



Viral replication

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Basic Structure of Viruses

- **Components**

- **Genetic Material:** DNA or RNA (not both)
- **Protein Coat (Capsid):** Protects genetic material
- **Envelope (in some viruses):** Lipid membrane derived from host cell

- **Shapes and Sizes**

- Helical, icosahedral, complex structures

- **Examples**

- Enveloped Viruses: HIV, Influenza virus
- Non-Enveloped Viruses: Adenovirus, Poliovirus



Viral Classification

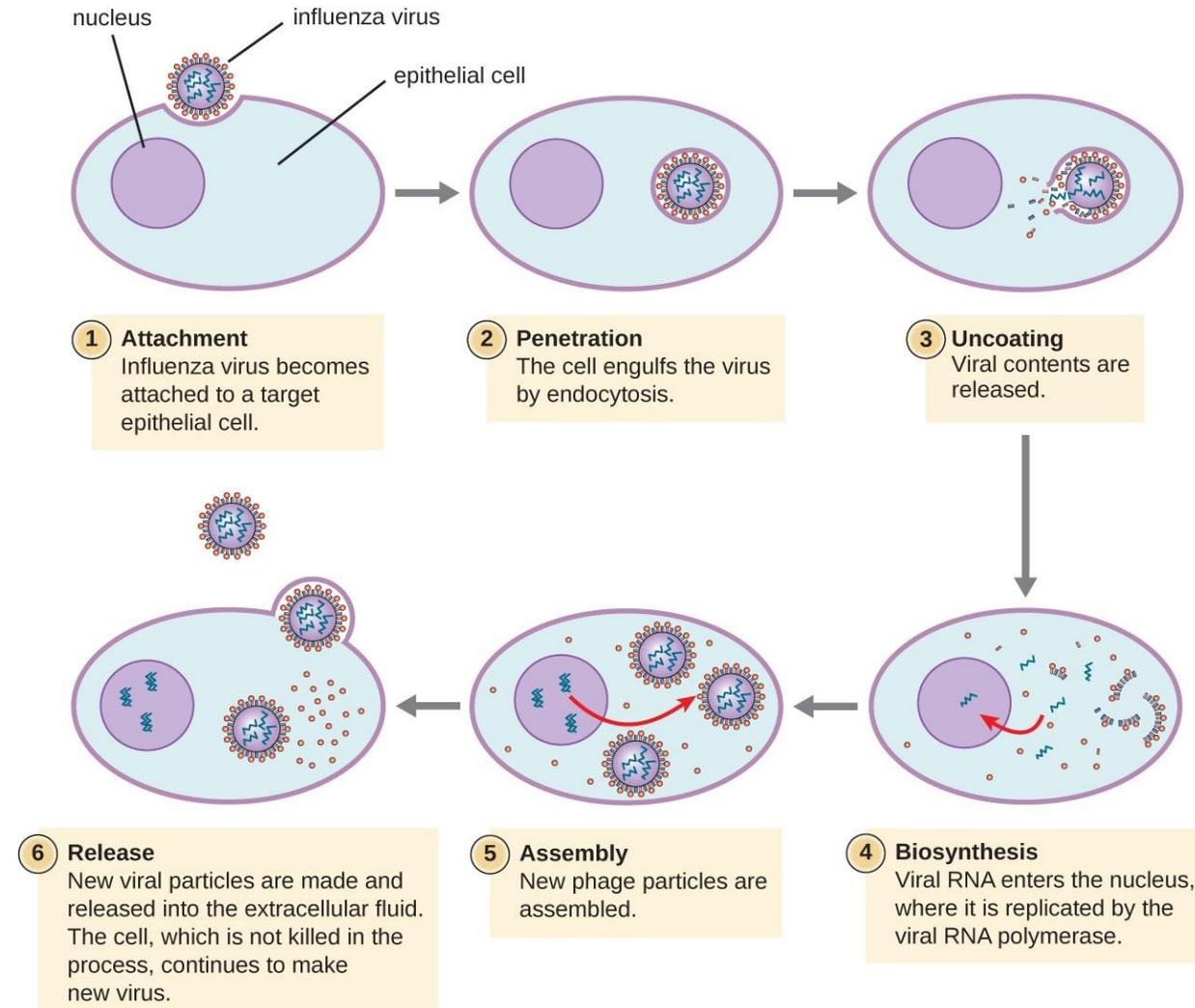
- **Based on Genetic Material**
 - DNA Viruses
 - RNA Viruses
- **Based on Replication Strategy**
 - Baltimore Classification (detailed later)



