Multivalent 9-O-Acetylated-sialic acid glycoclusters as potent inhibitors for SARS-CoV-2 infection

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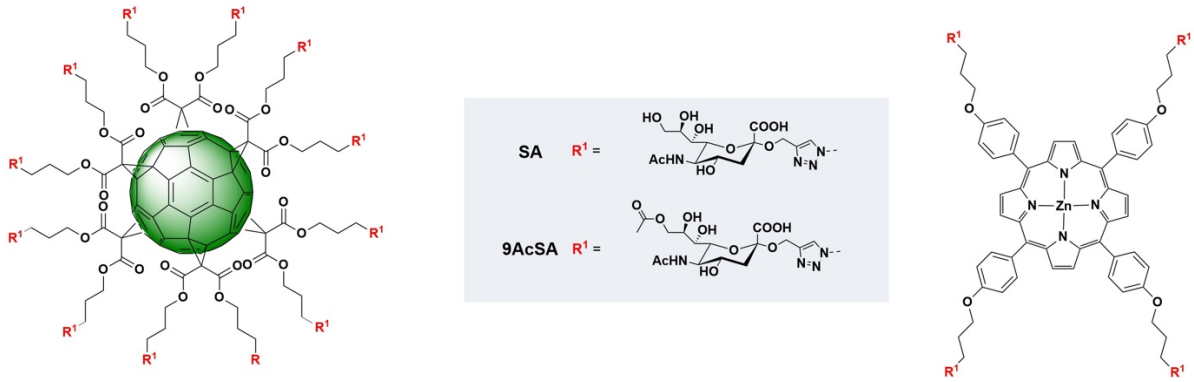
The recent emergence of highly transmissible SARS-CoV-2 variants illustrates the urgent need to better understand the molecular details of the virus binding to its host cell and to develop anti-viral strategies. While many studies focused on the role of the angiotensin-converting enzyme 2 receptor in the infection, others suggest the important role of cell attachment factors such as glycans.

The early binding events of the virus were studied using biophysical methods with the focus on the role of sialic acids (SA). We showed that SARS-CoV-2 binds specifically to (monomeric) 9-*O*-acetylated-SA with a moderate affinity, supporting its role as an attachment factor during virus landing to cell host surfaces. We demonstrated that 9-*O*-acetyl-sialic acid (9-AcSA) had a much stronger affinity towards the spike protein than sialic acid (SA) itself.

Four multivalent glycoclusters (with different topologies and valencies) presenting either SA or 9-AcSA were prepared. We identified 9-AcSA-derived porphyrin having high-binding inhibitory capacity (in the sub-µM range) both on purified receptors and on living cells. In addition, infection assays on living cells showed this molecule has a very promising neutralization potential.[1]



Sialic acid (SA) and 9-AcSA glycoclusters as potent SARS-CoV-2 ligands

Bibliographic references:

[1] S. Petitjean, W. Chen, M. Koehler, R. Jimmidi, J. Yang, D. Mohammed, B. Juniku, M. Stanifer, S. Boulant, S.P. Vincent, D. Alsteens (2022), Nat. Commun. (13) 2564.