

Role of Spike Protein in COVID-19

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Editorial Note

A surface structure called the spike glycoprotein is used by SARS-CoV-2 to bind the human angiotensin-converting enzyme 2 (ACE2) cellular receptor to gain entry into host cells. The presence of Spike proteins is one of the key biological characteristics of SARS-CoV-2, as well as several other viruses to penetrate host cells and cause infection as the viral envelopes typically consist of three proteins, including the membrane protein (M), the envelope protein (E) and the spike protein (S).

The RNA genome of coronaviruses is the longest among all RNA viruses with a median length of 29 kb comprised of six to ten open reading frames (ORFs) that are responsible for encoding both the replicase and structural proteins for the virus. SARS-CoV-2 would never be able to interact with the cells of prospective hosts such as animals and humans and cause infection without the S protein, so it acts as a potential target for vaccine and antiviral research activities.

The S protein plays a crucial role in penetrating host cells and initiating infection as it is a highly glycosylated type I transmembrane fusion protein that is made up of 1,160 to 1,400 amino acids. S proteins of coronaviruses can be further classified into N-terminal S1 subunit, which forms the globular head of the S protein and the C-terminal S2 that forms the stalk of the protein and undergoes two large conformational changes once the S1 subunit binds to the host cell receptors to complete the virus fusion to the cell membrane. The first conformation referred to prehairpin, includes the transformation of an unstructured linker to become helical within the S2 subunit.

The second conformational change to occur involves the inversion of this subunit's C-helix to the coil, resulting in the formation of a six-helix bundle. The fusion peptide is anchored to the membrane of the host cell once these conformations are completed to allow the virus to move closer towards the cell membrane and eventually deliver the nucleocapsid to the target cell.

Recent studies revealed that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) enhances its infectivity, replication, and early transmission of the virus that is caused by a common mutation in the spike protein as the people who were infected with COVID-19 have only experienced mild or asymptomatic disease while others had serious health issues such as heart problems, coagulopathy, stroke or acute respiratory distress syndrome.. SARS-CoV-2 engineered to host the D614 G mutation observed that this strain replicated more effectively than the wildtype virus in the primary human proximal airway epithelial cells. The D614 G strain also demonstrated much faster transmission of respiratory droplets in a hamster model of infection than the wild virus.

The Importance of the spike protein and its applications in the studies aims to develop vaccines and therapies as a virus may select its virulence, pathogenesis, or transmissibility to alter for mutations so the spike protein has become a central focus of interest in studies aiming to develop vaccines and therapies. The D614 G substitution in the spike glycoprotein has recently been identified as the most prevalent strain of SARS-CoV-2.