

Figure 1. Origin and transmission of pathogenic human coronaviruses. Yellow and red arrows indicate mild and severe infections in humans, respectively. The figure is inspired from Jie Cui et al. [49] and the illustrations of coronaviruses (left) are adapted from “Desiree Ho, Innovative Genomics Institute”, available at <https://innovativegenomics.org/free-covid-19-illustrations/>.

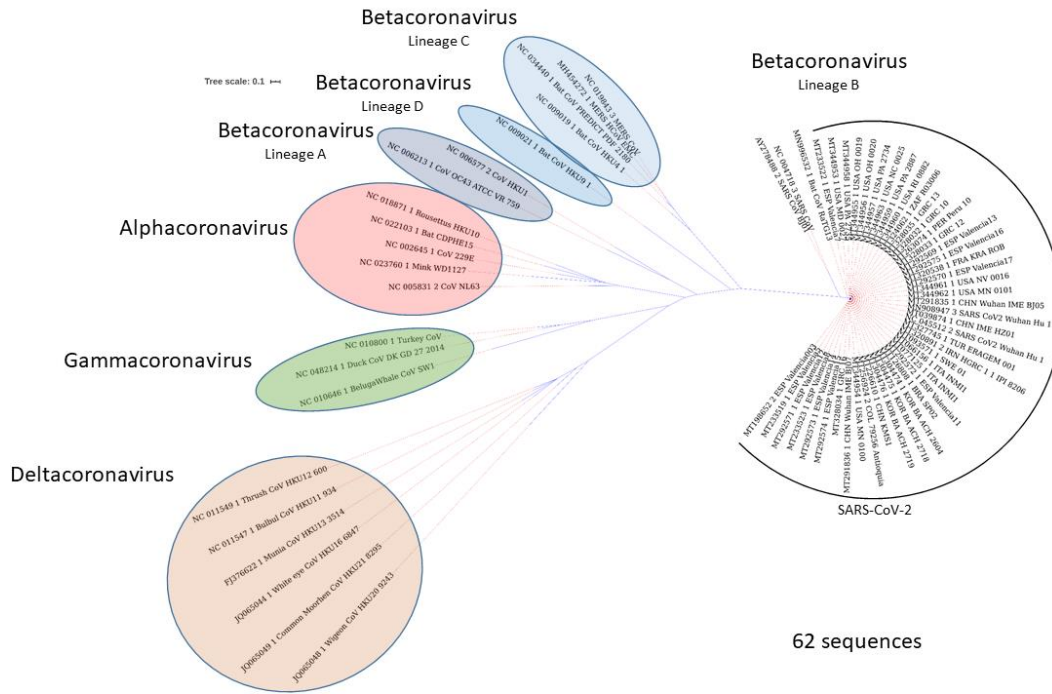


Figure 2: Phylogenetic relationships in the coronavirinae subfamily: the subfamily is formed by four genera: *Alphacoronavirus*, *Betacoronavirus* (linease A, B, C, and D), *Gammacoronavirus*, and *Deltacoronavirus*. We randomly picked 62 SARS-CoV-2 genome sequences, representing 15 different countries, together with other coronavirinae subfamily members. The phylogenetic tree was created using NgPhylogeny.fr tool. The analysis indicates that SARS-CoV-2 has a close relationship with Bat coronavirus RaTG13, and SARS-CoV; therefore classified as a new member of the lineage B *Betacoronavirus*.

