

Lecture 8-9:

Replication strategies of RNA Viruses

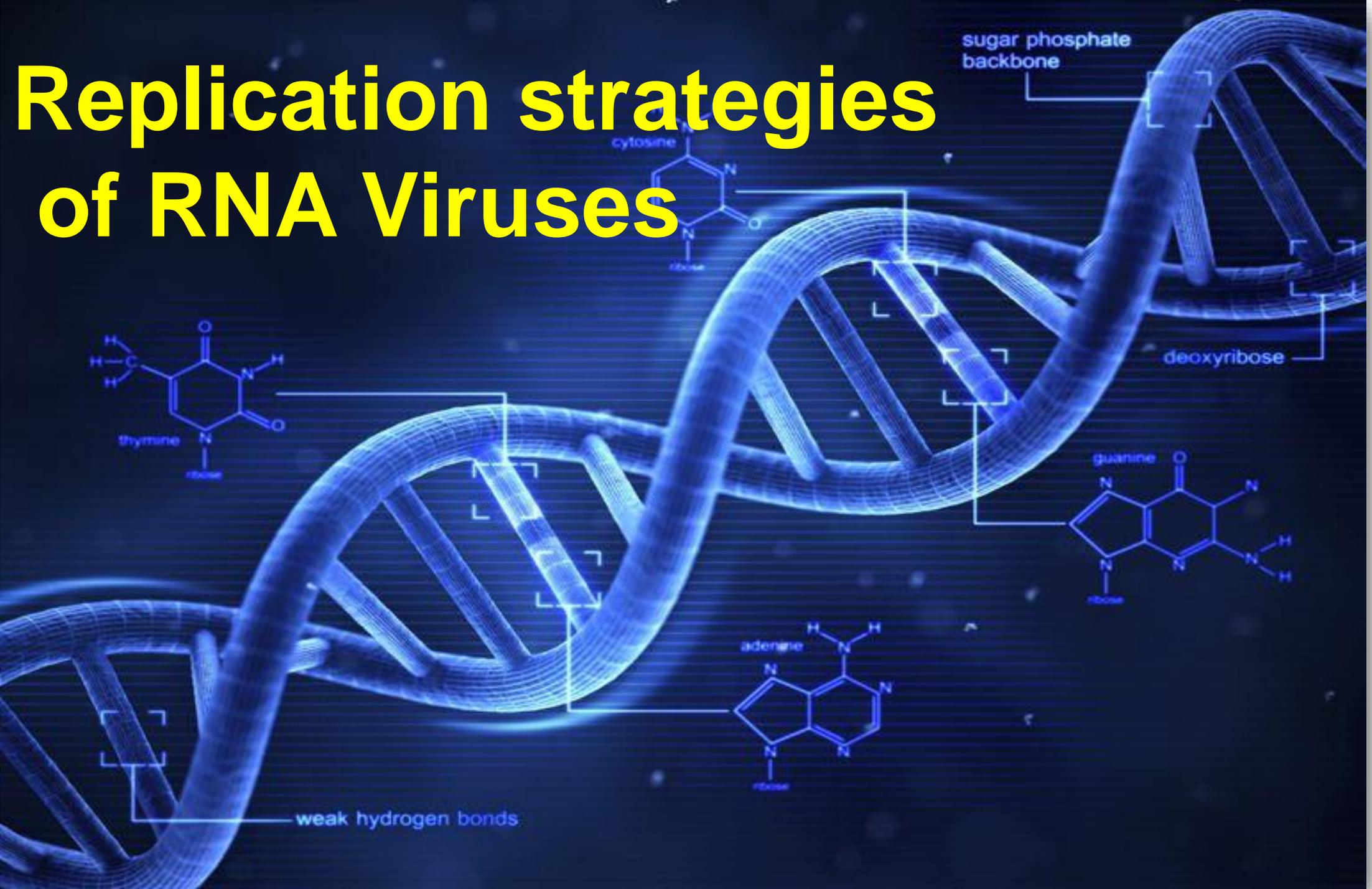
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Replication strategies of RNA Viruses



Important Notes

- Eukaryotic cells contain no **RNA dependent RNA polymerase** for transcription or replication of the viral RNA genome. So, RNA viruses should carry or code for their own **RdRp** for productive replication.
- Eukaryotic cells are not equipped to translate **polycistronic mRNA** into several individual proteins.
- RNA viruses mostly replicate in cytoplasm and have no access to the RNA splicing enzymes present in the nucleus. So they developed a diversity of solutions to that problem??



