

Coronavirus membrane fusion mechanism opportunistic model for SARS-CoV-2 fusion

Overview

Virus binding and it's fusion function.

Replication Process.

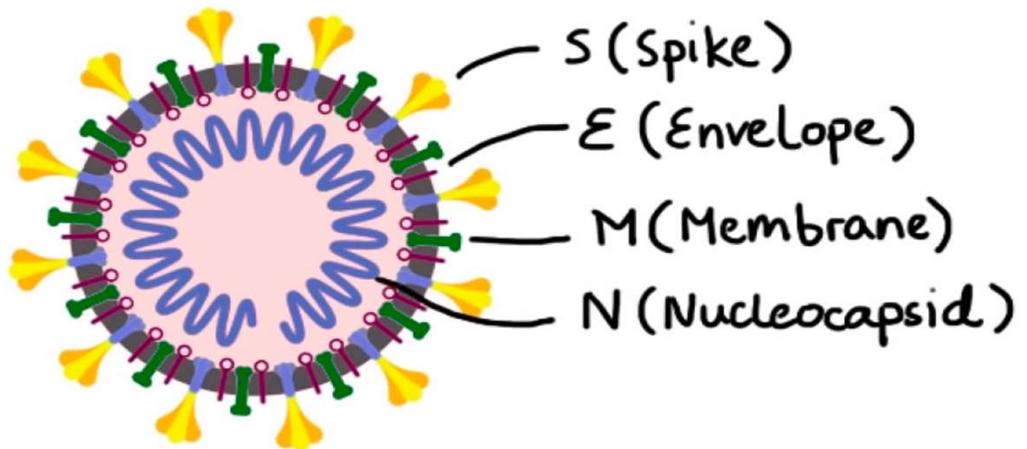
Sars-Cov Images and it's brief overviews.

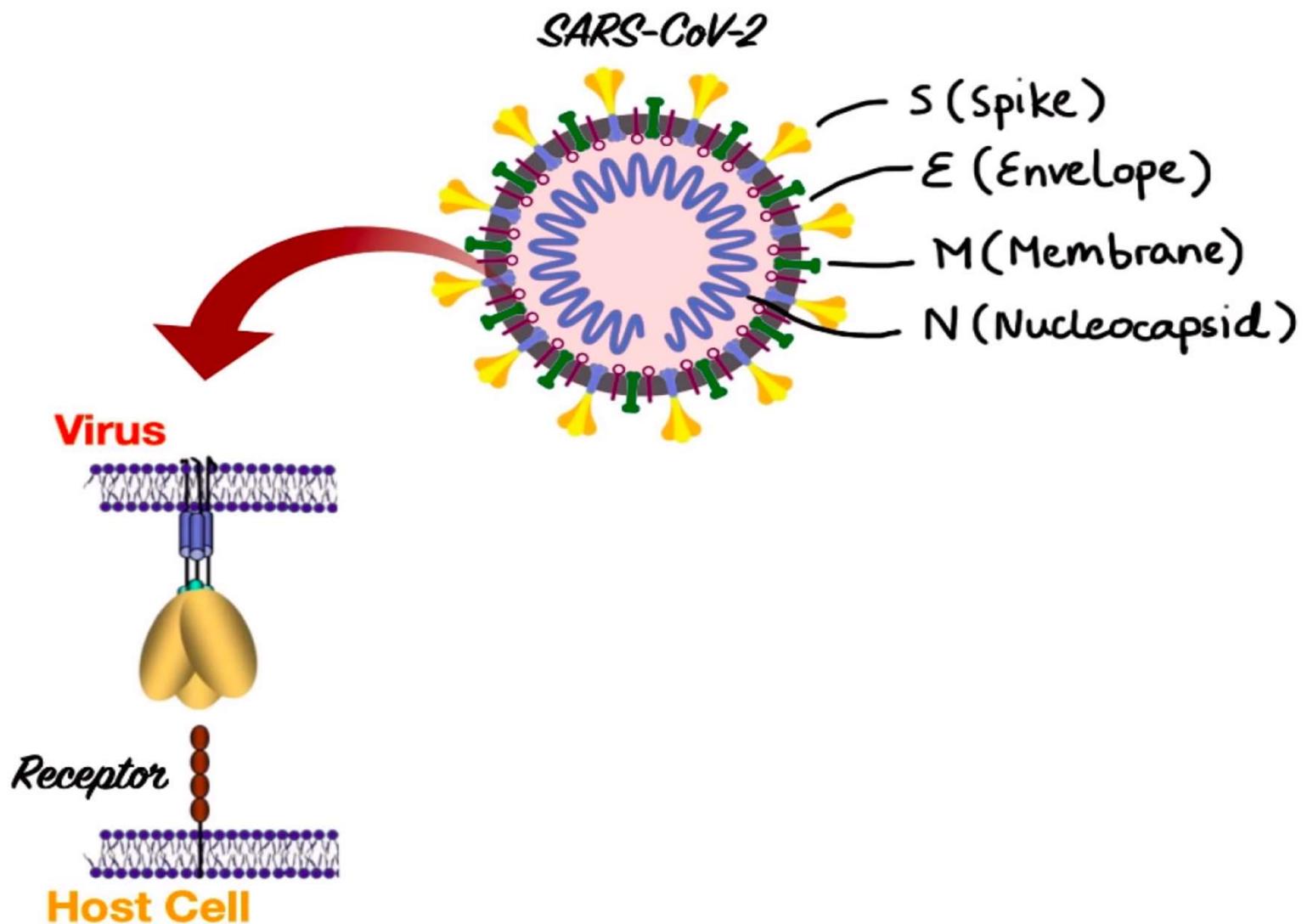
Life Cycle of SARS-CoV-2

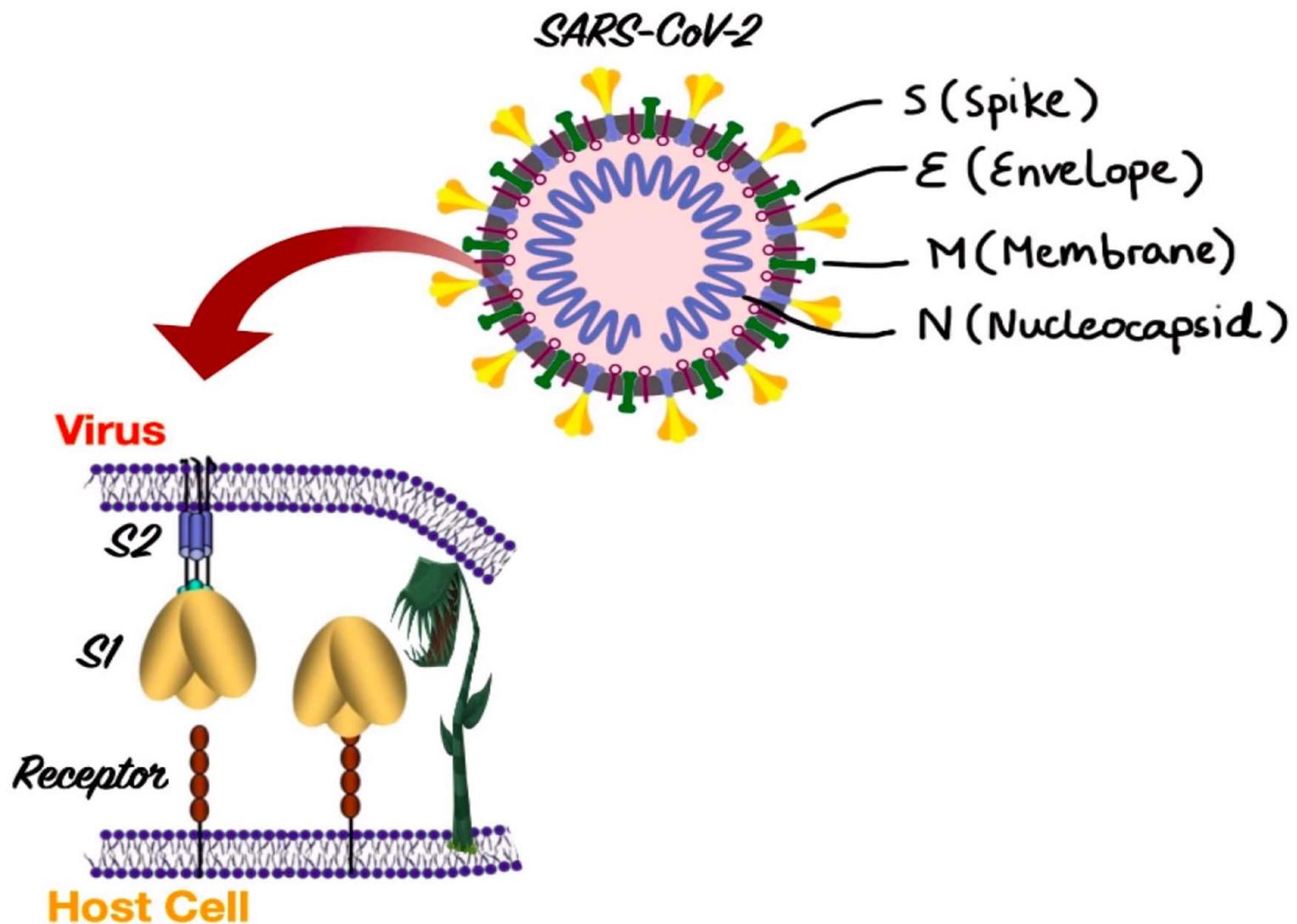
Virus Binding and it's fusion Functions

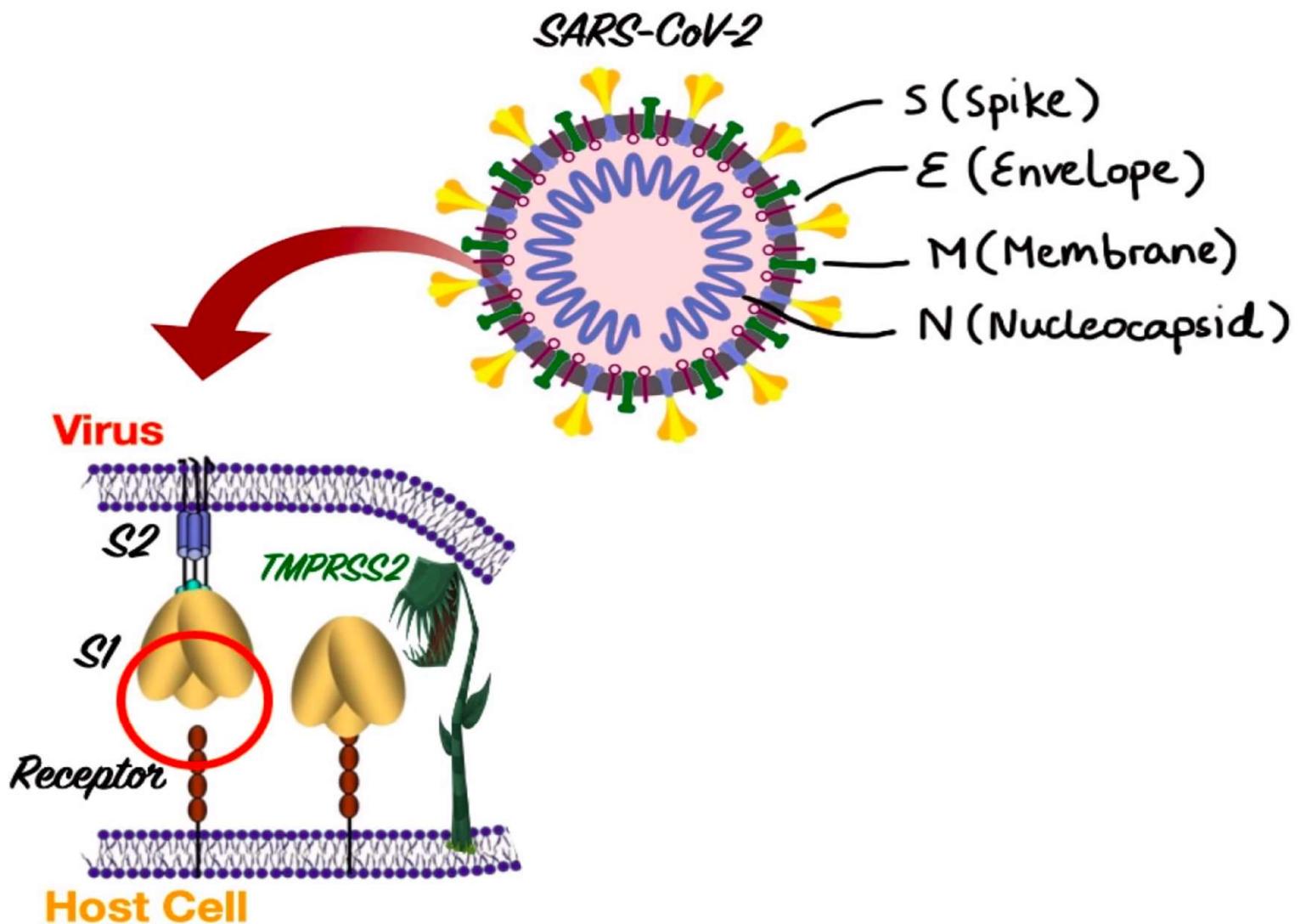


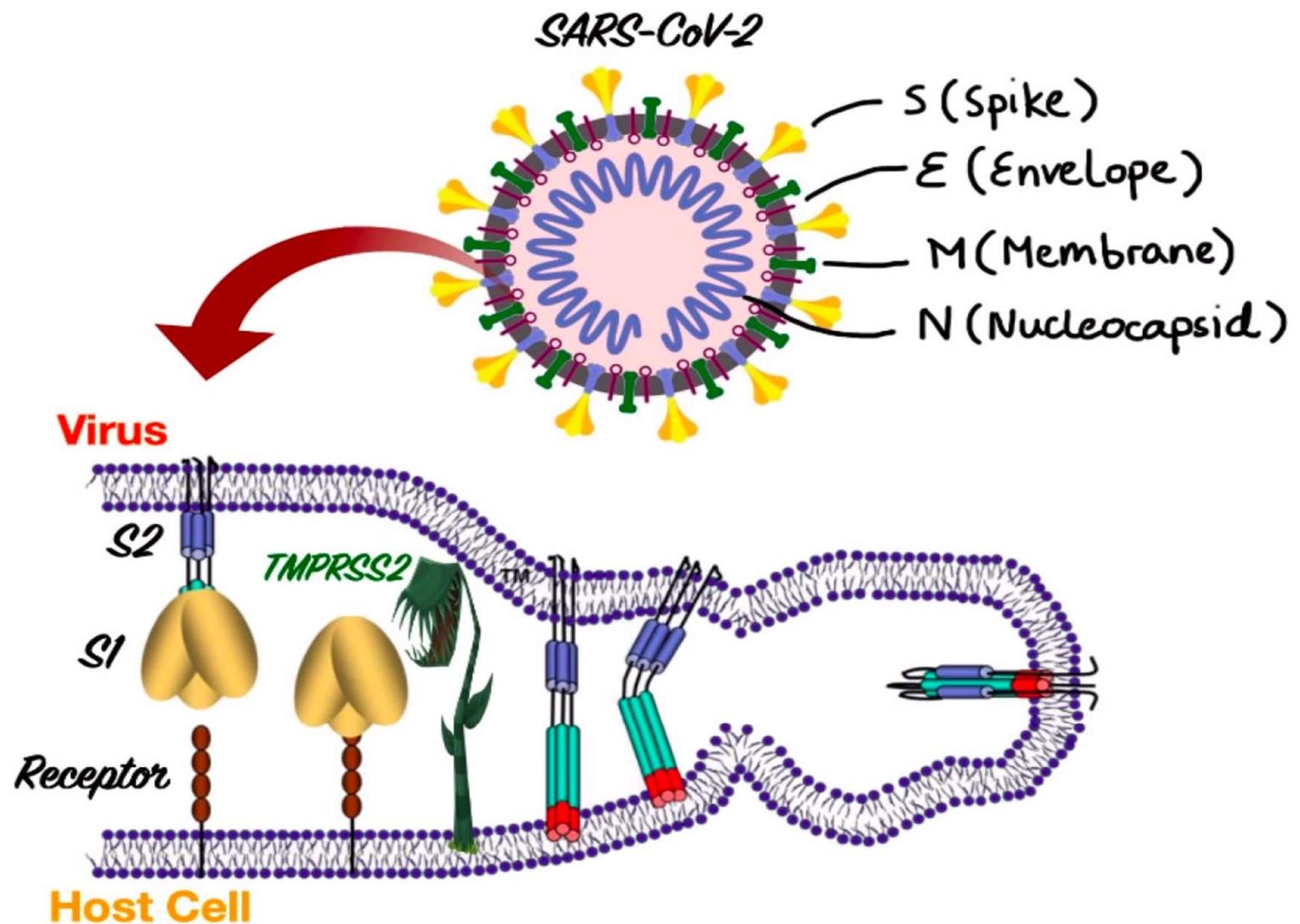
SARS-CoV-2

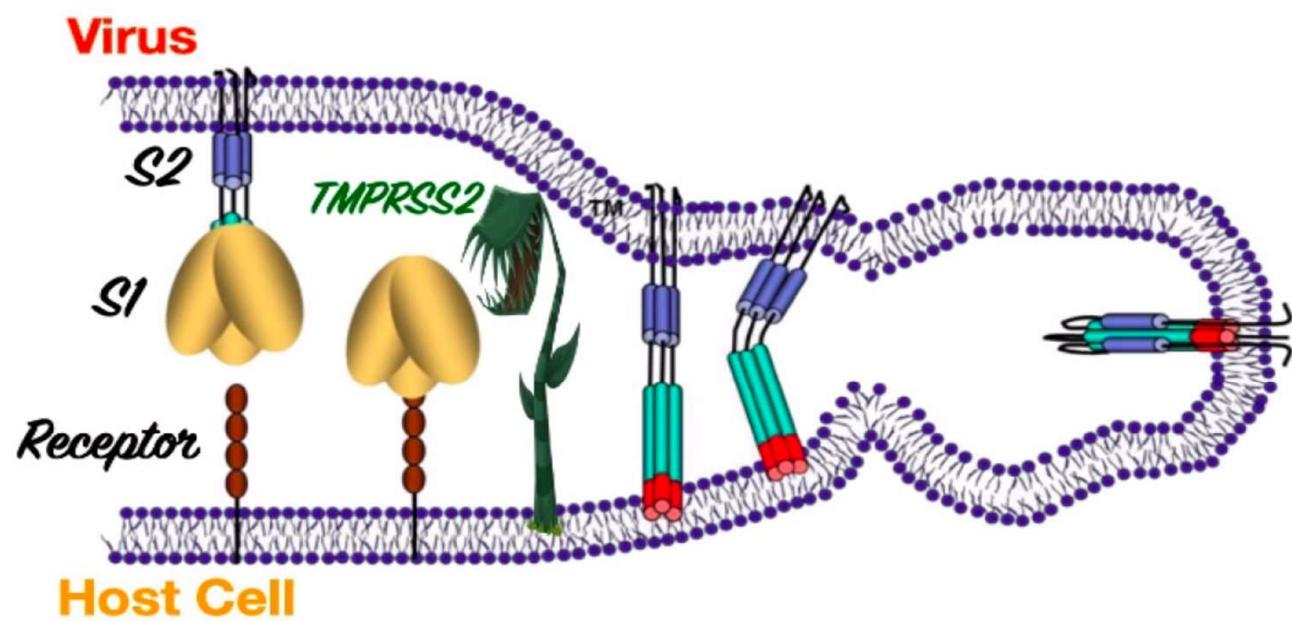
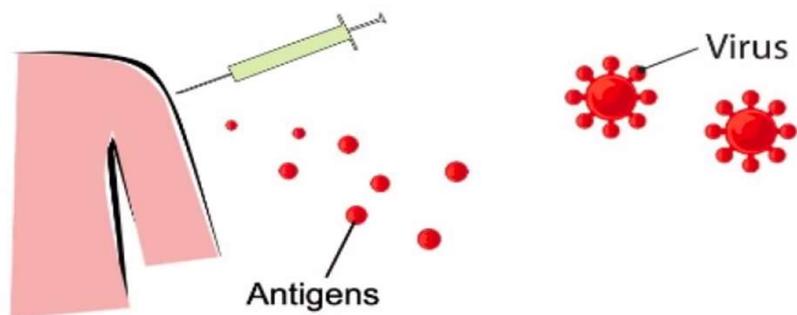


