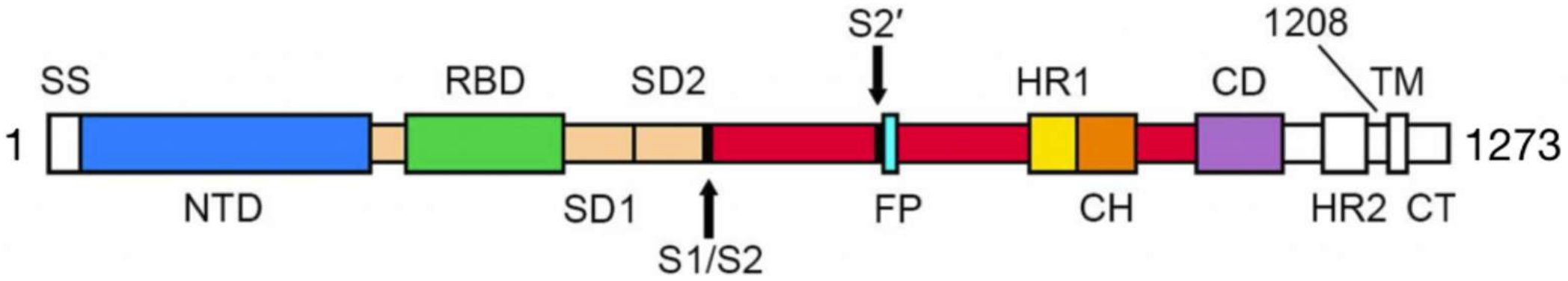
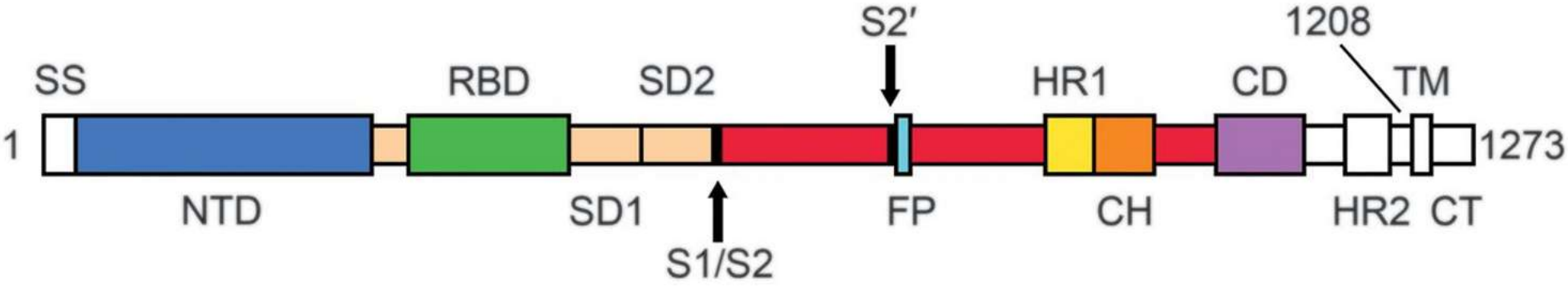
Schematic of SARS-CoV-2 S primary structure

