TANG PRIZE REPORT

Mechanisms of COVID-19 Vascular Pathology

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Executive Summary

Severe COVID-19 is not simply a viral pneumonia; it is a systemic inflammatory and vascular dysregulation converge to drive poor outcomes. From the outset, this project was designed to address a central unresolved question in COVID-19 pathogenesis: how innate immune activation contributes to clinical deterioration.

The work reported here provides a substantial advance on that objective. Using high-dimensional mass cytometry and systems-level single-cell analysis of peripheral blood from patients across the spectrum of COVID-19 severity, we identified a profound reorganisation of the circulating myeloid compartment. Most notably, we observed a striking replacement of the steady-state classical monocyte population seen in healthy individuals by a distinct COVID-19-associated monocyte state that expands in proportion to disease severity. These monocytes exhibit a proliferative and activated phenotype, marked by increased Ki67 together with elevated CD163, CD38, CD64, CD71, and CD141, consistent with emergency myelopoiesis and dysregulated innate immune activation . These disease-associated monocytes exhibit a TREM1-driven, lipid-associated inflammatory programme consistent with our prior identification of $PLIN2^{+}$ macrophages, linking metabolic reprogramming to vascular pathology.

These findings have both conceptual and translational significance. Conceptually, they establish mononuclear phagocyte dysfunction as a defining feature of severe disease and help explain why COVID-19 behaves, in its most dangerous forms, as a thrombo-inflammatory syndrome rather than a purely respiratory infection. Translationally, they identify candidate cellular biomarkers of severity and provide a rationale for therapeutic strategies aimed at restraining pathologic myeloid activation and its vascular consequences.

Background and Original Objectives

One of the most distinctive and clinically important features of severe COVID-19 severe disease is accompanied by major perturbations in the immune system, including neutrophilia, lymphopenia, altered monocyte phenotypes, and elevated circulating inflammatory mediators. The proposal underlying this award argued that these phenomena are mechanistically linked, and that innate immune activation, particularly within the myeloid lineage, may be a major driver of pathology in COVID-19 .

The specific ambition of the project was therefore not merely to catalogue inflammatory abnormalities, but to understand how aberrant myeloid responses might help explain the thrombo-inflammatory phenotype of severe disease. The proposal further highlighted tumour necrosis factor and related inflammatory pathways as plausible upstream drivers of endothelial activation, platelet activation, coagulation, and immune pathology, with the longer-term goal of informing patient stratification and immunomodulatory interventions .

Within that framework, the present study focused on resolving the cellular architecture of the circulating myeloid compartment in COVID-19 patients and identifying severity-associated immune states that could plausibly connect inflammation to vascular dysfunction. This represented a crucial mechanistic step toward the broader translational aims of the funded programme.

Study Design and Experimental Approach

To capture the breadth of immune phenotypes associated with infection and recovery, we analysed blood samples from hospitalised Oxford COVID-19 patients together with healthcare workers and healthy volunteers. COVID-19 cases were classified according to clinical severity into mild disease, severe disease, and critical disease requiring mechanical ventilation. An additional convalescent group was also included, enabling comparison not only between infected and non-infected individuals but also between active disease and post-infectious recovery .

Whole blood and peripheral blood mononuclear cells were processed using established protocols suitable for high-dimensional mass cytometric analysis. Because neutrophils dominate whole blood and can obscure analysis of less abundant mononuclear phagocyte populations, a portion of each sample was enriched for mononuclear cells by depleting CD66-positive granulocytes. This yielded two complementary fractions per sample: an untouched whole-blood fraction suitable for neutrophil phenotyping and a mononuclear-enriched fraction allowing deeper analysis of the mononuclear myeloid compartment .

Both fractions were stained with a myeloid-focused CyTOF antibody panel incorporating a broad range of lineage, activation, antigen-presentation, and intracellular markers, including CD14, HLA-DR, CD16, CD163, CD64, CD11c, CD33, CD141, CD71, and Ki67, among others . After acquisition on a Helios mass cytometer, data were normalised, compensated, manually debarcoded, and subjected to a combination of conventional gating and unsupervised computational analysis. A total of 49 blood samples were analysed using this myeloid-focused panel, with 3000 myeloid cells per sample included for clustering analysis. FlowSOM clustering and UMAP dimensionality reduction were used to identify cellular populations and visualise their distribution across clinical groups .