Replication strategies

- dsRNA viruses (e.g. Reoviridae and Birnaviridae)
- ssRNA viruses (-ve sense), non-segmented (e.g. Mononegavirales)
- ssRNA (-ve sense), Segmented viruses (e.g. Orthomyxoviridae)
- ssRNA viruses (+ve sense) (e.g. Picornaviridae)
- ssRNA viruses (+ve sense) of nested mRNA set (e.g. Coronaviridae)
- Reverse transcribing RNA viruses (e.g. Retroviridae)



1- dsRNA viruses **Reoviridae**

- The viral genome is segmented dsRNA.
- The virus carries its own “virion associated RdRp”.
- The negative strand of dsRNA (each segment) is transcribed by the RdRp to produce mRNA (positive) copies.
- The transcripts (mRNA) are monocistronic.
- The positive strands also serve as templates for synthesis of the genomic dsRNA.



2- ssRNA [-] viruses (Non-segmented) **Mononegavirales**

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- The viral genome is **non-segmented** negative-sense, single-stranded RNA.
 - The virus carries its own “virion associated RdRp”.
 - The viral genome (-) is transcribed by the RdRp to produce 5-7 mRNA (positive) copies by termination and reinitiation strategy.
 - The transcripts (mRNA) are monocistronic.
 - In the replication mode, RdRp transcribes the viral genome (-) to produce full-length positive strands for use in synthesis of new negative strands of viral genomic RNA

3- ssRNA [-] viruses (Segmented) **Orthomyxoviridae**

- The viral genome is **segmented** negative-sense single-stranded RNA.
- The virus carries its own “virion associated RdRp”.
- Each segment is transcribed separately by the use of RdRp to positive (mRNA) copies.
- The transcripts (mRNA) are monocistronic.
- Positive strands act bidirectionally for: production of the coding proteins and as templates for synthesis of the genomic negative strand RNAs.



4- ssRNA [+] viruses

Picornaviridae

- The viral genome is non-segmented **positive-sense**, single-stranded RNA.
- The virus genome acts as mRNA (polycistronic) and translated directly to a single polyprotein.
- The polyprotein is cleaved to give individual **structural** and **non-structural** (including RdRp) proteins.
- The viral encoded RdRp acts on the viral genome to produce a complementary negative copy, which acts as a template for production of the viral (+) RNA genome.



6- RT-RNA viruses

Retroviridae

- The viral genome is a diploid, non-segmented, single-stranded RNA.
- The viral RNA is reverse transcribed to dsDNA which proceed to produce his own protein like Herpes viruses (Replication strategies of DNA viruses, group II).



5- ssRNA [+] viruses (Nested mRNA) **Coronaviridae**

- The viral genome is **LARGE** non-segmented **positive-sense**, single-stranded RNA.
- The virus genome acts as mRNA and part of the virion RNA translated to produce the RdRp.
- RdRp acts on the viral genome to produce a complementary full-length negative RNA strand.
- Then, RdRp used the RNA (-) to produce a nested set of mRNA (starting from the full length till a single gene-coding) with a common 3' end.
- Only the 5'-terminal gene is translated from each mRNA.





