T-SPOT.COVID

Oxford Immunotec

Frequently Asked Questions

T-SPOT.COVID

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About SARS-CoV-2

What is SARS-CoV-2?

Severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2, is the virus that causes the respiratory illness coronavirus disease 2019 (COVID-19)[1]. SARS-CoV-2 was first identified in Wuhan, China in December of 2019, and has since caused an ongoing global health emergency which was declared a pandemic by the World Health Organization in March 2020[2].

What is COVID-19?

COVID-19 is the infectious disease caused by the SARS-CoV-2 virus[3]. Most people infected with SARS-CoV-2 will develop mild to moderate symptoms of COVID-19, with some individuals suffering no symptoms at all (asymptomatic infection). Mild to moderate symptoms include a dry, persistent cough, fever and a loss of smell or taste. A small number of people infected with SARS-CoV-2 will develop more severe symptoms of COVID-19, including difficulty breathing, severe acute respiratory distress syndrome, pneumonia, and in some cases unfortunately death[4].

What do we know about the immune response to SARS-CoV-2?

In general, most people infected with SARS-CoV-2 develop a T cell and an antibody response against the virus within several weeks after initial exposure[5].

What are T cells and antibodies and why are they important?

T cells produce a cellular-level immune response. Helper T cells orchestrate immune responses and activate B cells to release antibodies, while cytotoxic T cells kill host cells that have become infected by pathogens (bacteria and viruses)[6]. An antibody is a protein formed and released from specific B cells in response to a signal from a helper T cell. Antibodies attach to antigens, proteins on the surface of pathogens. They can also inhibit movement or stop some viruses from forming essential proteins[7].

Antibody tests are useful for showing whether a patient has recently been infected with SARS-CoV-2, the virus that causes the disease known as COVID-19[8]. However, research suggests antibody immunity to SARS-CoV-2 wanes over time[9]. There is also evidence that some infected individuals do not produce detectable levels of antibodies against SARS-CoV-2. As such, using antibody tests alone may underestimate the prevalence of population level exposure to the virus[10]. T cell testing can be used as an adjunct test to provide further information about immune responses to SARS-CoV-2.

Testing for SARS-CoV-2 infection

What is the current testing landscape for SARS-CoV-2?

The main categories for SARS-CoV-2 infection testing are molecular and antigen tests used to confirm whether an individual is currently infected with SARS-CoV-2, and antibody (serology) tests that tell whether an individual has been infected previously[11].

While molecular and antibody tests can detect current and past infection respectively, these technologies also have specific challenges, and using only these tests may not give a complete overview of whether an individual has been exposed.

There is strong evidence to suggest that SARS-CoV-2 triggers robust T cell responses[12]. Measuring T cell responses to SARS-CoV-2 may be reliable at detecting infection, and thus may be an important adjunct to current diagnostic methods.

What are the different diagnostic tests?

Molecular tests:

Molecular tests such as polymerase chain reaction (PCR) and antigen tests (such as lateral flow tests) are used to tell if a patient is actively infected with SARS-CoV-2[13]. Both types of test require swabs to be taken from the patient. Antigen tests look for virus-specific proteins called antigens, while molecular tests check for viral RNA. Both can show false negatives if the viral load is too low.

Antibody (serology) tests:

Antibody (serology) tests are relatively cheap and quick to process. These tests are useful for showing whether a patient has recently been infected with SARS-CoV-2, the virus that causes the disease known as COVID-19[13]. However, research suggests antibody immunity to SARS-CoV-2 wanes over time[9]. False negative results may occur if a patient has a delayed immune response or is able to eliminate SARS-CoV-2 infection without a strong antibody response[14]. As a consequence, antibody tests may underestimate the number of people previously infected.

The T-SPOT.*COVID* test:

The T-SPOT.*COVID* test has been developed using the standardised T-SPOT® technology testing platform to provide information on the T cell mediated immune response to SARS-CoV-2 infection[15]. A better understanding of the T cell response to infection is critical to providing a better understanding of the immune response to the SARS-CoV-2 virus. Measuring T cell responses to SARS-CoV-2 may be reliable at detecting infection, and thus may be an important adjunct to current diagnostic methods.

About T-SPOT technology

What is T-SPOT technology?

Oxford Immunotec's T-SPOT technology is based on the established ELISPOT assay method for measuring cells. Over the past 18 years we have worked to standardise it, industrialise it and make it suitable for routine clinical use in diagnosing tuberculosis.

