

The Number of SARS-CoV-2 Infections Among Vaccinated People Could Be Overestimated Unless Appropriate Diagnostic Tests Are Used, Says ISGlobal Study

The research team found that some COVID vaccines induce antibodies that recognise a viral antigen which is not included in the vaccine

Barcelona, 18 November, 2021- A considerable percentage of people immunised with the Pfizer-BioNTech and Moderna vaccines, which target the **SARS-CoV-2 Spike protein** generate antibodies that can recognise a fragment of another viral protein (the **N protein**), according to a [study](#) by the Barcelona Institute for Global Health (ISGlobal), an institution supported by "la Caixa" Foundation. These rather unexpected findings have implications for **the detection of infections in vaccinated people**.

All vaccines approved in Europe use the SARS-CoV-2 Spike protein as **antigen**, and therefore induce the **production of Spike-specific antibodies**. Because of this, serological tests to establish whether a vaccinated person has been infected measure antibodies to other viral proteins that are not included in the vaccine, such as the N (nucleocapsid) protein.

"With the emergence of **new variants** that can potentially evade vaccine immunity, it becomes of particular importance to monitor the percentage of vaccinated people that become infected," explains **Carlota Dobaño**, first author of the study.

An unexpected finding

From the beginning of the pandemic, Dobaño and her team have been closely following the production and duration of antibodies against different viral antigens **in two cohorts of healthcare workers in Catalonia** ([SeroCov](#) and [Covicatcentral](#)). In this study, carried out in collaboration with the Catalan Institute of Health Central Catalonia, they describe an **unexpected finding**: the mRNA vaccines (Pfizer-BioNTech or Moderna) induce antibodies that not only recognise the Spike protein, but can also recognise a fragment of the N protein (the C-terminal region) of SARS-CoV-2.

The research team detected, in a considerable percentage of vaccinated individuals, a significant increase of **IgG antibodies that can recognise the C-terminal** region of the N protein (36% of people who received **Moderna** and 13% of people who received **Pfizer**). The Moderna vaccine also induced an increase in antibodies that recognise the full-length N protein, although in a lower percentage of people.

"This phenomenon does not seem to result from the reactivation of immunity acquired by infection, since it was observed both in people who had been previously infected and in people who had no history of prior infection," explains **Gemma Moncunill**, senior author of the study. The most probable **explanation**, according to the authors, is that Spike vaccination can induce antibodies that **cross-react** with the C-terminal fragment of N.

Multiple viral antigens are better to detect breakthrough infections

These results are **relevant in terms of public health**, since it has been proposed to use the N protein to monitor breakthrough infections in vaccinated people. “This could lead to an overestimation of breakthrough infections, since a considerable percentage of cases would be misclassified as asymptomatic infections,” explains Dobaño. In consequence, vaccine effectiveness against **infections would be underestimated**.

The authors conclude that the N protein (in any case the N-terminal region) should not be used to detect breakthrough infections and that ideally a combination of **multiple viral antigens** should be used. This would allow a better estimation of vaccine effectiveness.

The study was funded by the [Daniel Bravo Foundation](#) and [EIT-Health](#), among others.

Reference

Dobaño C, Jiménez A, Rubio R et al. [Spike-based COVID-19 immunization increases antibodies to nucleocapsid 1 antigen](#). 2021. Translational Research. <https://doi.org/10.1016/j.trsl.2021.10.004>

About ISGlobal

The Barcelona Institute for Global Health, ISGlobal, is the fruit of an innovative alliance between the “la Caixa” Foundation and academic and government institutions to contribute to the efforts undertaken by the international community to address the challenges in global health. ISGlobal is a consolidated hub of excellence in research that has grown out of work first started in the world of health care by the Hospital Clínic and the Parc de Salut MAR and in the academic sphere by the University of Barcelona and Pompeu Fabra University. Its working model is based on the generation of scientific knowledge through Research Programmes and Groups, and its translation through the areas of Training and Analysis and Global Development. ISGlobal has been named a Severo Ochoa Centre of Excellence and is a member of the CERCA system of the Generalitat de Catalunya.

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