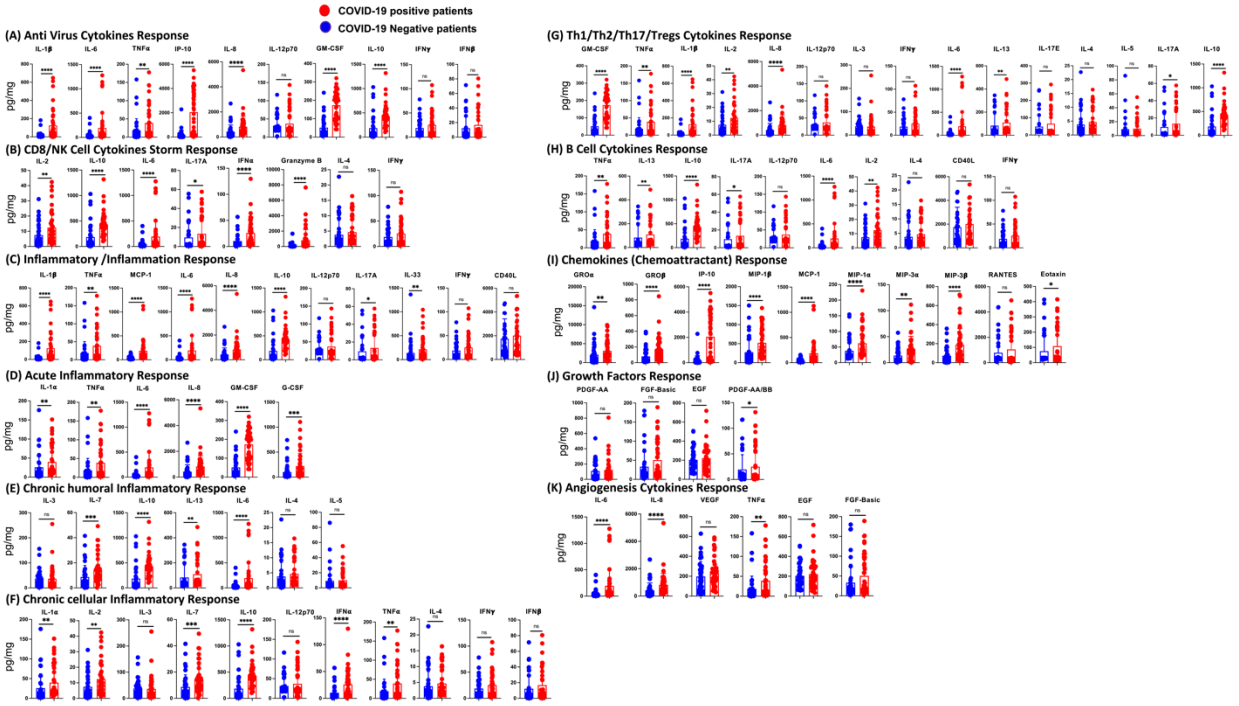
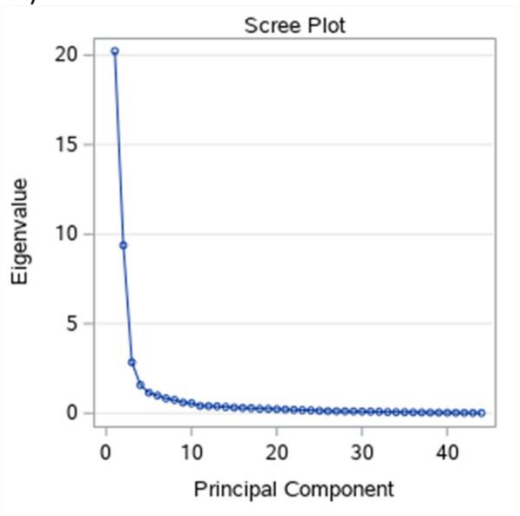
## Supplementary Figures

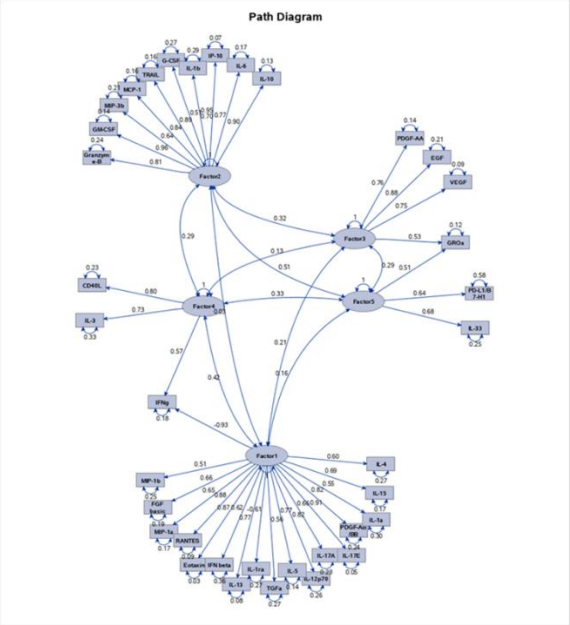



**Supplementary Figure S1:** The COVID-19 cytokine/chemokine storm in the nasopharyngeal microenvironment belongs to the responses, **(A)** Anti-virus cytokines, **(B)** CD8/NK cell cytokines storm, **(C)** Inflammatory /inflammation, **(D)** Acute inflammatory, **(E)** Chronic humoral inflammatory, **(F)** Chronic cellular inflammatory, **(G)** Th1/Th2/Th17/Tregs cytokines, **(H)** B cell cytokines, **(I)** Chemokines (Chemoattractant), **(J)** Growth factors, and **(K)** Angiogenesis cytokines. **(A-K)** Cytokine storm in nasal swabs of COVID-19 positive (N = 44) and negative (N = 40) patients was measured by a bead-based multiplex assay and analyzed by FLEXMAP 3D. Each dot represents an individual.

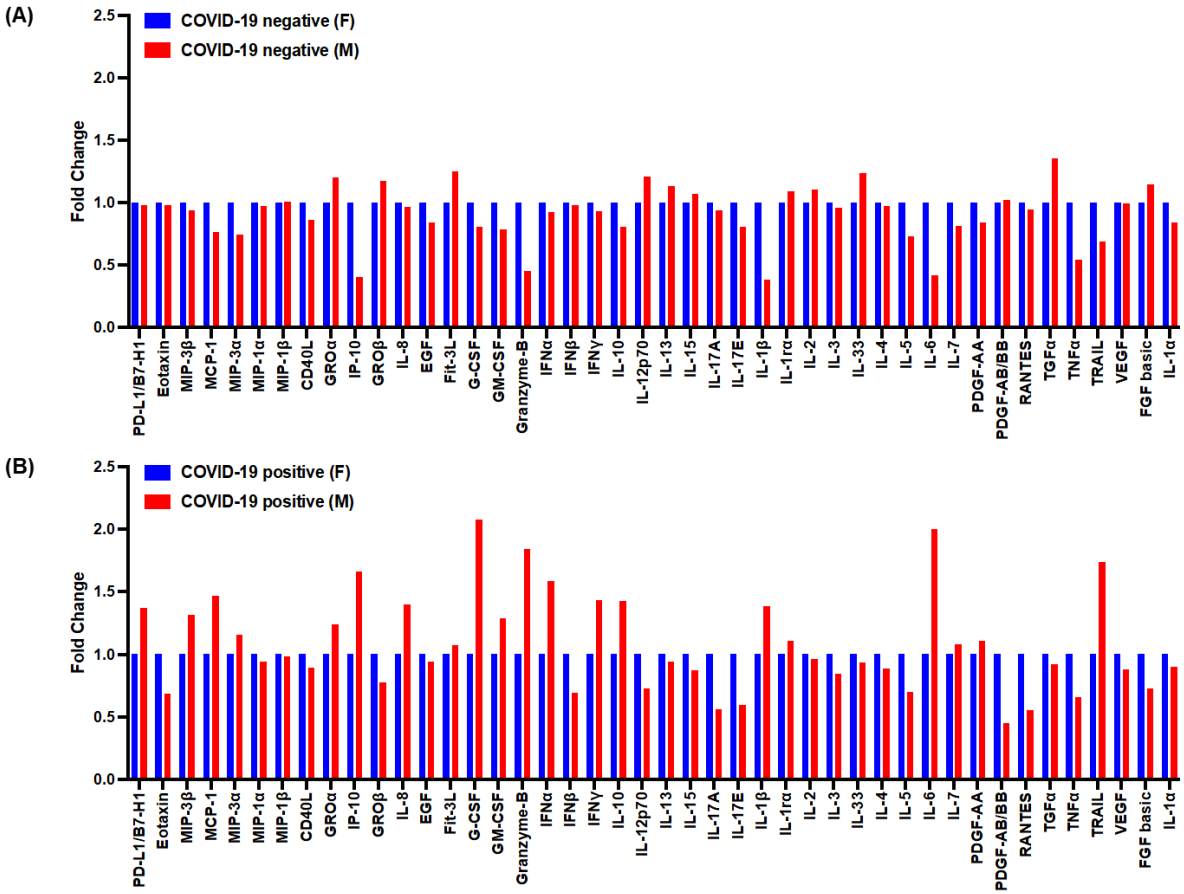
A)