Overview of Viral Replication Steps

- **General Steps:**

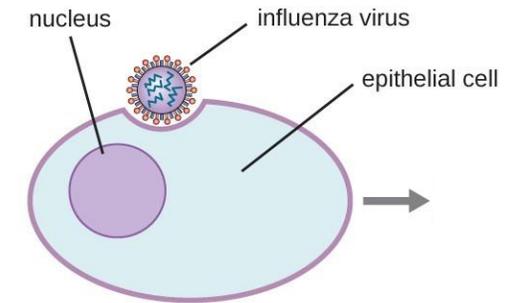
1. Attachment (Adsorption)
2. Penetration (Entry)
3. Uncoating
4. Synthesis (Replication and Protein Production)
5. Assembly (Maturation)
6. Release (Egress)



Viral Replication Steps

Step 1 - Attachment (Adsorption)

- **Mechanism:**
 - Viral surface proteins (ligands) bind to specific receptors on the host cell membrane.
 - The receptors on cells are protein or carbohydrate or lipid components of the cell surface.
- **Specificity:**
 - Determines host range and tissue tropism.
 - Cells without the appropriate receptors are not susceptible to the virus.
- **Examples:**
 - **HIV:** gp120 binds to CD4 receptors on T-helper cells.
 - **Influenza Virus:** Hemagglutinin binds to sialic acid residues on respiratory epithelial cells.



- 1 **Attachment**
Influenza virus becomes attached to a target epithelial cell.

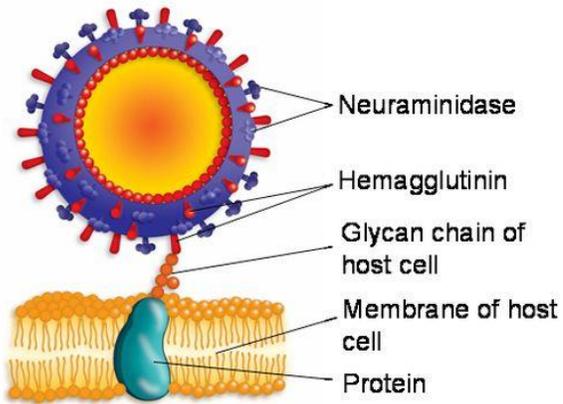


Viral Replication Steps

Step 1 - Attachment (Adsorption) - Examples

Influenza virus

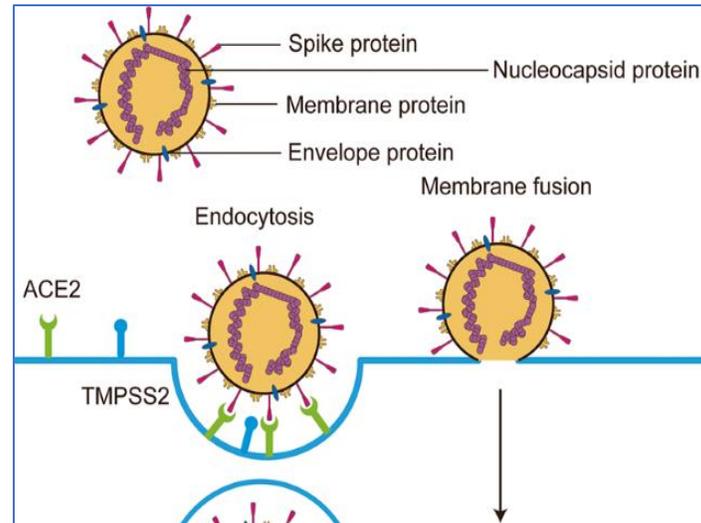
Influenza A virus infects a host cell



Hemagglutinin (HA): attaches to sialic acid-containing receptors on respiratory epithelial cells

