Classification and Replication

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Viral Taxonomy

- Virus classification is the process of naming viruses and placing them into a taxonomic system.
- The earliest efforts to classify viruses were based on the properties such as:-

- **Common clinical outcomes** (e.g. foot-and-mouth disease virus for the virus that causes foot-and-mouth disease in cattle),
- **Common organ tropisms** (e.g. canine hepatitis virus for the virus that causes hepatitis in dogs)
- **The geographic location** (e.g. Rift Valley fever virus for the virus that causes a febrile disease in the Rift Valley of Africa.

- Viruses that were **transmitted by insect vectors** were defined as **"arboviruses"**—arthropod-borne viruses.

Viral Taxonomy

- Viruses are mainly classified by phenotypic characteristics, such as morphology, nucleic acid type, mode of replication, host organisms, and the type of disease they cause.
- Currently, two main schemes are used for the classification of viruses:

1. The International Committee on Taxonomy of Viruses (ICTV) system:

- The system was established in 1966 for refining and maintaining universal virus taxonomy.
- The hierarchy of recognized viral taxa is as follow with the taxon suffixes given in italics:
- Order (*virales*) - Family (*viridae*) – Subfamily (*virinae*) – Genus (*virus*) - Species.

Example: Mononegavirales – Paramyxoviridae – Paramyxovirinae – Avulavirus - Newcastle disease virus

Viral Taxonomy

2. Baltimore classification system:

- This classification was given by David Baltimore in 1971 where viruses are placed into one of following seven groups depending on a combination of their method of transcription (mRNA synthesis).
- This grouping is also based on nucleic acid (DNA or RNA), strandedness (single-stranded or double-stranded), sense and method of replication.

2. Baltimore classification system:

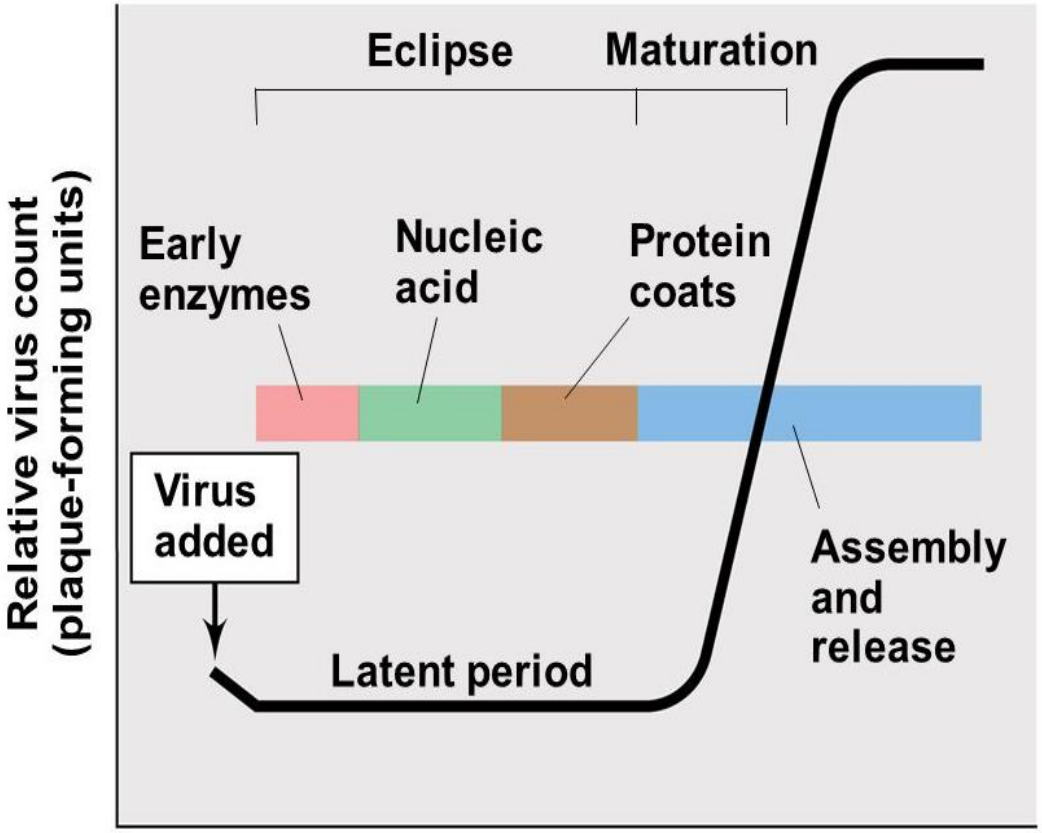
Group-I:	dsDNA viruses (e.g. Adenoviruses, Herpesviruses, Poxviruses)
Group-II:	ssDNA viruses (+ strand or "sense") DNA (e.g. Parvoviruses)
Group-III:	dsRNA viruses (e.g. Reoviruses)
Group-IV:	(+)ssRNA viruses (+ strand or sense) RNA (e.g. Picornaviruses, Togaviruses)
Group-V:	(−)ssRNA viruses (− strand or antisense) RNA (e.g. Orthomyxoviruses, Rhabdoviruses)
Group-VI:	ssRNA-RT viruses (+ strand or sense) RNA with DNA intermediate in life-cycle (e.g. Retroviruses)
Group-VII:	dsDNA-RT viruses (e.g. Hepadnaviruses)