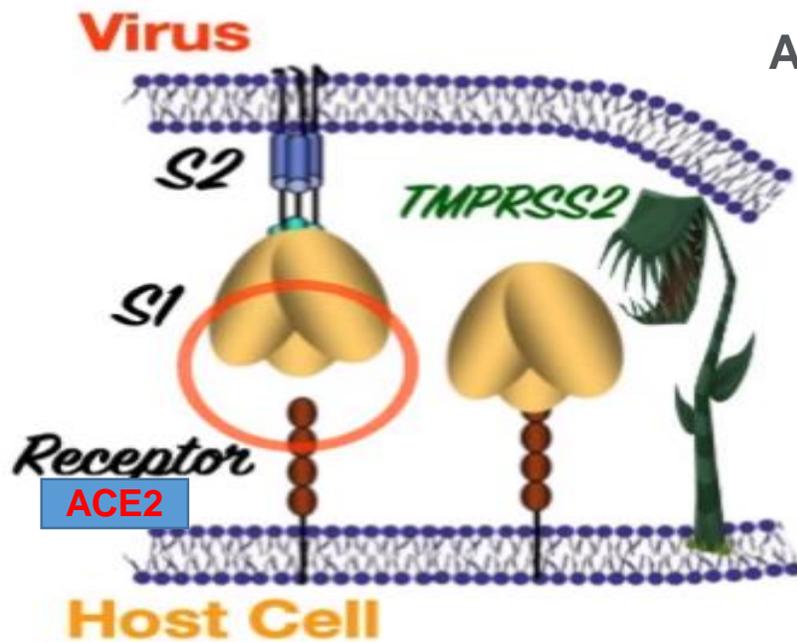
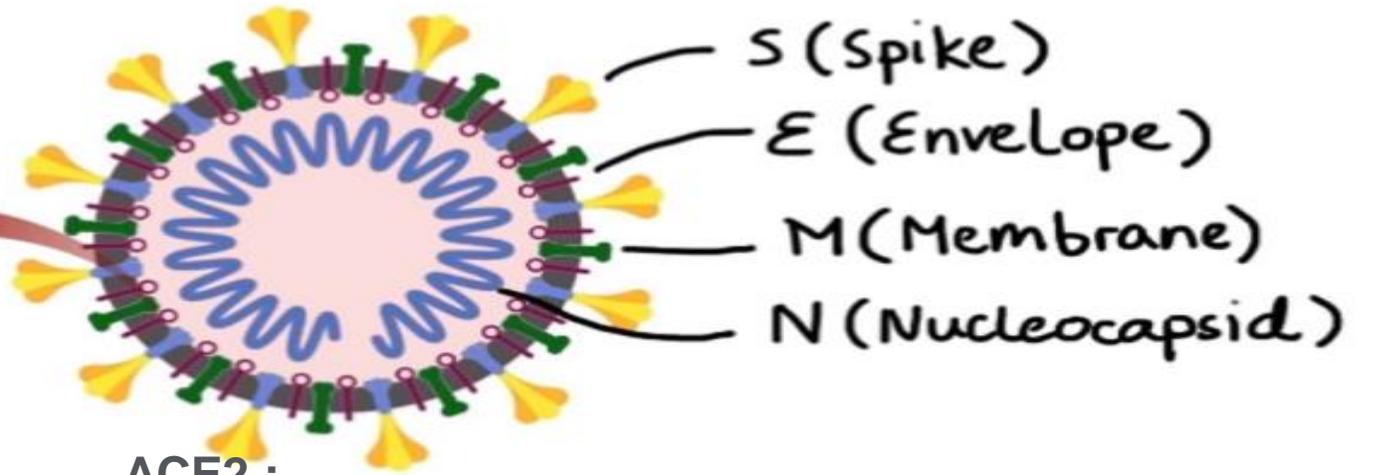
RNA viruses mostly replicate in cytoplasm and have no access to the RNA splicing enzymes present in the nucleus.

So they developed a diversity of **solutions to that problem??**

1. Some have a segmented genome in which each segment encodes for only one mRNA (mono-cistronic).
2. Some have a polycistronic genome but produce monocistronic RNA transcripts by termination and reinitiation of transcription.
3. Some make use of a nested set of overlapping RNA transcripts each of which is translated into a single gene product.
4. Some have a polycistronic viral RNA that is translated into a polyprotein, which is cleaved to yield the final products.



