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PRESS RELEASE

SARS-CoV-2: a new mode of transmission of the virus involves immune cells

Scientists from CNRS, CEA and Université Grenoble Alpes have confirmed in PLOS Pathogens, in an article to be published on May 20, 2021, that the Covid virus can use immune cells to increase its transmission to other cells. They also showed that it is possible to inhibit this new mode of virus transmission by using glycomimetics, previously developed at IBS. This work is the result of an international collaboration with Spanish (Hospital Universitario 12 de Octubre, Madrid) and Italian (Universita degli Studi di Milano) groups.

Broadly speaking, cells have receptors on their surface, some of which are only used for the attachment of viruses, while others can act as locks that viruses use to enter. They have an arsenal of proteins, like a set of keys, that allow them to cross the cell barrier. For example, the S-glycoprotein on the surface of SARS-CoV-2 allows the virus to enter human cells through its interaction with the ACE2 receptor on the surface of infected cells.

IBS scientists and their colleagues found that the S protein also interacts with other receptors than ACE2 of the lectin family of proteins (DC-SIGN, L-SIGN, MGL and Langerin), present on immune cells. "This interaction involves a multi-site recognition of the S protein by exploiting the different surface glycans (sugars) of the S protein," explains Franck Fieschi, professor at Université Grenoble Alpes. The S glycoprotein would therefore have a whole set of keys to allow SARS-CoV-2 to proliferate.

The scientists showed that this interaction did not cause the direct infection of cells by SARS-CoV-2. However, among these receptors, DC-SIGN and L-SIGN are able to transmit the virus to permissive cells possessing ACE2 once they have attached the virus to the cell. They also show that it is possible to inhibit this mode of virus transmission by using glycomimetics, molecules that can mimic the surface sugars of the virus.

These results, already demonstrated on pseudo viruses a few months ago in pre-publication, are now confirmed by the use of authentic SARS-CoV-2 viruses and on human respiratory cells. It is thus a new mode of transmission in the global infection process this publication work highlights. The glycomimetic inhibitors developed will thus be able to constitute a first tool to study its relative importance in the months to come.

References:

DC/L-SIGN recognition of spike glycoprotein promotes SARS-CoV-2 trans-infection and can be inhibited by a glycomimetic antagonist.
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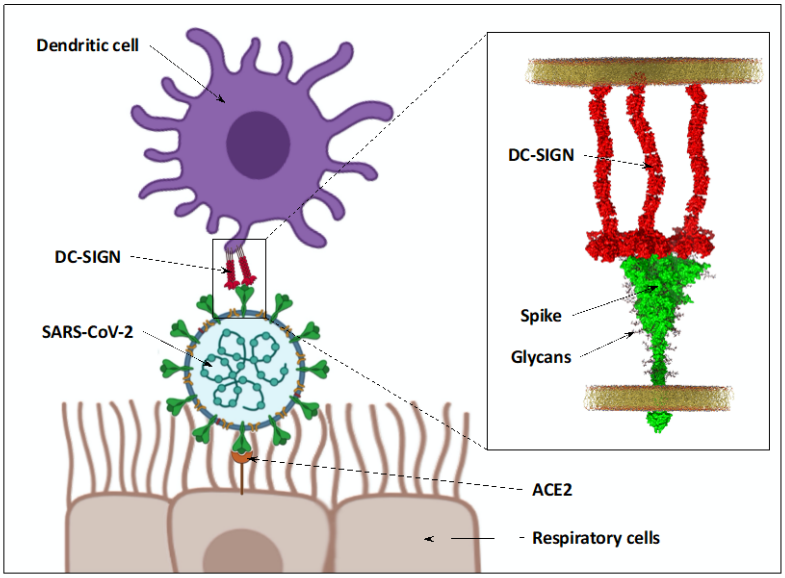

Caption:

Capture of SARS-CoV2 virus by DC-SIGN and/or L-SIGN receptors promotes trans-infection of virus-permissive cells (ACE2+). Right insert: The interaction between DC-SIGN or L-SIGN and the Spike protein involves recognition of the glycan "shield" (the sugars coating the Spike protein) by the sugar recognition domains of the lectin receptors.

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