immunoSEQ® T-MAP™ | COVID

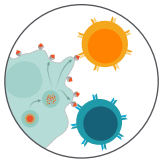
Assessing & monitoring T-cell responses to SARS-CoV-2 with immunoSEQ® T-MAP™ COVID

The COVID-19 pandemic has affected millions of people worldwide, igniting an extraordinary effort from the scientific community to understand the biological foundation of COVID-19 pathophysiology. This research has established a critical role for T cells in the immune response against SARS-CoV-2. Adaptive's immunoSEQ T-MAP COVID offering is a high-throughput approach to accurately, quantitatively, and reproducibly measure the T-cell immune response in COVID-19 clinical trial, vaccine and drug development research.

- Researchers can search our SARS-CoV-2-specific TCR database to determine if their samples show SARS-CoV-2 specific TCRs, the antigens to which these TCR responded, and deeper insights about their samples.
- Another feature provides a simple positive or negative result that can help determine past SARS-CoV-2-specific T-cell response in research samples.

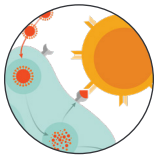
ROLE OF T CELLS IN COVID-19

T cells circulate in the blood and can quickly expand in response to pathogens like SARS-CoV-2 helping to clear the virus, often before symptoms occur. This T-cell response is an essential component of the human immune response to viruses like SARS-CoV-2.



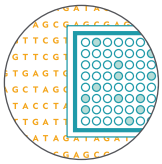
COMPREHENSIVE TOOL TO PROPEL YOUR COVID-19 RESEARCH

immunoSEQ T-MAP COVID allows researchers to comprehensively and quantitatively measure and monitor the T-cell immune response to SARS-CoV-2, allowing differentiation from other diseases.[1]



ASSESSING T-CELL RESPONSE IN COMPARISON TO OTHER METHODS

Preliminary data suggests T-cell based assays may better detect an immune response to COVID-19 when compared to tests that detect antibody responses.



APPLICATIONS OF IMMUNOSEQ TECHNOLOGY IN VACCINE RESEARCH

The immunoSEQ Assay is a validated, accurate, & standarized assay for measuring and monitoring the adaptive immune response, which can be leveraged with COVID-19-specific data to assess vaccine efficacy and durability.

Role of T cells in COVID-19

T cells are the adaptive immune system's first responders to any virus, circulating in the blood to detect and quickly multiply to help clear the virus, and also support the development of antibodies by B cells. This central role for T cells makes them a desirable target for assessing the immune response to viruses and specifically SARS-CoV-2 infection.

The combination of global scientific focus and the number of people infected with the SARS-CoV-2 virus in such a short period of time has led to an understanding of the variability of individual responses on a greater scale. In the setting of COVID-19, we are seeing:

- T-cell responses arise earlier than antibodies and last through clearance into convalescence.[2]
- T cells play a critical role in supporting the development of antibodies by B cells and can serve as the first signs of an immune response to SARS-CoV-2 infection.[3]
- The majority of COVID-19 patients generate a T-cell response comprised of both CD8⁺ T cells, or "killer" T cells which destroy virus-infected cells, and CD4⁺ "helper" T cells, which help other immune cells, including B cells which produce antibodies.[4]
- CD8⁺ and CD4⁺ T cells were observed in convalescent patients with mild and severe COVID-19 disease.[5]

Figure 1.

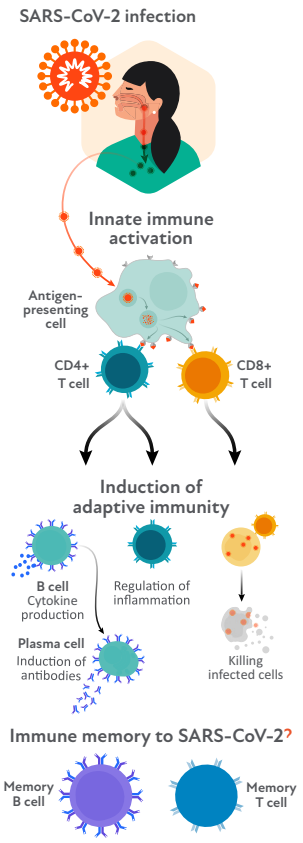


Figure 2.

