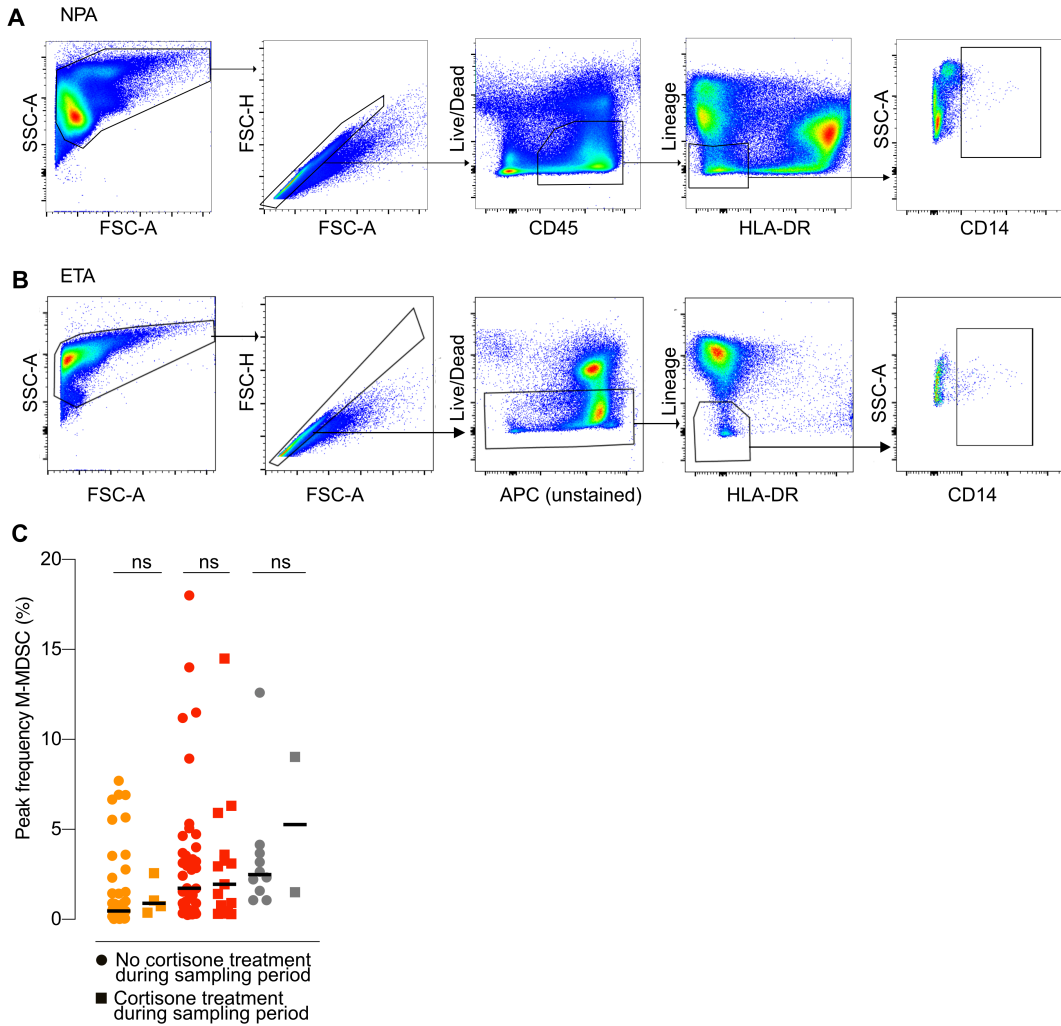
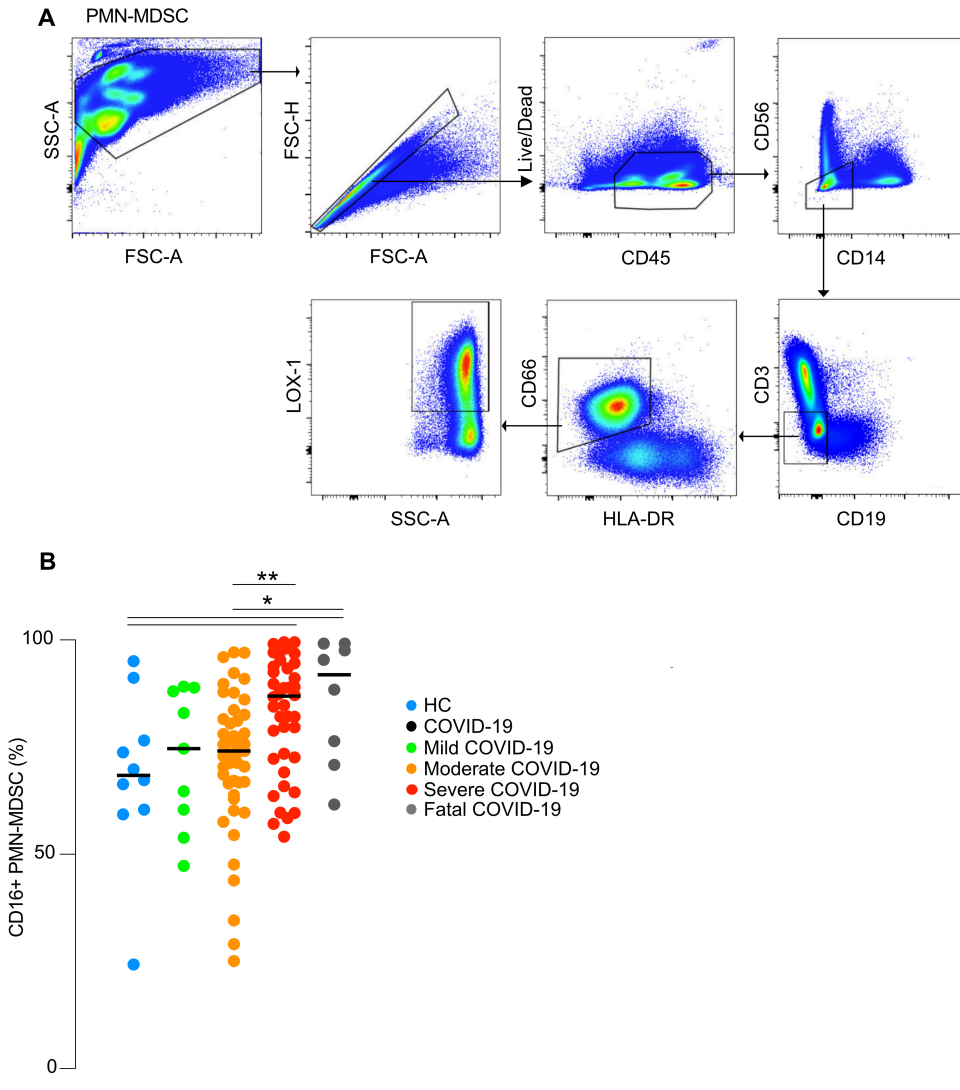


