**Chapter 2: Classification of viruses**

The categorization of viruses serves multiple purposes, including facilitating comparisons between different viral types and providing insights into newly identified viruses by comparing them to similar ones. Additionally, virus classification enables investigation of the origins and evolutionary trajectories of viruses over time. However, virus classification (Figure 21) is a complex endeavour, given the vast diversity of over 2800 distinct viral species, each with unique characteristics.

**Classification of DNA virus**:

DNA virus

Single stranded

Double stranded

Non-enveloped

Non-enveloped

Enveloped

Adenoviridae

* Common cold
* Viral meningitis

Hepadnaviridae

* Hepatitis B
* Liver Cirrhosis

Parvoviridae

* Parvo B19
* 5th didease
* Gastroenteritis

Poxviridae

* Smallpox

Papillomaviridae

* Warts
* Cervical cancer

Herpesviridae

* Chickenpox
* Cold sores
* Shingles
* Mononucleosis

Poliomaviridae

* BK, JCV
* progressive multifocal leukoencephalopathy (PML)

**Figure 21: The flowchart illustrates the classification of DNA viruses**

One notable classification framework, established in the 1970s by Nobel laureate David Baltimore, organizes viruses based on their nucleic acid genome type and replication methods. This system further subdivides single-stranded RNA viruses (Figure 22) into positive strand (+) and negative strand (−) groups. Positive-strand RNA can be directly translated into proteins, akin to cellular messenger RNA (mRNA), while negative-strand RNA requires transcription into positive-strand RNA before protein synthesis can occur.

**Classification of RNA virus**:

RNA virus

Picornaviridae

* Common cold, Polio
* Hepatitis A

Orthomyxoviridae

* Influenza

Filoviridae

* Ebola, Marburg
* Fatal hemorrhagic fever

Calciviridae

* Gastroenteritis

Coronaviridae

* SARS
* Respiratory distress

Togaviridae

* Rubella
* Encephalitis

Flaviviridae

* Dengue, Yellow Fever, Zika, West Nile
* Febrile illness
* Hepatitis C, liver damage

Enveloped

(-) RNA

Retroviridae

Reoviridae

Enveloped

Double capsid

(+/-) RNA

Enveloped

Non-enveloped

(+) RNA via DNA

(+) RNA

Arenaviridae

* Lassa fever

Rhabdoviridae

* Rabies
* Hydrophobia
* Paralysis

Paramyxoviridae

* Mumps
* Measles

Bunyaviridae

* Hunta virus
* Pulmonary distress

**Figure 22: The flowchart illustrates the classification of RNA viruses**

Baltimore's classification

Baltimore's classification also accounts for viruses capable of reverse transcription, a process in which DNA is synthesized from an RNA template, a capability absent in cells. Collectively, these criteria delineate the seven classes within the Baltimore classification system.

* class I: dsDNA viruses
* class II: ssDNA viruses
* class III: dsRNA viruses
* class IV: positive-sense ssRNA viruses
* class V: negative-sense ssRNA viruses
* class VI: RNA viruses that reverse transcribe
* class VII: DNA viruses that reverse transcribe

**Class I: dsDNA viruses-**

* Double-stranded DNA (dsDNA) genome (Figure 23), such as T4 bacteriophages and lambda (ʎ), possess a genome identical to that of their host cells, enabling them to utilize host enzymes for replication and protein synthesis.
* Genome replication necessitates a DNA-dependent DNA polymerase from either the virus or the host cell.
* Viruses often regulate gene expression to produce viral products during replication. For instance, in T4 phage, early viral proteins modify host RNA polymerase to transcribe early genes immediately upon DNA injection into the cell, followed by modification to recognize viral genes for middle and late-stage proteins, ensuring orderly protein production.
* dsDNA viruses produce concatemers, where multiple viral genomes are linked due to short single-stranded regions with terminal repeats. As the genome is packaged into the capsid, a viral endonuclease cleaves the concatemer to an appropriate length.

**(+)**

**(-)**

**Transcription copies (-) DNA strand**

**Translation**

Translation

(+)

**DNA dependent DNA polymerase**

**Viral protein**

**Viral dsDNA**

**Copies (+) and (-) DNA strand**

**(+)Viral RNA**

**DNA dependent DNA polymerase**

**(-)**

**(+)**

**Virus dsDNA**

**Figure 23: dsDNA replication**

**Class II: ssDNA viruses-**

* The flow of information in single-stranded DNA (ssDNA) viruses, such as parvoviruses, generally adheres to the conventional pathway: DNA → mRNA → protein.
* However, the viral genome (Figure 24) may have the same base sequence as the mRNA (plus-strand DNA) or be complementary to it (minus-strand DNA).
* A complementary DNA strand must be synthesized first to form a double-stranded replicative form (RF), which serves as a template for viral genome copies and protein production.
* For minus-strand DNA viruses, the genome can directly produce mRNA, but a complementary copy is still required for genome replication.

**(-)**

**(+)**

**(+)**

**DNA dependent DNA polymerase**

**DNA dependent DNA polymerase**

**Copies (+) DNA strand**

**Copies (-) DNA strand**

**ss(+) DNA viral genome**

**Copies (+) DNA strand**

**DNA dependent RNA polymerase**

(+)

**Translation**

**Viral protein**

**(+) Viral mRNA**

**Figure 24: ssDNA replication**

* Rolling-circle replication (Figure 25) can occur using the replicative form, where one strand is nicked and replication enzymes extend the free 3’ end. As a complementary strand is synthesized, the 5’ end is displaced, resulting in a growing displaced strand.

