Viewpoint: Forty years with coronaviruses

As a career researcher of coronaviruses, Susan R. Weiss, PhD offers insight from 40 years of research.

**Transcription**
- Coronaviruses use noncontiguous transcription involving viral polymerase, which jumps from one part of the genome template to another

**Implications**
- High rate of recombination, which plays a role in interspecies infections
- The sequence change that enabled bat to human transfer has yet to be characterized

**Cellular Receptor**
- MERS uses DPP4 receptor
- SARS-CoV and SARS-CoV-2 use ACE2 receptors

**Implications**
- Cell receptor expression does not necessarily correlate with viral tropism
- Cannot infer viral pathogenesis from knowledge of the spike protein and receptor alone

**Glycoprotein Cleavage**
- SARS-CoV-2 spike protein (S) is cleaved by the enzyme furin into S1 and S2 subunits
- The second cleavage creates S2', which exposes fusion peptide for viral entry

**Implications**
- Furin cleavage site in S1/S2 differentiates SARS-CoV-2 from SARS-CoV, but makes it similar to other bat viruses
- This makes furin a potential target for a protease inhibitor antiviral

**Conserved Sequences**
- Virally-encoded enzymes conserved across the coronavirus family function in both replication and evasion of host-directed immune responses

Understanding the roles of these viral proteins will reveal how they evade host-directed responses and serve as antiviral targets. Further studies on background genes (nucleocapsid, replicase, accessory) are needed to define tropism.

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