Replication of Viruses

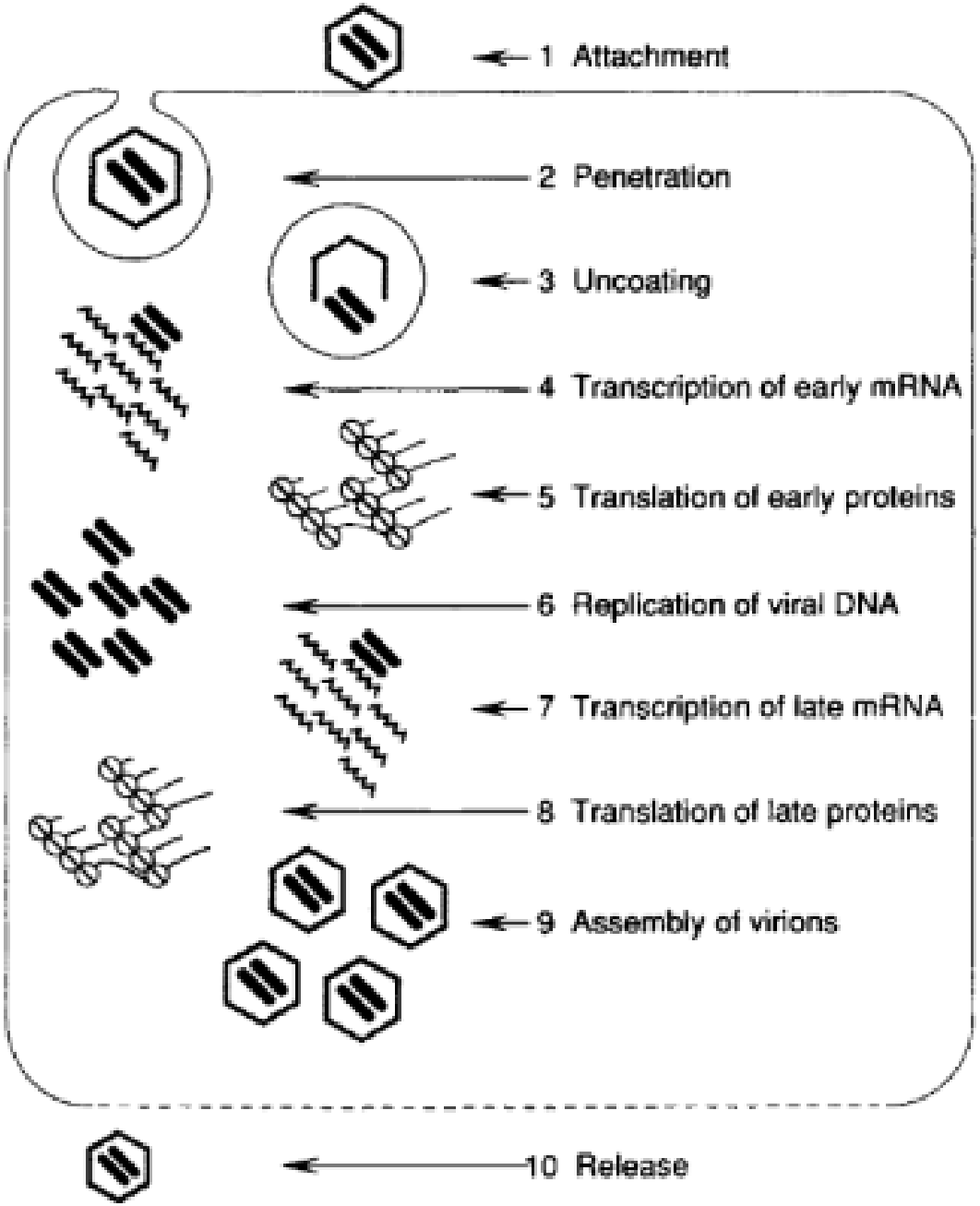
One-step growth curve

- After attachment and penetration, the infectious virus “disappeared” from the infected cultures for a variable period of time, depending on the virus–host-cell system.
- This time period is referred to as the eclipse period, and represents the time needed for the various parts of the virus particle to be synthesized and assembled.
- Then, there is an exponential increase in progeny virus particles. Depending on the type of virus, there may be sudden release of virus particles (lysis of the host cell) or a more slow release (maturation of the virus particle at a cell membrane site).
- The one-step growth curve can be used to divide the virus replication cycle into following parts-

- Attachment,
- The eclipse period (penetration, uncoating, replication of component parts)
- Release of virus particles



- *Latent period*: *eclipse* + *maturation*
- *Burst size*: number of virions released


1 Attachment
2 Penetration
3 Uncoating
4 Transcription of early mRNA
5 Translation of early proteins
6 Replication of viral DNA
7 Transcription of late mRNA
8 Translation of late proteins
9 Assembly of virions
10 Release

Attachment

- Attachment occurs via one or more of virus surface proteins to specific molecules of host cell. These cellular molecules are known as receptors.
- The recognition of the receptor by the virion is highly specific. Some viruses have to bind to a second type of cell surface molecule called co-receptor in order to infect a cell.