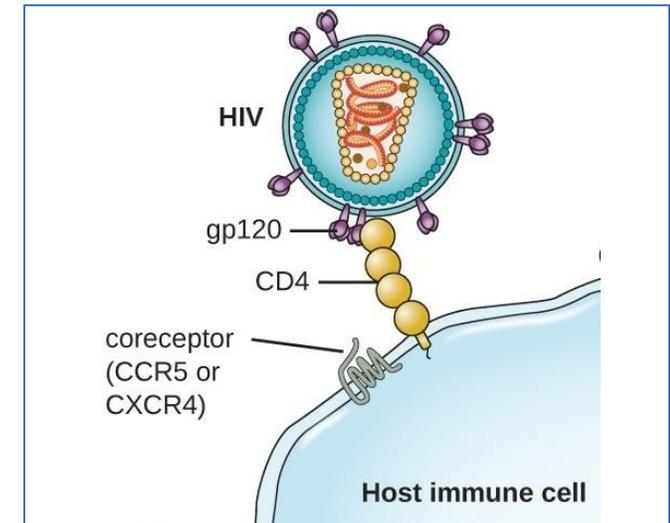
Neuraminidase (NA): cleaves newly formed virions off the sialic acid-containing receptor, allowing the virus to exit cells

COVID-19



The spike protein binds to the membrane protein angiotensin-converting enzyme 2 (ACE2). Membrane fusion and uncoating of the viral RNA occur.

HIV



The joining ligand of HIV is **gp120** which binds to the most common cellular receptors glycoproteins (CD4).



Viral Replication Steps

Step 2 - Penetration (Entry)

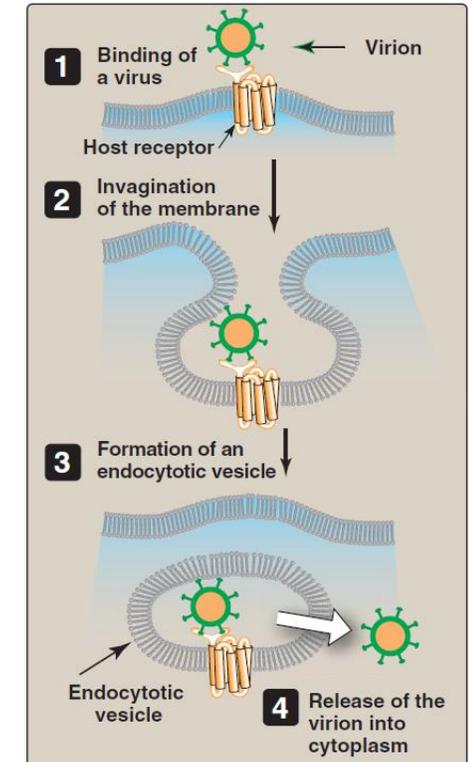
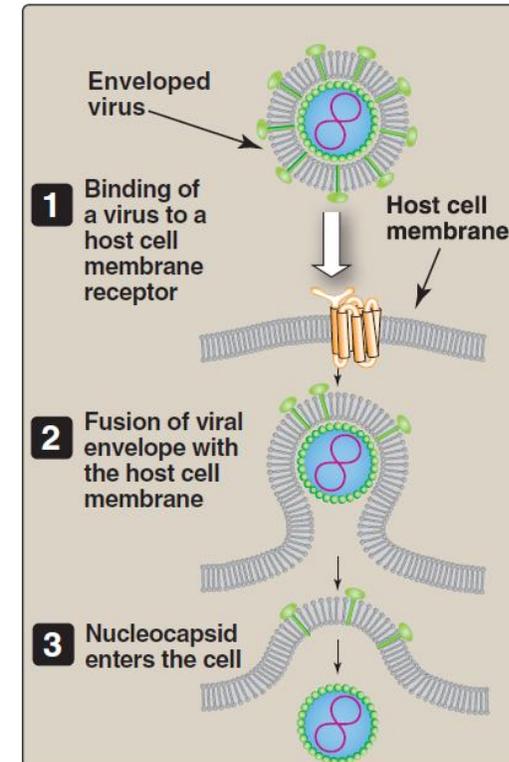
Mechanisms:

- **Direct Fusion (Enveloped Viruses):**

- Viral envelope fuses with the plasma membrane of the cell.
- The end result of this process is that the nucleocapsid is free in the cytoplasm, whereas the viral membrane remains associated with the plasma membrane of the host cell.
- Example: HIV entering T-cells.

