Immune responses in mild and severe COVID-19

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Methods

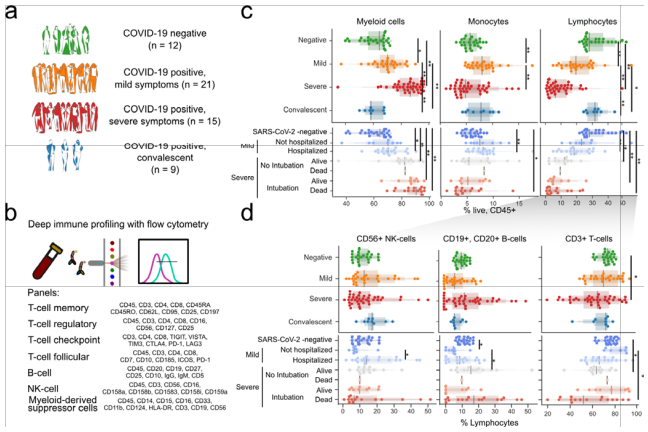
We conducted an observational of 45 COVID-19 patients treated at Weill Cornell Medicine (IRB 20-03021645) between April and July 2020. The disease was categorized as "mild" if the patient was not admitted or required <6 L non-invasive supplemental oxygen to maintain SpO2 >92% (n = 21). Patients with "severe" disease required hospitalization and received >6 L /high flow supplemental oxygen or mechanical ventilation (n = 15). Samples were also collected from non-hospitalized individuals who had recovered from mild COVID-19 ("convalescent" group, n = 9) and from healthy COVID-19 negative donors (n = 12) Longitudinal sampling at enrollment and every 7 days thereafter was performed in eight patients, making a complete dataset including 102 samples from 57 individuals.

We performed high-dimensional immune cell profiling of circulating blood by flow cytometry based on seven independent fluorochrome-conjugated antibody panels, each targeting a specific surface protein marker of T, B, NK, and myeloid-derived suppressor cells (MDSCs).

Background

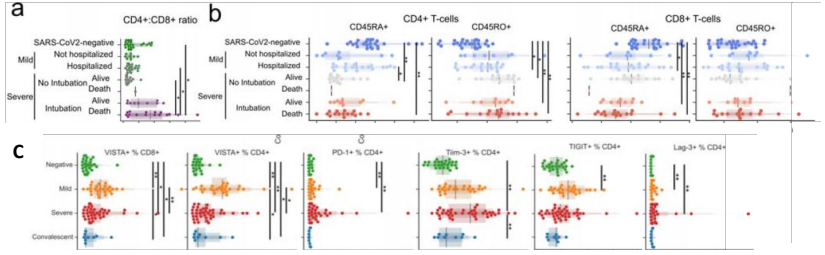
- Coronavirus disease-2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global pandemic that has affected over 25 million people worldwide.
- Clarifying the early immunological alterations associated with mild versus severe COVID-19 may offer therapeutically actionable targets and enable the identification of cases at highest risk for clinical deterioration and death.

SARS-CoV-2 infection causes major changes in the circulating immune system



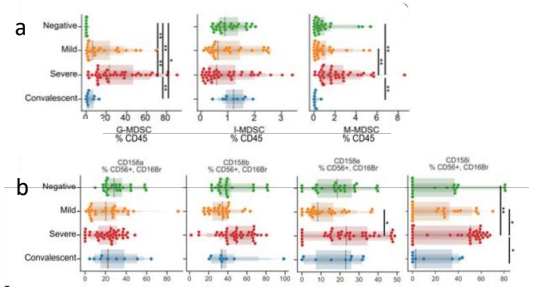
a) Composition of the cohort
b) Description of immune panels and their target epitopes.
c) Composition of major immune compartments as a percentage of all live CD45⁺ cells.
d) Abundance of major lymphoid compartments as a percentage of all lymphocytes. Significance was assessed using Mann-Whitney U tests and corrected for multiple testing with the Benjamini-Hochberg false discovery rate (FDR). **, FDR-adjusted p-value <0.01; *, FDR-adjusted p-value of 0.01–0.05.

SARS-CoV-2 infection causes imbalances in the naive and memory T cell compartments and induces exhaustion



a) The ratio of CD4⁺ to CD8⁺ T cells is dependent on disease state and clinical intervention.
b) The abundance of naive (CD45RA⁺) and memory (CD45RO⁺) CD4⁺ or CD8⁺ T cells is dependent on disease state or clinical intervention.
c) T cell exhaustion markers correlated with disease severity.

SARS-CoV-2 induces expansion of PMN MDSCs and biases NK KIR usage



a) Abundance of myeloid derived suppressor cells (MDSCs) as a percentage of all immune cells correlates with disease severity. **b)** Natural Killer (NK) cell Killer Immunoglobulin-like Receptor (KIR) receptor expression correlates with disease severity.

Conclusion

We observed that SARS-CoV-2 is associated with broad dysregulation of the circulating immune system, characterized by the relative loss of lymphoid cells coupled to expansion of myeloid cells. Severe cases demonstrated expansion of CD158i⁺ (KIR2DS4) NK cells and MDSCs, suggesting that the innate immune compartment may contribute to COVID-19-induced immune dysregulation.

Full Data

For full data: medRxiv 2020.09.08.20189092;
doi: https://doi.org/10.1101/2020.09.08.20189092