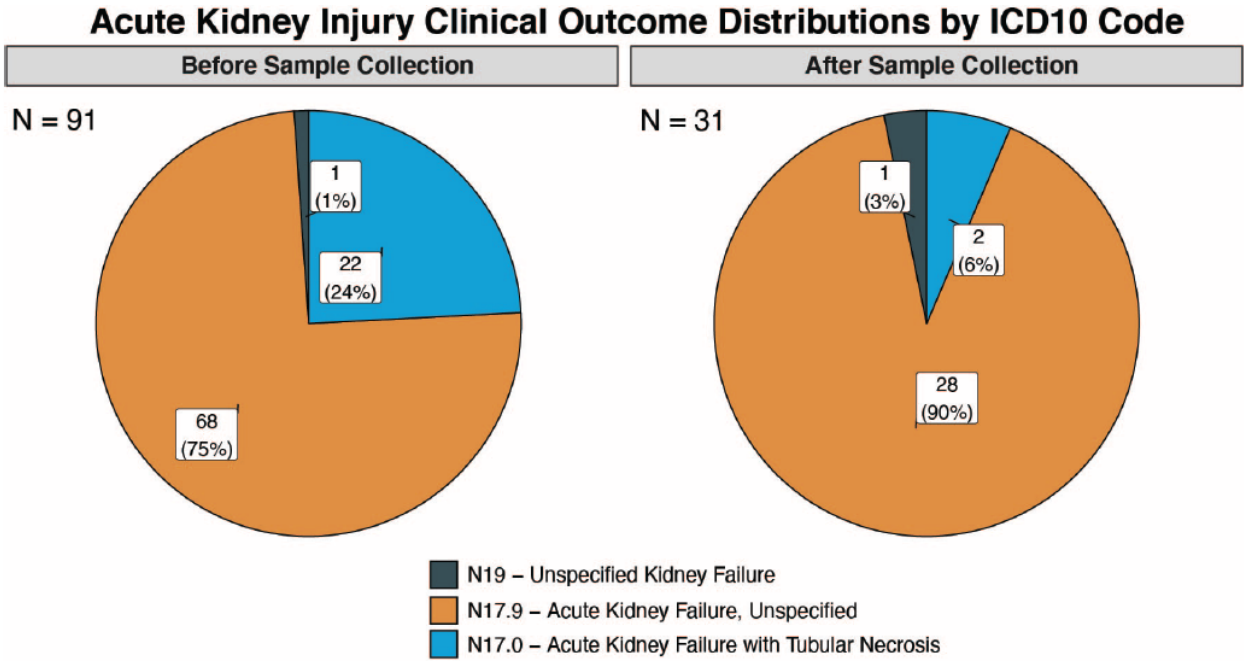
230 **derived platelets and comparison with human circulating platelets.**



Supplemental Figure 8. Distribution of Respiratory Failure Clinical Outcomes. ICD-10 code derived outcomes were assessed at two time-points: 1) the first respiratory failure outcome found post COVID-19+ admission and prior to blood sample collection, 2) the first respiratory failure outcome found post COVID-19+ admission, within 60-days after blood sample collection. Total outcome count for each time-point (N) are noted in the upper left hand corner of each pie-chart.



Supplemental Figure 9. Distribution of Thrombotic Event Clinical Outcomes. ICD-10 code derived outcomes were assessed at two time-points: 1) the first thrombotic event outcome found post COVID-19+ admission and prior to blood sample collection, 2) the first thrombotic event outcome found post COVID-19+ admission, within 60-days after blood sample collection. Total outcome count for each time-point (N) are noted in the upper left hand corner of each pie-chart.



Supplemental Figure 10. Distribution of Acute Kidney Injury Clinical Outcomes. ICD-10 code derived outcomes were assessed at two time-points: 1) the first acute kidney injury outcome found post COVID-19+ admission and prior to blood sample collection, 2) the first acute kidney injury outcome found post COVID-19+ admission, within 60-days after blood sample collection. Total outcome count for each time-point (N) are noted in the upper left hand corner of each pie-chart.