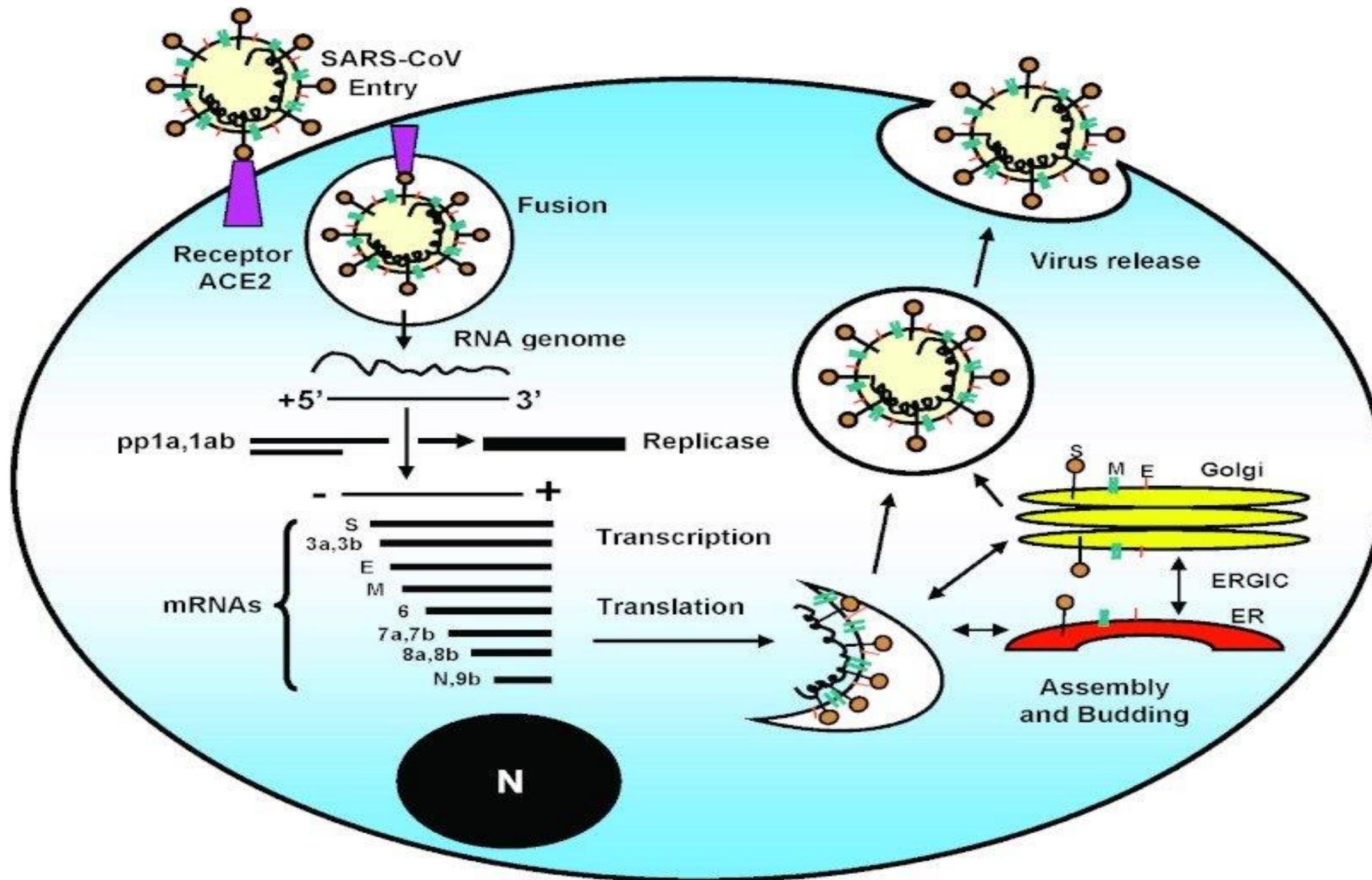
SARS-CoV-2