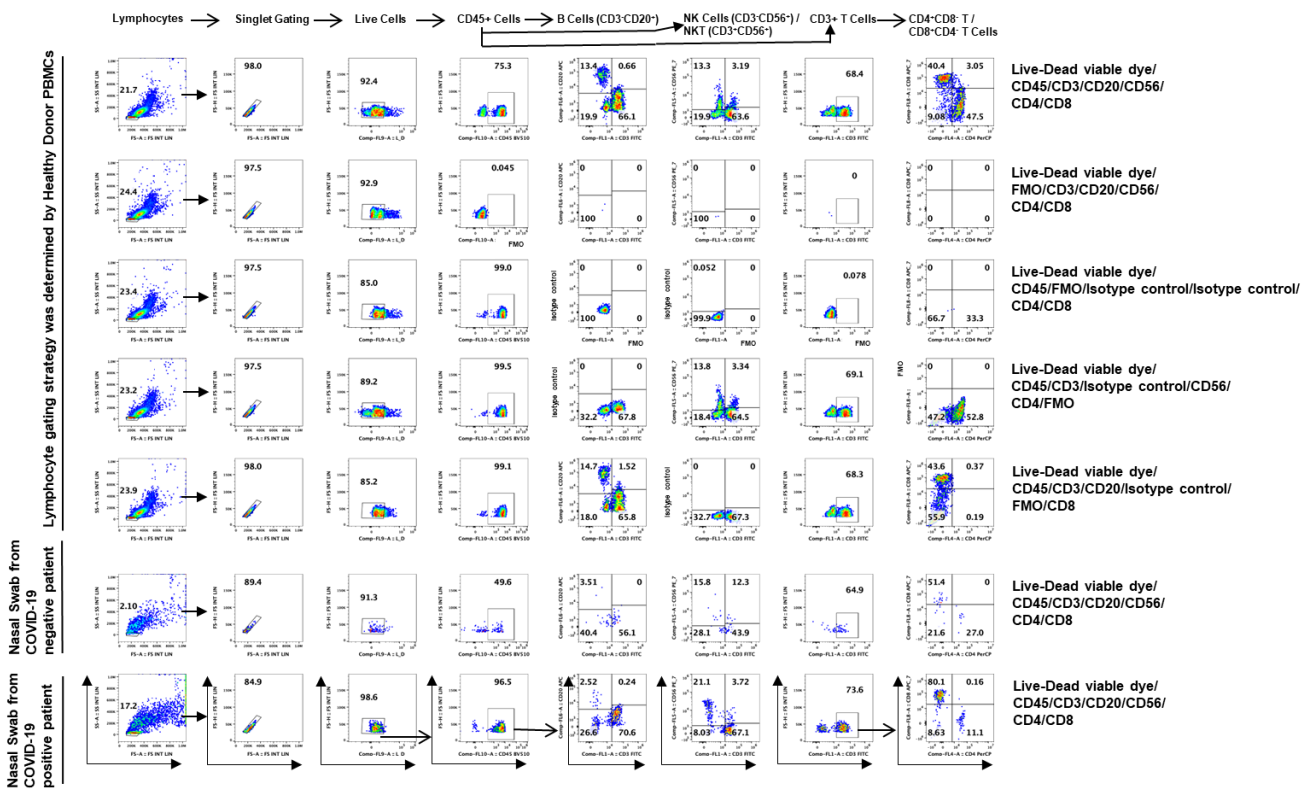

B)



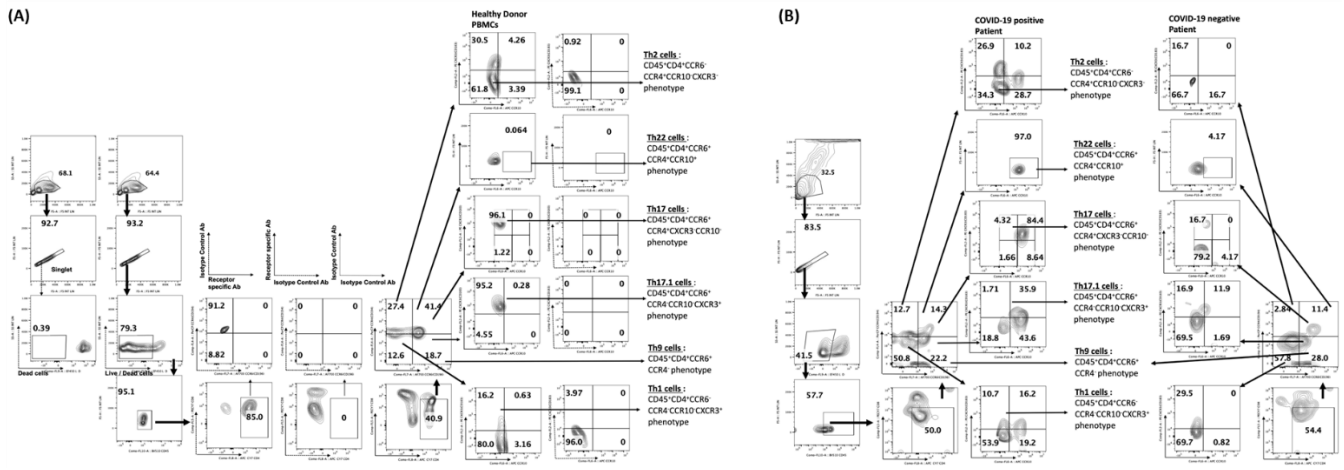

**Supplementary Figure S2:** Exploratory factor analysis. A) Principal component scree plot. Scree plot showed the eigenvalue for each principal component using 44 cytokine data. Eigenvalue>1 was used to select the optimal number of principal components, which resulted in five factors. B) Path diagram for factor analysis. Path diagram showed the quartimin-rotated factor solution and represented correlations among factors by double-headed links or paths and factor variance and error variances by double-headed links. Factors with lower explained variance have smaller magnitude loadings. The path diagram displayed only the links that have loading greater than 0.5 in magnitude.