- **Receptor-mediated endocytosis (Enveloped and Non-Enveloped Viruses):**

- The cell membrane invaginates, enclosing the virion in an endocytotic vesicle (endosome).
- Example: Adenovirus (non enveloped virus).



Viral Replication Steps

Step 3 - Uncoating

- **Definition:**

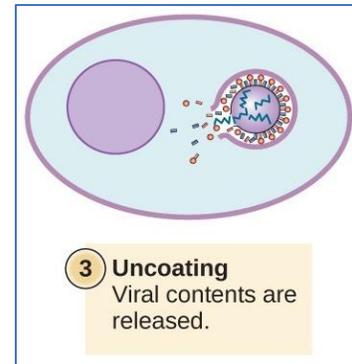
- Refers to the separation of the capsid from the viral genome. It results in the loss of virion infectivity.

- **Mechanisms:**

- Lysosomal Enzymes: degrade the proteins of the viral capsid.
- Conformational Changes: Triggered by pH shifts.

- **Examples:**

- Influenza Virus: Uncoating facilitated by M2 ion channel in acidic endosome.

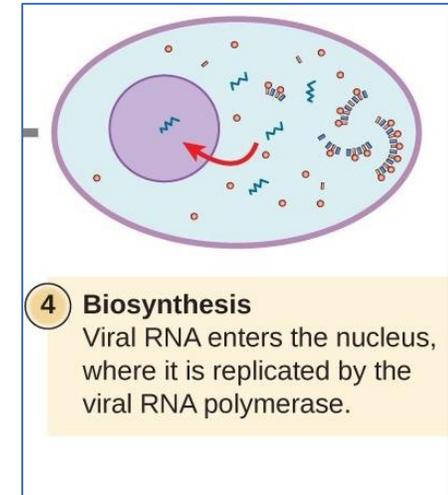


Viral Replication Steps

Step 4 –Synthesis: Replication and Protein Production

- Once uncoating has taken place, synthesis of viral nucleic acid starts.
- The site of production of nucleic acid also varies between viruses.
 - Most of the DNA viruses except Pox and Herpes replicate in nucleus.
 - All RNA viruses replicate in cytoplasm except Orthomyxoviruses and Retroviruses, which for certain stages of replication get into the nucleus of the cell
- How different viruses with different genome replicate?

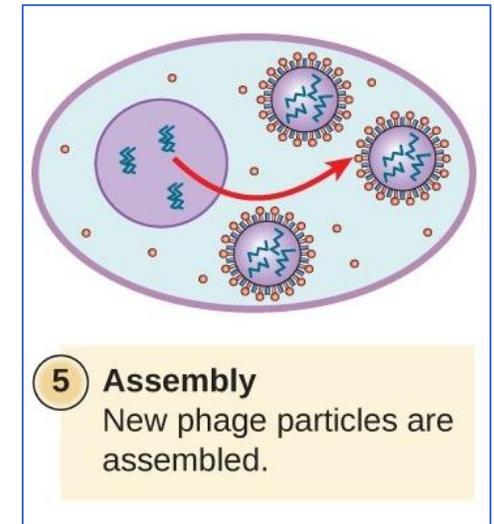
Baltimore Classification



Viral Replication Steps

Step 5 – Assembly (Maturation)