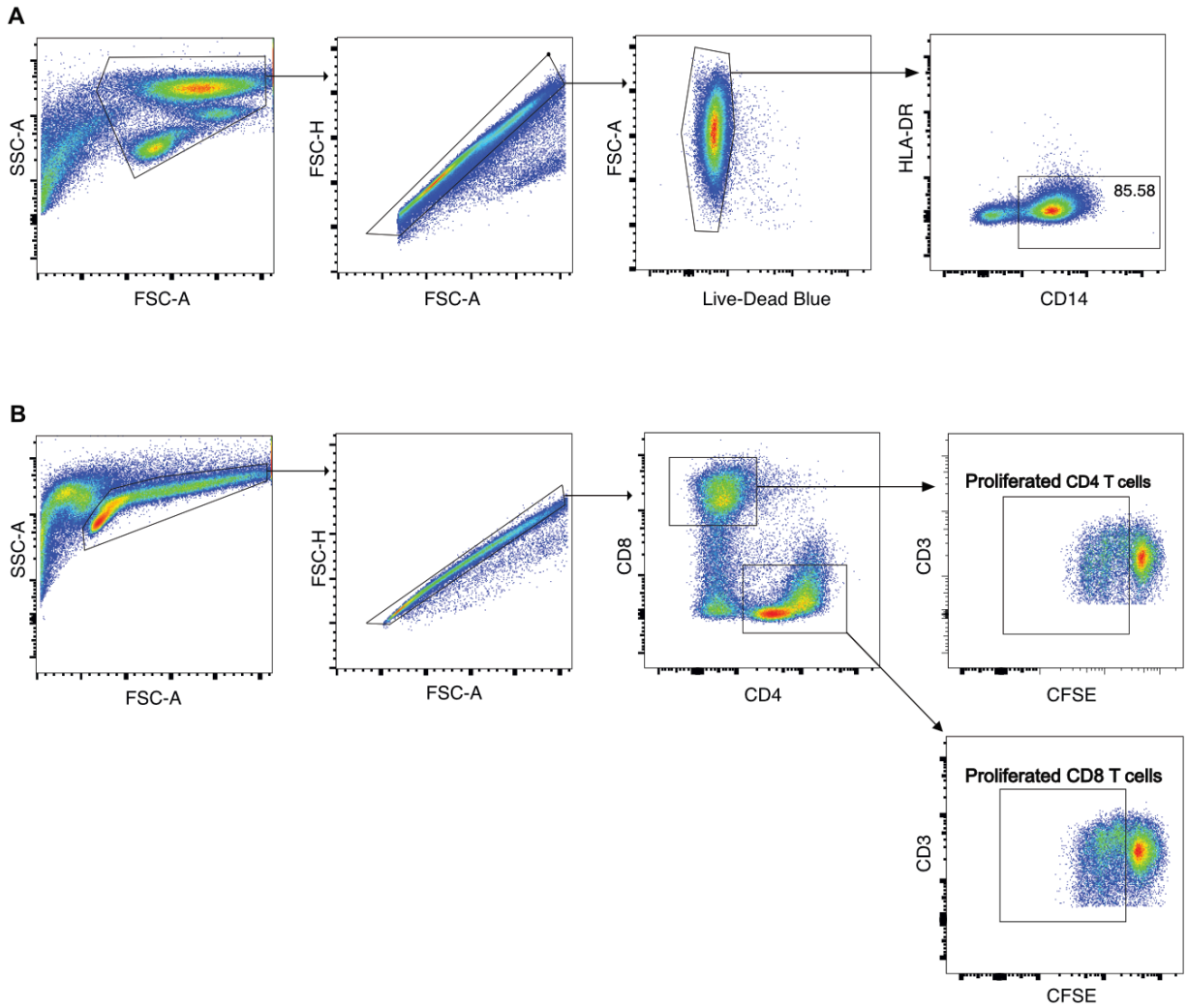
Supplementary figure 1. Patient characteristics over time. (A) Patient sampling overview. Schematic figure of timeline for each patient, including sampling timepoints, hospital admission/discharge, level of care and outcome. Patients are categorized based on peak disease severity. (B-D) Locally estimated scatterplot smoothing (LOESS) lines with shaded 95% confidence intervals of laboratory parameters in different disease severity groups over time, (B) CRP, n=144, (C) Lymphocytes, n=140, and (D) Neutrophil/lymphocyte ratio (NLR), n=140.