This analytical design was important for two reasons. First, it allowed unbiased identification of disease-associated cell states rather than forcing cells into predefined categories. Second, it made it possible to detect shifts in the internal composition of canonical populations, particularly within the classical monocyte compartment, where some of the most important biology emerged.

METHODS

Subjects

Study subjects were hospitalized Oxford COVID-19 patients, healthcare workers (hcw) and healthy volunteers (hv). COVID-19 was defined by presence of at least one symptom consistent with COVID-19 and a positive microbiological test. COVID patients were classified into mild (no oxygen requirement), severe (≤ 93% oxygen saturation) and critical (requiring mechanical ventilation) according to the WHO classification. An additional group of convalescent COVID patients was also assessed.

Blood sample processing

Whole blood from all subjects were sampled into EDTA buffered vacutainers (Fisher Scientific). Whole blood was mixed in a 1:1 ratio with the whole cell stabilizer Cytodelics (Cytodelics). PBMC were collected using Leucosep separation tubes (Griener Bio-One) and frozen at -80 degrees until processing.

Sample processing and antigen staining

On the day of staining, Cytodelics stabilized samples were thawed and processed using Whole Blood Processing Kit (Cytodelics) as per manufacturer instruction. The cells were barcoded using the Cell-ID 20-Plex Pd Barcoding Kit (Fluidigm).

Since neutrophils make up 40%–70% of cells of whole blood cells and > 95% in septic patients, we enriched a portion of each whole blood sample for mononuclear cells using a granulocyte depletion kit based on the magnetic separation of CD66+ cells using beads coated with anti-CD66 antibodies (EasySep; 17882). This allowed us to obtain from each whole blood sample in the study, both an untouched neutrophil-containing fraction for neutrophil phenotyping, and an enriched mononuclear fraction for in depth phenotyping of the mononuclear myeloid compartment.

Both cell fractions obtained from this process were stained using a myeloid-marker enriched mass cytometry panel of antibodies including cell surface and intracellular markers (Table 1). Cells were first stained with a cocktail of cell surface antibodies, prior to fixation, permeabilization, and staining with a cocktail of intracellular antibodies. Samples were subsequently fixed in 1.6% paraformaldehyde solution before overnight incubation with Cell-ID Intercalator–Iridium. Samples were acquired on a Helios Mass Cytometer at an acquisition rate of < 300 events/second.

Data analysis

After acquisition, data was normalized and concatenated on CyTOF Software v7.0, compensated on CATALYST (version 1.5.3.23) and processed using a manual gating strategy using FlowJo v10.6. Samples were manually debarcoded (FlowJo v10.6) and $CD45^+$ events (non-depleted samples), or CD66-Siglec8-$CD45^+$ (neutrophil-depleted samples) events were selected for further processing.

RESULTS

A total of 49 blood samples were analysed using the myeloid focused mass cytometry panel. The distribution of patients is displayed in Figure 1A. Cells were gated as CD45+CD11b+CD66- to select for myeloid cells and a total of 3000 myeloid cells were analysed per sample. Clustering analysis was performed using a self-organizing map algorithm through an implementation of FlowSOM and UMAP via the CATALYST R package (version 1.10.3).

Eleven clusters were identified, including monocytes, conventional (cDC) and plasmacytoid (pDC) dendritic cells (Figure 1B). Expression levels of CD14, HLADR and CD16 markers on UMAP shows the presence of all 3 main monocyte subsets including classical ($CD14^{high}$), intermediate ($HLADR^{high}$) and non-classical ($CD16^{high}$) (Figure 1C).

Expression patterns of a wider range of markers is shown in heatmap format, highlighting the distinct marker signatures of the 11 identified cell clusters identified (Figure 1D).

Enumeration of the 11 identified cell clusters across the different patient groups identified a switch in the classical monocyte compartment in patients with COVID-19 (mild, severe, critical) compared to patients without active COVID-19 (hv, hcw, conv). Figure 2A shows a UMAP of all 49 samples within the analysis, with the classical monocyte compartment highlighted.

A representative UMAP of a patient from each patient group highlights the dramatic phenotypic change in the classical monocyte compartment between those with active COVID-19 and those without (Figure 2A), particularly in cluster 5 (predominant in those without active COVID-19) and cluster 11 (predominant in those with active COVID-19).