- In some viruses binding to the receptor causes conformational changes in the virus protein that enables it to bind to the co-receptor.
- Receptors and co-receptors are cell surface molecules usually glycoproteins. Eg: intrcellular adhesion molecule–I (ICAM-I, rhinoviruses),CD155, CD4, sialic acid containg glycoproteins (orthomyxoviruses), signaling lymphocyte activation molecule (SLAM)

Attachment

- Virus attachment sites of naked viruses are on the capsid surface. For some viruses attachment occurs through specialized structure such as fibres and knobs of adenovirus and the spikes of rotavirus.
- For enveloped viruses the attachment sites are on the surface glycoproteins present on the envelope.
- Initially a virion is weakly bound to a cell at only one or few receptors. At this stage the attachment is reversible. Subsequently binding to many receptors occurs and the attachment becomes irreversible.

Uptake (Penetration)

Receptor-Mediated Endocytosis

- Many enveloped and nonenveloped viruses use this essential cell function to initiate infection.
- Virion attachment to receptors, which cluster at **clathrin-coated pits (togavirus)**, is followed by endocytosis into clathrin-coated vesicles.
- Vesicles enter the cytoplasm and, after removal of the clathrin coat, fuse with endosomes (acidic prelysosomal vacuoles).
- Acidification within the vesicle triggers changes in virion proteins and surface structures.

