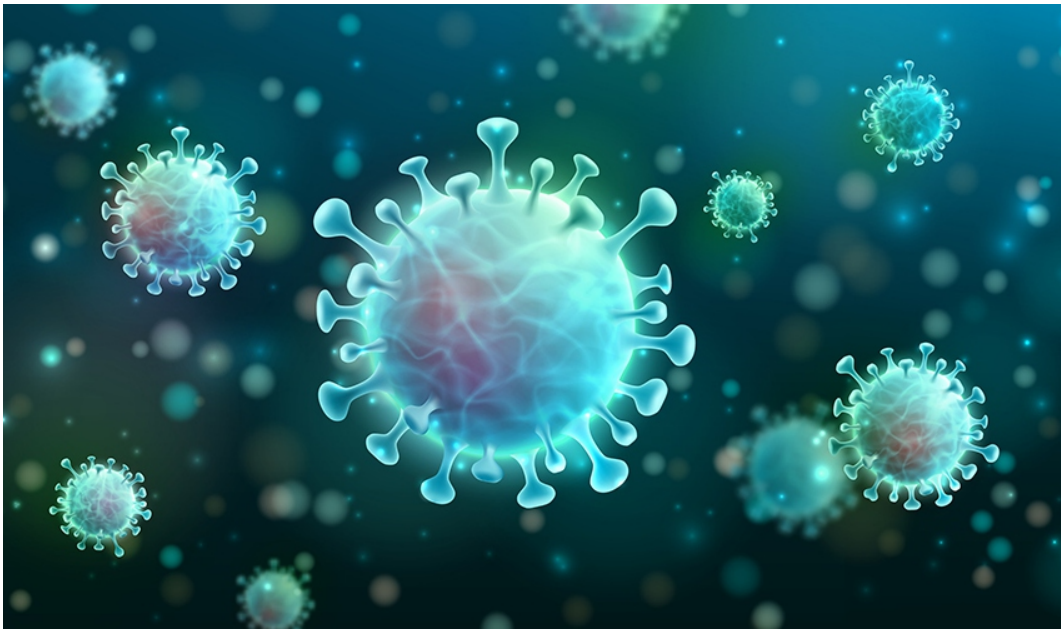
# VIRUSES



Dr. Sunita Rao,
Dr. Prithpal Singh Matreja

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# CHAPTER 1

# AN OVERVIEW OF THE EVOLUTION OF THE VIRUS

Dr. Sunita Rao, Assistant Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id-sunita.rao@jnujaipur.ac.in

**ABSTRACT:**

Viruses are nonliving and living particles. The virus is a simple virion made up of genetic material and protein capsids. In nature, numerous viruses are present which are either DNA or RNA viruses. There are theories suggesting the origin of this virus in nature. In this chapter we discussed the origin of the virus, and the different theories which support the evolution of the virus in nature.

**KEYWORDS:** Contagious Agents, Genetic Material, Hepatitis Virus, Tobacco Mosaic, Yellow Fever.

## INTRODUCTION

Viruses are everywhere there is life, and they have undoubtedly been around ever since the origin of living organisms. Because viruses do not leave remains, it is unknown where they came from, so their genesis is being studied using genetic methods. Additionally, rarely, virus genetic material fuses with the host species' germlines, allowing for long-term vertical transmission to the host's progeny. Paleovirologists can use this as a priceless resource of knowledge to track down historic viruses that date back millions of years. To describe the beginnings of viruses, there are three major theories. When Louis Pasteur, a French scientist, was unable to identify the rabies-causing agent, he conjectured the presence of a submicroscopic creature or particle.

In 1884, Louis Pasteur's colleague Charles Chamberland created a screen known as the Chamberland filter that had holes that were smaller than microorganisms.German scientist Adolf Eduard Mayer released his research demonstrating the tobacco mosaic illness. By pressing the liquid extract between diseased and healthy plants, he demonstrated how the illness could spread from one to the other, leading him to believe it was a bacterial infection. Then, a Russian scientist named Dmitri Ivanovski used the Chamberland filter to show for the first time that leaf extract from plants with the tobacco mosaic disease retained its contagious properties even after filtering.Adolf Mayer's tests were replicated by Dutch horticulturist Martinus Beijerinck in 1898, and he came to the opinion that a novel contagious agent was responsible for the illness. He noticed that the agent only reproduced in living cells and gave it the term virus after naming it contagium *vivumfluidum* (soluble liquid germ). He was certain that the substance was soluble and liquid in character. In 1992, "One Hundred Years of Virology" was released as a tribute to Ivanovsky and Beijerinck's efforts[1]–[3].

Two German researchers, Friedrich Loeffler, and Paul Frosch identified the second viral that causes foot and mouth disease in 1898. (FMDV). They are thought to be the ones who discovered the virus because they concluded that it was a particle rather than a watery substance. The first human viral to be identified as the yellow fever virus.This theory proposes that the evolution of viruses was a gradual process. Mobile genetic elements, or genetic components that can move around inside a chromosome, developed the capacity to

leave one cell and join another. Let's look at the reproduction of retroviruses, the family of viruses to which HIV belongs, to understand this change.The RNA DNA of retroviruses is single-stranded. Reverse transcriptase, a viral enzyme, transforms the single-stranded RNA into double-stranded DNA as soon as the virus penetrates a recipient cell. The host cell's nucleus then receives the virus DNA. Integrase, a different viral enzyme, integrates the freshly produced viral DNA into the genome of the host cell. Afterward, viral DNA can be translated and copied. The single-stranded RNA DNA of the virus can be replicated by the RNA polymerase of the recipient cell. Virus progeny form, leave the cell and repeat the process (Figure 2). This mechanism closely resembles the migration of retrotransposons, a significant but uncommon element of the majority of cell genomes. A staggering 42% of the human genome is made up of these movable genetic elements, which can travel around the genome using an intermediary RNA molecule. Certain groups of retrotransposons, including the retrotransposons that resemble retroviruses, contain an integrase and, frequently, a reverse transcriptase. These enzymes allow for the transcription of these elements into RNA, reverse transcription of those RNAs into DNA, and integration of those elements into a new position in the genome (Figure 1). We can hypothesize that the element could become a contagious agent by entering a new cell after acquiring a few structural proteins. Indeed, there are striking parallels between the genomic architecture of retroviruses and retrotransposons that resemble viruses.

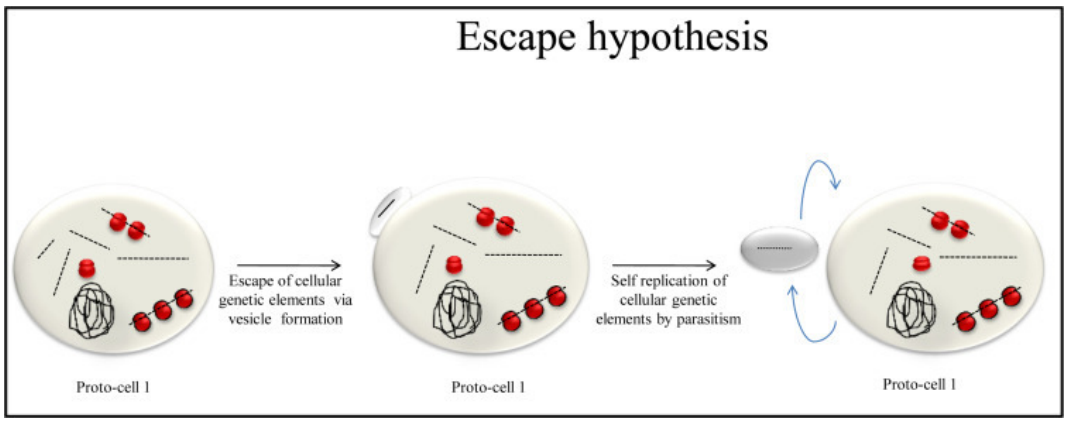


**Figure 1: Virus first model: Diagram showing the schematic presentation of the virus first hypothesis (Science direct.com).**

Viruses may have developed through a backward, or reduced, process as opposed to the advanced process just outlined. Most microbiologists concur that some bacteria, such as the Chlamydia and Rickettsia species, which are obligatory internal pathogens, developed from free-living progenitors. Indeed, genetic research suggests that Rickettsia prowazekii and eukaryotic cells' mitochondria may have derived from a single, free-living progenitor. Therefore, it is possible that current viruses developed from more advanced, potentially free-living creatures that gradually lost genetic material as they switched to a parasitic mode of reproduction. This theory is best illustrated by viruses from one specific category, the nucleocytoplasmic large DNA viruses (NCLDVs). These viruses, which also include the newly identified Mimivirus and the smallpox virus, are much larger than the majority of viruses. For instance, a normal brick-shaped poxvirus may be 200 nm broad and 300 nm long. Mimivirus is about twice that size, with an overall circumference of about 750 nm. On the other hand, poliovirus particles have a diameter of only 30 nm, or about 10,000 times smaller than a flake of salt, and influenza virus particles, which are spherically structured, may only be 80 nm in diameter. Large chromosomes are another feature of NCLDVs. Again, the genomes of poxviruses frequently reach 200,000 base pairs, and the genome of the

Mimivirus is 1.2 million base pairs, whereas the genome of the poliovirus is only 7,500 bases in total. The NCLDVs are also much more complicated than other viruses and rely less on their hosts for reproduction than other viruses, in addition to being very big. For example, a plethora of viral enzymes and associated components are present in poxvirus particles, enabling the production of functional messenger RNA within the cytosol of the recipient cell. Some virologists have suggested that NCLDVs may be offspring of more complicated progenitors due to the magnitude and intricacy of these viruses. Supporters of this theory contend that commensal relationships were originally formed between independent creatures. The connection eventually developed into a parasitic one as each organism's reliance on the other increased. The once-free-living bug dropped previously crucial genes as it grew more reliant on the host. It eventually lost its ability to reproduce on its own and evolved into a virus, an obligatory internal infection. This theory might be confirmed by an examination of the enormous Mimivirus. A sizable number of potential translation-related genes are found in this virus; these genes may be the remains of a once-full translation system. It's interesting how little Mimivirus differs from infectious microbes like Rickettsia prowazekii. Both the progressive and the retrograde theories imply that cells predated viruses. How about if pathogens came first? Several researchers recently suggested that the first reproducing organisms might have been viruses. According to Koonin and Martin's (2005) theory, viruses were self-replicating organisms in the precellular universe. They contend that these groups evolved to become more ordered and sophisticated. Cells were eventually created when enzymes for the production of cell walls and membranes emerged. Therefore, it is possible that viruses evolved before bacteria, archaea, or eukaryotes. The majority of scientists now concur that RNA, not DNA, made up the first reproducing molecules.

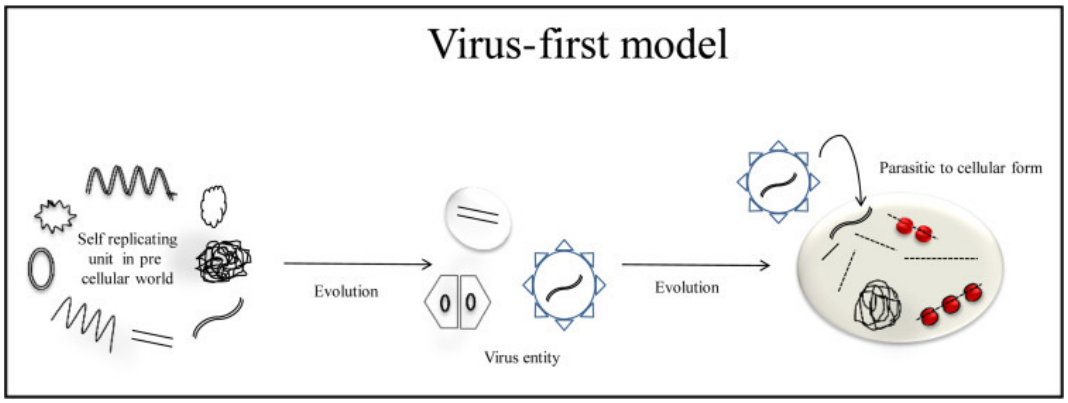


**Figure 2: Virus first model: Diagram showing the schematic presentation of the virus first hypothesis (Science direct.com).**

Additionally, we are aware that some RNA structures called ribozymes have enzyme characteristics and can initiate molecular processes. Maybe before the first cell was created, basic repeating RNA molecules acquired the capacity to infiltrate new cells. Could these precellular RNA molecules be the ancestors of modern single-stranded RNA viruses? Both groups speculate that the current eukaryotic cell nucleus may have developed as a result of an endosymbiotic-like occurrence in which a complex, enclosed DNA virus became a long-term inhabitant of an arising eukaryotic cell[4]–[6].

Bits of DNA or RNA that "escaped" from the genes of a bigger creature may have given rise to some viruses. The escaped DNA may have originated from plasmids, which are naked DNA fragments that can move between cells, or from transposons, which are mobile genetic elements that can replicate and move to different locations within a cell's genes. Transposons, also known as jumping genes, may have been the source of some viruses. They were found in

corn in 1950 by Barbara McClintock.The "escape hypothesis" or the "vagrancy hypothesis" are other names for this. The "virus-first hypothesis" puts forth the idea that viruses may have developed from intricate protein and nucleic acid structures at the same time that cells first emerged on Earth (Figure .2). As a result, viruses may have been reliant on cellular life for billions of years. Because they don't have a protein covering, RNA entities known as viroids are not considered viruses. They are frequently referred to as subviral agents because they share traits with several viruses. Important plant diseases include viroids. Although they communicate with the host cell and use the host apparatus for reproduction, they do not code for proteins. Although the human hepatitis delta virus's RNA sequence is comparable to that of viroids, it cannot make its protein covering and instead uses one from the hepatitis B virus. Therefore, it is flawed malware. Once inside a host cell, the hepatitis delta virus DNA can reproduce autonomously; however, to spread to new cells, it needs the assistance of the hepatitis B virus, which contributes a protein covering. Similar to how the mimivirus, which attacks the protozoan *Acanthamoeba castellanii*, is necessary for the sputnik virophage to function. These viruses, known as "satellites," may be evolving intermediaries of viroids and viruses because they rely on the existence of other viral types in the recipient cell.

## DISCUSSION

Mammalian and bird species make up the two divisions of the Hepadnaviridae family. The discovery of endogenous avian hepadnavirus DNA incorporated into the zebra finch genomes has disclosed a previously unknown, profound evolutionary genesis for hepadnaviruses, going back at least 40 million years and potentially more than 80 million years. The woodchuck hepatitis virus (WHV), ground squirrel hepatitis virus, arctic squirrel hepatitis virus, and a handful of the newly identified bat hepatitis virus are among the nonprimate mammalian members of the Hepadnaviridae. A more complicated genesis for this virus is further suggested by the discovery of hepatitis B viruses (HBV) in higher animals like chimpanzees, gorillas, orangutans, and gibbons that cluster with the human HBV. We address the prevailing hypotheses regarding the genesis and development of HBV and put forth a model that takes into account interspecies transfers and subsequent recombination events on the genetic basis of genotype C HBV infection. The existence of HBV is necessary for the hepatitis delta virus (HDV), a faulty RNA virus, to complete its life cycle. Although some new studies have indicated primordial African radiation, the virus's beginnings are still unclear. It is also unclear how long HDV and HBV have been linked**.**

Hepatitis B virus (HBV) etiology is intricate, and it appears that molecular variations contribute to this development. Within an infected host, HBV is produced in multiple cycles, each of which is prone to mistakes. The resulting quasispecies is heterogeneous, and without archaeological evidence of previous infections, it is only possible to deduce implicitly from epidemiology and genomic research how HBV evolved. This study compiled the debates surrounding the quasispecies of HBV and its genesis. Additionally, it offered some proof of the relationship between HBV genes and migratory trends and human history. We think this subject merits further study, so we anticipate that more in-depth research will be done to clarify the as-yet-unidentified methods and processes in this field**.**

The majority of the Hepadnaviridae family's members are viruses that reproduce their double-stranded DNA genomes through reverse transcription from a genomic RNA template. Within this family, there are two subgroups: mammals and birds. Duck hepatitis B virus (DHBV), heron hepatitis B virus, Ross swan hepatitis B virus, stork hepatitis B virus and the newly discovered parrot hepatitis B virus are among the avian members. Hepadnaviruses have a long evolutionary history that dates back over 40 million years, as newly discovered endogenous avian hepadnavirus DNA incorporated into the genomes of zebra finches has

been disclosed. The woodchuck hepatitis virus (WHV), ground squirrel hepatitis virus, arctic squirrel virus, and the newly discovered bat hepatitis virus are all non-primate rodent members of the Hepadnaviridae. The discovery of hepatitis B virus (HBV) in higher apes, including chimpanzees, gorillas, orangutans, and gibbons, which combine with human genotypes, suggests that the virus's origins are more nuanced. We develop a model for the genesis and evolution of HBV that includes numerous cross-species transmissions and subsequent recombination events on a backdrop of genotype C HBV infection by researching the molecular epidemiology of HBV in indigenous and relict populations in Asia-Pacific.

In terms of both physical abundance and genetic variety, viruses and other self-centered genetic components are the main organisms in the biosphere. All cellular living forms are parasitized by various selfish components. Prokaryotes and eukaryotes have significantly varying proportional abundances of various virus groups. In prokaryotes, the vast majority of viruses have double-stranded (ds) DNA chromosomes, with single-stranded (ss) DNA viruses making up a sizable percentage and RNA viruses being scarcely present. In comparison, RNA viruses dominate the virome variety in eukaryotes, though ssDNA and dsDNA viruses are also widespread. In particular, the probable origins of the main groups of eukaryotic viruses in prokaryotes are revealed by phylogenomic analysis. Although a primal beginning for this class of viruses cannot be ruled out, it is possible that the ancestral genome of positive-strand RNA viruses of eukaryotes was put together de novo from genes taken from prokaryotic retroelements and bacteria. Different subgroups of double-stranded RNA viruses can be traced back to either positive-strand RNA viruses or dsRNA bacteriophages. The bacterial rolling circle-replicating plasmids and positive-strand RNA viruses are thought to have contributed genes to the evolution of the eukaryotic ssDNA viruses. At least two separate eukaryotic dsDNA viral families appear to have descended from distinct bacterial phage populations. The largest known eukaryotic transposons, positions, were most likely the evolutionary intermediaries between bacterial tectiviruses and several groups of eukaryotic dsDNA viruses, including the proposed order "Megavirales," which unites various families of large and giant viruses. Polintons were predicted to also form virus particles. Surprisingly, the evolution of all eukaryotic viral classes appears to have involved the fusion of structural and replicative gene modules drawn from various sources as well as the purchase of additional diverse genes[7]–[9].

Because of their varied and patchy chemical and functional composition, viruses' origins remain a mystery. Although many theories have tried to explain the beginnings of viruses, none are supported by reliable evidence. We make the most of the abundance of structural and functional protein data that is currently accessible to investigate the development of the proteomic composition of thousands of cells and viruses. We discovered a primordial beginning for the "viral supergroup" and the presence of frequent instances of horizontal genetic information transfer despite the drastically reduced character of viral proteomes. Viruses harboring various replicon types and infecting distantly related hosts shared many metabolic and informational protein structural domains of primordial origin that were also prevalent in cellular proteomes. A global tree of life was discovered by phylogenomic analysis, and it was discovered that modern viruses descended from numerous prehistoric cells that contained segmented RNA genomes and coexisted with modern cells. Strong genomic and structural evidence supports the origin and evolution of viruses and cells, and this model can be resolved with other models of viral evolution if one assumes that viruses emerged from old cells rather than their contemporary equivalents.

The primate lentiviruses include HIV-1 and HIV-2, two viruses that cause AIDS in humans, as well as SIV strains from different host animals. Cross-species infections from chimps and

sooty mangabey monkeys, respectively, are the source of HIV-1 and HIV-2. To determine how long these pathogens have evolved, two methods have been used. Some SIV strain groups appear to have developed in a host-dependent way over many thousands or even millions of years. In stark comparison, only tens or hundreds of years have previously been estimated using molecular clock estimates. The heterogeneity of evolutionary rates across various locations within sequences was mainly disregarded in those estimates. The time depth of the monkey lentivirus phylogenetic tree may have been understated by at least a factor of ten because the distribution of rates at various sites in HIV-1 appears to be very skewed. These time frames, however, appear to be much too recent to be in line with host-dependent evolution[10].

## CONCLUSION

Wondering about the origins of life fascinates both life and nature in general. It is possible to better understand how viruses evolve, which could contribute to the understanding of this intriguing topic. The past virus still lacks a definite resolution. It's conceivable that mobile genetic elements that developed the ability to move between cells gave rise to viral. They might be related to extinct animals which were immediately free-living but later evolved an invasive mode of breeding. It's could be possible that viruses existed before biological life developed and helped to shape them.

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# CHAPTER 2

# AN OVERVIEW OF THE STRUCTURE AND GENETIC MATERIAL OF THE VIRUS

Dr. Manish Soni, Assistant Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id- manishsoni@jnujaipur.ac.in

**ABSTRACT:**

A contagious microorganism with DNA or RNA as its hereditary material is referred to as a virus. The virus protein sheath surrounds the genomic material. There are many different kinds of viruses in the world, some of which are active. Viruses are classified as helix, icosahedral, enveloped, and complicated according to their structural characteristics. The pathogen had either DNA or RNA as its molecular makeup. The host's mechanism was used by the pathogen to multiply. Consequently, viruses are also referred to as non-living entities. In this chapter, we summarized the genome and structure of the virus.

**KEYWORDS:**

DNA Viruses, Capsid Proteins, Enveloped Viruses, Genetic Material, And Nucleic Acid.

## INTRODUCTION

Viruses exhibit a broad variety of forms, sizes, and shapes. More than a thousand bacteriophage viruses could squeeze inside the cell of an *Escherichia coli* bacterium because viruses are typically much smaller than bacteria. The width of many viruses that have been examined ranges from 20 to 300 nanometers, and they are typically circular. Some filamentous filoviruses, which can reach lengths of up to 1400 nm, have widths of only about 80 nm. Scanning and transmission electron microscopes are used to visualize most viruses because optical microscopes cannot typically see them. Electron-dense "stains" are used to make the difference between the viruses and the backdrop stand out more. These are heavy metal salt solutions, such as tungsten, that deflect electrons away from stained areas. Fine detail is lost when virions are stained (positive staining). Only coloring, the backdrop, and negative staining solve this issue[1]–[3].

A full viral particle, or virion, is made up of nucleic acid encased in a protein shell for protection. These are made of capsomeres, which are protein-based components. A lipid "envelope" that is generated from the recipient cell membrane can surround viruses. The structure of the capsid, which is constructed from proteins written by the viral DNA, forms the foundation for physical differentiation. The existence of the virus DNA is typically necessary for the virally-coded protein components to self-assemble into a capsid. Complex viruses have the ability to code for proteins that help build their capsids. Nucleoproteins are proteins that are connected to nucleic acid, and a nucleocapsid is a combination of viral capsid proteins and viral nucleic acid. Atomic force microscopy allows for mechanical (physical) probing of the capsid and the complete viral structure. There are five major categories of structural viruses:

A single variety of protein components makes up helical capsids, which are layered around a center axis to create a helix shape. The middle of the spiral might be empty, giving it the appearance of a cylindrical tube. Rod- or filamentous-shaped virions are the product of this configuration. These virions can range in length from very short and stiff to very long and

pliable. A well-known example of a helix virus is the tobacco mosaic virus (TMV), which is depicted in Figure 1.

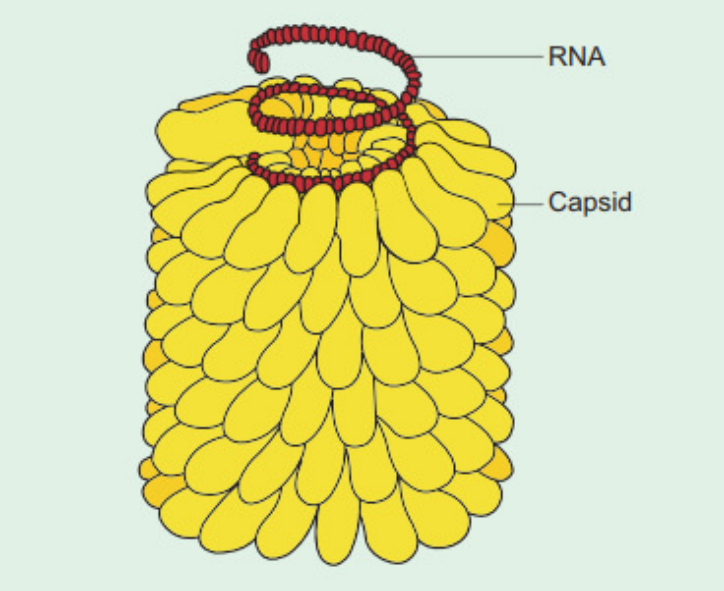


**Figure 1: Helical structure: Diagram showing the Helical structure of the virus (Brainkart).**

The tobacco mosaic virus is a spiral viral. Some helix viruses can be quite lengthy, as demonstrated here, even though they may have a very tiny circumference. DNA, viral protein molecules, and capsid are the three components. TMV causes tomato, cucumber, pepper, and tobacco plants to develop tobacco mosaic disease.

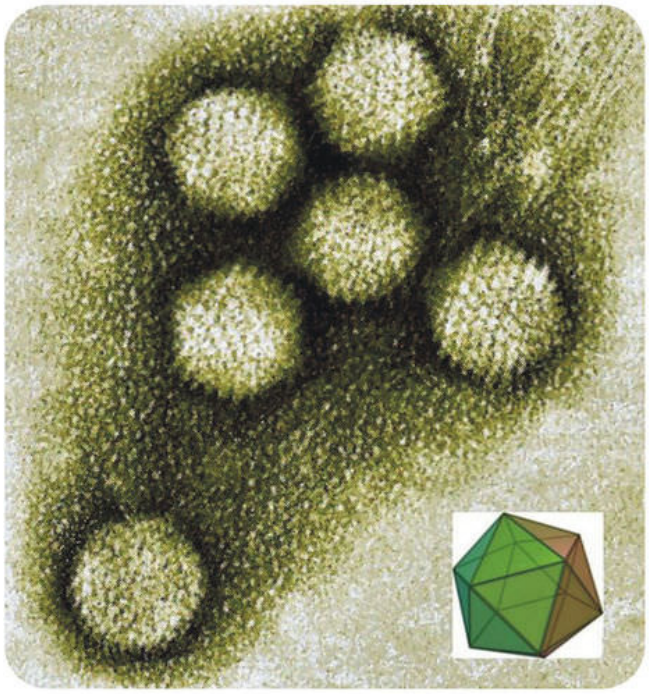

**Figure 2: Icosahedral-shaped virus: Diagram showing the icosahedral-shaped virus (CK-12).**

The majority of mammal viruses have chiral icosahedral symmetry and are icosahedral or nearly spherical (Figure.2). The best method to create a closed container out of identical

components is to arrange them into a standard icosahedron. For each triangle face, three capsomeres are the bare least needed, resulting in a total of 60 for the icosahedron. Many viruses maintain this symmetry despite having more than 60 capsomers and appearing circular, like the rotavirus. To accomplish this, the capsomeres at the apices known as pentons are encircled by five other capsomeres. Hexons are the six additional capsomeres that encircle each capsomere on the triangle sides. Pentons, which make up the 12 edges, are bent, whereas hexagons are fundamentally flat. Pentamers and hexamers may both contain the same protein as their component or they may be made up of distinct proteins.

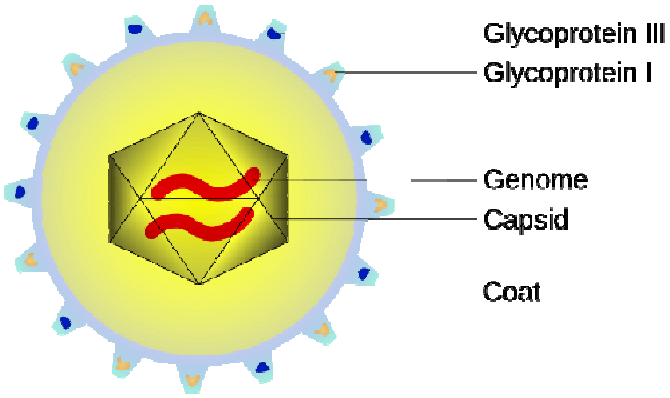


**Figure 3: Enveloped Viruses: Diagram showing the structure of the Enveloped Viruses (Wikipedia).**

Some virus species enclose themselves in a modified version of a cell membrane, such as the cell's exterior membrane that encircles an infected host cell or an interior membrane like the nuclear membrane or endoplasmic reticulum, resulting in the formation of an outer lipid bilayer known as the viral envelope (Figure.3). The lipid membrane and any extant carbs are completely derived from the host, but this membrane is peppered with proteins that are encoded by both the virus and host genomes. The majority of enclosed viruses rely on the membrane for their infectiousness. Influenza, human cytomegalovirus (HCMV), HIV, respiratory syncytial virus (RSV), vaccinia virus, and human coronaviruses are examples of enclosed viruses. (such as NL63, 229E, OC43, and SARS-CoV-2).

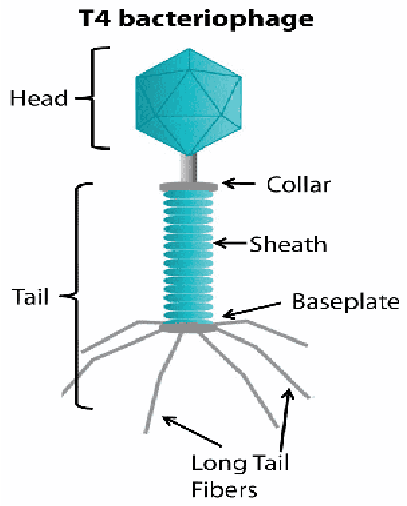


**Figure 4: Complex virus: Diagram showing the example of the complex virus (Morgridge Institute).**

These viruses have a capsid that is neither entirely helical nor entirely icosahedral, and it may also contain additional structures such as protein ends or a complicated exterior wall. Some bacteriophages, like Enterobacteria phage T4, have a complicated shape made up of an icosahedral head connected to a helix tail that may have a hexagonal base plate with sticking-out protein tail fibers (Figure.4). By adhering to the bacterium host and then delivering the virus DNA into the cell, this tail structure functions as a molecular needle. Viral genomes are made up of either DNA or RNA, never both. DNA and RNA units can be straight or circular, double or single-stranded, segmented (made up of several segments of nucleic acid), or nonsegmented (Figure.5)As the word "genomic segment" is used for both naming rules and historical purposes, its definition may be unclear. In the strictest sense, a genome segment is a discrete, isolated fragment of nucleic acid that is a part of the larger virus genome. For instance, the eight ssRNA segments that make up the influenza A virus's segmented genome (Figure.5). The so-called UL (unique long) and US (unique short) segments of herpesviruses, which have nonsegmented genomes made up of a single linear dsDNA molecule, are sections of their genomes that are bordered by repetitions. The fact that each virion contains two versions of the same ssRNA molecule adds to the complexity of the HIV genome.

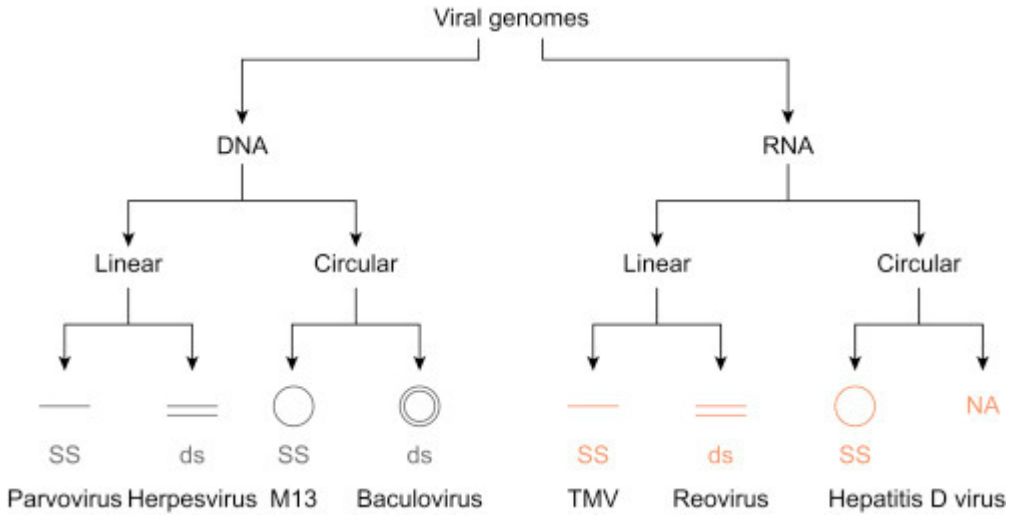


**Figure 5: Virus genomes: Diagram showing the genetic material which is present in the different viruses (Science direct.com).**

The two ssRNA molecules are referred to as clones rather than segments because the HIV genome is not thought to be divided. The extremities of the genome in many viruses contain repetitive sequences, chemical alterations, or secondary structures, many of which serve regulating purposes. Because of the close packing of the genomes inside the capsids, the genome and the capsid are commonly referred to as nucleocapsids. Amazingly, viruses can enter us productively and, of course, cause disease despite having very little genetic material. For instance, the genome of the flu virus only has 15,000 bases. The human genome is 3,200,000,000 bases longer than other genomes, or about 200,000 times longer. Viruses must be extremely effective in their attempts to enter and spread within the target cell. One of the tiniest RNA viruses, Bacteriophage Q, has only 4 genes and a genome made up of 4217 nucleotides. The TT virus, which has a genome of less than 4000 nucleotides long and 4 expected genes, is one of the tiniest mammal DNA viruses that is currently understood. The enormous *Megavirus chilensis*, with a genome as big as 1.3 MB and 1000 genes, is on the other end of the spectrum[4]–[6].

The mystery of the roles that virus chromosomes encode is intriguing. Approximately 80% of viral genomes, according to the analysis of viral genome sequences, code for virus-specific genes, many of which have no known homologs or functions. The extent of each species' genome differs considerably. The tiniest is the ssDNA circoviruses, family Circoviridae, which have genomes of only two kilobases and only code for two proteins; the biggest is the pandoraviruses, which have genomes of roughly two megabases and code for about 2500 proteins. Rarely do virus genes contain introns, and their placement in the genome frequently causes them to intersect.Due to their greater rate of replication errors, RNA viruses typically have lower genome sizes than DNA viruses. They also have a maximal top-size limit. Beyond this, replication mistakes make the virus ineffective or uncompetitive. To make up for this, RNA viruses frequently have segmented genomes (the genome is broken up into smaller components), which lessens the likelihood that a mistake in a single component of the genome will render the complete genome inoperable. In comparison, DNA viruses typically have bigger genomes because their reproduction enzymes are highly faithful. The exception to this norm is single-strand DNA viruses, whose genome change rates can be as high as those of ssRNA viruses[7], [8].

## DISCUSSION

Mengo virus, an example of the cardiac picornaviruses, has a structure that differs significantly from that of rhino- and polioviruses. As an 8-resolution structural estimate, human rhinovirus 14 was used to determine the Mengo virus structure. The use of icosahedral symmetry allowed for the extension of phase information to a 3  precision. With the help of this method, it is possible to predict the shapes of many other viruses without using the isomorphous substitution method. Large insertions and deletions, mostly in VP1, drastically change the surface characteristics of Mengo virus's main capsid proteins, VP1, VP2, and VP3, even though their structure is the same as that of rhino- and polioviruses. In particular, protein insertions in VP1 that occupy part of the canyon cause the hypothesized receptor binding "canyon" of human rhinovirus 14 to transform into a deep "pit" in the Mengo virus. Although the minor capsid peptide (VP4) of the Mengo virus is entirely intracellular, its interaction with the other capsid proteins differs significantly from that of rhino- or poliovirus. However, because the location of its carboxyl end is comparable to that of human rhinovirus 14 and poliovirus, all of these picornaviruses may undergo the same autocatalytic cleavage of VP0 to VP4 and VP2 during assembly. The foundation of mechanistic virology continues to be virus structures, which also act as a model for answers to issues with macromolecular construction and function in general.

In addition to providing information on the structural folds of individual viral components, X-ray crystallography, electron cryomicroscopy, and computational, and biochemical methods have also shed light on the structural underpinnings of viral assembly, nucleic acid packaging, particle dynamics, and interactions with cellular molecules. During the recovery stage of the EBOV illness, 98 semen tissues from 68 men in Guinea have collected for Ebola virus (EBOV) RNA sequencing. Up to nine months after the start of the illness, ten samples from eight males tested positive for EBOV, with declining patterns in the percentage of positive samples and the amount of virus RNA. After leaving treatment facilities, safe intercourse procedures should be followed. Zika virus (ZIKV) is regarded as a contagious illness that is both highly relevant clinically and epidemiologically. The viral epidemic that erupted in Southeast Asia and Latin America in 2014 demonstrated the pressing need for quick and accurate testing instruments. ZIKV is currently diagnosed in laboratories using genetic and antibody techniques. Serological detection may suffer from cross-reactivity, while molecular instruments require costly, complex apparatus, trained people, and trained

personnel. Genosensors present a compelling option for a field-ready, rapid, and precise detection of ZIKV in this situation. The creation of genosensors for ZIKV differential detection and differentiation from dengue (DENV) and chikungunya (CHIKV) related arboviruses is discussed in this study. The hepatitis B virus (HBV) is a tiny, circular, double-stranded DNA virus that can produce either an acute or persistent infection that is self-limited and may or may not result in liver cell damage. (hepatitis). Hepatocellular cancer growth is 200 times or more likely to occur in people with persistent hepatitis B that has been present for a long time.1 Even though the structure and arrangement of the HBV genome, its gene products, and its replication strategy have all undergone significant research recently, little is known about the processes underlying viral eradication and survival, liver damage, and cancerous change. Monkeypox, also known as mpox, is a current public health disaster that calls for more potent preventative and therapeutic measures. Peng et al. concentrated on a complex that is essential to the mpox virus's genome reproduction mechanism. The structure of the DNA polymerase F8, which catalyzes the production of viral DNA, in combination with the processivity factor made up of A22 and E4 and the DNA substrate was determined using cryo-electron imaging. The structure's explanation of the processivity factor's mode of operation departs from conventional wisdom and might serve as a starting point for the development of antiviral drugs[9], [10].

