# Glycans are crucial in COVID-19 infection

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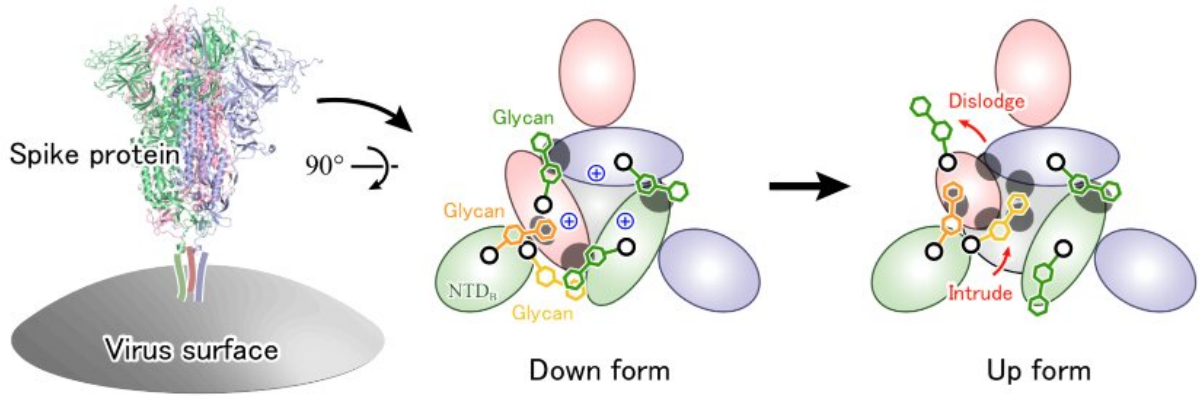


Molecular mechanism underlying the structural change of the SARS-CoV-2 spike protein. Credit: RIKEN

A research group at the RIKEN Center for Computational Science (R-CCS) has found that glycans—sugar molecules—play an important role in the structural changes that take place when the virus which causes COVID-19 invades human cells. Their discovery, which was based on supercomputer-based simulations, could contribute to the molecular design of drugs for the prevention and treatment of COVID-19. The research was published in the *Biophysical Journal*.

When SARS-CoV-2—the coronavirus that causes COVID-19—invades a human cell, a spike protein on its surface binds to an enzyme called ACE2 on the surface of the cell. The spike protein consists of three

polypeptide chains, and glycans—sugar molecules—are attached to the surface of the protein. Though these glycans are believed to be used to allow the proteins to recognize each other, it is also thought that viruses use them to evade attack by antibodies.

Structural analyses have shown that the spike proteins of SARS-CoV-2 have Down- and Up-form structures. These analyses have advanced our understanding of the three-dimensional structure of the spike proteins, but the detailed molecular structure of the highly fluctuating glycans is still not understood, and in fact the role of glycans in the process of cell invasion remains unclear.

To get a better understanding of their role, the research team led by Yuji Sugita of R-CCS conducted molecular dynamics simulations for the Down- and Up-form structures of the proteins, using two supercomputers—Fugaku at the R-CCS and Oakforest-PACS at the University of Tokyo. Using these powerful machines, they performed molecular dynamics simulations of the spike proteins at a timescale of 1 microsecond (one-millionth of a second).

From the calculations, they were able to identify specific glycan -attached amino acids in the spike protein that play an important role in stabilizing the structure of the receptor binding domain. Their results suggested that the conformational change to the Up-form structure is driven by electrostatic repulsion between the domains, and that glycans which stabilize the Down-form structure are dislodged and replaced by other glycans after the domains are displaced. The study thus provided new insights into how glycans help stabilize the dynamic structure of proteins.

According to Sugita, "We need to develop better preventative and therapeutics to bring the pandemic to an end. It would be very useful to be able to design drugs taking the structural changes of spike proteins

into account, by stabilizing the Down-form or inhibiting the change to the Up-form, for example."

"Research projects like this," he adds, "show us how the new generation of powerful supercomputers will allow us to gain new insights into many phenomena by performing simulations at a level of detail that would have been impossible previously."

**More information:** Takaharu Mori et al. Elucidation of interactions regulating conformational stability and dynamics of SARS-CoV-2 S-protein, *Biophysical Journal* (2021). DOI: 10.1016/j.bpj.2021.01.012

Provided by RIKEN

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