Uptake (Penetration)

Fusion with Plasma Membrane

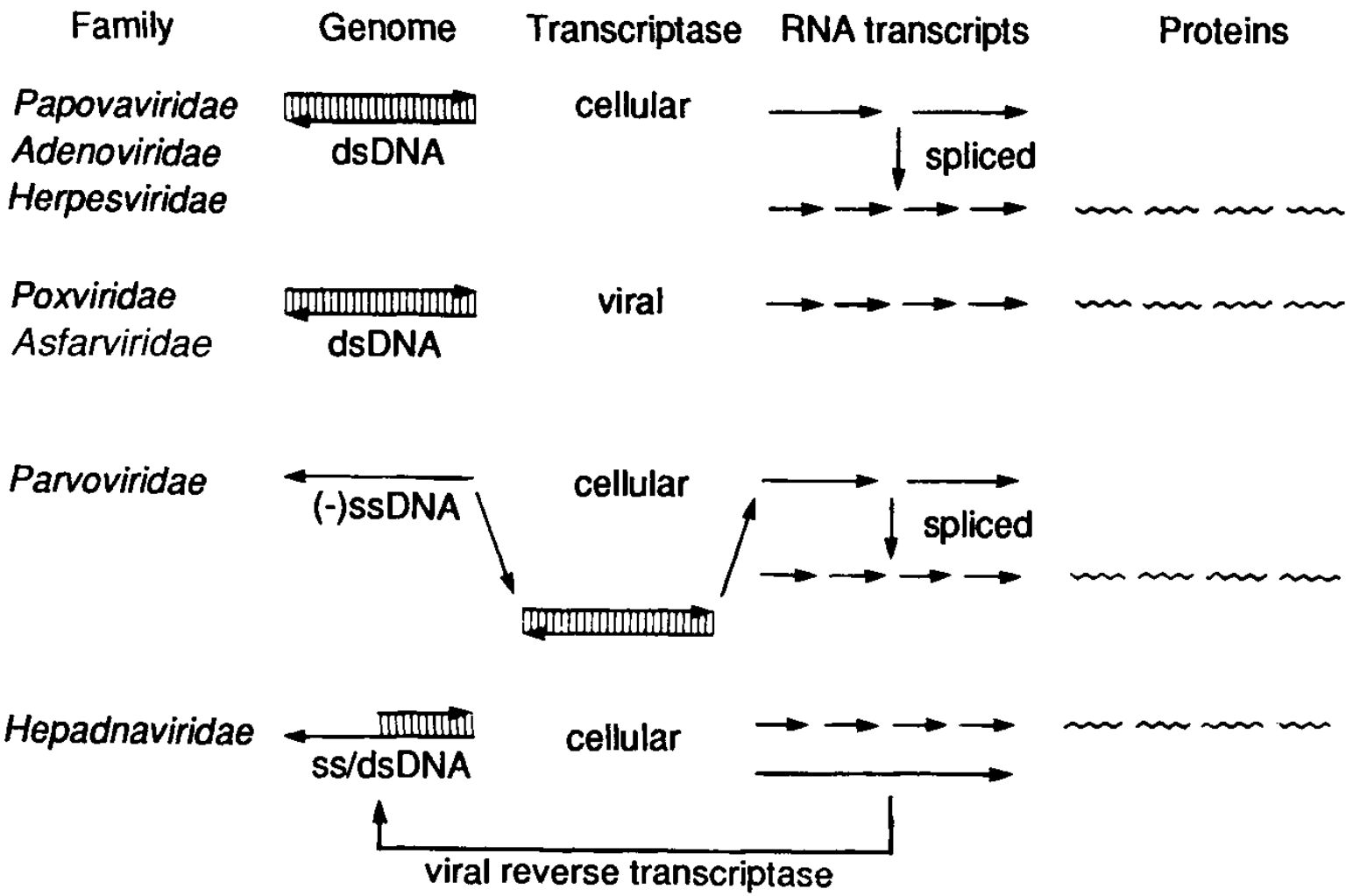
- The F (fusion) glycoprotein of paramyxoviruses causes the envelope of these viruses to fuse directly with the plasma membrane of the cell, even at pH 7.
- This allows the nucleocapsid to be released directly into the cytoplasm.
- A number of other enveloped viruses have the ability to fuse the host cell plasma membrane with their own envelope, thereby gaining entry of their nucleic acid.

