# IMG_8208

ical for ACE2 binding, namely Y455L, L486F, N493Q, D494S and T501N” (FIG. 3b,c). Owing to these residue changes, interaction of SARS-CoV-2 with its receptor stabilizes the two virus-binding hotspots on the surface of hACE2 (REF. (FIG. 3d). 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 our-residue motif 0 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 ocytic route. It has been shown that host proteases icipate in the cleavage of the S protein and activate entry of SARS-CoV-2, including transmembrane ease serine protease 2 (TMPRSS2), cathepsin L and in‘”*5, Single-cell RNA sequencing data showed TMPRSS2 is highly expressed in several tissues body sites and is co-expressed with ACE2 in nasal helial 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”.