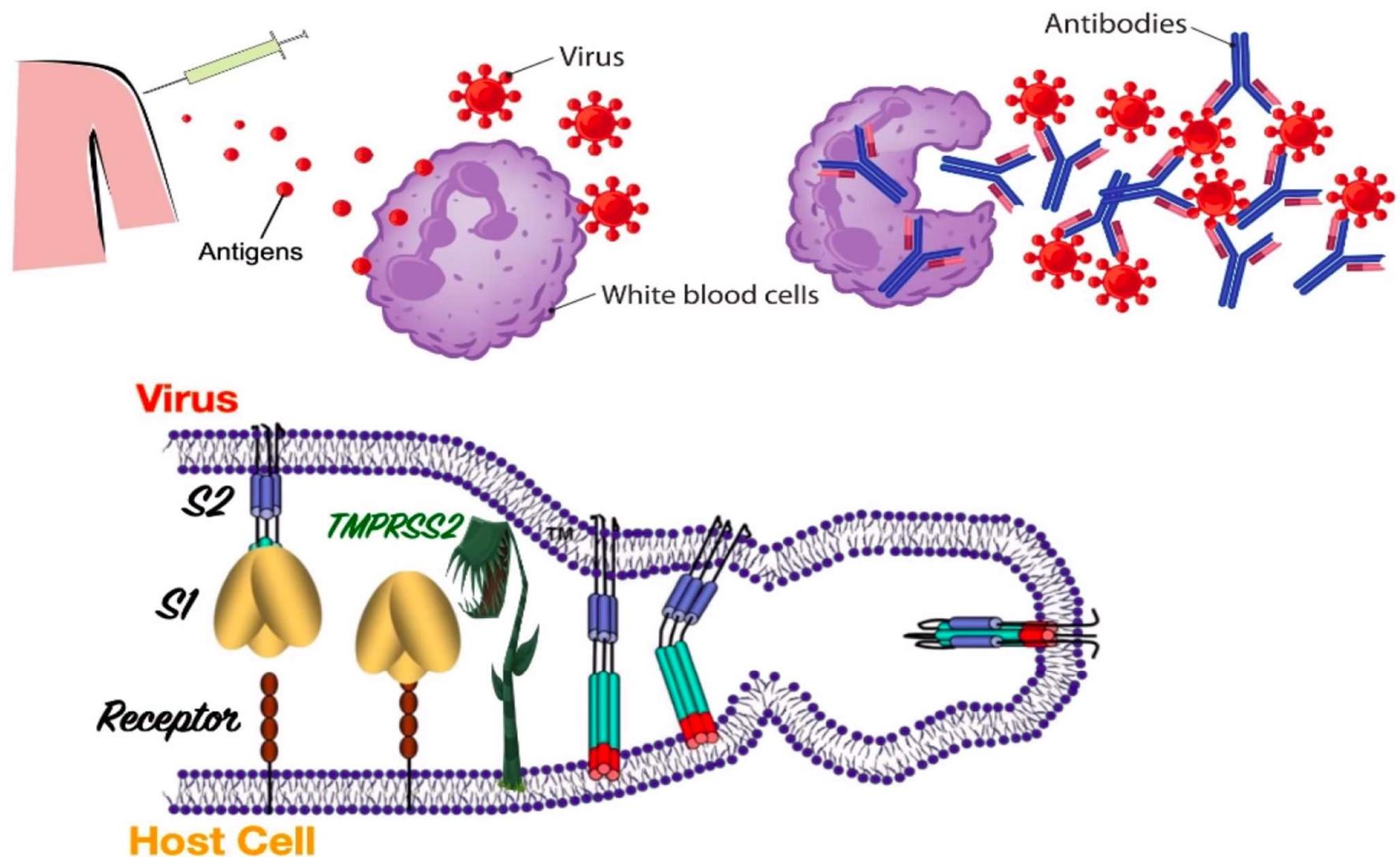


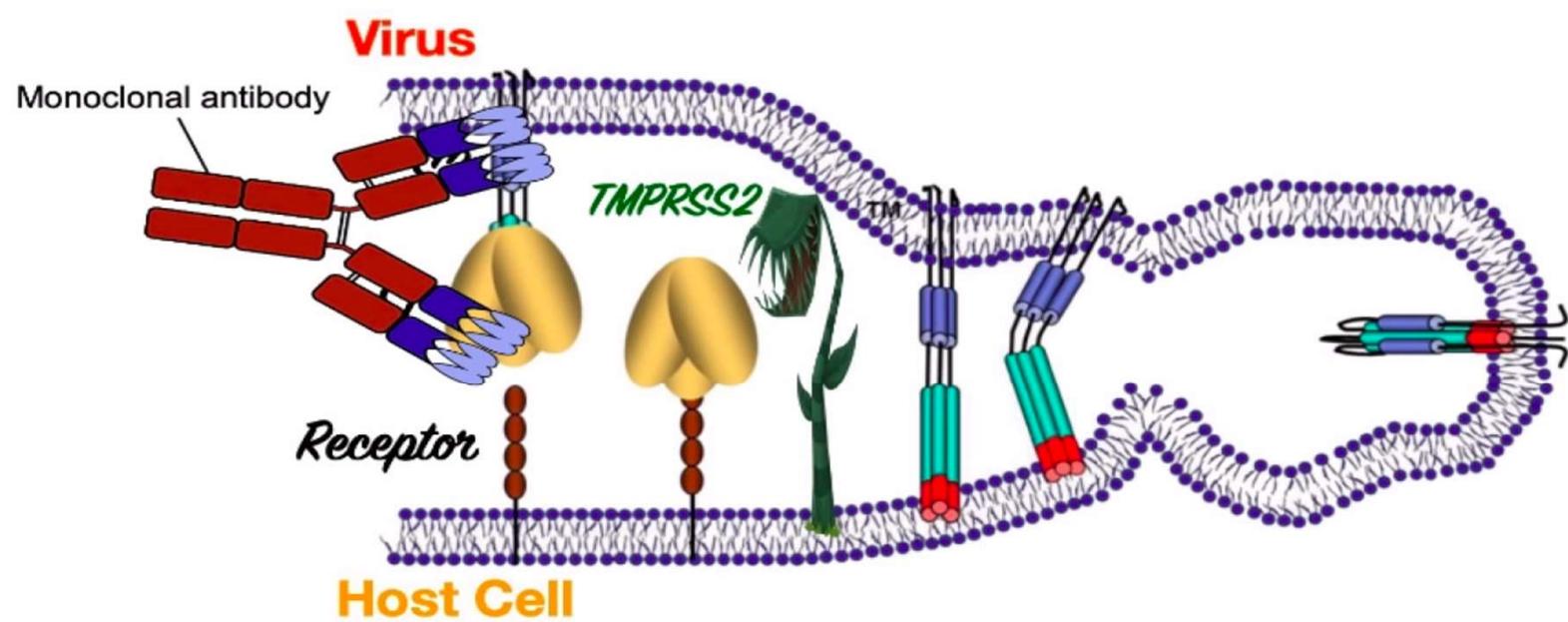
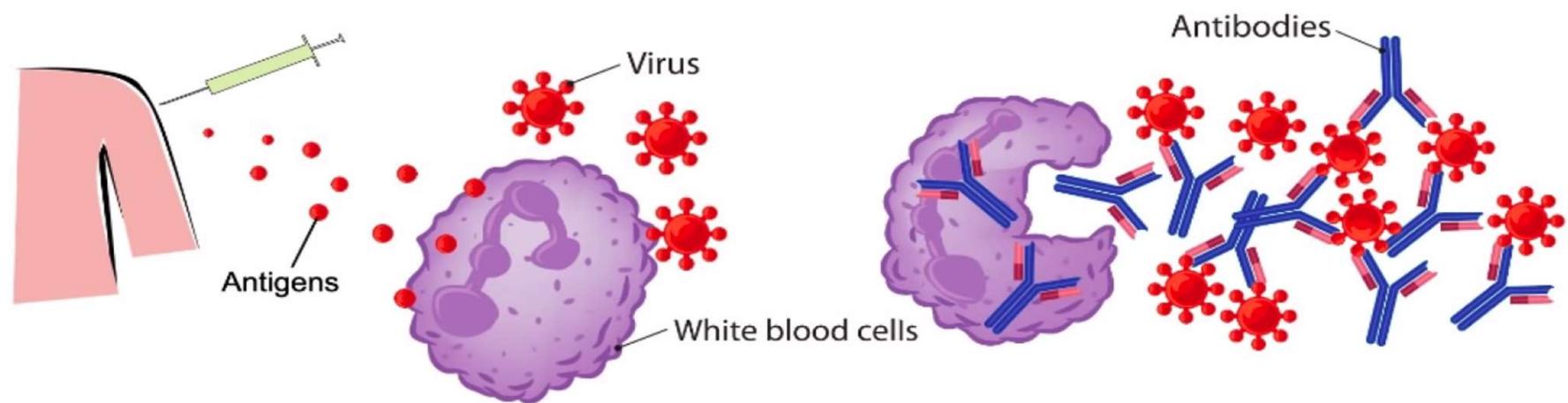


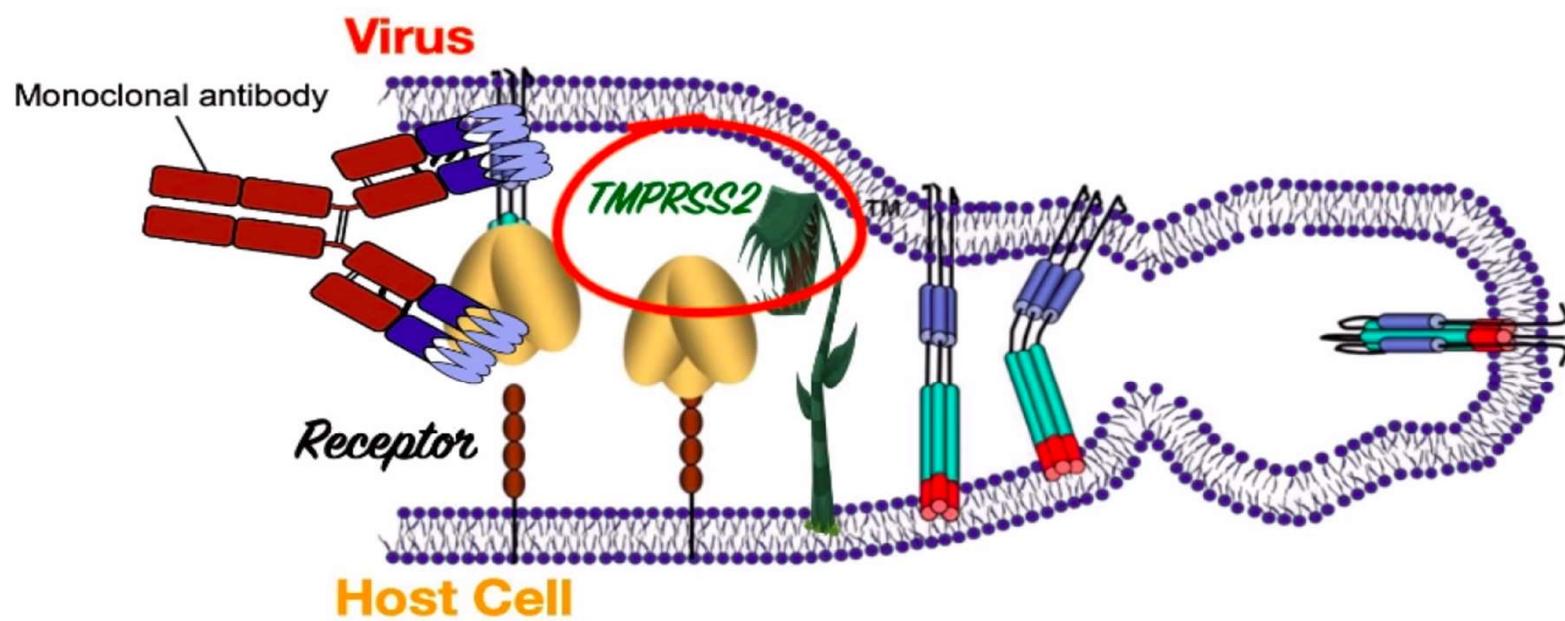
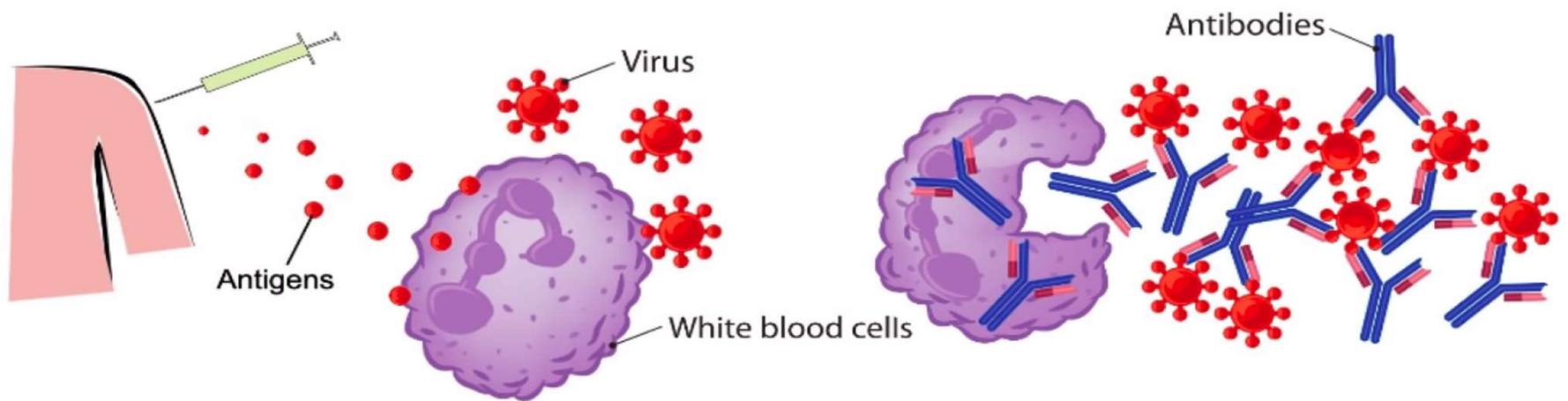


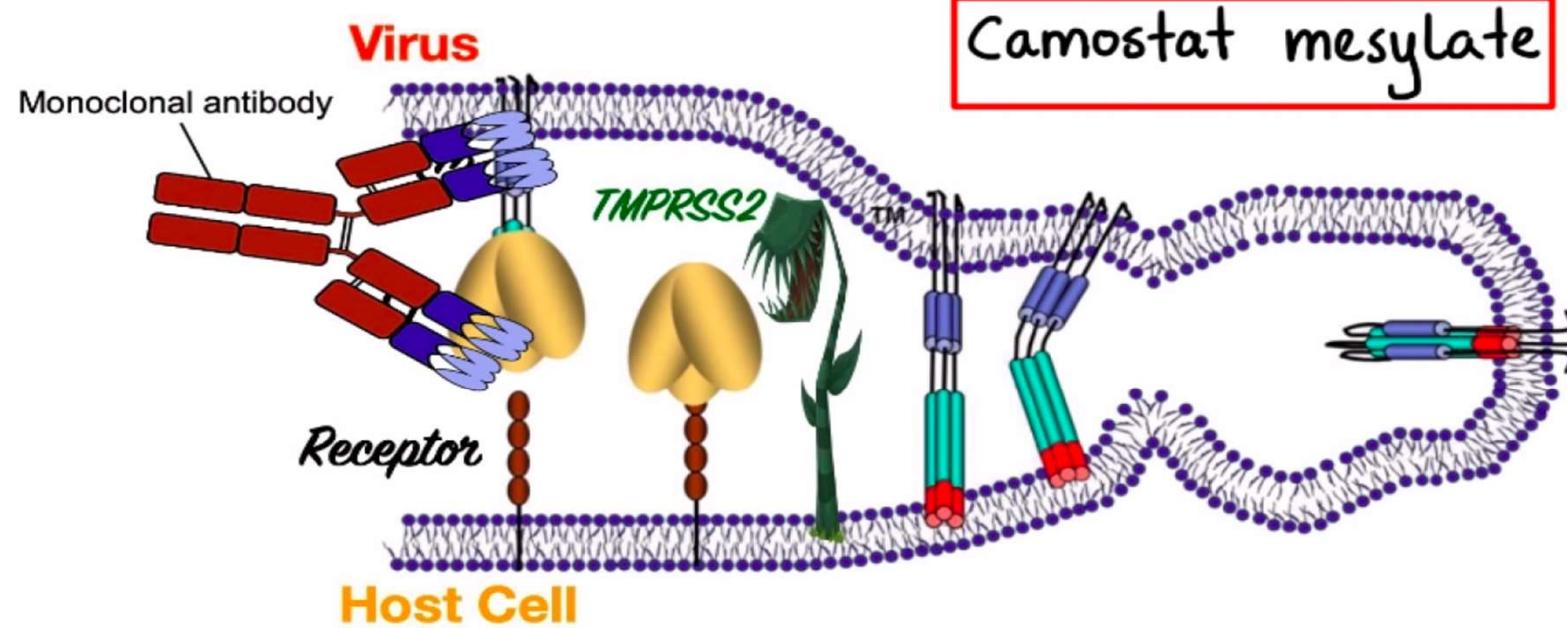
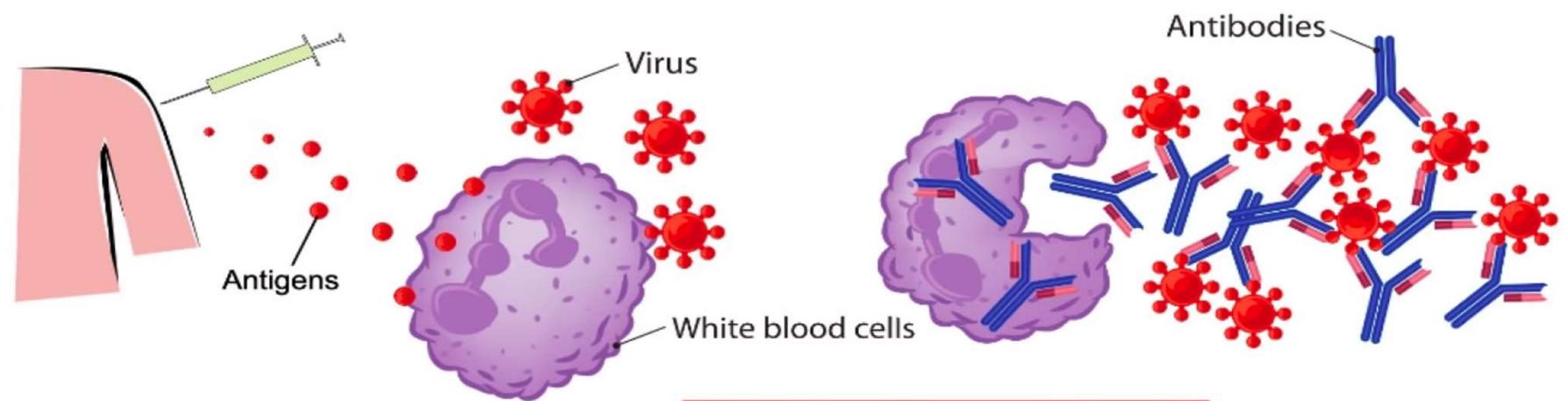