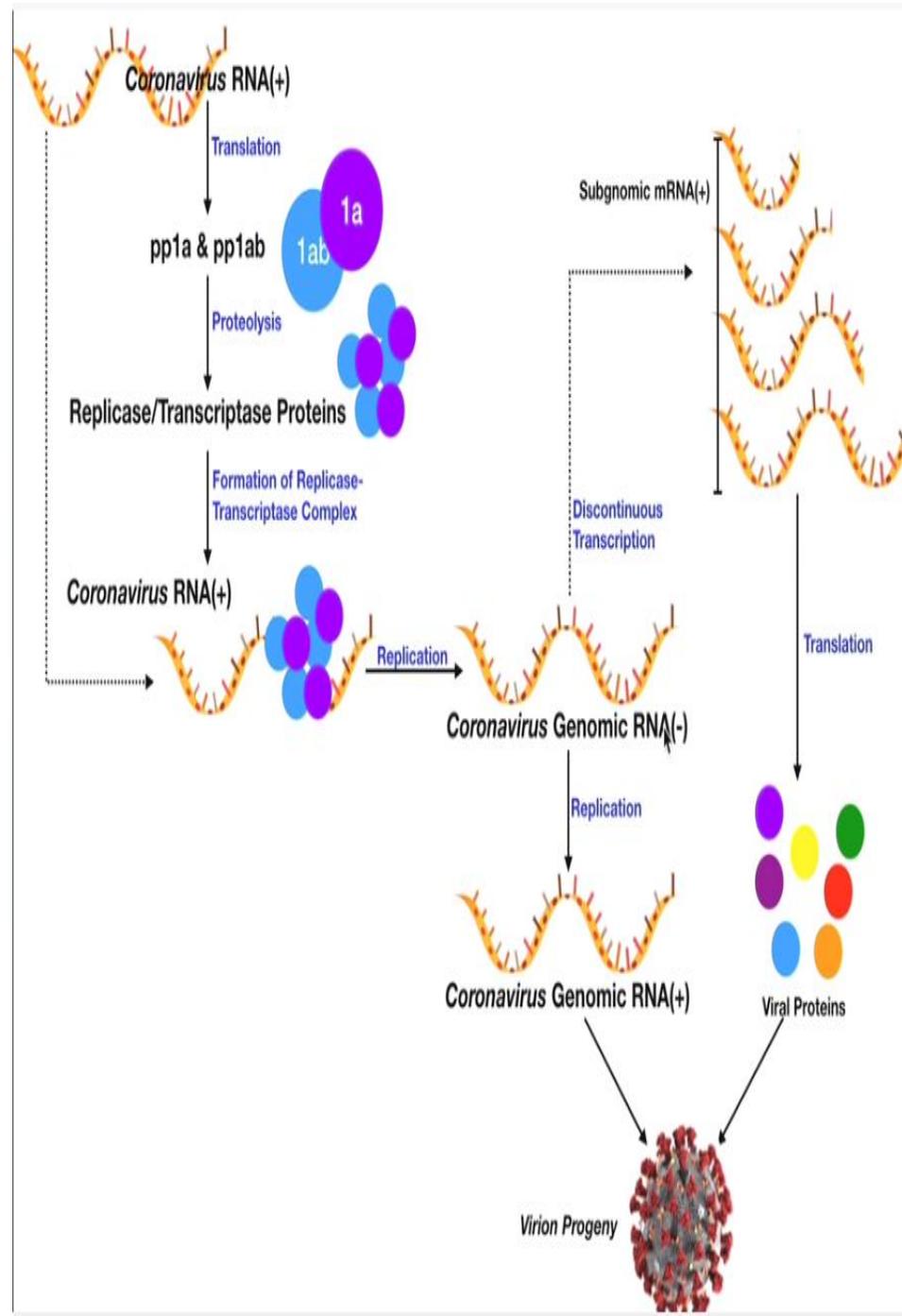


ACE2 :

