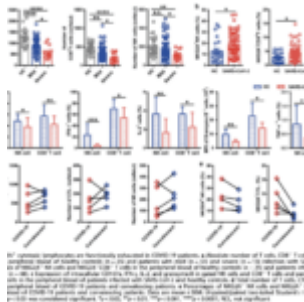
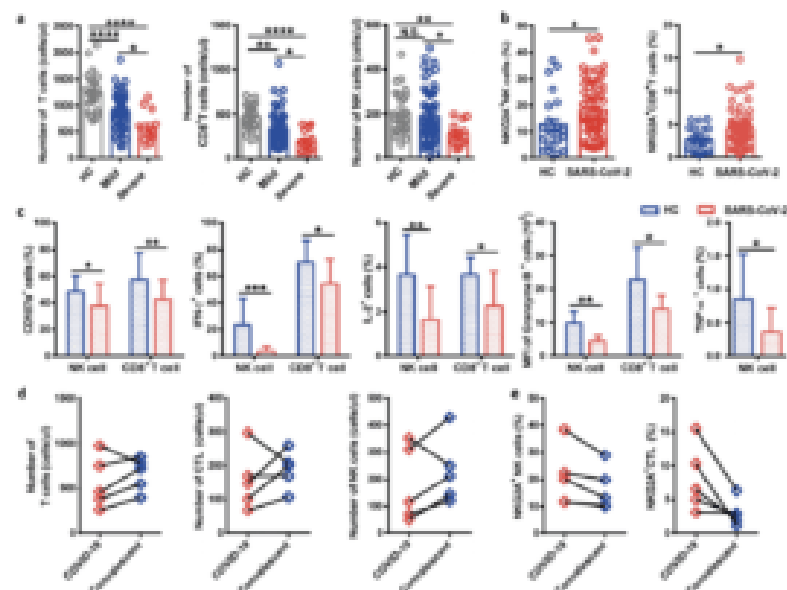


# Exhaustion of antiviral NK and CD8 T cells in SARS-CoV-2 infection



## Exhaustion of antiviral T cells in SARS-CoV-2 infection



**Fig. 1** NKG2A<sup>+</sup> cytotoxic lymphocytes are functionally exhausted in COVID-19 patients. **a** Absolute number of T cells, CD8<sup>+</sup> T cells, and NK cells in the peripheral blood of healthy controls ( $n = 25$ ) and patients with mild ( $n = 15$ ) and severe ( $n = 13$ ) infection with SARS-CoV-2. **b** Percentages of NKG2A<sup>+</sup> NK cells and NKG2A<sup>+</sup> CD8<sup>+</sup> T cells in the peripheral blood of healthy controls ( $n = 25$ ) and patients infected with SARS-CoV-2 ( $n = 68$ ). **c** Expression of intracellular CD137a, IFN- $\gamma$ , IL-2, and granzyme-B in gated NK cells and CD8<sup>+</sup> T cells and percentage of TNF- $\alpha$ <sup>+</sup> NK cells in the peripheral blood of patients infected with SARS-CoV-2 and healthy controls. **d** Total number of T cells, CTLs, and NK cells in the peripheral blood of COVID-19 patients and convalescing patients. Data are mean  $\pm$  SEM. Unpaired/paired two-tailed Student's  $t$  tests were conducted.  $p < 0.05$  was considered significant. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , \*\*\*\* $p < 0.0001$ ; N.S., not significant.

Source: Zheng et al., 2020

Natural Killer (NK) cells and CD8+ Cytotoxic T Lymphocytes (CTLs) play key roles in the control of viral infections. Zheng *et al* have studied the function of these lymphocytes in 68 COVID-19 patients, including 55 and 13 patients with mild and severe disease, respectively. Total numbers of T cells, NK cells and CTLs were reduced in all patients compared to

healthy controls, with severe cases having significantly lower proportions than those seen in mild cases. CD8<sup>+</sup> T and NK cells from COVID-19 patients had increased expression of the inhibitory receptor NKG2A compared to healthy controls. Furthermore, cells expressing NKG2A had diminished production of CD107a, IFN- $\gamma$ , IL-2, TNF- $\alpha$  and granzyme B. These findings suggest functional exhaustion of NK and CD8<sup>+</sup> T cells and inhibition of antiviral immunity during SARS-CoV-2 infection.

Following antiviral therapy, convalescing patients had an increased number of T cells, CTLs, and NK cells. Importantly, the percentage of NKG2A<sup>+</sup> NK and CTLs was reduced, suggesting that downregulation of NKG2A may be crucial for disease control.

A separate study also reported reduced expression of IFN- $\gamma$  by T helper cells, CTLs and NK cells in severe COVID-19 cases (Chen et al, 2020). Additionally, Qin et al have shown that both helper and cytotoxic T cell subsets are markedly reduced in COVID-19; however, they found no changes in IFN- $\gamma$  production.

Overall, these data suggest that dysregulation of the immune response, especially exhaustion of T lymphocytes, is a consequence of SARS-CoV-2 infection and may play a role in pathogenesis of the disease. Therapeutic approaches aimed at improving the immune response early on in the infection may, therefore, be beneficial for viral elimination.

## References:

- Qin et al., 2020. [Dysregulation of immune response in patients with COVID-19 in Wuhan, China](#). Clinical and Infectious Diseases.
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- Zhou et al., 2020. [Risk factors associated with disease progression in a cohort of patients infected with the 2019 novel coronavirus.](#) Annals of Palliative Medicine

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