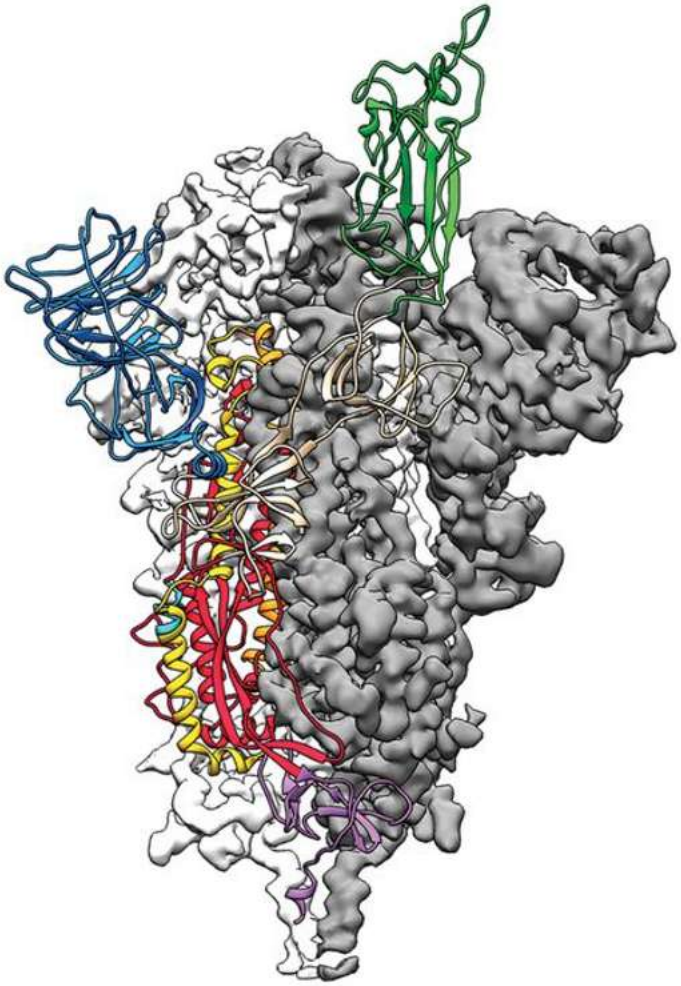


SS - signal sequence
NTD - N-terminal domain
RBD - receptor-binding domain
SD1 - subdomain 1
SD2 - subdomain 2
S1/S2 = S1/S2 protease cleavage site
S2' = S2' protease cleavage site

FP = fusion peptide
HR1 = heptad repeat 1
CH = central helix
CD = connector domain
HR2 = heptad repeat 2
TM = transmembrane domain
CT = cytoplasmic tail

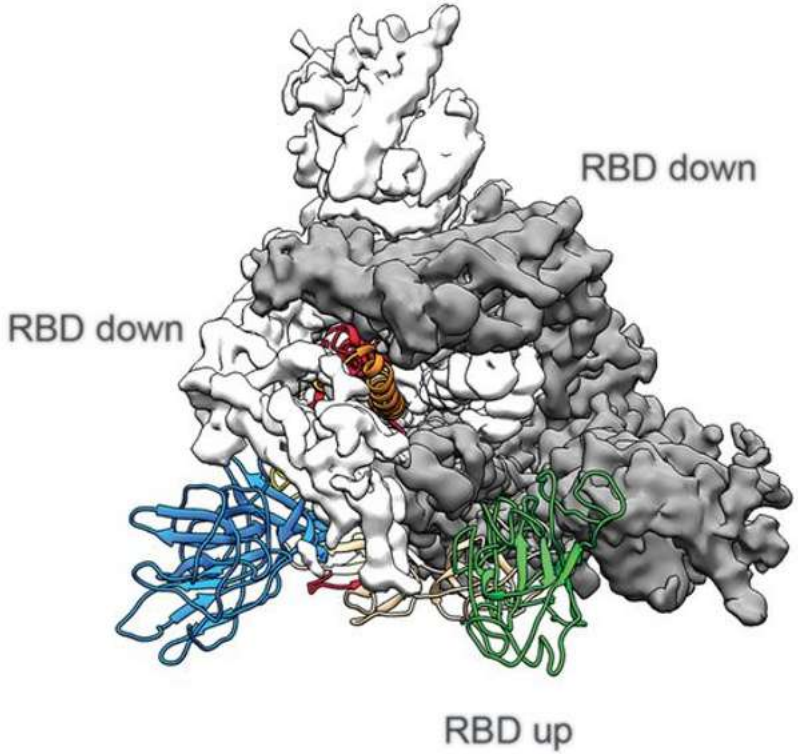
Figure adapted from Wrapp et al. 2020





Viral membrane

90°



The outbreak of COVID-19 caused by SARS-CoV-2 virus has now become a pandemic, but there is currently very little understanding of the antigenicity of the virus. We therefore determined the crystal structure of CR3022, a neutralizing antibody previously isolated from a convalescent SARS patient, in complex with the receptor-binding domain (RBD) of the SARS-CoV-2 spike (S) protein to 3.1 Å. CR3022 targets a highly conserved epitope, distal from the receptor-binding site, that enables cross-reactive binding between SARS-CoV-2 and SARS-CoV. Structural modeling further demonstrates that the binding epitope can only be accessed by CR3022 when at least two RBD on the trimeric S protein are in the “up” conformation and slightly rotated. Overall, this study provides molecular insights into antibody recognition of SARS-CoV-2.