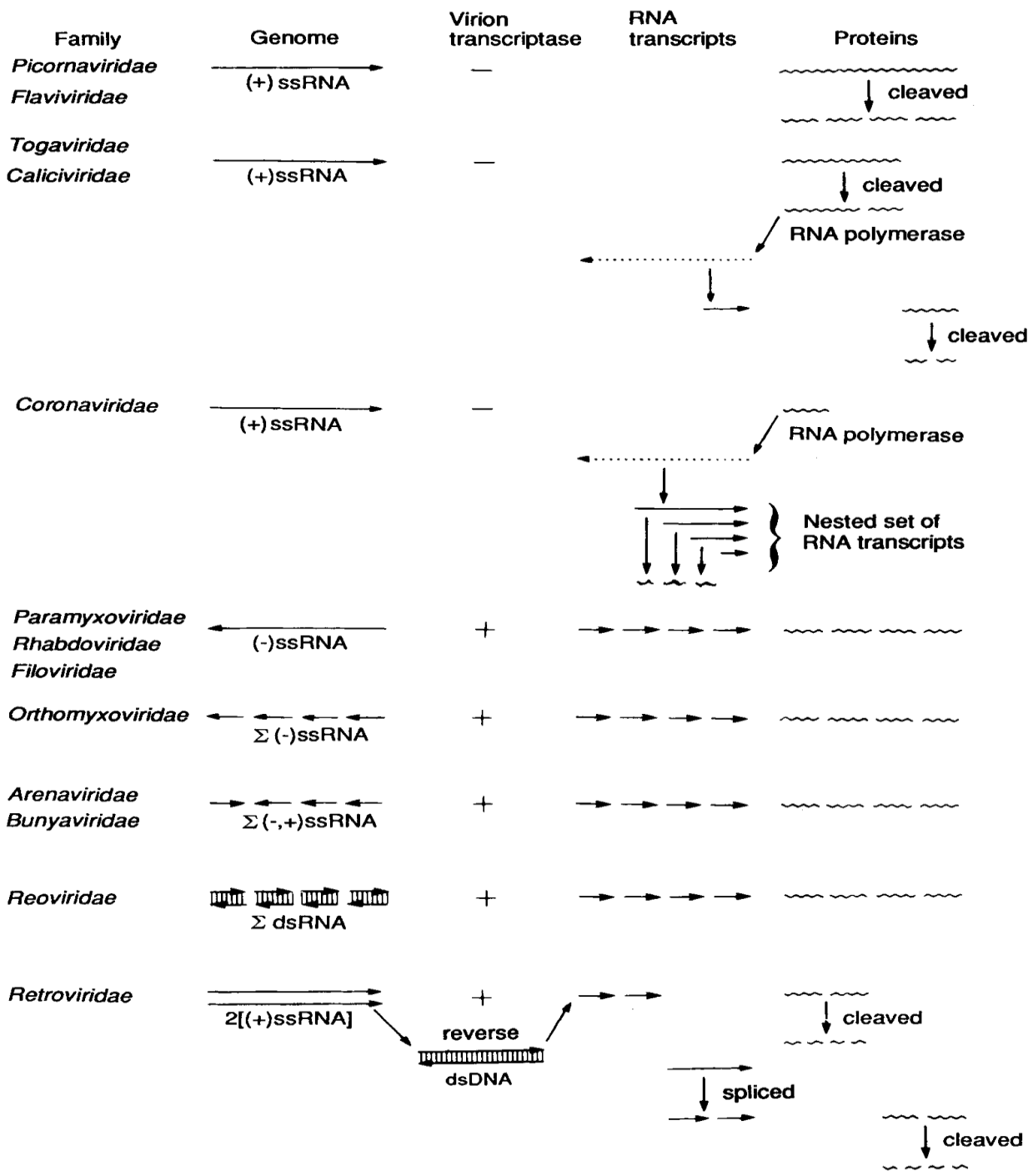
UNCOATING

- Genome uncoating is the complete or partial removal of the capsid to release the virus genome. Depending on the virus the process can take place
  - At the cell surface with the capsid remaining at the exterior surface of the cell.
  - Within cytoplasm
  - At nuclear pore
  - Within nucleus
- From the stage of penetration till the appearance of mature progeny virions the virions cannot be demonstrated inside the host cell. This period during which the virus seems to disappear is known as eclipse phase.

Strategies of Replication

DNA Viruses




Family
Genome
Virion transcriptase
RNA transcripts
Proteins
Picornaviridae
Flaviviridae
(+) ssRNA
cleaved
Togaviridae
Caliciviridae
(+)ssRNA
cleaved
RNA polymerase
cleaved
Coronaviridae
(+) ssRNA
RNA polymerase
Nested set of RNA transcripts
Paramyxoviridae
Rhabdoviridae
Filoviridae
(-)ssRNA
Orthomyxoviridae
Σ (-)ssRNA
Arenaviridae
Bunyaviridae
Σ (-,+)ssRNA
Reoviridae
Σ dsRNA
Retroviridae
2[(+)ssRNA]
reverse
dsDNA
cleaved
spliced
cleaved

Transcription

- The viral RNA of most positive-sense, single-stranded RNA viruses binds directly to ribosomes and is translated in full or in part without the need for any prior transcriptional step.
- From all other classes of viral genomes, mRNA must be transcribed in order to begin the process of expression of the infecting viral genome.
- In the case of DNA viruses that replicate in the nucleus, cellular DNA-dependent RNA polymerase II performs this function.

Transcription