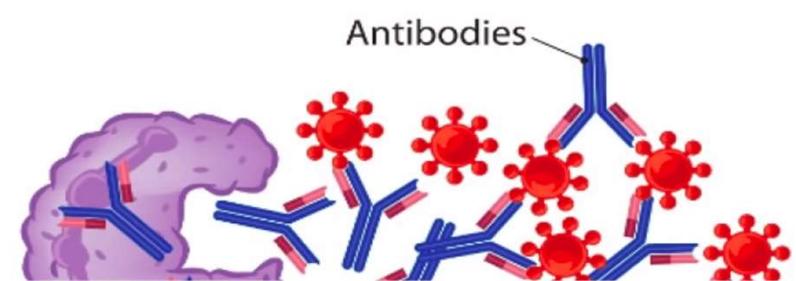
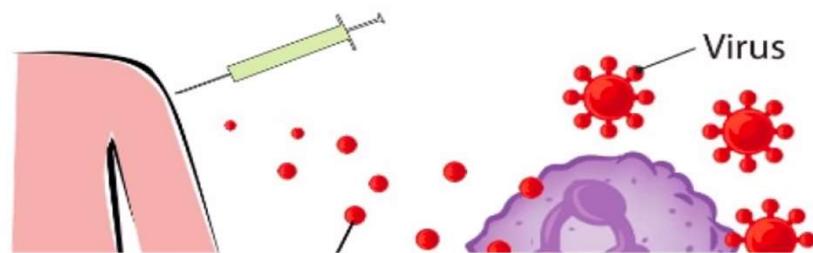


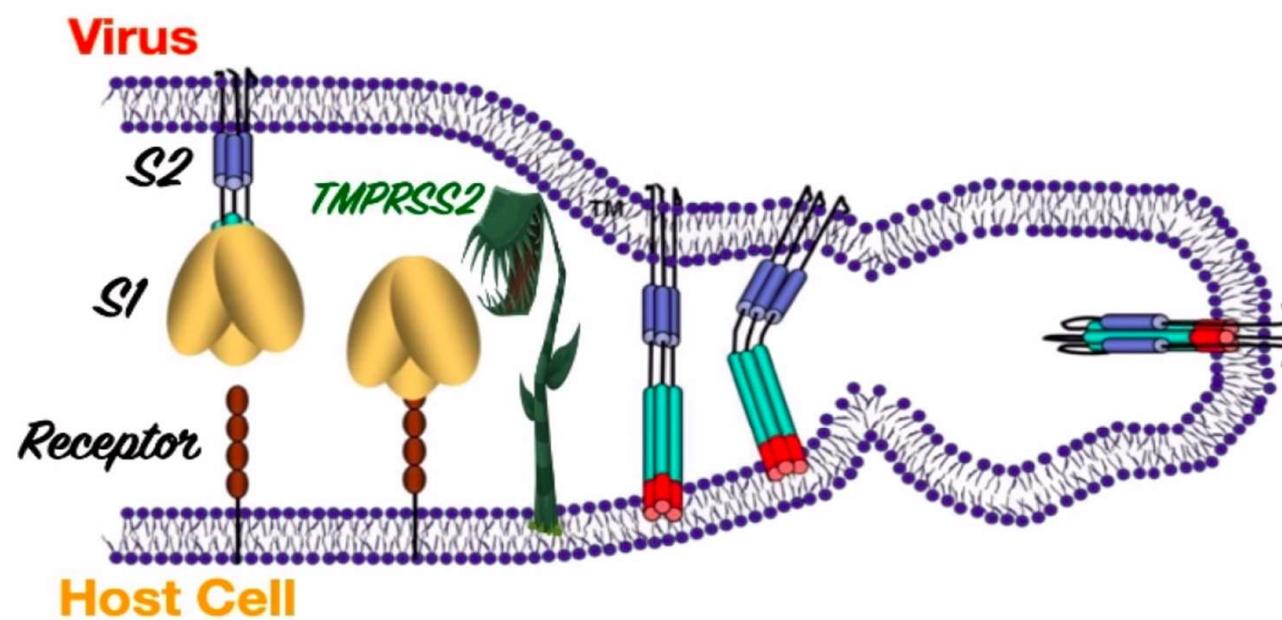


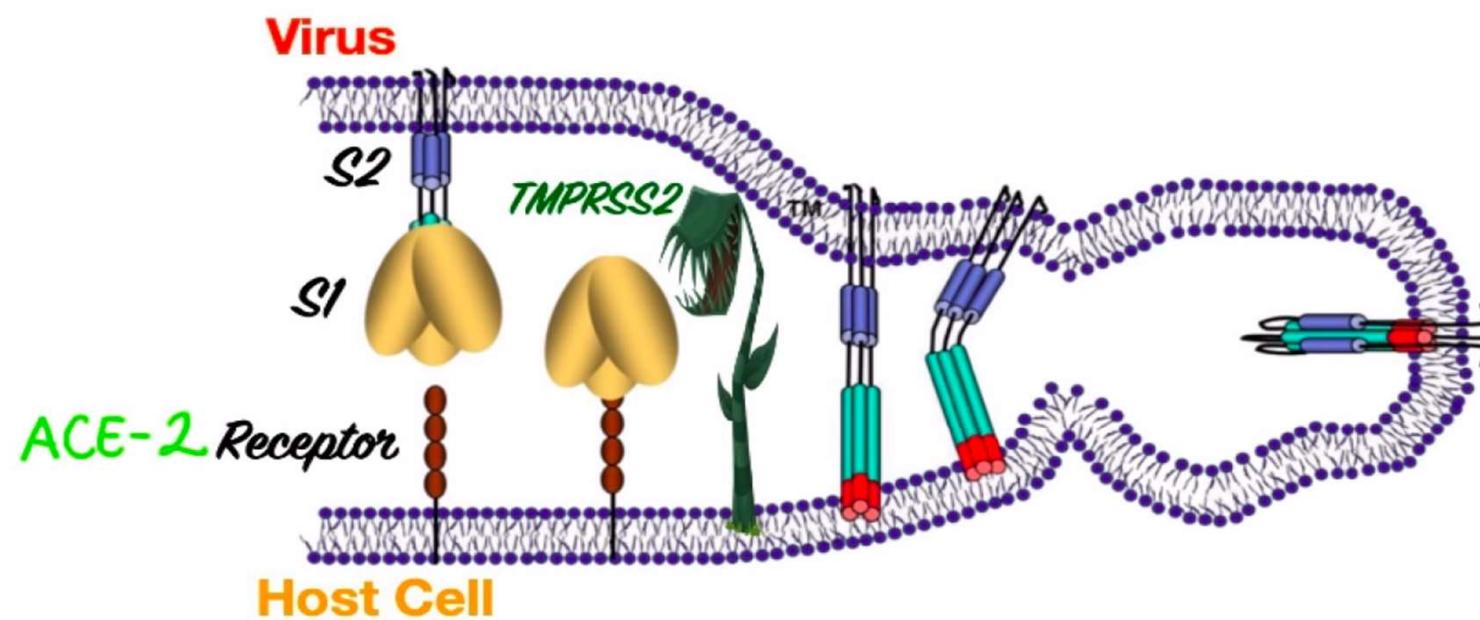


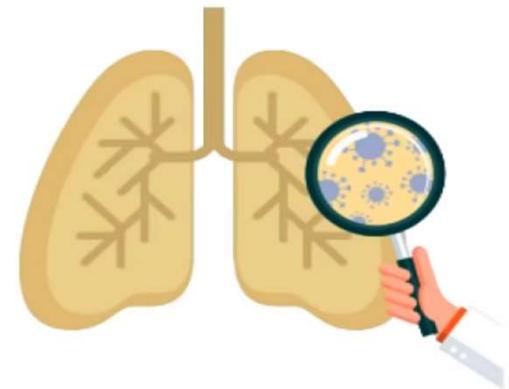
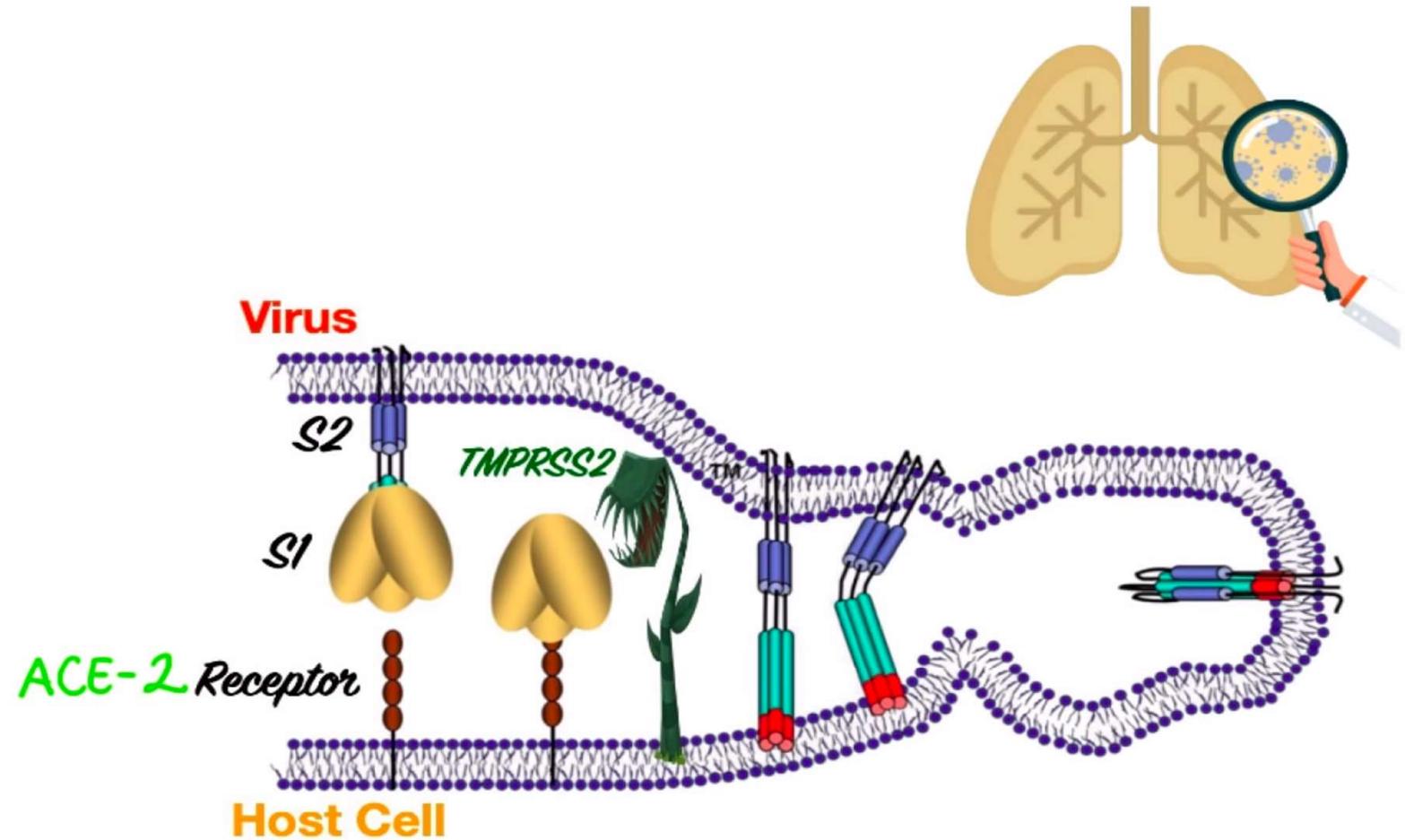


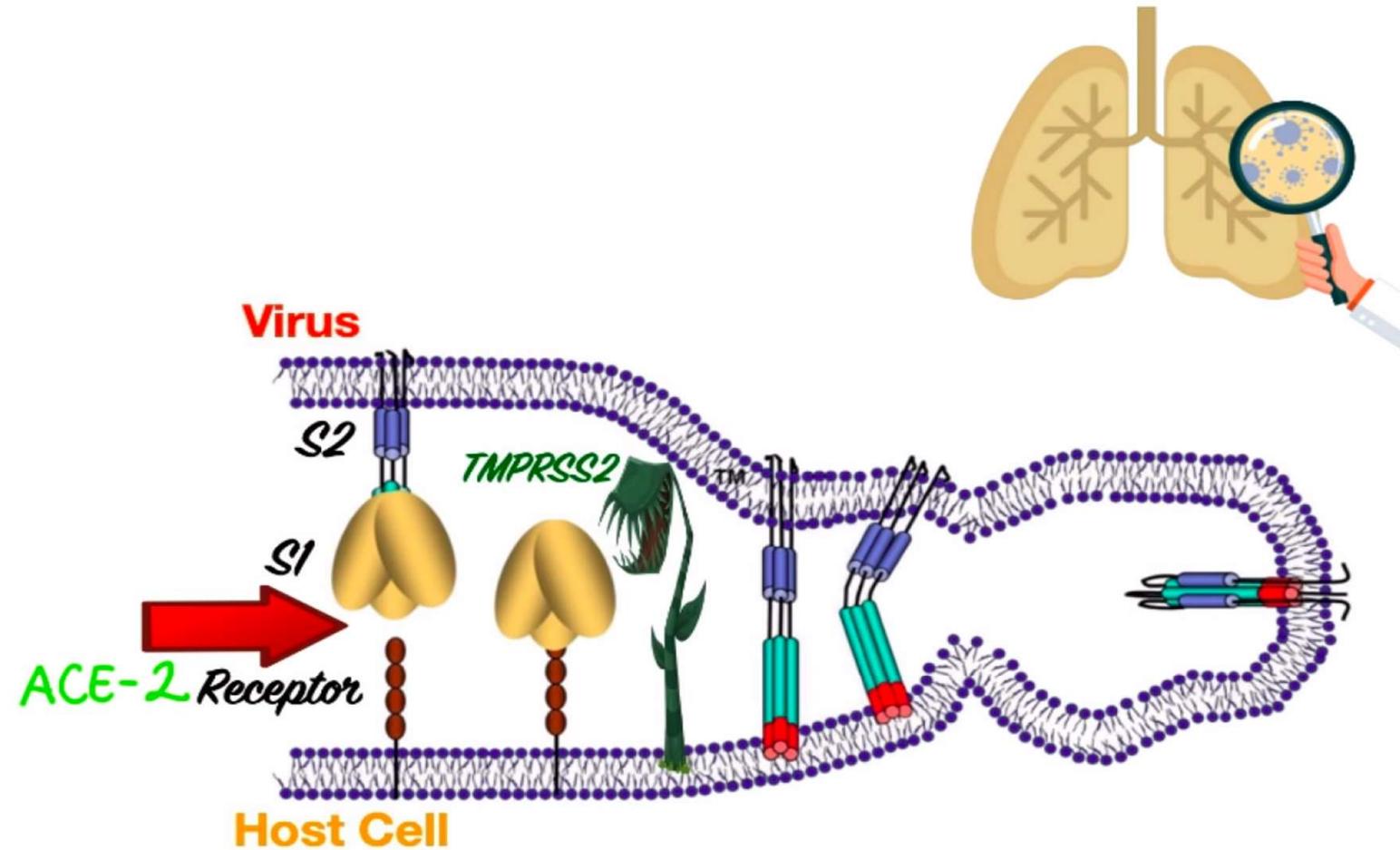


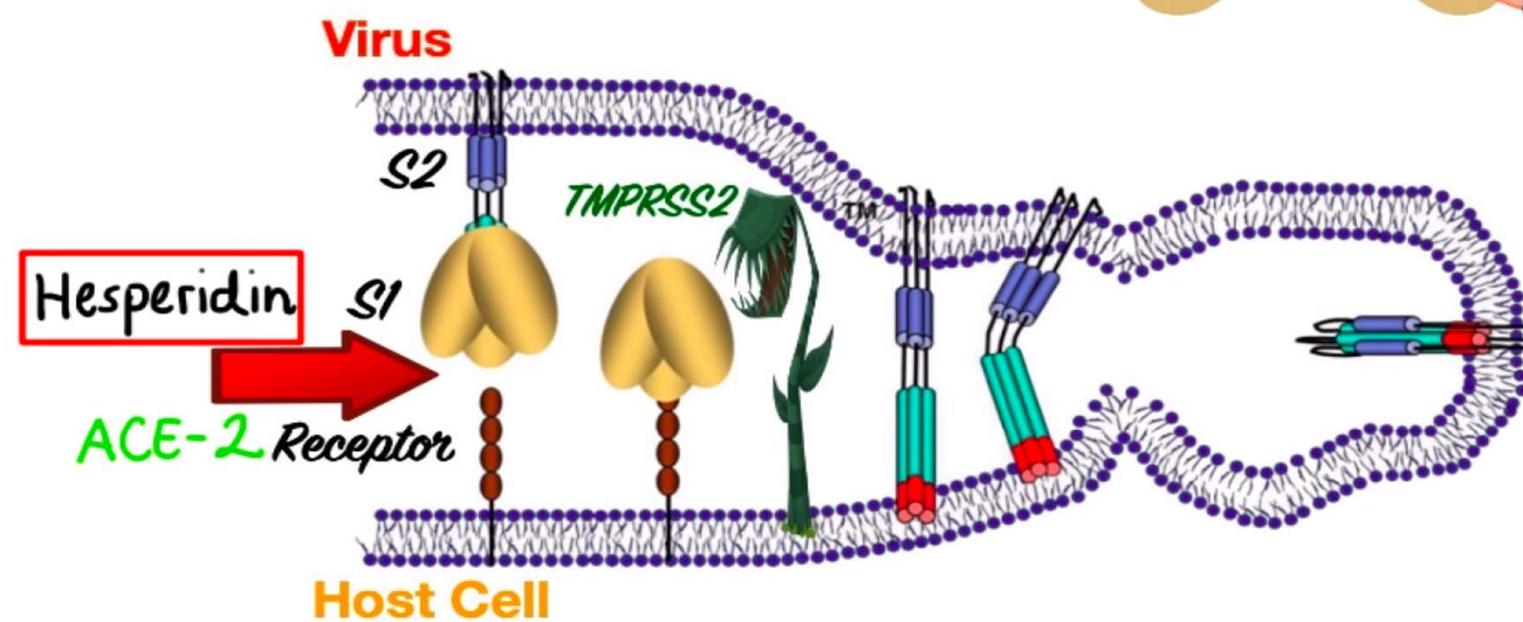
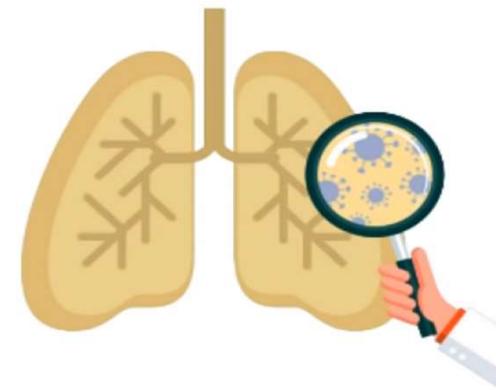