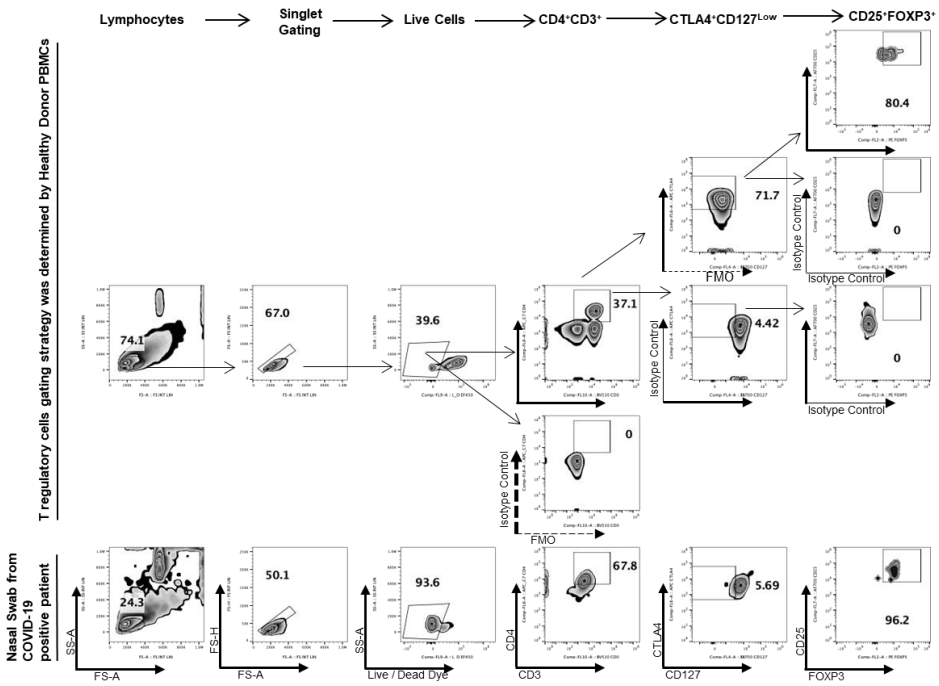

**Supplementary Figure S3:** The nasopharyngeal cytokines/chemokines storm is associated with male gender susceptibility to being infected by the SARS-CoV-2. The fold change of cytokines/chemokines in **(A)** COVID-19 negative male versus female and **(B)** COVID-19 positive male versus female.



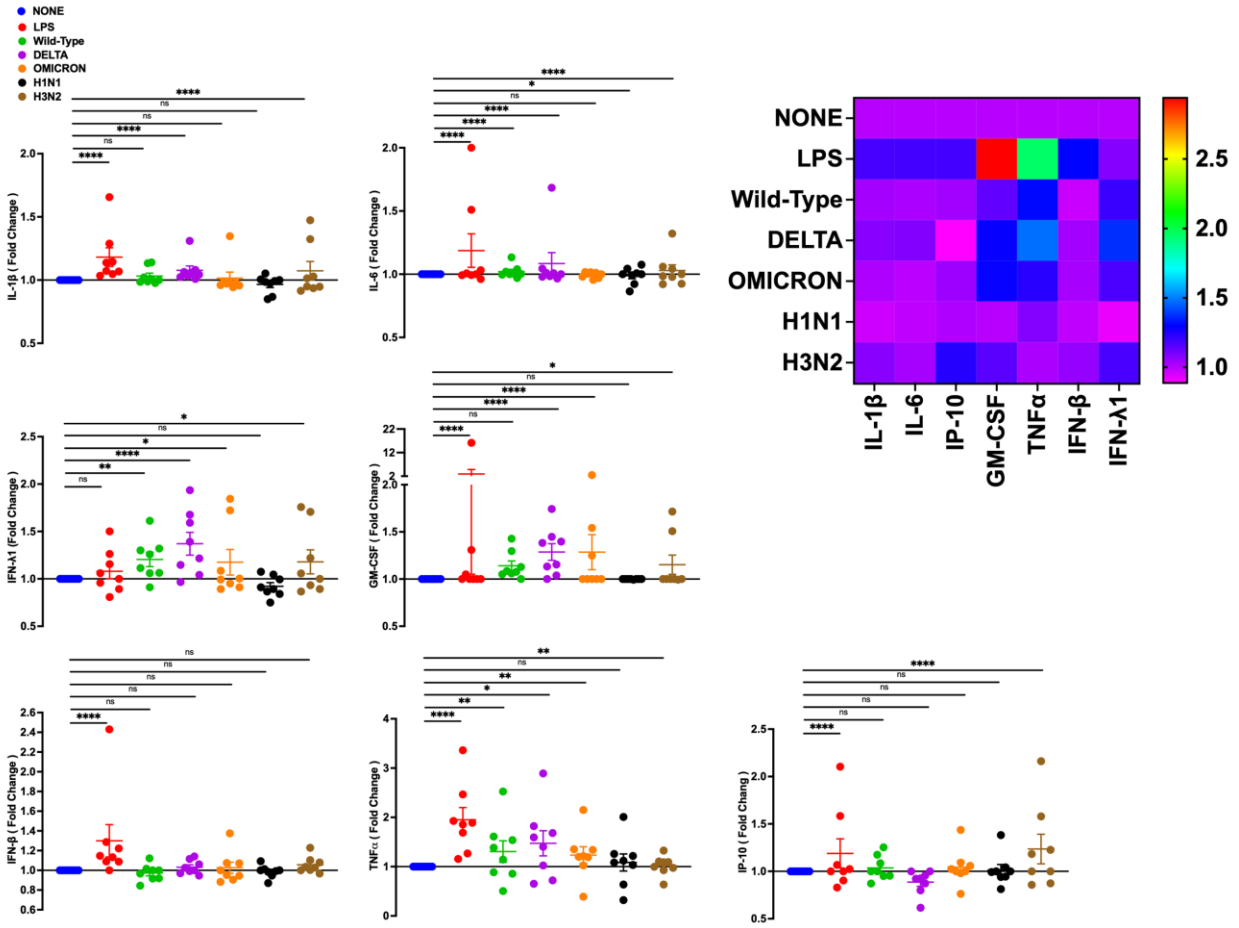

**Supplementary Figure S4.** A representative gating strategy illustrating the lymphocyte population being subgated to the level of $CD3^{-}CD20^{+}$ B cells, $CD3^{-}CD56^{+}$ (NK), $CD3^{+}CD56^{+}$ (NKT), $CD3^{+}$ T cells, $CD3^{+}CD4^{+}CD8^{-}$ T cells, and $CD3^{+}CD4^{-}CD8^{+}$ T cells.



