COVID Plus: A New Diagnostic Tool to Protect Transplant Patients in the Fight Against COVID-19

Abstract

We do not yet fully understand the impact of a COVID-19 infection on the HLA antibody status of transplant recipients. Researchers have long observed that episodes of viral infection can lead to alterations in the HLA antibody profiles of transplant patients. We must consider, therefore, that a COVID-19 infection, as well as any future COVID-19 vaccine, may trigger changes in HLA antibody profiles. This, in turn, may have a profound effect on patients' eligibility for transplant and risk of rejection after transplant. Additionally, an assay for transplant patients that could both detect neutralizing antibodies and rule out false positives will be critical for fully characterizing the immune response to COVID-19. The LABScreen™ COVID Plus assay can uniquely characterize these changes with greater accuracy by detecting multiple distinct antibodies and fragments, making it not only more specific than current assays but also more adept at reducing false positives caused by seasonal coronaviruses. These powerful features will enable physicians to adapt patient care for better transplant outcomes.

Key Considerations

- The impact of an episode of COVID-19 infection and of future vaccine administration on HLA antibody status is unknown.
- Distinguishing a true instance of COVID-19 infection will help to differentiate the impact of other seasonal respiratory infections.
- Identifying multiple distinct antibodies to COVID-19 will be vitally important as some have demonstrated neutralizing capabilities.

Background

The effect of the global coronavirus disease 2019 (COVID-19) pandemic on the field of transplantation has been profound. In excess of 75% of kidney and liver transplant programs have either been suspended or are operating with greatly reduced capacity[1]. The overwhelming need to protect our immunologically vulnerable transplant patients and the healthcare workers who care for them has been key to guiding these drastic protective efforts.

However, the time has come to reopen the clinics and operating theaters to resume transplant activity. In order to do this safely, the development of new diagnostic tools is required to enable the transplant laboratory to assess the risk of SARS-CoV-2, the underlying disease of COVID-19. Current data shows the mortality rate among transplant recipients who test positive for COVID-19 can be as high as 32%[2].

Consider the body of evidence currently available that indicates how active infectious episodes can result in profound changes to the patients' HLA antibody profile[3]. While the exact mechanisms that underpin these processes remain controversial, the emerging consensus is that pathogenic viral infections, such as COVID-19, may trigger an anamnestic B-cell response. Such memory responses can result in an increase in both the breadth and strength of the HLA antibody response[4].

Additionally, the current mass mobilization of the scientific community for the development of a safe and effective COVID-19 vaccine may pose additional challenges for transplant patients. Data has indicated that vaccine administration also has the potential to induce changes in the HLA antibody repertoire of our transplant patients[5,6]. By monitoring antibody responses post COVID-19 vaccination, we can detect changes and, if transplant eligibility or existing graft health is impacted, better manage the associated risk factors for these conditions.

In order to fully understand a patient's risk factor, transplant teams need be able to characterize the immune response to COVID-19 by simultaneously detecting the response to the spike protein, receptor-binding domain, nucleocapsid and other SARS-CoV-2 proteins.

Solution

Viral- and vaccination-induced changes to HLA sensitization status can have a profound impact on both transplant waitlist candidates and on those looking to preserve function in their transplanted organ. In response to this unmet patient need, we have developed the LABScreen COVID Plus assay, a comprehensive SARS-CoV-2 specific antibody detection panel that takes advantage of the multiplex capability offered by the Luminex platform. It can be run in parallel with conventional LABScreen products to give the full picture of a patients' HLA and COVID antibody status.

By uniquely targeting multiple subunits of the extracellular domain (commonly referred to as the "spike" protein) as well as the internal nucleocapsid protein, the LABScreen COVID Plus assay provides a reliable detection system (Fig. 1). The kinetics of the antibody response to SARS-CoV-2 are now reasonably well described with antibodies being routinely detected within 7-14 days after the onset of symptoms[7]. The added specificity of the LABScreen COVID Plus assay takes on greater importance since recent studies have indicated that individuals who develop antibodies to the viral nucleocapsid suffer increased mortality compared to those whose humoral response is limited to the recognition of spike protein[8]. In contrast, studies have indicated that the antibodies to the spike subunits RBD and S1 may have a neutralizing effect[9] (Fig. 2). The benefit of the antibody to Spike S2 is unknown, although detection of the Spike S2 antibody would indicate exposure to COVID-19. Clinical relevance of antibodies to Spike S2 may be established with future studies.