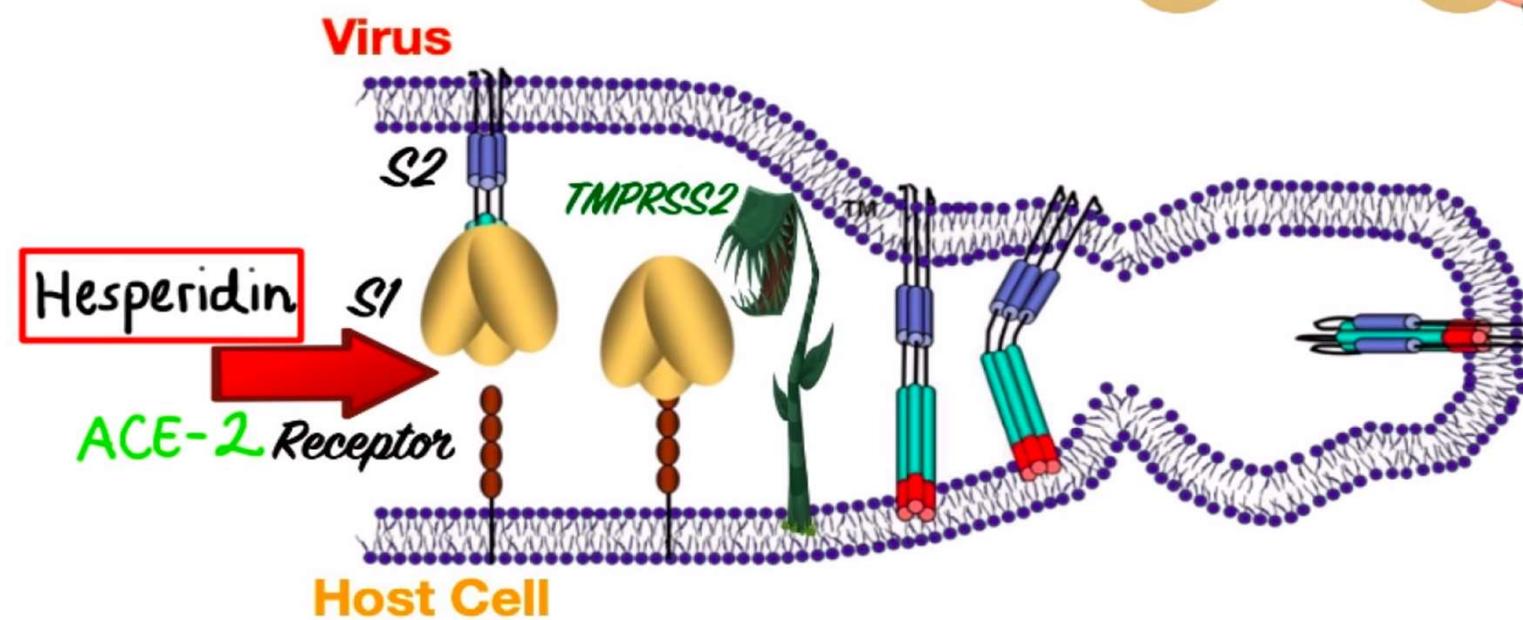
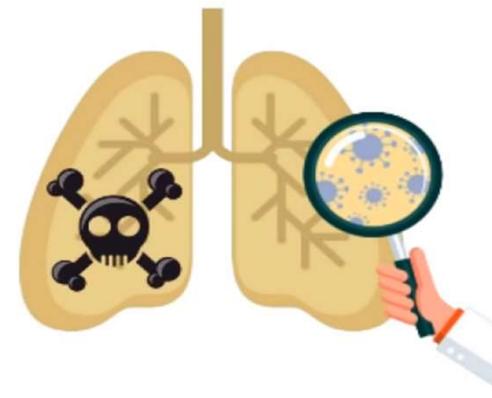


