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Molecular Interplay between SARS-CoV-2 and Human proteins for viral activation and entry, potential drugs and scope of new therapeutics

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The pandemic Coronavirus Disease 2019 (COVID19) caused by SARS-CoV-2 is a serious public health concern with global mortality reaching 1 million. Whilst the search for a vaccine is underway, there a several antiviral and antibody treatments being clinically evaluated to fill the “therapeutic gap”. The development of potential drugs requires an understanding of SARS-CoV-2 pathogenicity and mechanism of action. Thus, it is essential to understand the full repertoire of viral proteins and their interplay with host factors. Here, we show how the SARS-CoV-2 spike protein undergoes 3 stages of processing to allow virion activation and host cell infection. We also conduct pre-clinical and cohort studies and found effective viral clearance by Arborol drug treatment inpatients. Our comprehensive structural studies reveal why COVID19 is hypervirulent and the reason for the failure of several antibody treatments to date. We demonstrate via molecular dynamics and functional studies how the host proteins CD26, Furin and TMPRSS2 process the viral spike glycoprotein and assist in the viral entry in addition to ACE2. These results cognize the detailed mechanism of spike glycoprotein and reveal new avenues for potential therapeutics to block different stages of viral entry and new pathways for vaccine development.

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