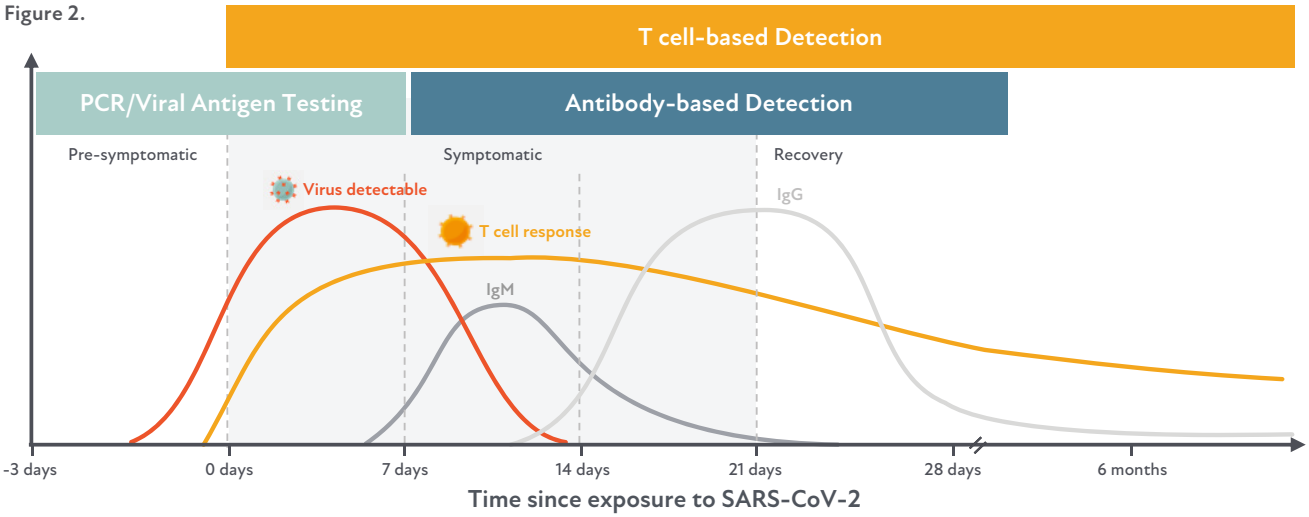


Figure 1. CD8⁺ T cells directly target infected cells via perforin/granzymes, FAS ligand/TRAIL pathways, or secretion of proinflammatory mediators. CD4⁺ T cells activate B cells that recognize the antigen. Plasma cells secrete antibodies to target the SARS-CoV-2 virus. Adapted from Gutierrez, et al. Elsevier Current Trends, 2020.[6]

Figure 2. Timeline of the adaptive immune response. T-cell responses, which occur prior to antibody responses, are detected within approximately one week of the onset of COVID-19 symptoms. Antibody responses wane over time, while memory T cells may be detectable months or years after infection. Based on data from Gallais, et al., 2020, Peng, et al. 2020, Snyder et al., 2020, Subbarao, et al., 2020, Channappanavar, et al., 2014, and Zuo, et al., 2020.[1,7,8,9,10,11]

Assessing T-cell response in comparison to other assessment methods

Historically, researchers measured the immune response primarily based on antibody levels. However, as we learn more about the role of T cells, researchers and vaccine developers are recognizing the need to measure the T-cell response in addition to the antibody response to both infection and vaccines.