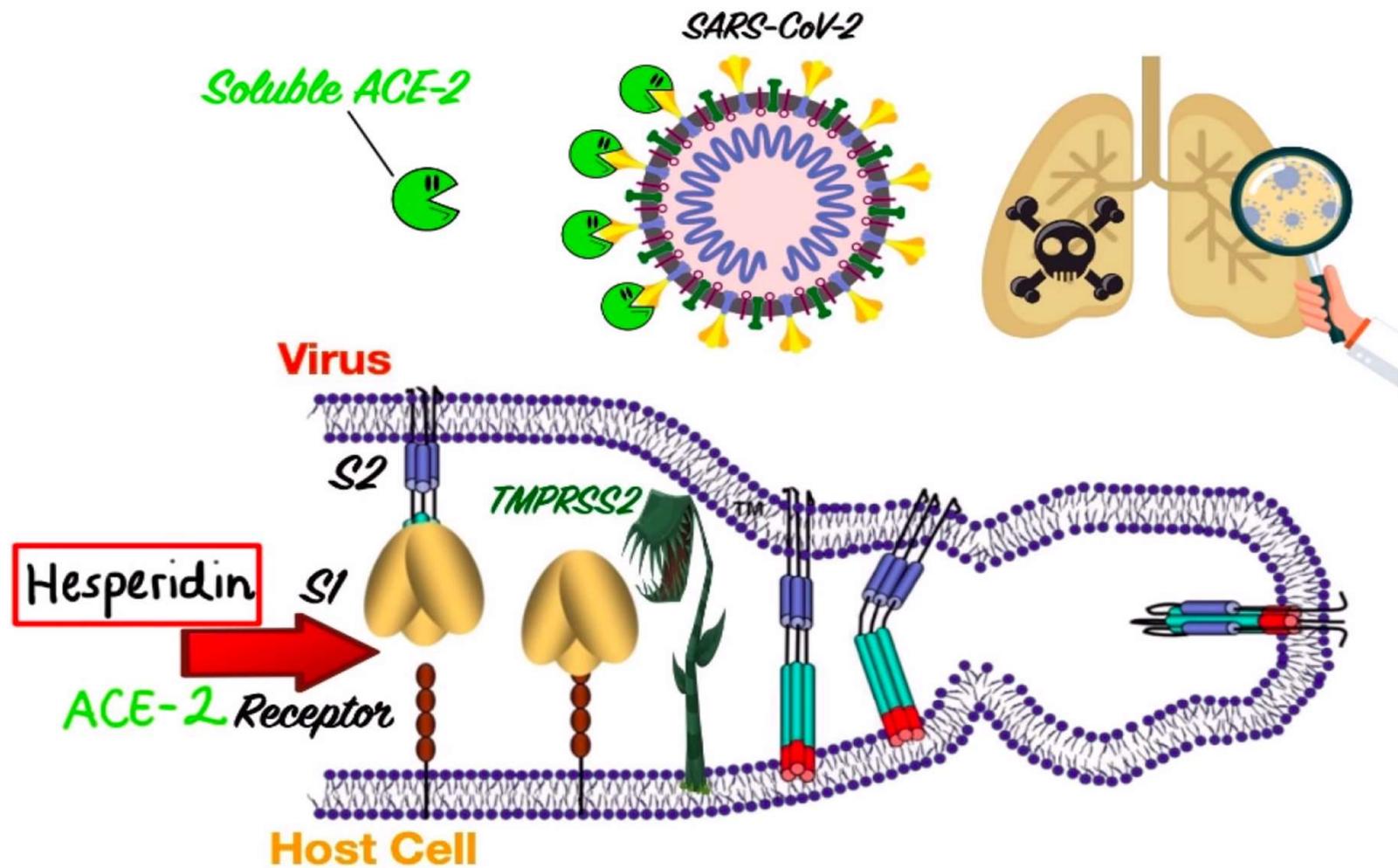






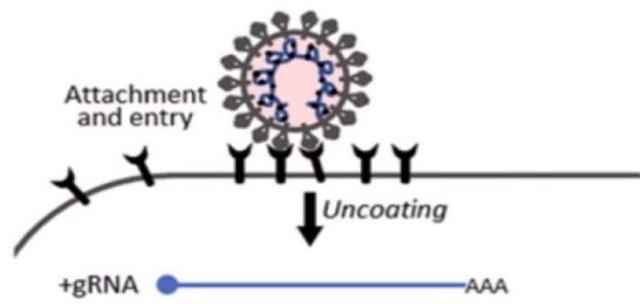


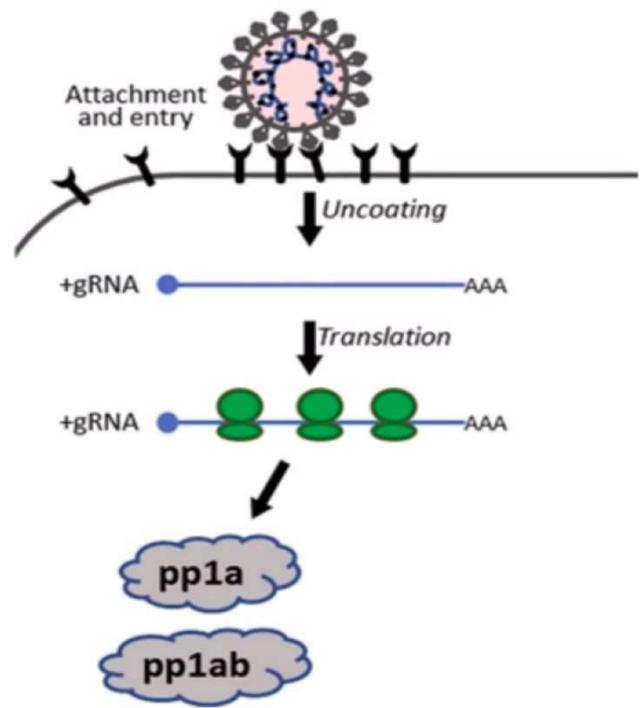


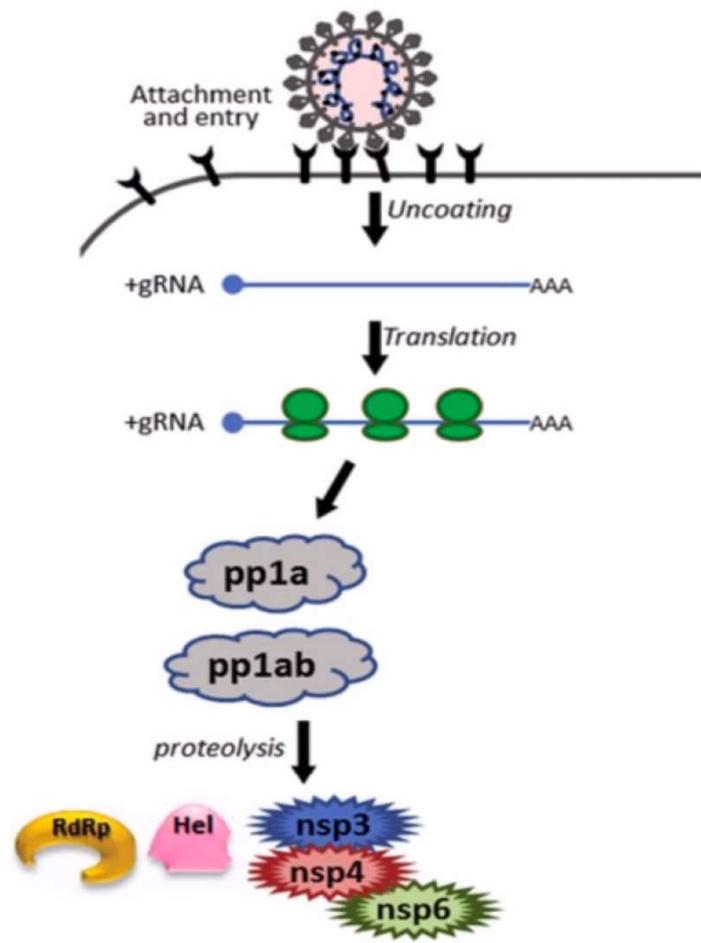


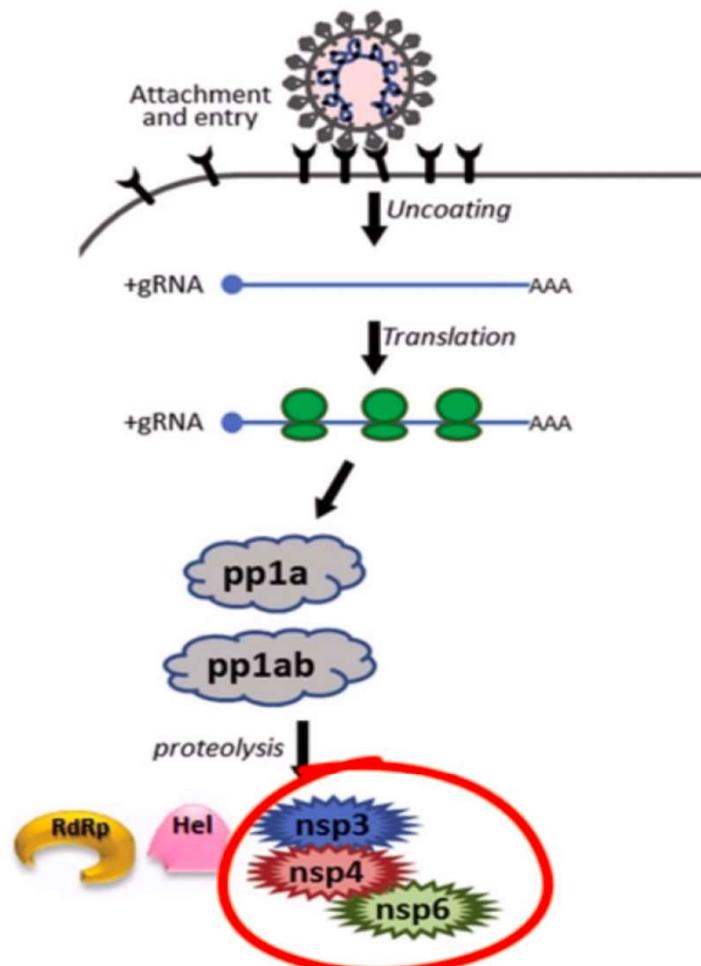
Replication Process

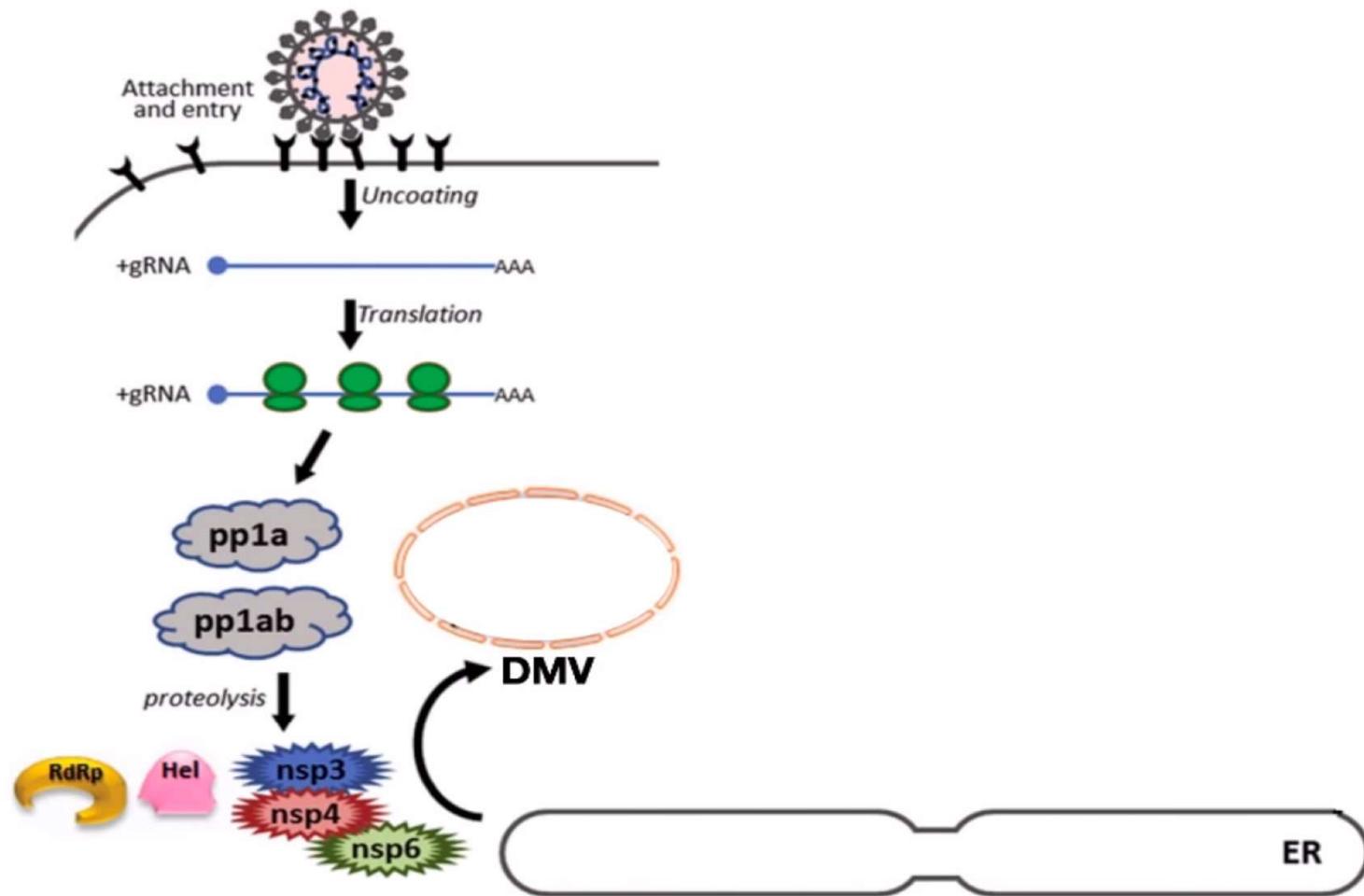


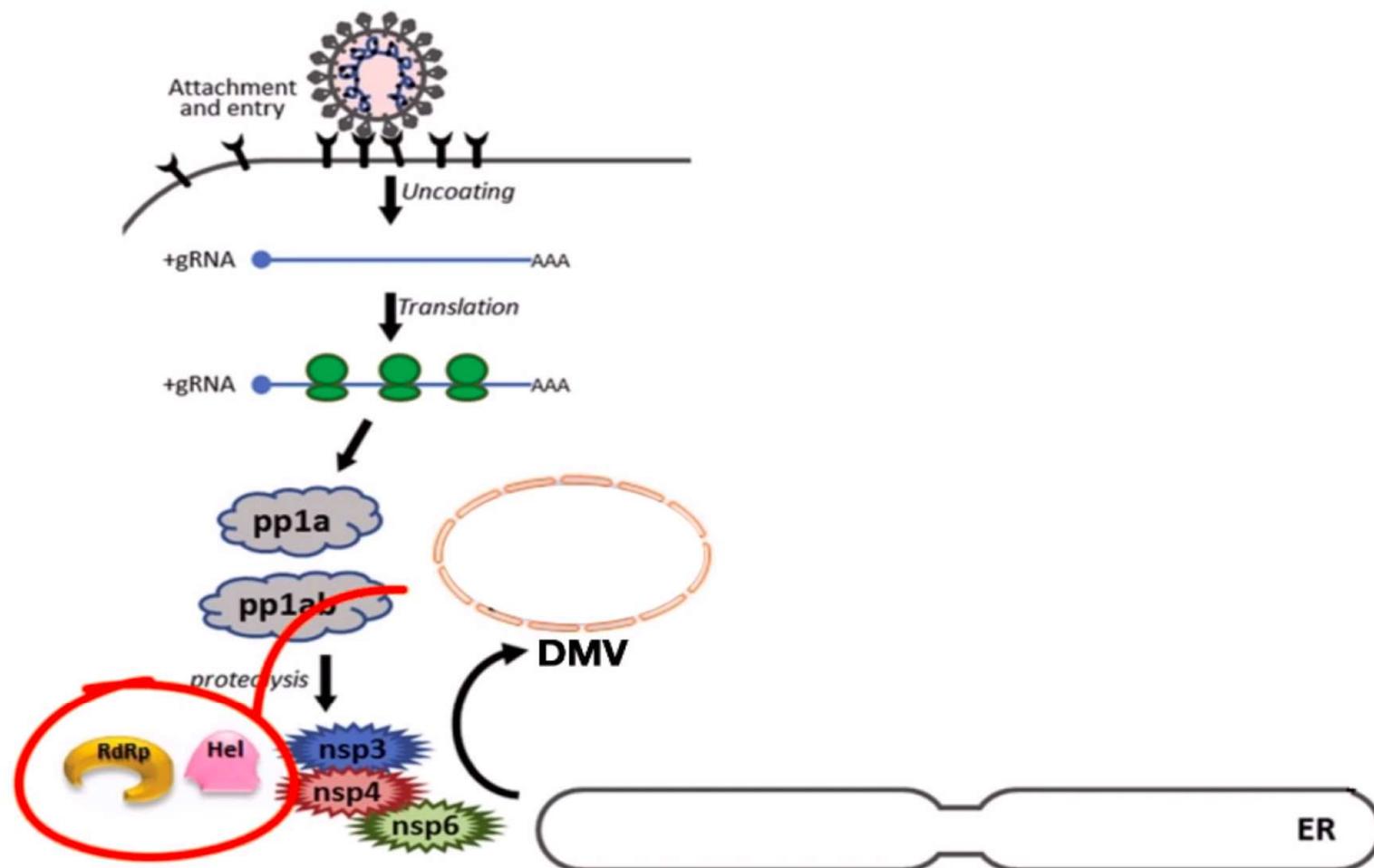


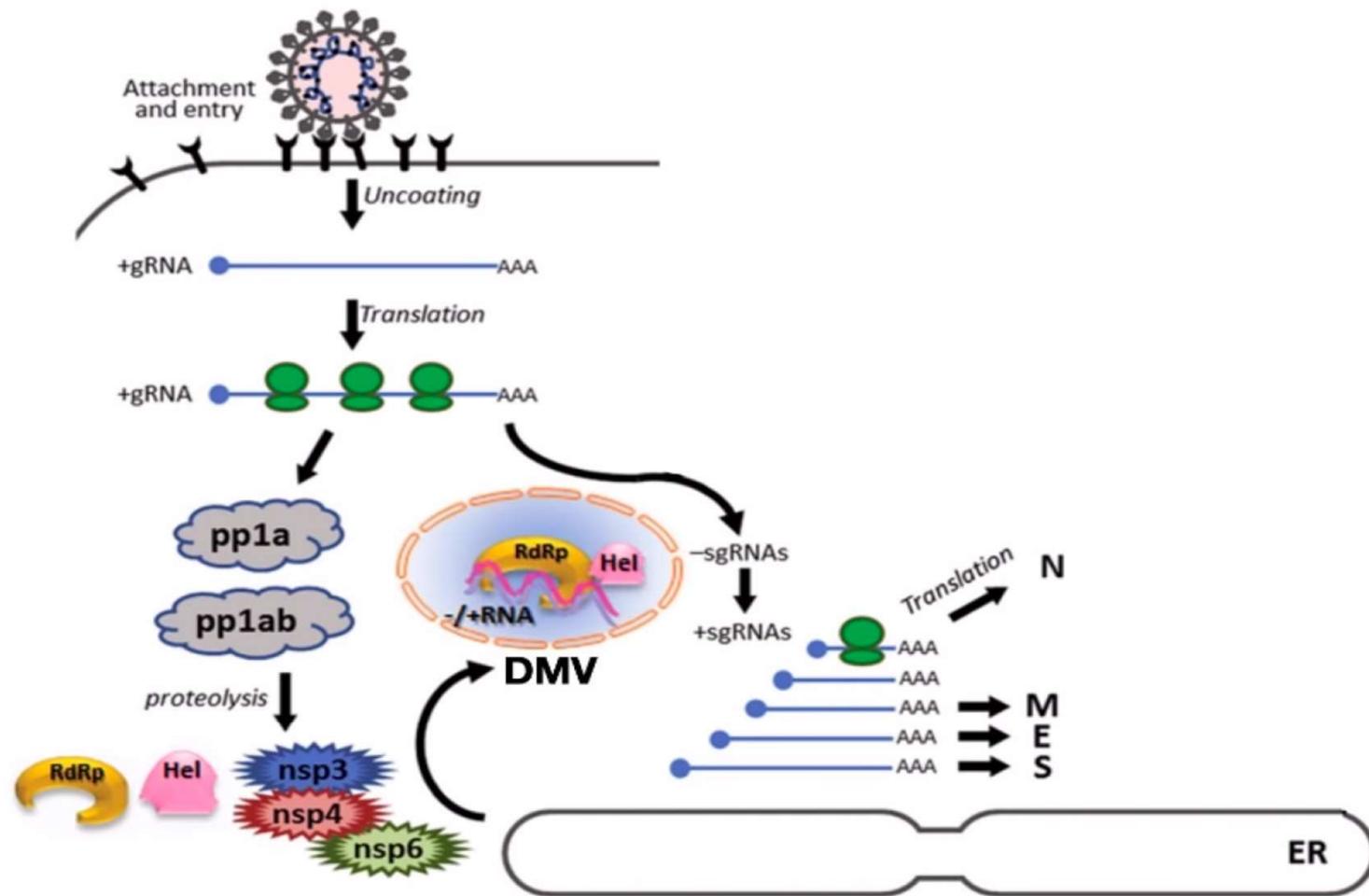