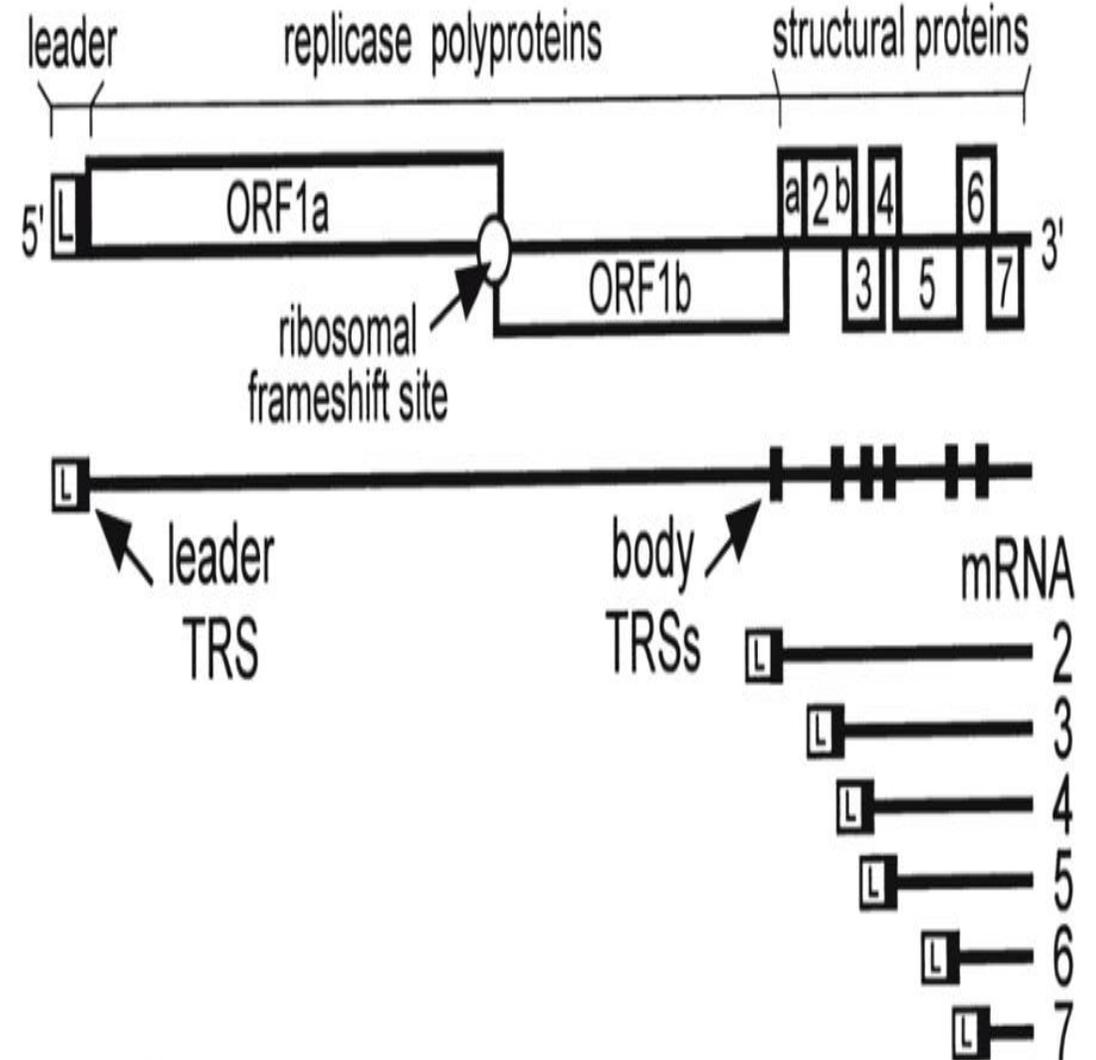
ACE2 : Angiotensin converting enzyme 2

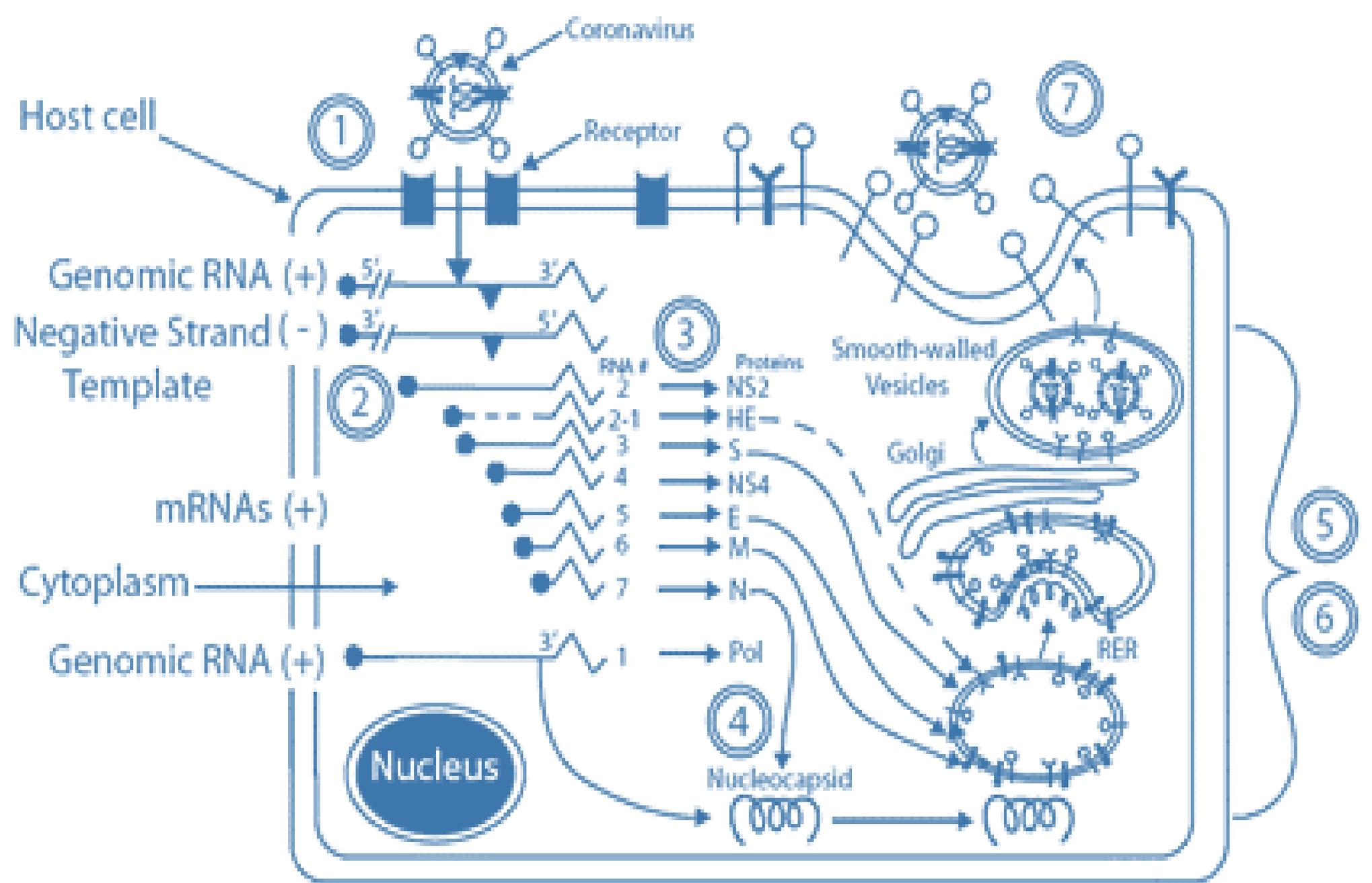
TMPRSS2: Transmembrane protease, serine 2