As shown in **Figure 2**, all four insertions are located outside the Receptor Binding Domain (RBD) of spike, in contrast to the original conclusion made by Pradhan *et al*. which stated that the insertions are located on the interface with ACE2.

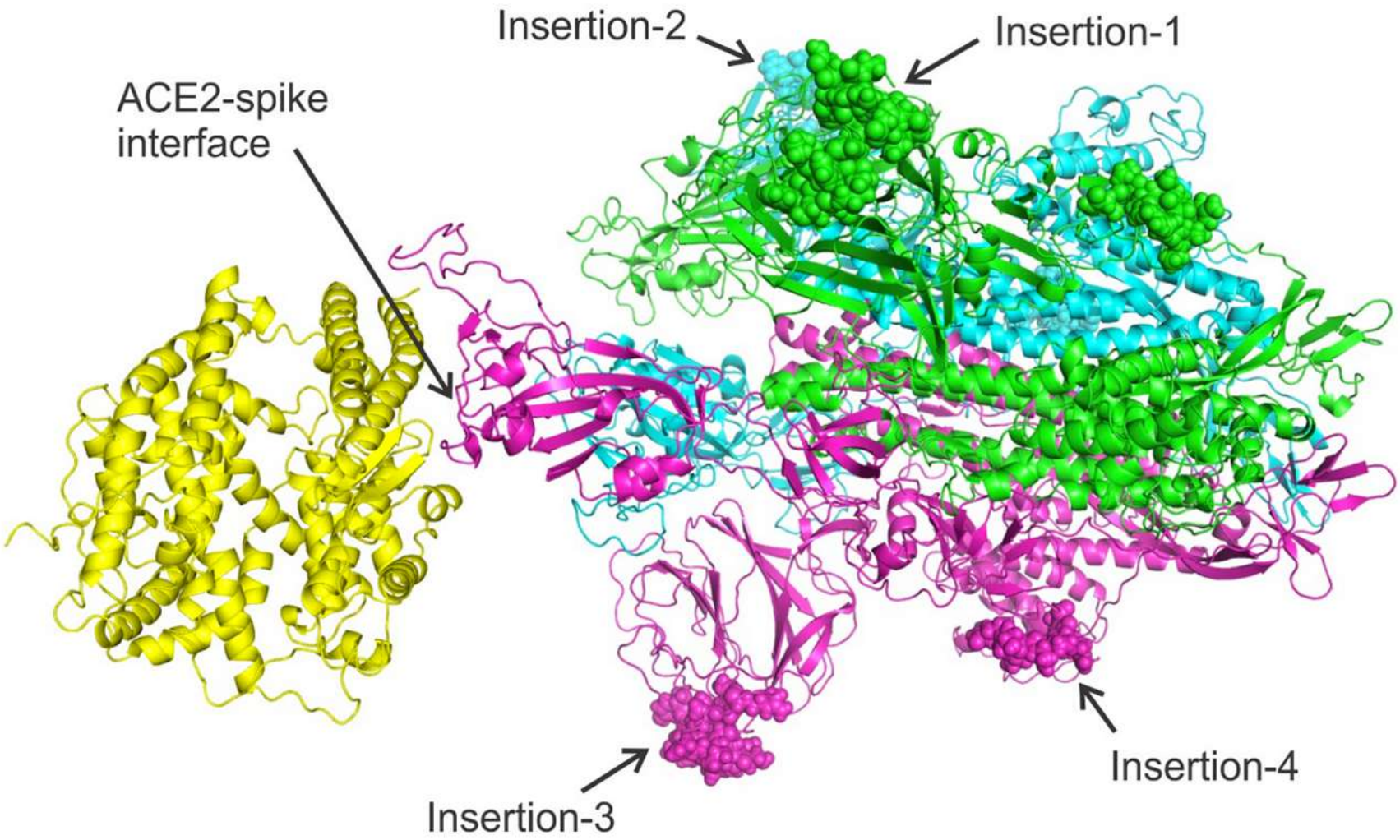