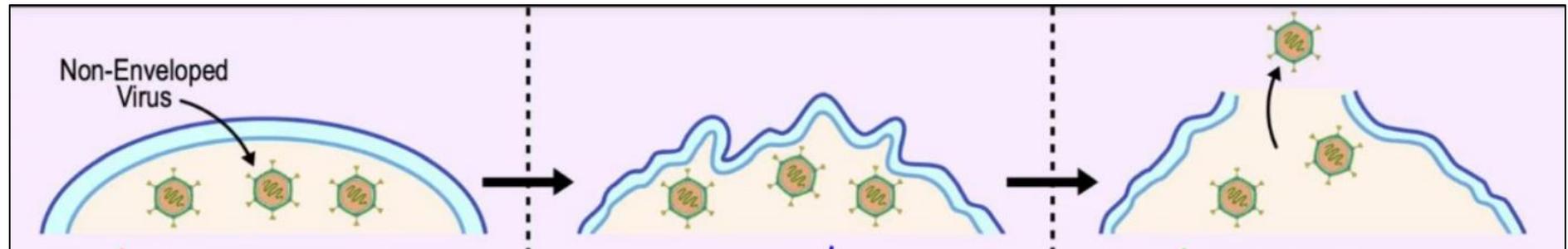
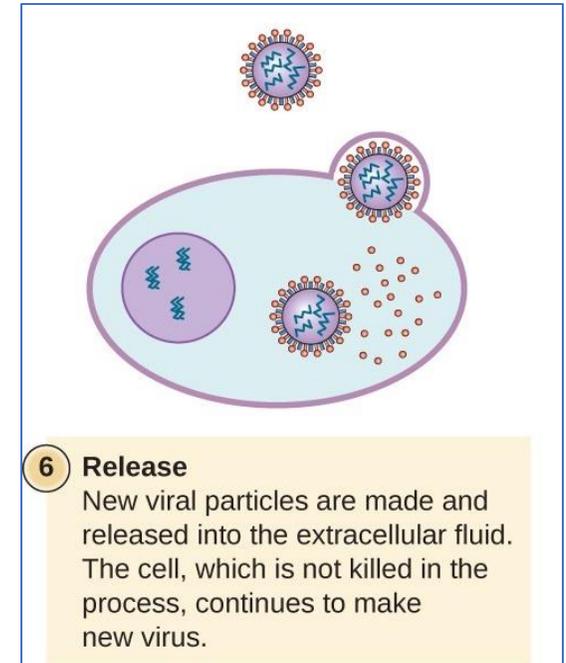
- **Process:**
 - Assembly of viral genome and proteins into new virions.
- **Locations:**
 - Assembly of nucleocapsids generally takes place in the host cell compartment where the viral nucleic acid replication occurs (that is, in the cytoplasm for most RNA viruses and in the nucleus for most DNA viruses).



Viral Replication Steps

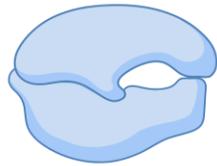
Step 6 –Release

- Release is a simple process – the cell breaks and releases the virus.
- Enveloped viruses acquire the lipid membrane as the virus buds out through the cell membrane.
- Non-enveloped viruses are released from the host cell after it has died by triggering apoptosis.