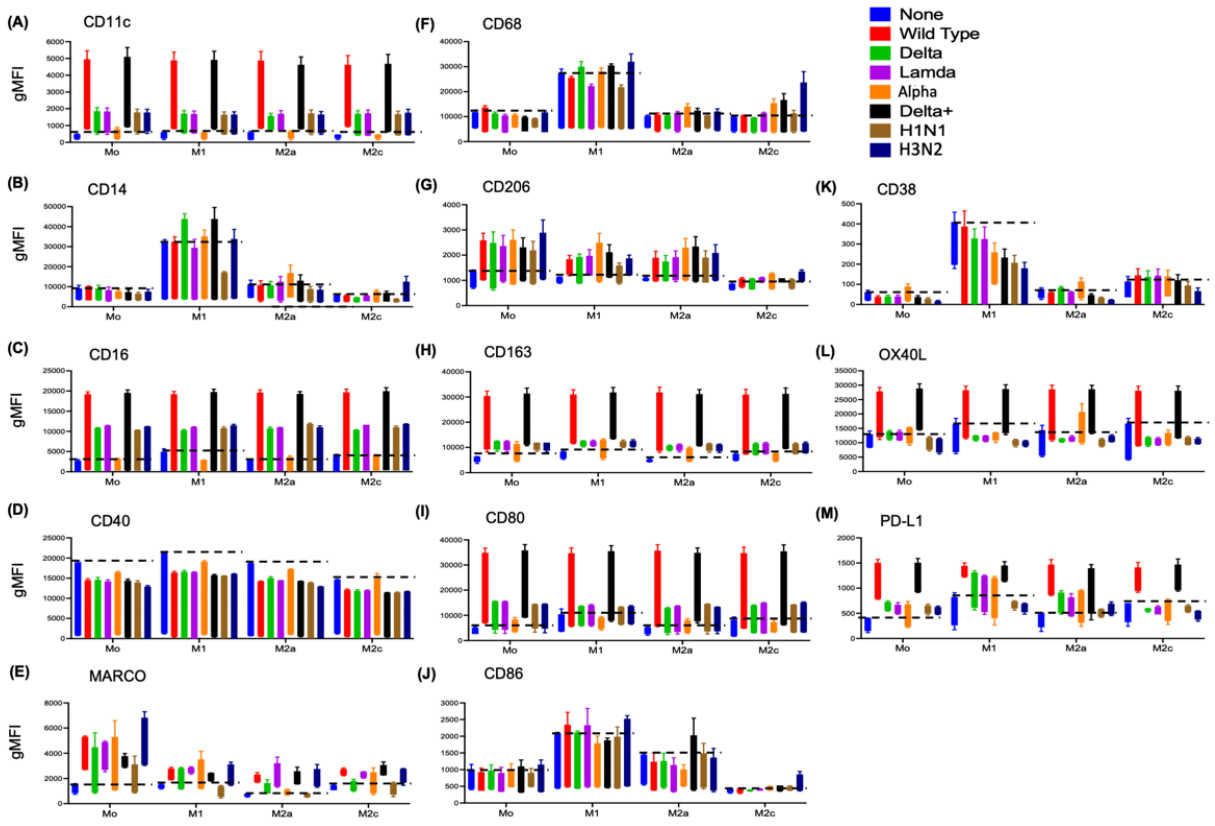

**Supplementary Figure S5.** Gating strategy for assessing the percentages of T cell subsets (Th2, Th22, Th17, Th17.1, Th9, and Th1) in nasopharyngeal swabs of COVID-19 positive and negative patients. (A) Healthy donor PBMCs were stained to determine the gating of T cell subsets and a similar gating strategy was used to determine T cell subsets in (B) nasopharyngeal swabs of COVID-19-positive and negative patients. The dotted arrow denotes staining with isotype control antibodies. The solid arrow shows staining with receptor-specific antibodies.



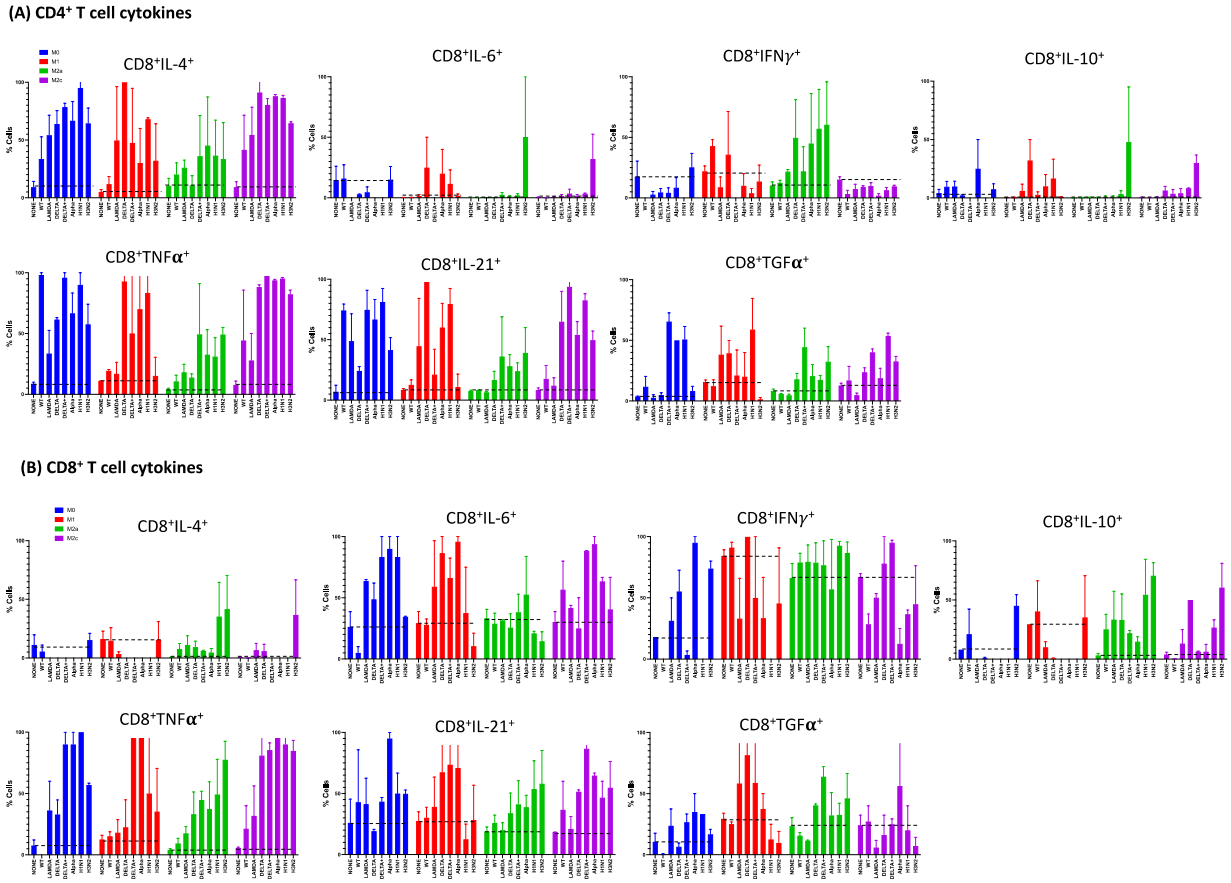

**Supplementary Figure S6.** A representative gating strategy illustrating the T regulatory cells (Tregs) lymphocyte subset being gated to the level of $CD3^{+}CD4^{+}CTLA4^{+}CD127^{LOW}CD25^{+}FOXP3^{+}$.