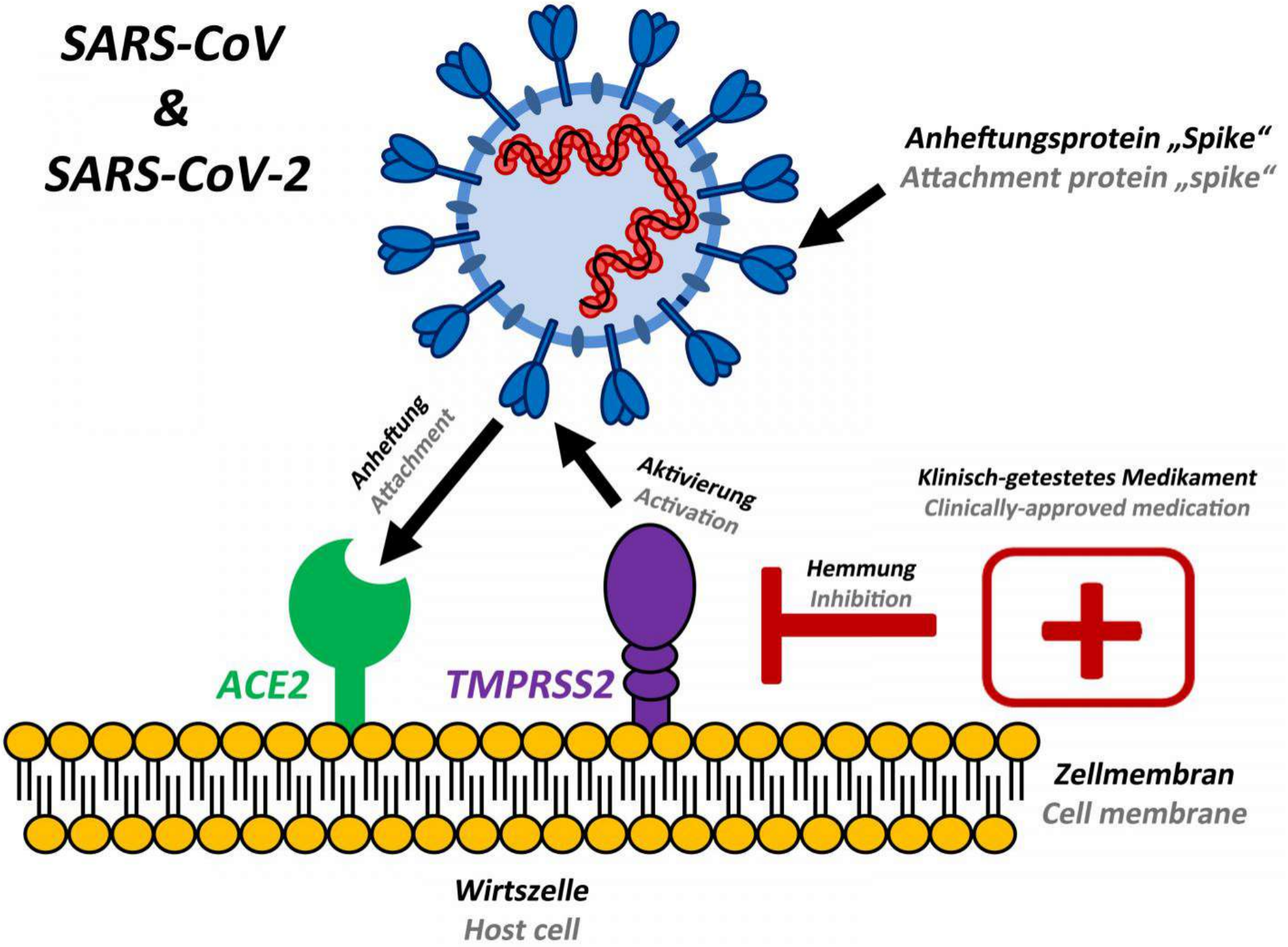
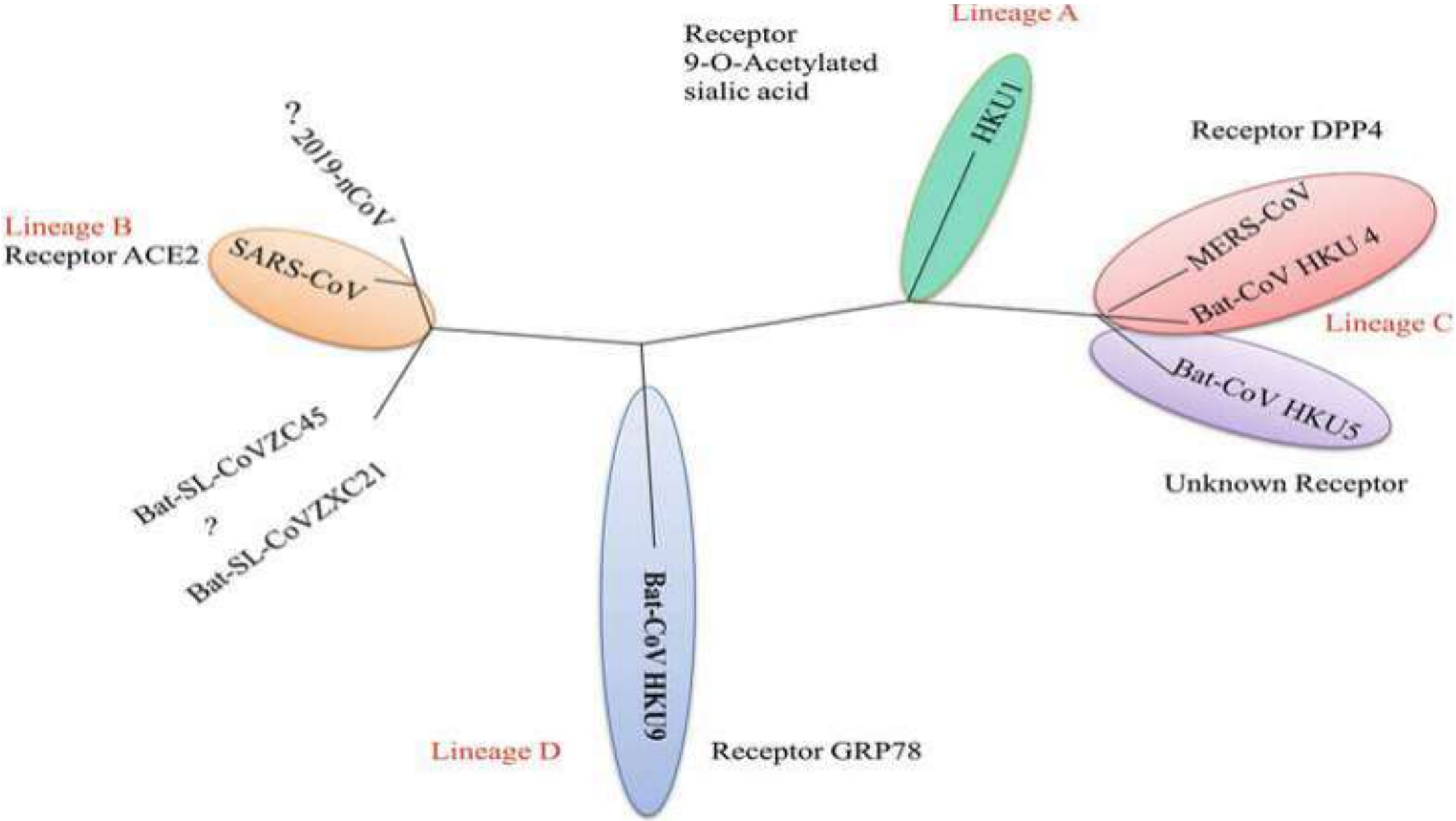
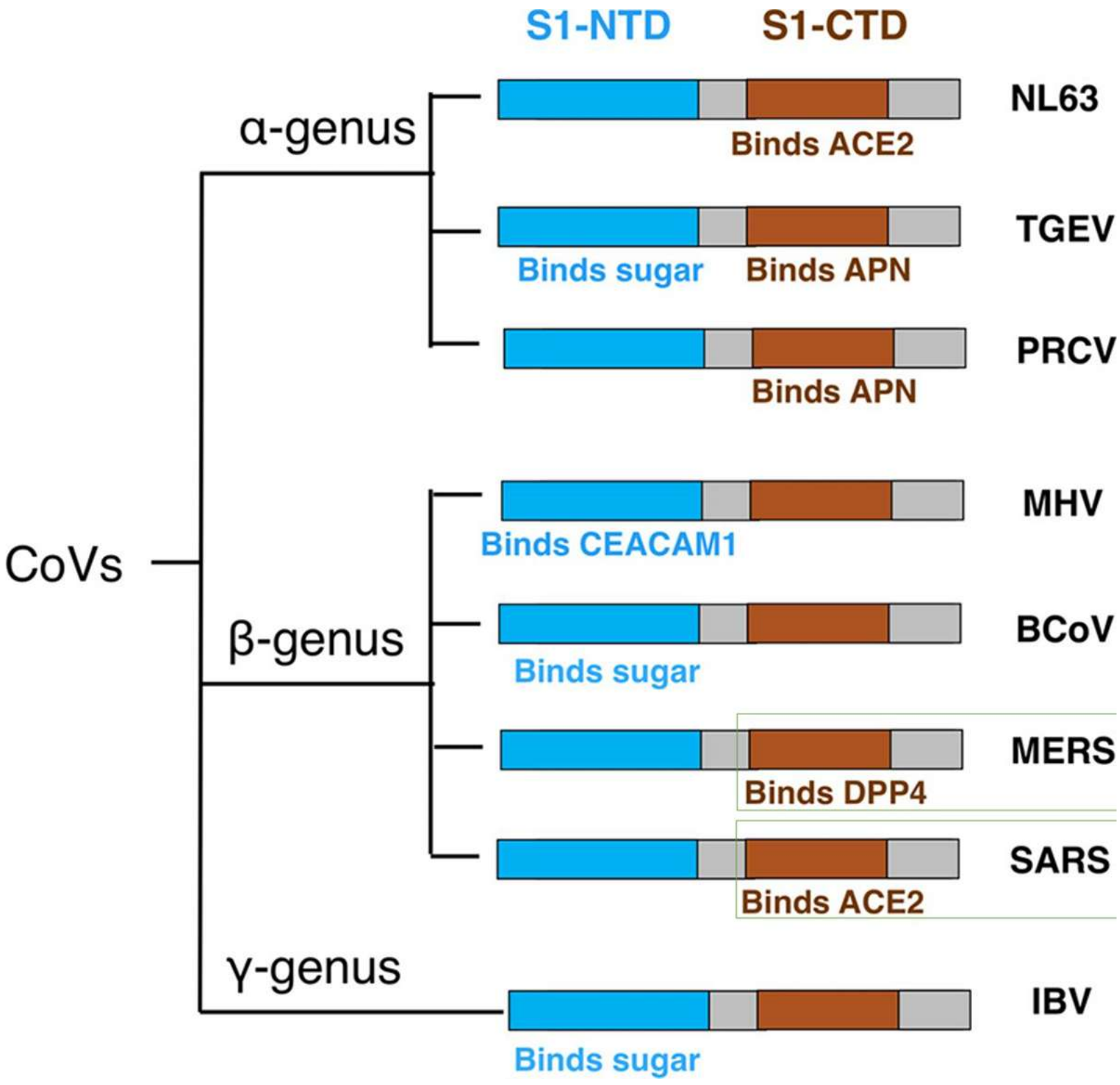