Antibody tests, or serological tests, detect the antibodies that are produced against the SARS-CoV-2 virus.[12] Antibody production can vary across patients with COVID-19, so these tests may be less reliable.[12,13] Studies indicate that although antibody responses are detectable for months post-exposure, these responses wane over time.[14]

Measuring T cells typically involves using functional assays that require live cells, and such techniques are expensive, bespoke, low throughput and are not suitable to support large clinical studies. For example, ELISpot, an assay that detects proteins secreted by specific immune cells, has historically been used in vaccine research to measure immune responses.[15] However, the ELISpot technology is not capable of quantitatively tracking the longitudinal clonal expansion or contraction of specific T-cell clones, has a limited detection range to measure immune responses from specific cell types, and involves several hands-on steps to culture live cells.[15]

In contrast, Adaptive's immunoSEQ T-MAP COVID is the first molecular T-cell monitoring tool for SARSCoV-2, is a high-throughput approach to accurately, quantitatively, and reproducibly measure the T-cell immune response. The assay can be performed on whole blood and the analyte, genomic DNA, is highly stable, making specimen handling ideal for applications requiring scale.

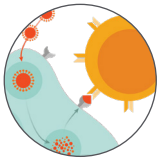
	Antibody-based Assays	ELISpot Assay	immunoSEQ T-MAP COVID
What it detects	Antibodies against SARS CoV-2	Proteins secreted by immune cells	T-cell response
Sample type	Blood	Fresh Cells	Flexible sample input including FFPE
How many targets are detectable	1-2	2-3	>100s of viral targets recognized by complete T-cell repertoire
Quantitative assessment?	×	×	✓
Longitudinal assessment?	×	×	✓

Table 1. Methods to detect an immune response in vaccine development. Commonly used assays to detect an immune response to a vaccine are antibody-based assays and ELISpot assay.[15,16] These assays have limited numbers of targets that they can assess and they cannot provide quantitative or longitudinal assessments. The immunoSEQ T-MAP COVID offering provides a highthroughput approach to quantitatively measure T-cell immune responses over time and across a range of flexible sample types.

A comprehensive tool to propel your COVID-19 research

Access the underlying technology that powers the first and only T-cell-based clinical test for COVID-19 to receive Emergency Use Authorization (EUA).

Adaptive Biotechnologies' robust immune medicine platform has identified >160,000 TCRs responsive to COVID-19 and mapped these TCRs to their putative antigens or epitopes. This has created a high resolution "map" of the T-cell response, launched as immunoSEQ T-MAP COVID. This offering provides invaluable, novel capabilities that have the power to advance SARS-CoV-2 clinical research and development, including the ability to detect past SARS-CoV-2-specific immune response in research samples and the ability to track responses longitudinally.



SARS-CoV-2-specific Antigen-TCR sequence-level data

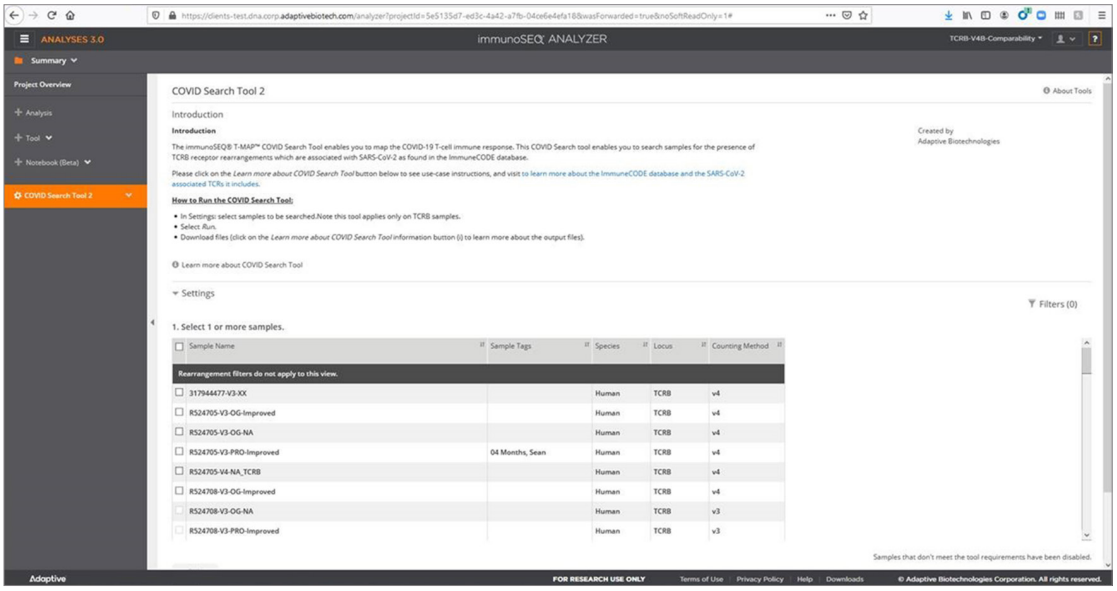
Quantitative sequence level data for SARS-CoV-2 specific antigens and TCR repertoires