Clinical Outcomes	ICD10 Codes
Thrombotic Events	I21.A1, I21.4, I63.9, I51.3, I24.0, I26.99, I82.409, I26.94, I82.401, I82.629, I82.413, I82.412, I21.01, I21.19, I22.2, I82.90, I82.411, I26.93, I82.403, I82.432, I82.811, I63.511, I21.3, I82.442, I82.452, I82.C11, I82.A13, I82.B12, I82.612, T82.868A, G45.9, I63.40, I82.621, I82.441, I82.431, I82.451, I82.C12, I82.210, D73.5, I81, I82.402, K76.3, N28.0, I63.431, I63.113, I21.9, I63.541, I21.11, I82.B11, I82.813, I82.A11, I82.611
Acute Kidney Injury	N17.9, N19, N17.0
Respiratory Failure	J96.01, J80, J96.21, J96.91, J96.90, J96.00, R06.03, J96.02, J96.92, J96.22

Table S1. ICD10 Billing Codes Used for Clinical Outcomes.

Model Variable	30-day Outcome Adjusted OR (95% CI)[2]	p-value[3]
Respiratory Failure		
Age (per 1 year)	1.03 (1.00, 1.08)	0.068
Body Mass Index (per 1 point)	1.00 (0.94, 1.05)	0.96
Charlson Comorbidity Score (per 1 point)	1.19 (0.98, 1.48)	0.067
S100A8/A9+ Spike+ Megakaryocyte Proportion (per 20% increase)	2.42 (1.55, 4.36)	<0.001
ICU Admission		
Age (per 1 year)	1.01 (0.97, 1.06)	0.55
Body Mass Index (per 1 point)	1.01 (0.95, 1.05)	0.74
Charlson Comorbidity Score (per 1 point)	1.32 (1.07, 1.69)	0.012
S100A8/A9+ Spike+ Megakaryocyte Proportion (per 20% increase)	2.05 (1.05, 3.64)	0.011
Acute Kidney Injury		
Age (per 1 year)	1.01 (0.97, 1.05)	0.73
Body Mass Index (per 1 point)	1.01 (0.96, 1.04)	0.83
Charlson Comorbidity Score (per 1 point)	1.21 (1.02, 1.46)	0.039
S100A8/A9+ Spike+ Megakaryocyte Proportion (per 20% increase)	1.82 (1.12, 2.96)	0.010
Thrombotic Events		
Age (per 1 year)	1.00 (0.95, 1.05)	0.93
Body Mass Index (per 1 point)	0.99 (0.94, 1.03)	0.70
Charlson Comorbidity Score (per 1 point)	1.04 (0.85, 1.26)	0.70
S100A8/A9+ Spike+ Megakaryocyte Proportion (per 20% increase)	1.91 (1.13, 3.15)	0.012
Mechanical Ventilation		
Age (per 1 year)	0.99 (0.95, 1.04)	0.77
Body Mass Index (per 1 point)	0.97 (0.92, 1.03)	0.47
Charlson Comorbidity Score (per 1 point)	1.02 (0.81, 1.26)	0.82
S100A8/A9+ Spike+ Megakaryocyte Proportion (per 20% increase)	2.75 (1.48, 5.56)	<0.001
Mortality		
Age (per 1 year)	1.02 (0.99, 1.05)	0.16
Body Mass Index (per 1 point)	0.99 (0.96, 1.02)	0.56
Charlson Comorbidity Score (per 1 point)	0.96 (0.83, 1.12)	0.59
S100A8/A9+ Spike+ Megakaryocyte Proportion (per 20% increase)	1.71 (1.18, 2.51)	0.005

[1] OR = Odds Ratio

[2] Bootstrapped 95% Confidence Intervals (n=1,000)

[3] Wald Test

Table S2: Logistic Regression Models for 20% Increase in S100A8/A9+ Virus+ Megakaryocyte Proportion for 30-day Adverse Events.

