Promoting COVID-19 Vaccine Efficacy through T Cell Immunity

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The rapid production of COVID-19 vaccines in response to the Sars-Cov-2 pandemic is a notable medical and scientific feat. Currently, COVID-19 immunizations recruit high titers of neutralizing antibodies (NAb) that block an infection from manifesting in the nasal passageways (1). However, the progression of the pandemic has exposed some flaws in current mRNA vaccines. First, the duration of immunity provided by vaccine-induced NAbs is only four to six months (1). In addition, mutations in the COVID-19 spike protein have allowed novel variants to evade NAb defenses (1). Due to the challenges posed by mutant Sars-Cov-2 strains and the lack of a vaccine that provides long-term immunity, researchers are looking towards utilizing T cell responses alongside stimulating NAb titers to mitigate severe complications in the lower respiratory tract.

Recent studies have demonstrated that T cells can inhibit the progression of COVID-19 infection regardless of the viral strain. Initial interest in the use of T cells began when researchers found that cancer patients who had COVID-19 but had higher concentrations of CD8+ T cells were less likely to develop serious complications (2). In addition, a deficit in CD8+ T cells was correlated to vaccine failures against the Omicron variant in macaques (3). Unlike NAbs, T cells can identify 8- to 15- long amino acid peptide sequences found in the COVID-19 genome outside of the spike protein domains (1). Since most mutations occur within the spike protein, T cell responses are still effective towards novel strains with over 80% of T cell binding epitopes remaining intact in recent variants (4). In addition, T cells recognize antigens presented by human leukocyte antigen (HLA) class I or II molecules, which then generate effector responses ranging from CD8+ T cells inducing apoptosis of infected cells to CD4+ T cells carrying out helper functions such as the recruitment of cytokines (4). Furthermore, memory T cells that are produced to recognize COVID-19 proteins can be maintained in the body for decades, providing

long-term immunity for recovered patients (1). Therefore, although T cells only respond after an infection has begun, their ability to recognize and prevent viral propagation by targeting multiple parts of the COVID-19 virus induces a potent immune response.

Researchers hope to implement T cell immunotherapy alongside vaccines to improve treatments towards novel COVID-19 variants. In this process, high concentrations of vaccine-induced NAb titers first enter the nasal passageways to bind to the receptor binding domains (RBD) and N-terminal domains (NTD) of the spike protein, inhibiting Sars-CoV-2 from infiltrating the host cell (1). However, if novel variants escape initial NAb mechanisms, having the additional layer of T cells suppresses the development of severe disease in the lower respiratory passages (1). Even if vaccine-mediated immunity eventually wears off, patients who receive T cell treatments would still possess long term immunity from memory T cells (1). Therefore, the upregulation of NAb titers through vaccines and the use of T-cell mediated immunity can provide the ideal immune response towards COVID-19 infection.

Despite the promising outlook of the combined use of vaccines and T cell treatments, some questions remain in using T cell therapy. First off, there is speculation that updated booster vaccines that target the Omicron variant might proliferate NAb responses which would lessen the need for T cell therapy (1). Additionally, researchers are questioning the exact mechanisms that each T cell uses to contribute to long-term immunity (1). Therefore, more research should be conducted to identify the distinct role of each T cell and the possible ways that new booster vaccines and T cells can function together.

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