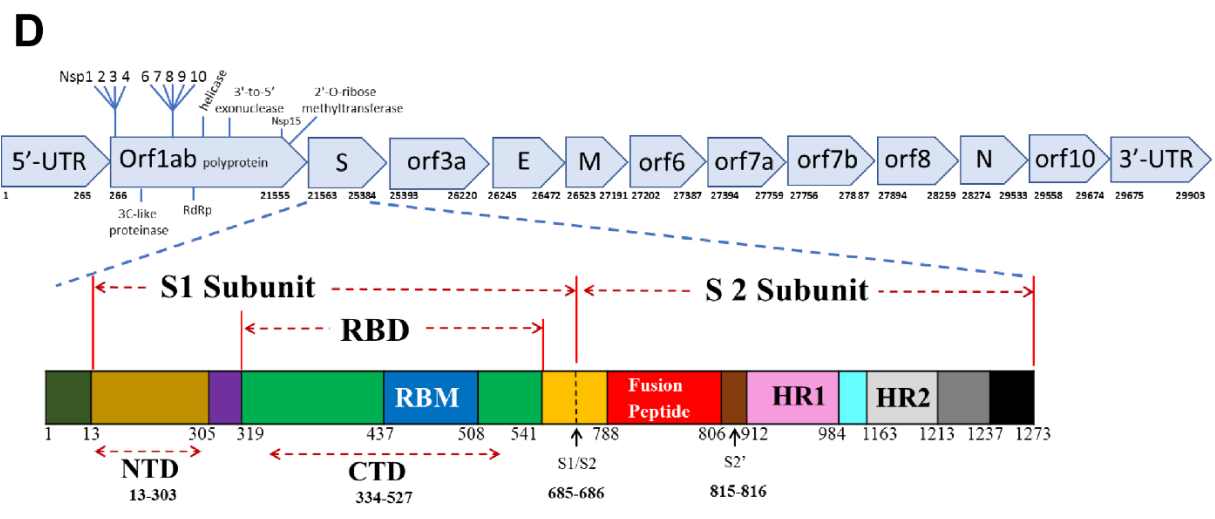
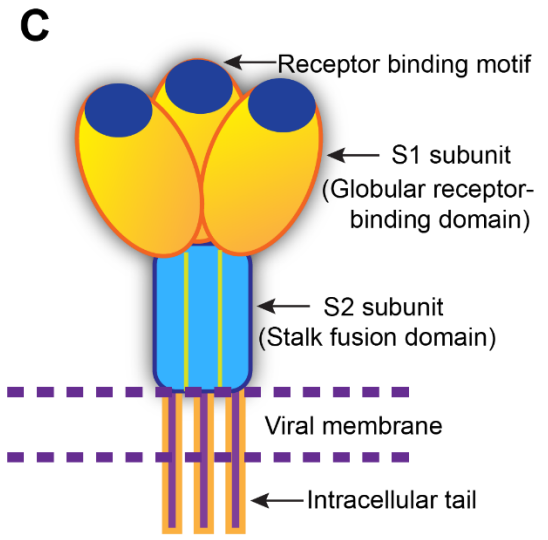