## CONCLUSION

In order to function, viruses must be small, obligatory intracellular pathogens with either a DNA or RNA genome encased in a safe, virus-coded protein sheath. Viruses can be thought of as movable genetic components that most likely have biological origins and have long coevolved with their hosts. The molecule of DNA or RNA that makes up a virus's gene can be a single-strand (ss), a two-strand (ds), linear, or circular. The first nucleic acid structure (a monopartite genome) or multiple nucleic acid fragments can include the complete gene.Viruses are contagious organisms that can affect all living things, including microbes, plants, and mammals.

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# CHAPTER 3

# CLASSIFICATION OF THE VIRUS BASED ON ITS STRUCTURE AND THE GENETIC MATERIAL

Prof. Kapilesh Jadhav, Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id-kapilesh@jnujaipur.ac.in

**ABSTRACT:**

The contagious molecule known as a virus is made up of a protein covering and DNA/RNA. According to their dimensions, different types of viruses can be found in nature.Human-infecting viruses are presently divided into 21 families, which only represent a tiny portion of the wide variety of viral that target encompasses vary from mammals to protozoa. Viruses are classified according to their molecular makeup and appearance. In this chapter, we covered different viral classification schemes.

**KEYWORDS:**

Committee Taxonomy, Dobule Stranded, International Committee, Nucleic Acid, Virus Taxonomy.

## INTRODUCTION

The process of identifying viruses and classifying them into a taxonomy scheme akin to those used for biological creatures is known as viral categorization. By identifying and categorizing viruses according to their commonalities, classification aims to explain the variety of viruses. The Linnaean hierarchy method of viral categorization was first developed in 1962 by André Lwoff, Robert Horne, and Paul Tournier. This method used phylum, class, order, family, genus, and species to categorize things. The common characteristics of viruses not those of their hosts—and the kind of nucleic acid that makes up their DNA were used to classify them. The International Committee on Taxonomy of Viruses, or ICTV, was established in 1966. Since viruses' tiny genome sizes and high rates of change made it challenging to identify their lineage beyond order, the ICTV originally rejected the Lwoff, Horne, and Tournier method. The more conventional order has thus been supplemented by the Baltimore categorization scheme. With the adoption of a 15-rank categorization scheme that ranges from domain to species, the ICTV started acknowledging deeper genetic connections between viruses that have been found over time in 2018. Additionally, a genogroup is used to classify some animals that belong to the same family. Phenotypic traits, such as appearance, nucleic acid type, method of reproduction, target species, and the sort of illness they produce, are used to categorize viruses. Although the Baltimore classification system can be used to classify viruses into one of seven categories based on how they synthesize mRNA, the official taxonomy categorization of viruses is handled by the International Committee on Taxonomy of Viruses (ICTV) system. The ICTV has established specific nomenclature standards and additional categorization rules[1]–[3].

Early in the 1970s, the International Committee on Taxonomy of Viruses started developing and putting into practice guidelines for identifying and categorizing viruses. The International Union of Microbiological Societies has entrusted the creation, improvement, and upkeep of a global viral classification exclusively to the ICTV. The method has many similarities with the taxonomic framework used to categorize biological entities. However, there are some variations, such as the fact that all taxonomy names are always italicized, in contrast to the

International Code of Zoological Nomenclature and the International Code of Nomenclature for Algae, Fungi, and Plants.

Beginning at the realm level, viral categorization proceeds as follows, with the genus prefixes in brackets.There is presently no defined format for viral species names, unlike the binomial naming used for biological species. Currently, the ICTV requires that a species name has as few syllables as possible while still being unique, and it cannot just have the word virus and the hostname. Especially for higher plants and animals, species names frequently take the shape of [Disease] viral. The ICTV released a plan 2019 for a referendum in 2020 to implement a more structured system of binomial naming for viral species names. Later, some virologists disagreed with the proposed change to the naming convention, claiming that the discussion took place when many experts in the field were concerned with the COVID-19 epidemic. All taxonomic categories, except subrealm, subkingdom, and subdivision, are in use as of 2021. There are two incertaesedis groups, 19 incertaesedis families, one incertaesedis class, and six kingdoms. According to some theories, the similarity between the virion assembly and structure of some viral groups that infect hosts from different domains of life (such as bacterial tectiviruses and eukaryotic adenoviruses or prokaryotic Caudovirales and eukaryotic herpesviruses) indicates that these viruses have evolved together. To define higher-level species - structure-based viral families - that could supplement the ICTV categorization system of 2010, it has been proposed that the structural relationships between viruses be used as a foundation. Using connections in protein structures, the ICTV has progressively introduced a large number of higher-level species. A protein belonging to a specific molecular family must be present for any of the four worlds described in the 2019 version to exist.

The Baltimore classification system, which was first described in 1971, divides viruses into seven categories based on a variety of factors, including their nucleic acid (DNA or RNA), strandedness (single- or double-stranded), sense, and reproduction strategy (Figure.1). These groups are identified by Roman numbers and are named for the scientist David Baltimore, who was awarded the Nobel Prize. Other categories are based on the illness the virus causes or its appearance, neither of which are acceptable because various viruses can either cause the same illness or have a striking resemblance. Furthermore, it can be challenging to identify virus components under a microscope. When viruses are categorized based on their genomes, those in a particular group will all act similarly, providing some guidance for future study. Viruses can be classified into one of the following seven categories:

1. I: viral dsDNA (e.g. Adenoviruses, Herpesviruses, Poxviruses)
2. II: ssDNA viruses with an added "sense" component DNA (e.g. Parvoviruses)

dsRNA viruses, third (e.g. Reoviruses)

Viruses with (+)ssRNA (+ strand or sense) RNA (e.g. Coronaviruses, Picornaviruses, Togaviruses)

1. V: (ssRNA viruses (sense or antisense strand) RNA (e.g. Orthomyxoviruses, Rhabdoviruses)
2. VI: Positive strand or sense ssRNA-RT viruses DNA and RNA are intermediates in the life cycle. (e.g. Retroviruses)
3. dsDNA-RT viruses RNA and DNA are intermediates in the life cycle. (e.g.Hepadnaviruses)

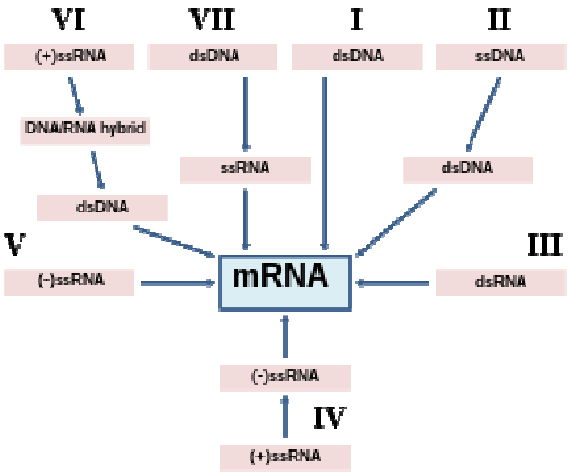


**Figure 1: Baltimore Classification of viruses Diagram showing the Baltimore Classification of viruses based on the viral mRNA (Wikipedia).**

Apart from that the next virus classification system is based on their nucleic acid (Figure.2).

Except for viruses that reverse-transcribe DNA, all viruses with DNA genomes belong to one of three known viral realms: Duplodnaviria, Monodnaviria, or Varidnaviria. However, numerous other incertaesedis families and groups as well as the incertaesedis order Ligamenvirales are also used to categorize DNA viruses. Double-stranded DNA viruses are found in the categories Duplodnaviria and Varidnaviria; other double-stranded DNA viruses are incertaesedis. Single-stranded DNA viruses in the class Monodnaviria typically contain a HUH endonuclease; other single-stranded DNA viruses are incertaesedis.

1. Group, I viruses have double-stranded DNA. These areas contain herpes and varicella viruses.
2. Group II viruses have DNA that is single-stranded.

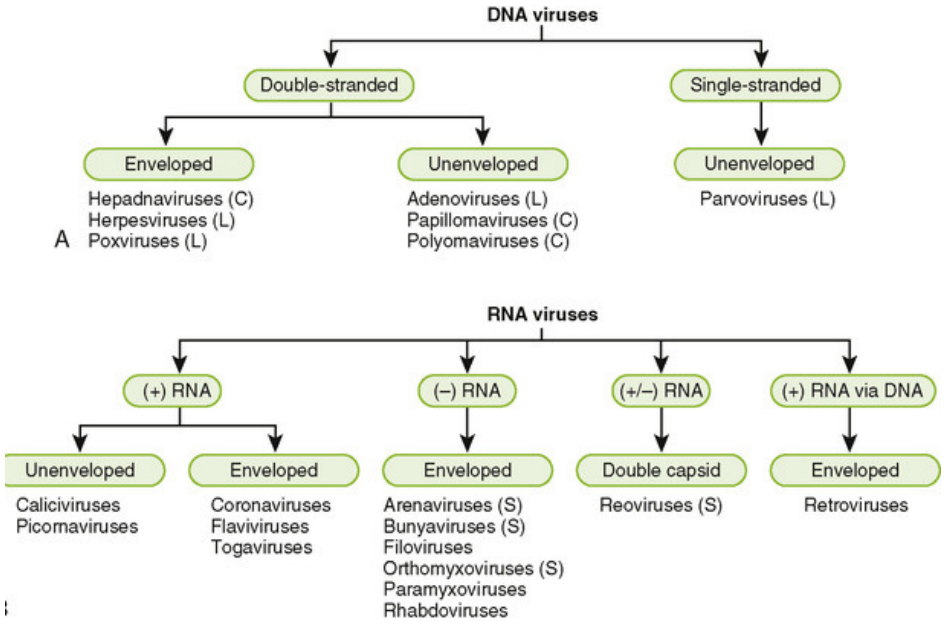


**Figure.2: Classification: Diagram showing the classification of the virus based on their nucleic acid (online biology).**

In the kingdom Orthornavirae of the phylum Riboviria, all viruses that have an RNA genome and contain an RNA-dependent RNA polymerase (RdRp) are considered to be viruses. Group III viruses, such as the rotavirus, have double-stranded RNA chains. Viral genomes in Group IV are positive-sense single-stranded RNAs. The picornaviruses are a family of viruses that includes well-known viruses like Hepatitis A virus, enteroviruses, rhinoviruses, poliovirus, foot-and-mouth virus, SARS virus, hepatitis C virus, yellow fever virus, rubella virus, among the well-known viruses found in this group. Group V viruses have single-stranded RNA sequences with a negative sense. Along with the influenza virus, measles, mumps, and rabies, well-known members of this category include the Ebola and Marburg viruses.

## DISCUSSION

The phenetic, biological, evolutionary, and polythetic ideas are examined concerning some conflicting views on the species notion in biology. The idea of species in virology is explored, and the distinguishing characteristics of various viral species are described. Considerations include the categorization of plant viruses and the oneness of the viral universe. The polythetic character of viral species, it is determined, precludes the use of a single type of indicator for identifying them, whether it be a recombinant complementation test, the existence of a specific antigenic marker, or host vulnerability. However, it is necessary to recognize the need for viral species classification and seek the ICTV's Plant viral Subcommittee's approval [6]. A huge new viral collection has been discovered thanks to high-throughput sequencing (HTS) and its application in retrieving and building novel virus genomes from ambient, human clinical, veterinary, and plant materials. Their categorization, which is determined solely by their genomes, poses a significant challenge to conventional viral taxonomy, particularly at the family and species levels, where it has traditionally relied heavily on descriptive taxon classifications.

These frequently require some understanding of their morphological characteristics, such as reproduction tactics, and virion structure, and clinical and epidemiological characteristics, such as host range, regional spread, and illness results. However, there is scant to no evidence of these characteristics for viruses found in metagenomic databases. Such viruses must be assigned based mostly or completely on genomic relatedness measures if they are to be included in the viral classification. The first issue is that the International Committee on Taxonomy of Viruses (ICTV), which approves the taxonomic classification of viruses, gives scant or no guidance on how similar or how divergent viruses must be to be considered members of new species or new families. We recently created a technique (Genome Relationships Applied to Virus Taxonomy - GRAViTy) for evaluating the genomic (dis)similarity between viruses among the eukaryotic and bacterial viruses presently categorized by the ICTV. We discovered widespread agreement between genetic connections and taxonomy classifications for eukaryotic viruses of all genome shapes and genome sizes at the family and genus levels. However, bacterial viral family designations have been made at a very distinct genomic level, and contemporary classifications of categories as sub-families are a much better fit for the eukaryotic virus family level. These results confirm the ICTV Phage Study Group's continuing reclassification of bacteriophages. It is crucial to have a quick and accurate way to examine the variety of metagenomic viruses and designate them to particular taxonomy layers based on evidence[4]–[6].

A categorization structure that aims to arrange and make sense of the variety of viruses affecting animals, plants, and microbes is provided by the separation of viruses into orders, families, groups, and species. Based on homologous genes, sequence patterns, homologous genome structure, and organization, as well as more fundamental factors like species, host range, nucleotide and immunological relatedness, and disease, classifications are made.

Phylogeny and the evolutionary paths of viruses must both be taken into account when classifying organisms below the family level. Alternative techniques for genus and species classifications that are solely based on the degree of difference between genome segments are offered by recently created methods like PASC, DEMaRC, and NVR. They provide the opportunity for the massive amount of new viral genomes being produced by next-generation metagenomic sequencing to be automatically classified. Although biological groups develop at varying rates and viral genomes undergo recombination and reassortment, distance-based techniques have trouble coping with their complicated evolutionary histories. Classifications in biology that are solely based on differences in sequence are also random, but the present system of viral taxonomy is useful exactly because it is based mainly on behavioral traits. However, a different method is required so that viral variations without biological information could still be classified by the ICTV using only genetic links to existing species. To add to the current viral categorization and record our quickly expanding knowledge of virus variety, simpler nomenclature suggestions, and naming standards represent an effective solution[8].

The International Committee on the classification of Viruses authorized and confirmed modifications to viral classification in February 2018, which are listed in this document. The classification now includes 451 species, 69 names, 11 subfamilies, 9 families, and 1 novel order. There are currently 9 orders, 131 families, 46 subfamilies, 803 names, and 4853 species at each classification level. The International Code of Virus Classification and Nomenclature was altered to permit the use of people's names in taxon titles in the right situations [9]. The categorization of viruses below the species level is not ruled on by the International Committee for the Taxonomy and Nomenclature of Viruses. For all known viral kinds, the term "species" cannot be specified precisely. The complex and fascinating ecology of human immunodeficiency viruses necessitates a thorough and educational naming system, but it also presents difficulties that necessitate flexible application or modification of many of the rules over time. This review summarizes the monkey lentivirus naming scheme and offers an update on fresh research since the previous review was published in 2000 [7]–[9].

Based on the traits of the virion, Lwoff and Tournier's general categorization system for viruses has been significantly altered to account for additional features. The Lwoff-Tournier method separates viruses into riboviruses or deoxy viruses depending on whether their nucleic acid is RNA or DNA. Next, based on the shape of the nucleocapsid, viruses are divided into helical or cubic classes, creating four classes: ribocubica, ribohelica, and deoxy cubica. Finally, the nucleocapsid may be bare or enclosed, establishing eight classes and a second division. The typical bacteriophages, which have icosahedral heads and helix tails, as well as some viruses with complicated - and occasionally still unidentified - structures, cannot fit into this system. Lwaff and Tournier (1996)[11] describe the categorization that is presently being created by a multinational group.

Concerned with our hypothetical species groups that include viruses as members. A viral species can only be characterized by enumerating a few of its component characteristics that are specific to that species. A viral species cannot, however, be identified by a singular species-defining characteristic. The updated description of a viral species from 2013 is incorrect because it also refers to virus families. A nucleotide motif is a molecular component of a viral genome, not a trait that can be used to categorize novel virus species. A categorization of viral genomes rather than viruses occurs when virus classification is exclusively based on nucleotide patterns. As this would create the contradiction that every polythetic class is also a monothetic one, the varying distribution of species-defining

characteristics of a polythetic species class is not itself a unique shared property of all the members of the class[10].

## CONCLUSION

Since it enables the biological, biochemical, and genetic characteristics of a virus to be arranged into a structure that accepts and links all viruses, viral classification is significant. The physical and molecular properties of the virus particles or the method of viral reproduction serve as the most crucial categorization factors. In the summary of this chapter, virus stored their genetic information in the different types of nucleic acid which transcribe in the mRNA.The virus used the host cell machinery the transcribed its genetic information.

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# CHAPTER 4

# A DETAILS STUDY OF THE ADENOVIRUS GENOME, HOST INFECTION, AND MECHANISM

Dr. Sunita Rao, Assistant Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id-sunita.rao@jnujaipur.ac.in

**ABSTRACT:**

The viruses are non-enveloped, icosahedral, and medium in size (90–100 nm) viral with double-stranded DNA known as the adenovirus. Infection of the adenovirus leads to chronic bronchitis and pneumonia. Adenoviruses can reproduce in the nucleus of mammalian cells by utilizing the host's reproduction apparatus and having a straight dsDNA genome. Adenoviruses engage with the target cell through two different pathways to enter the cell. At the edges, activity mostly takes place. In this chapter, we discussed the adenovirus genome, its mode of replication, infection, and the symptoms

**KEYWORDS:**

Adenovirus genome, DNA virus, Human adenovirus, Transcription unit, Viral DNA,

## INTRODUCTION

Adenoviruses, which belong to the Adenoviridae family, are double-stranded DNA-containing, medium-sized (90–100 nm), nonenveloped (viral particles without an exterior lipid membrane) nucleocapsid viruses. Their moniker comes from the fact that they were first separated from human adenoids in 1953. In humans, more than 50 different adenoviral serotypes have been found to cause a wide range of illnesses, from minor respiratory infections in young children (common cold) to life-threatening multi-organ diseases in people with weakened immune systems. They have a wide range of vertebrate hosts.

Adenovirus is a non-enveloped, icosahedral-symmetric virus with a width of 80–110 nm. The straight, double-stranded DNA genome of human adenoviruses has a terminal protein (TP) chemically linked to the 5' termini. The DNA is enveloped in a protein resembling histones and has inverted terminal repeats (ITRs) of 50–200 bp that serve as replication sites. The DNA is about 36,000 bp in length. The most crucial capsid proteins for gene transport are the hexon, penton base, and knobbed fiber. The 20 triangle sides of the virus capsid are made up primarily of the protein hexon. Each of the 240 trimer hexon capsomers in the capsid interacts with six other trimers. The penton capsomere, a compound made up of five duplicates of the penton base and three copies of fiber forms the 12 edges. Five hexon capsomeres, one from each of the five sides that meet at the apex, engage with each penton capsomere. From the fiber base, the knobbed fiber protrudes[1]–[3].

Adenovirus genomes are 23–46 protein-coding genes long, linear, non-segmented double-stranded (ds) DNA strands that are usually 26–46 Kbp in size. Human adenovirus E, a mast adenovirus with a 36 Kbp genome having 38 protein-coding genes, is used as an illustration in the following explanation. All adenoviruses share the fundamental concepts of genome structure and the roles of the majority of the genes outlined in this paper, despite differences in the exact number and identification of genes among adenoviruses.

The Human adenovirus E genome contains 38 genes that are arranged in 17 transcription units, each of which has 1–8 coding segments. One transcription unit can create numerous

distinct mRNAs by processing the pre-mRNAs generated by each transcription unit through alternative splicing. Early in the virus reproductive cycle, the transcription components E1A, E1B, E2A, E2B, E3, and E4 are sequentially produced (Figure.1). The majority of the proteins that these transcription units' genes encode work to control viral transcription, replicate viral DNA, and inhibit the host's immune reaction to infection.

The L1-L5 transcription units are produced later in the viral reproductive cycle and primarily code for proteins that are either engaged in capsid construction or make up the components of the viral capsid (Figure.1). The same promoter region controls all L1–L5 transcription units, and they all use the same transcription start point. Thus, transcription of each of the five late transcription units starts at the same time in the virus reproduction cycle. A community of transcripts with five varying lengths is created when transcription of pre-mRNAs starting at the late promoter is arbitrarily stopped at one of five termination sites. After that, alternative splicing is used to create 1-4 distinct mRNAs, each of which codes for a specific amount of proteins [3].

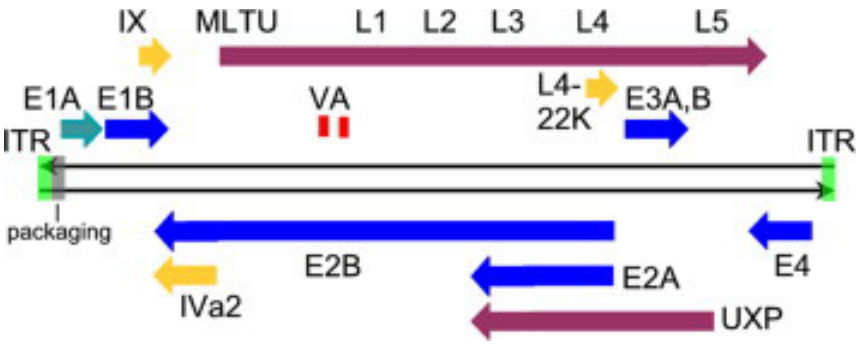


**Figure 1: Adenovirus genome: Diagram showing the genome of the adenovirus (Science direct.com).**

Adenoviruses can reproduce in the nucleus of mammalian cells by utilizing the host's reproduction apparatus and having a straight dsDNA genome. Adenoviruses engage with the target cell through two different pathways to enter the cell. At the edges, activity mostly takes place. The knob domain of the fiber protein binds to the cell receptor to begin entry into the target cell. The two recognized receptors at this time are the coxsackievirus/adenovirus receptor (CAR) for all other serotypes and CD46 for group B human adenoviruses. MHC molecules and sialic acid groups may also play a role in this, according to some reports [4].

Following this, an integrin molecule engages with a region in the penton base protein (see capsomere) in a secondary interaction. The co-receptor contact promotes the viruses' entrance. V integrin is the co-receptor protein in question. The viral particle is endocytosed when it binds to the v integrin via holes covered in clathrin. Virion entrance into the recipient cell occurs within an endosome as a consequence of attachment to the V integrin, which triggers cell communication and causes actin polymerization. Once the virus has effectively entered the recipient cell, the endosome begins to acidify, which changes the structure of the virus by causing the capsid components to break apart. Protein VI, one of the components of the capsid, is freed from the capsid as a result of its destabilization. The endosome is destroyed by these modifications and the pentons' toxicity, which causes the virion to migrate into the cytoplasm [4]. The virus travels to the nuclear pore complex with the aid of cellular microtubules, where the adenovirus particle disassembles. The following release of viral DNA allows it to pass through the nuclear opening and infiltrate the nucleus. The DNA then interacts with the host cell transcription mechanism by joining with histone molecules that

are already in the nucleus (Figure.2). Then, new virus particles can be produced without the viral DNA being integrated into the chromosomes of the recipient cell[4]–[6].

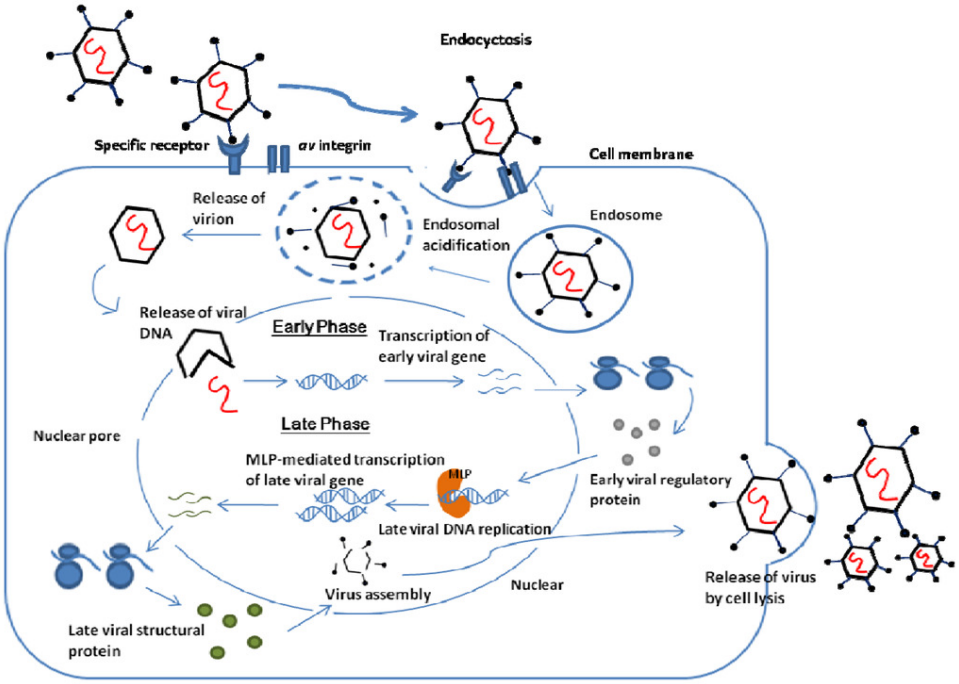


**Figure 2: Replication of the adenovirus: Diagram showing the steps involved in the replication of the adenovirus (Research gate).**

The DNA duplication mechanism divides the viral life cycle into two phases: an early phase and a late phase. Both stages result in the production of a main transcript that is variably spliced to create monocistronic mRNAs that can be translated by the host's ribosome (Figure. 2). The majority of non-structural, regulating proteins are produced by the early genes. These proteins work to prevent the infected cell from being killed too soon by the host immune system, trigger other viral genes (like the virus-encoded DNA polymerase), and change the translation of host proteins required for DNA synthesis. (blockage of apoptosis, blockage of interferon activity, and blockage of MHC class I translocation and expression). Under specific circumstances, some adenoviruses can change cells using their early gene products. It has been discovered that E1A (binds Retinoblastoma tumor suppressor protein) can immortalize progenitor cells in vitro, enabling E1B (binds p53 tumor suppressor) to help and stabilize the cells' transformation. But to effectively change the host cell and produce malignancies, they are dependent on one another. The CR3 region of the largely inherently unstructured protein E1A is essential for activating transcription. The early and late stages are separated by DNA reproduction. The adenovirus genome can be replicated once the early genes have released sufficient viral proteins, replication apparatus, and replication substrates. The 5' end of the viral genome is chemically attached to a terminal protein, which serves as a reproduction trigger. After that, the viral DNA polymerase replicates the genome using a strand relocation method as opposed to the traditional Okazaki pieces used in human DNA replication[5]. The goal of the adenovirus's late stage of development is to make enough structural protein to store all the genetic material created by DNA duplication. The virus is formed into its protein casings after the viral components have effectively been reproduced, and the virus is then expelled from the cell as a consequence of virally caused cell death. Adenovirus has the ability to multiply again (MR). (Yamamoto and Shimojo, 1971). The interaction of two or more viral genomes with fatal harm to create a functional virus genome is known as molecular recombination (MR). After virions were exposed to UV light and

permitted to infiltrate recipient cells numerous times, such MR for adenovirus 12 was observed. Numerous instances of MR in various viruses were reported in a study, and it was proposed that MR is a typical type of sexual contact that offers the survival benefit of recombinational healing of genome damage.

Adenovirus infection is a viral illness that spreads easily and frequently causes a respiratory system infection. Common cold symptoms like nose obstruction, coryza, and cough to pneumonia-like respiratory difficulties are among the typical symptoms. Fever, exhaustion, pains in the muscles, headaches, stomach pain, and enlarged neck glands are additional common signs. Onset typically occurs two to fourteen days after viral infection. A minor eye infection may develop on its own, in conjunction with a temperature and scratchy tongue, or as a more serious case of adenoviral keratoconjunctivitis, which includes a stinging red eye, sensitivity to light, and secretion. Young toddlers may only experience an earache. The signs of an adenovirus illness can include sickness, diarrhea, and stomach discomfort, along with or without breathing symptoms. Some individuals, though, show no signs.

Humans typically contract adenovirus infections from Adenovirus kinds B, C, E, and F. Spread primarily happens when a sick person is near another individual. The virus can spread through respiratory transfer, the fecal-oral pathway, or tiny particles. The virus can less frequently propagate through infected surfaces. severe respiratory distress syndrome, bronchiolitis, and severe bronchitis are additional breathing problems [5]. People with weakened immune systems may develop myocarditis, meningoencephalitis, or hepatitis as a result [6]. cleaning hands, avoiding contacting one's eyes, lips, or nostrils before cleaning hands, and avoiding being around ill people can all help prevent viral infection. Strict adherence to excellent infection control procedures is successful in preventing the spread of adenovirus-associated diseases, such as pandemic keratoconjunctivitis, in institutions. To stop viral eye epidemics linked to swimming pools, sufficient amounts of chlorination must be maintained. Some military members have received a live adenovirus immunization to guard against kinds 4 and 7 adenoviruses. After the advent of live sublingual immunization against kinds 4 and 7, rates of viral illness in military trainees decreased. After the vaccine's supplies ran out in 1999, illness rates rose until 2011, when it was once again made available. The majority of treatments are clinical and helpful. It is possible to purchase over-the-counter medications to relieve discomfort and lower temperature. A cool cloth and lubricants may ease pain from adenoviral conjunctivitis. The retina may need to be treated with steroid eye solutions. The majority of viral illnesses resolve on their own.

## DISCUSSION

DNA viruses known as adenoviruses (AdV) usually produce minor illnesses of the upper or lower nasal system, GI tract, or eye. Hepatitis, ulcerative colitis, pancreatitis, nephropathy, and encephalopathy are uncommon symptoms of AdV infections. Because they lack humoral defense, newborn infants are more likely to contract adenovirus illnesses. In confined or congested environments, epidemics of AdV illnesses can affect fit infants or adults. (particularly military recruits). In individuals with compromised antibodies, the illness is more serious and spread is more probable. (eg, organ transplant recipients, human immunodeficiency virus infection, congenital immunodeficiency syndromes). Untreated serious AdV pneumonia or widespread illness may have mortality rates of more than 50%. There are more than 50 different AdV serotypes known. Different serotypes exhibit various tissue tropisms and are associated with specific clinical signs of illness. Different nations or areas have different prevalent serotypes and these changes over time. New variants can supplant prevalent serotypes through transmission between nations or regions. Because planned, controlled therapy studies have not been conducted, the treatment of AdV diseases

is debatable. Although cidofovir is thought to be the best medication for treating serious AdV illnesses, not all individuals need to be treated. There are presently no vaccines accessible, even though they are extremely effective in lowering the chance of lung AdV infection [7].

A substantial portion of the 53 distinct human adenoviruses (HAdV) serotypes (species A–G) are linked to severe lung, gastric, and eye illnesses. Additionally, replication-defective HAdV-5-based vectors continue to be crucial in clinical vaccine administration and gene transfer studies. Even though studies of AdV biology have made considerable progress, we still don't fully comprehend the structure of AdV or its complex relationships with the host. For elucidating the processes of AdV disease and enabling the best use of AdV vectors for medicinal purposes, ongoing attempts to advance understanding in these fields, as addressed in this chapter, will be essential [8].

As the concentration of viral study moves from fundamental biology to adenovirus-based vector technologies, structural studies continue to play a crucial role. Modifying the virion is frequently an essential stage in the development of new treatments for gene substitution, cancer, and immunizations. Such tailored modifications aim to retarget the virus or lessen the immune reactions to infection. When these attempts are founded on thorough systemic understanding, they are far more successful. This minireview offers a succinct overview of the extensive knowledge amassed through the joint use of X-ray diffraction and electron microscopy. The virion's physical arrangement is now well understood, and the molecular shapes of all three main capsid proteins hexon, penton, and fiber are now known at the atomic level. We emphasize recent advances, such as the finding of the penton base's structure and the fact that adenovirus has several cousins. We outline how structural data can be used to design new virions before outlining the possibilities for further advancement[7]–[9].

Adenoviruses are double-stranded DNA viruses that are non-enveloped and linked to a variety of clinical conditions in people. Adenoviruses have been categorized into one of seven (A-G) species based on hemagglutinin characteristics, DNA similarity, carcinogenic potential in rats, and clinical disease [10]. There are currently 67 immunologically different adenovirus serotypes that have been identified. It was stated in a 1996 chapter on the biology of adenoviruses that "the identity of the cellular receptor remains a mystery." (78). Numerous viral targets have been discovered in recent years, and more knowledge has become available about the early phases of adenovirus transmission. The desire to transport remedial genes to particular regions using viral vectors has greatly fueled interest in receptors. The interplay of adenoviruses with receptors and the function of receptors in viral entrance and tissue tropism will be succinctly discussed in this review [11]. When first discovered, the immortalizing oncoproteins known as adenovirus early region 1A (E1A) proteins were thought to affect RNA in rat cells. Surprisingly, it was later discovered that many human tumor cells could be reverse-transformed by adenovirus-5 E1A in its 243-amino-acid version. E1A's capacity to re-program RNA in tumor cells appears to be the cause of tumor inhibition, and the biochemical foundation for this interesting impact is just now starting to become clear. These findings have given researchers an instrument with which to investigate how basic biological processes are regulated [12]. The adenovirus penton, which makes up the corners of the capsid and includes all the elements required for viral attachment and uptake, is a noncovalent combination of the pentameric penton base and trimeric fiber proteins.

The human adenovirus 2 (hAd2) penton base's 3.3 resolution crystal structure reveals that the monomer has a basal jellyroll domain and a distal irregular domain made by two long insertions, a shape that is comparable to the viral hexon. A pliable surface loop contains the Arg-Gly-Asp (RGD) pattern, which is necessary for contact with cellular integrins. A localized structural change occurs in the penton base's insertion domain as a consequence of

the universal fiber motif FNPVYPY binding at the interface of neighboring penton base monomers, as demonstrated by the complex of the penton base with bound N-terminal fiber peptide, which was found at 3.5  resolution. These findings will be helpful for gene therapy uses because they shed light on the composition and shape of the viral capsid [13]. Adenoviruses are responsible for several self-limiting but frequently extremely contagious illnesses that impact a variety of systems, most frequently those related to the lung, genitourinary, and gastric pathways as well as the surface of the eye. Adenoviruses have become the target of a broad hunt for potent dermal and systemic antivirals.

The startling recent trend of high morbidity and rising mortality associated with systemic adenoviral infections in the immunosuppressed, particularly pediatric bone marrow transplant recipients, is one of these. It includes patient morbidity, economic losses, and chronic visual disturbances linked to epidemic keratoconjunctivitis. Since several and frequently genetically distinct adenovirus serotypes can induce related illnesses, it has proven to be difficult to create effective antivirals. In the USA or Europe, there are still no approved cosmetic or systemic treatments. Though many substances have been tested for their ability to inhibit adenoviruses, some of them have undergone clinical testing for eye illness, general therapy, or even life-threatening adenovirus infections. Such substances are described in this paper along with their potential for clinical development and some challenges that might arise when trying to determine their therapeutic efficacy[10].

## CONCLUSION

Adenovirus is a double-stranded DNA virus that caused infection in humans. Adenovirus infection mostly affects the respiratory tract. There most of the symptoms are like the normal flu. Most of the infections caused by the adenovirus are cured by treatment. Adenovirus genome replication and the multiplication cycle depend on the host enzyme. Adenovirus is important in biotechnology for the formation of vectors.Adenovirus-based vectors possess multiple benefits over other viral vectors, like their capacity to produce strong transgene-specific T cells and antibodies, a broad spectrum of tissue tropism, a well-characterized genome, ease of genetic modification, including acceptance of large transgene DNA insertions, and associated adjuvant features.

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# CHAPTER 5

# AN OVERVIEW OF THE HERPESVIRIDAE; HERPESVIRUS

Dr. Manish Soni, Assistant Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id- manishsoni@jnujaipur.ac.in

**ABSTRACT:**

A particular viral variety with DNA as its hereditary makeup and the ability to induce herpes outbreaks. Human herpesviruses come in two different varieties. Cold ulcers on the cheeks or sinuses are brought on by type 1 viral infections. Virus type 2 infections result in vaginal ulcers. The 152-kb linear genome of the herpes simplex virus type 1 (HSV-1) is a double-stranded DNA (dsDNA) virus. HSV-1 DNA replication happens in the recipient cell's nucleus. Herpesviruses go through two stages in their life cycle: lytic infection and dormant infection. Active reproduction and the generation of numerous offspring virions take place during lytic infection. A lifelong dormant infection of the host results from the subsequent inhibition of the host immunological reaction. In this chapter, we discussed the Herpesviridae family virus herpesvirus.

**KEYWORDS**

Human Herpesvirus, Herpes Simplex, Simplex Virus, Viral DNA, Vaginal Herpes.

## INTRODUCTION

Herpesviridae is a sizable family of DNA viruses that affect mammals, including people, and can also cause some illnesses. Members of this family are also referred to as herpesviruses. The term "herpes" is derived from the Greek verb "herpein," which means "to creep," and refers to the creeping skin sores that appear during outbreaks of herpes simplex 1, herpes simplex 2, and herpes zoster. Herpesvirus was recognized as a genus in 1971 by the International Committee on the Taxonomy of Viruses (ICTV), which classified the 23 viruses into four categories. There are 115 identified species as of 2020, and all but one of them belong to one of the three subfamilies. Herpesvirus illnesses can be lytic or dormant[1]–[3].