Past SARS-CoV-2-specific immune response

Detect past SARS-CoV-2-specific immune response in research samples and track responses longitudinally

Study the T-cell response for SARS-CoV-2 variants

Assess the T-cell immune response for vaccine research across SARS-CoV-2 variants



Easily explore COVID-19 TCR-Antigen sequence data, de-identified subject level data and more in the immunoSEQ Analyzer. You can compare your COVID-19 samples against our COIVD-19 samples to identify Public vs. Private clones or download the full repertoire data set. The database is constantly updated with new findings and COVID-19 TCR-Antigen sequence data.

Identification of SARS-CoV-2-associated TCRs during natural infection

- Using immunoSEQ T-MAP COVID we can map the known SARS-CoV-2 associated TCRs during a natural course of infection or vaccine trial.
- immunoSEQ Assay was run with a subject's peripheral blood at 1 & 14 days post diagnosis, we can identify 19 of 77 expanded clones as illustrated in Figure 3.
- 17 of the 19 TCRs that are present are reactive to ORF1ab peptide and 2 to the Spike protein, suggesting that the ORF1ab may be the dominant epitope in this subject's response.

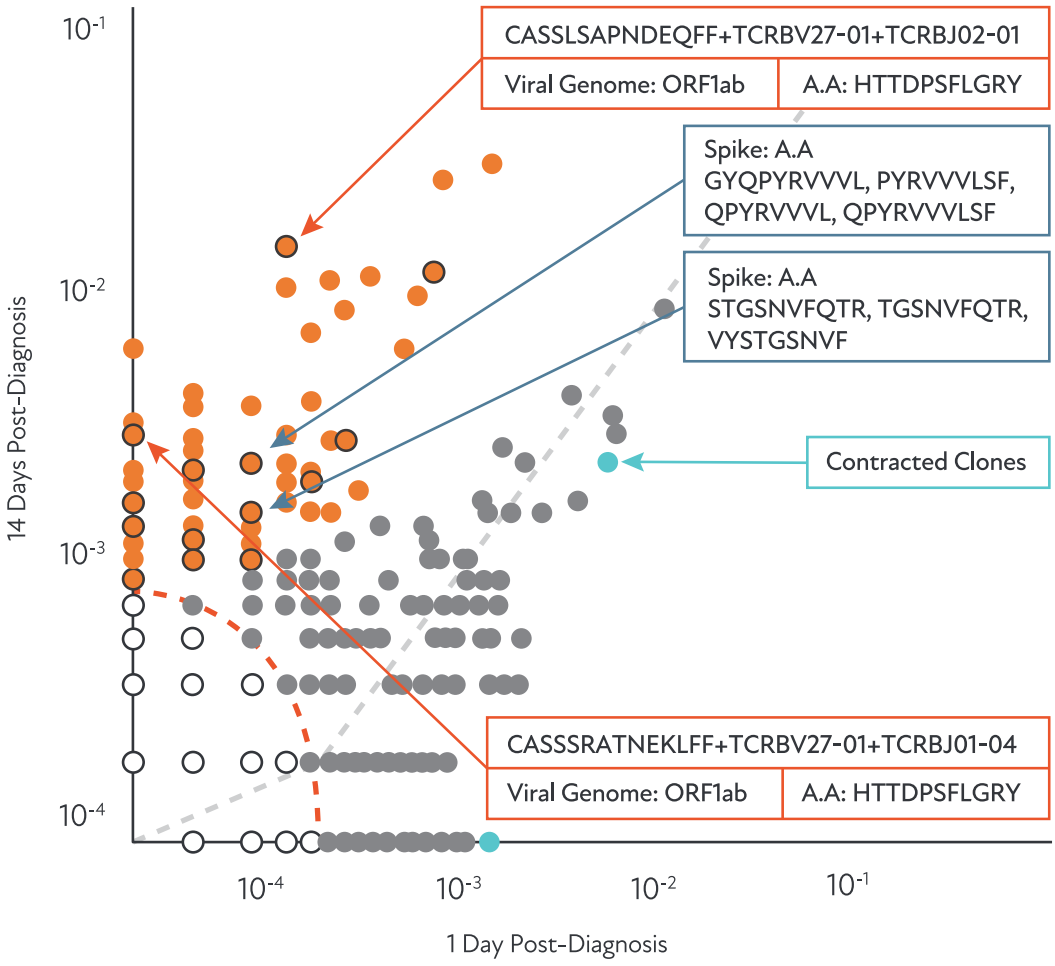
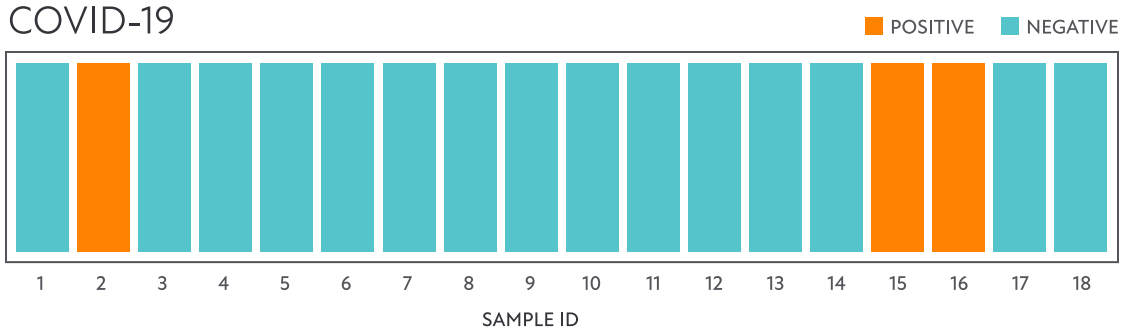


