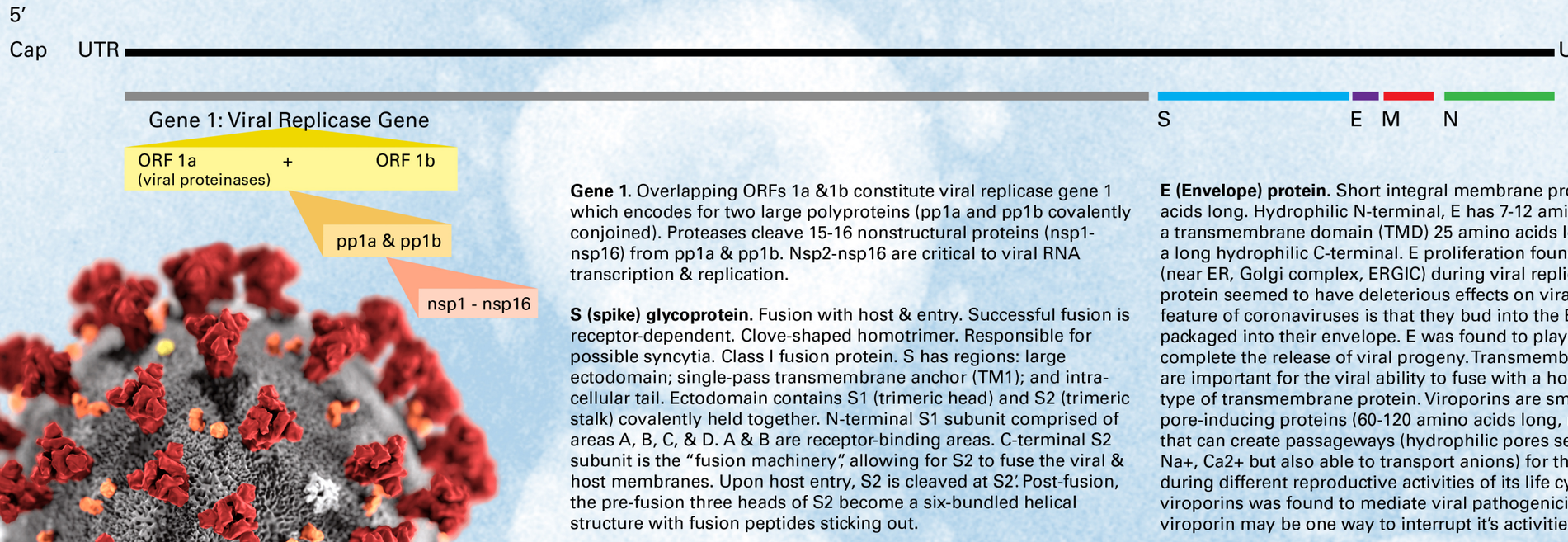
Order: *Nidovirales* Family: *Coronaviridae*

Surrounded by a fringe/crown of S (spike) glycoproteins. Largest +ssRNA genome 26-32 kilobases long. Tubular nucleocapsid helical symmetry. Pleomorphic. 5'capped leader (untranslated sequences, UTR 65-78 nucleotides long). UTRs help regulate replication and transcription. Nested mRNAs all share the same 5'end sequence. Gene 1 (20-22 kilobases long, ~2/3 entire genome). Spike (S) protein gene; E (envelope) protein gene; M (transmembrane) protein gene; N (nucleocapsid) gene; another 200-300 nucleotide UTR sequence; plus poly-A tail at 3' end. 7-14 open reading frames (ORF proteins) interspersed plus HE (hemagglutinin-esterase) glycoprotein gene, and accessory protein genes. Replication in cytoplasm. Assembly of virions and budding into endoplasmic reticulum & Golgi cisternae; virions exocytosed.



2019-nCoV by CDC/ Alissa Eckert, MS; Dan Higgins, MAM [Public domain]

Gene 1. Overlapping ORFs 1a &1b constitute viral replicase gene 1 which encodes for two large polyproteins (pp1a and pp1b covalently conjoined). Proteases cleave 15-16 nonstructural proteins (nsp1-nsp16) from pp1a & pp1b. Nsp2-nsp16 are critical to viral RNA transcription & replication.

S (spike) glycoprotein. Fusion with host & entry. Successful fusion is receptor-dependent. Clove-shaped homotrimer. Responsible for possible syncytia. Class I fusion protein. S has regions: large ectodomain; single-pass transmembrane anchor (TM1); and intra-cellular tail. Ectodomain contains S1 (trimeric head) and S2 (trimeric stalk) covalently held together. N-terminal S1 subunit comprised of areas A, B, C, & D. A & B are receptor-binding areas. C-terminal S2 subunit is the "fusion machinery", allowing for S2 to fuse the viral & host membranes. Upon host entry, S2 is cleaved at S2'. Post-fusion, the pre-fusion three heads of S2 become a six-bundled helical structure with fusion peptides sticking out.