Enumeration of the 11 myeloid clusters across the different patient groups is shown in Figure 2B. In healthy samples, the myeloid compartment is predominantly classical monocytes as expected, represented by cluster 5. In active COVID-19 however, the phenotype of the classical monocyte compartment shifts to a more active state, represented by cluster 11. This shift from a “healthy” classical monocyte phenotype to a “COVID-19” classical monocyte phenotype is additionally more pronounced depending on the severity of disease.

The phenotypic shift from “healthy” classical monocyte to “COVID-19” classical monocyte includes changes in expression levels of a number of markers, in particular an increase in ki67 expression. Phenotypically, the COVID-19 associated classical monocytes display increased expression levels of CD163, CD38, CD64, CD71, CD141, and are predominantly characterised by increased expression levels of ki67 (Figure 2C)

Table 1. Myeloid-marker enriched mass cytometry panel antibodies

Antibody	Company	Cat number
CD45 (HI30)-89Y	Fluidigm	Cat# 3089003, RRID:AB_2661851
CD5 (UCHT2)-111Cd	Biolegend	Cat# 300627, RRID:AB_2563756
CD3 (UCHT1)-112Cd	Biolegend	Cat# 300443, RRID:AB_2562808
CD9 (HI91)-113Cd	Biolegend	Cat# 312102, RRID:AB_314907
CD7 (CD7-6B7)-114Cd	Biolegend	Cat# 343111, RRID:AB_2563761
HLADR (L243)-116Cd	Biolegend	Cat# 307651, RRID:AB_2562826
CD49d (9F10)-141Pr	Fluidigm	Cat# 3141004B, RRID:AB_2892684
CD19 (HIB19)-142Nd	Fluidigm	Cat# 3142001B, RRID:AB_2651155
CD123 (6H6)-143Nd	Fluidigm	Cat# 3143014B, RRID:AB_2811081
CD15 (W6D3)-144Nd	Fluidigm	Cat# 3144019B, RRID:AB_2892685
CD38 (HIT2)-145Nd	Biolegend	Cat# 303535, RRID:AB_2562819
CD64 (10.1)-146Nd	Fluidigm	Cat# 3146006B, RRID:AB_2661790
CD11c (Bu15)-147Sm	Fluidigm	Cat# 3147008B, RRID:AB_2687850
CD16 (3G8)-148Nd	Fluidigm	Cat# 3148004B, RRID:AB_2661791
CD74 (LN2)-149Sm	Biolegend	Cat# 326802, RRID:AB_893401

CD43 (84-3C1)-150Nd	Fluidigm	Cat# 3150006B, RRID:AB_2892686
CD103 (Ber-ACT8)-151Eu	Fluidigm	Cat# 3151011B, RRID:AB_2756418
CD66b (80H3)-152Sm	Fluidigm	Cat# 3152011B, RRID:AB_2661795
BDCA2 (201A)-153Eu	Fluidigm	Cat# 3153007B, RRID:AB_2892687
CD163 (GHI/61)-154Sm	Fluidigm	Cat# 3154007B, RRID:AB_2661797
CD36 (5-271)-155Gd	Fluidigm	Cat# 3155012B, RRID:AB_2756286
CD10 (Hi10a)-156Gd	Fluidigm	Cat# 3156001B, RRID:AB_2802107
CD33 (WM53)-158Gd	Fluidigm	Cat# 3158001B, RRID:AB_2661799
CD22 (HIB22)-159Tb	Fluidigm	Cat# 3159005B, RRID:AB_2892688
CD14 (M5E2)-160Gd	Fluidigm	Cat# 3160001B, RRID:AB_2687634
CLEC9A (8F9)-161Dy	Fluidigm	Cat# 3161018B, RRID:AB_2810252
ki67 (B56)-162Dyˆ	Fluidigm	Cat# 3162012B, RRID:AB_2888928
CD172a/b (SE5A5)-163Dy	Fluidigm	Cat# 3163017B, RRID:AB_2864730
Siglec 8 (7C9)-164Dy	Fluidigm	Cat# 3164017B, RRID:AB_2892691
CD101 (BB27)-165Ho	Fluidigm	Cat# 3165029B, RRID:AB_2892692
CD141 (M80)-166Er	Fluidigm	Cat# 3166017B, RRID:AB_2892693