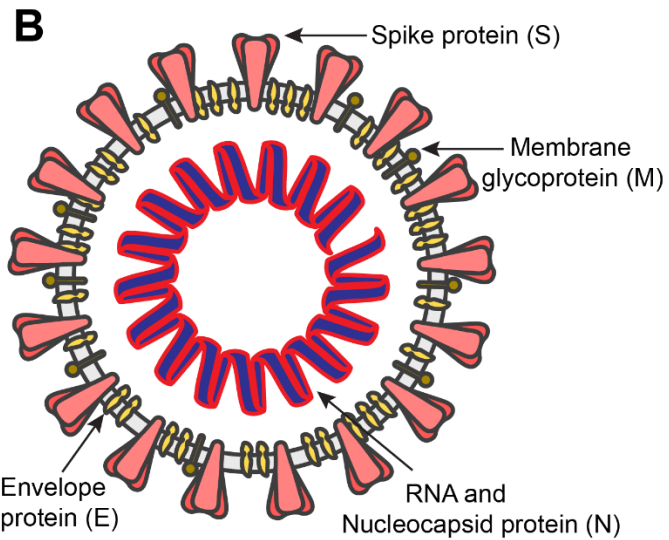
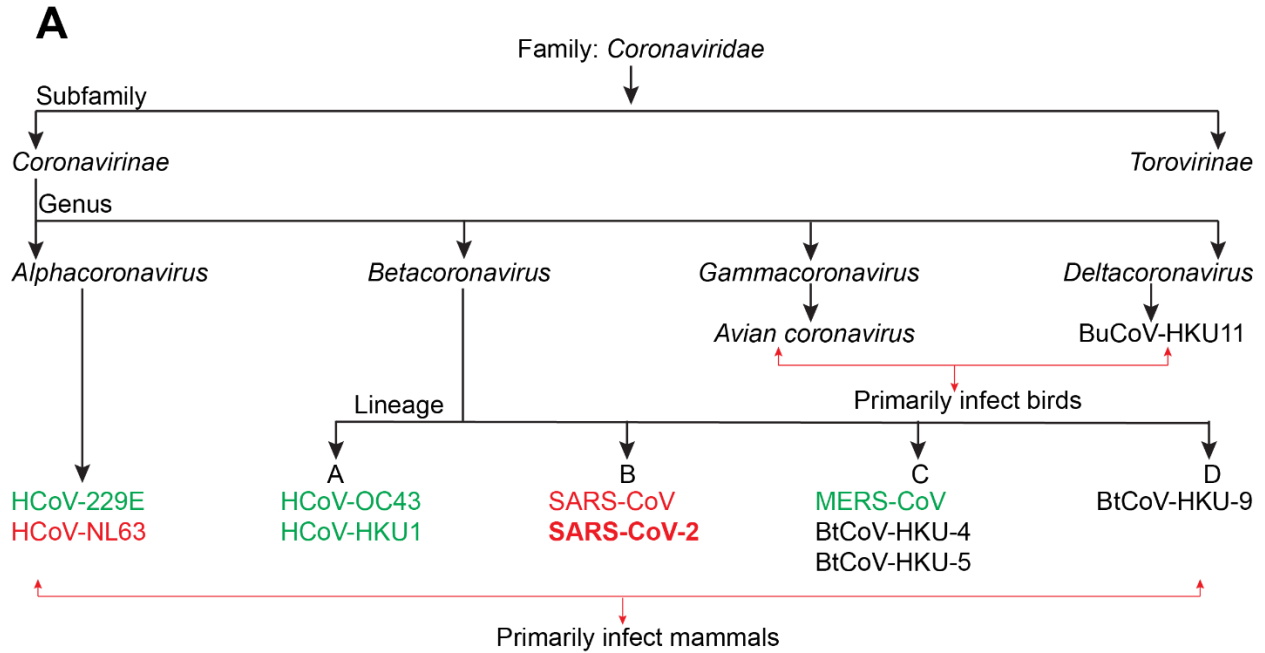