Figure 2. Complex structure model between human ACE2 (left yellow) and 2019-nCoV spike protein trimer (right, with three chains colored in magenta, cyan, and blue respectively) constructed by C-I-TASSER. The four insertions are shown as spheres. During different stages of coronavirus infection, the spike proteins may be post-processed (i.e. cleaved) to produce different isoforms. Therefore, the eventual spike complex might not include all residues of a full-length spike protein. Nevertheless, we construct the complex model using full-length spike sequence to illustrate the locations of the four insertions.


SARS-CoV
&
SARS-CoV-2
Anheftungsprotein „Spike“
Attachment protein „spike“
Anheftung
Attachment
Aktivierung
Activation
Klinisch-getestetes Medikament
Clinically-approved medication
Hemmung
Inhibition
ACE2
TMPRSS2
Zellmembran
Cell membrane
Wirtszelle
Host cell


Lineage A
Receptor
9-O-Acetylated
sialic acid
HKU1
Receptor DPP4
MERS-CoV
Bat-CoV HKU 4
Lineage C
Bat-CoV HKU5
Unknown Receptor
? 2019-nCoV
Lineage B
Receptor ACE2
SARS-CoV
Bat-SL-CoVZC45
?
Bat-SL-CoVZXC21
Bat-CoV HKU9
Lineage D
Receptor GRP78


S1-NTD
S1-CTD
CoVs
α-genus
β-genus
γ-genus
NL63
Binds ACE2
TGEV
Binds sugar
Binds APN
PRCV
Binds APN
MHV
Binds CEACAM1
BCoV
Binds sugar
MERS
Binds DPP4
SARS
Binds ACE2
IBV
Binds sugar