T CELLS AND COVID VACCINE

INTRODUCTION TO IMMUNOLOGY

BIOMEDICAL SCIENCE

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The rapid development and deployment of COVID-19 vaccines has been a big step forward in maintaining public health. Most of the research and conversations around this topic have focused on how neutralizing antibodies (Nabs) help stop infections. However, recent studies show that cellular immunity, particularly T cell responses, play an important role in protecting against severe illness, especially when antibody levels decrease or when new variants escape neutralization (1). This paper will explain how T cells help make COVID-19 vaccines effective, compare their role to that of antibodies, and discuss what this means for the future.

Protective immunity against viruses like SARS-CoV-2 involves two arms of the adaptive immune system: humoral immunity and cellular immunity. Humoral immunity is mediated by antibodies and memory B cells, while cellular immunity involves helper CD4+ T cells and cytotoxic CD8+ T cells. Antibodies are effective at preventing viral entry into cells, but they must be present at high levels to block infection. Studies have shown that transferring immunoglobulin G (IgG) into animals can prevent infection if the concentration is high enough (1).

T cells, in contrast, do not prevent infection from occurring, but they are essential in limiting the spread and severity of infection once the virus enters cells. CD8+ T cells directly kill infected cells and release antiviral cytokines, while CD4+ T cells help B cells produces antibodies and may also fight infections directly (1). These T cell responses are especially important when Nabs are not sufficient to block infection, such as with emerging variants like Omicron that escape antibody recognition (1).

When vaccines were first introduced, high Nab titers gave hope that they would prevent infection and transmission. However, Nab levels decline within a few months of vaccination, particularly with mRNA vaccines. Although adenovirus-based vaccines like Ad26.COV2.S produce more

durable Nab levels, they start at lower peak (1). Additionally, SARS-Cov-2 variants have developed mutations that make it harder for antibodies to neutralize the virus. These factors have lowered the ability of current vaccines to prevent infection, even after booster doses (1).

Despite reduced protection against infection, vaccines still provide strong defense against severe illness. In South Africa, for instance, vaccines like BNT162b2 and Ad26.COV2.S continued to protect against hospitalization during Omicron surges, even in people with low Nab levels (1). This suggests that mechanisms beyond antibodies, such as T cell responses, play a crucial role in protection against serious disease.

The immune system builds memory after infection or vaccination. Antibodies are produced in two waves: short-lived plasma cells produce immediate, low-quality antibodies, while long-lived plasma cells and memory B cells produce high-quality antibodies after undergoing changes in germinal centers (GCs) (1). Even when antibody levels in the blood decrease, memory B cells and T cells remain. These memory cells respond quickly when the body encounters the virus again, helping to reduce the severity of infection (1).

T cells recognize parts of the virus presented on infected cells through HLA molecules. CD8+ T cells attack infected cells and release signals to recruit other immune cells. CD4+ T cells assist in many ways, including supporting antibody production. Importantly, memory T cells can last for decades and are maintained after infection or vaccination (1).

Unlike antibodies, which target specific shapes on the virus surface (mainly the spike protein), T cells recognize short internal parts or viral proteins. Since these parts are less affected by mutations, T cell responses are more consistent across different variants, including Omicron.

This means that even if a variant escapes antibodies, T cells can still recognize and respond to the virus (1).

Evidence supporting the role of T cells includes studies in cancer patients who lacked B cells. These patients had milder COVID-19 symptoms when they had strong CD8+ T cell responses. In animal studies, the removal of CD8+ T cell s led to worse outcomes after viral exposure. Furthermore, vaccine failure against Omicron in monkeys was linked to a lack of CD8+ T cell responses, even when moderate Nab levels were present (1). This shows that Nabs alone are not enough and highlights the need to consider T cells in evaluating vaccine performance.

To improve future vaccines, researchers are looking into ways to increase T cell responses. This could include using parts of the virus beyond the spike protein, such as nucleocapsid or membrane proteins, to create broader and more durable protection. Additionally, it's important to understand whether vaccine-induced T cells can stay in mucosal tissues, such as the nose and lungs, where the virus enters the body (1).

In conclusion, while antibodies are essential for preventing SARS-CoV-2 infection, T cells play a vital role in controlling infection and preventing sever disease. Their long-lasting and broad response makes them crucial, especially when antibody levels drop or new variants emerge.

References

1. Seder, R. A., & Barouch, D. H. (2023). T cells in COVID-19 vaccine protection. Science, 381(6656), 502–503. https://doi.org/10.1126/science.add2897