

# **Replication of Positive Strand RNA Viruses (Polio)**

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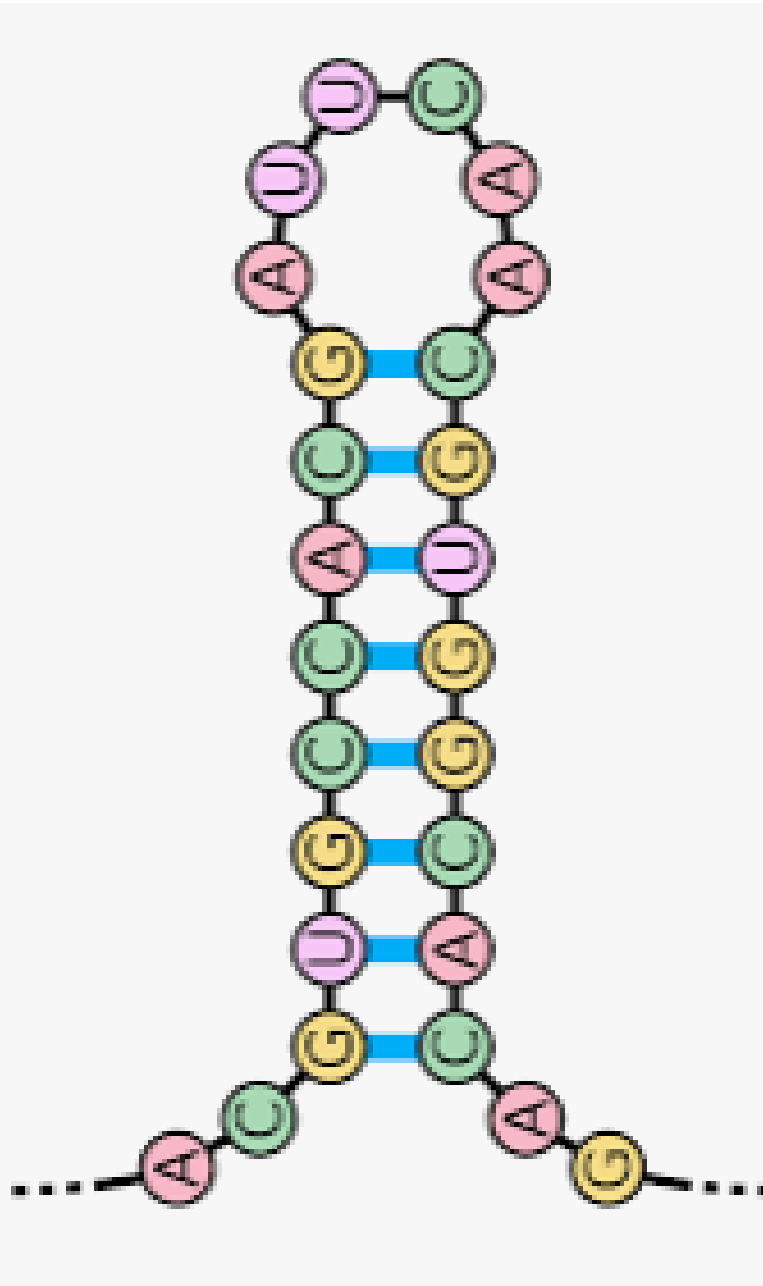
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# Positive Strand RNA Virus

- Positive strand RNA viruses are the single largest group of RNA viruses with 30 families.
- Important examples of +ssRNA viruses are severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), Hepatovirus A and polio virus, which cause corona, hepatitis A and poliomyelitis, respectively.
- Polioviruses are single-stranded RNA viruses belonging to the family Picornaviridae.
- They have a naked icosahedral protein capsid with a dense central core. The capsid consists of four structural proteins, VP1, VP2, VP3, and VP4.
- The poliovirus genome consists of ~7500 nucleotides and contains a poly(A) tail at the 3' end and a small peptide, VPg, covalently linked to the 5' end.
- The highly structured 5' untranslated region (UTR) regulates both translation and RNA replication.
- Two functional regions have been described within the 5' UTR:
  - a long element involved in cap-independent initiation of translation (IRES)
  - a shorter 5'-terminal structure (the cloverleaf RNA) involved in viral RNA replication

## Stem loop



- The genome of a positive strand RNA virus, unlike that of any other virus or organism, must function both as the repository of genetic information (i.e., as the genome) and also as a messenger RNA.
- Thus, the virus must coordinate the mutually exclusive activities of translation, RNA replication and encapsidation, all of which occur on the same genomic RNA molecule, but not at the same time.

# Translation

- To initiate infection virion attaches to specific receptor on the surface of a sensitive cell and enters the cell.
- Inside cell – virus particle uncoated
- Free RNA associates with ribosomes
- 5' end of poliovirus RNA has a long sequence that can fold into several stem loops.
- VPg protein and stem loops mimic the cap binding protein, permit binding of the viral mRNA to the ribosome.
- Viral RNA (monocistronic) but codes for all the proteins of the virus in a single protein called polyprotein (2200 amino acids).
- Polyprotein post-translational cleaved into ~ 20 small proteins (including VPg, RNA replicase).

# Replication of Poliovirus RNA

- Short time after infection replicate by RNA replicase.
- Transcribes positive sense viral RNA into a complementary RNA molecule of negative complementarity.
- Negative strand now template for repeated transcription of progeny positive strands catalyzed by viral-specific RNA replicase.
- Some positive strains again transcribe ~1000 negative strands, responsible for synthesis of millions positive strand.
- Both positive and negative strand linked to VPg protein (22 amino acids)
- Once poliovirus multiplication begins – protein synthesis inhibited.
- Host protein synthesis stops as destruction of important host protein, Cap binding protein, required for translation of capped mRNAs.
- The genomes that are encapsidated directly after synthesis keep the VPg in 5', which may be part of the encapsidation signal.

