

Recombinant SARS-CoV-2 (D614G Mutant) Spike Glycoprotein, His-tagged

Cat. No. HUM-346 **Lot. No.** (See product label)

SPECIFICATION

Product Overview SARS-CoV-2 (D614G mutant) trimeric spike glycoprotein is manufactured in CHO cells to high yield and purity. Protein has the D614G mutation and proline substitutions at residues 986 and 987, a GSAS substitution at the furin cleavage site (residues 682–685), and a C-terminal His-tag. SARS-CoV-2, previously known as the 2019 Novel Coronavirus (2019-nCoV), causes the pandemic COVID-19 disease.

Tag His

Background In late December, 2019, a number of patients with viral pneumonia (now called 2019-nCoV acute respiratory disease; COVID-19) were found to be epidemiologically associated with the Huanan seafood market in Wuhan, in the Hubei province of China. A novel, human-infecting coronavirus, provisionally named 2019 Novel Coronavirus (2019-nCoV) and since named SARS-CoV-2, was identified by genomic sequencing (Lu et al., 2020). SARS-CoV-2 is closely related (88% identity) to two bat-derived severe acute respiratory syndrome (SARS)-like coronaviruses, collected in 2018 in Zhoushan, eastern China, but were more distant from SARS-CoV (~79% identity) and MERS-CoV (~50% identity). However, although bats might be the original host of this virus, an animal sold at the seafood market in Wuhan may have acted as an intermediate host (Lu et al., 2020). Relative synonymous codon usage (RSCU) analysis suggests that SARS-CoV-2 is a recombinant between the bat coronavirus and an origin-unknown coronavirus, and it is thought that a Pangolin or other mammal is likely to have been the intermediate host. The recombination event occurred within the viral spike glycoprotein (Ji et al., 2020). Homology modelling

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shows that SARS-CoV-2 has a similar receptor-binding domain structure to that of SARS-CoV, despite amino acid variation at some key residues and is able to bind to the angiotensin-converting enzyme 2 (ACE2) receptor in humans (Lu et al., 2020). SARS-CoV-2 is a respiratory virus which spreads primarily through contact with an infected person through respiratory droplets generated when a person coughs or sneezes, or through droplets of saliva or discharge from the nose. The incubation period is believed to range from 2-11 days. Infection with SARS-CoV-2 can cause mild symptoms including a runny nose, sore throat, cough, and fever. However, it can be more severe for some people and can lead to pneumonia or breathing difficulties. The elderly, and people with pre-existing medical conditions (such as, diabetes and heart disease) appear to be more vulnerable to becoming severely ill with the virus (WHO, 2020).

The coronavirus spike (S) glycoprotein is a class I viral fusion protein on the outer envelope of the virion that plays a critical role in viral infection by recognizing host cell receptors and mediating fusion of the viral and cellular membranes (Li, 2016). SARS-CoV-2 entry into host cells is governed by the transmembrane spike (S) glycoprotein which forms homotrimers protruding from the viral surface. S contains an S1 subunit, responsible for binding to the host cell receptor, and a S2 subunit, facilitating fusion of the viral and cellular membranes. The S protein is a trimeric class I fusion protein that exists in a metastable prefusion conformation and which undergoes a substantial structural rearrangement to fuse the viral membrane with the host cell membrane. This process is triggered when the S1 subunit binds to a host cell receptor. Receptor binding destabilizes the prefusion trimer, resulting in shedding of the S1 subunit and transition of the S2 subunit to a stable postfusion conformation (Walls et al., 2017; Bosch et al., 2003; Li et al., 2020). The S1 subunit comprises the receptor-binding domain(s) and contributes to stabilization of the prefusion state of the membrane-anchored S2 subunit, which contains the fusion apparatus. For other CoVs, S is cleaved at the boundary between the S1 and S2 subunits, which then remain non-covalently bound in the prefusion conformation. S is then further cleaved by host proteases at the

S2' site located immediately upstream of the fusion peptide which is believed to activate the protein for membrane fusion via irreversible conformational changes. Different coronaviruses use distinct domains within the S1 subunit to recognize a variety of attachment and entry receptors, depending on the viral species. SARS-CoV-2 has been demonstrated to bind with the angiotensin-converting enzyme 2 (ACE2) to enter target host cells. SARS-CoV-2 also contains a novel furin cleavage site at the S1/S2 boundary, which is cleaved during biosynthesis. This polybasic cleavage site may help expand SARS-CoV-2 cell and tissue tropism and/or enhance its transmissibility, compared with other CoVs, due to the near-ubiquitous distribution of furin-like proteases and similar reported effects on other viruses, such as influenza (Walls et al., 2020). Wrapp et al. modified the SARS-CoV-2 spike ectodomain residues 1 to 1208 with two stabilizing proline mutations in the C-terminal S2 fusion machinery, scrambling the furin cleavage site and including a trimerization motif. This construct was used to produce a 3.5-angstrom-resolution structure of the trimeric spike protein by cryo-electron microscopy. Biophysical assays showed that it binds at least 10 times more tightly to the ACE2 host cell receptor than the corresponding spike protein of SARS-CoV.

Formulation	Presented in PBS, pH 7.4 at greater than 90% purity by SDS-PAGE.
Notes	This product is intended for research and manufacturing uses only. It is not a diagnostic device. The user assumes all responsibility for care, custody and control of the material, including its disposal, in accordance with all regulations.
Type	Recombinant
ClassID 1	Infectious Disease

GENE INFORMATION

Synonyms	SARS-CoV-2 (D614G Mutant) Spike Glycoprotein (Trimeric)
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