How does the Spike protein on the surface of SARS CoV 2 Work?

The corona virus bears its name from the crown-like structure around it. Constituting this are the spike proteins (S glycoprotein) which are key to cellular recognition and membrane fusion mechanisms.

→ Camouflaged by glycoproteins for host immune evasion.

Structure of the S protein.

The S protein is a homotrimer consisting of 3 similar subunits. Prior to viral packing in host cell, after synthesis of the viral polypeptides, at the golgi apparatus, the polypeptide chain bears a FURIN cleavage site at the S1/S2 boundary. This causes the S1 and S2 subunits to be non-covalently held together and this priming event is believed to confer extra virulence to SARS CoV 2 compared to previous lineages.

Not Sufficient for fusion competent.

RBD to ACE-2

S1 Subunit

S2 Subunit

- The S1 subunit is complementary to the ACE 2 receptor expressed mainly on the surface of lung epithelial cells.
- For interaction between receptor and RBD, RBD constantly flip between on and off state.
  - Can interact
  - cannot & has some degree of immune evasion.

From there, the va virus can enter the cell via 2 different pathways.

S1 binds to ACE2 to promote fusion of endosomes.

Late Entry: The virus binds to ACE 2, activating its endocytosis pathway. The ca virus is captured in an endosome.

→ As endosome matures, pH decreases to enhance activity of hydrolases.

→ When pH ~~decreases~~ decreases, to a certain point, Cathepsin L is activated and cleaves the S2' site on the virus.

→ Before the virus is fully destroyed, the cleaving at the S2' site engages the membrane fusion machinery by exposing the fusion peptides. ~~triggered~~ triggering event.

S1 Subunit is released during this process. ←

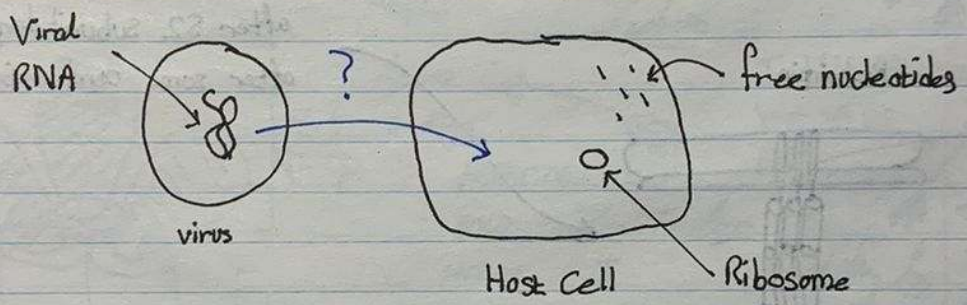
S2 Subunit

Fusion Peptide.

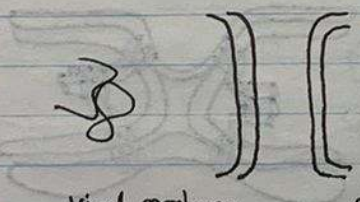
Early Entry Pathway

If the cell expresses TMPRSS2 on its surface, simultaneous to ACE 2 binding S2' site is cleaved initiating membrane fusion at plasma membrane, bypassing the endosomal pathway.

S2 Subunit

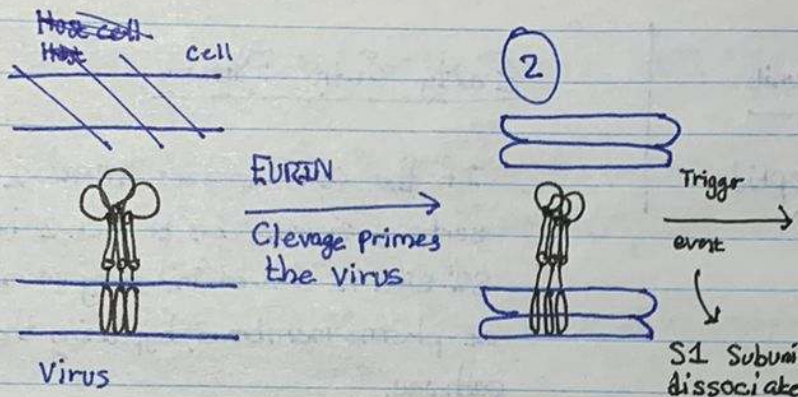


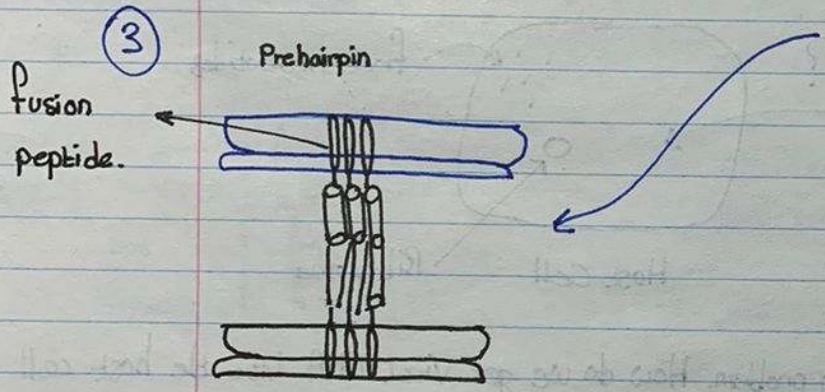
We have the following problem. How do we get Viral RNA into the host cell to be able to use its resources?

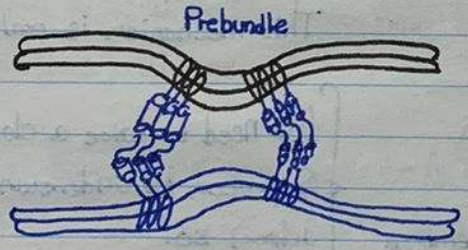


This mechanism is really fascinating

We need to take a closer look at the S protein to understand how it ~~achieves~~ achieves so.



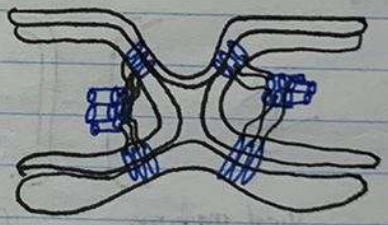




Close Apposition.

The extended S2 subunit breaks into 2 parts.

⑤ Bundle Hemifusion



These parts reassociate to form a hexamer.

In doing so, the membrane is pulled inwards.