Model Variable	30-day Outcome Adjusted OR (95% CI)[2]	p-value[3]
Respiratory Failure		
Age (per 1 year)	1.04 (1.01, 1.09)	0.027
Body Mass Index (per 1 point)	0.99 (0.94, 1.03)	0.78
Charlson Comorbidity Score (per 1 point)	1.19 (0.99, 1.43)	0.058
S100A8/A9+ Spike- Megakaryocyte Proportion (per 20% increase)	0.80 (0.46, 1.34)	0.37
ICU Admission		
Age (per 1 year)	1.02 (0.98, 1.06)	0.42
Body Mass Index (per 1 point)	1.00 (0.95, 1.04)	0.94
Charlson Comorbidity Score (per 1 point)	1.31 (1.06, 1.67)	0.011
S100A8/A9+ Spike- Megakaryocyte Proportion (per 20% increase)	0.99 (0.48, 2.29)	>0.99
Acute Kidney Injury		
Age (per 1 year)	1.01 (0.98, 1.05)	0.52
Body Mass Index (per 1 point)	1.00 (0.95, 1.04)	0.92
Charlson Comorbidity Score (per 1 point)	1.23 (1.00, 1.48)	0.034
S100A8/A9+ Spike- Megakaryocyte Proportion (per 20% increase)	0.99 (0.60, 1.74)	0.94
Thrombotic Events		
Age (per 1 year)	1.01 (0.97, 1.06)	0.78
Body Mass Index (per 1 point)	0.99 (0.93, 1.03)	0.60
Charlson Comorbidity Score (per 1 point)	1.06 (0.86, 1.26)	0.59
S100A8/A9+ Spike- Megakaryocyte Proportion (per 20% increase)	0.79 (0.44, 1.44)	0.45
Mechanical Ventilation		
Age (per 1 year)	1.01 (0.97, 1.05)	0.66
Body Mass Index (per 1 point)	0.97 (0.92, 1.01)	0.37
Charlson Comorbidity Score (per 1 point)	1.04 (0.79, 1.30)	0.70
S100A8/A9+ Spike- Megakaryocyte Proportion (per 20% increase)	1.06 (0.49, 2.43)	0.89
Mortality		
Age (per 1 year)	1.02 (1.00, 1.05)	0.056
Body Mass Index (per 1 point)	0.98 (0.95, 1.02)	0.42
Charlson Comorbidity Score (per 1 point)	0.96 (0.82, 1.10)	0.61
S100A8/A9+ Spike- Megakaryocyte Proportion (per 20% increase)	1.16 (0.76, 1.79)	0.44

[1] OR = Odds Ratio

[2] Bootstrapped 95% Confidence Intervals (n=1,000)

[3] Wald Test

Table S3: Logistic Regression Models for 20% Increase in S100A8/A9+ Virus-Megakaryocyte Proportion for 30-day Adverse Events.