Nine herpesvirus types are known to primarily infect people, at least five of which are extremely common and are responsible for many common diseases. These include herpes simplex 1 and 2 (HSV-1 and HSV-2, also known as HHV-1 and HHV-2), varicella zoster (or HHV-3; the cause of chickenpox and shingles), Epstein-Barr virus (EBV or HHV-4; responsible for several illnesses, including monon (HCMV or HHV-5). At least one of these infections affects more than 90% of adults, and almost all affected people still harbor a dormant version of the virus. Human herpesvirus 6A and 6B (HHV-6A and HHV-6B), human herpesvirus 7, and Kaposi's sarcoma-associated herpesvirus are additional human herpesviruses. (KSHV, also known as HHV-8). There are currently known to be over 130 herpesviruses in total, some of which are found in mammals, birds, fish, reptiles, frogs, and mollusks. Bovine herpesvirus 1 and pseudorabies virus, which both cause pustular vulvovaginitis and Aujeszky's disease in swine, are examples of animal herpesviruses.

A relatively large, monopartite, double-stranded, linear DNA genome encoding 100–200 genes are shared by all members of the Herpesviridae. This genome is encased in an icosahedral protein cage (with T=16 symmetry) called the capsid, which is then wrapped in a protein layer called the tegument that contains viral proteins and mRNAs and a lipid bilayer membrane called the envelope (Figure 1). The word "virion" refers to the entire particle.

DNA, Tegument, Glycoprotein spikes, and Nucleocapsid are the basic elements of a normal HSV virion. The double-stranded DNA genome is encased in an icosahedral nucleocapsid by the four-part Herpes simplex virion. The tegument is present everywhere. Each thread in the tegument is 7-nanometer broad. It is a stratum that is nebulous with some organized areas. Finally, a lipoprotein shell is placed over it. Each virion has spines composed of

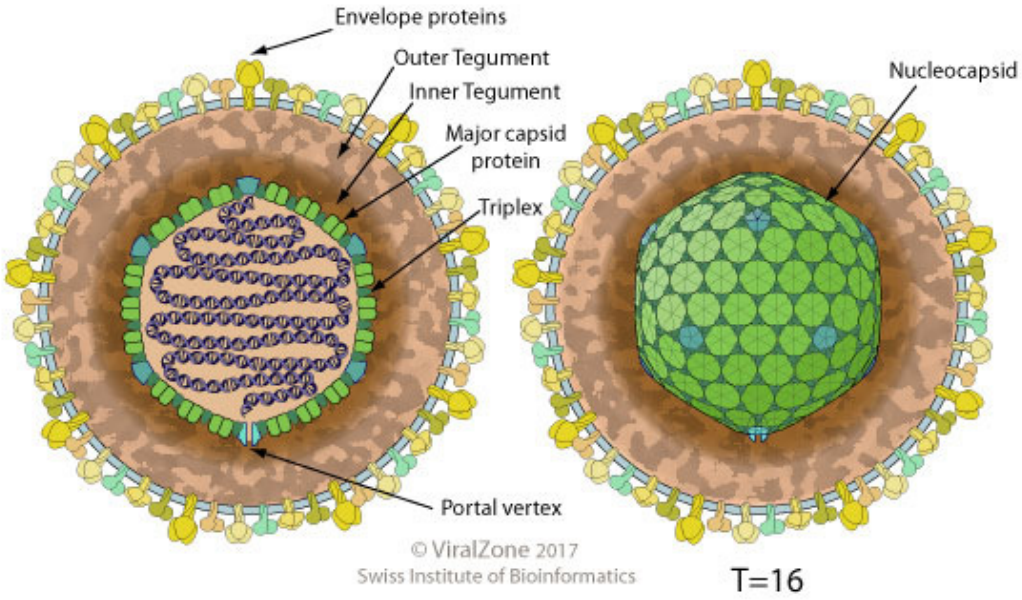


**Figure 1:Herpesvirus structure: Diagram showing the structure of the Herpesvirus (Viral zone).**

glycoprotein sticking out. These increase the virus's girth to 225 nanometers. Without spikes, virions have widths of about 186 nm (Figure.1) The virion's exterior coat contains at least two membrane proteins that are not glycosylated. There are 11 glycoproteins in total. gB, gC, gD, gE, gG, gH, gI, gJ, gK, gL, and gM are among them. There are 26 proteins in the tegument. They perform tasks like mRNA breakdown, early gene transcription initiation, and capsid transfer to the nucleus and other compartments. The nucleocapsid of icosahedral bacteriophages belonging to the group Caudovirales resembles tailed bacteriophages. This capsid has a gateway complex that enables DNA to enter and leave the capsid, as well as 161 capsomers made up of 150 hexagons and 11 pentons.

Herpesvirus genomes have a length between 120 and 230 kbp, a nucleotide that makes up between 31% and 75% G+C, and between 60 and 120 genes. Herpesviruses can sustain a sizable genome with intricate gene networks by using both the host's transcriptional apparatus and DNA repair enzymes because reproduction takes place inside the nucleus. Like the genes of their cellular hosts, herpesvirus genes are not organized in operons and typically have separate promoters. But very few herpesvirus genes are spliced, in contrast to eukaryotic genes. The genes are classified as either dispensable or necessary for cell culture development. Essential genes control transcription and are required for virion construction. The majority of disposable genes work to improve the cellular milieu for viral generation, protect the virus from the host defense system, and encourage cell-to-cell transmission. The vast majority of genes that are considered disposable are necessary for a successful in vivo transmission. They are only unnecessary in the constrained setting of laboratory cell preparations. Long terminal repetitions, both straight and reversed, are present in the DNA of all herpesviruses. There are six terminal repeat configurations, and it is an exciting area of an ongoing study to comprehend how these repetitions contribute to infectious success. All herpesviruses replicate within the nucleus of the affected cell; the viral DNA is converted to

mRNA there. When a virus particle comes into touch with a cell that has a particular set of receptor molecules on the cell surface, the infection begins. The virion is ingested and broken down after viral envelope glycoproteins attach to cell membrane receptors, enabling viral DNA to move into the cell nucleus. Viral DNA duplication and gene transcription take place inside the nucleus. Infected cells express lytic viral genes during clinical infection. Instead, a few virus genes known as latency-associated transcript (LAT) gather in some recipient cells. The virus can remain in the cell (and subsequently the host) forever in this way. Long-term latency is symptomless, in contrast to primary infection, which frequently comes with a self-limited time of clinical disease.

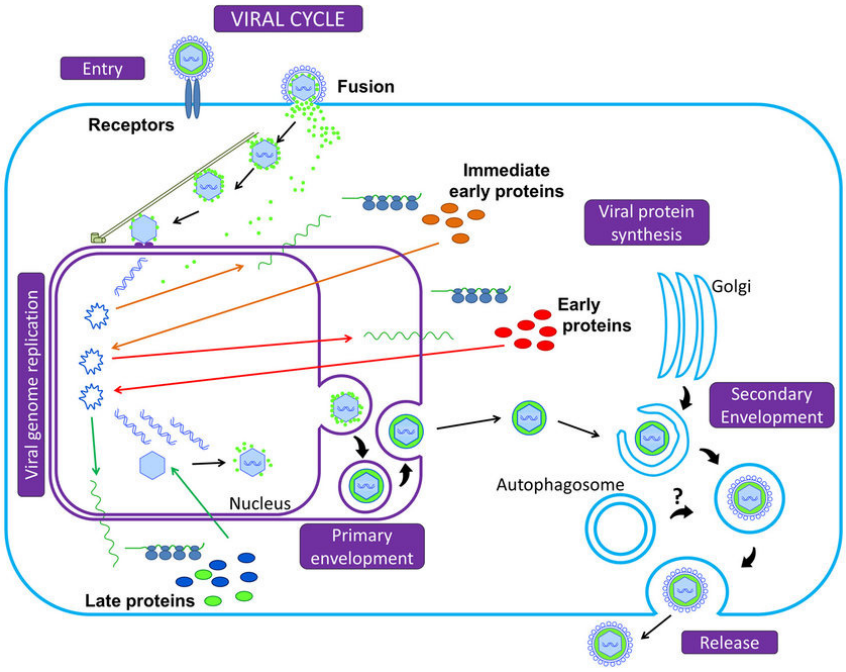


**Figure 2: Life cycle of herpesvirus: Diagram showing the life cycle of the herpesvirus (Research gate).**

The transcription capability of the complete herpes viral genome is governed by chromatin dynamics. The purpose of the cellular immunological reaction when a pathogen penetrates a cell is to safeguard the cell. The virus becomes inactive or latent as a result of the cell enveloping the viral DNA around histones and compacting it into chromatin. The virus DNA is still available if cells fail and the chromatin is loosely packed. The virus fragments have the ability to trigger their genes, reproduce using cellular machinery, and initiate a lytic attack. Several illnesses have been linked to the reactivation of dormant pathogens. (e.g. shingles, pityriasis rosea). After activation, the transcription of viral genes switches from LAT to several lytic genes, which promotes viral reproduction and production. Lytic stimulation frequently results in cell demise. Clinically speaking, lytic activation is frequently followed by the rise of vague symptoms like low-grade temperature, headache, scratchy neck, lethargy, and acne, as well as clinical indications like enlarged or sensitive lymph nodes and immune results like low levels of natural killer cells. Local injuries and systemic stress have been found to cause dormant herpesvirus infection to reactivate in animal models. Viral reactivation can also be brought on by cellular stresses like temporary protein synthesis disruption and oxygen[4]–[6].

Herpesvirus illnesses can be successfully treated using a variety of techniques. The first method is the virion's quick and effective entry into the host cell, which stops the creation of

host proteins and releases viral DNA into the nucleus, where reproduction and virion production begin right away. Herpesviruses can prevent host assaults, which is another tactic they all share. Techniques include preventing the display of epitope peptides on the cell membrane, stopping the processing of mRNA, and preventing the induction of apoptosis (cell death) by virus gene expression. Herpesviruses can conceal their naked, circularized genome in the nucleus of cancer and central nervous system cells and then resume active infection months or even years later. This is an essential third tactic shared by herpes viruses. Although these dormant herpesvirus illnesses are frequently harmless, they can be fatal for infants and people who have compromised immune systems.

All animal species are susceptible to herpes viruses. Except for the very young and the disabled, most illnesses are typically silent. Within the center of diseased cells, they all endure forever. Herpes simplex, varicella-zoster, Epstein-Barr, and CMV are the main human herpetic diseases. Three additional human herpesviruses have been identified in recent years; of these, HHV-8 is related to Kaposi's sarcoma, a sign of AIDS, while HHV-6 and HHV-7 produce only minor cases. The majority of the replication-needed enzymes are encoded by the double-stranded herpesvirus DNA. Antiviral treatment was one of the first to effectively cure herpes simplex infection, and immunizations against the varicella-zoster virus are now being gradually added to youth vaccination programs.

For those with HSV infection, antiviral drugs like acyclovir, famciclovir, and valacyclovir are the most efficient treatments. However, they cannot treat the illness; they can only help to lessen the intensity and recurrence of the symptoms. People who have oral herpes should refrain from sharing items that have come into contact with spit as well as any mouth interaction with others, including oral intercourse. When having signs, those who have vaginal herpes should refrain from engaging in sexual activity. Although HSV-1 and HSV-2 can spread even when no signs are felt or evident, they are most infectious when lesions are present. The most effective method to avoid contracting vaginal herpes and other STIs is for sexually active individuals to consistently and correctly use contraceptives. However, interaction with vaginal or anal regions not protected by the contraceptive can still result in HSV infection. In addition to offering lifetime partial protection against HIV and the human papillomavirus, medical male circumcision can also guard against HSV-2 infection. HIV testing should be made available to people who exhibit vaginal herpes signs. Women who are expecting should let their healthcare practitioners know if they have vaginal herpes signs. Preventing HSV-2 infection is crucial for pregnant women, as this is the time when the risk of newborn herpes is at its highest.

## DISCUSSION

The human herpesvirus 6 variants A (HHV-6A) and B (HHV-6B) are two similar but different viruses. These viruses, which are most closely linked to human herpesvirus 7 and then to human CMV, are members of the Roseolovirus species, a subgroup of betaherpesviruses. Current serologic techniques are unable to distinguish between infection with one variation and infection with the other, and more than 95% of individuals greater than 2 years of age are seropositive for one or both HHV-6 types. Although HHV-6A has not yet been etiologically connected to any human diseases, this connection will likely be made shortly. The prevalent pediatric sickness exanthem subitum (also known as roseola infantum or sixth disease) and associated fever diseases are caused by the HHV-6B virus. These viruses frequently cause sickness in vulnerable people, where they are also frequently active and may contribute to the pathogenesis of Hodgkin's disease and other cancers. Since HHV-6 is a common resident of the brain, patients who are immunosuppressed or who have a main HHV-6 infection may experience seizures and encephalitis, among other neural symptoms.

Patients with multiple sclerosis have changed levels of HHV-6 and its spread in the central nervous system; the meaning of this is still being researched. More than a hundred herpesviruses have been at least partly described in nature, where they affect both animal and non-vertebrate organisms. Only eight of these have been regularly separated from people and are covered in this article. The herpes simplex virus types 1, 2, varicella-zoster virus, CMV, Epstein-Barr virus, human herpesviruses 6, 7, and, most recently, Kaposi's Sarcoma herpesvirus are collectively referred to as the human herpesviruses. The B virus, a rare human infection that can induce potentially fatal illness, is a monkey herpes virus. The groups Herpesviridae, Alloherpesviridae, and Malacoherpesviridae of viruses that affect species ranging from mollusks to humans are all members of the order Herpesvirales. The nucleocapsid, envelope, and tegument are assembled from a variety of viral and cellular proteins found in herpes virions, which are among the most complicated viral particles.

The nucleocapsid is translocated to the cytoplasm by budding at the inner nuclear membrane followed by fusion of the primary envelope with the outer nuclear membrane after autocatalytic assembly of the capsid and packaging of the newly replicated viral genome, a process that occurs in the nucleus and is similar to head formation and genome packaging in the tailed double-stranded DNA bacteriophages. This "nuclear egress" involves significant modification of the nuclear architecture and is mediated by viral and cellular proteins. Tegument components connect with the translocated nucleocapsid, with themselves, and with the ensuing envelope carrying viral membrane proteins in a complicated network of contacts that leads to the creation of a contagious herpes virion during final growth within the cytoplasm. There is a remarkable duplication in the various interactions between the implicated proteins that are still not fully known. As an addendum to an earlier addition, new developments in our knowledge of the molecular mechanisms culminating in herpes virion growth will be given and debated in this overview[7]–[9].

Herpesviruses are among the most thoroughly researched big DNA viruses and are a common, widely dispersed collection of viruses that infect people and other animals. Numerous herpesvirus genome segments have been identified, and their gene contents have been analyzed to provide comprehensive perspectives of both general and lineage-specific functions. Evaluations of genetic connections have also been made possible by the availability of DNA transcripts. Mammal herpesviruses have a strong genealogical tree that exhibits many traits typical of the simultaneous evolution of the virus and host groups over extensive evolutionary timescales. It has also come to light that there are three different herpesvirus subgroups: the first includes viruses that naturally infect mammals, birds, and lizards; the second includes viruses that infect frogs and fish; and the third is made up of a unique invertebrate herpesvirus. Although there is abundant proof of shared ancestry within each of the first two groups, the connections between the three groups are incredibly distant. The strongest support for a shared genesis of the three groups comes from thorough studies of capsid structures. On a more detailed level, the capsid shell protein's structure further hints at a shared ancestor between tailed DNA bacteriophages and herpesviruses.

A dangerous British strain of horse herpesvirus-1, a lung virus that can result in miscarriage and brain illness, had its entire DNA sequence identified. The genome has a size of 150,223 bases, a nucleotide makeup of 56.7% G + C, and 80 open-reading frames that are probably going to generate proteins. The genome is thought to contain 76 unique genes because four open reading frames are replicated in the main inversion repeat, two are likely produced as spliced mRNAs, and one may contain an internal transcriptional regulator. Numerous horse herpesvirus 1 proteins' roles have been determined thanks to comparisons of expected amino

acid sequences with those in the genomes of the two previously sequenced alphaherpesviruses, varicella-zoster virus, and herpes simplex virus type-1[10].

## CONCLUSION

Herpesviruses possess a distinctive four-layered framework: an icosapentahedral shell made of capsomers encloses the center, which contains the big, double-stranded DNA gene. The tegument, a diffuse glycoprotein covering, envelops the capsid, or membrane. It is enclosed in a bilayer of lipid sheath that contains glycoproteins.Numerous species of animals, livestock rodents, piglets, poultry, tortoises, reptiles, fish, as well as some crustaceans, like mussels, have been found to harbor them. They also reproduce in the nuclei of a broad variety of mammalian the hosts, such as eight distinct human strains.

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# CHAPTER 6

# AN OVERVIEW OF THE COMPLEX VIRUS; POXVIRUS

Prof. Kapilesh Jadhav, Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id-kapilesh@jnujaipur.ac.in

**ABSTRACT:**
Pox virus belongs to the *poxvirus* family, and is a DNA virus. Poxviruses are brick-shaped (240 nm by 300 nm) and possess a double-stranded genetic genome (130–260 kb), and related enzymes. Infectious virions that are removed intentionally from sick cells lack a further outer coating that is present in normally produced viruses. In this chapter, we discussed the structure, genome organization, and life cycle of the pox virus.

**KEYWORDS:**

Amino Acids, DNA Virion, Enveloped Virion, Pox Virus, RNA Polymerase.

## INTRODUCTION

A genus of double-stranded DNA viruses is known as *poxviridae*. Natural carriers include vertebrates and arthropods. This family presently consists of 83 species spread across 22 groups and two subfamilies. This class of illnesses includes smallpox. Orthopoxvirus, Parapoxvirus, Yatapoxvirus, and Molluscipoxvirus are the four poxvirus families that can attack people. Smallpox (variola), vaccinia, cowpox, and monkeypox viruses are among the orthopoxviruses. Bovine papular stomatitis virus, orf virus, tanapox virus, and molluscum contagiosum virus are among the parapoxviruses. The most prevalent are vaccinia and molluscum contagiosum, which are both seen on the Indian peninsula, but monkeypox cases are on the rise (seen in west and central African rainforest countries). The herpesvirus varicella-zoster is the culprit behind the identically named condition known as chickenpox, which is not a real poxvirus [1]. Although the adult intracellular version of the Poxviridae virus, which has a different membrane, is also contagious, the viral particles (virions) of this family are typically enclosed (external enveloped virion). They can take on a variety of shapes based on the species, but because the endoplasmic reticulum surrounds them, they typically resemble bricks or have an elliptical shape resembling a rounded brick. The enormous virion is about 200 nm in circumference and 300 nm long. Its genome is contained within a single, linear, double-stranded stretch of DNA. (Figure 1A). In contrast, a normal Poxviridae virion is 1/10 the size of a rhinovirus [2].

The center section of the genome is conserved and includes about 90 genes, according to a phylogenetic study of the genomes of 26 distinct chordopoxviruses. Contrarily, the termini differ between species. The most diverse member of this category is the avipoxvirus. Molluscipoxvirus is the next-most diverse. The genera Capripoxvirus, Leporipoxvirus, Suipoxvirus, and Yatapoxvirus group together; Capripoxvirus and Suipoxvirus are separate from the family Orthopoxvirus and share a shared ancestor. Ectromelia virus, Monkeypox virus, and Cowpox virus variant Brighton Red do not cluster together with any other members of the Orthopoxvirus family. A family of viruses includes camelpox and variola viruses. CPV-GRI-90 and the vaccine virus have the closest genetic ties. The straight double-stranded DNA molecule that makes up the poxvirus genome has reversed terminal repetitions that range in size from 0.1 to 12.4 kb. The genomic makeup of the yoke poxvirus is identical, and it has a 2.3 kb reversed terminal repeat. The reversed terminal repeat area contained no tandem repeats (Figure 1 b).

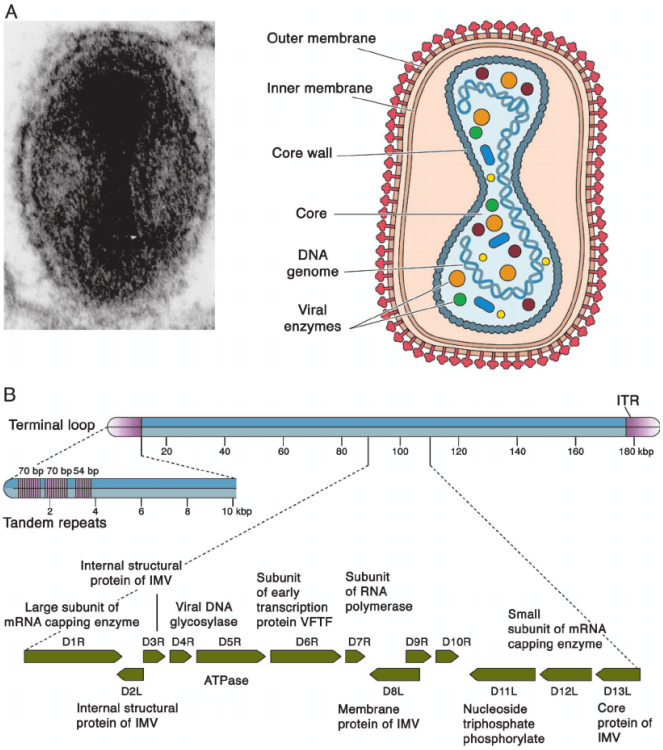


**Figure 1: Poxvirus structure and the genome: Diagramed showing the structure and genome organization of the pox virus (Research gate).**

The GC concentration of the DNA of family members varies greatly. Some Entomopoxviruses, such as Molluscipoxvirus, Orthopoxvirus, Parapoxvirus, and some unclassified Chordopoxvirus, have a relatively high G+C content while others, such as Avipoxvirus, Capripoxvirus, Cervidpoxvirus, Orthopoxvirus, Suipoxvirus, and Yatapoxvirus, have a low G+C content. It is unknown why these variations exist . There are multiple steps involved in poxvirus replication. The poxvirus's receptors are believed to be glycosaminoglycans, and they are found on the exterior of the host cell. The virus penetrates the cell where it uncoils after attaching to the receptor. The pathogen must be uncoated in two steps. The viral particle loses its outer membrane as it penetrates the cell, and then it fuses with the cellular membrane without it discharging its center into the cytoplasm. The genes of the pox virus manifest themselves twice. The early genes are produced before the viral genome is copied and are responsible for encoding non-structural proteins, such as those required for viral genome replication. After the genome has been copied, the late genes are expressed, and they produce the structural proteins that form the viral particle.

The viral particle is put together in five steps of maturation, the last of which results in the exocytosis of a fresh virion with an envelope. The immature virion assembles the A5 protein to produce the intracellular mature virion after the DNA has been copied. The internal virion's brick-shaped membrane and the protein line up. The cell-associated enclosed virion is created by fusing these particles into the cell plasma. This virion then interacts with the microtubules and gets ready to leave the cell as an extracellular encased virion. The complicated process of viral particle assembly, which takes place in the cell's cytoplasm, is presently being studied to better comprehend each step. Considering how big and complicated this virus is, replication happens fairly quickly, requiring only about 12 hours before the host cell dies from the discharge of viruses. Poxvirus reproduction takes place in the cytoplasm, which is uncommon for a virus with a double-stranded DNA genome but

common for other large DNA viruses. A DNA-dependent RNA polymerase that the adenovirus encodes for genome transcription enables cytoplasmic reproduction. The DNA-dependent RNA polymerase of the recipient cell is required for transcription by the majority of double-stranded DNA viruses.

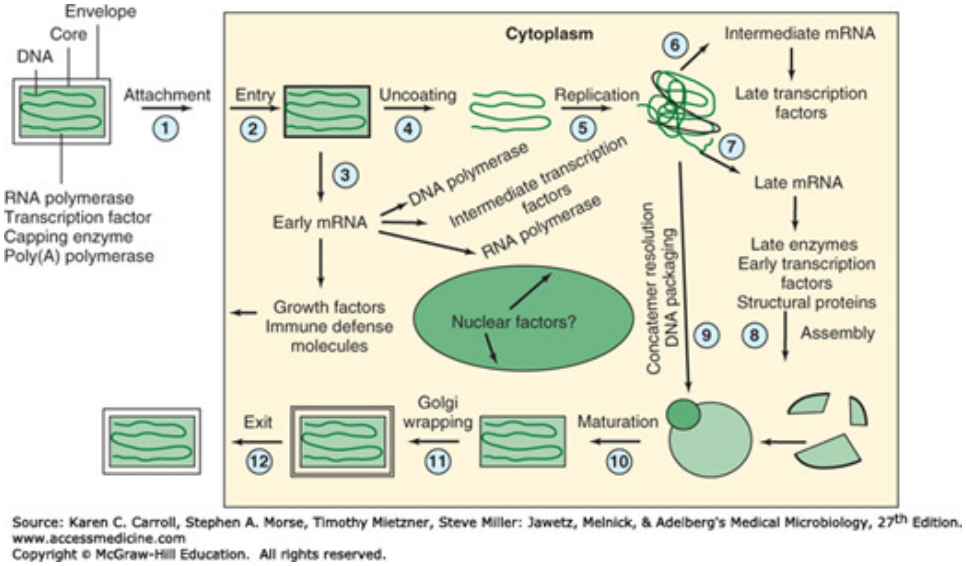


**Figure 2: Life cycle of the pox virus: Diagramed showing the life cycle of the pox virus (Basic medical key).**

Due to the presence of these host polymerases in the nucleus, a portion of the transmission cycle for the majority of double-stranded DNA viruses occurs there. Based on studies done in cell culture, a few genes identified in the poxvirus genome are not crucial for reproduction. They are necessary for the host's antibody production to be modulated, though. They are referred to as pathogenicity genes for this reason. Few of these genes are known as host range genes because they affect viral replication primarily in a subset of cell lines that originated from different organs or host species. More research has been done on the orthodox and leporine viral families to forecast since many poxviruses encode unique sets of host range genes. Twelve distinct poxvirus genes have been found, according to the most recent scientific classification; K3L, E3L, and K1L are among the groups with only one gene; other groups, such as separin, the C7L family, and the TNFRII family, have numerous members, which is expected as a result of actions related to lineage replication[3]–[5].

For studies that were generally linked to the operation of different cellular targets, including cellular kinases and phosphatases, apoptosis, and several antiviral pathways, laboratory animals were used to functionally characterize the factors by removing genes. These genes are necessary for infection on cell lines; without them, the illness cannot progress. Other research using experimental animals showed that viral pathogenicity is affected by an unidentified component, but the illness was still present in the animals. When referring to the cells affected by this virus but not the primary target mammals, these genes were formerly referred to as host range genes. The number of host species for various poxviruses and the variety of host range variables have been linked in some experimental studies, but this relationship is still debatable. Researchers needed to identify the natural hosts for the poxviruses that were formally allocated to viral species and acknowledged by the International Committee on Taxonomy of Viruses to evaluate these intriguing issues. (ICTV). Researchers conducted a thorough scan for various host range genes based on the data currently accessible.

## DISCUSSION

The most well-known member of the extremely effective family of pathogens known as variola viruses, which cause smallpox, is the variola virus. Poxviruses stand out among animal viruses in several ways. First, because the virus replicates in the cytosol, it encodes many enzymes needed to control the macromolecular precursor pool or to carry out biosynthesis processes. Second, the development of these viruses is extremely intricate and entails the de novo creation of inclusion bodies and membranes that are unique to the viruses. The genomes of these viruses also contain a large number of proteins that engage with host processes on both a cellular and systemic level, which is perhaps the most unexpected discovery of all. For instance, vaccinia virus infections of cultured cells, rabbits, and rodents are accompanied by the activity of a viral analog of epidermal growth factor. One viral protein, a 38-kDa protein encoded by the cowpox virus, is believed to obstruct a host route for producing a chemotactic substance.

At least five virus proteins with homology to the serine protease inhibitor family have been discovered. Finally, a protein that shares homology with complement-building blocks prevents the conventional complement pathway from being activated. Poxviruses can infect a host in a variety of ways, including mechanically through the skin (as in the case of molluscum contagiosum infections in humans), through the respiratory system (as in the case of variola virus infections in humans), or by oral methods. (e.g., ectromelia virus infection of the mouse). Poxvirus illnesses are typically acute, and there isn't much proof that they can be dormant, enduring, or chronic. They may be general or limited. Ectromelia viral infection in experimental mice can be systemic but not noticeable, with no mortality and minimal morbidity, or it can be extremely deadly, with death occurring within 10 days. On the other hand, the molluscum contagiosum virus does not disseminate systemically from the site of infection and only replicates in the stratum spinosum of the human epidermis, with little to no participation of the dermis. The host's reaction to infection is multifaceted and continuous. Interferons, the alternative complement activation pathway, inflammation cells, and natural killer cells may all help to delay the spread of the infection in the early stages of the infection process.

The most crucial component in the recovery from infection appears to be the cell-mediated reaction involving learned cytotoxic T cells and delayed-type hypersensitivity components. Specific antiviral antibodies and antibody-dependent cell-mediated cytotoxicity have not yet been shown to play a major role in the recovery from initial infection, but they are believed to be crucial in avoiding reinfection . Even though bug poxviruses don't seem to affect vertebrates, poxviruses are common in a variety of vertebrate and animal hosts. The majority of poxvirus cases are now found in other primates, mammals, and avian species because smallpox has been completely eradicated from the human community. Immunological techniques, protein analysis, nucleic acid hybridization, and restriction enzyme analysis have all been used to classify orthopoxvirus species. The vaccinia virus is covered in this chapter along with some key distinctions from other poxviruses. The first animal virus that was adequately purified for in-depth analysis was the vaccine virus. In between the palisade layer of the core and the exterior covering of the virion, the two lateral bodies of the vaccinia virus particles are ellipsoidal structures that resemble rugby balls. Although an entomopoxvirus has been shown to have a solitary lateral body, these structures have been reported to be present in a variety of poxviruses even though their functional importance is unknown. The Poxviridae family of viruses includes some of the biggest and most intricate viruses that attack mammals. A common trait of chordopoxviruses is their ability to colonize, reproduce, and cause pathology in the epidermis and, to a lesser degree, in some mucosae during the

course of infection of the host. A frequent way for the poxvirus to spread is through contact with contaminated material on broken or lacerated flesh.

The most well-known poxviruses are those belonging to the family Orthopoxvirus. Originally, cowpox was defined as a condition marked by teat sores in nursing cows brought on by the cowpox virus. Myxoma virus, the type member of the genus Leporipoxvirus, is the source of the serious illness myxomatosis in farmed rabbits. Worldwide, agricultural and untamed animals are infected by viruses of the genus Parapoxvirus, which also causes minor zoonotic illnesses in people. A severe, slow-moving illness that affects chickens and turkeys globally is called fowlpox. Cotia virus (COTV) SPAn232 was identified in 1961 from sentry mice at Cotia field station, São Paulo, Brazil. Findings from attempts to place COTV within a known family of the Poxviridae have produced conflicting results. A separate study classified COTV SPAn232 as a strain of the vaccinia virus, whereas studies by various researchers indicated some similarities to the myxoma virus and the swinepox virus.

We have carried out a separate biological and molecular analysis of COTV due to the absence of agreement. Virus DNA replication and a distinctive early/late pattern of viral protein synthesis were present along with virus growth curves as they achieved their highest outputs between 24 and 48 hours after starting. Intriguingly, COTV did not produce viral lesions until 8 days after infection and did not cause measurable cytopathic effects in BSC-40 cells until 4 days postinfection. Using a mix of the 454 and Illumina next-generation DNA sequencing methods, we were able to identify the full genomic genome of COTV. The 185,139 bp unique continuous sequence contained 185 genes, including the 90 genes shared by all chordopoxviruses. The COTV genome contains an intriguing panel of open reading frames (ORFs) involved in the escape of host defense, including two new genes that each encode a duplicate copy of a protein that is similar to the C-C chemokine. According to phylogenetic research, Cervidpoxvirus, Capripoxvirus, Suipoxvirus, Leporipoxvirus, and Yatapoxvirus had the greatest amino acid identity values. The fact that COTV formed a separate offshoot within this clade, however, obviously disqualified it from being categorized as an orthopoxvirus. Therefore, based on our findings, COTV might be a novel genus of poxvirus. Sharka disease, which is brought on by the PPV or Plum pox virus, was first identified in Bulgaria at the turn of the 20th century.

Since that time, the illness has gradually expanded throughout Europe and, more recently, to Asia, Africa, North America, and South America. Prunus has a limited number of naturally occurring PPV resistance genes, which has prompted research into biotech methods for creating resistance through genetic engineering. (GE). The "HoneySweet" apple is a well-known illustration of the value of this strategy. In this instance, PPV protection is founded on RNA interference (RNAi), and it has been demonstrated that resistance is extremely effective, stable, long-lasting, and heritable as a dominant trait. For more than 20 years, 'HoneySweet' has undergone extensive testing and risk analysis in the lab, garden, and field, proving both the technology's efficacy and safety. It is now legal to grow "HoneySweet" in the USA. by the relevant governing organizations. The creation and governmental approval of "HoneySweet" show how RNAi technology can support the viability of stone fruit cultivation in PPV-affected areas. Despite the fact that it has been nearly 100 years since the discovery of sharka, we can now successfully defend stone fruit species against this disease by using GE. The Poxviridae family has individuals all over the globe, and they can spread infectious illnesses. Although the genome sequences of representative isolates from all genera are openly accessible, research on the standards for genome-based categorization within the Poxviridae family have only occasionally been published. 60 Poxviridae genes were re-

annotated in our research using Prokka. Synteny and resemblance of whole genomic amino acid sequences were displayed using BLAST filtering and MCScanX[6]–[8].

The Chordopoxvirinae and Entomopoxvirinae subfamilies can be split into five and two groups, respectively, in accordance with the analysis pattern. This is compatible with the phylogenetic tree built using whole genomic amino acid sequences and Poxvirus core genes. By using replacement saturation analysis and phylogenetic tree proof, four genes (Early transcription factor, DNA-directed RNA polymerase, RNA polymerase-associated transcription-specificity factor, and DNA-dependent RNA polymerase) were chosen from the Poxvirus core genes. Concatenated sequences of the four chosen genes and single-gene phylogenetic trees both supported the categorization of divisions made by the genome-based phylogenetic trees. The use of the four qualified genes will help make phylogenic recognition of recently found Poxviridae isolates more easy and more accurate[9].

A novel approach based on the similarity of whole genomic amino acid sequences was suggested for Poxviridae taxon demarcation. The chemokine-binding protein (CBP), which is encoded by the parapoxvirus ORFV, reduces the host's immune reaction at the infection location by preventing the chemokine's induction of immune cell recruitment.

As part of continuing structure-function research on this protein, ORFV CBP was crystallized to provide insight into the structural basis of CBP-chemokine binding. Using the sitting-drop vapor-diffusion method and ammonium citrate as a precipitant, ORFV CBP crystals were produced. Small-molecule compounds were added to the crystallization mother liquid, considerably enhancing the crystal quality. The unit-cell characteristics of the ORFV CBP crystals were a = b = 75.62, c = 282.49, = 90, = 90, = 120° and they belonged to the hexagonal space group P6122 or its enantiomorph P6522 [10]. They also diffracted X-rays with a resolution of 2.50[9], [10].

## CONCLUSION

Poxviruses have big double-stranded DNA genomes and are structured like bricks or ovals. Large, enclosed DNA viruses called poxviruses attack both mammalian and invertebrate organisms and only reproduce in the cytoplasm.

Poxviruses are present all over the globe and can infect both people and a wide range of other animals. Poxvirus infections usually result in the development of infections, cutaneous nodules, which or generalized rash.Human system response to the pox virus by the cytoplasmic DNA sensor engages the adaptor throughout poxvirus disease, and the adapter consequently stimulates several effectors downstream to create interferons, cytokines, and interleukins for an immune reaction against the virus that causes infection.

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# CHAPTER 7

# AN OVERVIEW OF THE PARVOVIRIDAE; PARVOVIRUS

Dr. Sunita Rao, Assistant Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id-sunita.rao@jnujaipur.ac.in

**ABSTRACT:**

The parvoviruses are a family of very tiny DNA viruses which infect a wide variety of animal species. The virus's little quantity of DNA does not include enough genetic material to control how it replicates in the human host. In this chapter, we discussed the parvovirus classification, genome, structure, and the steps involved in their life cycle.

**KEYWORDS:**Canine Parvovirus, Human Parvoviridae, Host Cell, Family Parvoviridae, Parvovirus b19.

## INTRODUCTION

Animal viruses that make up the family Parvoviridae are known as parvoviruses. Their linear, single-stranded DNA (ssDNA) genomes usually contain two genes, one for the protein that makes up the virus capsid (NS1) and the other for a reproduction initiator protein. Telomeres at each end of the coding region of the genome create hairpin rings that are crucial for replication. The parvovirus DNA is contained in an icosahedral capsid with a rough surface, which is tiny compared to most viruses at 23–28 nanometers in diameter.

Endocytosis is the process by which parvoviruses penetrate a recipient cell. They then move to the nucleus where they wait for the cell to reach the replication stage. The genome is then exposed, and the coding region is duplicated. Following transcription and translation, viral messenger RNA (mRNA) causes NS1 to start reproduction. Rolling hairpin replication, which results in a molecule with many copies of the genome, is a process in which the hairpins continually unfold, are copied, and refold to shift the orientation of replication and advance back and forth along the genome. This concatemer is removed, and the progeny ssDNA genomes are packed into capsids. Mature virions exit the cell through disintegration or exocytosis[1]–[3].

Because parvoviruses encode a replication initiator protein that is linked to NS1 and has a comparable reproduction process, it is thought that they are derived from ssDNA viruses with circular genomes that create a loop. Bidnaviruses are a different family of viruses that resemble parvoviruses in origin. Three subfamilies, 26 names, and 126 species are known to exist within the family. The only family in the order Piccovirales, the only group in the class Quintoviricetes, is the Parvoviridae. The phylum Cossaviricota, which also contains papillomaviruses, polyomaviruses, and bidnaviruses, is home to this family.