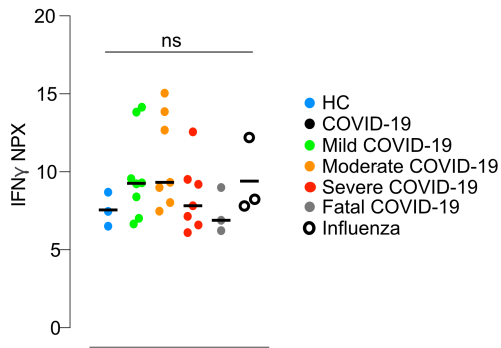
Supplementary figure 2. Representative MDSC gating strategy and cortisone treatment in the patient cohort. (A-B) Representative gating strategy to identify M-MDSCs by flow cytometry in nasopharyngeal aspirates (NPA) and endotracheal aspirates (ETA). Leukocytes were gated based on forward scatter (FSC) and side scatter (SSC). Live CD45+ cells were identified in NPA. In ETA, live cells were identified. Cells expressing lineage markers (CD3, CD19, CD20, CD56, and CD66abce) and HLA-DR were excluded. The lineage negative, HLA-DR negative cells were further gated to identify the CD14+ M-MDSCs. **(C)** Peak M-MDSC frequency in blood in patients with or without systemic cortisone treatment, divided by peak disease severity. No cortisone treatment: moderate (orange) n=49, severe (red) n=41 and fatal (grey) n=10. Cortisone treatment: moderate n=4, severe n=16 and fatal n=2. Comparison of medians between groups was performed using Kruskal-Wallis' test and subsequent post-hoc testing by Dunn's test of multiple comparisons.