Model Variable	30-day Outcome Adjusted OR (95% CI)[2]	p-value[3]
Respiratory Failure		
Age (per 1 year)	1.04 (1.00, 1.09)	0.034
Body Mass Index (per 1 point)	1.00 (0.94, 1.04)	0.81
Charlson Comorbidity Score (per 1 point)	1.17 (0.97, 1.43)	0.10
S100A8/A9- Spike- Megakaryocyte Proportion (per 20% increase)	0.48 (0.19, 0.80)	0.006
ICU Admission		
Age (per 1 year)	1.02 (0.98, 1.06)	0.5
Body Mass Index (per 1 point)	1.00 (0.95, 1.05)	0.8
Charlson Comorbidity Score (per 1 point)	1.32 (1.08, 1.74)	0.008
S100A8/A9- Spike- Megakaryocyte Proportion (per 20% increase)	0.43 (0.19, 0.76)	0.002
Acute Kidney Injury		
Age (per 1 year)	1.01 (0.98, 1.05)	0.6
Body Mass Index (per 1 point)	1.00 (0.96, 1.04)	>0.9
Charlson Comorbidity Score (per 1 point)	1.20 (0.99, 1.46)	0.054
S100A8/A9- Spike- Megakaryocyte Proportion (per 20% increase)	0.56 (0.29, 0.89)	0.010
Thrombotic Events		
Age (per 1 year)	1.00 (0.96, 1.05)	0.9
Body Mass Index (per 1 point)	0.99 (0.93, 1.03)	0.5
Charlson Comorbidity Score (per 1 point)	1.03 (0.84, 1.25)	0.8
S100A8/A9- Spike- Megakaryocyte Proportion (per 20% increase)	0.63 (0.32, 1.02)	0.064
Mechanical Ventilation		
Age (per 1 year)	1.00 (0.96, 1.04)	0.9
Body Mass Index (per 1 point)	0.98 (0.92, 1.03)	0.4
Charlson Comorbidity Score (per 1 point)	0.99 (0.77, 1.27)	>0.9
S100A8/A9- Spike- Megakaryocyte Proportion (per 20% increase)	0.23 (0.08, 0.45)	<0.001
Mortality		
Age (per 1 year)	1.02 (1.00, 1.05)	0.10
Body Mass Index (per 1 point)	0.99 (0.96, 1.02)	0.4
Charlson Comorbidity Score (per 1 point)	0.94 (0.81, 1.10)	0.5
S100A8/A9- Spike- Megakaryocyte Proportion (per 20% increase)	0.57 (0.37, 0.81)	0.004

[1] OR = Odds Ratio

[2] Bootstrapped 95% Confidence Intervals (n=1,000)

[3] Wald Test

Table S4: Logistic Regression Models for 20% Increase in S100A8/A9- Virus-Megakaryocyte Proportion for 30-day Adverse Events.

Characteristic	Overall N = 218[1]	Diabetic History N = 119[1]	No Diabetic History N = 99[1]	p-value
Age (years)	62 (52-70)	62 (52-69)	62 (54-72)	0.8[2]
Sex				0.4[3]
Female	92 (42%)	47 (39%)	45 (45%)	
Male	126 (58%)	72 (61%)	54 (55%)	
Charlson Comorbidity Score	3 (1-4)	3 (2-5)	2 (0-3)	<0.001[2]
Body Mass Index	32 (28-37)	33 (28-38)	31 (27-35)	0.15[2]
Calprotectin+ Spike+ Megakaryocyte Grouping				0.2[3]
Low (<12.8%)	72 (33%)	42 (35%)	30 (31%)	
Medium (12.8-27.7%)	72 (33%)	43 (36%)	29 (30%)	
High (>27.7%)	73 (34%)	34 (29%)	39 (40%)	
Inpatient Outcomes (within 30-days)				
Mechanical Ventilation	20 (9.2%)	10 (8.4%)	10 (10%)	0.6[3]
Respiratory Failure	69 (32%)	37 (31%)	32 (33%)	0.8[3]
Acute Kidney Injury	30 (14%)	19 (16%)	11 (11%)	0.3[3]
Thrombotic Event	25 (12%)	10 (8.4%)	15 (15%)	0.11[3]
Mortality	35 (16%)	23 (19%)	12 (12%)	0.2[3]
ICU Admission	19 (8.8%)	12 (10%)	7 (7.1%)	0.4[3]

[1]Median (25%-75%); n (%)
[2]Wilcoxon rank sum test
[3]Pearson's Chi-squared test

Table S5: Characteristics and Outcomes for UAB COVID-19+ Biospecimen Cohort Stratified by Pre-Admission Diabetic History.

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