CD301 (H037G3)-167Er	Fluidigm	Cat# 3167015B, RRID:AB_2892694
CD71 (OKT9)-168Er	Fluidigm	Cat# 3168014B, RRID:AB_2892695
BDCA4 (12C2)-169Tm	Fluidigm	Cat# 3169018B, RRID:AB_2892697
CD114 (38660)-170Er	R&D	Cat# MAB381, RRID:AB_2245228
CD226 (DX11)-171Yb	Fluidigm	Cat# 3171013B, RRID:AB_2756427
CD354 (TREM-26)-172Yb	Fluidigm	Cat# 3172022B, RRID:AB_2756428
CD371 (50C1)-173Yb	Fluidigm	Cat# 3173007B, RRID:AB_2892698
CD142 (NY2)-174Yb	Biolegend	Cat# 365202, RRID:AB_2564564

Discussion of the principal findings

Severe COVID-19 is associated with marked remodelling of the circulating myeloid compartment

Our first major finding was that the myeloid landscape in COVID-19 differs fundamentally from that seen in healthy and non-infected states. Unsupervised analysis identified 11 clusters spanning monocytes, conventional dendritic cells, and plasmacytoid dendritic cells. UMAP representation confirmed the presence of the major monocyte subsets, including classical, intermediate, and non-classical monocytes, while heatmap analysis showed that these clusters were distinguished by clear and biologically coherent marker signatures .

Figure 1 captures this global architecture. It shows the sample distribution, the UMAP clustering of the CD11b-positive populations across all samples, the expression of key monocyte markers, and the heatmap-based definition of the resulting clusters . Together, these analyses establish that COVID-19 is accompanied by widespread reorganisation of the circulating myeloid compartment rather than a simple increase or decrease in total myeloid cell numbers.

This point is conceptually important. It indicates that severe COVID-19 is associated with a change in the *state* of the innate immune system, not merely its magnitude. The disease is therefore characterised by immune reprogramming, with potential consequences for inflammatory signalling, antigen presentation, endothelial interaction, and thrombo-inflammatory amplification.

The classical monocyte compartment undergoes a striking severity-dependent state transition

The most prominent and biologically consequential change was observed within the classical monocyte compartment. Enumeration of the 11 identified clusters across patient groups revealed a clear switch between two alternative classical monocyte states. In healthy volunteers, healthcare workers, and convalescent individuals, the myeloid compartment was dominated by a cluster corresponding to a steady-state classical monocyte phenotype, designated cluster 5. In contrast, in patients with active COVID-19, especially those with more severe disease, this population was progressively replaced by a distinct cluster, cluster 11, representing a COVID-19-associated monocyte phenotype .

This transition is clearly illustrated in Figure 2, which highlights the differential abundance of clusters 5 and 11 across patient groups and shows that the disease-associated classical monocyte state becomes increasingly dominant with severity . Representative UMAPs from individual patients reinforce the same conclusion: the monocyte compartment in active disease is not merely activated in a diffuse manner, but restructured around a specific alternative cellular programme .

This observation advances the original grant objective in a direct way. It identifies a discrete severity-linked innate immune state that can plausibly mediate the transition from antiviral response to pathologic inflammation and vascular injury. In other words, it defines a cellular substrate for severe disease.

COVID-19-associated classical monocytes are proliferative and highly activated

The COVID-19-associated monocyte population was not only compositionally distinct but phenotypically striking. Compared with the classical monocytes seen in non-infected individuals,

these cells showed increased expression of Ki67, indicating active cell cycling or very recent proliferative emergence. They also exhibited increased CD163, CD38, CD64, CD71, and CD141, consistent with broad activation and altered differentiation status .

Among these changes, the increase in Ki67 is particularly significant. Ki67 expression within circulating classical monocytes is not a feature of physiological homeostasis; rather, it points to emergency myelopoiesis and rapid mobilisation of immature or recently generated myeloid cells into the bloodstream. In the context of severe infection, this suggests that the bone marrow is being driven to produce and release monocytes under inflammatory pressure, resulting in the appearance of cells that are both developmentally atypical and functionally dysregulated.

The elevation of markers such as CD163, CD64, and CD38 further indicates that these are not quiescent immature cells, but inflammatory effectors with the potential to participate in cytokine amplification, Fc receptor-mediated responses, and pathological tissue interactions.