**Nucleotide added to 3ʼOH end, displacing other end**

**5´P**

**5´P**

**3´OH**

**Nuclease cuts**

**Other strand copied discontinously**

**Direction of rolling**

**5´P**

**Figure 25: Rolling circle replication**

**Class III: dsRNA viruses-**

* Double-stranded RNA (dsRNA) viruses infect various organisms, such as the rotavirus, which causes diarrheal illness in humans (Figure 26).
* Cells do not utilize dsRNA in their processes and have mechanisms to destroy it. Therefore, the viral genome, in dsRNA form, must be shielded from cellular enzymes.
* Cells lack RNA-dependent RNA polymerases required for viral genome replication. The viral RNA-dependent RNA polymerase functions as transcriptase, transcribing mRNA, and a replicase, replicating the RNA genome.

**(+)**

**Translation**

**RNA dependent RNA polymerase**

**(-)**

**Viral protein**

**Transcription copies (-) RNA**

**(+)**

**(+) Viral mRNA**

**Copies (+) & (-) RNA strands**

**(-)**

**dsRNA viral genome**

**dsRNA viral genome**

**RNA dependent RNA polymerase**

**Figure 26: dsRNA virus replication**

**Class IV: positive-sense ssRNA viruses-**

* Viruses with plus-strand/positive strand RNA (Figure 27), like poliovirus, utilize their genome directly as mRNA, allowing translation by host ribosomes upon entry into the cell.
* Expressed viral gene produces an RNA-dependent RNA polymerase, which generates minus-strand RNA from the plus-strand genome. Minus-strand RNA serves as a template for more plus-strand RNA, used as mRNA or genomes for new viruses.
* Translation of the poliovirus genome results in a polyprotein, which self-cleaves into smaller proteins, including those needed for capsid formation and an RNA-dependent RNA polymerase.

**(+)**

**RNA dependent RNA polymerase**

**(+)**

**(-)**

**RNA dependent RNA polymerase**

**Copies (-) RNA strands**

**Copies (+) RNA strands**

**Viral genome ss (+) RNA**

**Translation (by host ribosome)**

**Viral genome ss (+) RNA**

**ss (-) RNA**

**Viral protein**

**Figure 27: +ssRNA replication**

**Class V: negative-sense ssRNA viruses-**

* Viruses that affect humans, such as influenza virus, rabies virus, and Ebola virus, belong to the category of minus-strand RNA viruses (Figure 28).
* The genome of these viruses cannot function directly as mRNA, they carry an RNA-dependent RNA polymerase within their capsid.
* Upon entering the host cell, this polymerase synthesizes plus-strand RNAs, which serve as mRNA for protein synthesis.
* When viral genomes are required, these plus-strand RNAs act as templates for the production of minus-strand RNA.

**RNA dependent RNA polymerase**

**(+)**

**RNA dependent RNA polymerase**

**(-)**

**(-)**

**Copies (-) RNA strands**

**Copies (+) RNA strands**

**Viral genome ss (-) RNA genome**

**ss (+) RNA**

**Viral genome ss (-) RNA genome**

**RNA dependent RNA polymerase**

**(+)**

**Transcription copies (-) RNA**

**Translation**

**Viral protein**

**(+) Viral mRNA**

**Figure 28: -ssRNA replication**

**Class VI: RNA viruses that reverse transcribe-**

* The virus employs its reverse transcriptase to produce a complementary ssDNA strand to the viral genome (Figure 29).
* This enzyme also exhibits ribonuclease activity, which degrades the RNA strand of the RNA-DNA hybrid.
* Additionally, the reverse transcriptase functions as a DNA polymerase, synthesizing a complementary copy to the ssDNA, resulting in a dsDNA molecule. This allows the virus to integrate its genome, in a dsDNA form, into the host chromosome, forming a provirus.
* Unlike a prophage, a provirus can remain dormant indefinitely or trigger the expression of viral genes, leading to the production of new viruses. Excision of the provirus does not occur for gene expression.

**(-)**

**DNA dependent RNA polymerase**

**(-)**

**(+)**

**(-)**

**(+)**

**NA dependent DNA polymerase**

**RNA dependent DNA polymerase**

**Copies (-) DNA strands**

**Copies (-) RNA strands**

**Copies (+) RNA strands**

**Viral genome ss (-) RNA genome**

**dsDNA intermediate**

**Viral genome ss (+) RNA genome**

**ss (-) DNA**

**(+)**

**Translation**

**Viral protein**

**(+) Viral mRNA**

**Figure 29: +ssRNA, retroviruses replication**

**Class VII: DNA viruses that reverse transcribe-**

* Hepadnaviruses harbor a DNA genome that is partially double-stranded, featuring a single-stranded region.
* Upon entering the cell nucleus, host cell enzymes facilitate the filling of the gap with complementary bases, resulting in the formation of a closed-loop double-stranded DNA (dsDNA).
* Gene transcription produces a plus-strand RNA known as the pregenome, along with the viral enzyme reverse transcriptase, which acts as an RNA-dependent DNA polymerase.
* The pre-genome serves as a template for reverse transcriptase to generate minus-strand DNA genomes, with a small segment of pre-genome serving as a primer for the production of the double-stranded region of the genomes.

**References:**

Louten, J., 2016. Virus Structure and Classification, in: Essential Human Virology. Elsevier, pp. 19–29. https://doi.org/10.1016/B978-0-12-800947-5.00002-8

The Baltimore Classification of Viruses 50 Years Later: How Does It Stand in the Light of Virus Evolution? | Microbiology and Molecular Biology Reviews [WWW Document], n.d. URL https://journals.asm.org/doi/10.1128/mmbr.00053-21 (accessed 4.13.24).