N (Nucleocapsid) protein. Responsible for phosphorylated helical nucleocapsid. Located near the endoplasmic reticulum (ER) and Golgi complex area. Expression of the N gene found to coincide with increased production of virus-like particles (VLPs) & N may contribute towards producing whole & viable virions.

M (Transmembrane) protein. 3 transmembrane areas influencing envelope shape. In the Golgi complex, M is glycosylated contributing to its ability to bind at receptor sites. M interacting with S caused S aggregation in the ER-Golgi intermediate compartment (ERGIC, mediate transport between the ER and Golgi complex) allowing for packaging into new virions. M interacting with N increased nucleo-capsid stability. M & E protein interaction contributed to the maintenance of the envelope, the production and release of VLPs.

E (Envelope) protein. Short integral membrane proteins 76-109 amino acids long. Hydrophilic N-terminal, E has 7-12 amino acids followed by a transmembrane domain (TMD) 25 amino acids long and ending with a long hydrophilic C-terminal. E proliferation found inside the host (near ER, Golgi complex, ERGIC) during viral replication. Lack of E protein seemed to have deleterious effects on viral progeny. An unique feature of coronaviruses is that they bud into the ERGIC where they get packaged into their envelope. E was found to play a role in scission to complete the release of viral progeny. Transmembrane areas (TMDs) are important for the viral ability to fuse with a host. Viroporins are a type of transmembrane protein. Viroporins are small viral pH-sensitive pore-inducing proteins (60-120 amino acids long, mostly hydrophobic) that can create passageways (hydrophilic pores selective for H+, K+, Na+, Ca2+ but also able to transport anions) for the virus to utilize during different reproductive activities of its life cycle. The lack of viroporins was found to mediate viral pathogenicity. Targeting a virus's viroporin may be one way to interrupt it's activities.

HE (Hemagglutination and Esterase) protein. Found in some betacoronaviruses & is associated with the viral envelope. HE acts like hemagglutinin (HA) and binds to sialic acid (Sia) which is a derivative of neuraminic acids, 9-carbon backbone acidic sugars (N-acetylneuraminic acid). Sia sometimes used synonymously as N-acetylneuraminic acid. Sia is important in maintaining a mucous defense. HA binds to Sia of mucins disrupting this mucous defense system.

Clinical. Upper respiratory tract infections (URTIs) like common cold; lower respiratory tract infections (LRTIs) like bronchitis, pneumonia, severe acute respiratory syndrome.

Last Update: 02.05.2020 Background photo: CDC/Dr. Fred Murphy. Poster ©2020 Shirley Chung

Coronavirinae

Virions: 80-220nm; enveloped; spherical.

Alphacoronavirus

HCoV-229E*
aminopeptidase N (hAPN) receptor; human (with 229E-variants in bats & camels).

HCoV-NL63*
zinc peptidase angiotensin converting enzyme 2 (ACE2) receptor; human.

Betacoronavirus

MHV mouse hepatitis virus.

HCoV-OC43*
9-O-acetylsialic acids receptor; human.

SARS-HCoV
zinc peptidase angiotensin converting enzyme 2 (ACE2) receptor; human.

HCoV-HKU1*
9-O-acetylsialic acids receptor; human.

HCoV-HKU4
serine peptidase dipeptidyl peptidase 4 (DPP4) receptor, bat.

MERS-CoV Middle Eastern Respiratory Syndrome
serine peptidase dipeptidyl peptidase 4 (DPP4) receptor; human.

Other animal coronaviruses.

Gammacoronavirus

Viruses of whales & birds.

Deltacoronavirus

Viruses isolated from pigs & birds.

Torovirinae

Virions 120-140nm; enveloped; disc, kidney, rod shaped; usually infects horses, cattle, pigs, cats, goats.

Bafinivirus

Torovirus

* Responsible for 1/3 of common cold in humans.

SARS-CoV-2

Origins & Genome

- SARS-CoV-2 is the virus causing the disease COVID-19.
- SARS-CoV-2 was first found & recognized in Wuhan, China.
- Genetically closest to SARS-CoV (shared 79.5% similarity) in the Betacoronaviruses (Nidovirales, Coronaviridae, Coronavirinae, Betacoronavirus, Sarbecovirus), and also shares similiarities with bat SARS-like variants, possibly BatCoV RaTG13 (96.2%).
- Virus was thought to have crossed over to humans from bats.
- The report trying to link HIV to SARS-CoV-2 was erroneous.
- Reports of SARS-CoV-2 originating from snakes were erroneous.
- Approx 29 kilobases (29,000 nucleotide bases) long.
- As of 02.05.2020, GenBank produced 44 nucleotide sequences for SARS-CoV-2 (https://www.ncbi.nlm.nih.gov/genbank/2019-ncov-seqs/#nucleotide-sequences).

Clinical Presentation

- Produces acute respiratory illnesses, fever, cough, difficulty breathing/shortness of breath. The severity of symptoms is variable.
- SARS-CoV-2 targets the angiotensin converting enzyme 2 (ACE2) receptor.
- Incubation ranges between 2-14 days.
- Use standard airborne disease precautions.