Paper #2: T-cells and COVID Vaccine

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BIOL302

11/12/2025

Previous COVID-19 vaccination research was focused on the neutralization of antibody responses, but currently researchers are questioning if T-cells perform a more vital role in vaccine protection than previously realized (1). This current research is highly relevant to this course's content, as it elaborates on how ATP is generated in response to T-cell activation in the SARS-Cov-2 vaccine, and how it contrasts with the previously highlighted antibody mediated neutralization discussed in class.

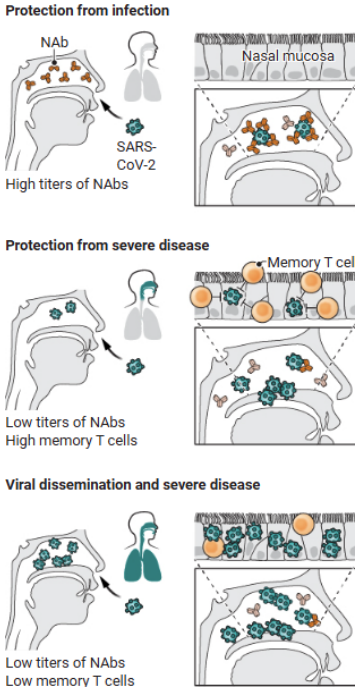
According to (1), through vaccination and past infection, individuals can develop protective immunity. Protective immunity is directed by the adaptive immune system, maintaining both humoral immunity and cellular immunity (1). The initial response to viral exposure is controlled by humoral immunity, which utilizes antibodies and memory B-cells that block viral infections by binding to and neutralizing the virus before it infects host cells (1). Many vaccines, including SARS-CoV-2, concentrate on this humoral mechanism by developing antibodies for their respective viruses (1). It should be noted that elevated levels of antibody concentration are required for the immune system to effectively fight viral infections (2). The secondary response of the immune system is the cellular immune response, which is mediated by helper CD4+ T-cells and cytotoxic CD8+ T-cells. Cellular immunity occurs if neutralization of the virus fails and is able to infect host cells. Because of this, the response occurs rapidly to limit the further spread of viruses in the host (1).

Figure 1 provides an illustration of the differences between the roles of NAbs and memory T-cells in the SARS-CoV-2 vaccine. This Image displays how upon entrance to the host, SARS-CoV-2 can be identified by the NAbs before infection can occur (2). It also shows how in situations with lower numbers of NAbs, the virus can avoid recognition by NAbs. If the virus is able to surpass neutralization, and infect host cells, they will then be thwarted by T-cell

responses. T-cell responses are facilitated by memory T-cells developed from the SARS-CoV-2 vaccine (3). If the virus is able to circumvent both immune responses due to sparse numbers or weak responses of NAbs and T-cells, then the virus will consequently spread to the upper respiratory tract (1).

Figure 1

Illustration of SARS-CoV-2 Immune Response Variations



Note. Adapted from (1)

There is growing interest in the data displaying the increased level of significance in the role of T-cell responses in vaccine protection (1). The original design of vaccines was to create a strong enough NAb response in order to entirely prevent infection and in turn suppress

transmission (1). For this to occur, vaccines need to provide high concentrations of NAbs and effector and memory durability. Unfortunately, viral variants such as Omicron are highly transmissible and capable of avoiding vaccine induced neutralizing antibodies (1,4,5). Because of this, researchers have come to realize that the original goals of vaccination may not be possible (1).

Difficulties managing Omicron continue, as it remains effective at avoiding immune system recognition, regardless of repeated booster vaccinations. Although Omicron is largely able to thwart the Nab immune response, it should be noted that during the Omicron surge in South Africa, individuals with vaccines and boosters were able to maintain protection from increasing death rates and hospitalization, regardless of the waning number of NAbs in current vaccines (6,7). The disconnect in this data suggests that there are other mechanisms at play allowing protection from severe variants (1).

The mechanisms used to fight viruses like Omicron have strong relevance in this course. B-cells along with long-lived plasma cells within the germinal center undergo changes and migrations in order to create more efficient antibodies (1). Memory B and T-cells play a vital role in this mechanism as well, because through booster shots, individuals can increase memory cell's already strong durability. These cells are necessary to generate recognition in HLA presentation scenarios because they help signal effector cells that are able to kill infected cells directly. Although this process is typically effective, for Omicron, it is more complicated (1).

Mutations in the spike proteins of Omicron are able to inhibit antibody binding, resulting in the incomplete neutralization of the newer viral variants (6). Although this is a major issue, the T-cells involved in this process are capable of remaining intact and largely unimpacted by COVID-19 variants such as Omicron (1).

Overall, the rapid development of COVID-19 vaccines and its research provided not only a major achievement for the field of biomedical sciences, but it also provided a new perspective on how the roles of T-cells and antibody mediated neutralization in vaccines is viewed (1). This paper displays how ATP is generated in response to T-cell activation in vaccines or infection, and how it is different from the antibody-mediated neutralization response.

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