Parvoviruses are responsible for a wide range of mammal illnesses. Notably, the canine parvovirus and the feline parvovirus, which affect cats and canines, respectively, both cause serious illness. The porcine parvovirus is a significant contributor to sterility in hogs. Human parvoviruses are less harmful; the two most noteworthy ones are human bocavirus 1 and parvovirus B19, the latter of which frequently produces acute respiratory illnesses, particularly in young children, and causes the fifth disease. Recombinant adeno-associated viruses (AAV) are now widely used in medicine as a carrier to carry genes into the cell nucleus during gene therapyThe first animal parvoviruses were found in the 1960s, including the mouse minute virus, which is still used today to research parvovirus propagation. During

this time, numerous AAVs were also found, and subsequent study on them has shown that they are useful as a type of medicine. .. and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and, and. In 1971, parvoviruses were first placed in the genus Parvovirus, but in 1975 they were given family classification. They get their name from the Latin term parvum, which means "small" or "tiny," and alludes to the virus's minuscule virions.

The subgroup Parvovirinae, which includes viruses of vertebrates, and the subfamily Densovirinae, which contains viruses of insects and other invertebrates, make up the family Parvoviridae. (that will not be discussed further). The subfamily Parvovirinae presently has eight recognized genera. Parvoviruses are classified into families based on their genetic characteristics rather than their host species of origin, which can lead to taxonomic confusion. Additionally, due to recent nomenclature changes that make it challenging to distinguish between historical names of viral species, this chapter will refer to specific parvoviruses that cause particular animal illnesses using their well-established colloquial names. The gray fox adenovirus and the Aleutian mink disease virus are both members of the family amdo parvovirus (earlier known as adenovirus). The intestinal parvoviruses of chickens and turkeys are now included in the genus Aveparvovirus, while some replication-competent parvoviruses of birds (such as goose and duck parvoviruses) are included in the genus Dependoparvovirus along with adeno-associated viruses of mammals that are dependent on the presence of a helper virus for their efficient replication.

The genus Bocaparvovirus includes several parvoviruses from marine animals, primates, ungulates, and canines (including canine minute virus, canine parvovirus 1, and canine bocavirus). (previously Bocavirus). There are at least two more ungulate parvoviruses in the family Copiparvovirus. The human parvovirus B19 and associated viruses of nonhuman apes and ungulates are all members of the family Erythroparvovirus (previously known as Erythrovirus). The feline panleukopenia virus, canine parvovirus, mink enteritis virus, raccoon parvovirus, parvoviruses of rats and lagomorphs, and parvoviruses of ungulates and primates are all members of the family proto parvovirus (previously known as parvovirus). Tetraparvovirus is the name given to a group of recently identified viruses, including human parvovirus-4 relatives and parvoviruses from ungulates and bats. Consequently, distinct parvoviruses from canines, birds, humans and nonhuman primates, rats, bovine cattle, as well as many exotic species, are categorized into various genera.

The parvovirus genome is a straight, monopartite, 5-kilo long ss DNA a (Figure .1). Palindromic sequences can coil back on themselves to create "hairpin" structures that are stabilized by self-hydrogen bonding and are found in the genome's 3' and 5' ends as well. For the replication of the DNA, these "hairpin" formations are essential.

Parvovirus reproduction and construction take place in the nucleus and are reliant on the operations of the host cell. The method of replication of the genome is specific to the virus family. To begin the production of plus-sense DNA, which produces double-stranded DNA, the hairpin structure at the 3' end is used as a self-primer. Then, more minus-sense strands from the ds DNA are translated using the hairpin structure once more as a template. According to the current theory, the developing strand repeats back on itself to create a tetrameric form, which is then split into two plus-sense and two minus-sense strands of DNA.

The three-dimensional structures of full10 and empty11 particles of CPV and of empty particles of feline panleukopenia virus (FPV)12 have been resolved to atomic precision using X-ray crystallography.

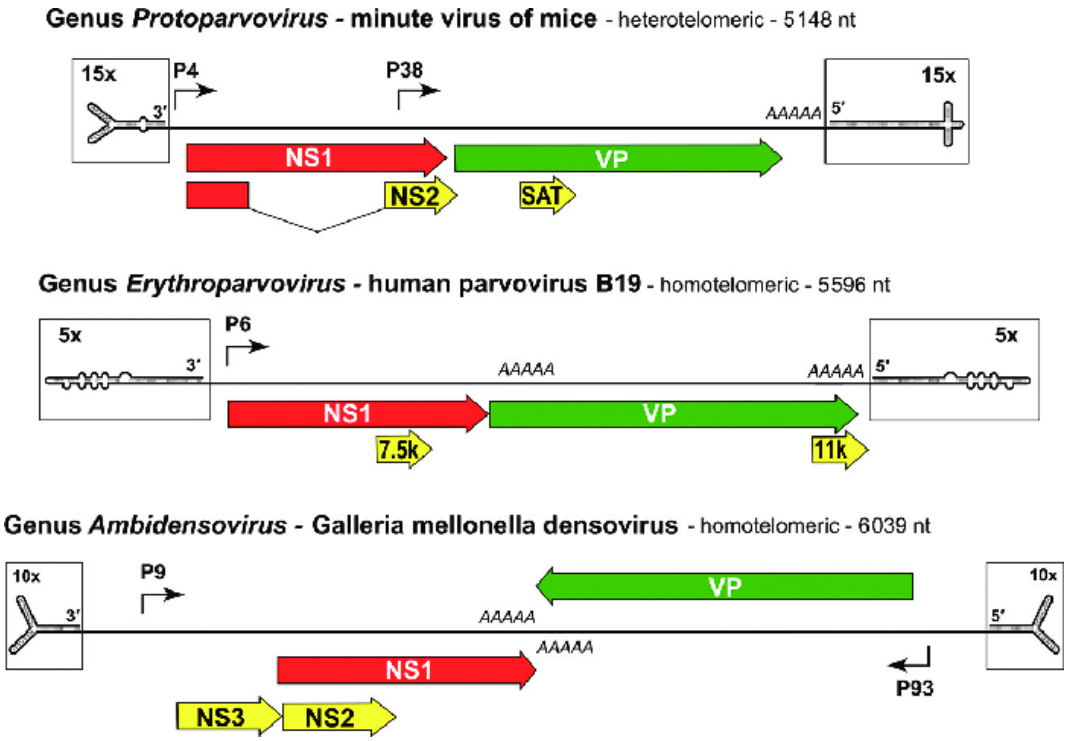


**Figure 1: Genome of the parvovirus: Diagram showing the genome of the parvovirus (Research gate).**

The capsid proteins VP1 and VP2 of CPV and FPV only vary by 8 to 10 amino acids and are more than 98% identical at the nucleotide level . The biological divergence between the two viruses is correlated with structural variations between CPV and FPV, which are primarily found on the capsid surface.12 Even though VP1, VP2, and VP3 are mixed within a virion, all 60 components share a similar structure that is organized with T = 1 icosahedral symmetry.

The majority of other known virus capsid structures share the eight-stranded anti-parallel "barrel motif," which is present in each component (Figures 1 and 2).13 Only about one-third of each polypeptide's amino acid composition is contained in this â-barrel structure, which is mostly below the capsid surface. Large insertions between the â-strands make up the other two-thirds of the CPV and FPV VP2 structure. Loop 1 is formed by 36 residues between strands B and C, Loop 2 by 74 residues between strands E and F, and Loops 3 and 4 by 223 residues between strands G and H. (Figures 2). The massive insertion between the âG and âH strands, which makes up the majority of the loops that make up the capsid surface, is what causes the 22-long spikes that surround the three-fold axis[4]–[6].

A cylindrical structure revolving around the five-fold axis is created by the insertion between the âD and âE strands, which creates an anti-parallel â-ribbon. This structure is also shared by four other polypeptides linked to five folds (Figure 2). Each of the five-fold axes has a 15-degree canyon-like depression circling it, and the two-fold axes have a dimple-like depression (Figure 2). By comparison with picornaviruses, these depressions could serve as receptor attachment sites. In the molecular structures of VP2 in CPV and FPV, the first 36 amino-terminal acids are disorganized. However, in roughly one out of every five subunits, the amino termini are externalized because residues 28 to 37 of VP2, which are conserved glycines among parvoviruses8, are located along the five-fold axial channel. Parvoviruses infiltrate cells through endocytosis and attach to the host cell using a range of cellular receptors.

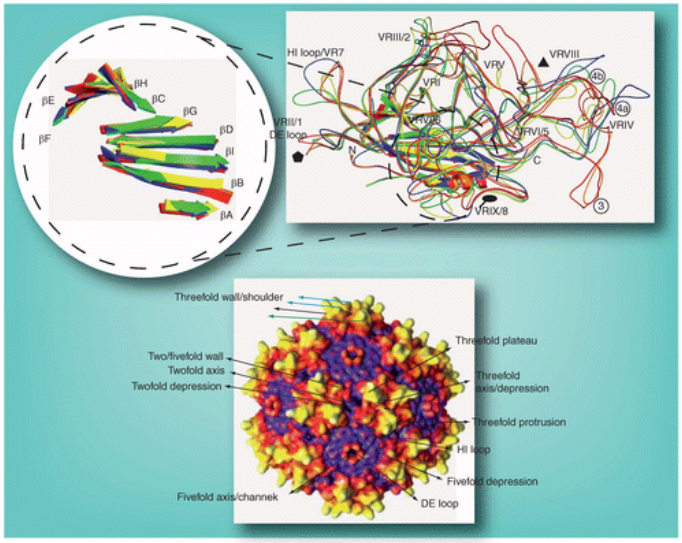


**Figure 2: Structure of the parvovirus: Diagram showing the structure of the parvovirus (Future medicine).**

Many parvoviruses experience a conformational shift in endosomes that exposes the phospholipase A2 (PLA2) domain on the VP1 N-termini, enabling the virion to cross lipid bilayer membranes. Virion intracellular trafficking differs, but eventually, virions reach the nucleus, where the DNA is released from the capsid. The genome is expelled from the capsid in a 3′-to-5′ orientation from one of the openings in the capsid, leaving the 5′-end of the DNA attached to the capsid, according to investigations of the minute virus of mice (MVM). Parvoviruses lack the capacity to drive cells into their DNA replication stage, termed S-phase, so they must wait in the nucleus until the host cell reaches S-phase on its own. This makes quickly dividing cell groups, like fetal cells, an ideal habitat for parvoviruses. Since coinfection modifies the cellular environment to facilitate reproduction, adeno-associated viruses (AAV) are reliant on helper viruses, which may be an adenovirus or a herpes virus. AAV's genome is incorporated into the recipient cell's genome up until coinfection happens in the absence of coinfection.

When infected cells reach the S phase, they are compelled to create virus DNA and are unable to exit. As the infection continues, parvoviruses create replication sites in the nucleus that get bigger and bigger(Figure. 3). A host DNA polymerase uses the 3′-end of the 3′ hairpin as a primer to create a complimentary DNA strand for the coding region of the genome, which is linked to the 5′-end of the 5′ hairpin, once a cell reaches S-phase and the genome is uncoated. The DNA polymerase then extracts the NS1-encoding messenger RNA (mRNA) from the genome, caps and polyadenylates it, and then the host ribosomes translate it to produce NS1 (Figure.3). Alternative splicing, inadequate translation start, or leaky scanning may be used to translate various gene products if proteins are stored in numerous co-linear frames. Rolling hairpin replication, a linear, strand displacement type of DNA replication that is started by NS1, is the method used by parvoviruses to reproduce their genome. Once NS1 attaches to and nicks a replication origin site in the duplex DNA strand at the end of one hairpin, replication can start. The 3′-end of the nicked strand is released during nicking as a free hydroxyl (-OH) to kick-start DNA synthesis while NS1 is still affixed to the 5′-end. The nearby hairpin expands into a linear, expanded shape as a result of the nick. The elongated telomere is copied by DNA polymerase using a replication fork created at the 3′-OH by the helicase activity of NS1. The replication fork is then repositioned to swap

templates to the other strand and proceed in the opposite direction toward the other end of the genome as the two telomere strands refold back into their original shapes.

The homo-telomeric parvoviruses are those that have comparable or identical termini, while the hetero-telomeric parvoviruses have distinct termini. The hairpin sequences of homo-telomeric parvoviruses, such as AAV and B19, are typically enclosed within larger (inverted) terminal repetitions that reproduce both ends of their genomes through the aforementioned process known as terminal resolution. To ensure that the telomere is replicated in the proper orientation, hetero-telomeric viruses like the minute virus of mice (MVM) reproduce one end by terminal resolution and the other end via an asymmetric mechanism called junction resolution. The duplex extended-form telomeres refold into a cruciform structure during asymmetric junction resolve. The lower arm of the cruciform unfolds into its expanded linear form after NS1 nicks a replication origin site on the lower strand of the right arm. The extended lower arm is moved down as a replication fork formed at the nick location copies the sequence of the lower arm.

The reproduction fork is then moved to move back toward the other end by folding the two strands of the lower arm, dislodging the top strand in the process. A concatemer comprising numerous clones of the genome is created by rolling hairpin replication in a back-and-forth, end-to-end sequence. Through the periodic nicking of this molecule by NS1, individual segments of the genome are removed from the concatemer using a mix of junction resolution and terminal resolution. Excised genes can be packed into progeny capsids or repurposed for additional reproduction cycles. The accumulation of capsid proteins in the nucleus that forms into these empty capsids is caused by the translation of mRNA-carrying VP proteins[7], [8].

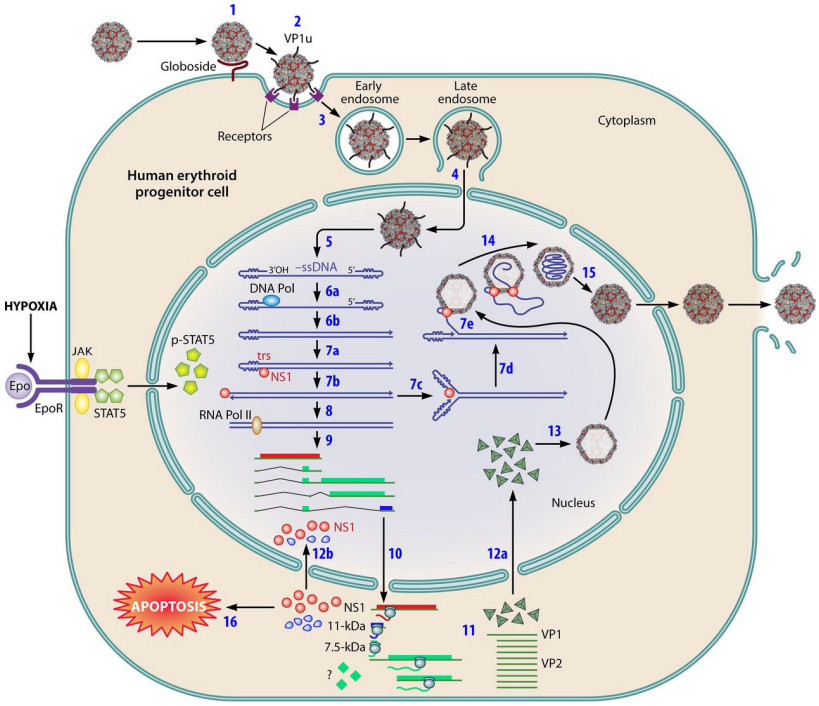


**Figure 3: Life cycle of the parvovirus: Diagramed showing the life cycle of the parvovirus (ASM journals).**

Through a portal, possibly the one opposite the portal used to eject the genome, genomes are enclosed at one of the vertices of the capsid. After the virions are finished being built, the nucleus can send them to the cell's surface before the nucleus breaks down. Later on in the

infection, the recipient cell milieu may also be disturbed. This causes death or apoptosis, which causes the cell to lyse and discharge virions into the surrounding tissue.

## DISCUSSION

The fifth illness in children is brought on by parvovirus B19, which can also induce transient arthropathy in adults. This page discusses the characteristics of the virus, how the host reacts to it, and how to avoid and cure infection [6]. The only Parvoviridae species known to be pathogenic in people, Parvovirus B19 (B19), was identified in 1974. Despite the virus' failure to grow in cell cultures, much has been discovered about its pathophysiology, including the discovery of the cellular receptor (P antigen) and the immune system's ability to regulate the virus. B19 is common, and depending on the host's hematologic and immune health, different infectious symptoms will appear. B19 is the cause of acute symmetric poly arthropathy and erythema infectiosum in immune-competent people, especially in adults. B19's affinity for erythroid precursor cells makes it so that infection in people with an underlying hemolytic disease results in a brief aplastic crisis.

Pure red cell aplasia and prolonged anemia are the only signs of continuous B19 infection in the immune-compromised host. The baby's underdeveloped immune system may also leave it vulnerable to infection, which could result in fetal mortality in utero, hydrops fetalis, or the onset of congenital anemia. Although causation is frequently challenging to deduce given the common character of the clinical symptoms, B19 has also been proposed as the causative agent in a variety of clinical syndromes. In order to diagnose an illness, particular antibodies must be found using an enzyme-linked immunosorbent test, and viral DNA must be found using a dot blot hybridization or PCR. Immunoglobulin therapy for a chronic illness lowers the viral burden and significantly improves anemia. Phase I vaccine studies have produced encouraging findings.

The late 1970s saw the emergence of the novel canine disease canine parvovirus type-2. Review of the virus's genesis, development, and dissemination. The contemporary illness pattern, as well as modern ideas for clinical treatment, prevention, and detection, are discussed. The single-stranded linear genome of the Parvoviridae family members, which has a size of about 5 kilobases, makes them some of the tiniest DNA viruses. The family currently consists of three families, two of which contain viruses that affect mammals, and a third that affect insects. The focus of this study is on viruses that infect vertebrates, with a particular focus on new developments in our understanding of the molecular biology of viral replication. The dependenceoviruses (adeno-associated viruses [AAV]) are thought to be defective because historically the vertebrate viruses have been differentiated by the presence or lack of a necessity for coinfection with a helper virus before fruitful infection can occur.

Recent research indicates that the two kinds of vertebrate viruses share a substantial amount of structural and genetic organizational resemblance as well as similarities in the molecular biology of fruitful reproduction. The host cell's metabolic state, which makes it receptive, is different. Healthy dividing cells are favorable for fruitful parvovirus reproduction, and these cells result in dependovirus dormant infection. A cell needs to have been subjected to toxic circumstances that trigger a dormant AAV genome for it to become permissive for fruitful AAV replication. These disorders may be brought on by exposure to some toxins or an infection with the helper virus. This article reviews the molecular biology of reproduction with a focus on the host's function and the effects of virus infection on the host[9], [10].

In 1978, the canine parvovirus was first identified. Since its emergence, isolates have been gathered, and analysis of those isolates has shown that viruses circulating after 1980 were antigenically distinct from early isolates. Monoclonal antibodies differentiated the two strains

distinctly, with some of them being particular to the ancient or new viruses. The post-1980 viruses were similar to previous isolates, according to a restriction enzyme study of viral DNA, but the new strain had some different restriction sites. These findings imply that a variant virus that supplanted the initial strain in 1980 is the source of the canine parvoviruses that infect canines in the seven regions of the United States that were sampled.

## CONCLUSION

Icosahedral, non-enveloped parvovirus particle range in size from 18 to 26 nm. Its linear single-stranded DNA genomic of parvoviruses is around 5 kb long and has short, incomplete terminal palindromes that fold back upon themselves to produce double hairpin telomere length.

About equal amounts of plus and minus DNA strands are packed into distinct virions. Two viral proteins are present. Inflammatory bowel sickness in pups is frequently brought on by the extremely infectious canine parvovirus (CPV), a viral infection that affects dogs. The condition primarily affects puppies between the ages of six and twenty weeks, while it can occasionally afflict older animals as well.Self-care at home is typically adequate for treating a simple parvovirus illness. Serious anemia may necessitate medical hospitalization and blood products for the patient.

Antibody titers infusions can provide antibodies for people who have impaired immune systems to treat the illness.

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# CHAPTER 8

# A NON-ENVELOPED RNA VIRUS; REOVIRUS

Dr. Manish Soni, Assistant Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id- manishsoni@jnujaipur.ac.in

**ABSTRACT:**

Reovirus is an extremely stable, non-enveloped double-stranded RNA virus that can cause either a moderate case of gastroenteritis or an asymptomatic, nonpathogenic infection in people.Reovirus, also ssRNAs additionally serve as substrates for the creation of negative-sense ssRNA, which is necessary for the production of nascent chromosomal dsRNA, inside the replicas particles .In this chapter we detail study the phylogenetic relationship, structure, genome and the life cycle of the reovirus.

**KEYWORDS:**Amino Acid, Genome Size, Family Reoviridae, RNA Virus, S1 Genome.

## INTRODUCTION

A genus of double-stranded RNA viruses is known as the Reoviridae. Vertebrate, invertebrate, plant, protist, and fungus are just a few of the vast variety of hosts that member viruses can infect. They contain their segmented DNA within multilayered capsids instead of lipid casings. These big complex viruses (diameter 60-100 nm) were able to have their three-dimensional structures determined thanks to the absence of a lipid envelope, showing a structural similarity to the cystovirus family of bacteriophages as well as a possible evolutionary connection. This family presently contains 97 species, distributed among 15 taxa in two subfamilies. Reoviruses can harm the breathing passages and digestive system (such as rotaviruses). Respiratory enteric orphan viruses are referred to by the prefix "reo-" in their nomenclature. The word "orphan virus" describes a group of viruses that have been found to exist independently of any recognized disease.

The initial name is still in use even though viruses in the family Reoviridae have been linked to several illnesses more recently. Humans frequently contract reovirus illnesses, but the majority of these are minor or subclinical. However, rotaviruses can produce very bad diarrhea and intestinal discomfort in children, and orthoreoviruses have been linked to coeliac disease in laboratory experiments in rodents. Feces are a good place to start looking for the virus, but it can also be found in blood, urine,cerebrospinal fluid, pharynx or nasal fluids, and urine. Reoviruses are frequently found in clinical specimens, but it is still unclear how they are used to cure or prevent human illness. Oryzaviruses and phytoreoviruses are two examples of viruses in this family that affect vegetation. Most plant-infecting reoviruses are spread from one plant to another by bug carriers. In general, the viruses cause illness in the plant but little to no damage, if any, to the infected bug. The viruses replicate in both the plant and the insect[1]–[3].

Icosahedral capsids are stacked in reoviruses. The Rotavirus family contains viruses with triple-layered particles. (Figure.1). A T=1 capsid, the thinnest and deepest layer, is created from 60 duplicates of the viral protein (VP) 2. VP6 at a molecular weight of 45 kDa forms the central portion of the T=13 capsid. Two extra structural proteins, VP4 and VP7, are combined to form the outermost layer of the rotavirus capsid. Members of the Reovirus family have two capsid layers, with an outer T=13 shell encasing an interior T=1 core.

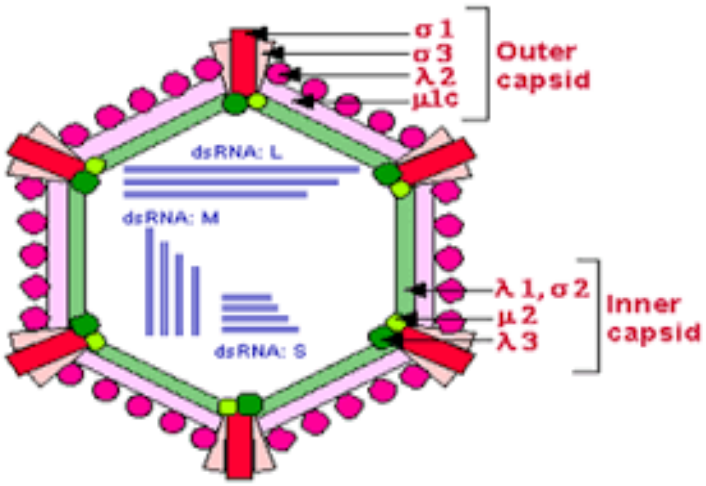


**Figure 1: Reovirus structure: Diagramed showing the structure of the reovirus (www.uta. Edu)**

Reoviruses are the family's group name for the viral particles, which have icosahedral symmetry but can have a spherical appearance. The linear dsRNA portions of the viral genome are surrounded by one, two, or three concentric layers of capsid proteins, which have a total width of 60–80 nm. Viruses with comparatively big spikes or turrets located at the 12 icosahedral corners of the virus or core particle belong to the subfamily Spinareovirinae. The viruses in the subfamily Sedoreovirinae lack prominent exterior projections on their virions or center particles, giving them a look that is almost spherical or smooth. Reovirus particles' interior protein layer covers the 9, 10, 11, or 12 linear dsRNA genome segments and has an internal diameter of 50–60 nm.(Figure. 2A). The enzymatically active minor proteins of the virion are affixed to the interior surface of the central space at the five axis of symmetry in the smooth-cored families. (Figure. 2B).

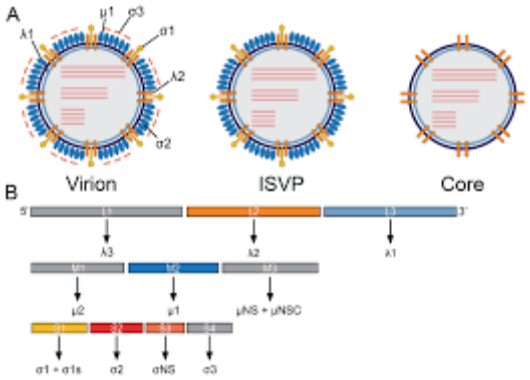


**Figure 2: Reovirus genome organization: Diagramed showing the genome organization of the reovirus (MDPI).**

The RNA-dependent RNA polymerase, NTPase, helicase, capping, and transmethylase enzymes are a few examples of these. Some species of particles have the ability to grow out of contaminated cells or to enter the endoplasmic reticulum during morphogenesis and acquire an envelope made of cellular membranes. According to the family, mature virions may have a myristyl residue covalently linked to one of the virion proteins but lack a lipid sheath. The intermediary in the morphogenesis or release of coltiviruses, rotaviruses, and orbiviruses may have a lipid sheath that is later lost or removed.

The genomes of viruses in the Reoviridae family are made up of segmented, double-stranded RNA. (dsRNA). As a result, only the cytoplasm is used for reproduction, and the virus specifies several proteins required for this process as well as the conversion of the dsRNA genome into positive-sense RNAs.

A cell surface receptor allows the viral to penetrate the recipient cell. Although the ligand is unknown, junctional adhesion molecules and sialic acid are believed to be involved. (JAMs). In the endolysosome, where the capsid is partly digested to permit additional cell entrance, proteases partially uncoat the virus. The genome is cautiously transcribed, resulting in an excess of positive-sense strands, which are used as messenger RNA templates to make negative-sense strands, before the core particle enters the cytoplasm through an as-yet-unidentified mechanism.(Figure.3). The rotavirus's DNA is composed of 11 regions. These regions are connected to the RNA synthesis-causing VP1 protein. Early events involve a selection procedure that allows 11 distinct RNA fragments to enter the cell. RNAs that have just been created carry out this process.

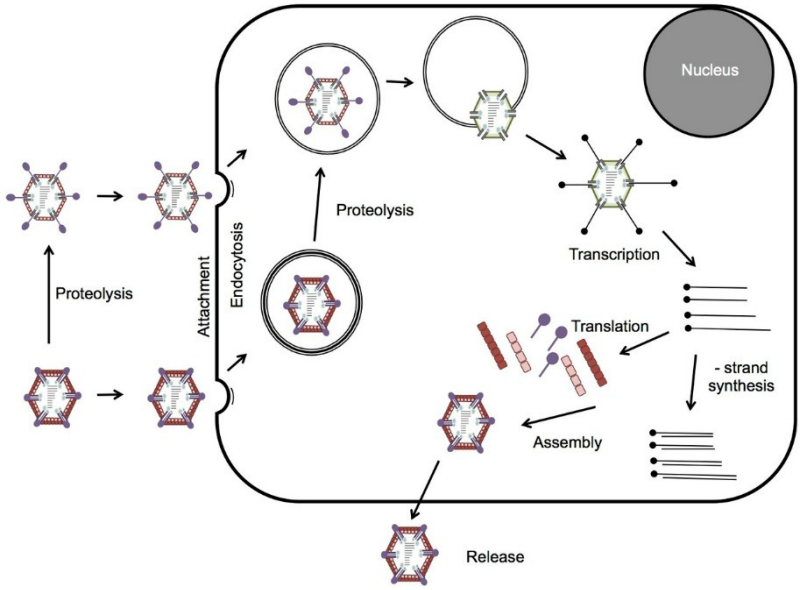


**Figure 3: Life cycle of the reovirus: Diagramed showing the life cycle of the reovirus (Science cracked).**

The 11 distinct RNA segments are all acquired as a result of this occurrence. In contrast to early events, the transcribing process is repeated in late events, but it is not limited this time. There is control machinery present during the translation stage because varying quantities of RNA are needed for viruses. (Figure.3). The number of RNA segments is the same, but the number of proteins is different. The RNA strands are not translated at the same pace, which is the cause of this. 6-7 hours after infection, viral particles start to form in the cytosol. By using ribosomal skipping, faulty screening, and termination suppression, translation is accomplished. The virus leaves the host cell through cell-to-cell transmission, monopartite non-tubule directed viral movement, and existence in occlusion bodies after cell death, where it remains contagious until it finds a new host. The biggest family of dsRNA viruses is the Reoviridae. It has viruses belonging to 15 families, each with a genome made up of nine, ten, eleven, or twelve linear dsRNA segments. A total of 75 viral species, including member viruses, have been identified from a variety of animals, birds, reptiles, fish, crustaceans, aquatic protists, insects, ticks, arachnids, plants, and mushrooms.

The various genera of reoviruses display amino acid sequence identities of less than 30%, according to phylogenetic studies using amino acid sequences of the RNA-dependent RNA polymerase. Two instances exist: Rotavirus B only shares a 22% amino acid sequence similarity with other rotaviruses. Aquareovirus and Orthoreovirus share an amino acid sequence up to 42%. Turreted viruses and non-turreted viruses are typically recognized as belonging to different clades on the evolutionary tree of the polymerase. However, it is notable that the RdRp family as a whole shares patterns in its functional core. The co-speciation theory, which states that reoviruses have co-evolved with their respective hosts and/or arthropod vectors, is generally supported by phylogenetic studies.

Reoviruses are a unique monophyletic group, but because they have been developing for over 550 million years, there are distinct structural variations between the more closely related genera as well as sequence divergence to nearly randomness. However, the internal proteins of the subcore shell and polymerase complexes (as well as some of their structural characteristics) continue to be essentially and strikingly identical. The non-turreted viruses may serve as an ancestor lineage from which the turreted viruses have developed, according to evolutionary studies.Structure-based studies of viral proteins have revealed closer relationships between some families, which may be suggested by the existence of signature sequences. For instance, structural studies of outer capsid proteins and similarities of the polymerase, capping enzyme, and capsid protein segments within the Sedoreovirinae family indicate that there has been an evolutionary leap between the rotaviruses and seadornaviruses. (Figure. 4)[4]–[6].

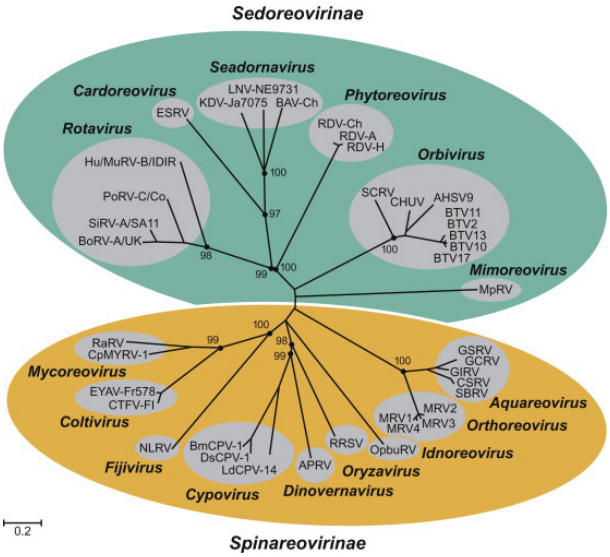


**Figure 4: Phylogenetic relationship tree of the *Reoviridae*: Diagramed showing the phylogenetic tree of the*Reoviridae***

The amount of genome regions may have changed as a result of gene duplication and rearrangement. (from 11 for the rotavirus to 12 for the seadornaviruses). Within the Spinareovirinae, closer connections have also been found between the aquareoviruses and orthoreoviruses, with identical proteins displaying up to 42% amino acid similarity and super-imposable particle morphology. (Revealed by cryoEM). The number of segments between aquareoviruses and coltiviruses increased from 11 (aquareoviruses) to 12 (coltiviruses), presumably as a result of gene amplification followed by rearrangement.

## DISCUSSION

It has been hypothesized that viral illnesses trigger pathological processes that begin the development of T helper 1 (TH1) antibodies against dietary gluten and celiac disease. (CeD). We created a viral infection model using two reovirus strains that infiltrate the intestine but vary in their immunopathological effects to test this theory and learn more about the processes underpinning virus-induced loss of tolerance to dietary antigens. Reovirus is an avirulent pathogen that induces protective immunity; however, we found that it can still disturb intestinal immune homeostasis at inductive and effector sites of oral tolerance by inhibiting peripheral regulatory T cell (pTreg) conversion and encouraging TH1 immunity to dietary antigen. Interferon regulatory factor 1 was necessary for the beginning of TH1 protection to dietary antigens, and this response was distinct from the type-1 interferon-mediated inhibition of pTreg conversion. Last but not least, research conducted on people suggests that the virus reovirus, which at first glance seems to be harmless, may play a part in CeD development.

For human reovirus to enter cultured cells, the Ras signaling system must be triggered. v-erbB-transformed mouse NIH 3T3 cells or human U87 glioblastoma cells were used to create tumors in extreme combined immune deficient animals, which were then given the virus to see if it could be used to cure cancer. In 65 to 80% of the rodents, a single intratumoral infusion of virus caused tumors to recede. Treatment of immune-competent C3H rodents with tumors derived from ras-transformed C3H-10T1/2 cells also caused the tumors to shrink, though this took a number of injections. These findings imply that reovirus might be useful in the therapy of cancer with additional research.

Reovirus infections in hens, turkeys, and other avian animals are widespread throughout the globe. Although lighter varieties and turkeys can also develop viral arthritis, meat-type poultry are the main species affected. In industrial hens, reoviruses have been found in a variety of illnesses besides tenosynovitis. They are runting/malabsorption syndrome, inclusion body hepatitis, hydropericardium, hepatitis in juvenile chickens, pulmonary disease, enteric disease, blue wing disease, and enteric disease. They are also simple to separate from the guts of hens that appear to be in good health. Several writers have reported molecular methods for finding avian reoviruses in infected tissues. Dot-blot hybridization was one of them, but reverse transcriptase polymerase chain reaction (RT-PCR) is now the method of choice. Reovirus vaccination has been attempted in a number of innovative ways, with different degrees of success. Among them are yeast, alfalfa, and thale grass (Arabidopsis thaliana) that produce C proteins[7]–[9].

The distinct patterns of virulence and central nervous system cell tropism displayed by reovirus types 1 and 3 have been defined molecularly using a genetic method. Reovirus type 3 intracerebrally injected into neonatal rodents results in a necrotizing encephalitis (without ependymal damage) that is always fatal. Reovirus type 1 infected animals typically live and may experience hydrocephalus and epedymal cell injury (without neuronal necrosis). We have been able to establish that the S1 genome region is responsible for the various cell tropism of reovirus serotypes and is the key determinant of neurovirulence using recombinant clones obtained from crosses between reovirus types 1 and 3. The type 3 S1 genome segment is responsible for neuronal necrosis and neurovirulence, while the type 1 S1 genome segment causes ependymal injury with later hydrocephalus. We hypothesize that these variations result from the distinct interactions of the protein encoded by the S1 genome segment, the 1 outer capsid polypeptide, with receptors on the surface of either ependymal cells or neural cells.

Reovirus is a nonenveloped double-stranded RNA virus. Initially thought to be unrelated to any particular illness, this virus was given the moniker Respiratory Enteric Orphan virus. However, it has been demonstrated that some reovirus family members can produce relatively minor ailments like gastroenteritis. Reovirus effectively infects the majority of human cells by attaching to the widely expressed sialic acid receptors and junction adhesion molecules (JAMs). Due to tumor-specific hyper-activated RAS signaling, this virus can preferentially multiply in cancerous cells, including glioma cells, despite its nontumor-specific infectivity. Reoviruses are better suited for use as oncolytic virotherapeutic agents than as carriers for gene delivery because they have the capacity to replicate only in tumors.

Reovirus type 1 was introduced into the mouse's digestive passage and was discovered to adhere to the surface of intestinal M cells but not other epithelial cells 30 minutes later. Within an hour, viruses were visible in the cytoplasm of M cells and were linked to mononuclear cells in the M cell's neighboring interstitial space. These results imply that the gut epithelium's M cells are the location of reovirus penetration. IgGs directed against 1 prevent reovirus particle adsorption, free protein 1 present in lysates of infected cells is capable of adsorbing to cells, and 1 competes with reovirus particles for cell surface receptors, making 1 the minor outer capsid shell component 1 that is the reovirus cell attachment protein. Reovirus particles of all three serotypes appear to adhere to the same cell surface receptor, according to competition tests. The main, if not the only, component of the 12 icosahedrally dispersed reovirus core projections or spikes, which pierce through the outer capsid shell to the reovirus particle surface, is shown to be found near 2 on the surface of reovirus particles as well[10].

