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Covid-19 : towards a simplified diagnostic test to better identify contagious subjects and those at high risk of developing a severe form

French scientists have published the results of a study showing that the measurement of the type-I interferon antiviral response (IFN-I) in nasal samples could be used to help identify patients at risk of transmitting the COVID-19 virus. This measurement of IFN-I, performed applying an innovative technique using the same swab as that used for the SARS-CoV-2 test, would also allow the identification of patients at risk of developing a severe form of COVID-19.

Type-I interferon (IFN-I) is a protein of the cytokine family usually produced rapidly by the immune system in response to a viral infection with the principal effect of inhibiting the replication of the virus in infected cells.

How long does the COVID-19 virus remain active in our body? Why do some patients develop a severe form? Is it possible to detect these potential severe forms in advance? In May 2020, several French and international teams demonstrated the absence of detection in blood of IFN-I in about 20% of patients hospitalized in intensive care with a severe form of COVID-19[1]. This absence could be explained, in particular, by the presence of auto-antibodies, preventing its antiviral action.

Further to this work, the clinical departments of the Hospices Civils de Lyon and the CHU St Etienne, as well as researchers at Université Claude Bernard Lyon 1, Université de Paris Inserm, the CNRS, and the ENS - Lyon at the InternationalCenter for Infectiology Research(the VirPath, LYACTS and GIMAP teams), and the HCL-bioMérieux joint laboratory in collaboration with the Imagine Institut des Maladies Génétiques (AP-HP, Inserm, Université de Paris) characterized the IFN-I anti-SARS-CoV-2 response for

[1] http://www.cnrs.fr/fr/deficit-en-interferon-alpha-des-patients-covid-19-de-nouvelles-perspectives-therapeutiques

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patients presentingwith mild COVID-19 symptoms as well as in patients presenting severe forms, admitted to intensive care. The results of this research have been published in the *Journal of Experimental Medicine*.

Interferon, a new marker for SARS-CoV-2 contagiousness

In this new study, researchers measured the IFN-I response from the same swab as that used for the SARS-CoV-2 test thanks to an innovative technique developed by bioMérieux, the BIOFIRE® FILMARRAY® system. Widely used for the diagnotics of other infectious diseases, this technique is based on a multiplex PCR system allowing the preparation, amplification, detection and analysis of samples in about one hour. Today, the PCR test allows the detection of viral genetic material but does not allow us to determine if the virus is active (alive) or inactive (dead) at the time the sample is collected. For subjects with mild COVID-19 symptoms, the IFN-I nasal response was proportional to the quantity of virus, itself linked to the risk of transmission. These results highlight the fact that measurement of the nasal IFN-I response could be used as a marker for active infection in combination with the detection of the SARS-CoV-2 virus. This measurement could thus be of help for the rapid identification of patients with a high risk of virus transmission, and conversely provide support to help avoid imposing quarantine measures on patients that do not represent, or no longer represent a possible source of contamination.

“We used type-I interferon as a marker for active virus replication, explains Dr Sophie Trouillet-Assant, associate researcher co-author of the study. If there is a small amount of virus and no IFN-I in your sample, you have been infected but are no longer contagious. Conversely, if there is a large quantity of both the virus and IFN-I, this would indicate the need for isolation”. She continues with her example: “For patients at risk of developing severe forms, the situation is again different: the samples may contain a large quantity of virus but no IFN-I. It ithen becomes possible to identify these profiles and prevent the deterioration of the illness”.

Predicting which patients are at risk of developing a severe form of COVID-19 thanks to the PCR test

In the same study, researchers demonstrated that in patients with anti-IFN-I auto-antibodies admitted to intensive care for a severe form of Covid-19, an absence of IFN-I response was demonstrated in nasal swabs that nevertheless contained large quantities of viral particles.. These results were confirmed in a laboratory model that mimicks what happens in the nasal epithelium (developed by the VirPath team): the anti-IFN-I auto-antibodies are capable of inhibiting the antiviral action of these molecules, resulting in significant viral replication and a loss of physiological integrity for the epithelial cells cultivated in vitro.

The measurement of the nasal IFN-I response and the evaluation of the presence of antibodies in the blood could thus be used as a support to stratify patients and identify those at risk of developing a severe form of the illness, right from theonset of infection and while swabbling for the standard SARS-CoV-2 test.

Beyond the diagnostic and prognostic aspects, the results of this study open up significant perspectives in terms of therapeutic strategy for COVID-19 patients. Indeed, treatments based on other types of interferons non-targeted by the auto-antibodies already exist, such as e recombinant interferon-beta. The researchers highlight their potential utility as an early treatment for COVID-19 patients presenting a deficit

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in interferon response, to prevent the development of severe illness symptoms while at the same time limiting SARS-CoV-2 viral replication.

Source

Early nasal type I IFN immunity against SARS-CoV-2 is compromised in patients with autoantibodies against type I IFNs, Journal of Experimental Medicine, August 6, 2021

Jonathan Lopez, Marine, Mommert, William Mouton, Andrés Pizzorno, Karen Brengel-Pesce, Mehdi Mezidi, Marine Villard, Bruno Lina, Jean-Christophe Richard, Jean-Baptiste Fassier, Valérie Cheynet, Blandine Padey, Victoria Duliere, Thomas Julien, Stéphane Paul, Paul Bastard, Alexandre Belot, Antonin Bal, Jean-Laurent Casanova, Manuel Rosa-Calatrava, Florence Morfin, Thierry Walzer, Sophie Trouillet-Assant

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