Supplemental Figure 1. Identification of immune cell subsets.
A) UMAP plot of all cells from all patients. B) Heatmap of genes differentially expressed by blood cells (downsampled). C) UMAP plots identify T cells (CD3G), NK cells (TYROBP, FCGR3A), B cells (MS4A1), plasma cells (JCHAIN), proliferating lymphocytes (MKI67 and CD3G or FCGR3A), monocytes (CD14 or FCGR3A), cDCs (CD1C), pDCs (SERPINF1), platelets (PF4) and erythrocytes (HBA2). Erythrocytes and platelets were excluded from further analysis.
Supplemental Figure 2. Identification of NK cell subsets.
A) UMAP of NK cells from all patients. B) Heatmap of genes differentially expressed by NK cell subsets (downsampled). C) NK cell clusters were identified as immature (KLRC1), mature (FCGR3A, PRF1) and memory (FCGR3A, KLRC2) cells. D) Proportions of NK cell subsets in mild, severe and recovering patients. E-F) Mean module scores for individual patients.
Supplemental Figure 3

A) UMAP of CD8 T cells from all patients. B) Heatmap of genes differentially expressed by CD8 T cell subsets (downsampled). C) CD8 T cell clusters were identified as naïve (CCR7, TCF7, LEF1), cytotoxic (GZMB, PRF1) and memory (GZMK) cells. D) Proportions of CD8 T cell subsets in mild, severe and recovering patients. E-G) Mean module scores for individual patients.

Supplemental Figure 3. Identification of CD8 T cell subsets.
A) UMAP of CD8 T cells from all patients. B) Heatmap of genes differentially expressed by CD8 T cell subsets (downsampled). C) CD8 T cell clusters were identified as naïve (CCR7, TCF7, LEF1), cytotoxic (GZMB, PRF1) and memory (GZMK) cells. D) Proportions of CD8 T cell subsets in mild, severe and recovering patients. E-G) Mean module scores for individual patients.
Supplemental Figure 4

A) UMAP of CD4 T cells from all patients. B) Heatmap of genes differentially expressed by CD4 T cell subsets (downsampled). C) CD4 T cell clusters were identified as naïve (CCR7, LEF1), central memory (CCR7, CD69), effector memory (ANXA1, PRDM1) cells and regulatory T cells (Tregs). D) Proportions of CD4 T cells subsets in mild, severe and recovering patients. E-F) Mean module scores for individual patients.

Supplemental Figure 4. Identification of CD4 T cell subsets.

A) UMAP of CD4 T cells from all patients. B) Heatmap of genes differentially expressed by CD4 T cell subsets (downsampled). C) CD4 T cell clusters were identified as naïve (CCR7, LEF1), central memory (CCR7, CD69), effector memory (ANXA1, PRDM1) cells and regulatory T cells (Tregs). D) Proportions of CD4 T cells subsets in mild, severe and recovering patients. E-F) Mean module scores for individual patients.
Supplemental Figure 5

A) UMAP of B and plasma cells from all patients. B) Heatmap of genes differentially expressed by B and plasma cell subsets (downsampled). C) B and plasma cell clusters were identified as immature B cells (IL7R), naïve B cells (IGHM, IGHD, IL4R, TCL1A), activated B cells (CD69), plasma cells (CD27, CD38, XBP1, JCHAIN) and memory B cells (AIM2). D) Proportions of B and plasma cells subsets in mild, severe and recovering patients. E-F) Mean module scores for individual patients.

Supplemental Figure 5. Identification of B and plasma cell subsets.
A) UMAP of B and plasma cells from all patients. B) Heatmap of genes differentially expressed by B and plasma cell subsets (downsampled). C) B and plasma cell clusters were identified as immature B cells (IL7R), naïve B cells (IGHM, IGHD, IL4R, TCL1A), activated B cells (CD69), plasma cells (CD27, CD38, XBP1, JCHAIN) and memory B cells (AIM2). D) Proportions of B and plasma cells subsets in mild, severe and recovering patients. E-F) Mean module scores for individual patients.
Supplemental Figure 6. B cell receptor signaling is enriched in the recovering group.

IPA canonical pathway analysis of genes significantly upregulated in B cells from recovering vs mild and severe COVID-19 patients. Analysis of the 539 DEGs upregulated (red) only in the recovering group shows increased signaling through the B cell receptor compared to mild and severe groups.
Supplemental Figure 7. IL-3 signaling in B cells is enriched in recovering groups.

IPA canonical pathway analysis of genes significantly upregulated in B cells from recovering vs mild and severe COVID-19 patients. Analysis of the 539 DEGs upregulated (red) only in the recovering group shows increased IL-3 signaling in recovering compared to mild and severe groups.
Supplemental Figure 8. PI3K signaling in B cells is enriched in the recovering group. IPA canonical pathway analysis of genes significantly upregulated in B cells from recovering vs mild and severe COVID-19 patients. Analysis of the 539 DEGs upregulated (red) only in the recovering group shows increased activation of CD79 signaling compared to mild and severe groups.
Supplemental Figure 9

Supplemental Figure 9. Increased B cell receptor signaling is the recovery group is regulated by SYK.

IPA causal pathway analysis demonstrates that SYK is the primary upstream mediator of the upregulated pathways in B cells from recovering vs mild and severe groups.
Supplemental Figure 10. Identification of monocyte and DC subsets.
A) UMAP of monocytes and DCs from all patients. B) Heatmap of genes differentially expressed by monocytes and DC subsets (downsampled). C) Monocyte and DC clusters were identified as classical monocytes (CD14), non-classical monocytes (FCGR3A), cDCs (HLA-DRB1, CD74) and pDCs (PLD4, LILRA4) cells. D) cDCs are predominantly DC2 cells (CD1C, FCER1A, CLEC10 with little/no monocyte gene expression). E) Proportions of monocyte and DC subsets in mild, severe and recovering patients. F-H) Mean module scores for individual patients.
Supplemental Figure 11. The eIF2 signaling pathway is differentially expressed in immune cells from COVID-19 patients.

Gene product interaction network analysis of the eIF2 pathway, which is down-regulated in lymphocytes, but not myeloid cells, in the severe vs mild group.