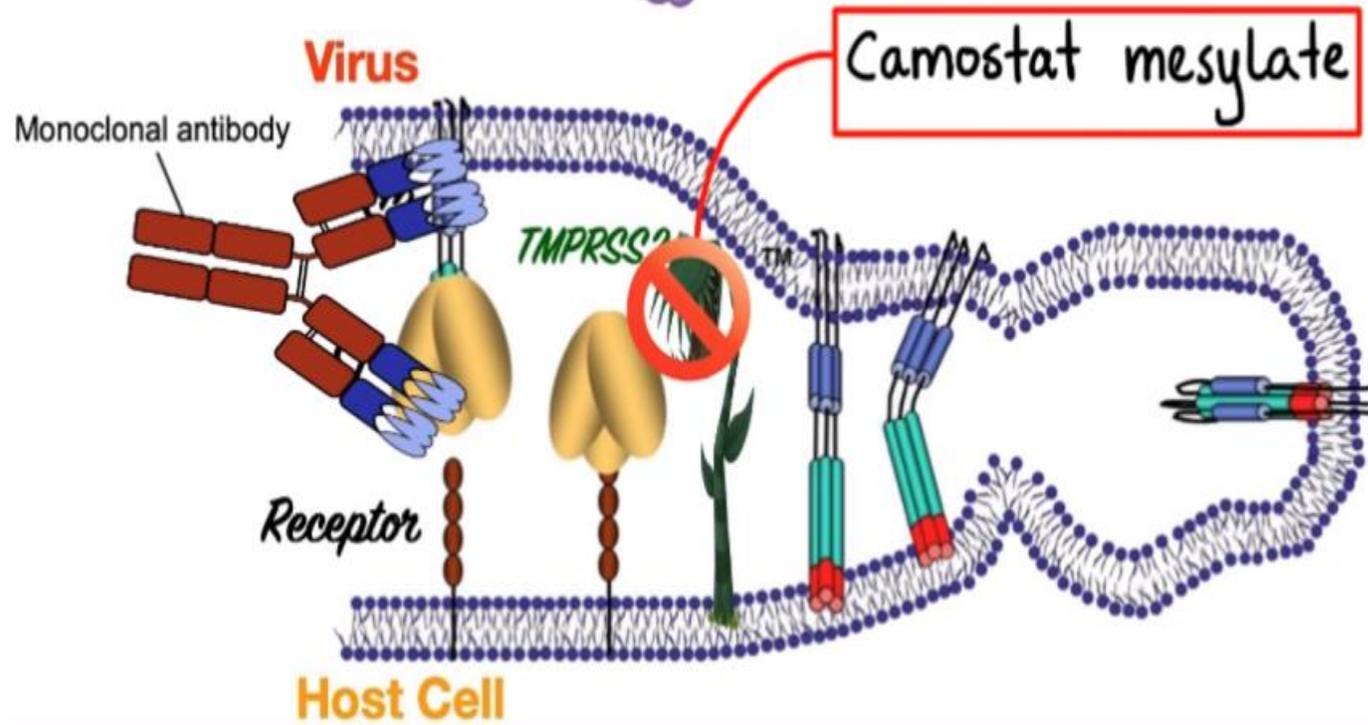
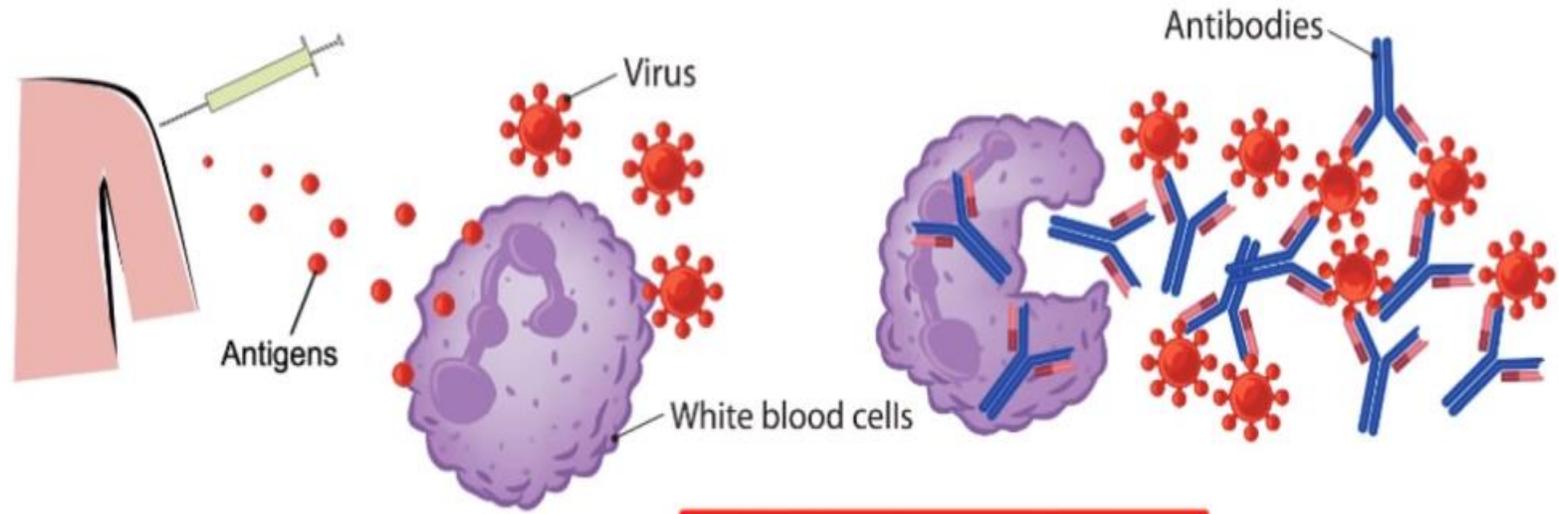