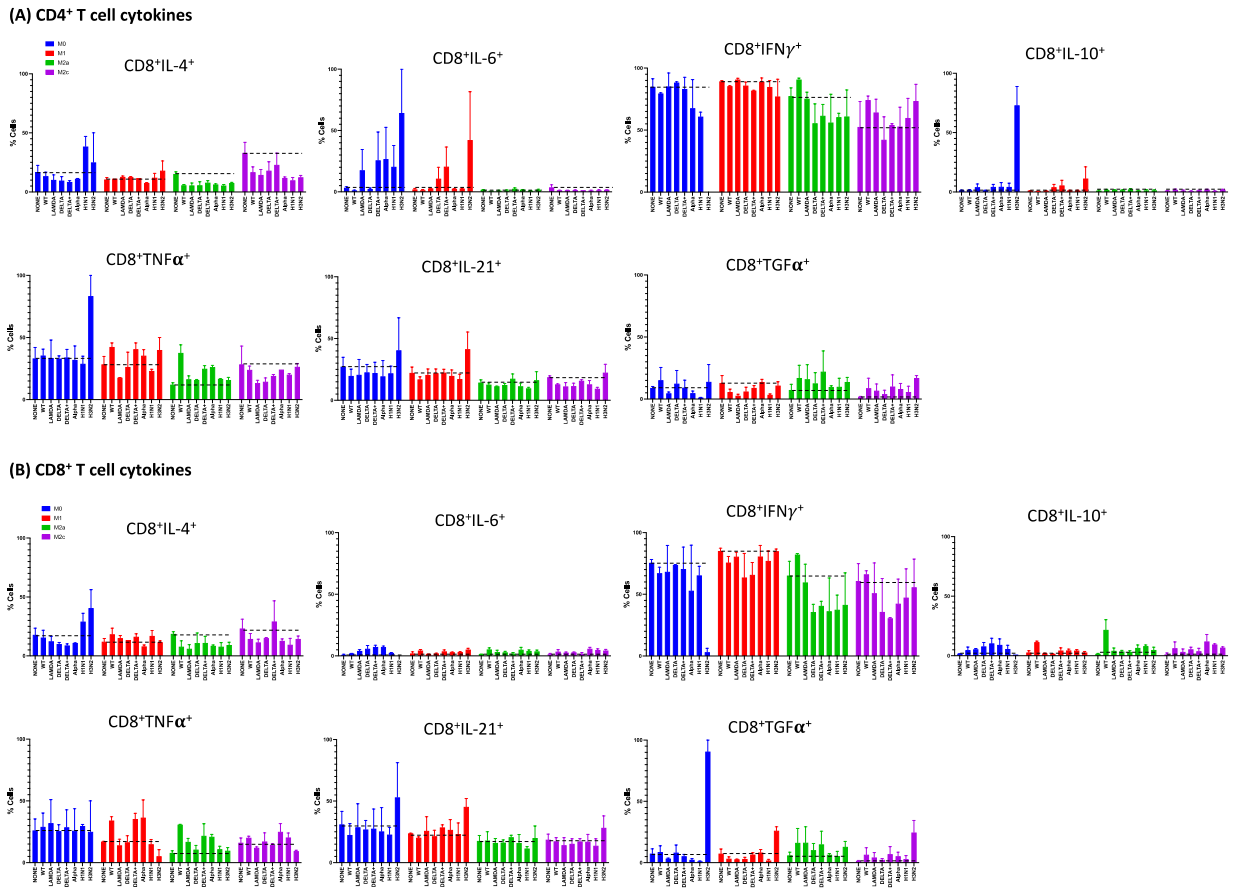

**Supplementary Figure S7.** Human PBMCs from healthy donors (n=8) cultured in the presence or absence of S protein of the SARS-CoV-2 wild-type strain, Delta- and Omicron-variants as well as H1N1 and H3N2 at 37ºC for 48 hr. The amount of cytokines secreted from PBMCs was assessed by the LEGENDplex Human Inflammation kit. Soluble analytes were quantified using flow cytometry and analyzed with BioLegend's LEGENDplex™ software. **(A)** The fold-change of cytokines normalized by none (unstimulated) and **(B)** the heatmap of the fold-change of cytokines. Data are expressed as mean ±SD. The *p* values were determined with unpaired Student t test. **p<0.05*, ***p<0.01* and *****p<0.0001*.



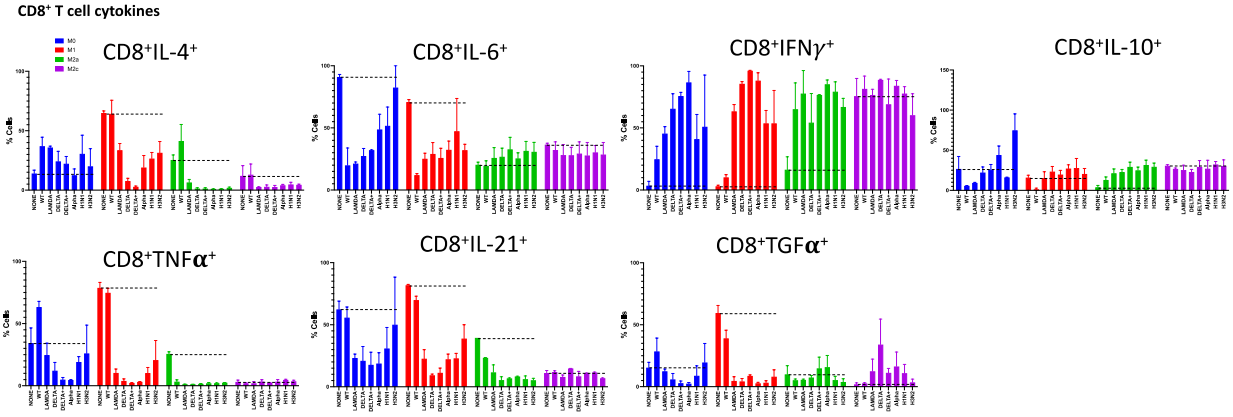

**Supplementary Figure S8.** Macrophage (Mϕ) subtypes in lymphocyte dysregulation during SARS-CoV-2 infection. Human monocyte-derived Mϕ (hMDMϕ) from PBMCs of 8 individual donors were polarized into M1, M2a, or M2c phenotype for 48 hrs. Unpolarized hMDMϕ was used as a control and considered M0. Macrophage subtypes stimulated in the presence or absence of SARS-CoV-2 spike (S) protein from the wild type of strain as well as Delta-, Lamda-, Alpha-, and Delta+-variants or positive controls such as hemagglutinin/HA antigen protein from H1N1 and H3N2 influenza A for 48 hrs. The expression of macrophage activation markers was assessed by flow cytometry. Data are shown in geometric mean fluorescence intensity (gMFI) belong to 8 individual donors' Mϕ.