Negative vs. Positive Sense Strand of DNA and RNA

DNA



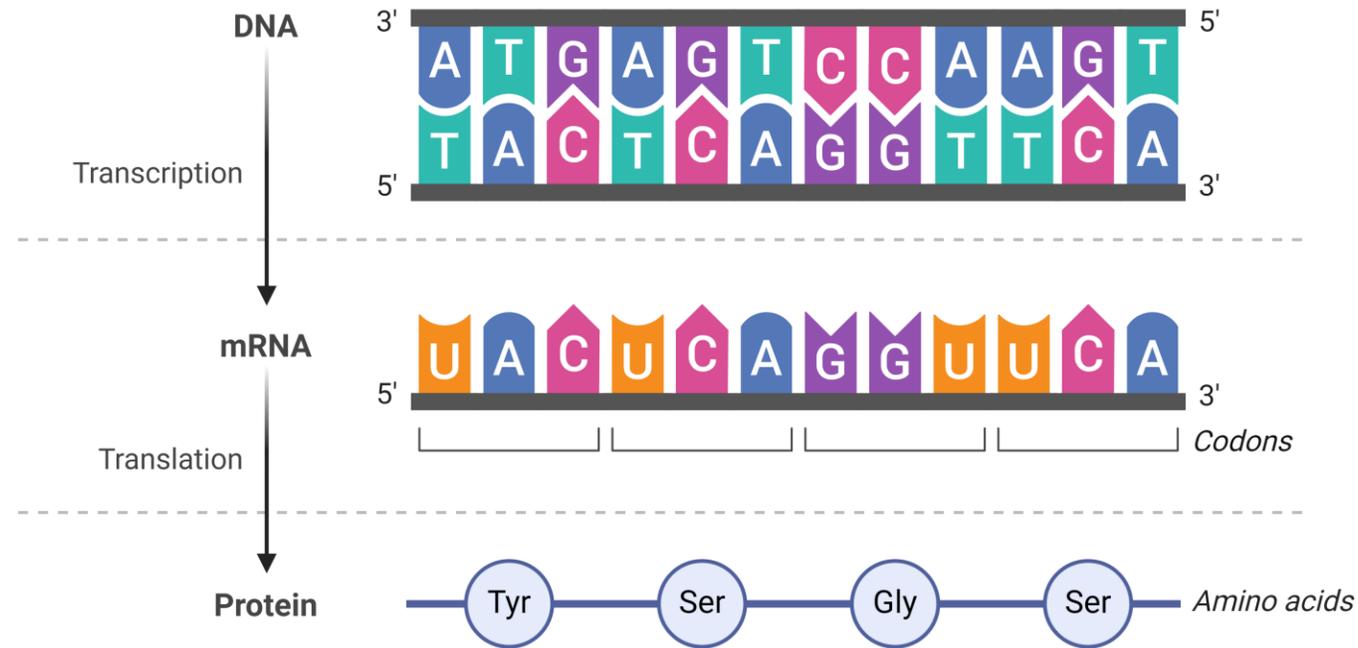
Negative-sense

Positive-sense

- Negative DNA strand was used to make mRNA (+ssRNA)
- mRNA can then be translated to make proteins



Negative vs. Positive Sense Strand of DNA and RNA



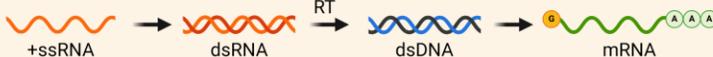
Viral replication = Protein synthesis + copying genetic material

BUT

It's not as simple—or as romantic—as it might seem. Viruses have their own complex dance with life!

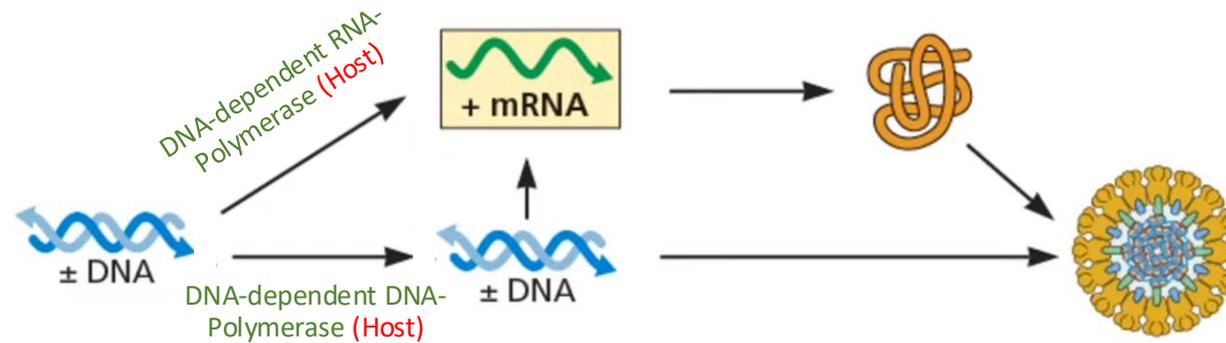


Baltimore Classification

Group	Example	Genetic Material Processing
Group 1 dsDNA	 Smallpox	
Group 2 +ssDNA	 Parvovirus	
Group 3 dsRNA	 Rotaviruses	
Group 4 +ssRNA	 Coronaviruses	
Group 5 -ssRNA	 Measles	
Group 6 +ssRNA-RT	 HIV	
Group 7 dsDNA-RT	 Hepatitis B	



