

## Cellular immunodiagnosics: SARS-CoV-2-EliSpot Determination of T cell activity against SARS-CoV-2

To regulate the immune response against a pathogen, the immune system relies on two important mechanisms: **the humoral and the cell-mediated immune response.**

As not all patients develop measurable levels of antibody after contact with a virus, the immunity can be assessed on the cellular level by the SARS-CoV-2-EliSpot test.

Laboratory routine diagnostic investigation assess immunity following infection based on the humoral immune response with antibodies against the SARS-CoV-2 virus. Neutralising antibodies can prevent an infection and help to eliminate a pathogen. **Not all patients develop measurable levels of antibody after contact with a virus**, especially if they are asymptomatic or have very mild symptoms (8). Further data indicate that after an initial antibody response, the detected antibodies may disappear later.

The cell-mediated immune response and the **T cells**, in particular, control the strength of the immune response by secreting **cytokines** to increase (7) or to suppress the immune response depending on the viral load. In addition, T cells mediate the differentiation into plasma cells and the associated subsequent antibody production of the humoral immune response.

T-cell responses thus play a central role in the clearance of viral infections, and T-cell memory can persist for several years to protect against severe reinfection (1, 2, 5).

**The specific detection of reactive T cells (effector cells) against SARS-CoV-2 indicates an acute or past infection and possible (vaccination) protection - regardless of whether antibodies have been formed.**

### A proven method: The EliSpot assay (Enzyme-linked Immuno-Spot Assay)

The test is able to detect the cytokine **release of T cells** at the single cell level and thus decisively complements the diagnostics of the immune response. T cells that have already been in contact with the virus, but also with vaccine, react with activation by **SARS-CoV-2 peptides** added in vitro. The production and release of interferon gamma (**IFN $\gamma$** ) is detected in the EliSpot test (T-Spot.COVID) and is characteristic of **effector T cells**. The detection succeeds over a longer period of time than it is possible with antibodies.

Highly specific **peptides of SARS-CoV-2** are used in our test:

1st. sequences of the **spike protein** located on the membrane and

2nd. of the **nucleocapsid** present in the nucleus.

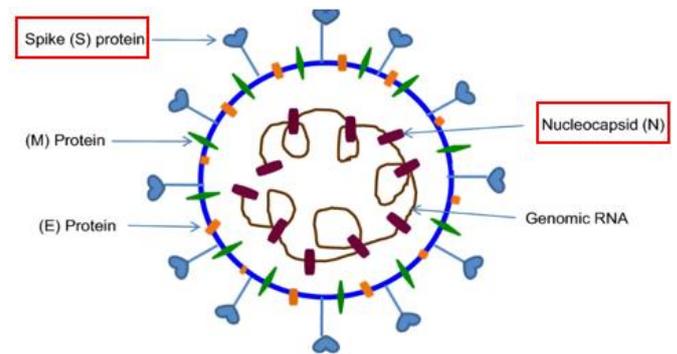
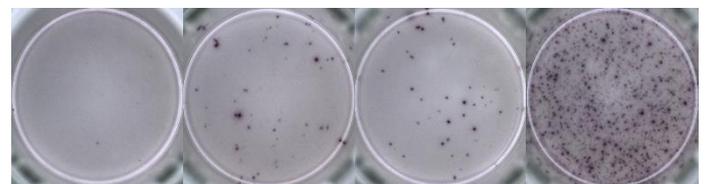


Figure 1: S- and N-protein of SARS-CoV-2 virus (3)

Previous research results indicate a possible distinction between a passed Covid-19 infection (reaction to both peptides) and vaccination (reaction to the S-peptide) (4, 6, 9, 10).



negative sample S-peptide N-peptide positive sample

Figure 2: sample of T-cell responses on S- and N-peptide on passed Covid-19 infection.

### Possible indication – questions:

#### Has an infection with SARS-CoV-2 occurred at all?

if a clinical course is mild and asymptomatic,  
if a PCR result is negative despite the presence of typical symptoms.

#### Uncertain, decreasing, or absent antibody response after PCR positivity or vaccination.

Detection of memory T cells that react with cytokine secretion against SARS-CoV-2 antigens in an EliSpot assay may indicate previous viral contact without antibody production. Detection of cross-reactivity may indicate **baseline immunity** independent of antibody detection.

### Requirement

SARS CoV-2 Elispot, profile 66911  
With indication of clinical information, treatment, PCR test, vaccination

### Price

CHF 177.00, no mandatory provision

### Material

10ml heparin blood

### Preanalytics

Due to limited sample stability, the sample must be processed in the laboratory within 24h.  
- Blood collection from Monday to Thursday. Sample preparation Monday to Friday at noon.  
- Collection via courier, no postal delivery  
- Do not use centrifugation  
- Do not store in the refrigerator  
- Do not expose to direct sunlight

### Tested antigens

SARS-CoV-2 S-peptide (spike protein), SARS-CoV-2 N-peptide (nucleocapsid protein)

### Approval

CE, IVD

### Result

The result of the cellular immune reaction is indicated as «negative», «borderline» or «positive».

### Literature and figures:

1. Braun J, Loyal L, Frentsch M, Wendisch D, Georg P, Kurth F, et al. Presence of SARS-CoV-2 reactive T cells in COVID-19 patients and healthy donors. medRxiv. 2020:2020.04.17.20061440
2. Channappanavar, R., Fett, C., Zhao, J., Meyerholz, D.K., and Perlman, S. (2014). Virus-specific memory CD8 T cells provide substantial protection from lethal severe acute respiratory syndrome coronavirus infection. *J Virol* 88, 11034-11044.
3. Das, S.K. The Pathophysiology, Diagnosis and Treatment of Corona Virus Disease 2019 (COVID-19). *Ind J Clin Biochem* 35, 385–396 (2020). <https://doi.org/10.1007/s12291-020-00919-0>
4. Folegatti PM, Ewer KJ, Aley PK et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomized controlled trial. *The Lancet*. 2020; 396(10249):467-478.
5. Grifoni A, Weiskopf D, Ramirez SI, Mateus J, Dan JM, Moderbacher CR, et al. Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. *Cell*. 2020;181(7):1489-501.e15
6. Jackson LA, Anderson EJ, Roupael NG et al. An mRNA vaccine against SARS-CoV-2 – Preliminary Report. *N Engl J Med*. 2020; 383:1920-1931.
7. Maisch B. SARS-CoV-2 as potential cause of cardiac inflammation and heart failure. Is it the virus, hyperinflammation, or MODS? *Herz*. 2020;45(4):321-2.
8. Mallapaty, S. (2020). Will antibody tests for the coronavirus really change everything? *Nature* 580, 571-572.
9. Sahin U, Muik A, Derhovanessian E et al. COVID-19 vaccine BNT162b1 elicits human antibody and Th1 responses. *Nature*. 2020; 586: 594-599.
10. Sauer K, Harris T. An effective COVID-19 vaccine needs to engage T cells. *Front. Immunol*. 2020. <https://doi.org/10.3389/fimmu.2020.581807>