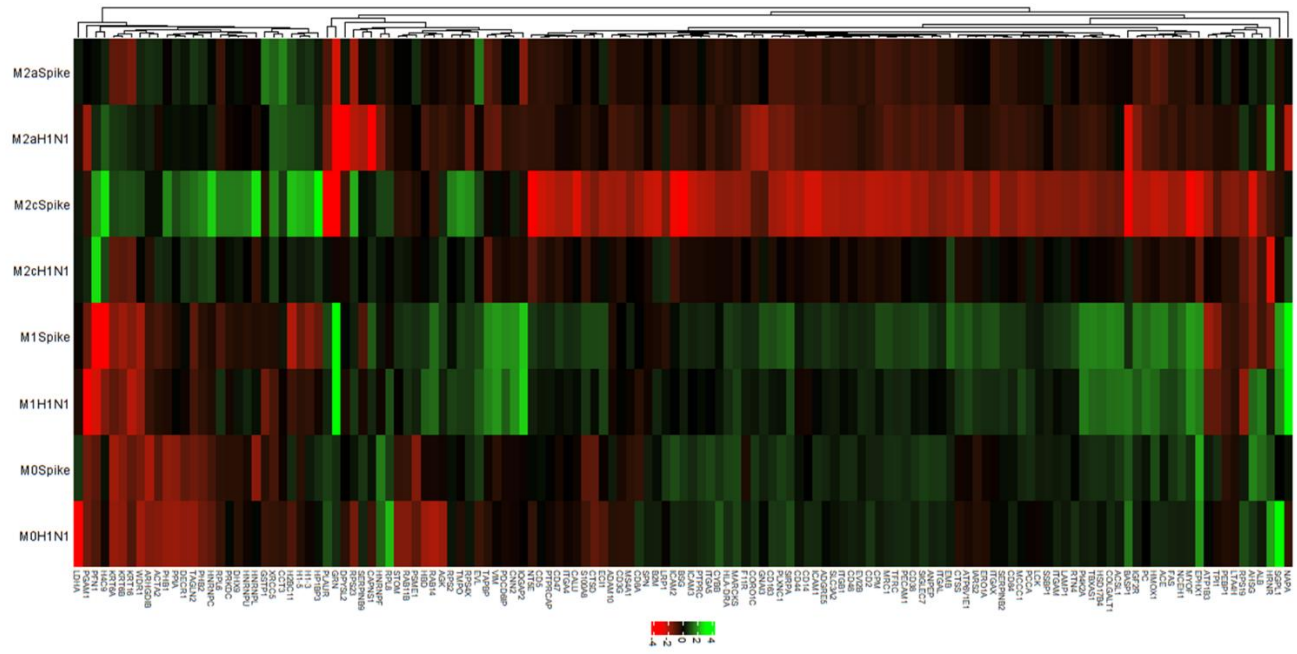

**Supplementary Figure S9.** Macrophage subtypes of SARS-CoV-2 infection affect T-cell cytokines responses. Human monocyte-derived Mϕ (hMDMϕ) from PBMCs of 8 individual donors were polarized into M1, M2a, or M2c phenotype for 48 hrs. Unpolarized hMDMϕ was used as a control and considered M0. Macrophage subtypes stimulated in the presence or absence of SARS-CoV-2 spike (S) protein from the wild type strain as well as Delta-, Lamda-, Alpha-, and Delta+-variants or positive controls such as hemagglutinin/HA antigen protein from H1N1 and H3N2 influenza A for 48 hrs followed by autologous human PBMCs co-culture. **(A)** CD4+ and **(B)** CD8+ T cell cytokines were assessed by flow cytometry. Each bar represents percent frequency of cells that belong to 8 individual donors' Mϕ co-cultured with PBMCs.



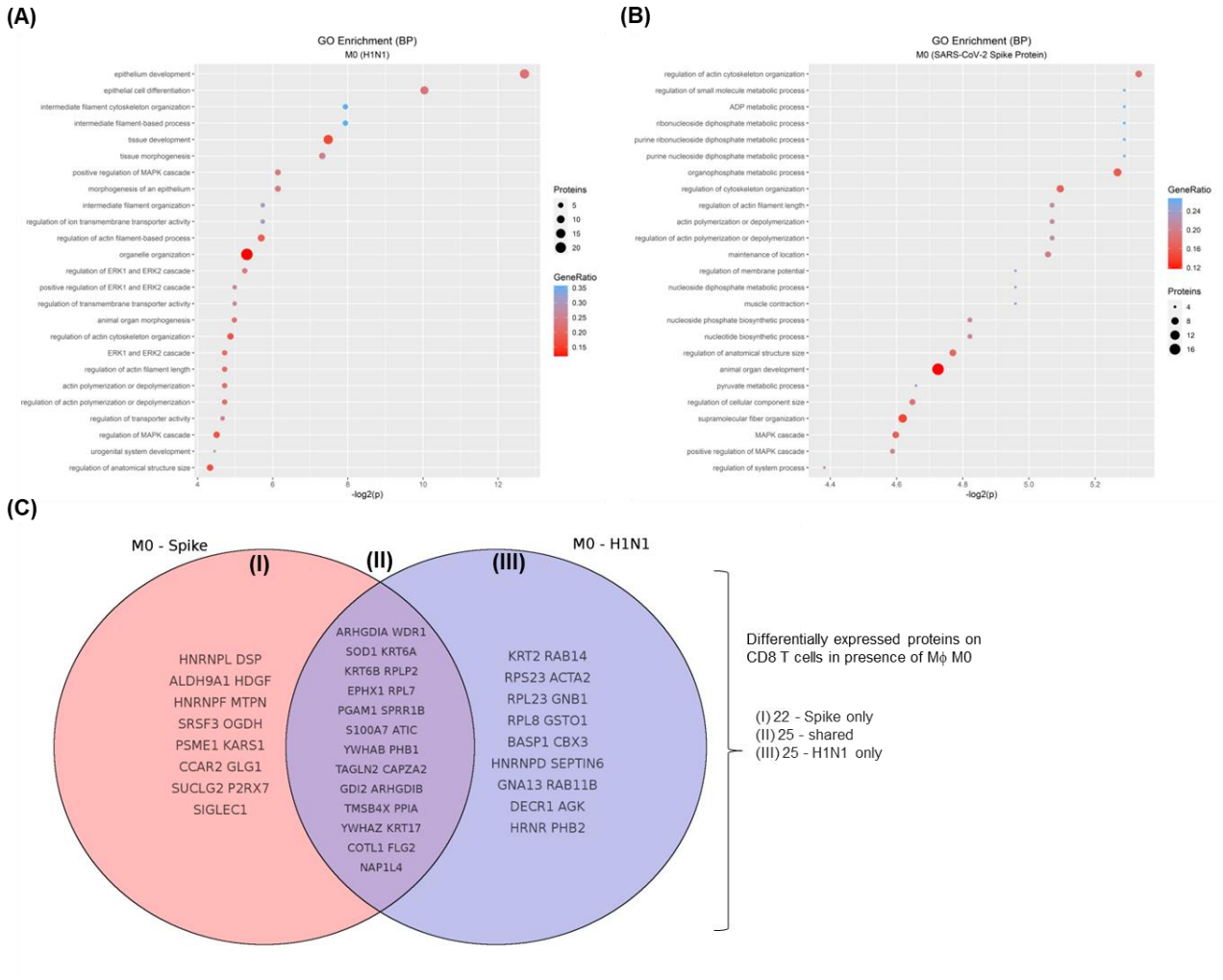

**Supplementary Figure S10.** Macrophage subtypes of SARS-CoV-2 infection affect T-cell cytokines responses. Human monocyte-derived Mϕ (hMDMϕ) PBMCs of 8 individual donors were polarized into M1, M2a, or M2c phenotype for 48 hrs. Unpolarized hMDMϕ was used as a control and considered M0. Macrophage subtypes stimulated in the presence or absence of SARS-CoV-2 spike (S) protein from the wild type strain as well as Delta-, Lamda-, Alpha-, and Delta+-variants or positive controls such as hemagglutinin/HA antigen protein from H1N1 and H3N2 influenza A for 48 hrs followed by co-culture of enriched autologousT cells from human PBMCs. **(A)** $CD4^+$ and **(B)** $CD8^+$ T cell cytokines were assessed by flow cytometry. Each bar represents percent frequency of cells that belong to 8 individual donors' Mϕ co-cultured with PBMCs.