## CONCLUSION

The reovirus gene consists of four small (S) regions that are each about 1.3 kbp long and are divided into three large (L), three medium (M), and three small (S) segments that are each about 3.9 kpb long. Reovirus reproduction takes place in the cytoplasm of cells that are infected and results in the development of crystalline clusters of offspring virions inside viral inclusions. From the beginning in reovirus infection, protein-RNA clusters are formed by structural protein 3, two viral nonstructural proteins, NS and NS, and NS. Reovirus exhibits potential as an immunotherapeutic drug that can improve a patient's defense the system's capacity to attack cancer cells in addition to its clinical use for the direct destruction of cancer cells.

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# CHAPTER 9

# CORONAVIRUS CAUSED OF THE PENDEMIC IN 2019

Prof. Kapilesh Jadhav, Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id-kapilesh@jnujaipur.ac.in

**ABSTRACT:**

The large viral family known as coronaviruses is responsible for a variety of illnesses, from the typical cold to more serious conditions like Middle Respiratory Syndrome and Severe Acute Respiratory Syndrome (SARS-CoV). The recent coronavirus was severally affected the worldwide population and become a cause of several people. In this chapter, we discussed the genome organization of the coronavirus, its life cycle, and the disease caused by coronaviruses.

**KEYWORDS:**

Acute Respiratory, RNA Synthesis, SARS COV, Sub Genomic, Severe Acute.

## INTRODUCTION

Coronaviruses are a family of related RNA viruses that infect both humans and birds and induce illness. They can induce mild to fatal respiratory system infections in both people and animals. Some instances of the common cold in humans (which is also brought on by other viruses, primarily rhinoviruses), while more deadly types can bring about SARS, MERS, and COVID-19, which is causing the current pandemic. They induce diarrhea in hogs and cows, and hepatitis and encephalomyelitis in mice. The subgroup Orthocoronavirinae of the family Coronaviridae, order Nidovirales and kingdom Riboviria are made up of coronaviruses. They have encapsulated viruses with a helical-symmetric nucleocapsid and a positive-sense single-stranded RNA DNA. Coronaviruses have one of the biggest RNA viral genomes, ranging in size from about 26 to 32 kilobases. Their name comes from the distinctive club-shaped spikes that protrude from their surface and can be seen in electron micrographs creating a picture that resembles the stellar corona.

A single-stranded positive RNA virus of about 29.9 kB in size, the SARS-CoV-2. The 14 open reading frames (ORFs) in the SARS-CoV-2 code for 27 distinct proteins. It has a poly (A) tail, a 5′ untranslated region (UTR), replication complex (ORF1a and ORF1b), Spike (S) and Envelope (E) genes, Membrane (M) and Nucleocapsid (N) genes, and 3′ UTR. The polyprotein pp1a, which has 10 naps, is encoded by the ORF1a gene, which is found at the 5′UTR. The polyprotein pp1ab, which has 16 nsps, is encoded by the ORF1b gene, which is present next to ORF1a. The virus replication complex is created by the autoproteolytic breakdown of the pp1ab and pp1a proteins. The four basic genes and eight auxiliary genes are all found in the 3′UTR. The role of the accessory genes, which are scattered among the structural genes, is largely unclear[1]–[3].

A non-segmented encapsulated virus with a width of 50–200 nm, the SARS-CoV-2. Spike glycoprotein (S), sheath protein (E), Membrane glycoprotein (M), and Nucleocapsid protein (N) make up its double-layered lipid sheath structurally. (Figure.1). The Spike glycoprotein covers the viral DNA that has an RBD for interacting with host cell receptors. The cytoplasmic domain, transmembrane domain, and N hydrophilic domain are the three domains of the M glycoprotein, which assembles virus particles. The Envelope protein is known to perform a part in pathogenesis as it links with the tight junction-related protein

PALS1. The viral DNA is enclosed in a ribonucleoprotein complex by the nucleocapsid protein. A phosphoprotein called the nucleocapsid participates in both the cell signaling cascade and virus genome replication.

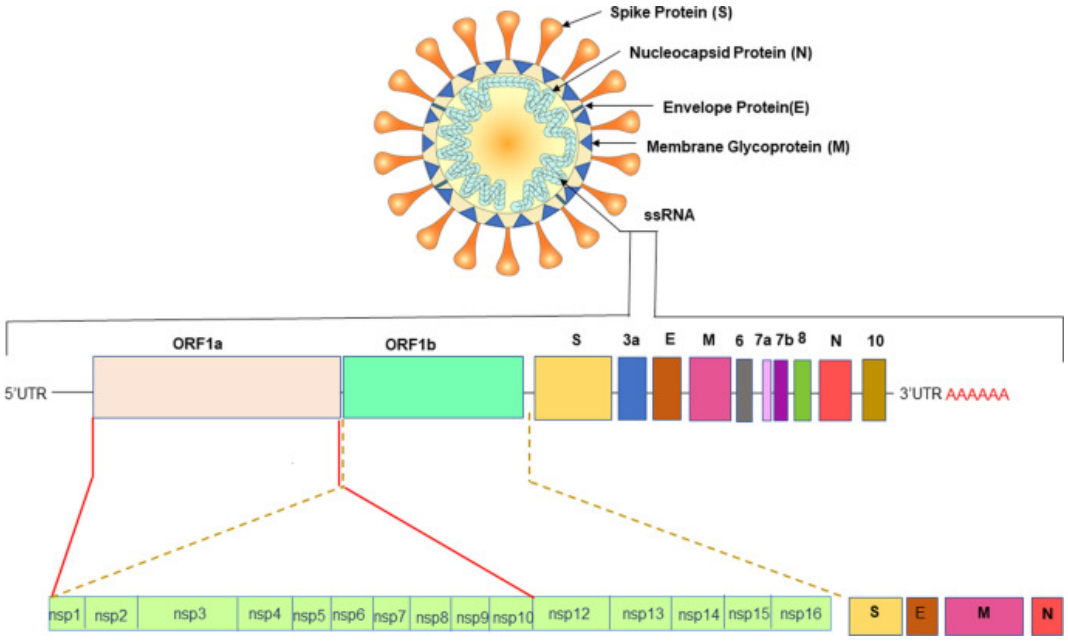


**Figure 2: Structure and genome of the coronavirus: Diagram showing the structure and genome organization of the coronavirus(respiratory. research).**

interactions between the S protein and its receptor start the early binding of the virion to the recipient cell. Different coronaviruses have different locations for their receptor binding domains (RBD), with some having them at the N-terminus of S1 (MHV), while others (SARS-CoV) have them at the C-terminus. The S-protein-receptor association is the key factor in coronavirus infection of a host species and controls the virus's tissue tropism. Peptidase is used by many coronaviruses as their cellular target. Given that entrance happens even when these proteins' enzymatic domains are absent, it is unknown why peptidases are used. As a receptor, many -coronaviruses attach to aminopeptidase N (APN), SARS-CoV and HCoV-NL63 bind to angiotensin-converting enzyme 2 (ACE2), MHV enters through CEACAM1, and the newly discovered MERS-CoV binds to dipeptidyl-peptidase 4 (DPP4). The virus must first attach to the receptor before making its way into the target cell's cytosol. This is typically done by cathepsin, TMPRRS2, or another protease cleaving the S protein under acidic conditions, followed by the union of the viral and cellular membranes.

Within the S2 region of the protein, S protein cleavage takes place twice, with the first cleavage being crucial for differentiating the RBD and fusion domains of the S protein and the second (cleavage at S2′) for revealing the fusion peptide. Although most coronaviruses combine within acidified endosomes, some, like MHV, can fuse at the plasma membrane. A fusion peptide that enters the membrane is exposed by cleavage at S2′, and two heptad repeats are then joined in S2 to create an antiparallel six-helix bundle. This bundle's creation enables the fusion of viral and cellular membranes, which eventually releases the viral DNA into the cytoplasm. The production of the replicase gene from the virion genomic RNA is the following phase in the coronavirus lifecycle. The replicas locus produces two co-terminal polyproteins, pp1a, and pp1ab, by encoding two big ORFs, rep1a, and rep1b. (Figure.2). The virus uses a slippery sequence (5′-UUUAAAC-3′) and an RNA pseudoknot to induce ribosomal frameshifting from the rep1a reading frame into the rep1b ORF to produce both polyproteins. The ribosome typically unravels the pseudoknot structure and carries on

translating until it comes across the rep1a halt codon. Sometimes the pseudoknot prevents the ribosome from extending translation into rep1b, causing it to pause on the slippery sequence and move the reading frame back one nucleotide, or a -1 frameshift, until the ribosome is able to melt the pseudoknot structure, extending translation into rep1b, which results in the translation of pp1ab. Ribosomal frameshifting may occur up to 25% of the time, according to in vitro research, but this hasn't been confirmed concerning a viral transmission. Although the precise purpose of these viruses' use of frameshifting to regulate protein expression is unknown, it is thought that it is either to regulate the precise ratio of rep1b to rep1a proteins or to postpone the production of rep1b until the environment for RNA replication is favorable.

The nsps 1-11 and 1-16 are found in polyproteins pp1a and pp1ab, respectively. Following the expansion of pp1a into pp1b, nsp11 from pp1a becomes nsp12 in pp1ab. However, -coronaviruses lack an equivalent nsp1. The individual nsps are then created by cleaving these polyproteins. The replicase polyproteins are cleaved by two or three proteases that are encoded by coronaviruses.

These are the papain-like proteases (PLpro), which are encoded by nsp3, and the major protease, or Mpro, which is encoded by nsp5. Except for the -coronaviruses SARS-CoV and MERS-CoV, which only produce one PLpro, most coronaviruses encode two PLpros within nsp3. The nsp1/2, nsp2/3, and nsp3/4 borders are cleaved by the PLpros, and the Mpro is in charge of the other 11 cleavage processes.After that, a large number of nsps come together to form the replica-transcriptase complex (RTC), which is eventually in charge of RNA replication and transcription of the sub-genomic RNAs. The nsps also contain other enzyme domains and functions, including those important for RNA replication, for example, nsp12 encodes the RNA-dependent RNA polymerase (RdRp) domain; nsp13 encodes the RNA helicase domain and RNA 5′-triphosphatase activity; nsp14 encodes the exoribonuclease (ExoN) involved in replication fidelity and N7-methyltransferase activity; and nsp16 encodes 2′-O-methyltransferase activity.

Other activities, including blocking innate immune responses (nsp1; nsp16-2′-O-methyl transferase; nsp3-deubiquitinase) have been discovered for some of the nsps, whereas others have largely unidentified functions (nsp3-ADP-ribose-1″-phosphatase; nsp15-endoribo-nuclease (NendoU)). see the following collection of non-structural proteins and their alleged roles.Interestingly, the Nidovirales group is the only one that has the ribonucleases nsp15-NendoU and nsp14-ExoN activities, which are regarded as genetic identifiers for these viruses.Viral replicase complexes are assembled and translated before being translated into viral RNA. Genomic and sub-genomic RNAs are both produced during viral RNA production. The structural and auxiliary genes located downstream of the replicase polyproteins are transcribed into messenger RNAs (mRNAs) by sub-genomic RNAs.

A distinguishing characteristic of the order Nidovirales is that all positive-sense sub-genomic RNAs are 3′ co-terminal with the full-length viral genome and thus create a collection of nested RNAs. Negative-strand intermediates are used to generate both genomic and sub-genomic RNAs. This poly-uridylate and anti-leader sequence-containing negative-strand intermediates are only 1% as common as their positive-sense cousins.It takes a lot of cis-acting regions for virus RNAs to replicate. Seven stem-loop structures that may stretch into the replicase 1a gene can be found in the genome's 5′ UTR. A pseudoknot, a bulged stem-loop, and a hypervariable area are all present in the 3′ UTR. It's interesting to note that the stem-loop and pseudoknot at the 3′ ends meet and cannot develop at the same time.

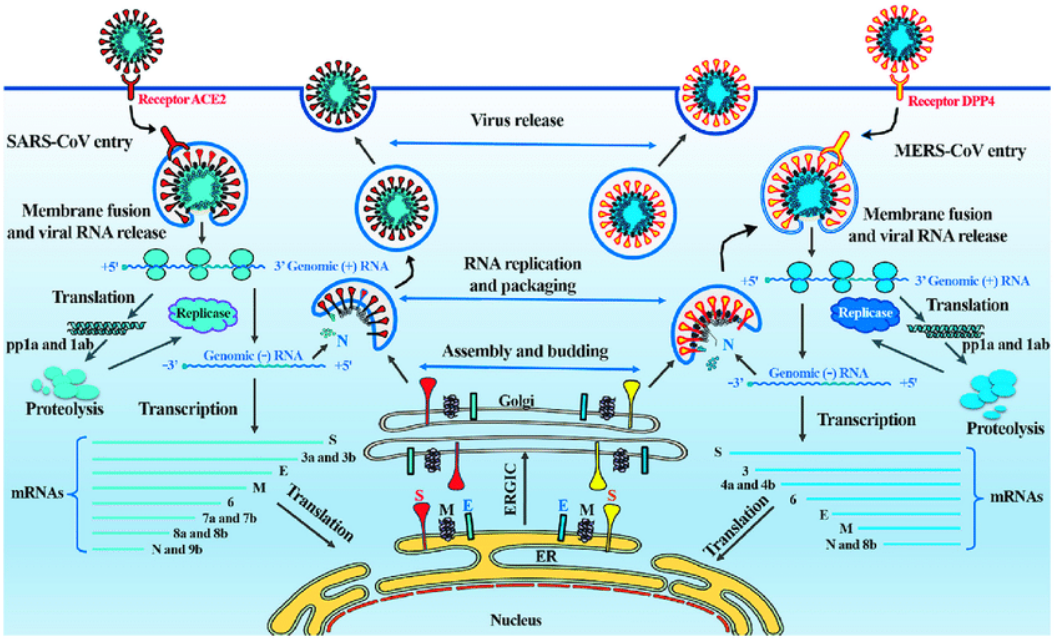


**Figure 2: Life cycle of the coronavirus: Diagram showing the life cycle of the coronavirus (Research gate).**

Therefore, it is suggested that these various structures control various stages of RNA synthesis, though it is still unclear precisely which steps are controlled and how. The fusion of the leader and body TRS segments during the generation of sub-genomic RNAs during coronavirus replication is possibly the most innovative feature of this process. The discontinuous extension of negative-strand RNA is now widely considered to be where this occurs. Originally, it was supposed to happen during positive-strand synthesis. According to the current model, the RdRp pauses at any of the body TRS sequences (TRS-B), and then either continues elongating to the next TRS or switches to amplifying the leader sequence at the 5′ ends of the genome under the guidance of complementarity between the TRS-B and the leader TRS. (TRS-L). This hypothesis is presently supported by a variety of data, including the anti-leader sequence found at the 3′ ends of the negative-strand sub-genomic RNAs. Last but not least, coronaviruses are renowned for their capacity for both homologous and nonhomologous recombination. The RdRp's capacity for strand swapping is linked to these viruses' capacity for recombination. Targeted RNA recombination, a reverse genetics technique used to create viral recombinants at the 3′ ends of the genome, is based on recombination, which most likely plays a significant part in viral evolution[4]–[6].

The virus structural proteins S, E, and M are translated and incorporated into the endoplasmic reticulum (ER) after replication and sub-genomic RNA synthesis (Figure.2). These proteins enter the endoplasmic reticulum-Golgi intermediate compartment (ERGIC) via the secretion route. From there, mature virions are formed when viral genomes encapsidated by N protein develop into membranes of the ERGIC harboring viral structural proteins. The majority of protein-protein interactions necessary for coronavirus formation are governed by the M protein. M protein expression alone cannot produce virus-like particles (VLPs), so it is not adequate for virion production. VLPs are created when M protein and E protein are produced together, indicating that these two proteins work together to make coronavirus envelopes. N protein promotes the formation of VLP, which implies that the union of encapsulated genomes with the ERGIC promotes the formation of the viral sheath. At this stage, the S protein is added to the virions but is not necessary for formation. For the S protein to be incorporated into virions, it must be able to traffic to the ERGIC and engage with the M

protein. The M protein is comparatively abundant, but the virion only contains tiny amounts of the E protein. Therefore, it is probable that M protein contacts give the envelope maturation process a boost. Although many theories have been put forth, it is unclear how E protein helps M protein during virion formation. While other studies have suggested that the E protein inhibits the aggregation of M protein, some studies have suggested that the E protein plays a part in causing membrane curvature. By changing the host secretory route, the E protein may additionally play a distinct function in fostering viral release. Additionally, the M protein interacts with the nucleocapsid, promoting the conclusion of virion formation. The C-terminus of the endodomain of M and the CTD of the N-protein has been identified as the site of these interactions. The precise mechanism by which the nucleocapsid complexed with virion RNA travels to the ERGIC to engage in an interaction with the M protein and integrate into the viral membrane is unknown.

How the N protein preferentially packages only positive-sense full-length genomes from the diverse range of RNA species generated during infection is another intriguing issue. A packaging signal for MHV has been found in the nsp15 coding sequence, but it is not yet known how this signal functions or how mutations in this signal appear to have no effect on viral generation. Additionally, the fact that the majority of coronaviruses lack comparable sequences at this locus suggests that packing might be virus-specific. After being assembled, virions are carried to the cell membrane by vesicles before being exocytosed and expelled. It is unknown if the virus has redirected a different, distinct pathway for its departure or if the virions use the conventional pathway for the transport of heavy cargo from the Golgi. The S protein, which is not formed into virions by some coronaviruses, travels to the cell surface and facilitates cell-cell fusion between infected cells and nearby, unaffected cells. Giant, multinucleated cells are produced as a result, which enables the virus to propagate throughout an infected organism without being noticed or stopped by viral-specific antibodies.

## DISCUSSION

Several mysterious pneumonia instances have been recorded in Wuhan, China, as of late December 2019. A new coronavirus was found to be the etiologic cause of this enigmatic pneumonia a few days later. According to the World Health Organization, the pertinent infected illness has been given the temporary names coronavirus disease 2019 (COVID-19) and severe acute respiratory syndrome coronavirus 2 accordingly. Presently, the COVID-19 pandemic is expanding throughout the globe and in China. This review's main goals are to examine COVID-19's pathogen, clinical characteristics, diagnosis, and therapy. It also briefly discusses epidemiology and pathogenesis in light of the available data.

Early in December 2019, Wuhan City, Hubei Province, China experienced an epidemic of the coronavirus disease 2019 (COVID-19), which was brought on by a brand-new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The epidemic was deemed a Public Health Emergency of International Concern by the World Health Organization on January 30, 2020. 49,053 laboratory-confirmed fatalities and 1,381 total deaths have been recorded as of February 14, 2020, worldwide. Many governments have implemented a variety of control methods due to the perceived danger of contracting illness. We performed a literature review of openly accessible material to summarize our understanding of the pathogen and the present epidemic. The causal agent, pathogenesis, immune responses, epidemiology, diagnostics, therapy, and care of the illness, as well as control and prevention methods, are all covered in this literature review.

A serious acute respiratory syndrome coronavirus 2 infection outbreak started in Wuhan, Hubei Province, China, in December 2019, and it quickly expanded throughout China and

beyond. The illness brought on by the novel coronavirus was formally referred to as coronavirus disease 2019 on February 12, 2020, by the World Health Organization. (COVID-19). Because most COVID-19 patients had pneumonia and recognizable CT imaging patterns, radiologic examinations have become essential for making an early diagnosis and gauging the progress of the illness. The primary source of proof for the clinical diagnosis of COVID-19 to date in Hubei, China, has been CT results. This study emphasizes the importance of chest CT in disease management and prevention while focusing on the etiology, epidemiology, and clinical signs of COVID-19.

It is thought that up to 16 virus components and a number of cellular proteins make up the replicase complex. In addition to the RNA-dependent RNA polymerase, RNA helicase, and protease activities that are common to RNA viruses, the coronavirus replicase was recently predicted to use a variety of RNA processing enzymes that are not (or very rarely) found in other RNA viruses. These include putative sequence-specific endoribonuclease, 3′-to-5′ exoribonuclease, and 2′-O-ribose methyl The organization of the coronavirus replicase gene, the proteolytic processing of the replicase by viral proteases, the functional and structural data that is currently available on specific replicase subunits, such as proteases, RNA helicases, and RNA-dependent RNA polymerases, are all covered in this chapter. Additionally, the subcellular localization of coronavirus proteins involved in RNA synthesis is covered. Coronaviruses and their distant nidovirus relatives appear to use a distinctive set of enzymatic activities and other protein functions to synthesize a set of 5′-leader-containing subgenomic mRNAs and to replicate the largest RNA virus genomes currently known. This is even though many molecular details of the coronavirus life cycle remain to be investigated.

With the emergence and dissemination of the 2019 novel coronavirus (2019-nCoV), also known as the severe acute respiratory syndrome coronavirus 2, there is a new public health crisis that threatens the entire globe. (SARS-CoV-2). In December 2019, the virus spread from bats to people via unidentified intermediary species in Wuhan, Hubei Province, China. As of today (05/03/2020), there have been approximately 96,000 confirmed instances of the coronavirus disease 2019 (COVID-2019) and 3300 confirmed fatalities. The illness has an incubation phase of 2 to 14 days and is spread through inhalation or interaction with infectious droplets. Common signs include a temperature, cough, sore tongue, shortness of breath, exhaustion, and lethargy. Most people with the illness have a minor case; however, some people (usually the aged and those with comorbid conditions) may develop pneumonia, acute respiratory distress syndrome (ARDS), and multi-organ failure. Many individuals don't show any symptoms[7]–[9].

According to estimates, the case mortality rate lies between 2 and 3%. Specialized genetic assays used for diagnosis show the virus in respiratory fluids. Normal or low white cell counts and increased C-reactive protein are typical laboratory results. (CRP). Even in people with no signs or moderate illness, the computerized tomographic chest image is typically abnormal. The function of antiviral agents has not yet been defined; the focus of treatment is primarily supportive. To prevent transmission, institutions must implement stringent infection control procedures, including contact and droplet safeguards, and isolate probable cases and patients with minor illnesses at home. The virus has a reduced fatality rate than its two progenitors, the Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV. This novel epidemic's effects on the entire world are still unknown.

Human coronavirus 229E (HCoV-229E), HCoV-OC43, and severe acute respiratory syndrome (SARS)-associated coronavirus are three human coronaviruses that have been identified. (SARS-CoV). Here, we report the finding of HCoV-NL63, a fourth human coronavirus, through a novel virus discovery technique. The virus was discovered in a 7-

month-old baby who had conjunctivitis and bronchiolitis. The entire genome sequence reveals that this virus is a brand-new group 1 coronavirus, not a hybrid. Because it multiplies on secondary monkey kidney cells and the monkey kidney LLC-MK2 cell line, HCoV-NL63's in vitro host cell range is noteworthy. The viral DNA has distinguishing characteristics, such as a peculiar N-terminal fragment in the spike protein. Seven additional HCoV-NL63-affected people were found through screening of clinical specimens from patients with respiratory illnesses, showing that the virus was broadly distributed among people.

Many mammal species, including people, are infected by coronaviruses, which can lead to both acute and chronic illnesses. The pathophysiology of murine coronaviruses, including mouse hepatitis virus (MHV) and serious acute respiratory coronavirus, is the main emphasis of this study. (SARS-CoV). One of the few animal models for the study of chronic demyelinating diseases like multiple sclerosis, MHV is a collection of strains that offer models systems for the study of viral tropism and pathogenesis in several organ systems, including the central nervous system, the liver, and the lung. SARS-CoV first infected humans in China in 2002, sparking a pandemic with serious morbidity and high fatality rates, especially in the elderly. We go over the pathogenesis of viruses as well as the various reverse genetics methods that enabled a lot of these investigations. We also go over the structural, enzymatic, and auxiliary roles that coronavirus proteins play, with a focus on their contributions to disease. In addition to their functions in virion structure and morphogenesis, structural proteins also play a major role in viral dissemination in vivo and in repressing host cell responses. The 16 conserved proteins encoded in the replicase locus and the small accessory proteins, many of which have enzymatic activities in RNA metabolism or protein processing in addition to functions in inhibiting host response, are examples of nonstructural proteins[10]. The severe acute respiratory syndrome coronavirus (SARS-CoV), the Middle East respiratory syndrome coronavirus (MERS-CoV), the new coronavirus, and six other human coronaviruses (HCoVs) have all been discovered to date examine the molecular virology of these widespread HCoVs in this paper and provide a current knowledge overview of HCoV-host interaction, pathogenesis, and other therapeutically significant perspectives.

## CONCLUSION

Viral infections can cause typical colds and other minor respiratory diseases in people, but they can also result in more severe conditions like pneumonia. The crown-shaped spines on the surfaces of coronaviruses give them their moniker. In the middle of the 1960s, coronaviruses that attack humans were first discovered. Authorities in charge of the public's health keep a careful eye on them.In December 2019, Wuhan, China, reported pneumonia. Chinese officials released the sequence of a new coronavirus called SARS-CoV-2, which was identified from a few clustered cases, on January 12, 2020.The coronavirus caused epidemic shows how susceptible the globe is to epidemics of public health with serious negative effects on the economy and health. The epidemic manifests itself differently in different geographical areas and nations within the globe.

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# CHAPTER 10

# PICORNAVIRIDAE FAMILY; LARGEST FAMILY OF THE VIRUS

Dr. Sunita Rao, Assistant Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id-sunita.rao@jnujaipur.ac.in

**ABSTRACT:**

Picornavirus is a positive sense RNA virus that belongs to the family of the Picornaviridae. Most of the human pathogenic viruses are belongsto thePicornaviridae family.Studies have found the IRES-derived translation, the human immune system's antiviral reaction, and the development of protein synthesis for their translation through the study of the molecular virology of the picornavirus. This chapter covered a general summary of the Picornaviridae family, the Picornavirus life cycle, and their defense strategy against the recipient cell.

**KEYWORDS:**

Single-stranded, Genetic material, RNA virus, RNA polymerase, Positive sense.

## INTRODUCTION

The foot-and-mouth disease viral was the first mammal virus to be found (1897). (FMDV). It belongs to the Picornaviridae family and is the archetypal member of the genus Aphthovirus. Poliovirus was also used in the development of the plaque test and the 1949 finding of viral propagation in culture. Infectious viral production in cultivated cells had never occurred before. Studying poliovirus-infected cells led to the identification of polyprotein synthesis, intracellular ribosome entry sites, and open mRNA. A poliovirus clone was also the first contagious DNA copy of an animal RNA virus. Poliovirus was the first mammal virus whose structure was established by x-ray diffraction, along with rhinovirus. Mengovirus, a family of picornaviruses, was found to contain RNA-dependent RNA polymerase [1]. One of the biggest and most significant families of viruses is the picornavirus. This group of viruses contains parechoviruses, polioviruses, and enteroviruses. Picornavirus, as its name implies, is a tiny RNA-containing virus. Pico denotes the virus's small dimension, which is approximately 27 nm, and RNA denotes that this virus's genetic material is RNA. The knowledge of picornavirus characteristics, its structure, picornavirus reproduction, and its toxicity in the human body are the topics of this essay. The categorization of picornaviruses and a review of the virus's therapeutically significant families are also covered in this article [2].

Since picornaviruses have a single-stranded, positive-sense RNA sequence, they are categorized as group IV viruses under Baltimore's viral categorization scheme. Their genomes vary in size from 6.7 to 10.1 (kilobases). The genetic material is contagious, similar to the majority of positive-sense RNA genomes; however, it is considerably less deadly than if it were confined within the virus particle. When transferred into cells, the RNA can have enhanced contagiousness. The genome RNA is unique because it contains a protein on the 5' end that RNA polymerase uses as a precursor during transcription. This primer, which goes by the name of VPg genome, is 2 to 3 kb long. Tyrosine residue is present at the 3' terminus of VPg. Covalently attached to the 5' end of RNA, tyrosine serves as a source of -OH.

The genome is positive-sense (read 5' to 3', the same sense as human mRNA) and not divided. Picornaviruses, unlike human mRNA, lack a 5' end in favor of the virally expressed

protein known as VPg. The genome does, however, have a poly(A) tail at the 3' end, just like human mRNA. On the picornavirus genome, an untranslated region (UTR) can be located at both extremities. When compared to the 3' UTR, which is typically between 30-650 nucleotides (nt) in length, the 5' UTR is typically lengthier (Figure.1). Though the 3' UTR is believed to be crucial for negative strand production and the 5' end for translation, the 5' end may also contribute to the virus' pathogenicity. The remaining portion of the genome specifies a single polyprotein with structural proteins at the 5' end and nonstructural proteins at the 3' end. The polyprotein is arranged as L-1ABCD-2ABC-3ABCD, where each character stands for a different protein, though other arrangements are possible.

The capsid proteins VP4, VP2, VP3, and VP1 are represented by the proteins 1A, 1B, 1C, and 1D, accordingly. The cleavages are carried out by virus-coded proteases, some of which are intramolecular (Figure.1). First, the polyprotein is divided into P1, P2, and P3. Before being cleaved into the proteins that make up procapsids, P1 is myristylated at the N end. VP0 will later be split to generate VP2 and VP4. 3B (VPg), 2C (an ATPase), and 3D (the RNA polymerase) are additional breakdown products.

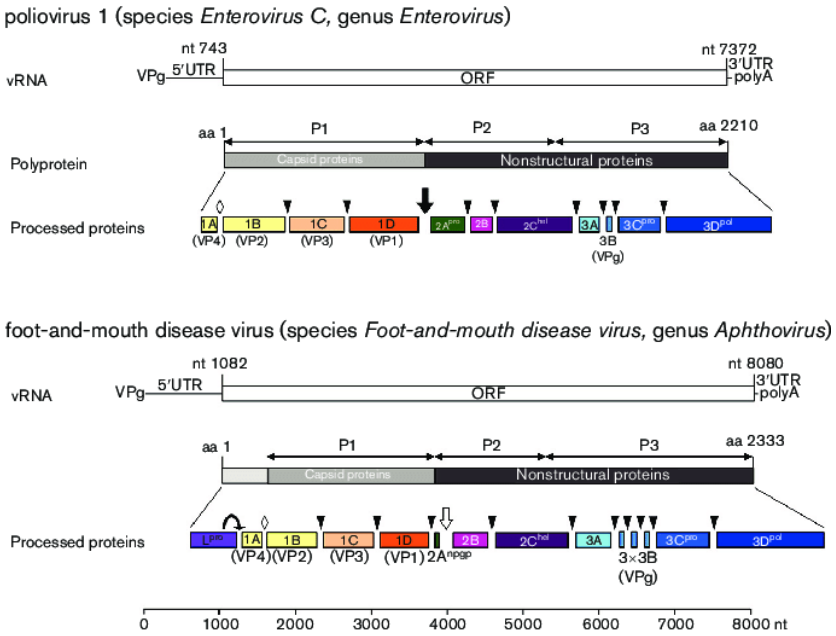


**Figure 1: Genome organization: Genome organization and proteins of enteroviruses and aphthoviruses(Wikipedia).**

The Order Picornavirales now includes the family *Picornaviridae* alongside the families *Dicistroviridae, Iflaviridae, Marnaviridae, and Secoviridae*. The following characteristics are shared by all viruses in this order: A conserved RNA-dependent RNA polymerase, a genome with a protein (VPg) affixed to the 5′ ends, a lack of contiguous open reading frames within the genome, and viral RNA processed into a polyprotein before processing are the first three characteristics. Viruses within the families Iflaviridae, Marnaviridae, and Secoviridae attack only animals, plants, or phytoplankton and will not be examined further in this volume. Insects and crabs are infected by viruses in the Dicistroviridae family, and the illness known as "Taura syndrome" has caused catastrophic deaths in prawn farms.

The "next-generation" sequencing of clinical and ambient samples has led to the discovery of previously unidentified picornaviruses, which has led to a substantial growth of the family Picornaviridae in recent years. Currently, there are 29 families in the family, 23 of which contain just one type of virus. The discovery and comparison study of novel and extant

picornavirus genomes has led to the establishment of 21 new genera, in addition to the well-established genera of Aphthovirus, Enterovirus, Teschovirus, Cardiovirus, Erbovirus, Kobuvirus, Hepatovirus, and Parechovirus: The following viruses are also known as *Aquamavirus, Avihepatitis virus, Avisivirus, Cosavirus, Dicipivirus, Gallivirus, Hunnivirus, Kunsagivirus, Megrivirus, Mischivirus, Mosavirus, Oscivirus, Pasivirus, Passerivirus, Rosavirus, Sakobuvirus, Salivirus, Sapelovirus, Senecavirus, Sicinivirus, and Tremovirus*. The largest genus in the family, Enterovirus contains viruses that are most important to human medicine.

These viruses include rhinoviruses, which infect the upper respiratory tract, as well as enteroviruses that primarily replicate in the gastrointestinal tract (e.g., polio, echo, and coxsackie viruses). Except for the aphthoviruses that are yet to be changed, picornavirus species have been renamed lately to eliminate host species names that have been substituted with alphanumeric designations. This chapter will be organized according to animal species rather than the taxonomic assignment of each virus because of the picornaviruses' seeming instability and potentially perplexing taxonomic organization, as well as the fact that taxonomic assignments don't always correspond with the biological behavior of specific picornaviruses (including the type of disease they inflict on animals if any)[4].

The cytosol of the host is where the picornavirus replicates. Single-stranded RNA with a molecular weight of 2 106 to 3 106 is present in the viral.

1. Because the virus relies on the host's reproduction mechanism to finish its replication, the virus can only replicate once it has invaded the ghost's cell. The virus DNA functions as an mRNA, thus triggering the synthesis of the protein using the components of the host (Figure.2).
2. The reproduction begins with the binding of the virion to the particular cell receptor. The plasma membrane is where the connection takes place. It is hypothesized that the hydrophobic N end of the core protein of the host's plasma membrane is introduced into the virion.
3. Following implantation, the protein is taken up by the endosome, leading to endosomal transfer. As a consequence, the virus nucleic acid is reached in the cytoplasm (Figure. 2).
4. The host's cellular enzymes then eliminate the VPg protein that is linked to the viral RNA, allowing the viral genetic material to become bare.
5. The viral RNA that is now exposed functions as viral mRNA and starts the translation process. The internal ribosomal entry site (IRES) in the 5′ UTR is where the ribosome attaches. It forms a clover leaf shape, enabling the host protein to attach to it (Figure.2).

It's crucial to remember that the virus DNA lacks internal translational stop codons. As a consequence, the solitary lengthy polyprotein chain is created. To guarantee the creation of the virus protein, this protein is then subjected to translational changes. To produce the desired end proteins, the encoded protein is cleaved by the virus protein known as a protease. Antisense RNA strand is another name for the negative strand of RNA. Its production is started by the VPg acting as a precursor at the 3′ ends of the virion RNA. The antisense RNA strand serves as a blueprint for the synthesis of the sense RNA strand, also referred to as the plus strand, as soon as the synthesis of the antisense RNA is finished. The viral capsid proteins and this sense RNA come together to create the viral head's encasing. Thus, it can be said that two distinct replicative stages are used for virion reproduction.

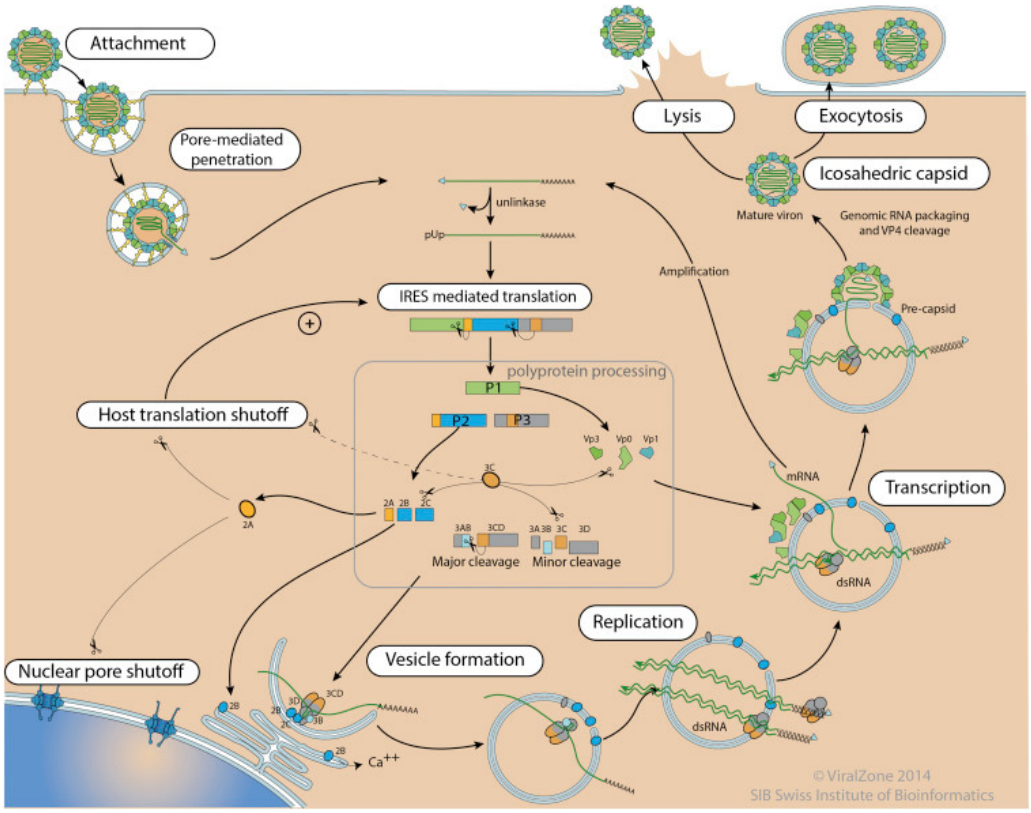


**Figure 2: Lifecycle of the Picornavirus: Diagram showing the life cycle of the Picornavirus (Science direct.com).**

Picornavirus typically enters the body through the lips and nostrils. The nasopharyngeal epithelium and a second location of viral reproduction in local lymphoid tissues are where the picornavirus typically multiplies. Replication can cause lung conditions or diseases without any symptoms. The fact that some types of these viruses can develop in the gut due to their resistance to digestive and biliary acidic content can be explained by the observation that some of these viruses can infiltrate the lower intestine. The virus strain then enters the circulation and targets tissues like the spinal cord, meninges of the brain, the heart, the liver, and the epidermis. Through the CNS, the pathogen also gets to the bone system.