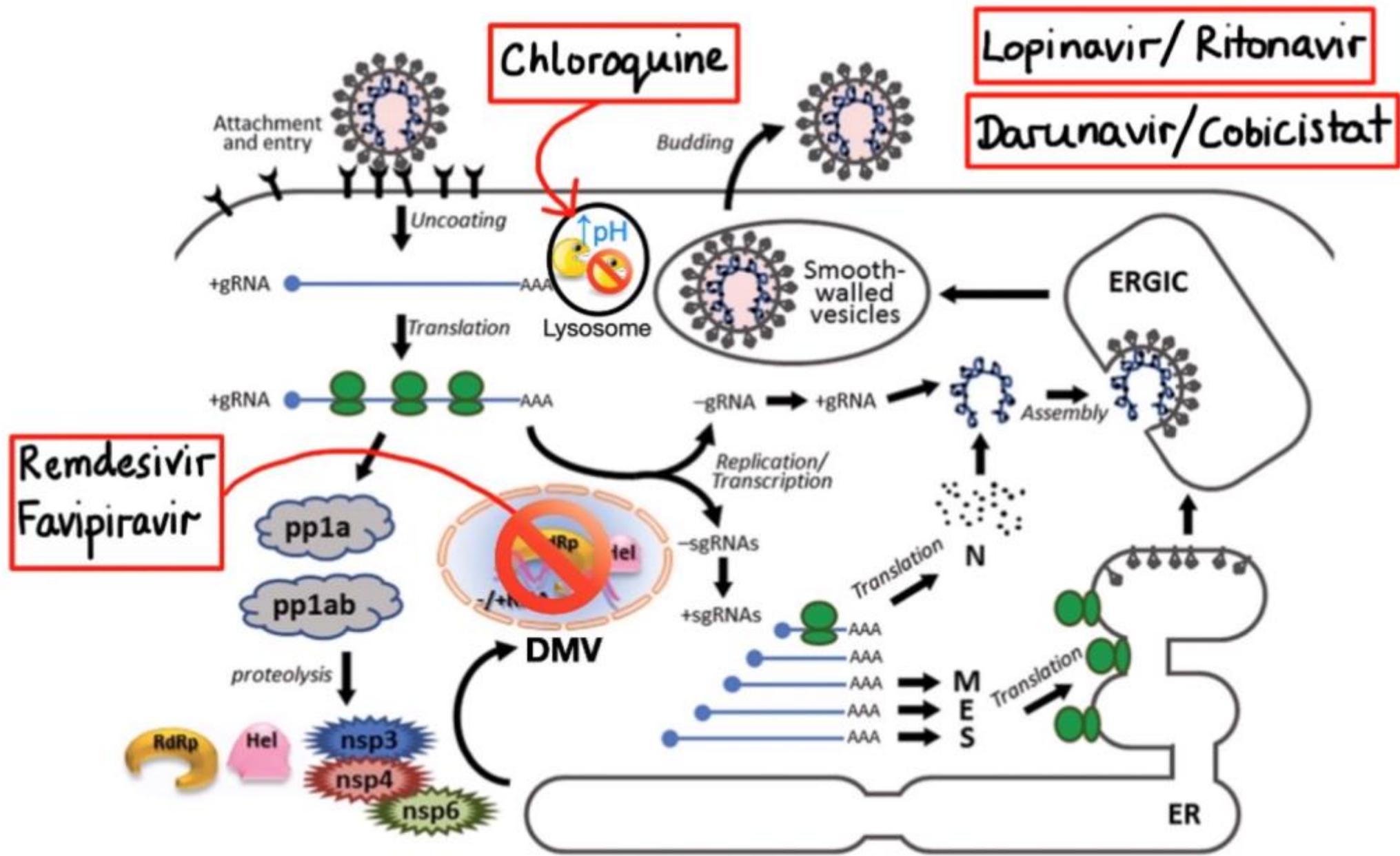


Coronavirus Subgenomic mRNA Synthesis









Questions

1. RNA viruses mostly replicate in cytoplasm and have no access to the RNA splicing enzymes present in the nucleus. So they developed a diversity of strategies to that problem? Discuss and mention these strategies?
1. What is the role/function of RNA dependent RNA polymerase during replication of the viral RNA genome?





TAKE HOME MESSAGES

Let us all do our part to stop SARS-CoV-2 and encourage one another. Together, we will overcome this COVID-19 pandemic and emerge stronger



Thank
You