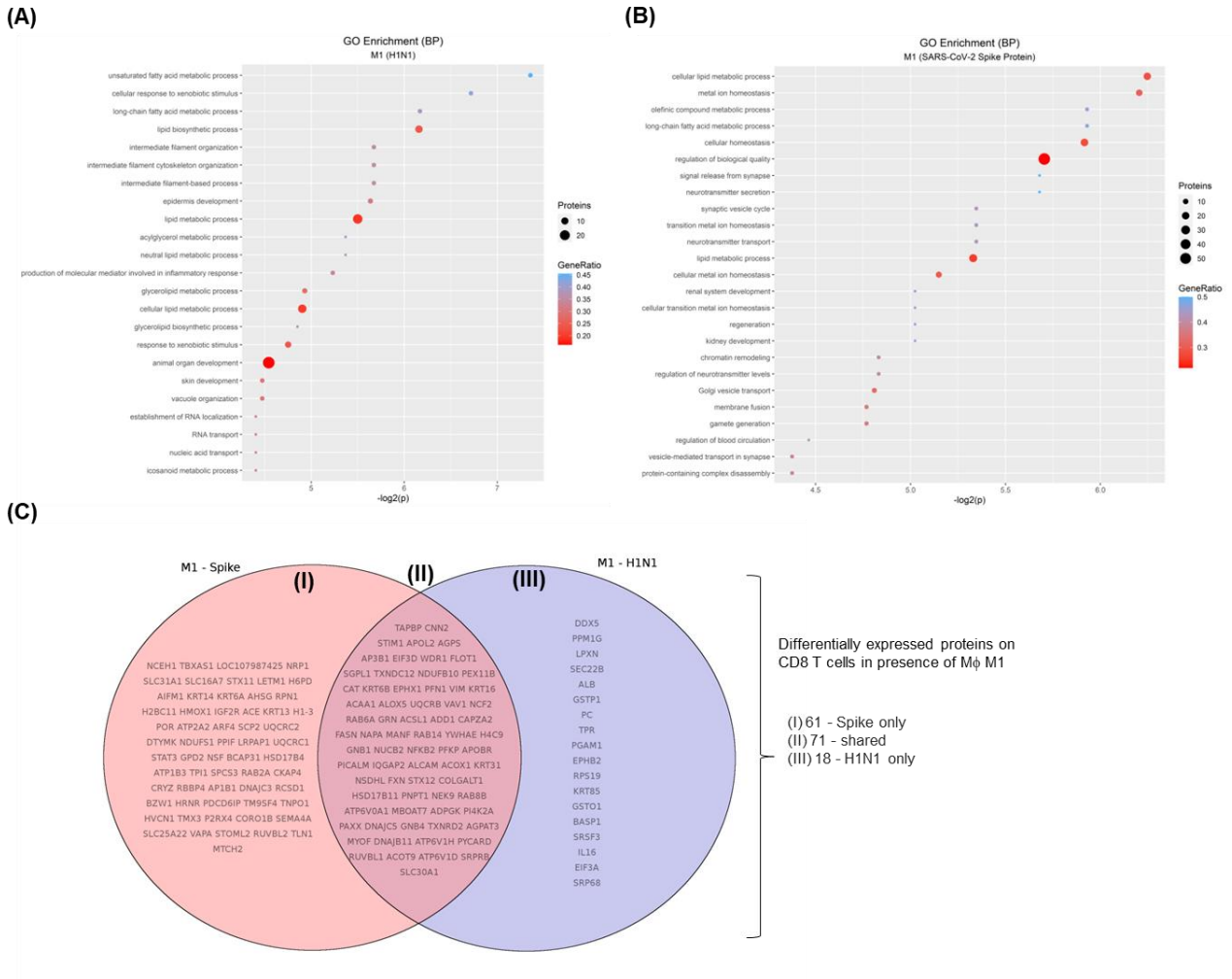

**Supplementary Figure S11.** Macrophage subtypes of SARS-CoV-2 infection affect T-cell cytokines responses. Human monocyte-derived Mϕ (hMDMϕ) were polarized into M1, M2a, or M2c phenotype for 48 hrs. Unpolarized hMDMϕ was used as a control and considered M0. Macrophage subtypes stimulated in the presence or absence of SARS-CoV-2 spike (S) protein from the wild type strain as well as Delta-, Lamda-, Alpha-, and Delta+-variants or positive controls such as hemagglutinin/HA antigen protein from H1N1 and H3N2 influenza A for 48 hrs followed by co-culture of enriched autologous CD8 T cells from human PBMCs. $CD8^+$ T cell cytokines were assessed by flow cytometry. Each bar represents percent frequency of cells that belong to 8 individual donors' Mϕ co-cultured with PBMCs.



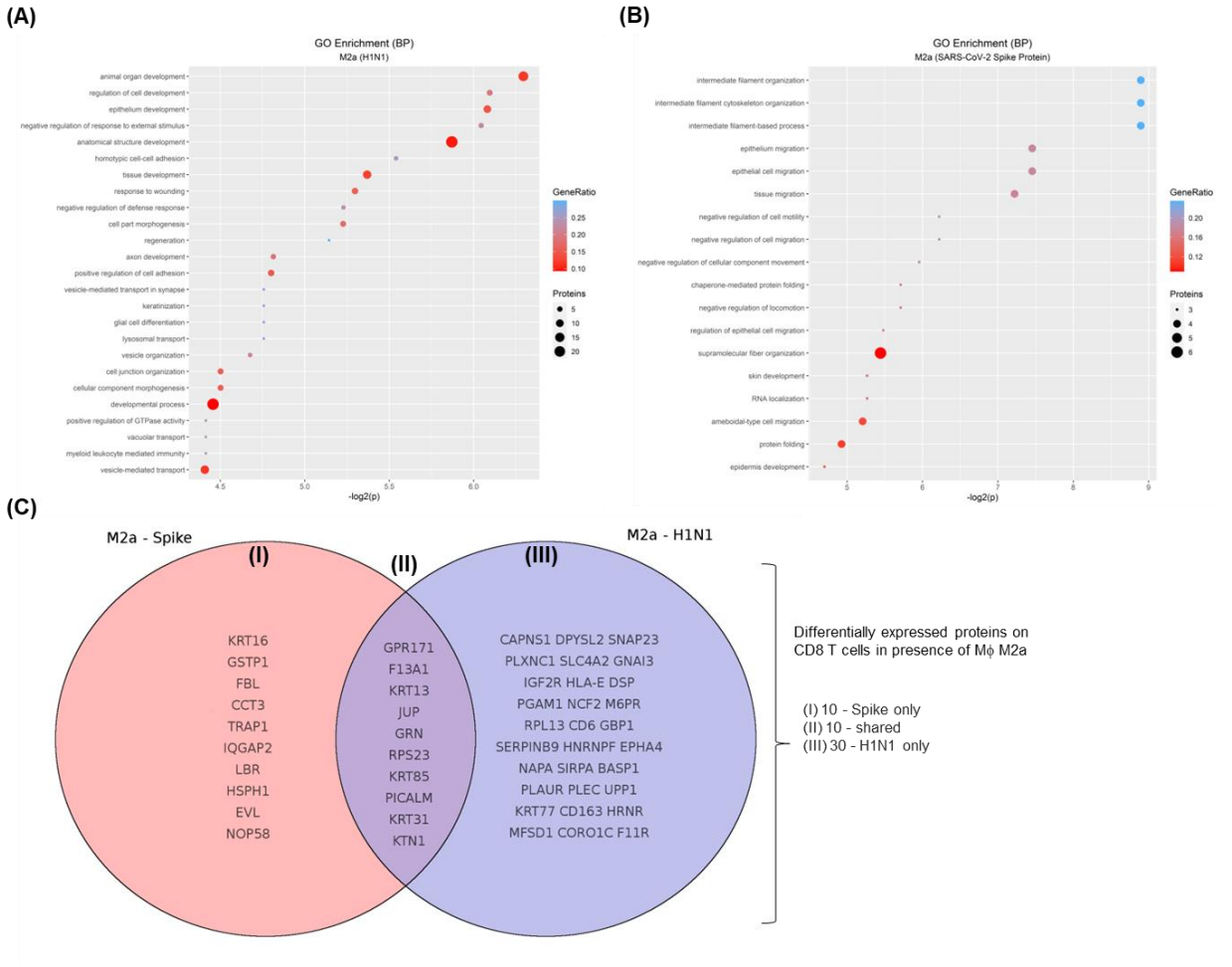

**Supplementary Figure S12.** Macrophage subtypes modulate immune-related protein interaction networks in CD8 T lymphocytes during SARS-CoV-2 infection. Heatmap of the differentially up- and down-regulated proteins in CD8 T cells cocultured with macrophage subsets stimulated in the presence of SARS-CoV-2 S protein or HA protein of H1N1. Color range illustrates the log2 fold change between the stimulated and unstimulated macrophages.