The quantity of IgA antibodies in the mucus increases as a result of the host's defense against the pathogen. Infections of the pulmonary system exhibit this. A higher IgA content can also be observed in the human body's intestines. The IgM antibody is the first one the body makes in reaction to the pathogen. After some time, there is class flipping, which causes the human body to produce more IgG antibodies. IgG antibody content peaks for two to three weeks before beginning to decline as the stable period draws near. It is also crucial to remember that absorption, metabolism, and elimination are how the antibody and antigen combination is cleared.

## DISCUSSION

There are many tiny RNA viruses in the picornavirus family, many of which are serious human and animal diseases. They are among the most basic viruses found in vertebrates, with a single-stranded positive-sense RNA genome contained within a T = 1 (quasi T = 3) icosahedral protein shell measuring about 30 nm in diameter. By using X-ray diffraction, the structures of several picornaviruses have been identified with nearly atomic precision. The X-ray diffraction method or cryo-electron imaging, with reduced precision, has also been used

to determine the shapes of intermediary particles that allow for cell entrance and combinations of viral particles with receptor molecules or antibodies. Different picornaviruses use a variety of receptors, and it is now known that many of them attach to and attack cells using co-receptors and substitute receptors. However, it is still unclear how these viruses liberate their genes and move them across a cellular barrier so they can reach the cytosol. In-depth investigations into cell entrance methods have only been conducted on a small number of family members, and it is still unknown how widely the findings of these investigations apply to the entire range of picornaviruses. For the enteroviruses, the picornaviruses that have been researched the most, working models of the cell entrance mechanism are currently being created. These viruses retain particle structure throughout the infectious process and act as DNA transport units. However, there is currently no paradigm to describe how viruses that appear to merely split into components during uncoating, such as cardio- and aphthoviruses, transport their DNA into the cytoplasm [2].

A sizable family of tiny plus-strand RNA viruses known as the Picornaviridae is responsible for a dizzying variety of serious human and animal illnesses. The stage of these viruses' morphogenesis that is least known is encapsidation, which is intricately linked to genome translation and RNA reproduction, making it challenging to research. Although the fundamental stages of assembly are well understood, there aren't many specifics about the method and variables that control this process. The majority of the knowledge has come from research on enteroviruses, particularly the poliovirus, where new data has unexpectedly revealed that the selectivity of encapsidation is controlled by a viral protein-protein association rather than by an RNA packing signal. In this review, we attempt to provide a concise summary of the current understanding of the following issues: (i) encapsidation intermediates; (ii) the specificity of encapsidation; (iii), viral and cellular factors required for encapsidation; (iv) encapsidation inhibitors; and (v) a model of enterovirus encapsidation. In the end, we make some comparisons between the morphology of picornavirus and other plus-strand RNA viruses [5].

IgSF-related cell-surface molecules serve as the cellular targets for a large number of picornaviruses. These molecules typically comprise tandem repetitions of two to five Ig-like domains, each of which has an amino-terminal domain (D1) that interacts with invasive viruses and a transmembrane, and a brief cytoplasmic area at their carboxy-termini. The majority of the Picornavirus family's rhino- and enteroviruses adhere to cellular receptors by using a canyon-like structure on their surface. Binding into the crevice causes the virus to become less stable, which starts the uncoating process. Contrarily, when picornaviruses use non-IgSF molecules as receptors, they attach outside the canyon and do not result in viral instability[6].

Positive-strand RNA viruses in the Picornaviridae family are responsible for several human illnesses, including poliomyelitis, the common cold, myocarditis, and hepatitis. The genome structure and the ways in which genes are expressed are extremely consistent among members of the same family, despite the diversity of illnesses brought on by picornaviruses. The processes of viral gene expression will be covered in this overview, including cap-independent translation start, host cell translation cut-off, processing of viral polyproteins, and RNA replication [7].

The transport of the RNA gene to the cytosol of a target cell, where reproduction takes place, is the crucial step in picornavirus entrance. Understanding the molecular alterations in the virion necessary for uncoating and RNA release has advanced over the past few years. Additionally, the cellular locations at which uncoating takes place as well as the endocytic processes accountable for the uptake of several viruses have been discovered. It is now

understood that entrance is not an inert process and that certain cues needed for entry are initiated by viruses. According to the specific target cell and the proteins that are present in that cell, there may be numerous entrance points for a given virus [8]. Picornaviral RNAs translate by a peculiar process in which ribosomes attach to an intracellular spot directly rather than scanning the RNA from the 5′ ends. A 450-nucleotide stretch of the picornavirus 5′ untranslated region is necessary for this intracellular entrance process. To find the real start site, the ribosome may first attach to a site at the 3′ ends of this section. Some cellular mRNAs' translations may be affected by this new mechanism [9].

The picornaviruses are a large family of viral diseases that collectively account for the majority of human illnesses in the industrialized world. Three well-known human diseases are members of the picornavirus family: the enteroviruses (which include the poliovirus, coxsackievirus, and echovirus), the rhinoviruses, and the hepatoviruses. (including hepatitis A). Recent research has identified the parechoviruses, formerly known as echoviruses 22 and 23, as a fourth family of human picornaviruses. The enteroviruses and rhinoviruses, for which significant effort has been made and recent results have been documented towards the creation of safe and efficient antiviral therapy[10], will be the main emphasis of this paper.

Although echovirus 22 is currently regarded as a part of the picornavirus family's enterovirus group, it has been noted to possess unique molecular characteristics when compared to other members of the family. The entire nucleotide sequence of the echovirus 22 (Harris strain) genome has been identified, and it appears to vary considerably from all the other examined picornaviruses. The genome's structure, which consists of 7339 nucleotides (excluding the poly(A) segment), is comparable to that of previously sequenced picornaviruses, though. In comparison to aphtho- and cardioviruses, this genome has a reasonably well-conserved 5' untranslated section, which is followed by an open reading frame that codes for a polyprotein with 2180 amino acids. Direct sequencing was used to identify the amino termini of the capsid polypeptides VP1 and VP3, and a comparison to other picornavirus proteins was used to infer the locations of the polyprotein's other protease cleavage sites. The amino acid similarities of echovirus 22 polypeptides with the equivalent proteins of other picornaviruses are in the 14-35% range, comparable to those numbers seen when members of the five picornavirus families (entero-, rhino-, cardio-, aphthous-, and hepatoviruses) are compared. Our findings imply that echovirus 22 is a member of a distinct clade of picornaviruses [11].

## CONCLUSION

The poliovirus, coxsackievirus, picornaviruses, and ECHOvirus are members of the Picornaviridae, a significant family of RNA viruses. Picornaviruses proliferate in the cytosol of affected cells and have positive-sense, single-stranded RNA genomes. These internal pathogens depend on cellular proteins for translation and chromosomal RNA reproduction due to the restricted coding capability of these viruses. Non-enveloped RNA viruses called picornaviruses penetrate cells through endocytosis mediated by receptors. Picornaviruses struggle to get their RNA genomes through the endocytic vesicle's membrane and into the cytosol to start an infection since they lack an envelope. We investigated the characteristics, structure, life cycle, and pathology of the Picornavirus.

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# CHAPTER 11

# AN OVERVIEW OF THE TOGAVIRIDAE FAMILY

Dr. Manish Soni, Assistant Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id- manishsoni@jnujaipur.ac.in

**ABSTRACT:**

The*Togaviridae* family is the family of the virus that enclosed, single-stranded, plus-strand RNA. The virus belongs to the *Togaviridae*family have a genome size of around 50-70 in diameter including a protein envelope containing the two and three glycosylated polypeptides. In this chapter, we discussed the members belonging to the *Togaviridae*family, the structure of the virus, their replication mode, and the disease caused by this virus.

**KEYWORDS:**

Epithelial Cells, Rubella Virus, Structural Protein, Sindbis Virus, *Togaviridae*Family.

## INTRODUCTION

A genus of enclosed, single-stranded, plus-strand RNA viruses known as the *Togaviridae* is found almost everywhere.*Alphavirus* (with 26 species), *Rubivirus*(one species), *Pestivirus* (three species), and *Arterivirus*are the four families that make up the family *Togaviridae*. (one species). Viruses from the genus Alphavirus, a collection of arthropod- (mainly mosquito-) transmitted, endemic viruses that are predominantly sustained in mice, primates, and birds by mosquito carriers, are included in this family. The two disease conditions that the alphaviruses can induce are encephalitis and arthritis with dermatitis, or a feverish sickness attended by both. Human illnesses typically happen when humans enter areas where enzootic alphavirus transmission occurs and are eaten by infected mosquitoes or when alphaviruses arise and spread through shifts in host range to cause epizootics and outbreaks.

The Rubella virus, the causative agent of 3-day measles (German measles), is the only member of the other group in the Togaviridae family, which is loosely linked. Host movement appears to control the genetic and immunological variety within alphaviruses, as the majority of alphavirus complexes are limited in their spread to either the Old or New World. *Alphaviruses* have evolved primarily through purifying selection, which is likely a reflection of the severe restrictions placed on them by their transmission cycles, which call for alternate reproduction in arthropods and mammals. Although a live vaccine has significantly decreased Rubella virus illnesses in many parts of the world [1], there is presently neither an approved vaccine nor a viable therapy for alphaviral infections.

The positive-sense, single-strand RNA genome of alphaviruses is icosahedral and mimics messenger RNA. (mRNA). They have an envelope (Latin for "cloak," 45 to 75 nm in circumference), which makes them marginally bigger than picornaviruses. The DNA of the togavirus encodes primarily late proteins. Two or three glycoproteins join together to create a singular spike in alphaviruses. The glycoproteins' carboxy (COOH) end is embedded in the capsid, causing the membrane to shrink-wrap and adopt the form of the capsid (Figure.1). All alphaviruses have capsid proteins that are structurally comparable and have cross-reactive antigens. The various antigenic markers on the membrane glycoproteins of the viruses can be used to classify and differentiate them into groups (complexes).

The alphaviruses bind to particular receptors found on a wide variety of cell types from a wide variety of organisms (Figure.1). These viruses can infect both mammals and invertebrates, such as people, primates, horses, birds, lizards, and frogs (e.g., mosquitoes, ticks). The various illness manifestations are somewhat explained by the fact that each virus has a distinct organ tropism. Through a process called receptor-mediated endocytosis, the virus penetrates the cell (Figure.1). When the vesicle becomes acidic, the viral envelope joins the endosome membrane to release the capsid and DNA into the cytoplasm. The alphavirus genomes attach to ribosomes as mRNA once they have been discharged into the cytosol. Both early and late stages of the alphavirus DNA translation occur.

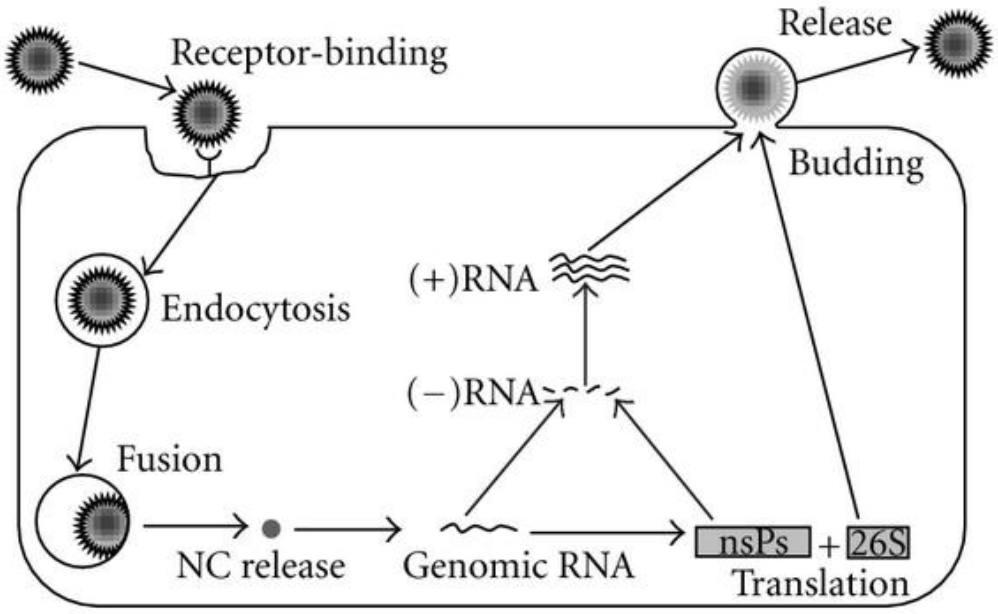


**Figure 1: Replication of the Alphaviruses: Diagram showing the overview of the replication of the Alphaviruses (Hindawi).**

The first two-thirds of the alphavirus RNA is transcribed into a polyprotein, which is then broken down into four nonstructural early proteins by proteases. (NSPs 1 through 4). The RNA-dependent RNA polymerase is made up of these early proteins. The enzymes for genome replication form in vesicles, as they do for all positive-strand RNA viruses, on a membrane framework. The production of 42S positive-sense mRNA follows the synthesis of a full-length 42S negative-sense RNA, which serves as a blueprint for the duplication of the genome. A 26S late mRNA is also produced from the template, accounting for one-third of the genome. The proteins for the membrane (E1 through E3) and capsid (C) are encoded by the 26S RNA. Viral mRNA can make up as much as 90% of the mRNA in the affected cell late in the reproduction cycle. The creation of a significant number of the structural proteins needed for viral packing is made possible by the plethora of late mRNAs.

The late polyprotein that was created from the 26S mRNA is cleaved by an enzyme to generate the structural proteins. The polyprotein is split from the C protein, which is processed first. The newly formed polypeptide is then connected to the endoplasmic membrane by a signal sequence. The E1, E2, and E3 glycoprotein spikes are then created by translating, glycosylating, and cleaving membrane glycoproteins from the residual polyprotein. The majority of alphavirus glycoprotein increases produce the E3. The glycoproteins are handled by the usual cellular mechanisms in the endoplasmic reticulum and

Golgi apparatus and are acetylated and acylated with long-chain fatty acids. The plasma membrane is then effectively exchanged with alphavirus glycoproteins. Rubella virus is the lone member of the genusRubivirus and belongs to the Togaviridae family together with alphaviruses. Rubella is an enclosed single-stranded RNA virus of 9757 nucleotides in length that includes two long open reading frames, the 5′ proximal of which encodes nonstructural proteins and the 3′ proximal of which encodes the structural proteins (Capsid, E1, and E2) (Figure.2) The virion has a 30-nm-dense center and is cylindrical, measuring 50–70 nm in circumference.

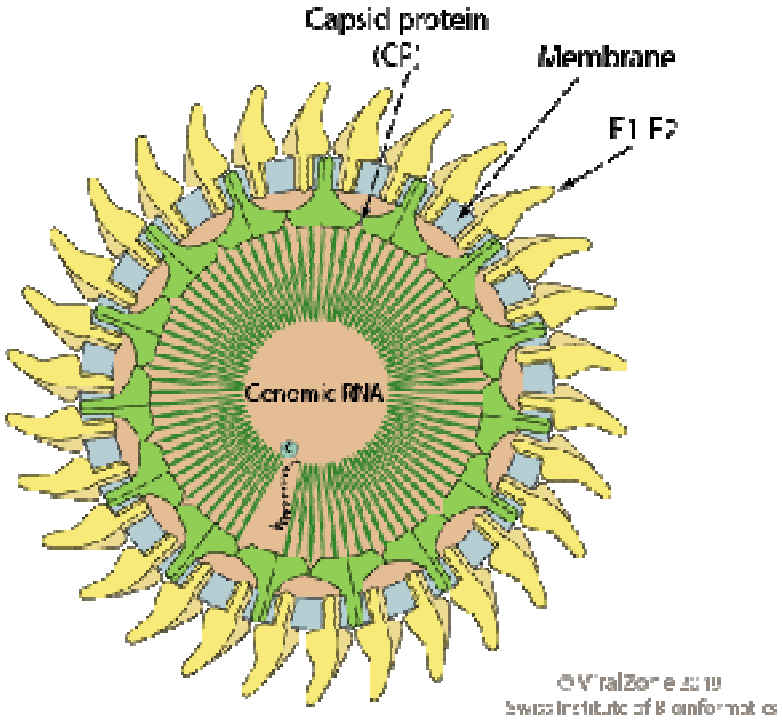


**Figure.2: Rubivirus: Diagram showing the structure of the rubivirus (Viral zone).**

Nasopharyngeal fluids are the means of transmission. Most infections result in a benign, self-limiting illness resembling measles, but when rubella affects a baby, it can cause abortion or fetal rubella syndrome, which are serious issues. (CRS). The ability of the rubella virus to infiltrate the placenta, disseminate to the baby, and change the way many systems work in CRS leads to systemic inflammation. Myelin oligodendrocyte glycoprotein (MOG), which the rubella E1 protein attaches to, promotes transmission when it is expressed ectopically on nonpermissive cells. Additionally, MOG and the rubella E2 protein have a high degree of similarity, which may help to explain why antibodies to rubella can, at least in vitro, induce demyelination. Joint complaints are a side effect of naturally obtained measles that affects more than 50% of adult females but is uncommon in toddlers and adult men.58 Synovitis does not happen as frequently as symmetric or migrating arthralgias.

The main sign is morning rigidity, and it typically goes away within a few days to a week. Proximal interphalangeal, metacarpophalangeal, wrist, elbow, foot, and knee joints are most commonly impacted. Carpal tunnel syndrome, tenosynovitis, and periarthritis may be present. The signs of some people could last for months or even years. Joint symptoms after immunization are less common, typically milder, and last for a shorter period than symptoms after spontaneously obtained measles.59 The high incidence of postvaccination myalgia and paresthesia, which start two weeks after vaccination and last for less than a week, has also

been linked to living attenuated rubella vaccines. But in some individuals, the signs might last longer than a year. In 15% or more of users, RA27/3, the vaccine type currently in use, may result in post-vaccination joint symptoms [2]. In joint cell preparations and as reported in tissues, persistent rubella infection can develop. Some individuals with persistent arthritis have greater levels of rubella-specific antibodies in their joint fluid than in their blood, indicating local production of the particular antibody. Our earlier research, which showed that virus-specific IgM may linger for up to 4 years after both a spontaneous infection and immunization, also points to RV persistence. Patients' joint tissues may contain measles RNA owing to recurrence, immunosuppression, or waning immunity with advancing age [3].

## DISCUSSION

Alphavirus and Rubivirus are the two families that make up the family Togaviridae. The eight antigenic complexes that alphaviruses fall under are based on antibody cross-reactivity. The Semliki Forest complex contains the Getah virus (GETV), the Sagiyama virus (SAGV), and the Ross River virus (RRV), while the Eastern equine encephalitis virus (EEEV) is in the EEEV complex. The endemic EEEV virus infects people and results in encephalitis, fever, lethargy, and nuchal stiffness. Confusion, immobility, convulsions, and unconsciousness are possible progressions of symptoms. Coordination problems, sadness, seizures, sickness, low temperature, and death are examples of clinical symptoms. GETV was first documented in pigs in 1987 and in neonatal piglets showing melancholy, trembling, yellowish-brown feces, and 100% case fatality. Though SAGV is regarded as a GETV variation, complement fixation can distinguish it from GETV because the capsid protein of SAGV contains the amino acid leucine. A chain of humans, mosquitoes, macropod marsupials, mosquitoes, and humans routinely transmits RRV. The greatest and most efficient clinical alleviation is provided by nonsteroidal anti-inflammatory drugs [4].

Rubella virus is unconnected to the hog cholera, cattle dysentery, and border disease viruses, but they are antigenically similar. Congenital illnesses caused by noncarbon togaviruses can result in a broad range of defects. The fetus with the infection may pass away in gestation, during the newborn stage, or it may be delivered with teratogenic abnormalities. Additionally, offspring that appear to be healthy can be born and go on to live a statistically typical life or acquire an illness that manifests itself years, months, or even decades after birth. The period of embryonic development at which infection develops has a significant impact on the final result of a hereditary illness. Rubella virus exposure causes fetuses to produce antibodies against the virus, whereas farmed animals commonly do not produce an immune reaction to a prenatal pestivirus infection. The rubella virus typically leaves the host's body 1-2 years after delivery in cases of hereditary rubella. However, in clinically sound animals, a lifetime and extensive survival of the virus may be a sign of hereditary pestivirus infections. These species are important for understanding the zootiology of diseases like swine cholera, border disease, and cattle viral diarrhea [5].

Both Sindbis and Kunjin togavirus RNA had a molecular weight of 4.2  106daltons as determined by polyacrylamide gel electrophoresis; either viral RNA was then treated with 8 M urea to produce a product with a molecular weight of 2.1  106 daltons. However, the cores produced by treating Kunjin virions with deoxycholate had characteristics similar to those reported for Sindbis virus cores (sedimentation coefficient, ribonuclease sensitivity, lack of phospholipid)[6]. Kunjin virus sedimented at a rate that was three-quarters that of the Sindbis virus. A prevalent, minor illness known as rubella (German measles) is marked by a rash. It can impact young people as well as toddlers and teenagers around the globe. Early rubella virus infection during pregnancy increases the risk of transmission to the baby and birth

abnormalities. Consequently, a correct prognosis is essential during pregnancy. The rubella virus belongs to the Togaviridae family's species Rubivirus [7].

Up until 1984, flaviviruses were considered to be part of the togavirus family. The International Committee for the Nomenclature of Viruses then decided to split Flaviviridae into its own family. Morphological standards had previously been used to identify the togavirus genus. Recent findings that flaviviruses, while usually comparable to alphaviruses in their appearance vary significantly from alpha to togaviruses in their virion structure, strategy of reproduction, and development led to the shift in classification [8].

After being vaccinated against either a group A or group B togavirus, rabbits were then exposed to a similar togavirus from a separate subset six weeks later. In hemagglutination-inhibition experiments, IgG antibodies in antisera cross-reacted widely with group B viruses at all times, but within group A, they were specific for the primary virus until challenge, at which point they reacted with both the primary and challenge viruses. IgM antibodies, however, were produced when the challenge and main viruses belonged to the same antigenic subtype because they were specific in both groups for the most recent immunizing virus. In connection to their envelope proteins, the antigenic makeup of both classes of togaviruses is examined, and theories are put forth to explain the antibody specificities of the observed IgG responses[9]. It was originally thought that arthropod-borne viruses did not manifest any pathogenic alterations in their native mosquito carriers.

We describe cytopathologic ulcers in the mosquito's midgut, *Culisetamelanura*, 2 to 5 days after oral exposure to the EEE virus. By using light and transmission electron microscopy, it was possible to see the sloughing into the midgut cavity of epithelial cells that were highly stained and infectious, as well as the epithelium's cellular deterioration. Pathological alterations in midgut epithelium cells sometimes included loss of brush boundary and basal lamina integrity. The midgut basal lamina may be damaged, circumventing defenses against viral spread inside the mosquito and allowing for quick transfer. As an alternative, mosquito infestations may be controlled by the lumen sloughing of severely diseased midgut epithelium cells. These results cast doubt on earlier assumptions about the innocuous character of arbovirus-invertebrate host interactions [10].

## CONCLUSION

The molecular properties of togaviruses are covered in the current section. There are over 80 single-strand viral genomes in the togavirus genus. The shell of the icosahedral nucleocapsid fits snugly. These viruses are prevalent in both moderate and equatorial temperature zones, with the latter having a higher prevalence due to the constant presence of numerous hosts and carriers. Rate-limiting variables for the regional spread of viral infections are vectors, hosts, and external factors. Although the vector may graze on numerous hosts, birds, and/or animals, each variety of alpha- and flavivirus typically only affects one species of it. The majority of hosts in endemic regions are latently sick but exhibit a high enough viremia to allow the virus to spread to carriers.

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# CHAPTER 12

# AN OVERVIEW OF THE ORTHOMYXOVIRIDAE FAMILY; INFLUENZA VIRUS

Prof. Kapilesh Jadhav, Professor
Department of Biotechnology, Jaipur National University, Jaipur, India
Email Id-kapilesh@jnujaipur.ac.in

**ABSTRACT:**

The virus is a single-stranded negative-strand RNA with a width of about 100 nm that belongs to the family Orthomyxoviridae. Influenza virus is one of the viruses which belongs to the Orthomyxoviridae family. The influenza virus can infect humans and animals, where it replicates in the respiratory system. Influenza A virus's genomic diversity results from the accumulation or tolerance of small changes, a process known as antigenic drift. The process of antigenic shift allows influenza viruses to rearrange their segmented genomes and form new viruses in changed host selection and pathogenicity. In this chapter, we discussed the structure, genome, and life cycle of influenza viruses.

**KEYWORDS:**

Hemagglutinin Neuraminidase, Influenza Virus, Matrix Protein, Negative Sense, Viral Particles.

## INTRODUCTION

Orthomyxoviridae a group of negative-sense RNA viruses is known as. *Alphainfluenzavirus*, *Betainfluenzavirus*, *Gammainfluenzavirus*, *Deltainfluenzavirus*, *Isavirus*, *Thogotovirus*, and *Quaranjavirus*are just a few of the seven species that make up this family. The first four families comprise influenza viruses that infect animals, including people, as well as birds (see also avian influenza). Salmon are infected by isaviruses, while arboviruses called thogotoviruses affect both mammals and crustaceans. (such as ticks and mosquitoes). In addition to attacking animals and mammals (birds), the guarana viruses are arboviruses. All flu pandemics are brought on by the alpha influenza virus, which affects people, other animals, and wildlife. Humans and seals can contract the beta-influenza virus. Humans and swine are both infected by the gammaretrovirus. Pigs and livestock are infected by the delta influenza virus [1]. The viral coat of the influenza virus can take the shape of a sphere or a thread. The virus typically has ellipsoidal particles that are 100–120 nm in diameter or elongated particles that are 80–100 nm in diameter and up to 20 m in length.

The membrane contains about 500 unique spike-like surface extensions, each of which projects 10–14 nm from the surface and has a different surface density. The main glycoprotein (HA) spike is separated sporadically by groups of neuraminidase (NA) spikes, with a ratio of HA to NA of about 10 to 1. The nucleocapsids, which are nucleoproteins of various size classes with a loop at each end and whose organization within the virion is unknown, are enclosed by the viral envelope, which is made up of a lipid bilayer membrane in which the glycoprotein spikes are attached (Figure.1). The spiral symmetry of the linear ribonuclear proteins ranges from 50 to 130 nm in length and 9 to 15 nm in diameter. Orthomyxoviridae viruses are made up of six to eight pieces of straight negative-sense single-stranded RNA. They have a complete genome length that is 10,000-14,600 nucleotides (nt). a case of the plague For instance, a genome contains eight segments of negative-sense RNA. (13.5 kilobases total). Hemagglutinin and neuraminidase, two sizable glycoproteins located

on the surface of the viral particles, are the influenza virus proteins with the best-known properties. Hemagglutinin, a protein, facilitates viral attachment to target cells and viral DNA entrance into the target cell. By cleaving the carbohydrates that bond the mature viral particles, neuraminidase is an enzyme that aids in the discharge of offspring viruses from infected cells. Key targets for antibodies and antiviral medications include the hemagglutinin (H) and neuraminidase (N) proteins, and they are employed to categorize various influenza A viral serotypes, thus the H and N in H5N1.

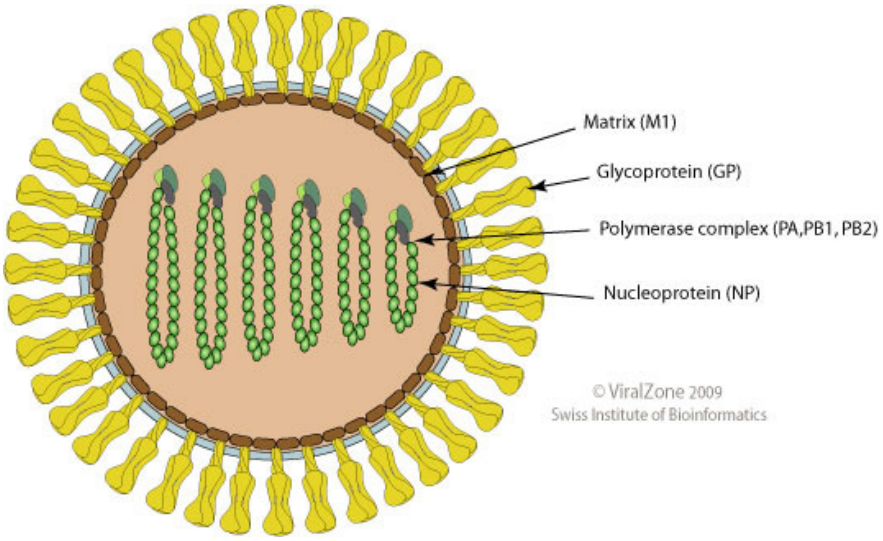


**Figure 1: Orthomyxoviridae structure: Diagram showing the structure of the Orthomyxoviridae family (Viral zone).**

The final repetitive segments in the genome sequence are duplicated at both extremities and the nucleotide terminal repetitions are present at the 5′ ends. similar 3′-terminal nucleotide sequences, shared by groups within the same family, the majority of RNA (segments), or all RNA species. nucleotide terminal repetitions at the 3′ end. Only chromosomal nucleic acid is encapsidated. Each virion may contain faulty conflicting duplicates. PB1-F2 is created in Influenza A (H1N1) from a different reading frame in PB1. Through alternative splicing, the M and NS genes generate two distinct transcripts.

Influenzavirus A, Influenzavirus B, Influenzavirus C, Thogotovirus, Quaranjavirus, and Isavirus are all members of the family Orthomyxoviridae. The Greek words myxa, which means phlegm, and orthos, which means accurate or right, were combined to create the family name. The term intended to set the orthomyxoviruses apart from the paramyxoviruses. Influenza is the Italian word for the Latin word influential, which means "influence." This word was used because it was thought that astronomical or other supernatural forces were to blame for outbreaks. In most of the globe, influenza A viruses are prevalent parasites of household chickens, equine, pigs, and people. However, they can also cause rare or locally specific illnesses and diseases in mink, seals, whales, and canines. Although influenza B viruses are known human diseases, accounts of seals contracting the illness have also been made. Even though influenza C viruses can affect both pigs and people and reassortants have been found, neither species is frequently severely harmed by influenza C viruses.

The thogotoviruses are tick-borne viruses that occasionally affect people and animals in Africa, Europe, Asia, and most recently North America. However, it is still unknown whether these viruses are dangerous. The newly discovered family Quaranjavirus contains viruses recovered primarily from insects and birds, but occasionally also from people suffering from feverish illness. Infectious salmon anemia virus, an extremely lethal condition affecting

Atlantic salmon raised in aquatic environments, is the only member of the family Isavirus. Newly identified orthomyxoviruses from bats and calves (influenzavirus D is suggested as a new family) are pending official taxonomy categorization. The practical need to evaluate the risk posed by the rise of novel variation viruses and the need to ascertain herd or community protection against previously prevalent strains to estimate vaccine needs led to the development of a categorization system for influenza viruses. Genetic shift, or chromosomal section reassortment, as well as genetic drift, or point changes (nucleotide replacements, insertions, and deletions), are both necessary for the development of mutant viruses. Before the development of improved sequencing technology, drift and shift in only the viral hemagglutinin and neuraminidase were closely watched. Now, however, other viral genes may be given more weight when determining risk. Although newly identified bat influenza viruses may raise the number of hemagglutinin subtypes, the present categorization scheme divides influenza A viruses into 16 hemagglutinin (H) and 9 neuraminidase (N) subgroups. Influenza virus subgroups (A, B, or C), hosts (swine, horse, poultry, turkey, duck, etc.) if not people, regional origin (at the provincial or state level), strain number, year of sample collection, and hemagglutinin and neuraminidase variants are all taken into account when identifying viral strains [2].

In tissues that are open to infection, the virus hemagglutinin is split into two components, HA1 and HA2, which are joined by disulfide bonds. When triggered hemagglutinin binds to sialic acid receptors on the plasma membrane, and virion attachment to cells occurs. Different orthomyxoviruses use sialic acid molecules with various carbohydrate side chains as receptors. Entry occurs through receptor-mediated endocytosis, and after the virus coat and endosomal membrane fuse, transcription complexes (nucleocapsids with accompanying RNA polymerase) are released into the cytoplasm (Figure.2). Low pH inside the endosomes causes this union, which leads to yet another structural shift in the hemagglutinin structure. RNA duplication and transcription are carried out in the nucleus by transcriptional complexes.The genome segments of orthomyxoviruses, like all other viruses with negative-sense RNA genomes, serve two purposes: first, as a template for the synthesis of messenger RNAs, and second, as a template for the synthesis of positive-sense replicative intermediate RNA, which in turn serves as a template for the synthesis of nascent RNA genomes.

The nucleus is where mRNA synthesis and DNA reproduction happen. The virus endonuclease (PB2) cleaves the 5′-methyl-guanosine cap plus roughly 10 to 13 nucleotides from diverse cellular RNAs during primary transcription, a peculiar process known as cap-snatching. The viral RNA polymerase then uses these cap structures as templates for the production of viral genes. Five of the eight gene regions that make up the influenza A and B viruses' main RNA transcripts are monocistronic and are transcribed immediately. The expression of M1 and M2 from segment 7, NS1 and NS2 from segment 8, and PB1 and PB1-F2 from segment 2 is caused by nuclear-dependent control of viral mRNA synthesis. The other three undergo splicing, each of which results in two mRNAs that are translated into different reading frames, each of which produces two proteins. Not produced by all influenza A viruses, PB2-F2 migrates into the cytoplasm and becomes linked with mitochondria, potentially increasing the death of infected cells.

A distinct method is employed by the influenza B virus, incorporating alternate translation start locations and reading frames. Viral mRNAs lack the 5′-terminal 16 nucleotides of the matching RNA genome section and are 3′-polyadenylated. Viral protein synthesis utilizes the cellular translation apparatus and takes place in the cytosol. It's interesting to note that the orthomyxoviruses have developed several methods, including frameshifting, paired stop-start translation of tandem genes, and mRNA splicing, to expand the genome's coding capacity.

Within the first few hours following infection, the proteins linked to the virion RNA are moved to the nucleus before moving on to the cytoplasm. Full-length positive-sense RNA intermediates, which, unlike the equivalent mRNA transcripts, must be devoid of 5′-caps and 3′-poly(A) tails, are necessary for the replication of RNA genome segments. These full-length positive-sense RNA templates attach to newly formed nucleoproteins, which aid in the production of developing RNA genome segments.

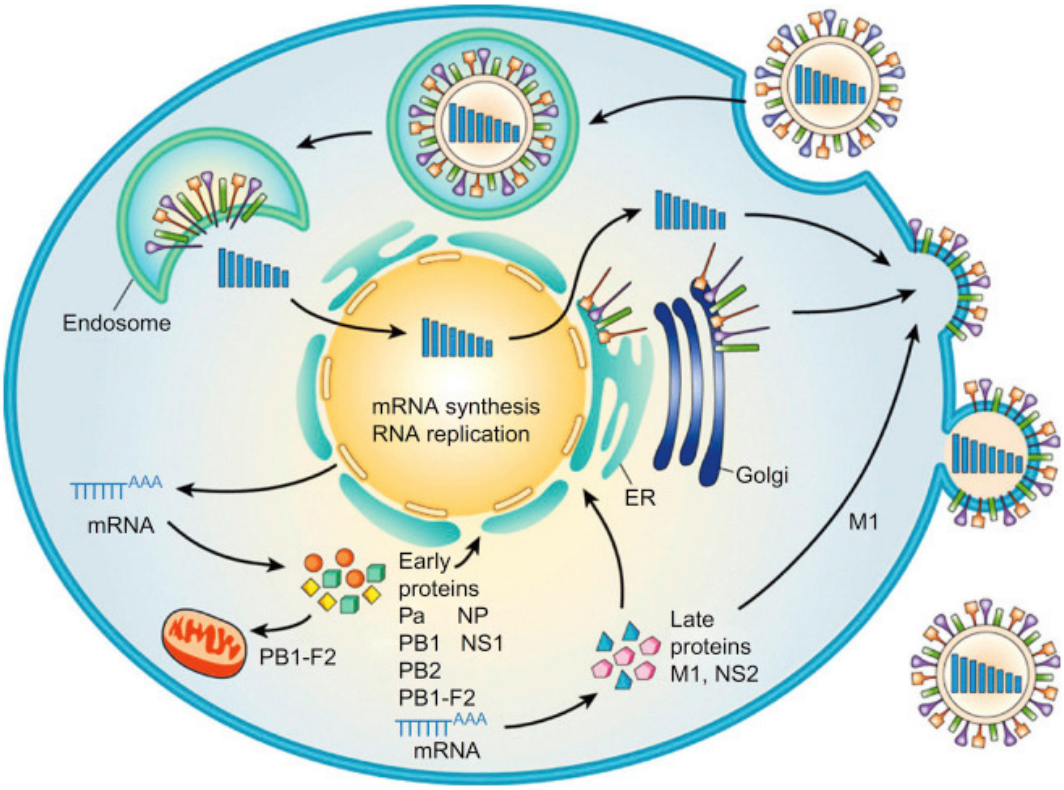


**Figure 2: Replication cycle of the influenza virus: Diagram showing the replication cycle of the influenza virus (Science direct.com).**

Late in the course of the infection, the matrix protein M1 penetrates the nucleus and attaches to developing RNA molecules, inhibiting transcription and enabling export from the nucleus and the following assembling of nucleocapsids into virions. M protein and nucleocapsids, which are positioned beneath regions of the plasma membrane where hemagglutinin and neuraminidase peplomers have already been introduced, are incorporated into budding to create viral particles. By removing plasma membrane sensors that would otherwise recover virions and keep offspring virions at the cell surface as they grow, neuraminidase peplomers assist in the "pinching-off" and release of virions. There is proof that the majority of virions contain no more than eight segments, and that at least one duplicate of each chromosomal RNA segment must be packed for a single virion to start a fruitful infection. The method by which this was accomplished was inadequately known until recently, but a better image of a mechanism, facilitated by cis-acting packing cues in the RNA segments, has started to appear. A sequence of protein-protein interactions between the virus proteins' intracellular ends is believed to be involved in packaging [3].