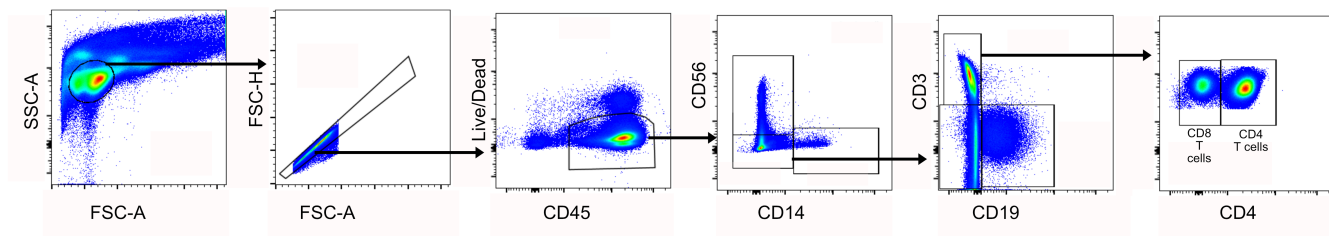
Supplementary figure 3. Representative PMN-MDSC gating strategy and CD16 expression. (A) Representative gating strategy to identify PMN-MDSCs by flow cytometry in PBMC. Live CD45⁺ cells were identified, and cells expressing CD56, CD14, CD3, CD19 were excluded. HLA-DR⁻ cells expressing CD66abce and LOX-1 were identified as PMN-MDSCs. (B) Frequency of CD16⁺ PMN-MDSCs of total PMN-MDSCs in blood from COVID-19 patients. HCs (blue) n=10. COVID-19 patients: mild (green) n=9, moderate (orange) n=47, severe (red) n=42 and fatal (grey) n=8. Comparison of medians between groups was performed using Kruskal-Wallis' test and subsequent post-hoc testing by Dunn's test of multiple comparisons.



Supplementary figure 4. Representative flow cytometry plots of M-MDSC isolation and T cell proliferation in vitro. (A) M-MDSCs were isolated from frozen PBMCs from COVID-19 patients and purity of isolated M-MDSCs from COVID-19 patient assessed. (B) CFSE labelled PBMCs were cultured with SEB for 3 days. Proliferation of T cells was assessed using CFSE.



Supplementary figure 5. IFN_γ levels in plasma. Level expressed in normalized protein expression (NPX). HCs (blue): n=3. Influenza patients (open circles): n=3. COVID-19 patients (color-coded by peak severity): mild (n=8), moderate (n=7), severe (n=7) and fatal (n=3). Comparison of medians between groups was performed using Kruskal-Wallis' test and subsequent post-hoc testing by Dunn's test of multiple comparisons.



Supplementary figure 6. Representative gating strategy for T cell frequencies. (A) Leukocytes were gated based on forward scatter (FSC) and side scatter (SSC). Single cells were identified by FSC-area (FSC-A) and FSC-height (FSC-H). CD14⁺ and CD56⁺ cells were excluded. CD3⁺ and CD19⁺ cells were identified. CD3⁺ cells were separated based on CD4 into CD4⁺ T cells and CD4-T cells (CD8⁺).

Supplementary table 1. Respiratory SOFA/mSOFA score.

Resp. SOFA Score	Definition
0	PFI >53 kPa or SFI > 400
1	PFI < 53 kPa or SFI ≤ 400
2	PFI < 40 kPa or SFI ≤ 315
3	PFI < 27 kPa or SFI ≤ 235 and mechanical ventilation*
4	PFI < 13 kPa or SFI < 150 and mechanical ventilation*

* Incl. non-invasive positive pressure ventilation.

SOFA=Sequential Organ Failure Assessment. mSOFA=modified SOFA.

PFI=PaO₂/FiO₂-index. SFI=SpO₂/FiO₂-index.

Supplementary table 2. Disease severity classification.

Severity score	Definition	
Mild	1	Peak resp. SOFA score 0, not admitted
	2	Peak resp. SOFA score 0, admitted
Moderate	3	Peak resp. SOFA score 1, admitted
	4	Peak resp. SOFA score 2, admitted
Severe	5	Peak resp. SOFA score 3, admitted
	6	Peak resp. SOFA score 4, admitted
Fatal	7	Fatal outcome

SOFA=Sequential Organ Failure Assessment