- All other viruses require a unique and specific transcriptase that is virus coded and is an integral component of the virion.
- The double-stranded DNA viruses that replicate in the cytoplasm carry a DNA-dependent RNA polymerase,
- Whereas, double-stranded RNA viruses have a specific double-stranded RNA-dependent RNA polymerase
- Negative-sense single-stranded RNA viruses carry a specific single-stranded RNA-dependent RNA polymerase.

Capping and Polyadenylation

Capping

- Most eukaryotic and viral mRNA have a cap at their 5' end. The cell enzymes that carry out the capping activities are guanylyl transferases (add guanosine 5' triphosphate) and methyl transferases (add methyl groups).
- Most viruses carrying out transcription in the nucleus use the cell enzymes. Some of the viruses replicating in cytoplasm eg: pox, reo and corona viruses encode their own capping and methylating enzymes.
- Negative sense RNA viruses with segmented genomes "snatch" caps from cell m RNAs eg: influenza. In this case the viral RNA polymerase binds to the cellular capped mRNA and cleaves the RNA 10-20 nucleotides from the 5' end.
- The capped oligonucleotide acts as primers to initiate transcription of viral mRNA.
- Not all m RNAs are capped. For example Picornaviruses do not cap their m RNAs.

POLYADENYLATION

- Series of adenosine residues are to 3' end of most m RNAs of eukaryotes and viruses.
- This probably increase stability of m RNA and plays a role in the initiation of translation.
- Some viruses (eg: Reoviruses) do not polyadenylate their m RNA.