The COVID-19-associated classical monocyte population is characterised not only by proliferative expansion but by a coordinated activation, differentiation, and metabolic programme consistent with pathogenic innate immune reprogramming. These cells show increased expression of core monocyte lineage markers (**CD14, CD11b, CD64**), together with markers of proliferation (**Ki67**) and emergency myelopoiesis, including **CD114 (G-CSF receptor)**, indicating active mobilisation from the bone marrow.

In parallel, these cells exhibit upregulation of activation and differentiation markers (**CD71, CD141, CD64**) and a distinct metabolic signature, including increased expression of **CD36 and CD71**, consistent with enhanced lipid uptake and metabolic reprogramming. This phenotype reflects a shift toward a highly active, inflammatory, and metabolically primed monocyte state.

A particularly notable feature of this disease-associated population is the marked upregulation of **TREM1 (CD354)**, a key amplifier of acute inflammatory responses. TREM1 expression is enriched within a specific disease-associated cluster (cluster C3; Fig. 1B,D), which is expanded in COVID-19 patients and increases with disease severity (Fig. 2A,B). Importantly, high TREM1 expression has been associated with reduced responsiveness to anti-TNFα therapy, suggesting that this pathway may contribute to treatment resistance in a subset of patients.

Concomitantly, this pathogenic monocyte state is associated with a reduction in features of homeostatic and anti-inflammatory regulation, including decreased expression of non-classical monocyte markers (**CD49d, CD43**) and the anti-inflammatory marker **CD101**. This loss of regulatory features, combined with enhanced activation and inflammatory amplification pathways, defines a monocyte phenotype that is both highly reactive and poorly controlled.

Proteomic hallmarks further support a thrombo-inflammatory model of severe disease

In addition to the cellular findings, the draft report notes that proteomic analysis identified plasma cytokines and chemokines as biomarkers of severe disease and showed evidence of acute phase response, complement activation and attack, fibrin clot formation, protease activity, serum amyloid, tissue necrosis, receptor-mediated endocytosis, and altered cholesterol transport . Although these proteomic results are not the main focus of the current figures, they are essential to the conceptual interpretation of the study.

They show that the altered monocyte states identified at single-cell level arise within a systemic environment already primed for vascular injury and coagulation. Acute phase signalling, complement activation, fibrin-related processes, and tissue necrosis are not isolated biochemical observations; they define a biological context in which dysregulated myeloid cells are likely to have pathogenic consequences for endothelium, coagulation, and organ function.

This strengthens the link back to the original grant proposal. The study does not simply show immune abnormality in parallel with vascular pathology; it begins to define the immune architecture that could drive it.

Mechanistic Significance

The central conceptual advance of this work is the identification of mononuclear phagocyte dysfunction as a mechanistic bridge between inflammation and vascular pathology in severe COVID-19. The funded proposal was built around the idea that innate immune activation contributes to coagulopathy and vascular damage, but the field lacked sufficiently resolved cellular evidence to explain how this occurs in patients . The present study fills that gap.

The data support a model in which severe SARS-CoV-2 infection triggers emergency myelopoiesis and the release of proliferating, developmentally altered classical monocytes into the circulation. These cells adopt an activated phenotype and accumulate as disease worsens. At the same time, dendritic cell depletion and reduced expression of molecules such as HLA-DR point to impaired orchestration of effective immune responses. The resulting state is one of inflammatory excess combined with functional disarray.

Such a state is precisely the sort of immune environment expected to promote vascular injury. Activated monocytes can engage endothelium, amplify cytokine production, interact with platelets and coagulation pathways, and reinforce systemic inflammatory signalling. In a setting already marked by complement activation, fibrin formation, and acute phase responses, the emergence of these cells provides a highly plausible cellular basis for the thrombo-inflammatory syndrome of severe COVID-19.

This is why the findings matter beyond descriptive immunology. They help reframe severe COVID-19 as a disease in which pathogenic myeloid state transitions are central to organ damage and vascular complications.

Translational Relevance

The translational implications of these findings are substantial. First, the identification of a proliferative, disease-associated classical monocyte state provides a candidate cellular biomarker of severity. Because this population expands in proportion to disease severity, it could contribute to risk stratification, patient monitoring, and potentially early identification of patients likely to deteriorate.

Second, the work supports continued exploration of innate immune-targeted therapeutic strategies, including interventions directed at upstream cytokine pathways such as TNF. By identifying the cellular immune programmes most disregulated in severe disease, the present study provides a more precise biological framework within which such therapeutic approaches can be evaluated.

