Why are some people hit harder by COVID-19?

Richard Béliveau

Translated from Le Journal de Montréal, September 28th, 2020

Two recent biochemical studies show that a significant proportion of severe forms of COVID-19 are due to genetic and autoimmune disorders that inactivate interferon, our first biochemical line of defense against viral infections.

One of the most intriguing features of the COVID-19 pandemic is the enormous inter-individual variation that exists in the severity of the disease. In the vast majority of healthy people, the infection does not cause serious complications of the disease and often even goes completely unnoticed in almost half of the cases.

Conversely, in the elderly and those with pre-existing health problems (obesity, diabetes, cancer, cardiovascular disease), the disease can progress rapidly and lead to serious complications. It is therefore a very discriminatory virus, which preferentially targets the most vulnerable people.

DEFICIENT INTERFERONS

Recent results suggest that in several cases this vulnerability is caused by the absence of the immune response involving type I interferons.

This class of proteins plays a very important role in our defense against viruses: from the first moments of infection, cells secrete interferons to stimulate the production of antiviral proteins by nearby cells and thus limit the spread of the virus.

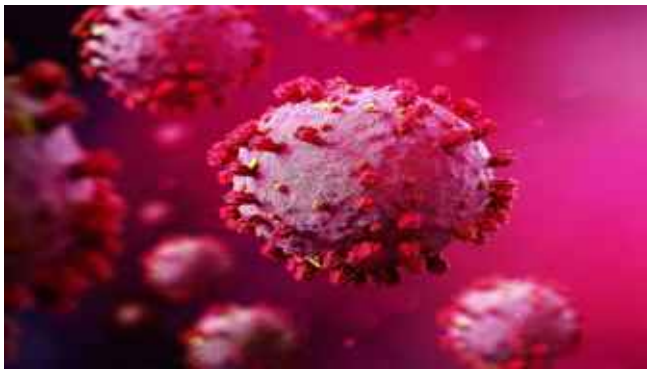
At the same time, these interferons attract circulating immune cells to the site of infection to fight the virus and activate B and T lymphocytes to build up an immunological memory capable of neutralizing the viral agent in the longer term.

According to a study recently published in the very prestigious *Science*, this activation of the response mediated by type 1 interferons is seriously compromised in a high proportion of patients severely affected by COVID-19 (1).

By analyzing blood samples from 987 very ill patients living in different parts of the world, the researchers observed that some of these patients produced antibodies that attacked and neutralized the action of their own interferons and therefore had no primary defense line against the coronavirus.

These antibodies were not detected in any of the 663 blood samples from people who developed a mild form of COVID-19 and also appear to be very rare in the general population (0.33% of healthy people tested in the study).

It therefore appears that a significant proportion (10%) of severe COVID-19 cases can be considered an autoimmune disease, which attacks the immune system itself and prevents it from activating in response to viral infection.



It should be noted that these anti-interferon antibodies are mainly found in men (94% of cases) and in people over 65 years old (50%) and therefore contribute to the greater vulnerability of men and the elderly to COVID-19.

GENETIC DEFECTS

Another study, also published in *Science*, finds that some very sick patients also have a deficient type I interferon-mediated response, but this time due to genetic variations that prevent the production of these proteins (2).

By analyzing the DNA sequences of 659 patients with a severe form of COVID-19, the researchers observed in some of these patients (3.5%) the presence of mutations in 8 of the 13 genes involved in the production of type I interferon.

Conversely, these mutations are absent in people who are infected but who were asymptomatic or mildly ill. This is therefore the first demonstration of a genetic variation that dramatically increases the risk of developing severe forms of COVID-19.

In sum, these two studies show that some of the severe COVID-19 cases (nearly 15%) are caused by a defect in the immune response mediated by type I interferon. People with these biochemical disorders are therefore more at risk of being strongly affected by this disease, even if they are in good health and do not have apparent risk factors.

Interestingly, none of the patients with anti-interferon antibodies or mutations that prevent the production of this class of proteins had a medical history of serious viral infections requiring hospitalization. So it appears that we are much more dependent on type I interferons to protect us from the coronavirus that causes COVID-19 than on other types of viruses.

This discovery has immediate therapeutic implications. For example, synthetic interferons have been used for several years to treat other diseases (multiple sclerosis, hepatitis C) and are therefore already available to treat some very sick patients (3).

We can also consider the development of a biochemical test capable of detecting anti-interferon antibodies to identify people at very high risk of complications of the disease and who must therefore redouble precautions to avoid exposure to the virus, or even be vaccinated as a priority when a vaccine is available.

(1) Bastard P et coll. Auto-antibodies against type I IFNs in patients with life-threatening COVID-19. Science (published on-line, September 24th, 2020)

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research

(2) Zhang Q et coll. Inborn errors of type I IFN immunity in patients with life-threatening COVID-19. Science (published on-line, September 24th, 2020)

(3) Wadman M. Can interferons stop COVID-19 before it takes hold? Science, 2020; 369 : 125-126

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research