We are the only company in the world with clinically approved ELISPOT technology which has obtained regulatory approval in more than 50 countries including the US, EU, UK, China and Japan. The technology is proven, and a test for tuberculosis, another deadly infectious disease, has been available for over 18 years, More than 20 million tests using T-SPOT technology have been shipped worldwide.

How does T-SPOT technology work?

Our T-SPOT test based on ELISPOT technology is normalised for both cell number and culture conditions. This means that the test standardises the number of cells and removes serum factors that could adversely affect results, making it the most sensitive and specific test for T cell measurement. A blood sample is collected using routine phlebotomy and a standard blood collection tube from which a subset of white blood cells, known as peripheral blood mononuclear cells (PBMCs), are isolated. The cells are washed, counted and normalised to create a standard cell suspension.

A standard number of cells are added into specially designed plates and stimulated with antigens specific to the disease under study. Cells responding to these antigens release a chemical messenger known as a cytokine.

Cytokine antibodies are used to directly capture the cytokine as it is released by the cells. A secondary labelled antibody is added and binds to the captured cytokine.

A detection reagent is added and reacts with the secondary labelled antibody. This reaction produces spots, which are a footprint of where the cytokine was released. Spots are then enumerated.

The T-SPOT.*COVID* test has been developed using this standardised T-SPOT technology testing platform to provide information on the T cell mediated immune response to SARS-CoV-2 infection. A better understanding of the T cell response to infection is critical to providing a better understanding of the immune response to the SARS-CoV-2 virus.

About the T-SPOT.*COVID* test

When should I use the T-SPOT.*COVID* test?

The T-SPOT.*COVID* test should be used to detect a cell mediated immune response to SARS-CoV-2. The test is intended to identify those individuals who are capable of generating an immune response to SARS-CoV-2, even if serologically negative.

How soon after infection is the T-SPOT.*COVID* test effective?

How soon T cells can be detected after infection remains to be seen. However, it has been reported that T cells have been detected in individuals infected with SARS-CoV-2 approximately 1 week after symptom onset[5]. Data from the US clinical study of the T-SPOT.*COVID* test showed 100% agreement with previous positive PCR test results at 7-14 days (in all 4 samples tested) and 0-6 days (in the one sample tested) after a PCR positive test[15]. Samples were not available for testing at earlier time points in this study.

What is the accuracy of the test?

The data from the US clinical study shows an average percent positive agreement between the T-SPOT.*COVID* test and PCR of 96.6 % (84/87) at <60 days after positive PCR result, and 83.3% (40/48) at >60 days after positive PCR result[15].

An overall negative agreement of 98.0 % (98/100) was seen in a cohort of individuals presumed negative (low risk of infection and no previous PCR positive result) but living in an endemic region[15].

What does a positive T-SPOT.*COVID* test result mean?

A positive test result means that a patient has T cells that are reactive to the SARS-CoV-2 specific peptides used in the T-SPOT.*COVID* test. It is highly likely that they have been exposed to the SARS-CoV-2 virus.

What does a negative test result mean?

A negative test result means that the patient does not have T cells that are reactive to the SARS-CoV-2 specific peptides used in the test. It is therefore unlikely that they have been exposed to the SARS-CoV-2 virus.

How does the T-SPOT.*COVID* test add to the information I get from antibody testing?

The T-SPOT.*COVID* test is intended to assess the cell mediated immunity to SARS-CoV-2. This is important as several limitations have been reported with the measurement of antibody-mediated immunity to SARS-CoV-2. As such, understanding cell mediated immunity may help to better understand the immune response to SARS-CoV-2 infection, especially in individuals who do not produce a measurable antibody response, or whose antibody responses have waned over time. The only way to understand the complete immune response to SARS-CoV-2 infection is to test for both antibodies and T cells.

Is the test suitable for use in acute COVID-19 diagnostics?

The T-SPOT.*COVID* test is not intended to be used to diagnose acute SARS-CoV-2 infection. T-SPOT.*COVID* should be used for the detection of a T cell response to SARS-CoV-2, which is generally detectable in the blood several days after initial infection, however the precise timing of the T cell responses post-infection is not well characterised at this time.

What regulatory approval does the T-SPOT.*COVID* test have?

The T-SPOT.*COVID* test is CE marked and has been submitted to the FDA for Emergency use authorisation.

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