differs from that in SARS-CoV in the

ical for ACE2 binding, namely Y455.

D494S and T501N” (FIG. 3b,¢). Owin

stabilizes the two virus-binding hotsp

of hACE2 (REF.\*°) (FIG. 4a). Moreover, a

in the RBM of SARS-CoV-2 (amin

G-V-E-G) results in a more compac

its hACE2-binding ridge than in SA

five residues crit-

L, L486K, N493Q,

g to these residue

changes, interaction of SARS-CoV-2 with its receptor

ots on the surface

our-residue motif

o acids 482-485:

conformation of

RS-CoV and ena-

bles better contact with the N-terminal helix of hACE2

REF.). Biochemical data confirmed that the structural

eatures of the SARS-CoV-2 RBD has strengthened

its hACE2 binding affinity compared with that of

SARS-CoV,

Similarly to other coronaviruses, SARS-CoV-2 needs

proteolytic processing of the S protein to activate the

endocytic route. It has been shown that host proteases

participate in the cleavage of the S protein and activate

he entry of SARS-CoV-2, including transmembrane

protease serine protease 2 (TMPRSS2), cathepsin L and

urin’?\*\*, Single-cell RNA sequencing data showed

hat TMPRSS2 is highly expressed in several tissues

and body sites and is co-expressed with ACE2 in nasal

epithelial cells, lungs and bronchial branches, which

explains some of the tissue tropism of SARS-CoV-2

(REFS\*°\*’), SARS-CoV-2 pseudovirus entry assays

revealed that TMPRSS2 and cathepsin L have cumu-

lative effects with furin on activating virus entry”.

Analysis of the cryo-electron microscopy structure of

SARS-CoV-2 S protein revealed that its RBD is mostly in

the lying-down state, whereas the SARS-CoV S protein

assumes equally standing-up and lying-down conforma-

tional states\*\*'\*\*\*’. A lying-down conformation of the

SARS-CoV-2 S protein may not be in favour of receptor

binding but is helpful for immune evasion”.