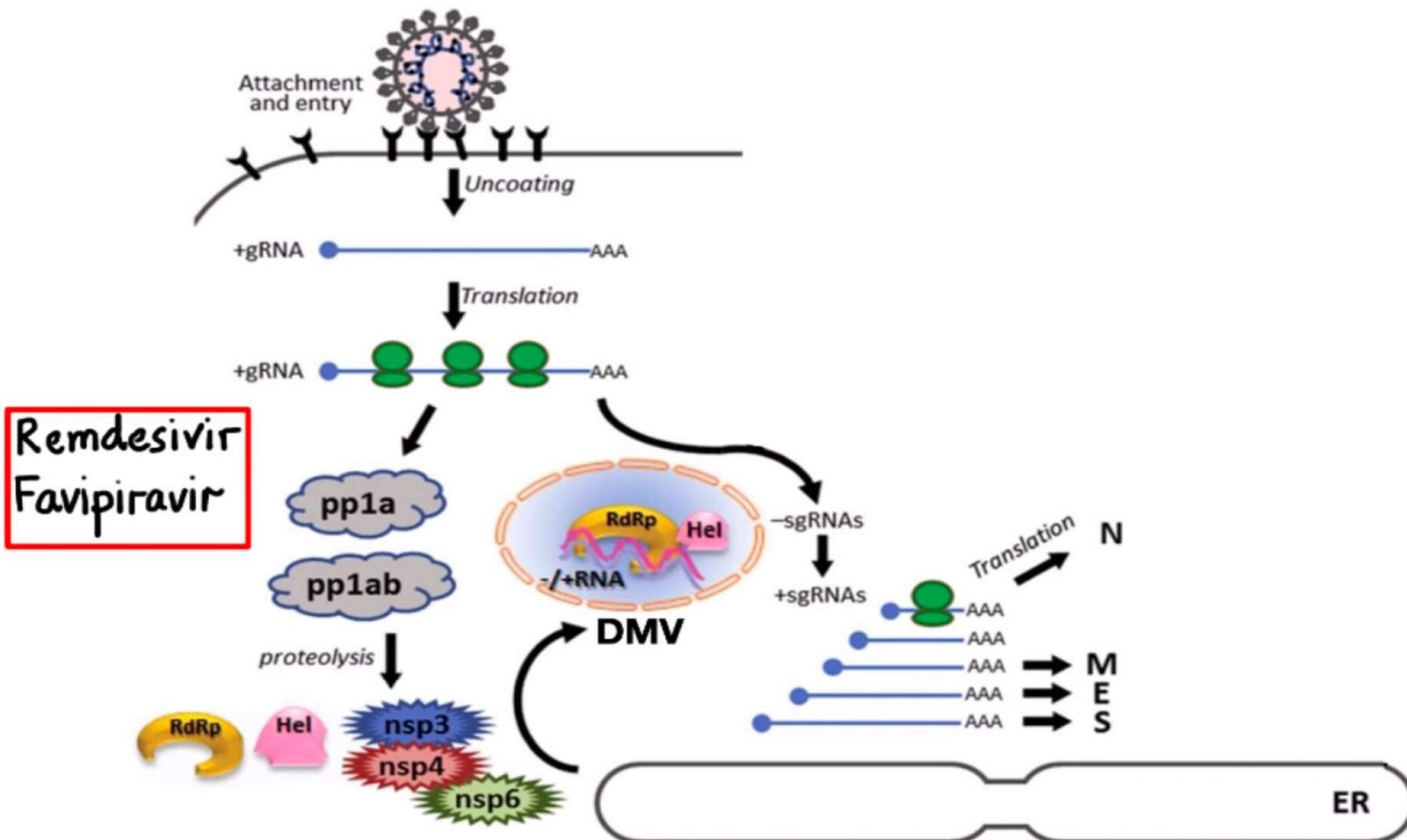


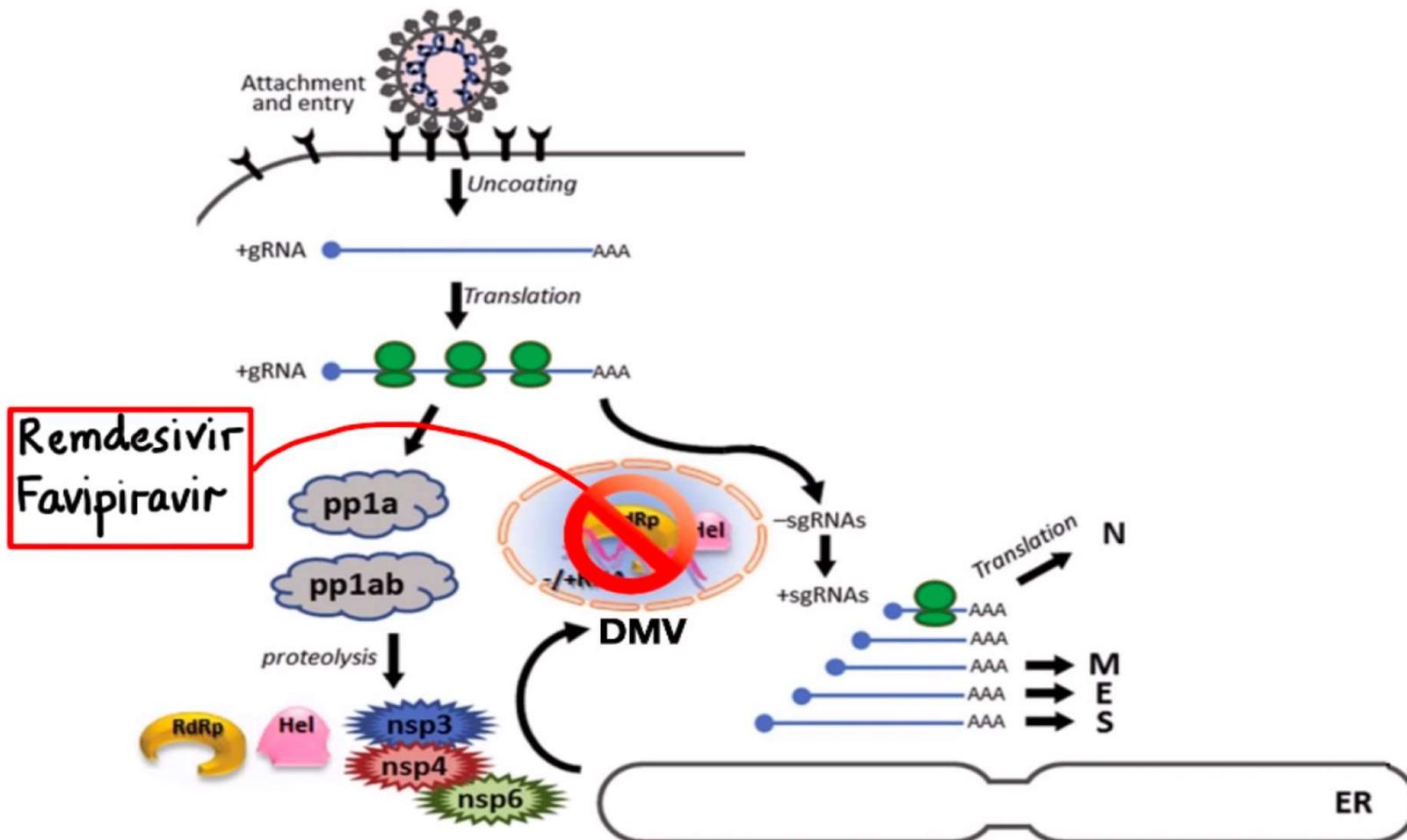


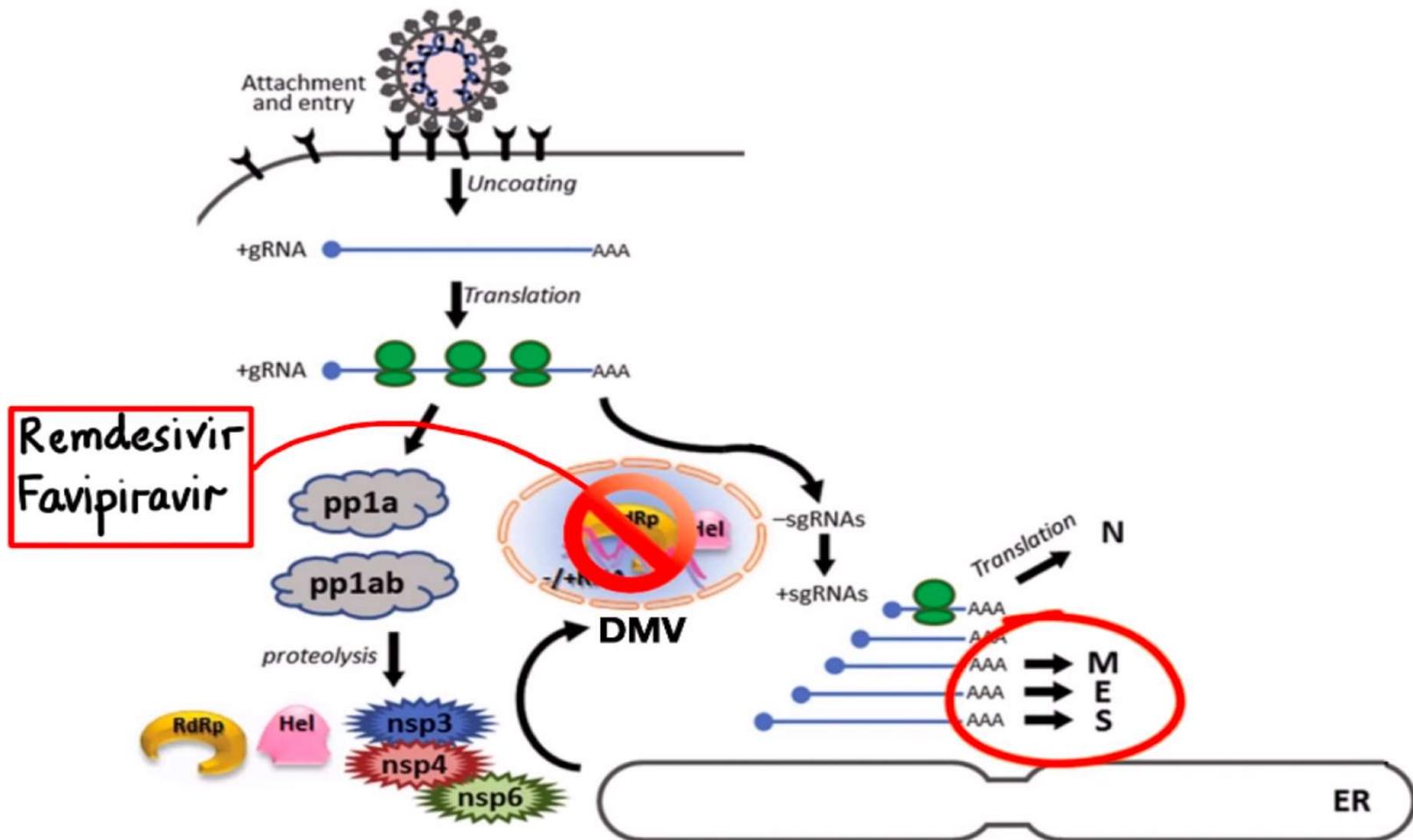


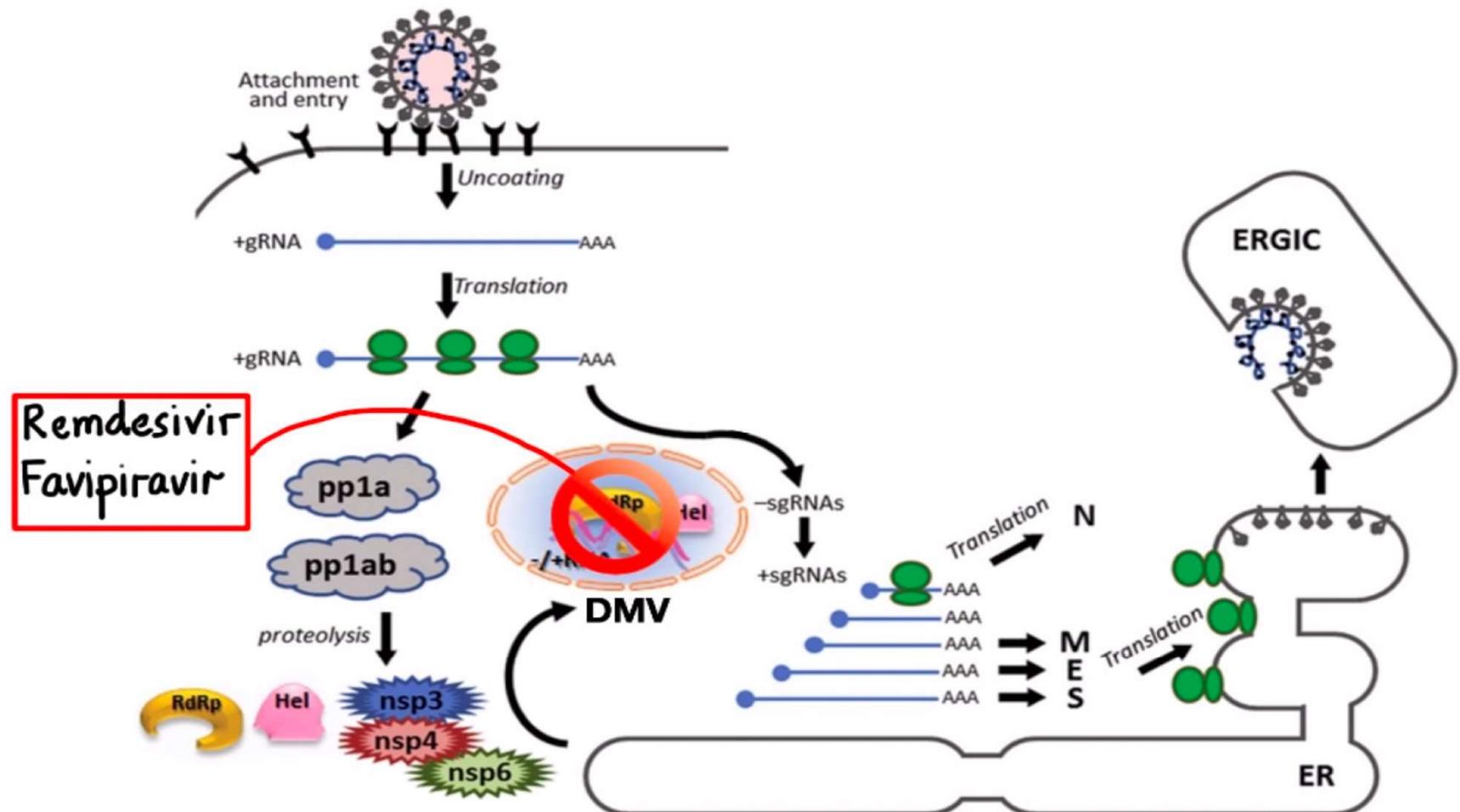


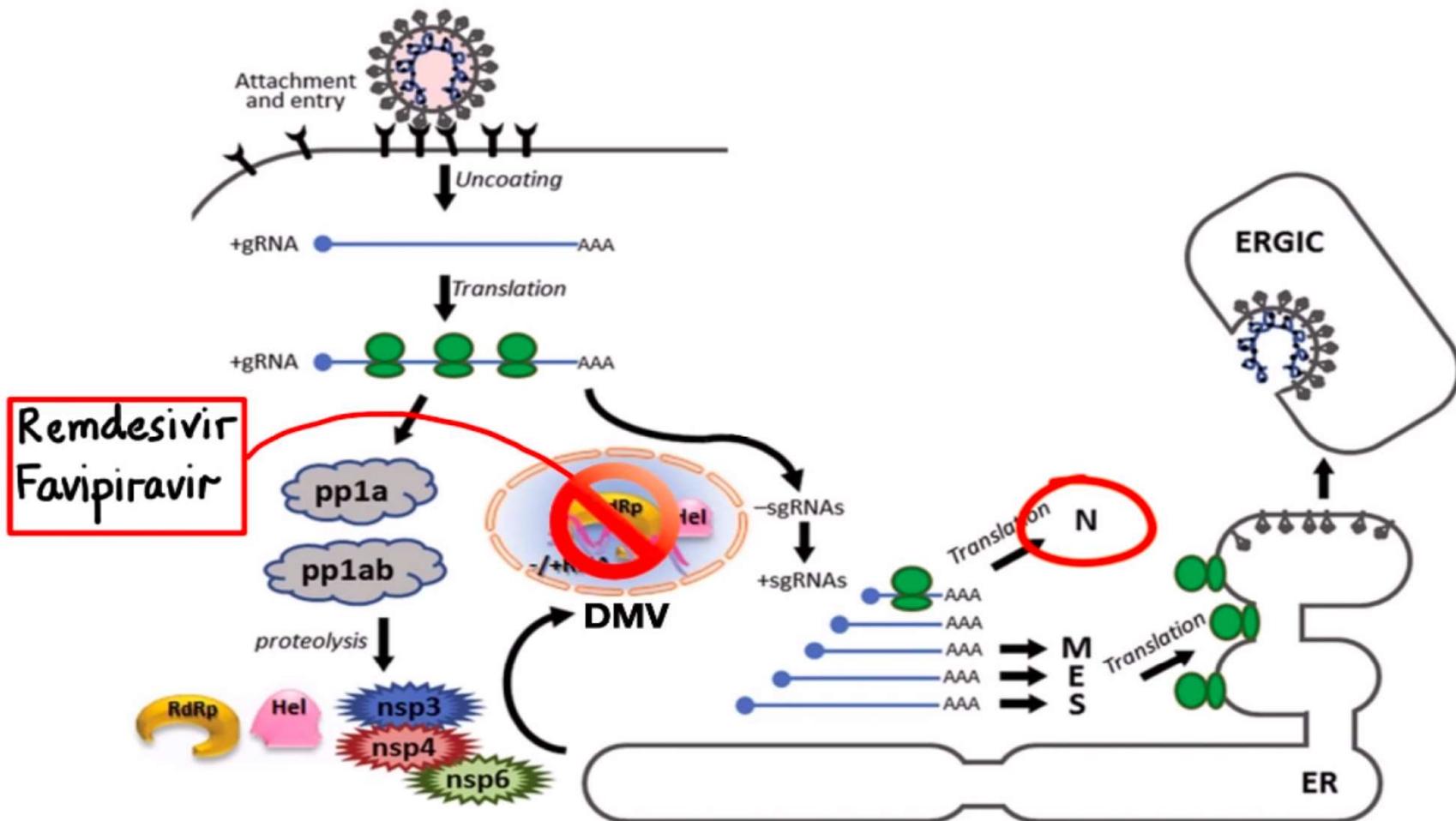


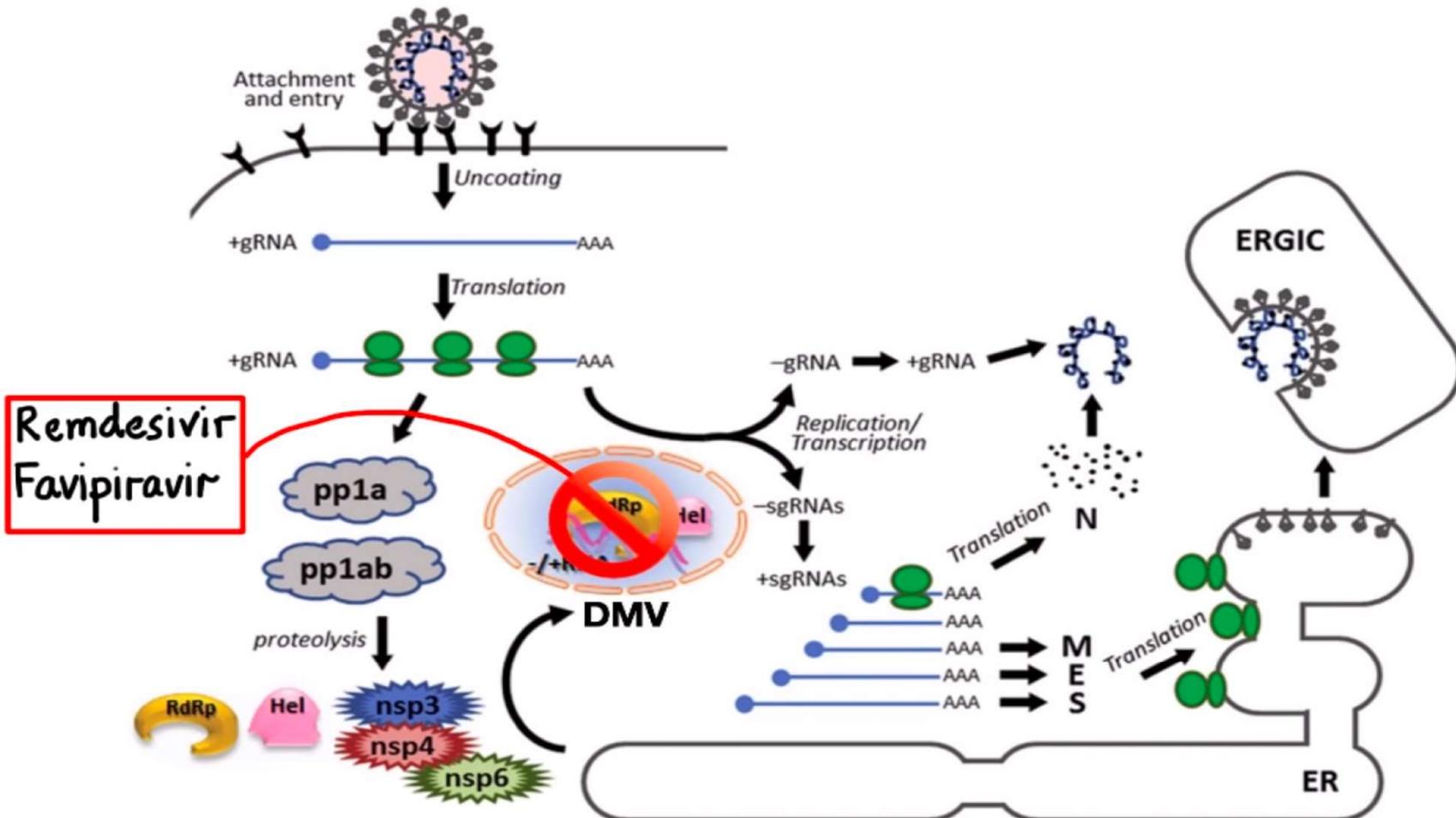


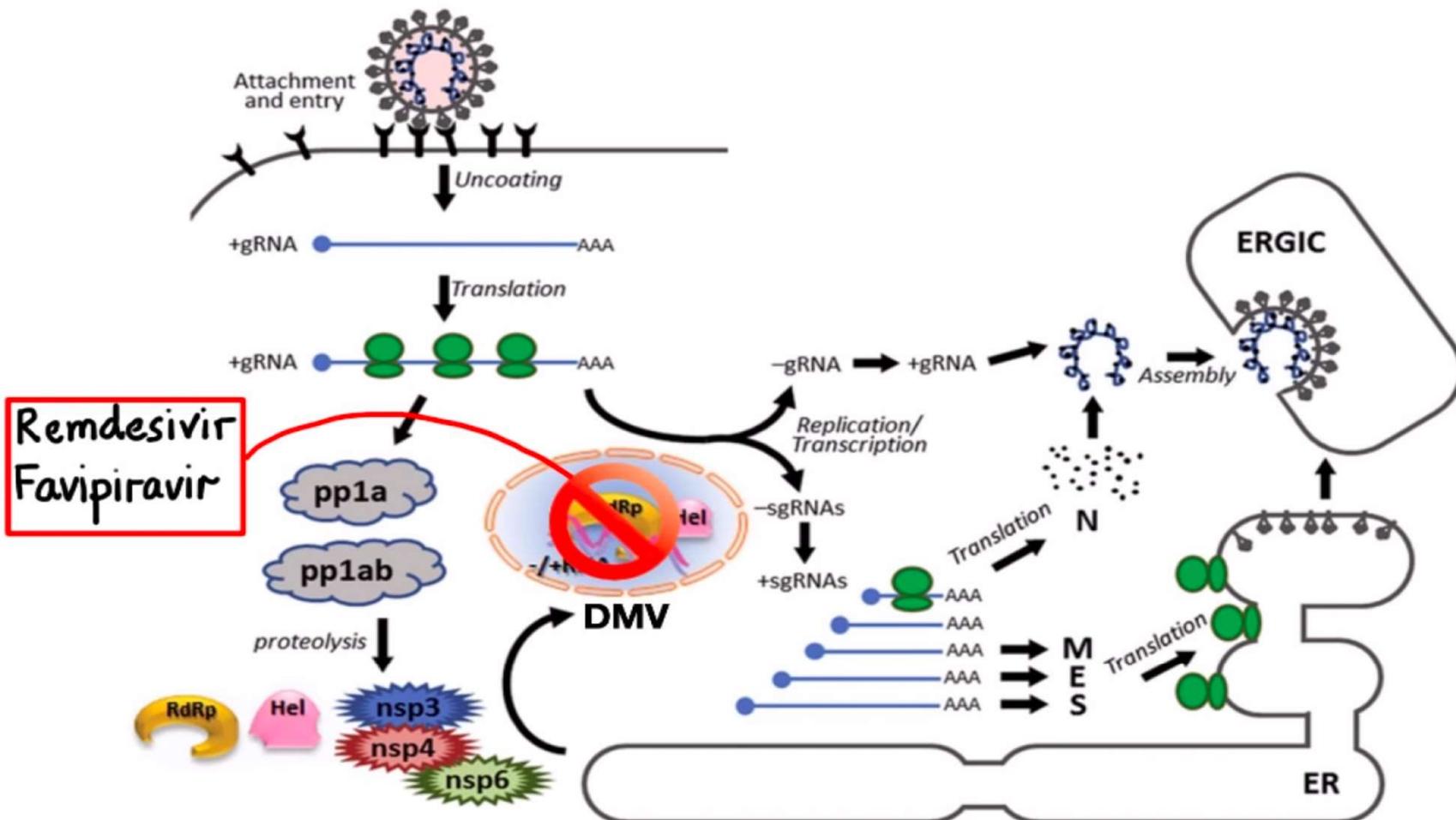


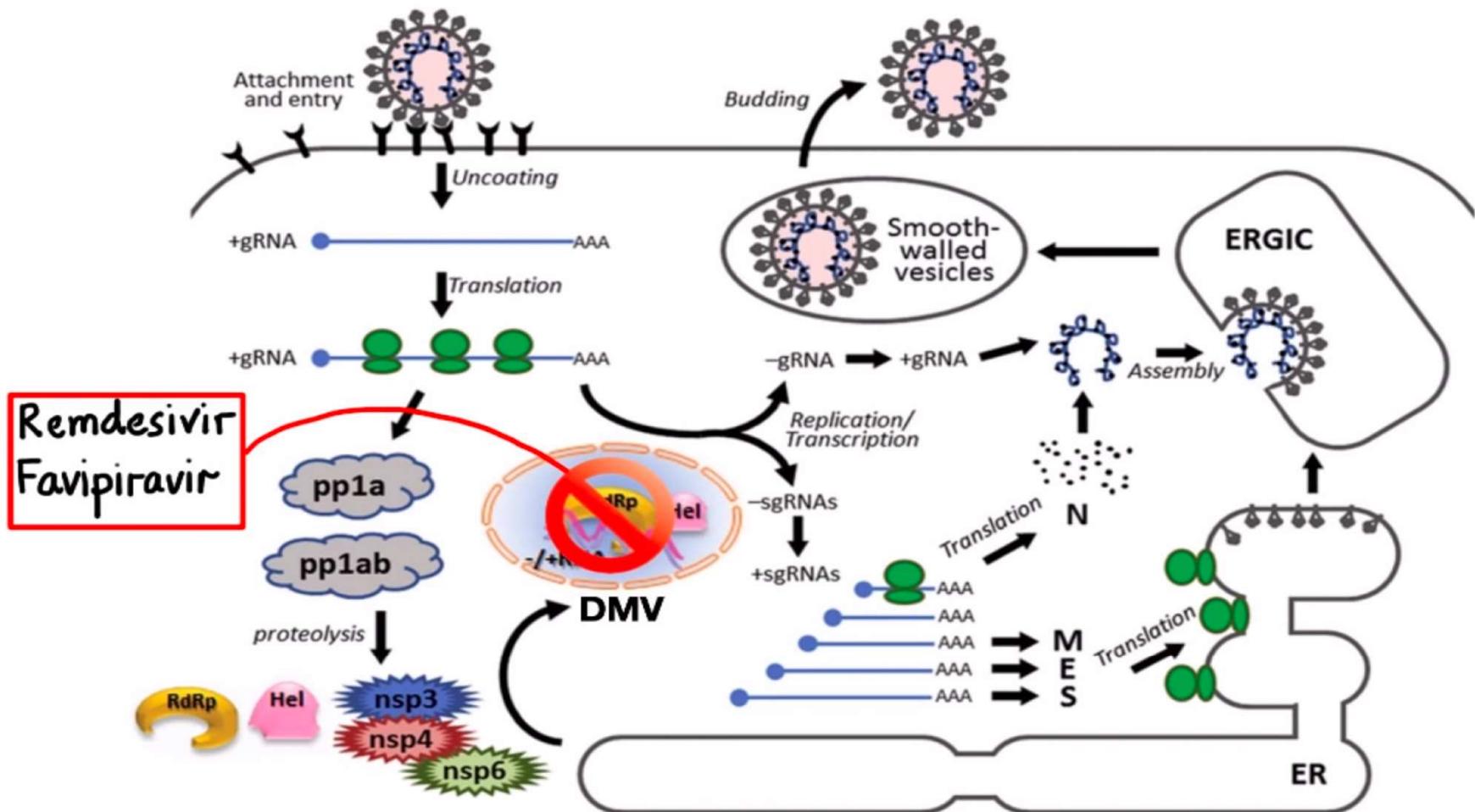


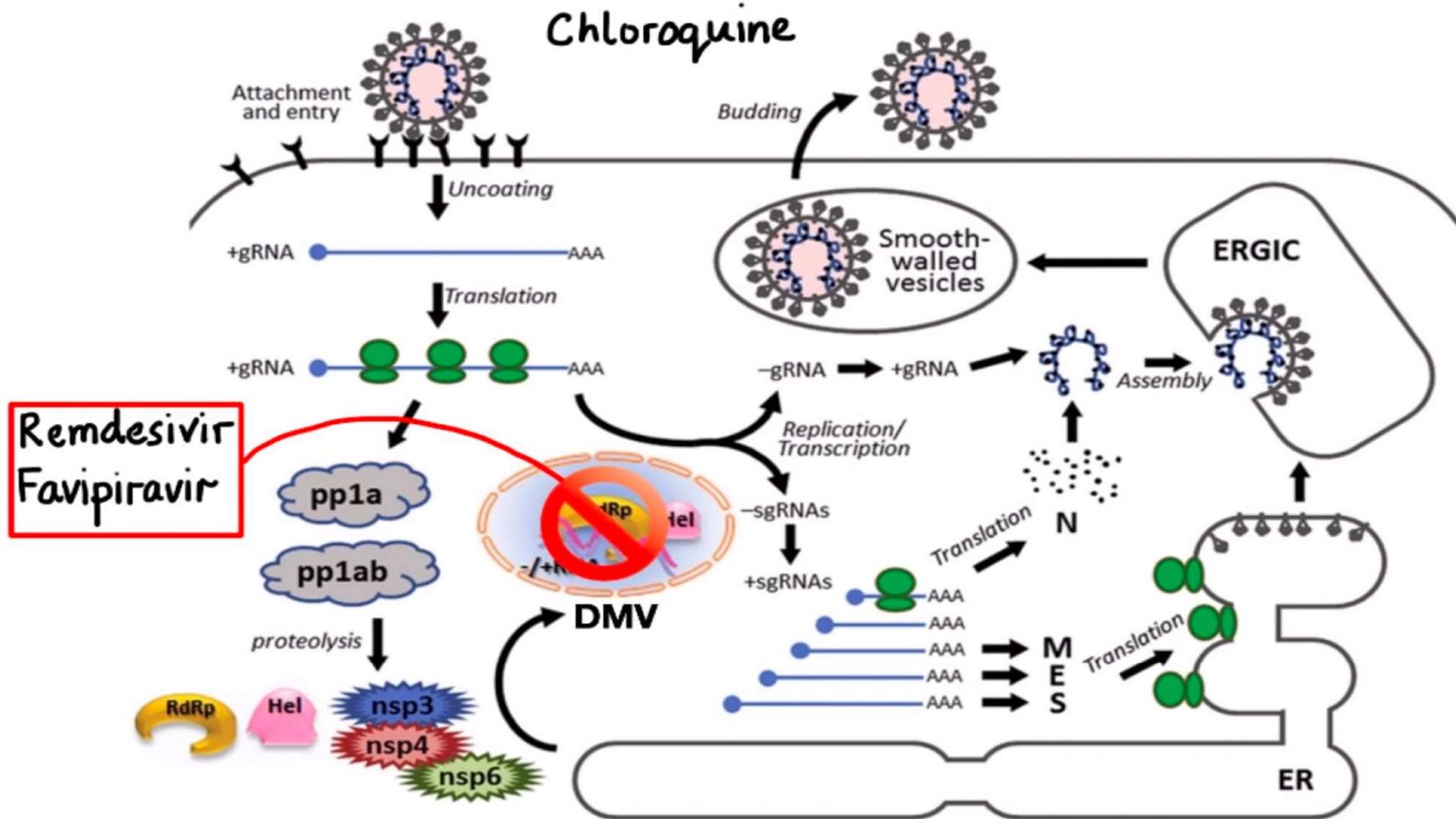