Figure 3. (A) Classification of coronaviruses: the seven known human coronaviruses (HCoVs) are shown in green and red. HCoVs in red bind the host receptor ACE2. (B) Schematic of the SARS-CoV-2 structure, illustration of virus is adapted from “Desiree Ho, Innovative Genomics Institute”, available at <https://innovativegenomics.org/free-covid-19-illustrations/>. (C) Cartoon depicts key features and the trimeric structure of the SARS-CoV-2 spike protein. (D) Schematic of SARS-CoV-2 genome (top) and spike protein (bottom); annotations are adapted from the NCBI (NC_045512.2) and Expaty (<https://covid-19.uniprot.org/uniprotkb/P0DTC2>), respectively.

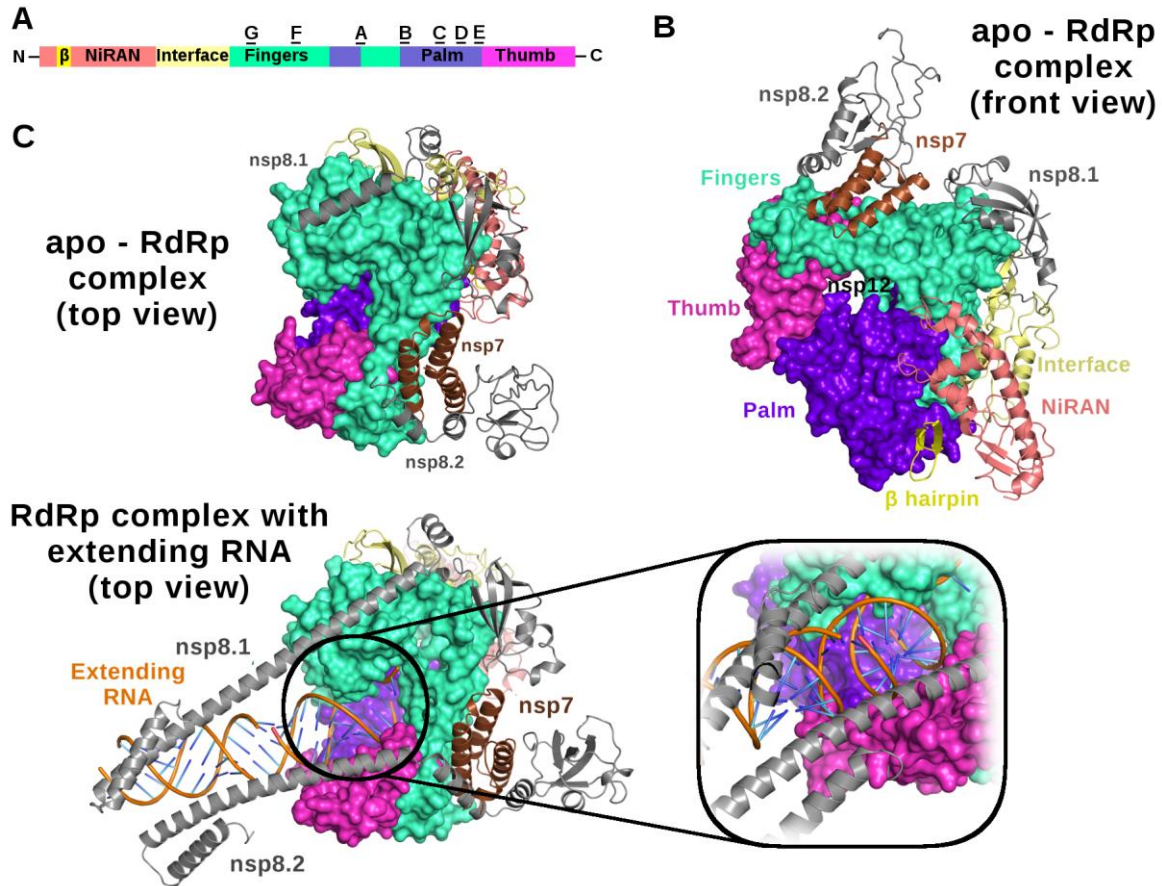


Figure 4. Cryo-EM structure of RNA dependent RNA polymerase (RdRp) of SARS-CoV-2. **(A)** The domain architecture of RdRp or nsp12 gene of SARS-CoV-2 subdivided into NiRAN, interface, finger, palm, and thumb subdomains, with A-G indicating the conserved motifs. **(B)** The cryo-EM structure of apo RdRp, PDB ID: 7BV1, complex (designated as front view) consisting of RdRp or nsp12, nsp7 (brown) and two chains of nsp8 (nsp8.1 and nsp8.2, both in grey), the subdomains of RdRp are colored according to the scheme (A) mentioned previously. A clear groove formed by the intersection of finger and thumb can be seen. While the nsp8.1 interacts directly with nsp12, nsp8.2 binds to nsp7 that interacts with nsp12, **(C)** The cryo-EM structure of RdRp complex bound to RNA, PDB ID: 6YYT, showing the two nsp8 chains stabilizing the extending RNA chain with their extended alpha helix (designated here as top view). The active site is expanded to show the RNA molecules coming out of the groove formed between the finger and the thumb.