## DISCUSSION

There are now effective in vitro and in vivo methods available to investigate viral proteins' functions in transcription and/or reproduction, their control, the polyadenylation of viral mRNAs, the shapes of viral promoters, or the importance of non-coding viral areas for viral

replication. We recap the state of our understanding of RNA production by orthomyxoviruses in this chapter [4]. An orthomyxovirus called Infectious Salmon Anemia Virus (ISAV) infects farmed Atlantic salmon and causes a condition known as infectious salmon anemia. During an epidemic, the overall fatality in a net enclosure can range from negligible to over 90%. The virus can also potentially propagate through interaction with migratory fish when it comes to controlling activities like well-boat traffic. The ISAV and influenza viruses are comparable in many ways, including the shape of the viral particle and the method of reproduction. The majority of the changes between ISAV and influenza viruses can be attributed to the immunological responses of their respective recipient species and variations in the temperature at which reproduction takes place. Both haemagglutinating and receptor-destructive action is displayed by ISAV. The ISAV haemagglutinin molecule's variation is centered on a tiny segment near the transmembrane region. Although the purpose of this changeable area is unclear, it might be connected to the recent or continuing passage of a dividing line between species. The evolutionary distance between ISAV and the influenza viruses, as revealed by alignment studies based on genomic data, may call for the creation of a new family of Orthomyxoviridae for ISAV [5].

A challenging issue is frequently genome packing for viruses with segmented genomes. This is especially true for orthomyxoviruses like influenza, which have genomes made up of numerous negative-sense RNAs encapsulated as ribonucleoprotein (RNP) complexes. We found the crystal structure of the nucleoprotein (NP) of a fish orthomyxovirus, the infectious salmon anemia virus (ISAV), to comprehend the structural characteristics of orthomyxovirus RNPs that enable them to be packed. The ISAV-NP, which makes up the majority of the RNPs' proteins, has a bi-lobular shape akin to that of the influenza virus NP. We were able to quantify the NP RNA binding affinity as well as the stoichiometry using recombinant proteins and synthesized oligos because both RNA-free and RNA-bound ISAV NP forms stable dimers in solution. According to our study of RNA binding, each ISAV-NP only attaches 12 nts of RNA, as opposed to the 24-28 nts that the influenza A virus NP was initially predicted to bind based on the population average. Results from electron imaging and dynamic light scattering provided additional evidence for the 12-nt stoichiometry. Our results imply that NP-free RNA may exist on orthomyxovirus RNPs and that selective RNP packing may be achieved through direct RNA-RNA interactions [6].

This is consistent with the comparable shapes and measurements of ISAV and influenza virus RNPs. The virus that causes infectious salmon anemia (ISA) was first identified in 1984 in cultured Atlantic salmon. The infectious salmon anemia virus (ISAV), which is distantly related to influenza viruses in terms of development, is categorized as the parent species of the genus Isavirus in the Orthomyxoviridae family. The genome is made up of eight negative single-stranded RNA strands, and it enters and leaves cells using the same processes as influenza viruses. There are many parallels between ISAV and the influenza viruses in terms of appearance, reproduction cycles, and relationships with their respective hosts [7], even though a shared progenitor of ISAV and other families of Orthomyxoviruses could be traced back several million years. A matrix protein is encoded by many enclosed viruses. The influenza A virus employs the matrix protein M1 to help maintain the form and structural integrity of complete viruses by polymerizing them into a stiff protein layer beneath the viral membrane. It is also known that the influenza virus M1 mediates viral budding, nuclear export of the viral nucleocapsids, and the following packing of the viral nucleocapsids into immature viral particles. Even though the influenza A virus M1 (FLUA-M1) has been extensively studied, only crystal models of its N-terminal region are currently accessible. Here, we present the full-length crystal structure of the salmon anemia virus, a contagious orthomyxovirus that attacks fish. (ISAV). The ISAV-M1 structure resembles an elbow, and

its N domain is very similar to that of the FLUA-M1. Four -helices are tightly crowded together to form the C domain, which joins the N domain via a malleable linker. ISAV-M1 monomers organize into endless 2D groups in the crystal through a web of contacts involving both the N and C domains. According to the results of liposome floatation experiments, ISAV-M1 contacts membranes through electrostatic interactions, which are mainly driven by a positively charged surface loop from the N domain. The interior portion of the viral membrane is next to a layer of matrix proteins, which was discovered through the restoration of complete ISA virions using cryoelectron tomography. The 2D ISAV-M1 crystal lattice and the physical measurements of the virion-associated matrix layer are compatible, indicating that the crystal lattice is a reliable model for analyzing M1-M1, M1-membrane, and M1-RNP interactions in the virion [8].

A significant human disease capable of triggering catastrophic pandemics is the influenza A virus (FLUAV). The inherent immunological reaction to FLUAV and other human diseases has recently been studied using cotton rats as an animal model. The cell-autonomous innate immune reaction to viruses includes the interferon (IFN)-induced Mx GTPases. So, we examined the two newly discovered Mx proteins from cotton rats for antiviral action. It was discovered that the cotton rat Mx1 protein in the nucleus was a potent regulator of FLUAV, but the cotton rat Mx2 protein was inert. The rhabdovirus Vesicular Stomatitis Virus (VSV) and the bunyavirus Rift Valley Fever Virus (RVFV), which are known to reproduce in the cytosol of infected cells, were both inhibited by cotton rat Mx2, but not cotton rat Mx1. As a result, cotton rats have two Mx proteins that, depending on their subcellular location, have specific antiviral action. To investigate experimental outbreaks with FLUAV and other RNA viruses, cotton rats are an appropriate animal model [9].

The parent species of a brand-new genus in the Orthomyxoviridae family is the tick-borne Thogoto virus (THOV). Its single-stranded, negative-sense RNA genome is made up of six parts. At the 3' and 5' termini of each section are preserved areas of semi complementary nucleotides that closely match those of influenza viruses. The activity of an in vitro polymerase test based on reassembled THOV viral cores was demonstrated to be primer sensitive and to depend on an interaction between the conserved 3'- and 5'-terminal regions. The inclusion of globin mRNA stimulated transcription, which catalyzed the transcription of an additional nucleotide, corresponding to the 5'-terminal m7G cap character, to the transcripts. According to base matching and priming studies with different cap analogs, THOV transcription is preferentially started with m7GpppAm. This is the first scientific proof that THOV has endonuclease activity as a component of a distinct cap-snatching mechanism [10].

## CONCLUSION

The *Orthomyxoviridae* family, which consists of seven species, belongs to the RNA virus. The *Orthomyxoviridae* family member influenza virus causes respiratory disease in both humans and poultry. Based on their membrane glycoproteins, influenza viruses are divided into four distinct types. Rearrangements in the influenza viral DNA and a build-up of changes resulted in the development of an infectious disease. Follow-up on influenza viruses is essential due to the potential of changes or re-assortment in these viruses.

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# CHAPTER 13

# RHABDOVIRUS; CHARACTERISTICS, LIFE CYCLE, AND THE EPIDEMIOLOGY

Dr Prithpal Singh Matreja, Professor
Department of Pharmacology,Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- drpsmatreja@yahoo.co.in

**ABSTRACT:**

The Rhabdoviridae family of basic viruses includes rhabdoviruses, which are bullet-shaped encapsulated viral particles with a width of 50 to 95 nm and a length of 130 to 380 nm. These viruses only encode five proteins. One single-stranded, negative-sense RNA molecular structure with about 12,000 bases and the nucleoprotein, big, and non-structural protein molecules make up the nucleocapsid, which is a protein. The trimer of the glycoprotein makes up the membrane spike. In this chapter, we discussed the structure, life cycle, and epidemiology of the rhabdoviruses.

**KEYWORDS:**

Plasma Membrane, RNA Virus, Rabies Virus, Stomatitis Virus, Virus Particles.

## INTRODUCTION

The group Mononegavirales contains the family of negative-strand RNA viruses known as *Rhabdoviridae*. Natural hosts include animals (including mammals and people), insects, plants, fungi, and protozoans. The rabies virus, which causes encephalopathy, and vesiculoviruses, which produce flu-like symptoms in people, are diseases linked to member viruses. The term comes from the Greek word rhabdos, which means "rod" and alludes to the form of the virus particles. The 40 species in the family are primarily divided into three subfamilies [1].

History of Rhabdovirus: The Sanskrit word rabhas, which means "to commit violence," is where the word "rabies" first appeared. The Greek word "lyssa" comes from the same origin as the word for violence: These allusions to ailments brought on by animal bites reveal the awareness of rabies that existed in earlier societies. In the 23rd century BC, the Eshmuna Code of Babylon states: "If a dog is mad and the authorities have informed the owner; if he does not keep it in, and it bites a man and results in his death, then the owner shall pay two-thirds of a minimum (40 shekels) of silver. He must pay 15 pieces of silver if it kills a prisoner by biting. The use of words like "rabid dog" in well-known Greek writings from 700 BC, such as The Iliad, shows that this society was aware of rabies. Due to his incorrect assumption that rabies is an animal illness, Aristotle "exempted humans from contracting rabies" from a crazed dog's attack in the 4th century BC.

By positing that the slippery state is brought on by a "poison" in the saliva, the Roman author Cordamus showed a growing level of specific knowledge of rabies. The Roman Aulus Cornelius Celsus, a colleague of his, wrote a clinical account of rabies in people. According to Celsus, patient with rabies develops a changed mental state that makes them tortured by hunger and an "invincible repulsion toward the water." Celsus advised "[excising] bitten tissue, [cauterizing] the wound with a hot iron, and ducking the victim into a pool" as rabies treatments. In the 1800s, nitric acid was used as a substitute for heated iron in this therapy.

Additionally, consumption of crustacean eyes, cock's brain, cock's comb, and crazy dog liver was advised for rabies prevention. Girolamo Fracastoro, an Italian surgeon and scholar, wrote The Incurable Wound during the Renaissance, which details a real-life instance of rabies transmission in a person. Even today, his detailed depictions of the patient "flinging himself about like a madman, shrinking from water and all liquids" are still accurate.

Reports like the De Rebus Oceanicis et de Orbi Novi Decades Octo, which was penned by the first bishop of Oceania after the finding of the Americas, provide proof that rabies existed in the Americas and Oceania. Thus, the understanding of the existence of rabies and its contagious transfer from animals to people became increasingly obvious as the global society reached the 1800s. The dread of acquiring rabies reached panic during the nineteenth century when rabies devastated Europe, and patients who were attacked by dogs even in the remotest chance of getting the disease committed suicide. As a result, a global sphere of fear began to develop, which could only be subdued by the scientific advances that Louis Pasteur would soon oversee.

Rhabdoviruses produce individual viral particles called virions, which are made up of RNA, protein, glucose, and fat. They are shaped like complicated bacilli or bullets. Given their molecular similarity, these viruses have been grouped into a singular family. The virions are 180 nm in length and 75 nm broad. Rhabdoviruses are enveloping, have helix nucleocapsids, and have linear, 11–15 kb–long genomes. Negative-sense single-stranded RNA is the genetic carrier used by rhabdoviruses. They usually contain the genes for the following five proteins: matrix protein (M), large protein (L), glycoprotein (G), and nucleoprotein (N) (Figure.1). These protein genes are located in the chromosome in the following order: N-P-M-G-L from the 3' end to the 5' end. These five proteins are encoded in the DNA of all rhabdoviruses. Many rhabdoviruses also encode one or more proteins in addition to those mentioned above. The first four genes produce the main structural proteins involved in creating the virion membrane.

Between the rhabdovirus's virion membrane and its nucleocapsid center, there is a layer made up of the matrix protein (M). Reverse genetics experiments with the rabies virus, a member of the Rhabdoviridae family, revealed additional functions in addition to those related to virus assembly, morphogenesis, and budding off enveloped from the host plasma membrane, such as the regulation of RNA synthesis, affecting the balance of replication and transcription products. The large (L) protein performs several biochemical tasks during the production and handling of viral RNA. This L protein, which has numerous regions, is produced by the L gene. It is believed to be involved in polyadenylation action and methyl capping in addition to RNA production. During RNA genome replication and transcription, the P protein performs numerous crucial functions. The P gene codes for the versatile P protein.

P protein functions as a big protein polymerase component that is not active. It binds to the proteins N and L. There are two separate binding areas on the P protein. It can maintain the N protein in a shape that is appropriate for particular packaging by creating N-P compounds. P protein disables the cellular type 1 interferon pathway by inhibiting the actions of interferon regulatory factor 3 (IRF3) and signals transducer and activator of transcription 1 (STAT1). This conflicts with the host's natural defense system. P protein also inhibits PML's ability to operate as an antiviral. Bullet-shaped rhabdoviruses are typically found infecting plants, invertebrates, and animals, particularly fish and mammals. Rhabdoviruses lack hemagglutinating and neuraminidase functions, in opposition to paramyxoviruses. The Vesicular Stomatitis Virus serves as the model for the propagation of rhabdoviruses and all other negative-stranded RNA viruses. The following processes take place during replication: The G glycoprotein on the exterior of the virion initially attaches to host cell receptors.

Endocytosis allows the virion to penetrate the cell. The membrane of the endosome and the virus envelope join. The helix nucleocapsid is released into the cytoplasm as a consequence of the acidification of the vesicle. The virus transcriptase complex (L+P), an RNA-dependent RNA polymerase, is responsible for the transcription.

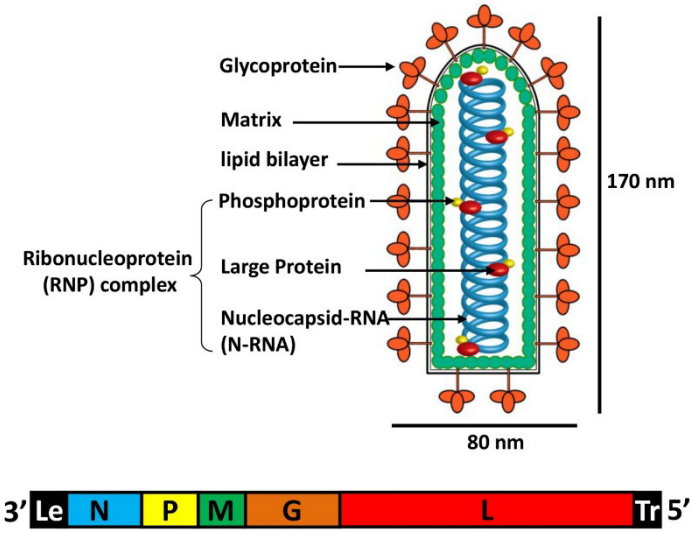


**Figure 1: Structure of the rhabdovirus: Diagram showing the Structure of the rhabdovirus(Wikipedia).**

Five distinct monocistronic mRNA species—N, P (NS), M, G, and L—are produced as a consequence of this transcription, and these five mRNA species are then transformed into five virus proteins (Figure.2). The L protein encodes a multipurpose enzyme that enables 5' capping and polyadenylation to take place at each length of non-coding intergenic segments. Since there is only one promoter, the polymerase complex moves to the following open reading frame when it comes into contact with the intergenic sequence of seven U acids.

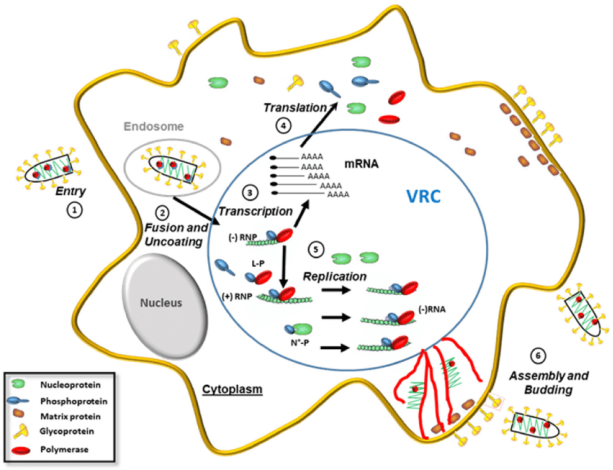


**Figure 2: Life cycle of the Rhabdovirus: Diagram showing the replication, transcription, and translation steps involved in the life cycle of the Rhabdovirus(Research gate).**

The transcription of the five genes occurs in diminishing molar abundance from N at the 3' end to L at the 5' end, which is explained by the complex's movement being less efficient than 100%. Following N protein synthesis, the virion switches to replication mode, allowing the polymerase to disregard polyadenylation, capping signals, and intergenic transcription

termination to create the corresponding positive strand of genomic RNA. This positive segment functions as a model for creating new genomes. In the meantime, the Golgi apparatus processes the G protein that is then produced by the membrane-bound ribosomes and transported to the cell surface in membrane vesicles.The virus reforms in two stages: The nucleocapsid is formed during the first step of the process, which starts in the cytoplasm with the association of the plus and minus strands of the genome with the N protein and later with the polymerase proteins L and NS. The nucleocapsid is encased and released at the cell plasma membrane during the second phase. The plasma membrane glycoprotein G-modified regions and the M protein interact to cause the nucleocapsid to spiral back into a compacted state. Once the complete nucleocapsid has been enclosed, the virus branches through the plasma membrane and is then released(Figure.2). The cytoplasmic region known as a Negri body, which functions as a viral factory and exhibits the look of a distinctive cytoplasmic inclusion body, is where the aforementioned events all take place. The behavior of VSV and Rabies viruses differ significantly in that fast cytopathology develops in VSV due to protein M's inhibition of cellular mRNA transcription, whereas rabies virus proliferation is typically non-ncytopathic. Defective Interfering Particles are necessary for the propagation of the rabies virus. In comparison to typical contagious particles, these DI virus particles are smaller, shorter, and have complicated deletion changes in their DNA. Because of their shorter RNA genomes, which require less time to reproduce, are less frequently redirected to serve as templates for the production of mRNA, and have increased attraction for the viral replicase, DIs are more common in serial passing.

All regions, except Antarctica, have rabies. In North America and Western Europe, rabies has been completely eradicated in domestic predators thanks to extensive control measures, such as immunization programs in populations of dogs and land mammals. The majority (99%) of rabies-related fatalities in humans still occur in the poor world, primarily in Africa and Asia, where the WHO believes that 59,000 people die from the disease each year. Significantly, a high percentage of illnesses affect children under the age of 16, frequently in underdeveloped remote regions where vaccines and postexposure treatments are difficult to obtain. There is little statistical data on rabies transmission in places where it is prevalent, and the information that does exist is typically based on clinical accounts and test findings from samples that were presented to public health or veterinarian diagnosis labs. In areas where rabies is a common disease, there is typically a general dearth of testing tools, so the real number of rabies cases is probably greatly underestimated. There are no statistics on the number of household and untamed animals infected.

In prevalent regions where dog-derived rabies predominates, sylvatic rabies, which refers to the disease's transmission among animals, typically presents less of a danger to the human population. All animals can contract rabies, but based on the area, sylvatic transmission is typically limited to a few specific species. For example, rabies is reported in red foxes(Vulpes vulpes) in continental Europe, Canada, and southern states of the United States, in arctic foxes(*Vulpes lagopus*) in Arctic areas, in the yellow mongoose(*Cynictispenicillata*) populations of the West Indies and Africa, in raccoon dogs(*Nyctereutesprocyonoides*) and ferret badgers(*Melogalemoschata*) in China, and in African wild dogs(Lycaon pictus) and Ethiopian wolves(*Canis simensis*) in Africa. Reintroduction of the illness from common regions can take place in regions devoid of soil rabies. A rabid Algerian canine that was transported into France in 2015 and a rabid dog that attacked several persons in Spain in 2013 both serve as recent instances of disease invasions into the European Union. 26 instances of rabies in humans were recorded in the UK between 1946 and 2016. Most of these instances were obtained overseas. One noteworthy exception, though, was the death of a bat rescuer in Scotland in 2002 as a result of infection with the locally prevalent European bat lyssavirus

type-2 (EBLV-2). Terrestrial rabies has been eradicated from most areas of Western Europe. Approximately 80,000 rabies instances have been recorded in Europe over the past ten years, with the majority occurring in Eastern European nations like the Russian Federation (34.3%), Ukraine (24.5%), Belarus (10.3%), Croatia (6.0%), Romania (5.8%), Lithuania (5.6%), and Turkey (5.0%). Out of these, 45% of cases were found in tamed animals, 55% in natural species and only a small number of cases were found in humans and bats. Except the Russian Federation and Turkey, there has been a marked decline in the number of recorded rabies cases in these nations in recent years [2].

## DISCUSSION

One of the most environmentally varied groups of RNA viruses, the Rhabdoviridae, infects a broad variety of species, including marsupials, birds, fish, invertebrates, plants, and mammalian mammals. The variety and intricacy of their genomes are mirrored in their biological diversity, which has been shown by the growing availability of full nucleotide sequences for rhabdoviruses. The five universally shared classical rhabdovirus structural protein genes—N, P, M, G, and L—are overprinted, overlapping, and intermingled with a plethora of new and varied auxiliary genes. Most, however, produce proteins with unclear functions that are unconnected to any other proteins that are currently known. In addition to providing opportunities for the development of new anti-viral therapies, understanding the functions of these accessory genes and the methods by which rhabdoviruses use them to engage, divert, and re-direct cellular processes may also reveal aspects of cellar function with wider implications in biology, agriculture, and medicine [3].

Rhabdoviridae, a big family of rhabdoviruses, includes people as well as other animals, insects, and vegetation as hosts. There are at least 90 rhabdoviruses that can attack plants, and several of them are significant agricultural diseases from a commercial standpoint. A small number of potential plant rhabdoviruses are transmitted by mites, and all final plant-infecting and many vertebrate-infecting rhabdoviruses are consistently carried by insect carriers. Plant rhabdoviruses reproduce in their invertebrate and plant hosts, and each viral species is spread by one or a small number of closely related bug species, primarily aphids, leafhoppers, or planthoppers. Here, we give a summary of the interactions between plant rhabdoviruses and the insects that serve as their hosts as well as how these interactions relate to those between viruses that attack vertebrates and the Sigma rhabdovirus that affects Drosophila flies. We concentrate on the cellular and molecular characteristics of the uniqueness of the vector/host, the transmission obstacles, and the viral receptors in the vectors. We also quickly go over recent developments in our knowledge of rhabdovirus-plant interactions [4].

A varied and widely dispersed class of encapsulated viruses called rhabdoviruses form and emerge from the plasma membrane of their target cells. We have been able to improve upon current models of rhabdovirus budding and describe in greater detail the interplay between viral and cellular components involved in the budding process as a result of recent advances in the identification of domains on both the envelope glycoprotein and the matrix protein of rhabdoviruses that contribute to virus assembly and release. In this review, we go over the steps in rhabdovirus assembly, starting with genome encapsidation, the association of nucleocapsid-matrix protein pre-assembly complexes with the inner leaflet of the plasma membrane, how condensation of these complexes may happen, how microdomains containing the envelope glycoprotein facilitate bud site formation, and how various forms of the matrix protein may take part in virion extrusion and release [5].

The neurotropic rabies virus (RV), which is directly passed between animals, and the insect-borne vesicular stomatitis virus (VSV) are among the significant diseases of people, cattle,

and crops that belong to the family Rhabdoviridae. The RNA genes, proteins, and viral particles of VSV and RV are organized very similarly, but their cell biology differs in several ways, especially in how they interact with the cellular host defense. The intracellular RNA helicase/translocase RIG-I detects infection with both rhabdoviruses via viral triphosphate RNAs, but the viral responses to suppress the reaction are different. Due to numerous actions of the matrix (M) protein that influence host polymerase functions and mRNA nucleus export, VSV infection is marked by a fast general cessation of host gene expression, serious cytopathic effects, and high-level viral reproduction. On the other hand, maintaining the viability of host cells, especially neurons, is essential for RV proliferation and dissemination. RV phosphoprotein (P) has evolved separate roles to obstruct the stimulation of IRFs and STAT signaling, even though a general cell shutoff by RV M is not seen. The utilized molecular processes demonstrate the development of IFN inhibitors to particularly support viral survival in the natural niches [6]. They vary from those of the paramyxovirus P gene products performing comparable functions.

An RNP complex is packaged by the negative-strand RNA virus known as rhabdovirus. The nucleoprotein fully encapsidates the DNA that makes up the RNP. (N). Despite their absence of substantial similarity in amino acid sequence, structural studies of the RNA-nucleoprotein complexes from two members, vesicular stomatitis virus (VSV) and rabies virus (RABV), showed highly conserved features of folding, RNA binding, and assembly. The positively charged residues that interact with the phosphate groups are at various locations in the RNA binding pocket, which is sandwiched between two conserved domains created by -helices. However, various positions give varying interpretations of the preserved structure of the intermolecular contacts between N molecules. In the molecular structure, the RABV N-RNA complex has a greater curve than the VSV N-RNA complex. The RNA bases can stack more compactly due to the loosened curve, and at the same time, the helices close to the C-terminus shift into the open area to cover the attached RNA. This could explain why the RNP can take on various conformations, such as a flexible linear shape once it enters the cytoplasm from being compressed as a superhelix in the virion [7].

Rhabdoviruses are single-stranded RNA-containing, membrane-enveloped viruses that are comparatively straightforward. The chromosomal RNA is non-infectious and is equivalent to messenger RNAs (mRNAs) in the negative sense. To produce the mRNAs, the viral particles must therefore possess an RNA-dependent RNA polymerase. (Baltimore et al., 1970). Rhabdoviruses are found to attack plants, animals, and mammals and have a bacilliform, bullet-, or cone-shaped appearance. McSharry has examined how different rhabdoviruses are made. (1979). The genetic RNA and protein form a spiral nucleocapsid center within the viral particles. The nucleocapsid is typically discovered to be linked with three proteins known as N (nucleocapsid), NS (initially signifying nonstructural), and L (large). Within the membrane, the sheath is another matrix (M) protein that may associate with both the membrane and the nucleocapsid nucleus. The membrane is covered by a single species of glycoprotein (G), which also creates spikes on the exterior of the viral particle [8].

The fish rhabdovirus viral hemorrhagic septicemia virus's entire nucleotide sequence has been identified. The genome is 11158 nucleotides long and has six long open reading frames that each code for a different protein, including the polymerase L, glycoprotein G, matrix protein M, phosphoprotein P, and nucleoprotein N. The sequence of the genes is 3′-N-P-M-G-NV-L-5′. After RNA-oligonucleotide binding, also known as RACE, the precise 3′, and 5′ ends were identified. As in other rhabdovirus genomes, they exhibit inverted matching. The significant similarity between nucleotide and derived amino acid sequences and matching sequences in the related fish rhabdovirus contagious hematopoietic necrotic virus can be seen

[9]. A new rhabdovirus (Bas-Congo virus, or BASV) linked to a 2009 epidemic of three human cases of severe hemorrhagic fever in Mangala hamlet, Democratic Republic of Congo (DRC), Africa, was found using deep sequencing. The cases, which manifested over three weeks, were distinguished by a sudden start of the illness, a high temperature, nasal bleeding, and, in two patients, mortality within three days. Acute blood from the lone survivor contained 1.09 106 copies of BASV, and 98.2% of the genome was later de novo constructed from approximately 140 million sequence sequences. According to phylogenetic research, BASV is extremely diverse and only matches 34% of its amino acid sequences with other rhabdoviruses. Both the survivor and a healthy caregiver who was directly caring for him had high convalescent neutralizing antibody titers of >11000, indicating the possibility of BASV spread from person to person. Uncertainty exists regarding the virus' exact method of propagation as well as its native animal storage host or invertebrate carrier. A new human virus called BASV has been linked to severe hemorrhagic fever in Africa [10].

Alpha/beta interferon induces the synthesis of three Mx proteins in rat cells. The three proteins in question are taken from three different genes, according to a sequencing study of the respective cDNAs. A rat cDNA that is most similar to the mouse Mx1 cDNA and codes for a nucleus protein that, like the mouse Mx1 protein, suppresses influenza viral proliferation is known as Mx1. The difference between this protein and rat Mx1 protein is that it also prevents the rhabdovirus vesicular stomatitis virus (VSV). A second rat cDNA, which has a stronger affinity for the mouse Mx2 cDNA, controls the production of an intracellular protein that prevents VSV but not the influenza virus from spreading. The third rat cDNA produces an intracellular protein that is identical to the second in all but eight locations and exhibits no discernible antiviral activity. The study of the mouse Mx1 protein did not predict the antiviral specificities of the rat Mx proteins, according to these findings [11].

## CONCLUSION

The Rhabdoviridae family virus rhabdovirus is discussed in this chapter. Numerous invertebrate species are among the many host species that are infected by rhabdoviruses. Rhabdoviruses rarely switch between distantly related hosts, which is consistent with earlier findings that both invertebrate and vertebrate rhabdoviruses (such as the rabies virus in bats) exhibit a declining capacity to infect hosts that are more distantly related to their natural host. To anticipate important biological characteristics in other classes of viruses where the present information is lacking, another evolutionary method could be expanded.

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# CHAPTER 14

# AN OVERVIEW OF THE RETROVIRUS GENOME AND THE MOLECULAR MACHINERY USED FOR THE REPLICATION

Dr Shilpa Patrick, Professor
Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- drshilpapatrick@gmail.com

**ABSTRACT:**

Retrovirus is belong to the family of *Retroviridae* is having RNA as their genetic material. During the infection to the host cell, they convert their genetic material RNA into the Double stander DNA in their genome. As an advantage in their genome machinery, they spread from cell to cell as the RNA molecule but it also leaves a duplicate of its DNA in each affected cell's chromosomes, where it can pass from one cell generation to the next. In this chapter, we discussed the characteristics of the retrovirus genome, their replication cycle, and the virus responsible for the disease in humans.

**KEYWORDS:** Endogenous Retroviruses, Host Genome, Life Cycle, Reverse Transcription, RNA Genome.

## INTRODUCTION

There are 7 species in the family Retroviridae. Because BIV is the only member of the Lentivirus family of retroviruses identified from bovine, it has many characteristics in common with other members of this genus. In contrast to most biological systems, all retroviruses are protein-enveloped, positive-stranded RNA viruses that contain the RT enzyme, which is capable of mediating the transfer of genetic material from RNA to DNA. To incorporate into the host genome, retroviruses have a DNA intermediary in their life cycle. Retroviruses can be further divided into groups according to how they spread horizontally or vertically (via the genome). Most often, the appearance of retroviruses as seen under an electron microscope, a few aspects of their biology and pathobiology, and how their genome is organized are used to classify them into one of the three retrovirus subfamilies. The lentiviruses are exogenously obtained retroviruses that are frequently linked to sluggish, enduring, and life-threatening illnesses[1]–[3].

A retrovirus is a form of the virus that alters a cell's genome by inserting a DNA duplicate of its RNA genome into the target cell's DNA. After entering the cytosol of a recipient cell, the virus employs its reverse transcriptase enzyme to create DNA from its RNA genome, which is the opposite of the typical pattern. (backward). An integrase enzyme then incorporates the new DNA into the genome of the recipient cell; at this stage, the retroviral DNA is referred to as a provirus. The host cell then handles the viral DNA as if it were a component of its genome, interpreting and transcribing both the viral and cellular genes to create the proteins needed for the virus's replication. Serious illnesses are brought on by many retroviruses in people, other animals, and wildlife. Retroviruses can be divided into three main subfamilies. The human T-lymphotropic virus (HTLV), which causes a specific form of leukemia in people, and the murine leukemia viruses (MLVs) in rodents are examples of oncoretroviruses (retroviruses that cause malignancy). HIV-1 and HIV-2 are lentiviruses (slow viruses), which are the root of acquired immune deficiency syndrome (AIDS) in people. Spumaviruses (foamy viruses) are harmless and have no connection to any human or animal diseases. Retroviruses are icosahedral-enclosed viruses that are between 100 and 120 nanometers in

size. The virion is enclosed in the envelope. There are several spines with glycoproteins on the exterior of the virion(Figure.1). The virus covering contains many proteins; usually seven intracellular proteins, four of which are structural and three of which are catalytic. Reverse transcriptase, DNA endonuclease (integrase), and protease are the enzymes found in the virion. Additionally, certain cellular tRNA molecules are present in the virion. In addition to all of these, the genome, which is symbolized by RNA, is located in the middle.

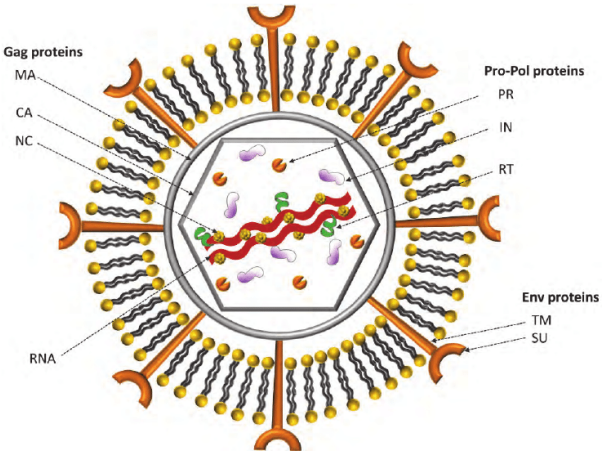


**Figure 1: Structure of the retrovirus: Diagram showing the structure of the retrovirus (Research gate).**

These traits include(1) The structural proteins encoded by the gag gene, (2) Reverse transcriptase and DNA endonuclease (integrase)-encoding Pol genes, and (3) The membrane protein-encoding Env gene. A fourth gene found in some retroviruses, such as the Rous sarcoma virus, is thought to play a role in cellular change and malignancy. Figure 2 depicts a genomic diagram of a normal retrovirus genome.

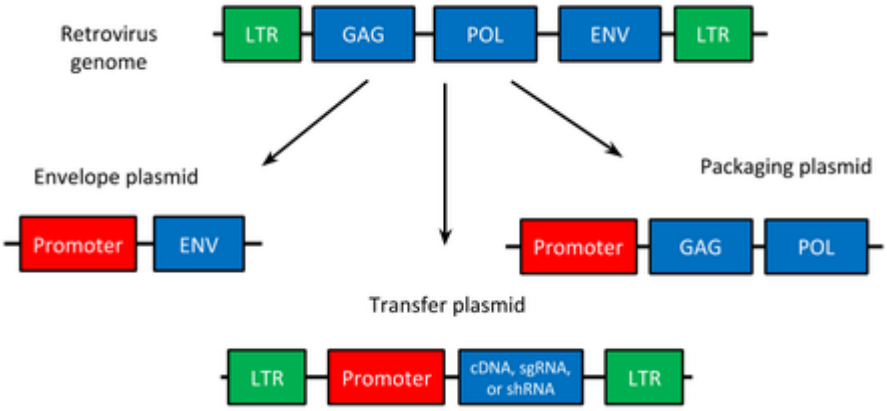


**Figure 2: Retrovirus genome: Diagram showing the genome of the retrovirus(Addgene).**

When retroviruses have incorporated their genome into the cell line, their genome is passed on to a subsequent generation. In contrast to foreign retroviruses, these endogenous retroviruses (ERVs) now make up 5-8% of human DNA. Most insertions are referred to as "junk DNA" because they are thought to have no known purpose. Many indigenous retroviruses, however, have crucial functions in the biology of the host, including the regulation of gene transcription, cell union during placental development during embryonic hatching, and resilience to foreign retroviral infection. Although endogenous retroviruses have not yet been shown to play a causative role in this type of illness, they have also attracted particular interest in the study of immunology-related disorders like inflammatory

diseases like multiple sclerosis. Reverse transcriptase transcribes RNA into DNA, whereas transcription was once believed to only happen from DNA to RNA(Figure.3). The word "retro" in the word "retrovirus" alludes to this reversal of the normal path of transcription (creating DNA from RNA). It still adheres to the fundamental tenet of molecular biology, according to which data can be moved from one nucleic acid to another but cannot be returned from a protein to a nucleic acid or protein to a protein. Almost all organisms have been discovered to have reverse transcriptase activity outside of retroviruses, allowing for the creation and introduction of novel retrotransposons into the host genome. These inserts are translated into new RNA molecules that infiltrate the cytoplasm by the host's enzymes. The translation of some of these RNA molecules into virus proteins follows. Gag and Gag-Pol polyproteins are created by the translation of the proteins encoded by the gag and pol genes from genome-length mRNAs.

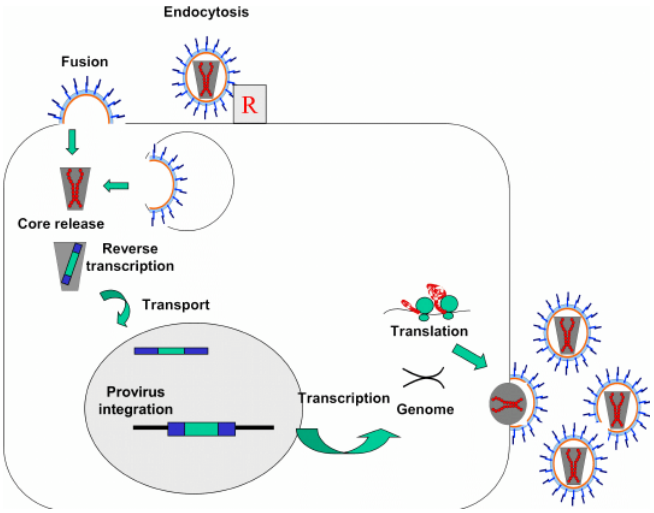


**Figure 3: Life cycle of retrovirus: Diagram showing the lifecycle of the retrovirus (Research gate).**

For instance, the pol gene is translated into molecules of reverse transcriptase, and the gag gene is translated into molecules of the capsid protein. Retroviruses have sophisticated mechanisms to make the necessary quantity of each because they require a lot more Gag proteins than Pol proteins. As an illustration, following the production of Gag, nearly 95% of the ribosomes stop translating, while the remaining ribosomes carry on translating to produce Gag-Pol. The env gene is transcribed from altered mRNAs into molecules of the envelope protein in the rough endoplasmic reticulum, where glycosylation starts. A host enzyme splits the envelope protein molecules into surface glycoprotein and transmembrane glycoprotein once they reach the Golgi complex. Following additional glycosylation, these two glycoprotein molecules are carried to the plasma membrane while maintaining a close association. Due to the peculiarity of creating DNA from RNA, a retrovirus must "bring" its reverse transcriptase into its capsid if it is to be able to use the affected cell's enzymes to complete the job.

