Press information

An Immune "Signature" to Identify Diabetic Patients at Risk of Developing Severe Covid-19

Researchers have identified biomarkers in blood samples taken from diabetic patients. © Inserm/Latron, Patrice

Type 2 diabetes is a risk factor for the development of a severe form of Covid-19. Identifying the immune- and inflammatory markers associated with these severe forms of the disease in this patient population would enable earlier and more appropriate care. Researchers from Inserm, the Paris hospitals group AP-HP and Université de Paris have identified an immune signature in hospitalized diabetic patients that would make it possible to predict the risk of admission to intensive care. Their findings have been published in *EMBO Molecular Medicine* and supplement those of other studies published in recent months on the identification of biomarkers predictive of severe forms of Covid- 19.

In the early months of the Covid-19 pandemic, type 2 diabetes was identified as a risk factor for developing a severe form of the disease and has been linked to higher mortality. Therefore, understanding why this is and identifying biomarkers to predict which diabetic patients will progress to a severe form of Covid-19 requiring intensive care constitutes a research priority in order to improve their care and increase their chances of survival.

Type 2 diabetes is characterized by chronic inflammation, related to the disruption of adipose tissue which produces lipids recognized as "danger signals" by certain cells of the immune system. The immune response is then deregulated, leading to local and then systemic inflammation.

As part of the team led by Inserm Research Director Nicolas Venteclef at Cordeliers Research Center (Inserm/Université de Paris/Sorbonne Université), researchers Fawaz Alzaid and Jean-Baptiste Julla prepared an observational study in a hospital setting. It was conducted at the University Center for the Study of Diabetes and its Complications led by Jean-François Gautier, a diabetologist researcher at Lariboisière Hospital AP-HP. The objective was to better understand the link between pre-existing inflammation in diabetes and the risk of developing a severe form of Covid-19. The scientists sought to characterize the immune and inflammatory "signatures" of diabetic patients hospitalized following infection with SARS-CoV-2 and who presented severe symptoms of the disease.

They looked at the immune response of 45 patients hospitalized with Covid-19, thirty of whom had type 2 diabetes. Among the study participants, 35% of the diabetic patients developed a severe form of the disease requiring a stay in intensive care, compared to 25% of the non-diabetic hospitalized patients.

The researchers analyzed blood samples from all of the patients. They found that those most severely affected had fewer lymphocytes (a type of white blood cell) than those who had not been in intensive care. The team observed particularly low levels of cytotoxic CD8+ lymphocytes, immune cells particularly involved in the antiviral response with important functions of recognizing and eliminating infected cells. This was observed in all of the intensive care patients, regardless of diabetic status.

However, the diabetic patients having required intensive care differed from non-diabetic patients in the same case because they also had fewer monocytes (another type of white blood cell) in their blood. Changes in the morphology of these monocytes were also observed, as these immune cells in patients with type 2 diabetes had a larger average size than those found in blood samples from non-diabetic patients.

Finally, the researchers noted an increased presence of inflammatory markers associated with the type 1 interferon pathway, powerful antiviral molecules.

"These findings have major clinical implications as they suggest that there is an immune- and inflammatory signature specific to diabetic patients at risk of developing severe Covid-19. If physicians notice a decrease in monocyte frequency and a change in their morphology, they have the possibility to identify patients who will require further follow-up and potentially a place in intensive care. This will make it possible to refine and improve care," explains Inserm researcher Fawaz Alzaid.

This research also provides data to support ongoing clinical studies that suggest the importance of a disruption of the type 1 interferon pathway in the development of severe forms of the disease, and the potential therapeutic value of anti-interferon drugs, already highlighted in recent research involving Inserm, published in *Science.*

Sources

Monocytopenia, monocyte morphological anomalies and hyperinflammation characterise severe COVID-19 in type 2 diabetes

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