# Why T Cells Are Key to Durable Protection Against SARS-CoV-2

Tyler Rector

Biomedical Sciences

Biol 302

10/3/2025

The article “T cell immunity to COVID-19 vaccines” examines the current state of SARS-CoV-2 vaccine design strategies and how a focus on generating high neutralizing antibody (NAb) titers limits variant resistance and long-term protection. The authors argue that because of these limitations of the current vaccine design strategies, the focus of future designs should be on inducing T cell immunity of $CD8^+$ T cells. Neutralizing antibodies block SARS-CoV-2 through targeting the spike receptor-binding domain (RBD) and preventing engagement with the ACE2 receptor on host cells. But as the NAb titers decline or as variants mutate, especially on their spike proteins, the authors argue that infection will continue without the involvement of $CD8^+$ T cells. T cell immunity can overcome the limitations of an NAb focused approach, as infected cells can present viral peptides, made from highly conserved viral proteins, on MHC 1, and $CD8^+$ T cells can recognize these presented peptides and kill the infected cell. Exemplifying this, the authors note that even against the SARS-CoV-2 variants, greater than 80% of T cell epitopes were conserved. T cells cannot, however, prevent the initial infection like neutralizing antibodies and can only respond once an infection occurs.

The authors utilize a series of immunological and clinical case studies to substantiate their hypothesis that long-lasting protection against SARS-CoV-2 will need to utilize T-cell immunity rather than neutralizing antibodies alone. The authors found that NAb titers decline within 4-6 months after mRNA vaccination and that the Omicron variant escapes demonstrate NAb immune escape. Demonstrating the effects of decreased NAb titers, the efficacy of mRNA vaccination protecting against SARS-CoV-2 infection appeared to be transient, even after booster vaccination. The authors found that robust protection against hospitalization can happen in the absence of high-titer NAbs, demonstrating that the more durable T cell and B cell immunity was likely responsible for preventing hospitalization. To demonstrate the efficacy of

specifically T cell immunity, the authors find that in cancer patients with B cell deficiencies, a $CD8^+$ T cell response was correlated with milder disease outcomes. This is also supported by the finding that in Omicron vaccination failures, a lack of $CD8^+$ T cells was demonstrated.

The figure in the article summarizes the key findings of the article into three scenarios: when NAb titers are high, when there are low titers of NAbs with a High amount of memory T cells, and both low titers of NAb and a low amount of memory T cells. The first scenario demonstrates that high NAb titers can block the initial infection of the upper respiratory tract. But once those NAb titers decrease, the second scenario demonstrates T cells becoming essential to halting viral spread towards the lower respiratory tract. Through this visual, the figure reinforces the central argument that $CD8^+$ T cell immunity is essential for long-term protection against SARS-CoV-2 infection.

The article discussed how $CD8^+$ T cell cytotoxic mechanisms limited the spread of infection towards the lower respiratory tract. This matches what was learned in class about how Cytotoxic T Lymphocytes utilize Granzyme B to initiate a cascade to activate the apoptotic pathway in an infected cell. The authors make a compelling case for reframing how we can evaluate the performance of SARS-CoV-2 towards prevention against not just infection and transmission but severe disease and Long Covid. There is potential in utilizing viral vectored vaccines, which have been demonstrated an effective method for inducing strong and broad T cell responses (Gilbert, 2011). Overall, the articles give an evidence-based argument for focusing scientific attention on the induction of T cell immunity in future SARS-CoV-2 vaccine designs.

References

Wherry, E. J., & Barouch, D. H. (2022). T cell immunity to COVID-19 vaccines. *Science*, *377*(6608), 821–822. https://doi.org/10.1126/science.add2897

Gilbert, S. C. (2011). T-cell-inducing vaccines – what's the future. *Immunology*, *135*(1), 19–26. https://doi.org/10.1111/j.1365-2567.2011.03517.x