

Infection and transmission of SARS-CoV-2 depends on heparan sulfate proteoglycans

*Bermejo-Jambrina M^{1¶}, Eder J^{1¶}, Kaptein T.M¹, van Hamme J.L¹, Helgers L.C¹,
Vlaming K.E¹, Neeltje A. Kootstra¹, Marit J. van Gils², Rogier W. Sanders^{2,3}, Teunis
B. H. Geijtenbeek^{1*}*

¹Dept. of Experimental Immunology, Amsterdam institute for Infection and Immunity, Amsterdam University Medical Centers, University of Amsterdam, Meibergdreef 9, Amsterdam, The Netherlands.

²Dept. of Medical Microbiology, Amsterdam institute for Infection and Immunity, Amsterdam University Medical Centers, University of Amsterdam, Meibergdreef 9, Amsterdam, The Netherlands.

³Dept. of Microbiology and Immunology, Weill Medical College of Cornell University, New York, NY 10021, USA.

* Corresponding author:

Email: t.b.geijtenbeek@amsterdamumc.nl (TBHG)

¶ These authors contributed equally.

Abstract

The current pandemic caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and outbreaks of new variants highlight the need for preventive treatments. Here we identified heparan sulfate proteoglycans as attachment receptors for SARS-CoV-2. Notably, neutralizing antibodies against SARS-CoV-2 isolated from COVID-19 patients interfered with SARS-CoV-2 binding to heparan sulfate proteoglycans, which might be an additional mechanism of antibodies to neutralize infection. SARS-CoV-2 binding to and infection of epithelial cells was blocked by low molecular weight heparins (LMWH). Although dendritic cells (DCs) and mucosal Langerhans cells (LCs) were not infected by SARS-CoV-2, both DC subsets efficiently captured SARS-CoV-2 via heparan sulfate proteoglycans, and transmitted the virus to ACE2-positive cells. Moreover, human primary nasal cells were infected by SARS-CoV-2 and infection was blocked by pre-treatment with LMWH. These data strongly suggest that heparan sulfate proteoglycans are important attachment receptors facilitating infection and transmission, and support the use of LMWH as prophylaxis against SARS-CoV-2 infection.