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Editorial

Hematopoietic Stem Cell Transplant

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EDITORIAL

Scientists can harvest T-cells from the blood of recovered COVID-19 patients and multiplied in the lab and maintain the ability to target proteins that are key to the virus's function, according to a new study.

We found that many people who recover from COVID-19 have T-cells that recognize and target viral proteins of SARS-CoV-2, giving them immunity from the virus because those T-cells are primed to fight it," study leader Michael Keller, MD, a pediatric immunology specialist at Children's National Hospital, said. "This suggests that adoptive immunotherapy using convalescent T-cells to target these regions of the virus may be an effective way to protect vulnerable people, especially those with compromised immune systems due to cancer therapy or transplantation.

Investigators from the Cellular Therapy Program at Children's National believed that the expanded group of COVID-19 virus-targeting T-cells could be infused into immunocompromised patients, helping them build an immune response before exposure to the virus and therefore protecting the patient from a serious or life-threatening infection.

This hypothesis came after previous research done looking at the safety of T-cells with antiviral activity in a phase 1 trial looking at adenovirus, BK virus, cytomegalovirus, Epstein-Barr virus, Human Herpesvirus 6 and human parainfluenza-3.

The T-cells were mainly grown from the peripheral blood of donors who were seropositive for SARS-CoV-2. The study also identified that SARS-CoV-2 directed T-cells have adapted to predominantly target specific parts of the viral proteins found on the cell membrane, revealing new ways that the immune system responds to COVID-19 infection.

In this study, we demonstrate that ex vivo expanded CSTs may be easily generated from convalescent patients, following recovery from COVID-19, and recognize multiple immunodominant epitopes within membrane protein, which represent class II restricted T-cell epitope "hot spots.

In addition, the authors note that using T-cells to develop a vaccine may offer another viable option for researchers. The current development has been targeting the spike proteins.

The Cell Therapy Program is now seeking approval from the U.S. Food and Drug Administration for a phase 1 trial that will track safety and effectiveness of using COVID-19-specific T-cells to boost the immune response in patients with compromised immune systems, particularly for patients after bone marrow transplant.

Immunocompromised patients are at elevated risk of complications from primary and reactivation infections with herpesviruses, including varicella zoster virus (VZV) and human papillomavirus (HPV). In the past several decades, vaccines have been become available to prevent primary VZV infection (chickenpox), reactivation VZV infection (herpes zoster, or shingles), and primary HPV infection, and all are routinely recommended for distinct age groups in the general population. The presence of immunocompromise requires special attention to several aspects of vaccination. The first is safety: Live attenuated vaccines are "weakened" but potentially have viable virus. This may cause disseminated infection in severely immunocompromised patients, and live vaccines are therefore generally avoided. Inactivated vaccines do not contain live virus and cannot cause disseminated infection; therefore, they are safer. However, many inactivated vaccines contain adjuvants, which might theoretically increase the risk of rejection and/or graft-versus-host disease (GVHD) in solid organ transplant (SOT) and allogeneic hematopoietic stem cell transplant (HSCT) recipients, respectively. The second consideration is efficacy: Immunocompromised patients may not mount the expected immune response to a vaccine and may therefore derive less benefit.

As a general principle, vaccines should be administered prior to initiation of immunosuppression whenever feasible (eg, patients being listed for SOT should be vaccinated prior to transplant). Live vaccines should be administered 4 weeks or more prior to initiation of immunosuppression, and they should especially be avoided within 2 weeks prior to immunosuppression given the risk of developing disseminated disease. Inactivated vaccines should be given at least 2 weeks prior to immunosuppression to allow time for an adequate immune response.

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