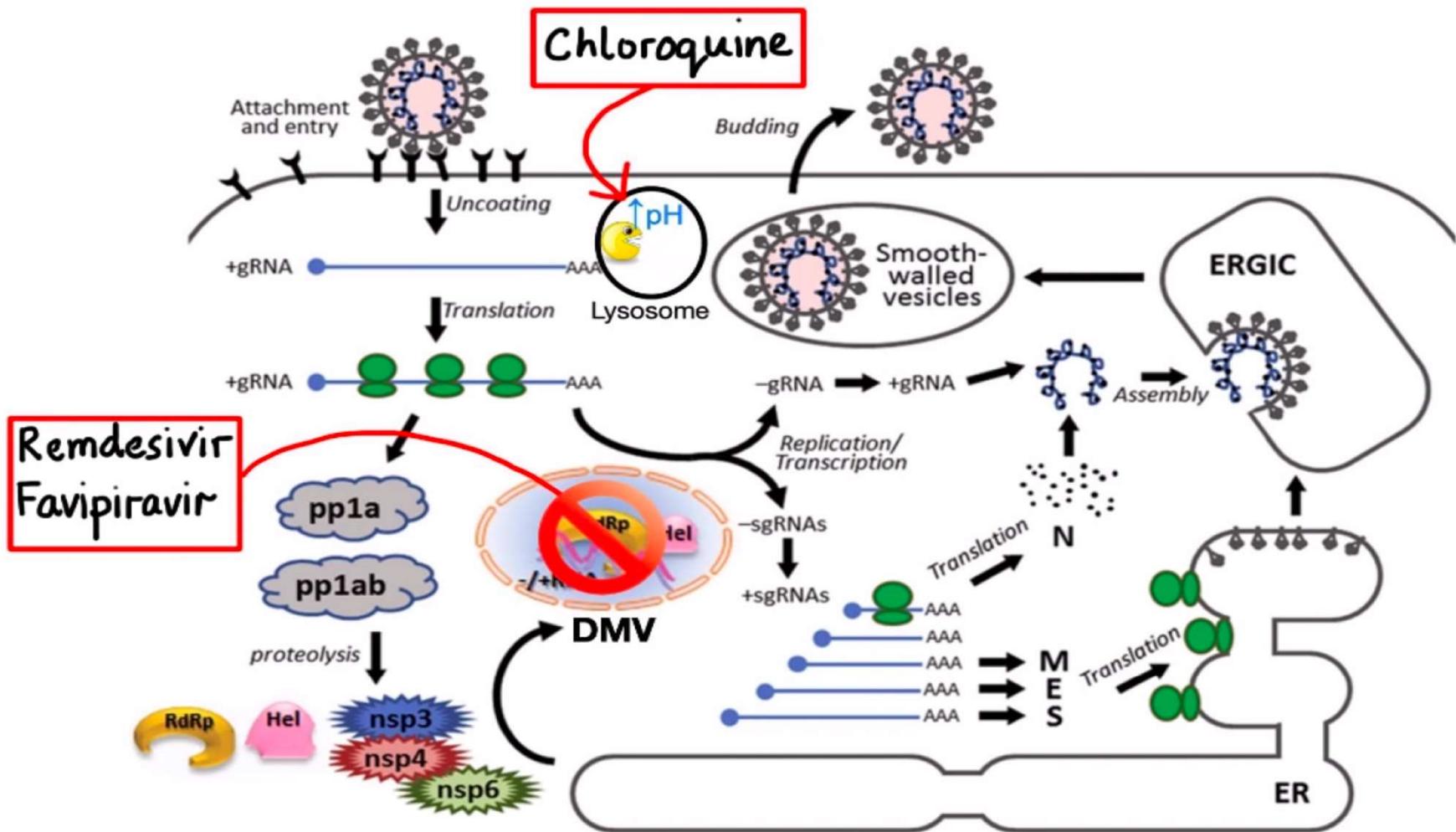


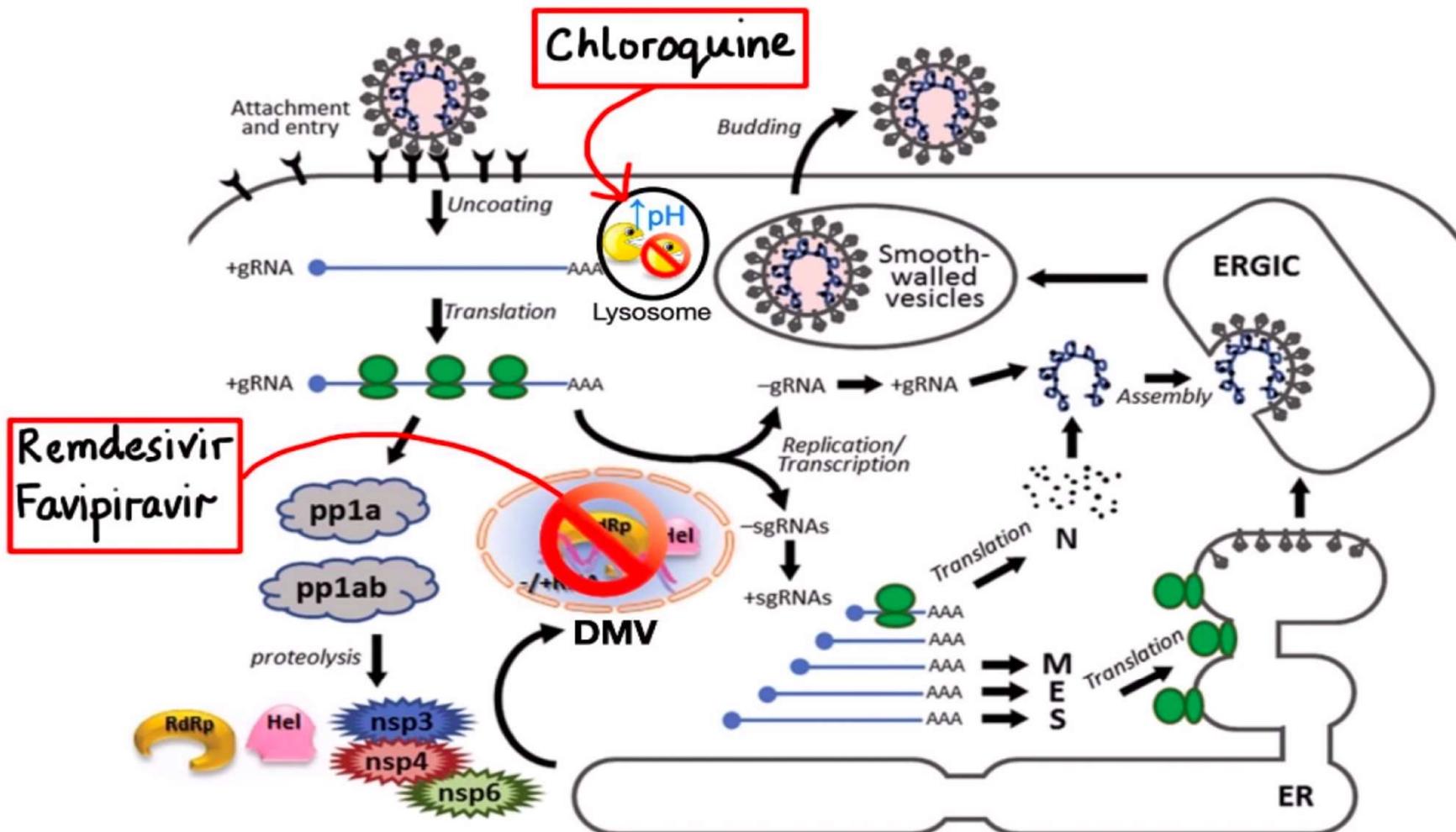


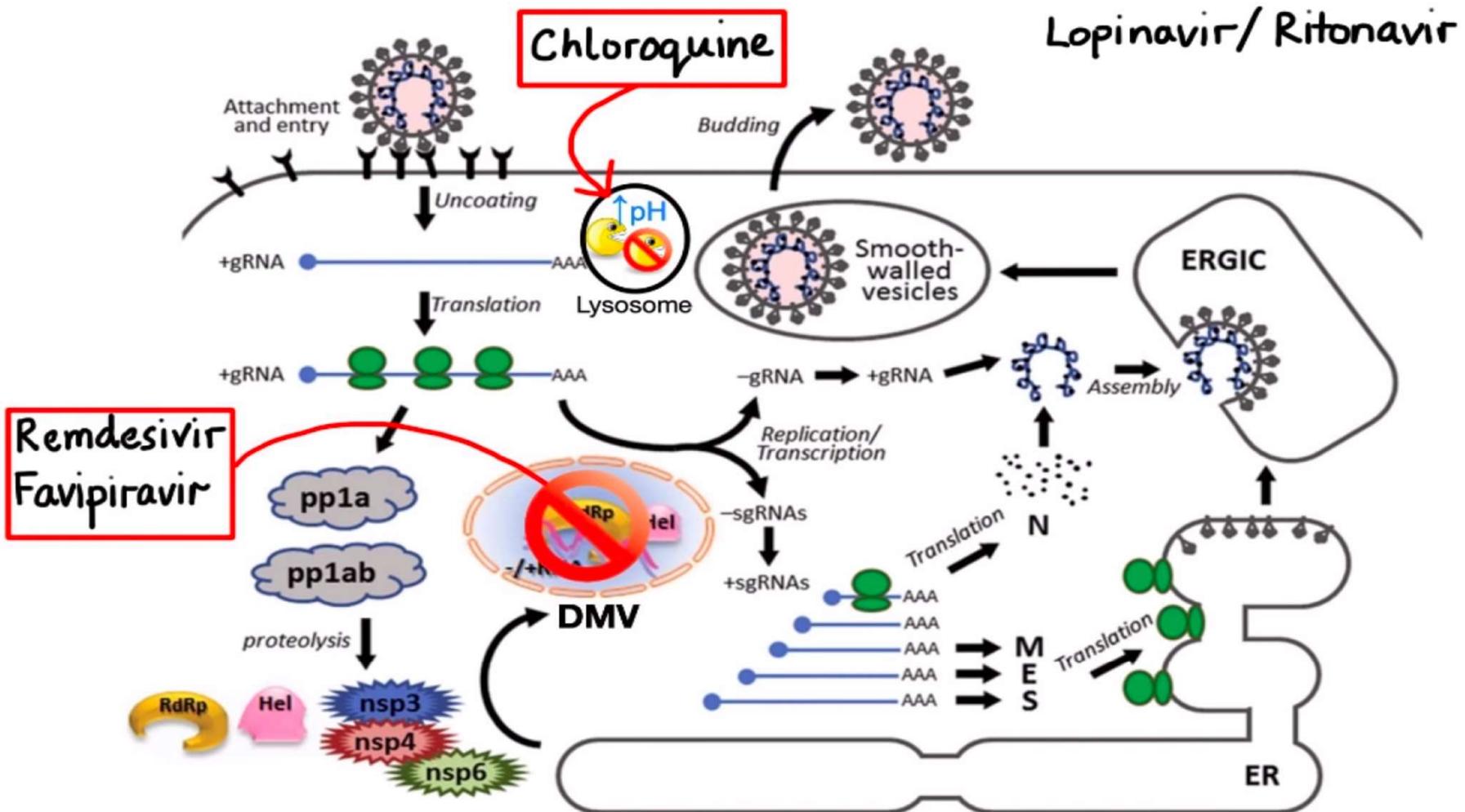


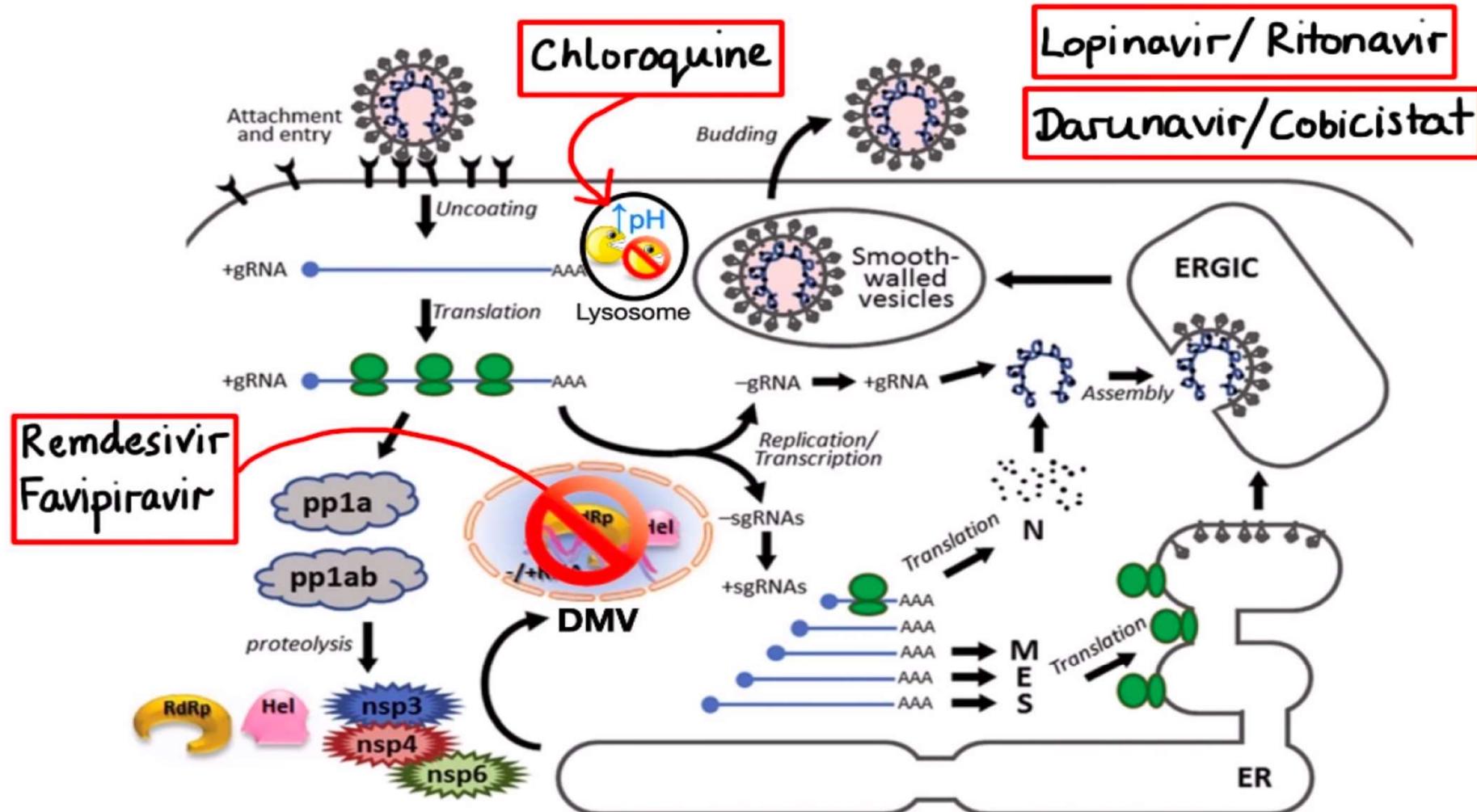


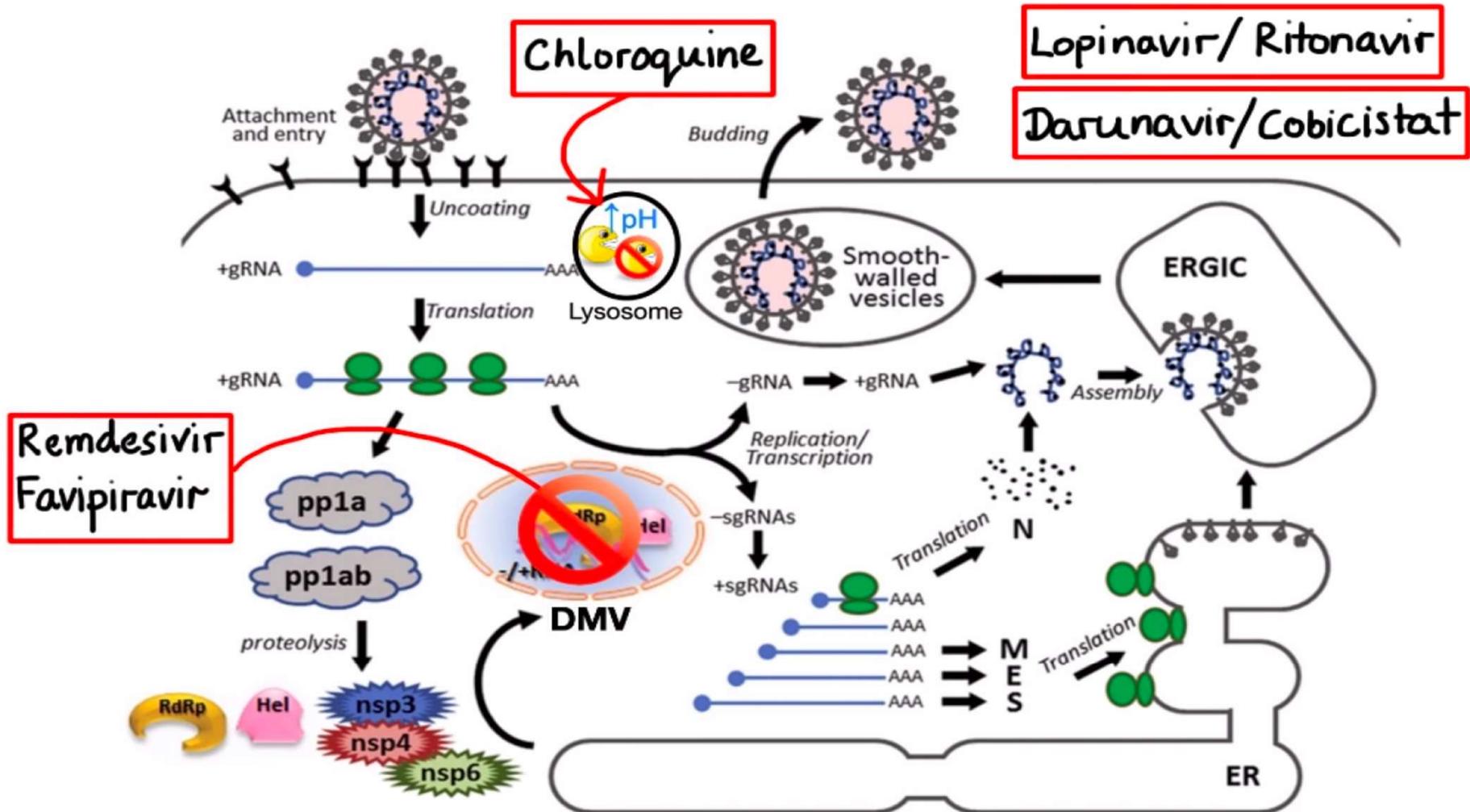




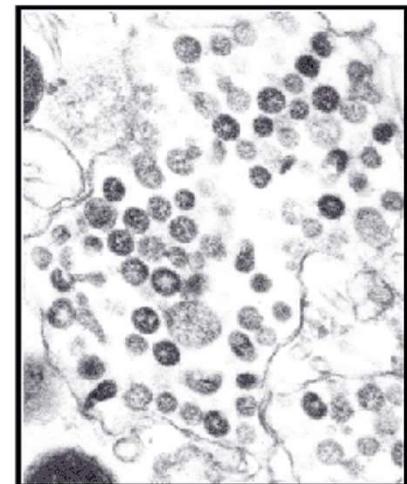
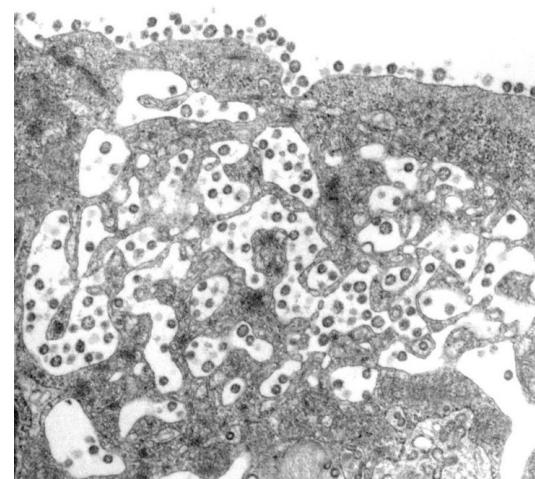
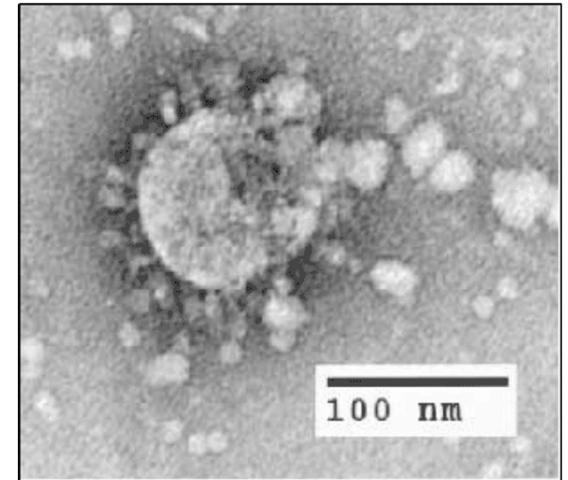
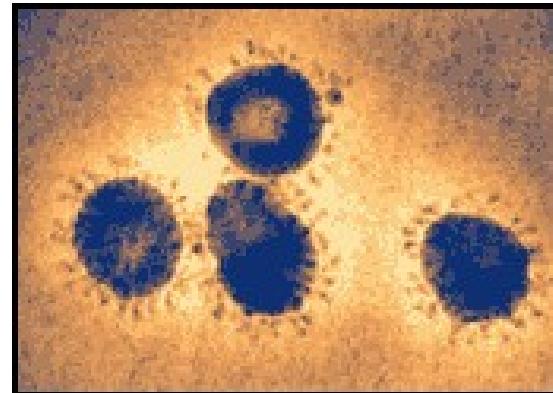