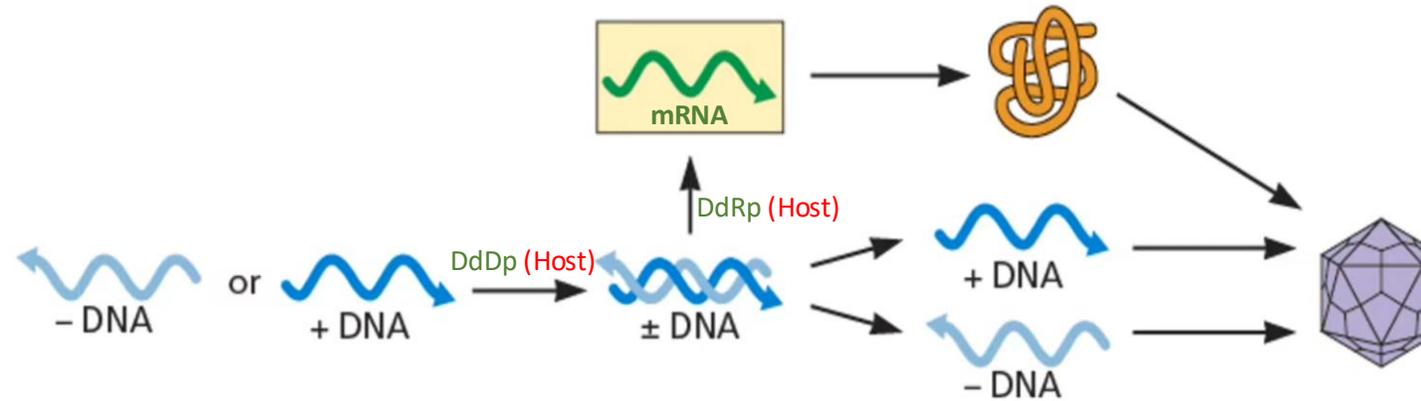
Group 1: Replication of dsDNA Virus



- The replication of dsDNA viruses is a straight-forward.
- They use the cell's replication machinery to transcribe their genome into mRNA immediately.
- Host enzymes for mRNA synthesis and DNA replication are available in nucleus hence, it needs to enter the nucleus.
- **Example:** papillomaviruses, polyomaviruses, adenoviruses and herpesviruses.



Group 2: Replication of ssDNA Virus



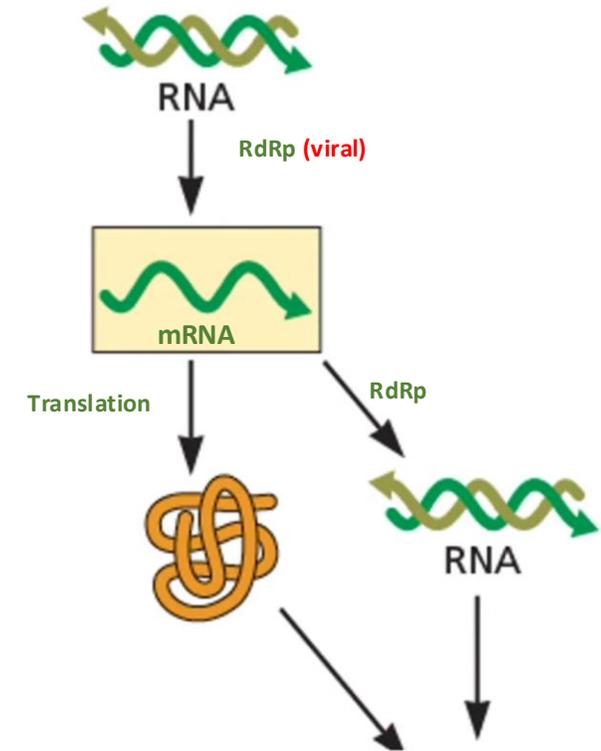
- This can be used to both manufacture viral proteins and as a template for viral genome copies.