Figure 3. Example Analysis: Longitudinal comparison of the peripheral repertoire of a subject at 1 and 14 days post-diagnosis. Significantly expanded clones are annotated based on SARS-Cov-2 reactive T cells from ImmuneCODE results.[17]

Detection of past T-cell immune response to SARS-CoV-2

- Adaptive has now developed an additional feature for immunoSEQ T-MAP COVID, called the Classifier, that can determine recent or past T-cell immune response to COVID-19.
- The Classifier uses a set of sequences that are known to be specific to COVID-19 cases compared to control subjects to identify a T-cell signature of SARS-CoV-2.
- Samples are annotated as POSITIVE (+) or NEGATIVE (-) based on the presence of these T cells.
- The Classifier can be used to monitor changes over time or as a baseline biomarker.



immunoSEQ T-MAP COVID sample requirements

Sample Type	Desired gDNA concentrations	Total gDNA
PBMCs	206 ng/µL	20,600 ng
Whole blood	360 ng/µL	36,000 ng

Applications of the immunoSEQ Technology in infectious disease and vaccine research

The adaptive immune system plays a leading role in the physiologic response to vaccines and it's clear that T cells play a pivotal role in the host immune response. Characterizing the T-cell response to a vaccine is critical to fully understanding safety and efficacy, as well as immunogenicity and durability of protection.