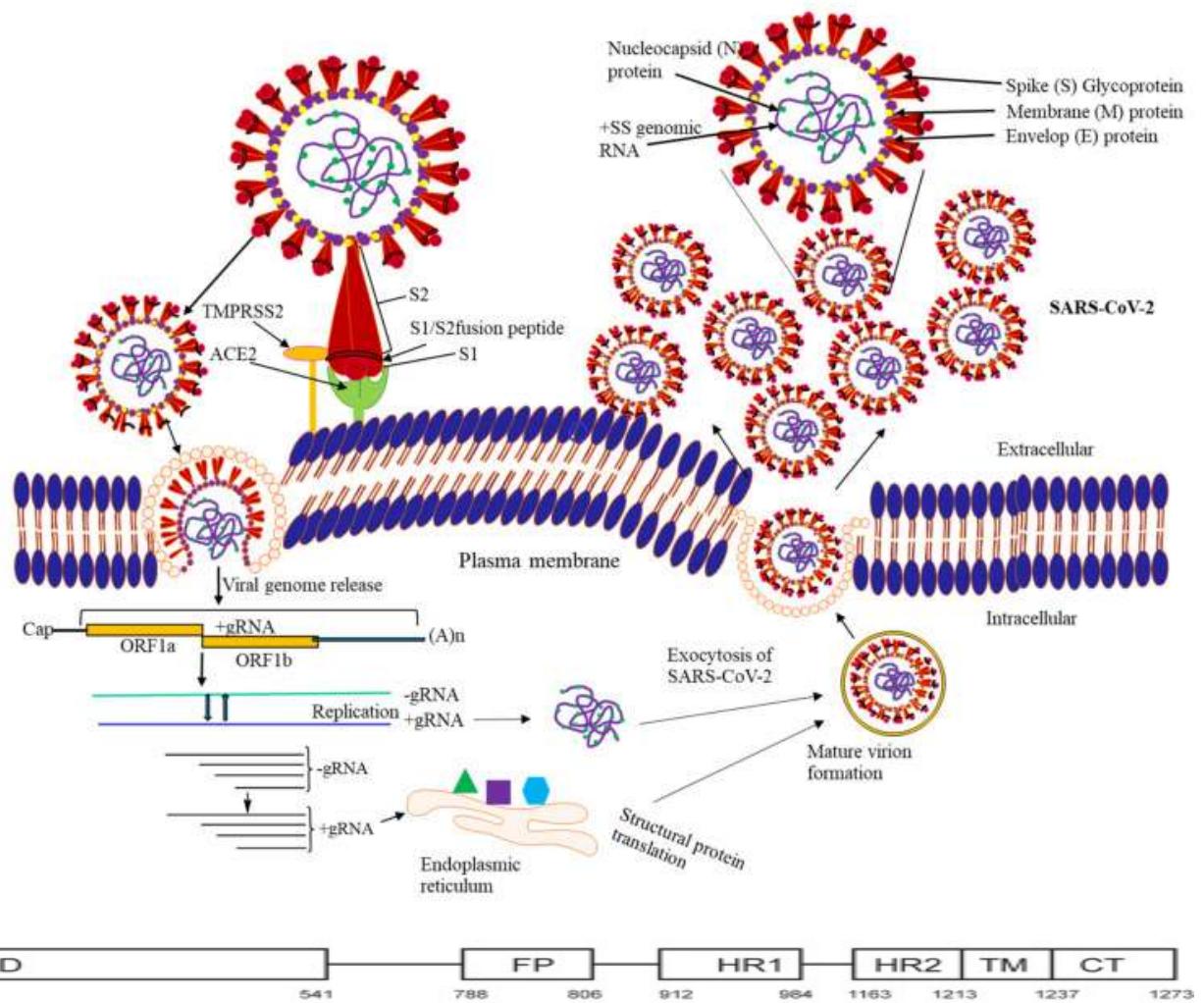


SARS-CoV Images

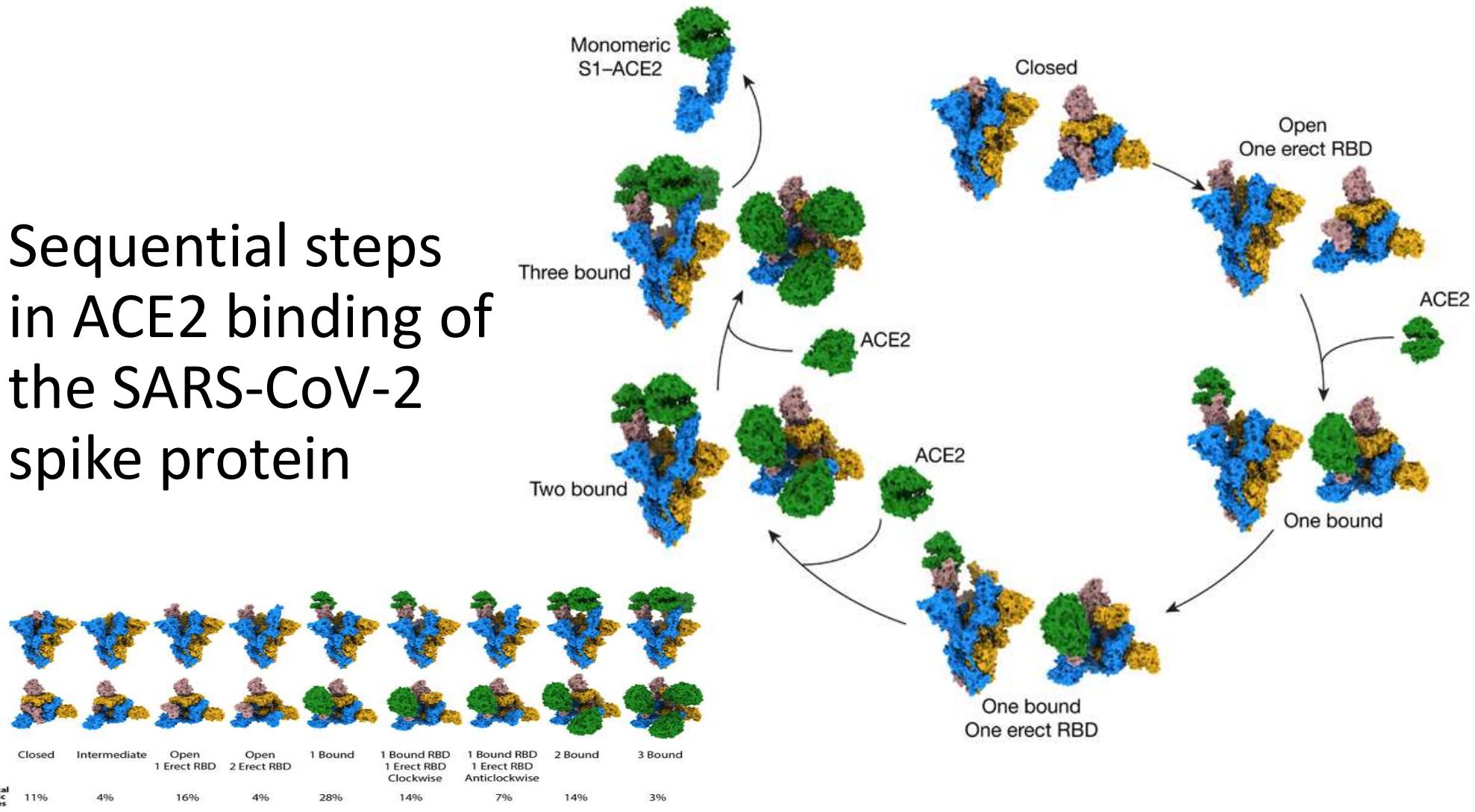


Life Cycle of SARS-CoV-2

- Life cycle of SARS-CoV-2 consists of following 5 steps
- 1. Attachment to Host Cell Surface
- 2. Viral Penetration and Uncoating
- 3. Replication-Transcription Complex (RTC) Formation
- 4. Synthesis of Viral RNA
- 5. Molecular Assembly and Release of SARS-CoV-2

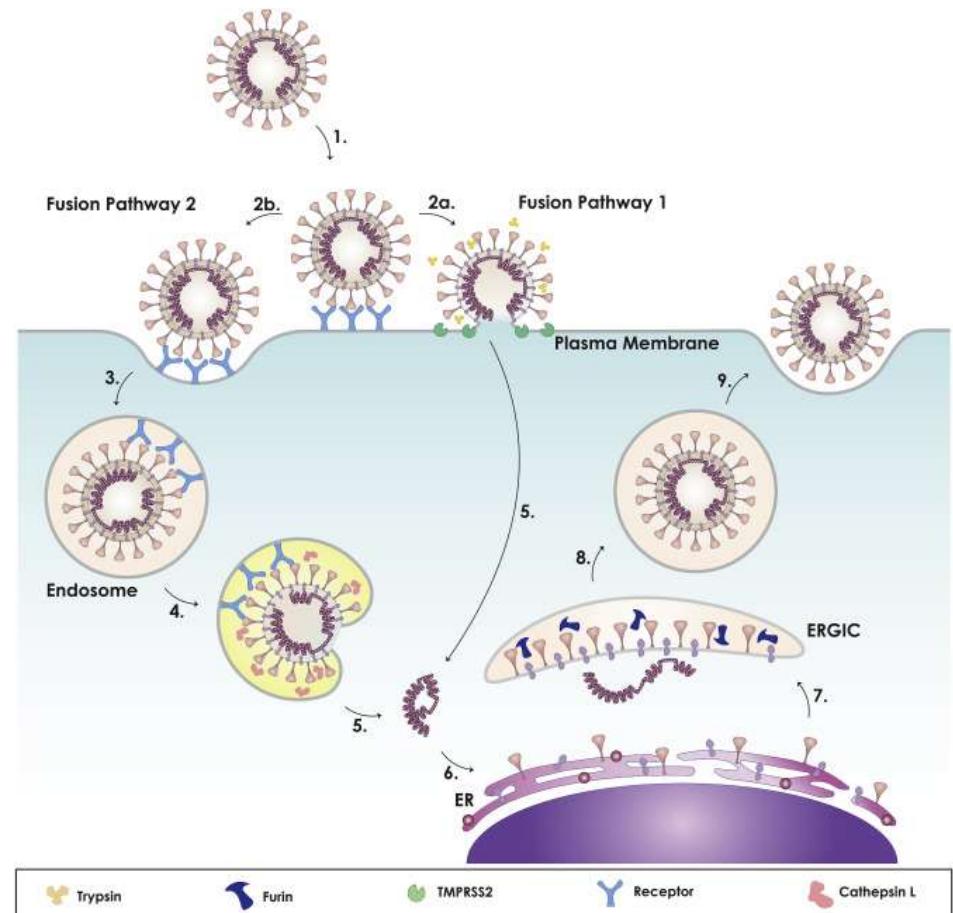


Sequential steps in ACE2 binding of the SARS-CoV-2 spike protein



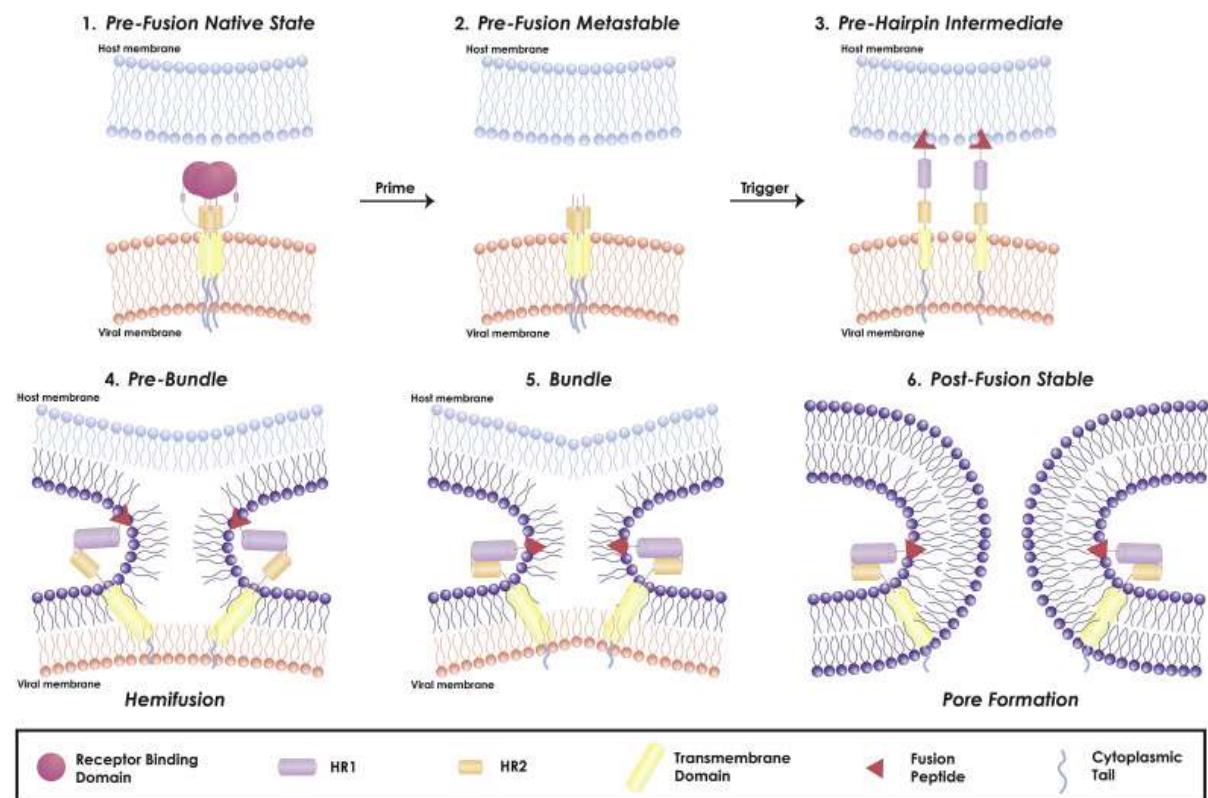
Summarize

- Model of coronavirus dual entry pathway. This model depicts the two methods of viral entry: early pathway and late pathway. As the virus binds to its receptor (1), it can achieve entry via two routes: plasma membrane or endosome. For SARS-CoV: The presence of exogeneous and membrane bound proteases, such as trypsin and TMPRSS2, triggers the early fusion pathway (2a). Otherwise, it will be endocytosed (2b, 3). For MERS-CoV: If furin cleaved the S protein at S1/S2 during biosynthesis, exogeneous and membrane bound proteases, such as trypsin and TMPRSS2, will trigger early entry (2a). Otherwise, it will be cleaved at the S1/S2 site (2b) causing the virus to be endocytosed (3). For both: Within the endosome, the low pH activates cathepsin L (4), cleaving S2' site, triggering the fusion pathway and releasing the CoV genome. Upon viral entry, copies of the genome are made in the cytoplasm (5), where components of the spike protein are synthesized in the rough endoplasmic reticulum (ER) (6). The structural proteins are assembled in the ER-Golgi intermediate compartment (ERGIC), where the spike protein can be pre-cleaved by furin, depending on cell type (7), followed by release of the virus from the cell (8, 9). For SARS-CoV-2: Studies currently show that SARS-CoV-2 can utilize membrane bound TMPRSS2 or endosomal cathepsin L for entry and that the S protein is processed during biosynthesis. Other factors that can influence the viral entry pathway are calcium and cholesterol (*not shown*).

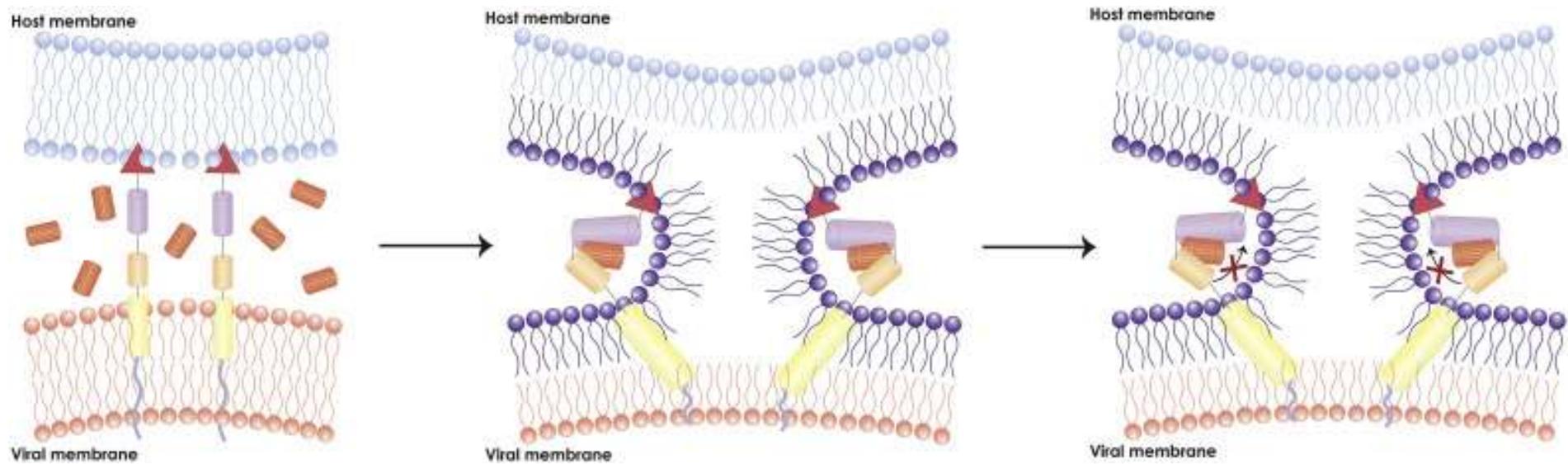


Coronavirus viral fusion pathway model based on class I fusion protein understanding

In this metastable state, the fusion protein must overcome a kinetic barrier to transition to the next state. The energy to overcome this barrier can be provided by a trigger that will interact with the fusion protein, resulting in a series of conformational changes that will enable the fusion protein to insert its FP into the host membrane, forming a pre-hairpin intermediate state. The triggering event(s) are usually environmental cues that inform the virus about its microenvironment. As an example, the influenza virus fusion protein is triggered by low pH; as the virus is trafficked through the endosome, the increasingly acidic conditions eventually destabilize its fusion protein, so that the fusion peptide is able to insert into the endosomal membrane and commence the fusion process.



- Model of major antiviral inhibitor pathway



Thank You