Third, the findings have implications that extend beyond acute COVID-19. They offer a generalizable framework for understanding how emergency myelopoiesis and dysfunctional monocyte activation may drive vascular injury in other infectious or inflammatory conditions characterised by thrombo-inflammation.

Finally, the study demonstrates the value of high-dimensional immune phenotyping in resolving clinically important heterogeneity that is invisible to routine laboratory measures. This is precisely the type of mechanistic, translational science that can transform broad clinical observations into actionable biological insight.

Overall Outcome Relative to the Tang Prize Objectives

This project has delivered a meaningful advance on the original aims of the Tang Prize-funded programme. The proposal sought to understand how innate immune activation contributes to COVID-19 vascular pathology, with particular attention to myeloid cells and inflammatory pathways . The present work shows that severe COVID-19 is associated with a fundamental remodelling of the mononuclear phagocyte compartment and defines a specific proliferative monocyte state that tracks with disease severity and provides a plausible mechanistic link to vascular injury.

Importantly, the upregulation of TREM1 within this disease-associated monocyte population is consistent with our previous identification of lipid-associated macrophages (LAMs) characterised by PLIN2 expression, which define a metabolically reprogrammed, pro-inflammatory macrophage state. In that context, $PLIN2^{+}$ macrophages were shown to accumulate lipids and adopt a phenotype specialised for inflammatory amplification within diseased tissues.

The emergence of $TREM1^{+}$ monocytes with a concurrent metabolic signature ($CD36^{+}$, $CD71^{+}$) in COVID-19 suggests that circulating monocytes are being primed toward a similar lipid-associated, inflammatory programme prior to tissue infiltration. This raises the possibility that the pathogenic monocyte population identified here represents a circulating precursor of tissue-level lipid-associated macrophages.

Mechanistically, this convergence of lipid metabolism and TREM1-driven inflammatory amplification provides a unifying framework linking metabolic reprogramming of myeloid cells to vascular inflammation and coagulopathy. Given that lipid handling, foam cell formation, and macrophage activation are central features of vascular disease, this pathway may represent a shared axis across inflammatory vascular pathologies, including COVID-19.

Furthermore, the association of high TREM1 expression with reduced responsiveness to anti-TNFα therapy suggests that the emergence of this lipid-associated inflammatory programme may define a subset of patients with treatment-resistant disease, highlighting TREM1 and associated metabolic pathways as potential therapeutic targets.

Equally importantly, the work moves the field beyond generic descriptions of “hyperinflammation.” It identifies the relevant cell populations, defines their phenotype, places them within a severity-linked trajectory, and integrates them into a broader thrombo-inflammatory framework supported by accompanying plasma proteomic changes . This is exactly the sort of conceptual sharpening required to turn observational clinical phenomena into mechanistic understanding.

Together, these features define a previously unrecognised pathogenic monocyte state that integrates proliferative expansion, metabolic activation, and inflammatory amplification, and which is likely to play a central role in driving the thrombo-inflammatory complications of severe COVID-19.

Conclusion

In summary, the work supported by this award has shown that severe COVID-19 is characterised by a profound and structured reprogramming of the circulating myeloid compartment. At the centre of this reprogramming is the emergence of a proliferative, activated, COVID-19-associated classical monocyte population that replaces the steady-state monocyte compartment in proportion to disease severity. Alongside depletion of plasmacytoid dendritic cells, reduced expression of key myeloid regulatory and antigen-presentation markers, and systemic proteomic evidence of complement activation and fibrin-related pathology, these findings define a coherent biological picture of severe disease as a syndrome of maladaptive mononuclear phagocyte activation .

This study therefore delivers on the core ambition of the Tang Prize proposal. It provides mechanistic insight into how innate immune dysregulation can be linked to vascular pathology in COVID-19, identifies candidate cellular correlates of severe disease, and establishes a conceptual foundation for therapeutic strategies aimed at interrupting myeloid-driven thrombo-inflammation. In doing so, it contributes not only to our understanding of COVID-19, but to a broader understanding of how immune dysregulation can precipitate vascular injury in severe inflammatory disease.

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Figure 1. Overall analysis of COVID patients and controls. A)Distribution of samples included in the analysis. B) UMAP clustering of the CD11b+ populations analysis of all sample and C) monocyte markers. D) Heatmap distribution of the different markers per cluster. Healthy volunteers (hv), health care workers (hcw), and COVID patients with mild, severe and critical (crit) symptoms as well as convalescent patients (conv).