The immunoSEQ Assay is a well-validated, accurate, and standardized assay for measuring and monitoring the adaptive immune response, which can be leveraged with SARS-CoV-2-specific data to assess vaccine efficacy and durability.

- In SARS-CoV, only antibodies against the Spike protein could neutralize the virus, so most SARS-CoV-2 vaccines in development include a portion of the Spike protein.18 Including antigens besides the Spike protein could help promote a more balanced immune response, comprising both B- and T-cell responses.[19]
- Safety can be impacted by antibody dependent enhancement of disease (ADE). Vaccine strategies should be designed to induce both neutralizing antibodies and T-cell immunity to protect against ADE.[19,20]

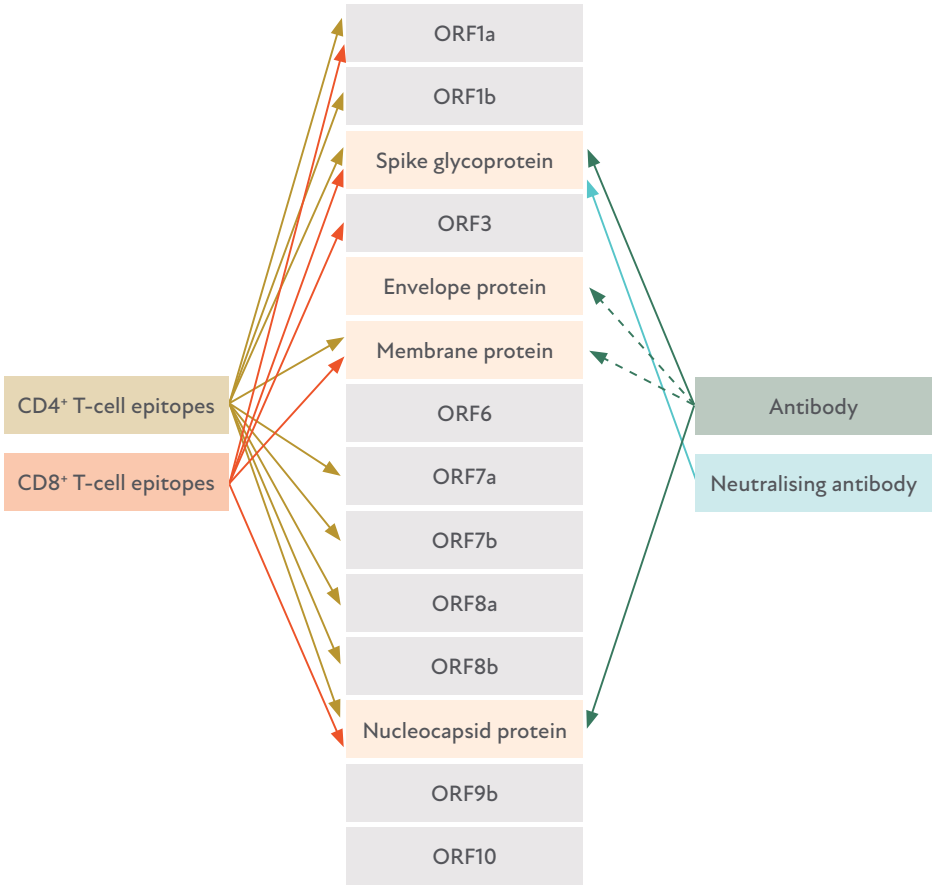


Figure 4. T-cell and antibody responses to SARS-CoV-2 proteins. CD4+ and CD8+ T cells can respond to SARS-CoV-2 antigens across the proteome, while antibody responses are limited to structural proteins. Adapted from Poland et al., 2020.

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