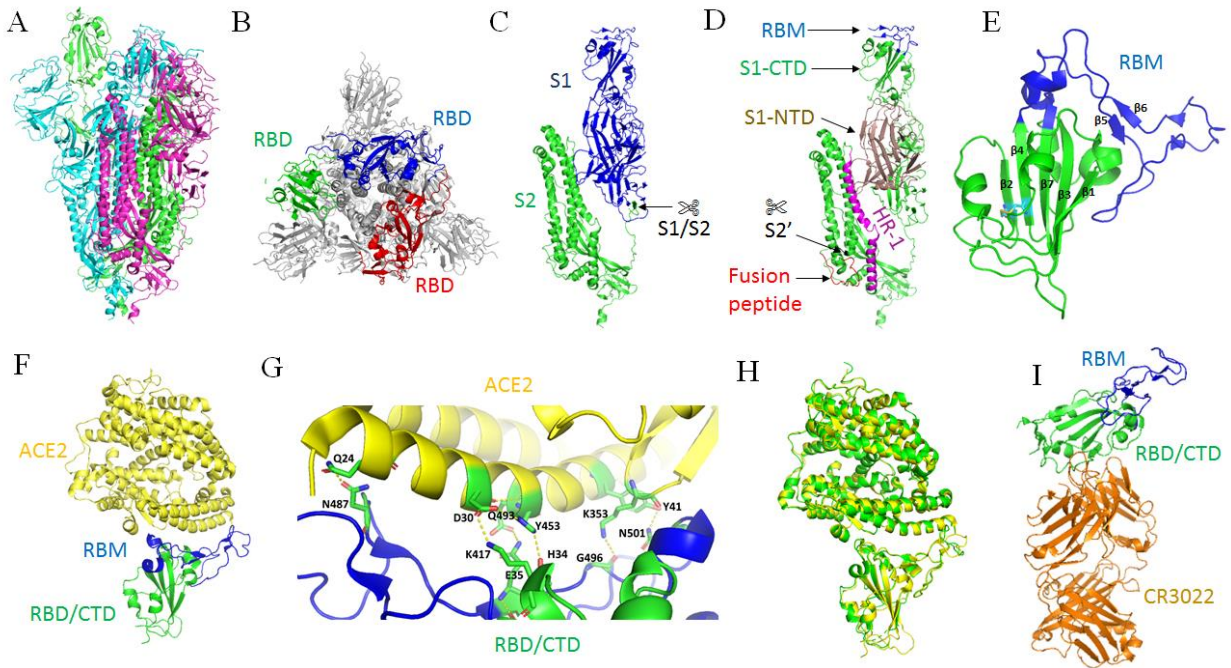


Figure 5. Structure of the SARS-CoV-2 spike protein alone and in complex with ACE2 receptor. **(A)** Side view of the trimeric SARS-CoV-2 spike ectodomain in the prefusion state (PDB ID: 6VSB). The protomer in green is in the “up” conformation and other two protomers in red and cyan are in “down” conformation. **(B)** Top view of the trimeric spike protein showing receptor binding domains (RBDs) in red, blue, and green on each protomer. **(C)** Structure of a single protomer showing the receptor-binding subunit S1 in blue and the membrane-fusion subunit S2 in green. The Furin-like protease site at the boundary of S1/S2 subunits is depicted. **(D)** The S1 subunit contain the receptor binding motif (RBM) in the CTD region in blue, and the NTD region in sand. The S2 subunit contain the fusion peptide in red, second cleavage site S2’ in black, and HR1 in pink. **(E)** Structure of the RBD, core subdomain in green and RBM in blue (PDB ID: 6LZG). **(F)** Structure of the SARS-CoV-2-RBD in complex with ACE2 receptor (PDB ID: 6LZG). **(G)** SARS-CoV-2-RBD: ACE2 receptor polar interface shown by specific residues. **(H)** Structural similarity between the SARS-CoV-RBD: hACE2 (green) and SARS-CoV-2-S-CTD: hACE2 (yellow) complexes. **(I)** Crystal structure of the SARS-CoV-2-RBD (green) in complex with a monoclonal antibody CR3022 (orange). The RBM and CR3022 binding sites do not overlap and are distantly located on the RBD (PDB ID: 6W41). The figures are prepared using Pymol.

Supplementary Figure S1

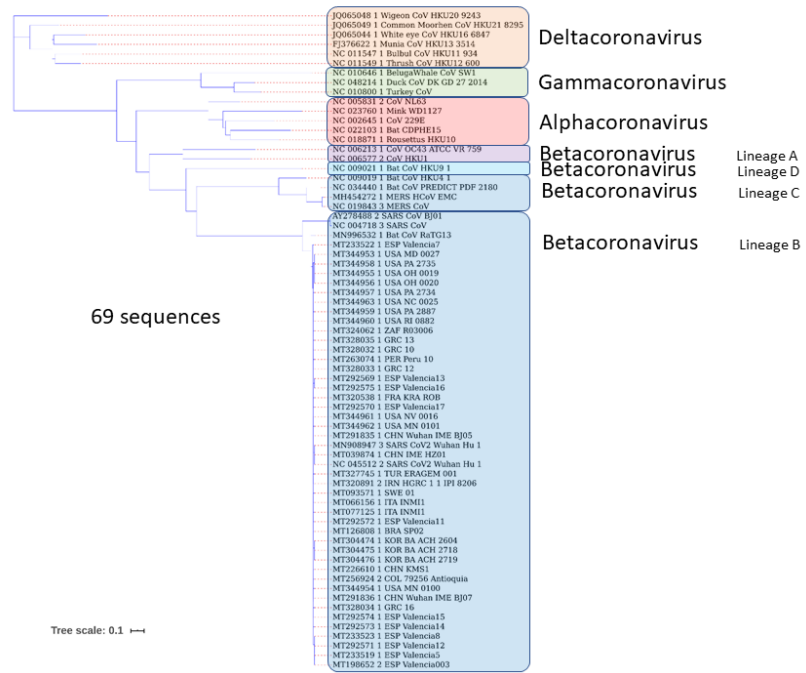


Figure S1. The figure depicts the phylogenetic tree drawn for 69 coronavirus genomic sequences including SARS-Co-2 sequences. Sequences belonging to different coronavirus subfamily have been labelled.