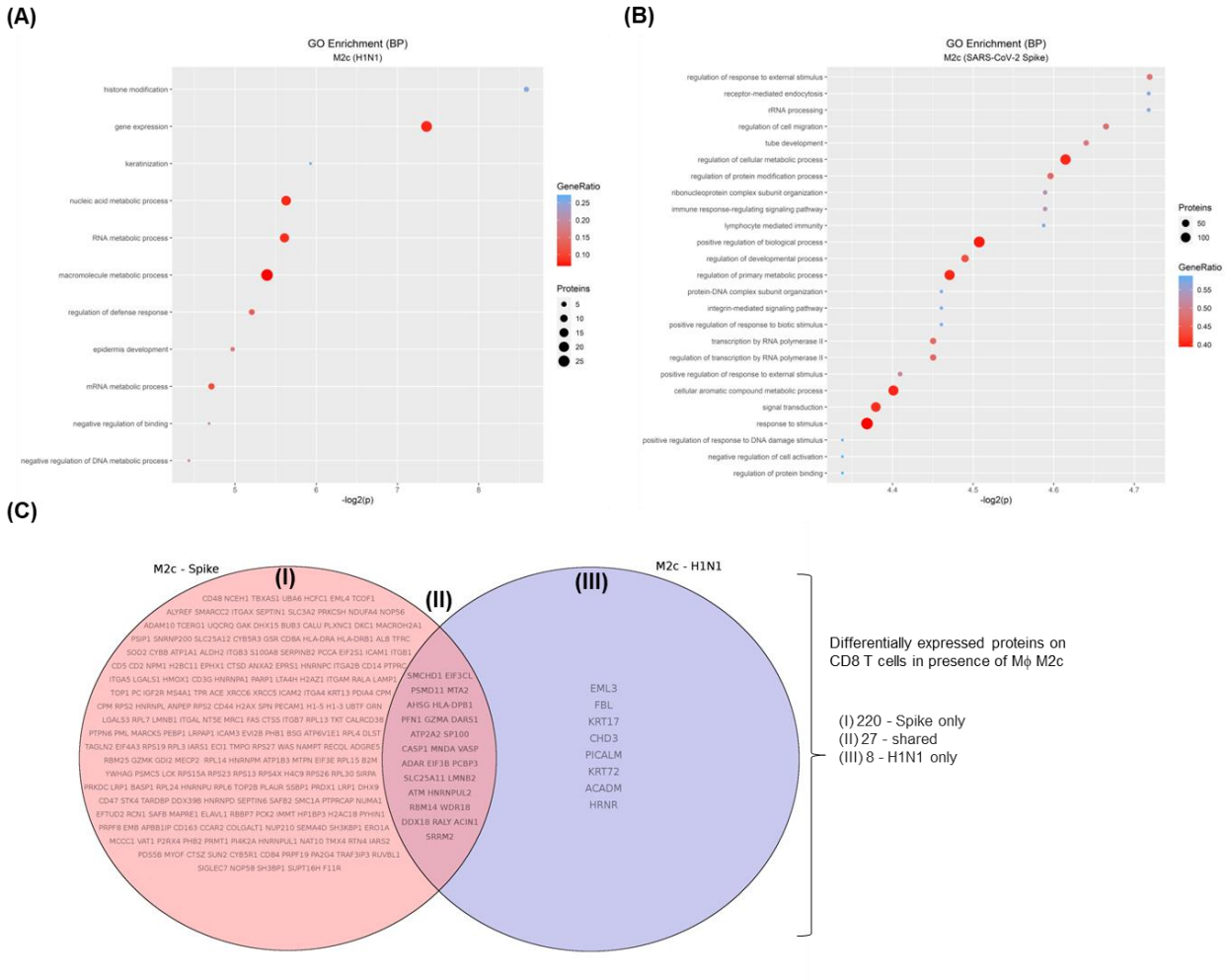

**Supplementary Figure S13.** Proteomics alterations-associated GO terms in CD8 T lymphocytes during SARS-CoV-2 infection identified using the TopGO package in R. CD8 T cells cocultured with macrophage subset, M0, stimulated in the presence of SARS-CoV-2 S protein or HA protein of H1N1. CD8 T cells in presence of stimulated M0 with **(A)** H1N1 shows the top 25 ontology terms- and **(B)** S protein shows the top 25 ontology terms significantly enriched with differentially expressed proteins using Gene Ontology (GO) biological process (BP) Enrichment. GO-based enrichment analysis of DEPs is arranged in terms of p-values of biological process ontologies (Fisher's exact test; $p < 0.05$). **(C)** Comprehensive comparative protein analysis of CD8 T cells from in vitro cocultured with S protein stimulated Mϕ M0 and with hemagglutinin/HA antigen protein from H1N1 stimulated Mϕ M0. Venn diagram shows the shared proteins among differentially expressed proteins.




**Supplementary Figure S14.** Proteomics alterations-associated GO terms in CD8 T lymphocytes during SARS-CoV-2 infection identified using the TopGO package in R. CD8 T cells cocultured with macrophage subset, M1, stimulated in the presence of SARS-CoV-2 S protein or HA protein of H1N1. CD8 T cells in presence of stimulated M1 with **(A)** H1N1 shows the top 23 ontology terms- and **(B)** S protein shows the top 25 ontology terms significantly enriched with differentially expressed proteins using Gene Ontology (GO) biological process (BP) Enrichment. GO-based enrichment analysis of DEPs is arranged in terms of p-values of biological process ontologies (Fisher's exact test; $p < 0.05$). **(C)** Comprehensive comparative protein analysis of CD8 T cells from in vitro cocultured with S protein stimulated Mϕ M1 and with hemagglutinin/HA antigen protein from H1N1 stimulated Mϕ M1. Venn diagram shows the shared proteins among differentially expressed proteins.




**Supplementary Figure S15.** Proteomics alterations-associated GO terms in CD8 T lymphocytes during SARS-CoV-2 infection identified using the TopGO package in R. CD8 T cells cocultured with macrophage subset, M2a, stimulated in the presence of SARS-CoV-2 S protein or HA protein of H1N1. CD8 T cells in presence of stimulated M2a with **(A)** H1N1 shows the top 23 ontology terms- and **(B)** S protein shows the top 18 ontology terms significantly enriched with differentially expressed proteins using Gene Ontology (GO) biological process (BP) Enrichment. GO-based enrichment analysis of DEPs is arranged in terms of p-values of biological process ontologies (Fisher's exact test; $p < 0.05$). **(C)** Comprehensive comparative protein analysis of CD8 T cells from in vitro cocultured with S protein stimulated Mϕ M2a and with hemagglutinin/HA antigen protein from H1N1 stimulated Mϕ M2a. Venn diagram shows the shared proteins among differentially expressed proteins.




**Supplementary Figure S16.** Proteomics alterations-associated GO terms in CD8 T lymphocytes during SARS-CoV-2 infection identified using the TopGO package in R. CD8 T cells cocultured with macrophage subset, M2c, stimulated in the presence of SARS-CoV-2 S protein or HA protein of H1N1. CD8 T cells in presence of stimulated M2c with **(A)** H1N1 shows the top 11 ontology terms- and **(B)** S protein shows the top 25 ontology terms significantly enriched with differentially expressed proteins using Gene Ontology (GO) biological process (BP) Enrichment. GO-based enrichment analysis of DEPs is arranged in terms of p-values of biological process ontologies (Fisher's exact test; $p < 0.05$). **(C)** Comprehensive comparative protein analysis of CD8 T cells from in vitro cocultured with S protein stimulated Mϕ M2c and with hemagglutinin/HA antigen protein from H1N1 stimulated Mϕ M2c. Venn diagram shows the shared proteins among differentially expressed proteins.