Furthermore, the panel for LABScreen COVID Plus includes specific targets for the common cold coronavirus families and markers for Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), thereby reducing the possibility that cross-reactive viral response may give rise to false positive COVID-19 tests.

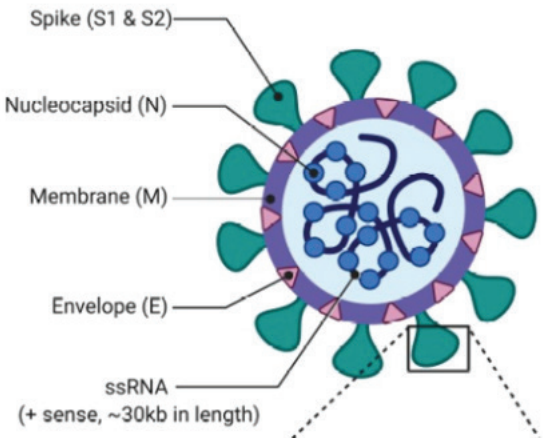

Figure 1: Schematic diagram indicating the viral structure highlighting the components featured as distinct targets on the COVID Plus panel
Cascella 2020

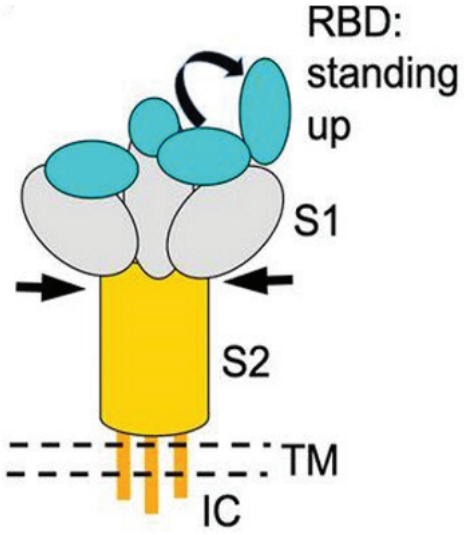

Figure 2: COVID-19 "Spike" protein showing arrangement of S1, S2, and RBD subunits
Shang 2020

The LABScreen COVID Plus assay will facilitate the detection and monitoring of the post-COVID antibody response, the assessment of antibody responses to vaccination (both COVID- and HLA-specific), and the exploration of changes to HLA antibody profiles. When combined with any of the currently available LABScreen HLA panels, the COVID Plus solution provides a tailored suite of antibody monitoring diagnostic tools specific for transplant patients.

LABScreen COVID Plus: Features & Benefits

- Batch with available LABScreen HLA assays to detect COVID-19 and HLA antibodies in a single run
- Comprehensive SARS-CoV-2 specific multiplex antibody detection panel
- Minimize cross reactivity with seasonal coronaviruses, MERS, and SARS infection
- Optimized assay workflow compatible with both LABScan™ 200 and LABScan3D™ instruments

Conclusion

The LABScreen COVID Plus assay is specifically designed to truly distinguish and characterize the humoral response to COVID-19 infection. With this product, transplant centers can know with confidence if a patient has been infected, even in asymptomatic cases, by identifying the specific COVID-19 antibody present and can then decide to manage the patient accordingly.

In this unprecedented time, we must adapt in order to meet the changing and unique needs of transplant patients. The LABScreen COVID Plus solution will help us rise to this challenge.

Disclaimer

The LABScreen COVID Plus assay is for professional, in vitro diagnostic use only:

1. This test has not been FDA cleared or approved.
2. Use of this product is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate or high complexity tests.
3. This test has been authorized only for the presence of IgG antibodies against SARS-CoV-2, not for any other viruses or pathogens.

References

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