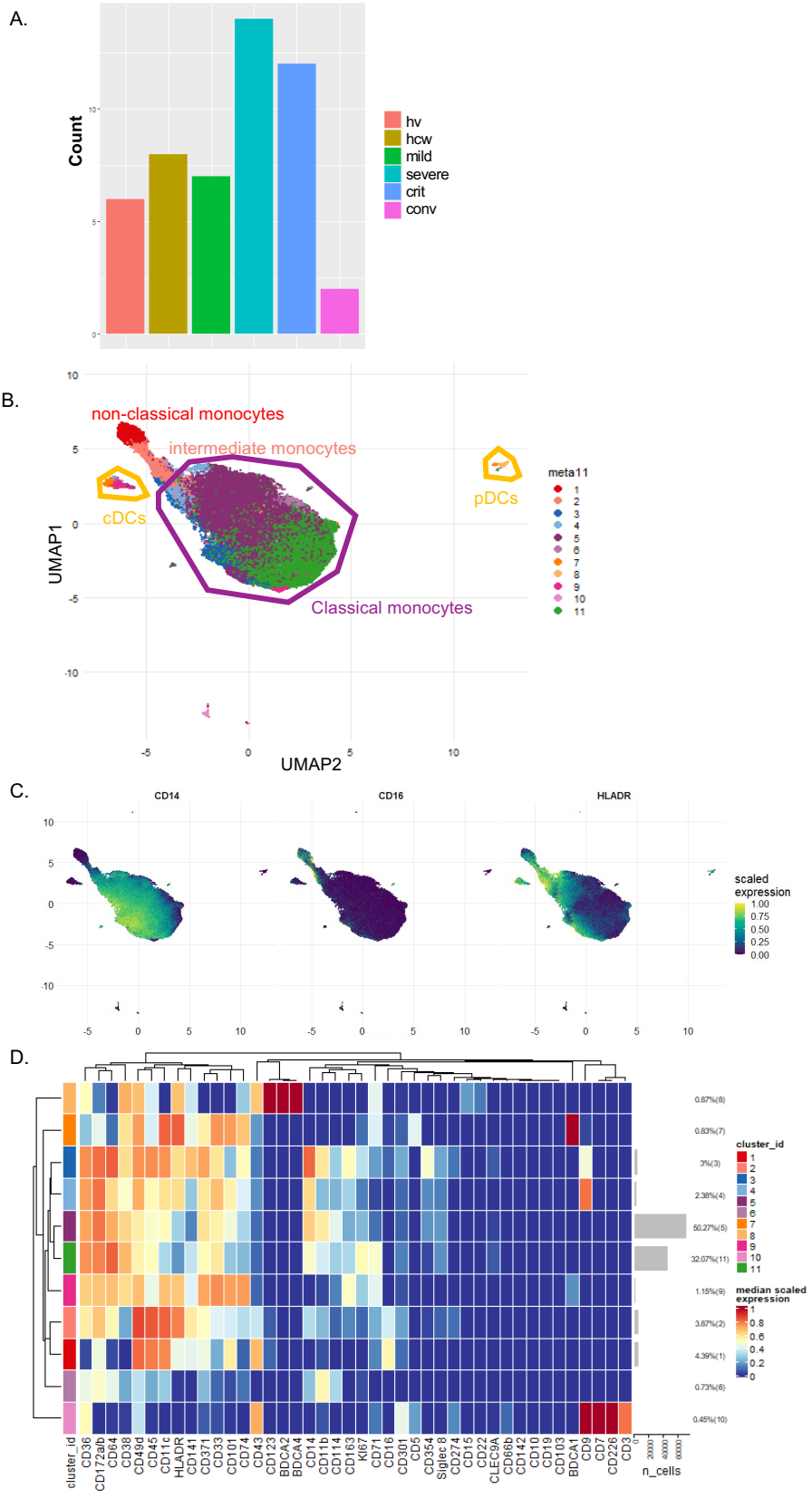


Figure 2. Compositional and marker differences between COVID patients and control samples. A) Cluster composition differences in the different set of subjects, with classical monocytes being the most affected especially clusters 5 and 11 being mostly affected between groups as shown in the percentage cells per cluster plot (B) C) Markers highly expressed in COVID patients compared to healthy controls