Genome replication

- Most DNA virus genomes are replicated in the nucleus but some ds DNA virus genomes are replicated in cytoplasm.
- Genomes of most RNA viruses are replicated in the cytoplasm but those of the minus strand RNA viruses with segmented genomes are replicated in the nucleus.
- In retro and pararetroviruses RNA to DNA replication occurs in the cytoplasm and DNA to RNA replication occurs in the nucleus.

Assembly and release

Assembly

- After synthesis of genomes and viral proteins they are assembled into virus particles in the nucleus and/or cytoplasm of the infected cell.
- DNA viruses (except poxviruses – assembled in cytoplasm) are assembled in the nucleus.
- RNA viruses are generally assembled in the cytoplasm. Maturation step may follow the initial assembly process.

Release

- It is the final step in virus replication.
- Naked virions are released by lysis of the cell.
- Enveloped animal viruses are released by budding through the host cell membranes.
- In a few viruses the host cells are not destroyed.
- The virions leave the cells through cytoplasmic channels over an extended period of time.

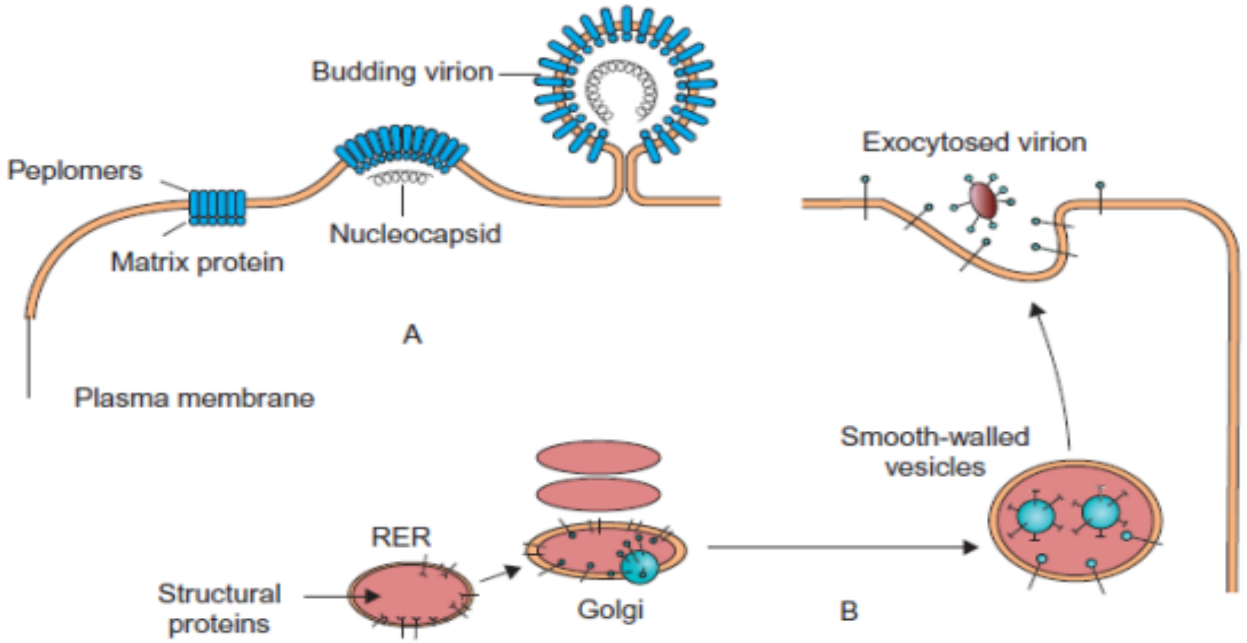


Figure- Maturation of enveloped viruses.

(A) Viruses with a matrix protein (and some viruses without a matrix protein) bud through a patch of the plasma membrane in which glycoprotein spikes (peplomers) have accumulated over matrix protein molecules.

(B) Most enveloped viruses that do not have a matrix protein bud into cytoplasmic vesicles [rough endoplasmic reticulum (RER) or Golgi, then pass through the cytoplasm in smooth vesicles and are released by exocytosis.

THANK YOU

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