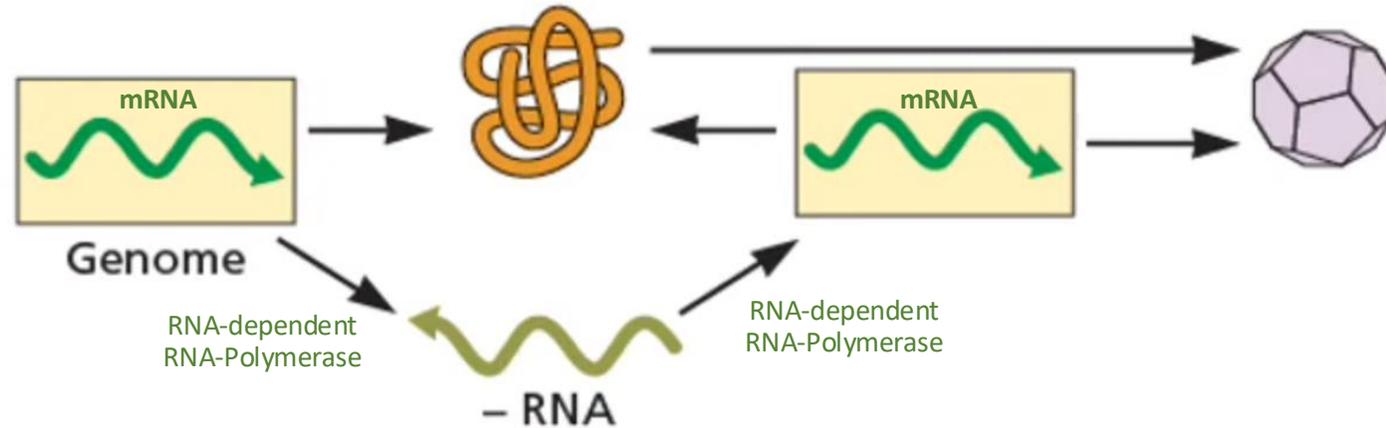
Group 3: Replication of dsRNA Virus

- Double-stranded RNA viruses infect bacteria, fungi, plants, and animals, such as the rotavirus that causes diarrheal illness in humans.
- The viral RNA-dependent RNA polymerase acts as both a **transcriptase** to transcribe mRNA, as well as a **replicase** to replicate the RNA genome.
- Prokaryotic and eukaryotic cells do not carry **RdRp**.

After entering the host body, the viral RNA-dependent RNA polymerase (RdRp) transcribed the dsRNA genome into mRNA, later this transcribed mRNA is used for the translation or replication.



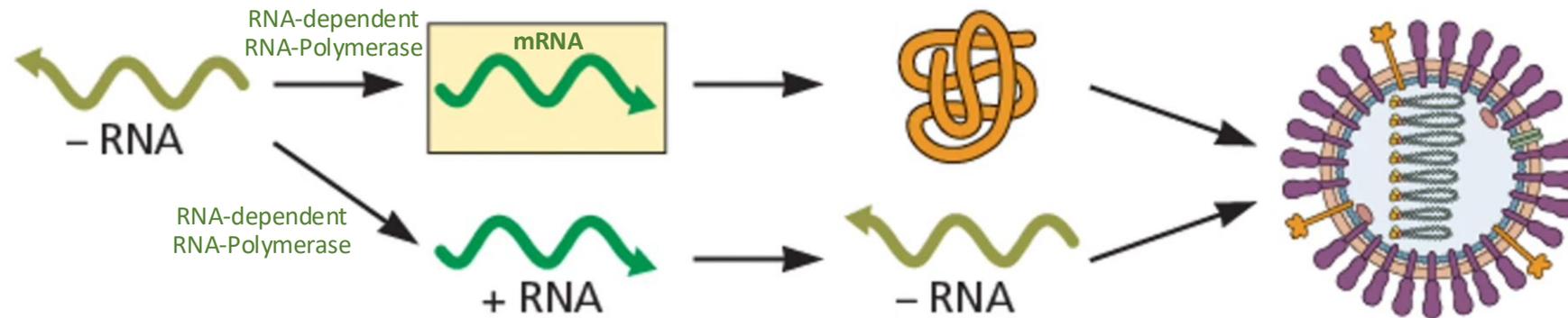
Group 4: Replication of (+) ssRNA Virus



- Viruses with plus-strand RNA, such as poliovirus, can use their genome directly as mRNA with translation by the host ribosome occurring as soon as the viral genome gains entry into the cell.
- One of the viral genes expressed yields an RNA-dependent RNA-polymerase (or RNA replicase), which creates minus-strand RNA from the plus-strand genome.
- The minus-strand RNA can be used as a template for more plus-strand RNA, which can be used as mRNA or as genomes for the newly forming viruses.



Group 5: Replication of (-) ssRNA Virus



- Minus-strand RNA viruses include many members notable for humans, such as influenza virus, rabies virus, and Ebola virus.
- Since the genome of minus-strand RNA viruses cannot be used directly as mRNA, the virus must carry an RNA-dependent RNA-polymerase within its capsid.
- Upon entrance into the host cell, the plus-strand RNAs generated by the polymerase are used as mRNA for protein production.
- When viral genomes are needed the plus-strand RNAs are used as templates to make minus-strand RNA.