Protease and reverse-transcriptase inhibitors are industrial medicines that are manufactured to target particular locations and patterns within the relevant enzymes (Figure.3). However, because the DNA regions that code for the protease and reverse transcriptase rapidly change, these medications may soon lose their effectiveness. To prevent drug targeting by missing the sites that the drug truly targets, these changes in bases cause particular codons and sites with the enzymes to change. A retrovirus mutates frequently because reverse transcription lacks the normal DNA reproduction correction process. This makes it possible for the virus to

develop antiviral drug resistance rapidly and hinders the creation of efficient retrovirus inhibitors and immunizations. Some retroviruses, like the Moloney retrovirus, have a problem in that transmission requires that cells be constantly growing. As a consequence, cells like neurons are highly immune to retrovirus invasion and transformation. This raises the possibility that insertional mutation brought on by incorporation into the host DNA could result in leukemia or cancer. This contrasts with Lentivirus, a family of Retroviridae, which can incorporate its RNA into the DNA of a recipient cell that is not replicating.

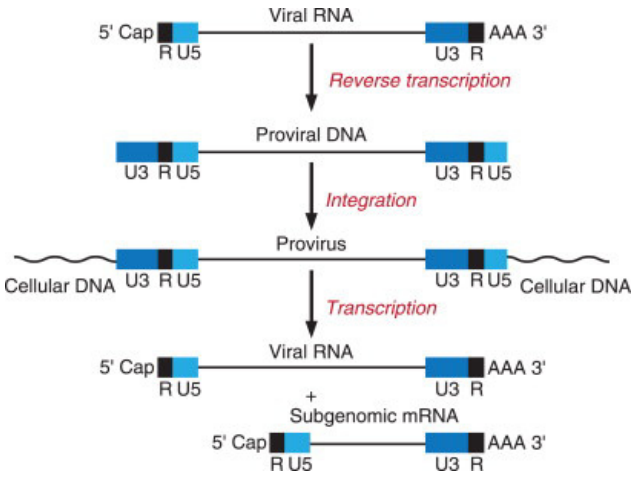


**Figure 4: Provirus: Diagrame showing the mechanism of the provirus formation in the retrovirus (Science direct.com).**

Due to the presence of the U3-R-U5 sequences, also known as long terminal repeats, at each of the terminals, the DNA created after reverse transcription (the provirus) is lengthier than the RNA genome. (LTR) (Figure.4). The additional U3 sequence is present at the 5' terminal while the U5 sequence is present at the other terminal. LTRs have the ability to transmit instructions for the execution of critical duties, such as the start of RNA synthesis or control of transcription rate. LTRs are able to regulate reproduction in this manner, and as a result, the complete virus life cycle. The non-integrated retroviral cDNA, despite being in the nucleus, is a very unreliable medium for transcription. For retroviral genes to be expressed permanently and effectively, an incorporated provirus is required. As a provirus that can be transmitted to offspring cells, this DNA can be integrated into the host genome. The host genome contains a random insertion of retrovirus DNA. It can therefore be introduced into oncogenes. Some retroviruses can change healthy cells into cancerous cells in this manner. Some proviruses take a while to become active in the cell before the environment change which causes them to do so[4]–[6].

Three types of retrovirus-affected humans. A person's immune system is attacked by HIV. The CD4 T-cells that are in charge of warding off pathogens are destroyed. As a result, a person's immune system progressively deteriorates. It can be passed from a woman to an infant during delivery or nursing, through injections, bodily secretions, or from one person to another. Medication and therapy won't be able to fix it. The final step of HIV transmission, AIDS, results in death for the patient. Types I and II of the HTLV (Human T-cell Lymphotropic Virus) are closely linked to one another. Acute T-cell leukemia is a disease that the HTLV I virus can cause in an individual. It results in a neural condition and has an impact on the spinal nerve. It was the first human retrovirus to be identified, and transmission methods include breastfeeding, intercourse, sharing needles, and blood transfusions.

In addition to blood malignancies and brain conditions, HTLV II is linked to both. However, little is understood about this particular viral variety. The genetic material from those

deceased viruses, whose genetic makeup is comparable to that of the living retroviruses, is what makes up endogenous retroviruses. As people have evolved, these diseases have spread among us. They are handed down from one generation to the next and makeup 5% of the human DNA.

## DISCUSSION

The vast family of contagious organisms known as the retroviruses (Retroviridae) that they belong to share a similar virion structure and method of reproduction. Most mammalian species where that have been sought after for isolation have yielded retroviruses, which have been discovered to exhibit a surprising variety in their relationship with the host. A summary of some of the more prevalent viruses is provided in Table I. At one extreme of the range, infections with some retroviruses can result in clinical conditions that are all universally deadly, such as AIDS, various types of cancer, neurodegenerative illnesses, and other conditions. On the other hand, some retroviruses only cause an innocuous viremia with no overtly harmful side effects. They can even establish DNA in the germ line and transmit from generation to generation as "endogenous" viruses. There is a very thin line separating indigenous viruses from the numerous retrotransposable elements found in the genomes of all organisms. (Chapters 1 and 4). The basic characteristics of retroviruses, the composition of their virions, and their categorization will be covered in this volume. Its application will be restricted to substances that can be proven to be pathogens.

Retroviruses were first identified as contagious cancer-causing agents nearly 80 years ago, and they are now widely used in modern biology for a variety of purposes. (i) Several processes take place during the virus life cycle, including the reverse transcription of the viral RNA genome into DNA, the orderly integration of viral DNA into host chromosomes, and the use of host mechanisms for gene expression in response to viral signals, provide general information about eukaryotic cells and viruses. (ii) Cellular genes are typically transduced or activated by retroviruses, and the separation of those genes has given the scientific community access to many of the molecular elements now thought to be involved in the regulation of healthy development and human disease. (iii) Retroviruses are the cause of two newly identified human pathogens, adult T cell leukemia/lymphoma and acquired immunodeficiency syndrome (AIDS), as well as many significant animal diseases. (iv) Retroviruses are hereditary carriers by nature, and they can be altered to act as carriers for both medicinal and experimental reasons. (v) Insertion of retroviral DNA into host chromosomes can be used to identify cell lines and to create embryonic mutations. Although there has been a significant advancement in these and other retrovirus-related biological fields over the past 20 years, there are still numerous theoretical and real issues that need to be resolved[7].

A total of 22 out of 45 people with AIDS who were arbitrarily chosen for testing also tested positive for other San Franciscans for infectious retroviruses. The AIDS-associated retroviruses (ARV) that were specifically examined had a type D shape, a reverse transcriptase that was Mg2+-dependent, and cytotoxic effects on cells. The HUT-78 mature human T cell type is a well-established platform for viral propagation. The lymphadenopathy-associated retrovirus identified in French AIDS patients causes them to cross-react with antiserum. All 86 AIDS cases and a sizable portion of the other 88 gay males in San Francisco tested positive for ARV antibodies. This finding suggests the ubiquitous prevalence of these lymphocytopathic retroviruses and their close connection with AIDS.

Endogenous retrovirus (ERV) genes make up 10% of the mouse genome, and the majority are leftovers from long-ago germ-line viruses. The abundance of various wild mouse species

and subgroups as well as the continuing study of the Mus genome sequence have helped us better understand the three different types of ERVs, which are negatively associated with their copy number. The three ERV groups still contain live rodent ERVs, in contrast to the virtually dead human ERVs. Over the course of evolution, host-virus interactions have shaped the distribution and diversity of ERVs, but ERVs have also played a significant role in shaping the mouse genome by co-opting host cells as retroviral resistance genes, changing host genes through insertional mutagenesis, and adding novel regulatory and coding sequences. We examine the evolutionary processes that have led to resilient cohabitation. The Betaretrovirus genus contains type D retroviruses, which are categorized in the family Retroviridae.

These viruses have positive strands of RNA and reproduce by reverse transcription to create an intermediary form of proviral DNA that can chemically bind to the host genomic DNA. Similar to the type B mouse mammary tumor virus (MMTV), M-PMV preassembles juvenile capsids (also known as intracytoplasmic A-type particles, or ICAPs) within the cytoplasm of infected cells. The adult external virion has a distinct shape than MMTV, with a center nucleoid akin to type C retroviruses and a much less thick glycoprotein border. With these variations, a novel structural family of retroviruses known as type D was identified as being of monkey origin[8]–[10].

## CONCLUSION

Retroviruses have a coat and a diploid RNA genome that typically ranges from 7 to 11 kb. The capacity to transmit hereditary material from RNA to DNA is a trait shared by all retroviruses. A common method of genetic interchange is exemplified by the development cycle of retroviruses, which involves reverse transcription, chromosome fusion, and transcription of the viral DNA back into RNA. Retrovirus research has significantly influenced genetics, molecular biology, nanotechnology, and biological medicine.

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# CHAPTER 15

# AN BRIEF OVERVIEW OF THE HEPADNAVIRUSES

Mayur Porwal, Associate Professor
Department of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id-mayur.porwal1@gmail.com

**ABSTRACT:**

A double-stranded DNA genome of the Hepadnaviruses, which are small enclosed viruses, belongs to the Hepadnaviridae family. Small DNA viruses known as hepadnaviruses, also known as para-retroviruses, reproduce through an intermediary RNA molecule. Three sets of proteins were present in hepadnaviruses for transcription and reproduction. Reverse transcription within nucleocapsids is used for genome reproduction in the host cytosol. The genome and the molecular machinery of the hepadnaviruses used for their replication were covered in this chapter.

**KEYWORDS:**

Aminoacid, Circular DNA, Hepadnavirus genome, Reverse transcription, Viral DNA.

## INTRODUCTION

*Hepadnaviridae* is a family of viruses. Natural carriers include people, primates, and animals. There are presently 18 species in this family, split among 5 families. The Hepatitis B virus is its most well-known component. Hepatocellular carcinomas (chronic infections), cirrhosis, and liver diseases like hepatitis are among the illnesses connected to this family. It is the only recognized genus within the Blubervirales group [1].Hepatitis A, a virus belonging to the *picornaviridae*family, was the first recognized hepatitis with a viral etiological agent, even though liver illnesses contagious among human groups were discovered early in the annals of medicine. Through its poisoning of measles, mumps, and yellow fever immunizations in the 1930s and 1940s, the Hepatitis B Virus (HBV) was discovered as a different illness from Hepatitis A. As a binding substance, these immunizations comprised human blood that had been exposed to HBV.

The flavivirus hepatitis C was discovered a few decades after HBV was discovered as a novel DNA virus in the 1960s. Blumberg and coworkers discovered HBV in the blood of an Aboriginal transfer patient, establishing it as the "Australia agent" for the first time in the laboratory. Blumberg won the 1976 Nobel Prize in Medicine for his efforts. The genome of hepadnaviruses is among the tiniest of all known viruses, and it takes the shape of a tiny, circular DNA structure that is partly single-stranded in virions (Figure 1). The single-stranded sections in the DNAs of the three mammalian viruses range in length from roughly 15 to 60% of the circular length of various molecules. According to reports, the single-stranded section of the DHBV is much smaller, and virions contain many full-length molecules.

As a result, these DNAs are made up of two strands: a long (or minus) strand that is constant in length across all molecules (between 3,300 and 3,300 bases in different viruses), known as the minus DNA strand, and a short (or plus) strand that varies in length across molecules, between 1,700 and 2,800 bases. The single-stranded section of the viral DNA is repaired by a DNA polymerase activity in the virion, resulting in completely double-stranded molecules. This process starts DNA synthesis at the 3' end of the short strand, which happens at various locations within a particular area (50%) of the DNA in various structures. When the short

strand's distinctive 5' end is reached, DNA production comes to a close. In human viruses , a break is present at a specific location about 225 base pairs (bp) from the 5' end of the plus strand and at 69 bp in the DHBV DNA, indicating that the viral strand is not a complete circle. The minus DNA strand of DHBV and GSHBV has approximately 9 nucleotide terminal repetitions (r), which may be significant in circularizing the DNA and in template swapping during synthesis of the plus DNA strand (see "Genome Replication"). By carefully heating the 225 bp area between the 5' extremities of the short and long strands under the right circumstances, mammalian viruses' circular DNA can be transformed into a linear shape with single-stranded continuous ends. By reassociating the complete single-stranded extremities, the resulting linear shape can be circularized [2].

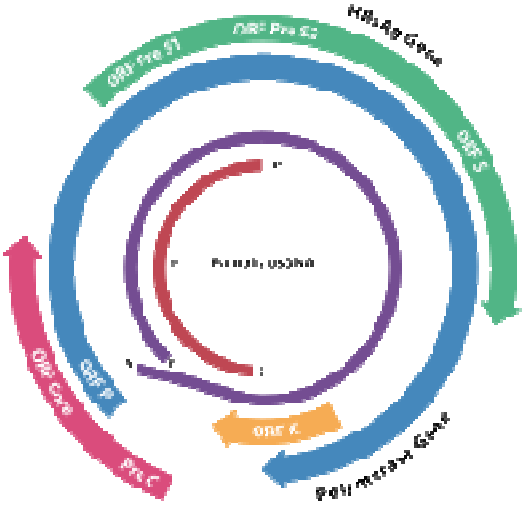


**Figure 1: Genome of the hepadnaviruses: Diagram showing the genome of the hepadnaviruses(Wikipedia).**

Hepadnaviridae family members do not co-opt host apparatus as some other viruses do; instead, they encode their polymerase. The only other human-pathogenic virus family that encodes a polymerase with this capability is Retroviridae. This enzyme is also unique among viral polymerases in that it has reverse transcriptase activity, RNAse activity (used when the DNA genome is synthesized from pgRNA that was packaged in virions for replication to destroy the RNA template and produce the pdsDNA genome), and DNA-dependent-DNA-polymerase activity. (used to create cccDNA from pdsDNA in the first step of the replication cycle). The virus preS1, preS2, and S genes are used to make the components of the hepatitis membrane proteins. All three components are found in the L envelope protein, which stands for "large". The M protein, which stands for "medium," only includes preS2 and S. Only the S (for "small") protein is present.

These membrane protein components' DNA segments share the same frame and stop codon, resulting in stacked transcripts on a single open reading frame. The pre-S1 is encoded first (nearest the 5' end), then the pre-S2, and finally the S. All three genes are present in the mRNA created from the start of the pre-S1 region, which results in the production of the L protein. The finished protein only includes the pre-S2 and S components when the mRNA begins after the pro-S1 at the commencement of the pre-S2, making it an M protein. Because it is written most closely to the 3' end and originates from the shortest mRNA, the tiniest envelope protein which only contains the S subunit is produced most frequently. These envelope proteins have the ability to come together without the help of the viral capsid and DNA to form non-infectious virus-like particles that give the virus a pleomorphic look and

stimulate the host's immune system. Hepadnaviruses propagate using an intermediary made of RNA. A brief 3- or 4-nucleotide primer is chemically joined to the reverse transcriptase. Most hepadnaviruses can only reproduce in particular hosts, which makes in vitro studies very challenging.

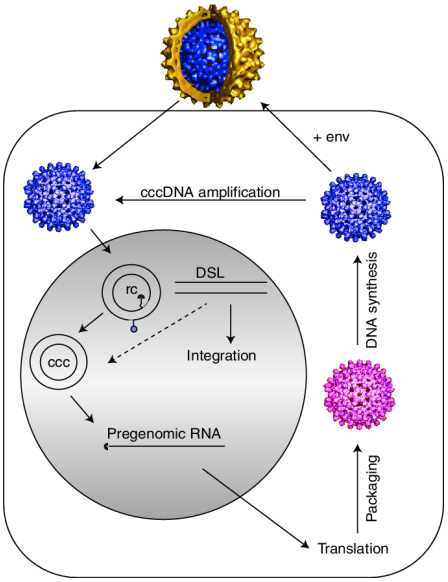


**Figure 2: Life cycle of the Hepadnaviruses: Diagram showing the life cycle of the Hepadnaviruses (Research gate).**

The virus's central particle penetrates the cytosol of the cell after the virus attaches to particular receptors on the cell (Figure.2). The partly double-stranded DNA is then moved to the nucleus, where the virus enzyme "repairs" it to create a full circular dsDNA gene. Pregenomic RNA (pgRNA) is then released from the nucleus following the synthesis of the genome by the host cell RNA polymerase. A formed viral capsid that contains the viral polymerase has the pgRNA introduced into it. By acting first as an RNA-dependent DNA polymerase and then as an RNAse to destroy the pgRNA mRNA, the polymerase inside this shell converts the genome from RNA to pdsDNA. These fresh virions either depart the cell to spread the infection to other cells or break apart right away to allow fresh viral genes to access the nucleus and spread the infection. The virus exit from the cell occurs through budding.

The spread of hepadnaviruses among their native hosts, including people, non-human animals, and wildlife, as well as between different types of organisms is a subject of research in the field of virology. A group of viruses known as hepadnaviruses can attack the livers of both people and animals. They are Group VII viruses that use reverse transcriptase to reproduce their double-stranded DNA genes. They have differentiated themselves sufficiently to be included in the family Hepadnaviridae due to their distinctive reproduction strategy, extremely tiny genomes, and extremely restricted host and tissue tropism. Two families have been recognized: Hepatitis B virus is a form of orthohepadnavirus. Duck hepatitis B virus is a form of avian hepatitis virus.

## DISCUSSION

A significant number of blood samples that had cross-reacted with human HBV proteins led to the suspicion that 195 formerly confined orangutans had a high frequency (42.6%) of hepatitis B virus (HBV) infection. Such virus illnesses were thought to have been acquired from people while held captive. The discovery of two wild orangutans with HBV surface

antigen positivity suggests that HBV or similar viruses may exist in the orangutan communities spontaneously. Orangutans were found to be infected with hepadnaviruses, but sequence studies of seven samples showed that these were distinct from the six known human HBV genotypes and those of other animal hepadnaviruses reported. Geographic grouping with Southeast Asian genotype C viruses and gibbon chimpanzee HBV was discovered through phylogenetic studies. This suggests that hepadnaviruses were spread among hominoids through interspecies contact within this geographical area [3]. Hepatocellular cancer (HCC) is linked to chronic hepadnavirus transmission in native carriers like people, woodchucks, and Beechey ground squirrels. The hepadnavirus x (hbx) gene, which transactivates transcription controlled by specific cis-acting sequences, such as regulatory sequences of the hepatitis B virus (HBV) and heterologous regulatory sequences of other viruses and cellular genes, has been implicated in one of the many potential oncogenic mechanisms.

The discovery of HCCs in hbx transgenic animals, the oncogenic change of cells producing hbx in culture, and the transactivation of oncogenes c-myc and c-jun by hbx all point to the oncogenic potential of hbx. In woodchuck hepatitis virus (WHV)-associated HCCs of woodchucks, viral promoter insertion has frequently been found to cis-activate the cellular oncogenes N-myc and c-myc. In virus-associated HCCs of ground squirrels or people, there hasn't been any evidence of such cis-activation of any cellular gene. Ground squirrel HCCs frequently exhibit c-myc gene amplification and upregulation, whereas human or woodchuck HCCs rarely do. In contrast to ground squirrels and woodchucks, which do not have HCCs, point changes in the p53 gene and allelic loss of p53 have both been frequently observed in human HCCs. It is unclear how each of these genetic alterations in the various hosts affects the formation of HCC, but the fact that different alterations appear in different hepadnavirus-infected hosts' HCCs suggests that a number of distinct genetic occurrences may do so.

These things could happen differently in every recipient, and some of them might not be caused directly by the infection. Cirrhosis, a pathological condition shared by several other risk factors for HCC, and persistent hepadnavirus infection are frequently linked. This indicates that independent of the initiating substance, this pathogenic process (necroinflammatory disease) may be hepatocarcinogenic. The same processes by which other risk factors for HCC cause chronic necroinflammatory liver disease and HCC also cause chronic hepatitis and HCC, suggesting that hepadnavirus infection may play a significant part in the formation of HCC [4].

The creation of covalently closed circular DNA (cccDNA) and the reverse transcription of a genomic RNA (pgRNA) in core particles, which results in the synthesis of the relaxed circular DNA (cDNA) genome, are hallmarks of the hepadnavirus replication cycle. The reason these viruses remain active in infected hepatocytes is that cccDNA serves as the blueprint for viral RNA production. We present a summary of the current understanding of the processes underlying hepadnavirus reverse transcription, as well as the molecular and structural characteristics of the viral reverse transcriptase, in this article. (RT). We draw attention to critical information voids in cccDNA production and stability. Additionally, we go over how contemporary antiviral treatments affect virus longevity, especially as it relates to cccDNA [5].

In old primary cultures of hepatocytes from congenitally infected ducklings, covalently closed circular (CCC) double-stranded DNA, thought to be the transcriptional template for duck hepatitis B virus (DHBV), is increased. The flexible circular DNA produced in the cytoplasm by reverse transcription is the main antecedent to the enlarged reservoir of nucleus viral CCC DNA, according to an analysis of 5-bromodeoxyuridine-labeled heavy/light CCC

DNA. It has been shown through in vitro DHBV infection of untreated hepatocyte cells that CCC DNA amplifies 50 times during an early stage of the infection before viral generation. Without requiring numerous cycles of infection or semiconservative reproduction, this increase enables the cell to create a reservoir of regulatory templates. This mechanism could explain why hepadnavirus-infected cells can continue to generate virus particles even in the lack of steady viral DNA integration [6]. It is unclear where monkey HBV (family Hepadnaviridae) originated. Hepadnaviruses are primordial diseases that may have long been connected to ancestral animal groups like bats. Hepadnaviruses in bats have evolved over a lengthy period, as evidenced by the fact that their genomic variety is greater than that of living hepadnaviruses in other host groups. Surprisingly, a newly discovered New World bat hepadnavirus can attack human hepatocytes and shares antigens with HBV. These viruses support the idea that primordial orthohepadnaviruses originated in the New World, along with genetically varied hepadnaviruses from New World mice and a non-human mammal. Bats are probable sources of ancestor hepadnaviruses obtained by primates, as evidenced by the multiple host changes of bat and ape viruses [7].

The viral polymerase polypeptide and an RNA fragment, found on genomic RNA, create a ribonucleoprotein (RNP) complex, which is necessary for hepadnavirus assembly. A tyrosine fragment on the polymerase primes the reverse transcription process, which is then activated by this contact. We now report that p23, a newly discovered chaperone companion for Hsp90, is necessary for RNP production as well as ATP breakdown. We also show that a polymerase-dependent process is involved in the incorporation of the chaperone complex into the viral nucleocapsids. Based on these findings, we propose a model for hepadnavirus assembly and protein priming of viral DNA synthesis [8]. In this model, the reverse transcriptase is maintained in a specific conformation that is capable of RNA packaging and protein priming of viral DNA synthesis by a dynamic, energy-driven process that is mediated by a multi-component chaperone complex composed of Hsp90, p23, and possibly additional factors.

To determine whether the development of the hepadnavirus family is host-dependent, a genetic lineage study was conducted. We made evolutionary trees using the DNA sequences of 18 different genotypes. The hepatitis B virus can be divided into four subsets, which are incompatible with traditional classifications, according to the trees found. For the hepatitis B virus, we calculated the rate of identical (silent) replacement to be 4.57 x 10(-5) per site per year. By extrapolating this rate to the phylogenetic tree, we calculated that the duck hepatitis B virus diverged from a common ancestor at the earliest 30,000 years ago, the ground squirrel hepatitis virus and woodchuck hepatitis virus diverged at the earliest 10,000 years ago, and the hepatitis B virus diverged within the last 3000 years. Because these separation dates of the viruses are much more recent than those of the host species, it indicates that the hepadnavirus family developed separately from host-species divergence [9].

An assessment of the mutation rate of the viral genome during reproduction in the host is crucial for tracing the development of hepadnaviruses. We infected 10 newborn woodchucks with a contagious molecular clone of the woodchuck hepatitis virus to ascertain the rate of change of the hepadnavirus genome under specified experimental circumstances. All 10 animals displayed antibody signs of the WHV virus 4 months after the initial exposure. One of the animals later developed a persistent infection and was used in additional research. WHV DNA from serum virions was cloned at 16 months after transfection, and the nucleotide sequences of three distinct offspring genomes were directly compared with those of the original hybrid DNA. We discovered three variations between the mother genome sequence and the individual offspring genomes, despite the average nucleotide sequence

remaining unaltered. As a result, we calculate that the WHV genome mutates at a pace of about 2 x 104 nucleotide changes per site per year. The mutation rate of the gag gene, the most slowly changing gene in retroviruses, is comparable to this number, which is one to two orders of magnitude lower than the mutation rates previously estimated for the positive- and negative-strand RNA viruses. Therefore, in contrast to other viruses that do not possess polymerase-associated editing functions, we discover that the hepadnavirus genome is comparatively steady during reproduction in host tissues [10].

The viral P gene product and the hepadnaviral polymerase polypeptide are chemically connected at their 5' termini, which has been interpreted to mean that the hepadnaviral polymerase polypeptide also serves as a protein precursor to starting reverse transcription of the RNA genome. By locating the nucleotide-linked amino acid in the duck hepatitis B virus's P protein structure, the current research supports this hypothesis. (DHBV). One set of studies found that only tyrosine 96 was necessary for both viral DNA synthesis in infected cells and stimulation of DNA synthesis in a cell-free system. The other two phylogenetically conserved tyrosine residues in the DNA terminal (TP) region were found to be only weakly or not at all necessary. This assignment was verified through direct biochemical analysis. Tryptic peptides from the DHBV P protein, which were isolated and analyzed in parallel to reference peptides chemically synthesized and 33P-labeled by a tyrosine kinase, were 32P-labelled at the priming amino acid by the initiating dGTP and additionally labeled internally by [35S]methionine. High-performance liquid chromatography mobility along with the release of [35S]methionine and phospholabel during sequential amino acid sequencing made it clear that the tyrosine in the sequence 91KLSGLYQMK99, which is found in the middle of the TP domain, is the initiating amino acid. Tyr-96 is predicted to be the triggering tyrosine in other hepadnaviruses thanks to conserved sequence patterns encircling it. The processes that use protein priming to start the production of viral DNA genomes or RNA genomes from an RNA template share a shared beginning, according to weak sequence homology to picornavirus genome-linked polypeptides (VPgs) and comparable gene organization [11].

## CONCLUSION

A class of DNA viruses known as hepadnaviruses attack hepatocytes and have been linked to the development of hepatocellular carcinoma (HCC) and liver damage in humans and birds. The genus of hepadnaviruses that produces acute and chronic hepatitis B, cirrhosis, and HCC in humans is represented by the hepatitis B virus (HBV). These viruses' DNA genes are relatively small and are reproduced by reverse transcription of RNA intermediates. They use contiguous open reading frames and polymerase enzymes with regions that have reverse transcriptase, RNase H, and priming functions to encode the envelope and nucleocapsid (core) proteins. The contacts among the large membrane peptide and the main receptor on the hepatocyte appear to be the source of the host specialization characteristic of this viral family. Human HBV illness is treatable with nucleoside and nucleotide analogs and is avoidable through vaccination.

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# CHAPTER 16

# AN OVERVIEW OF THE PLANT VIRUS

Mukesh Singh Sikarwar, Professor
Department of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- MUKESHSIKARWAR@GMAIL.COM

**ABSTRACT:**

The term "plant virus" refers to the viral that affects plants. Plant viruses completed their reproduction cycle by using the host cell's machinery, just like other kinds of viruses do. The protein sheath protects the DNA/RNA hereditary material of plant viruses. This part covered the anatomy of the plant virus and the life cycle of the tobacco mosaic virus.

**KEYWORDS:**

Mosaic Virus, Nucleic Acid, Plant Virus, Plant RNA, Viral Infection.

## INTRODUCTION

Plants can be harmed by viruses known as plant viruses. Plant viruses, like all other viruses, are obligatory intracellular pathogens that are unable to reproduce on their own. Vascular plants are susceptible to infection by plant viruses. The majority of plant viruses have a rod-like shape, with the viral DNA enclosed in a tube of protein plates. Isometric particles are another typical structure. They don't often carry an envelope. Although some viruses have double-stranded (ds), single-stranded (ss), or double-stranded DNA genomes, the vast bulk of viruses has an RNA genome, which is typically tiny and single-stranded. Plant viruses are divided into 49 families and 73 species. However, only domesticated plants, which make up a very small percentage of all plant types, are included in these statistics. The interactions between untamed plants and their viruses frequently do not seem to result in illness in the host plants, even though viruses in wild plants have not been thoroughly investigated.

Plant viruses typically need to employ methods that are distinct from those used by animal viruses to spread from one plant to another and from one plant cell to another. Since most plants are immobile, plant-to-plant transfer frequently includes vectors. Transport through plasmodesmata is the favored method for virions to travel between plant cells because they are encircled by solid cell walls. RNA viruses are believed to propagate from one cell to another using specific processes that plants have for transporting mRNAs through plasmodesmata. Plants use siRNA in reaction to dsRNA as one of their protections against viral infection. The majority of plant viruses express a protein that blocks this reaction. In reaction to damage, plants also decrease transport through plasmodesmata. Martinus Beijerinck, a professor of microbiology at the Technical University of the Netherlands, proposed his theories regarding the size of viruses in 1898. He also discovered that the "mosaic disease" stayed contagious after passing through a Chamberland filter candle.

The filter, however, kept bacteria microbes, which was the opposite of this. The word "virus" was first used by Beijerinck to refer to the contagious supernatant as a "*contagium vivumfluidum*". Even though microscopic inspection was ineffective after the original finding of the "viral concept," it was necessary to categorize any other viral illnesses that were currently recognized based on the method of spread. There were 977 formally designated and a few preliminary plant viral species in 1999 as a result of this expansion. Wendell Stanley was the first to purify (crystallize) TMV; he reported his results in 1935, but he did not conclude that the RNA was the contagious component. But in 1946, he was awarded the

Chemistry Nobel Prize. The case was strengthened in the 1950s by the simultaneous finding by two laboratories that the TMV's pure RNA was contagious. The genetic material used to write for the creation of new contagious particles is carried by RNA. The molecular biology and genetics of plant viral genes have lately been the center of virus study, with a special emphasis on figuring out how the virus can reproduce, migrate, and attack plants. The possibility for business application by biotechnology firms has been investigated using knowledge of the DNA of the virus and the functions of the protein. Sequences generated from viruses have been used in particular to comprehend new types of resilience. New methods for producing value-added proteins in plants may be made possible by the recent explosion in technology that makes it possible for people to control plant viruses [1]. Almost all viruses in their final version follow a straightforward structural concept. The genome, which is formed of nucleic acid, and a protective protein coating make up the two main components of virus particles (virions). Additionally, some viral particles have an outer barrier made of lipids and proteins around them. (lipoprotein membrane). Plant viruses' (capsids') protein envelopes are put together following one of the two basic symmetrical kinds. Helix-shaped virion is the first variety. (roughly elongated). There are two main types of elongated viruses: stiff rods (Figure 1) and flexuous strands.

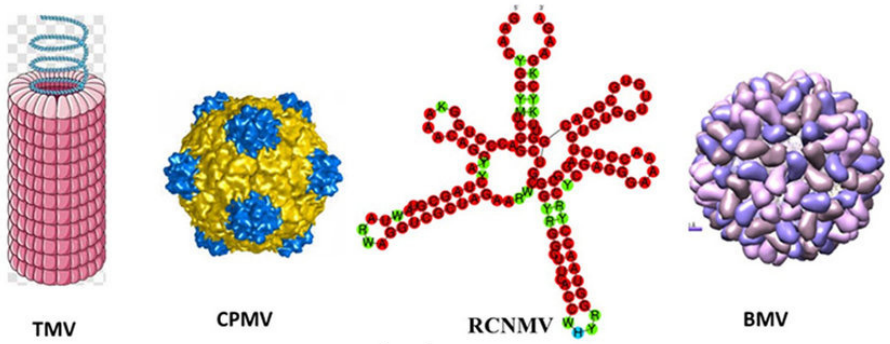


**Figure 1: Plant virus: Diagramed showing the structure of the different plant viruses (Research gate).**

The nucleic acid is highly organized in both of these forms and adopts the same helix shape as the proteinaceous capsid. The second kind of viral particle is an icosahedral one, which is approximately spherical (Figure .1)[2]. Its variants include bacilliform virions (Figure .1) and twin virions, which are made up of two connected incomplete icosahedra. (Figure .1). In the icosahedral virions, the genomic nucleic acid creates a partly organized spheroid inside the proteinaceous capsid. If the nucleic acid and protein components are cultured under the right circumstances, both icosahedral and elongated virions can self-assemble in a test tube.The tiniest known creatures are viruses. A spherical plant virus typically has a width of 30 nanometers or less. The TMV particle is 300 x 18 nm in size, stiff, and has a 6,400 nucleotide RNA genome that is encapsulated by 2,130 clones of the TMV coat protein. Some filamentous viruses can grow as long as 2000 nm or 2 m. For reference, a mesophyll cell in a leaf is typically 50 m in the area [2]. Only a small percentage of plant viruses have dsDNA sequences, even though double-stranded DNA makes up the genetic material for the majority of species (Figure.2). Single-stranded (ss) DNA makes up the genomes of a few plant viruses. However, DNA is not used at all by the vast bulk of plant viruses. Instead, almost all plant viruses have RNA as their DNA. The majority of these genomes are made up of short hairpin RNAs (ssRNA), which have the same (positive-sense) orientation as the cell's messenger RNAs. Some of the RNA viruses use ssRNAs of negative polarity, and yet others have genomes composed of dsRNA. Because viruses' genetic makeup varies so greatly from one

another, various viruses frequently have very varied life cycles and reproduction patterns. The entry of the virion into the cell initiates the life cycle of plant viruses because they are obligatory, biotrophic pathogens. Plant epidermis and cell walls are impermeable to plant viruses. The cuticle and cell wall are thought to be mechanically damaged wounds through which the virion quietly penetrates the cytoplasm of the cell. The elimination of the virion's cytoplasmic coat protein covering, either entirely or partially, is the next stage of viral infection. The cell then provides transcription machinery (for DNA viruses) and a translation mechanism to mediate the expression of the viral genome. To reach the cell proteins necessary for the synthesis of messenger RNA from viral DNA, the DNA viruses must be carried to the nucleus for transcription. Viral proteins are created during the translation of viral RNA in the cytosol and are necessary for the virus life cycle to be completed.

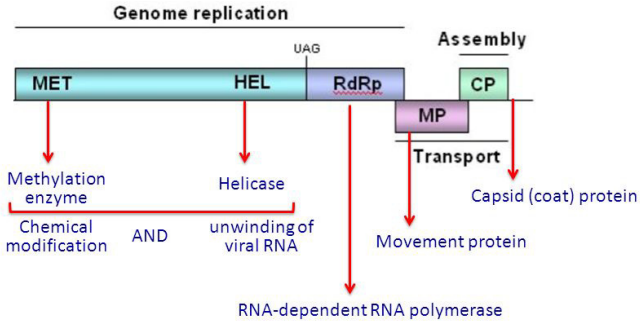


**Figure 2: Genome of the plant: Diagramed showing the organization of the Plant virus genome (Slide player).**

All viruses must control the production of at least three different kinds of proteins: replication proteins, which are necessary for the synthesis of nucleic acids, structural proteins, which form the protein shell and other parts of the virions, and movement proteins, which facilitate the movement of viruses between plant cells. A complex of proteins is created when the viral replication proteins join with cellular proteins to make numerous copies of the virus genome. To create new virions, these freshly created genes engage with the structural proteins. The stages that the Tobacco Mosaic Virus takes inside the cell during its replication are shown in Figure 3.

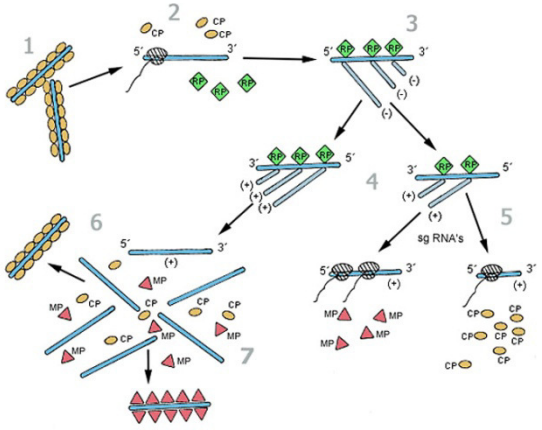


**Figure 3: Tobacco Mosaic Virus replication steps: Diagramed showing the different stages Tobacco Mosaic Virus takes inside the cell during its replication (American Phytopathology).**

Moving the virus into nearby cells is the next stage in the viral replication cycle. Depending on the virus, the viral genomes or the virions are carried into adjacent cells through tiny channels called plasmodesmata that create links between cells. Numerous viruses generate mobility proteins that alter plasmodesmata channels to make it easier for the virus to spread into nearby cells. The migration of the tobacco mosaic virus from an infected cell to a nearby cell is depicted in the accompanying figure 4 (Figure 4).

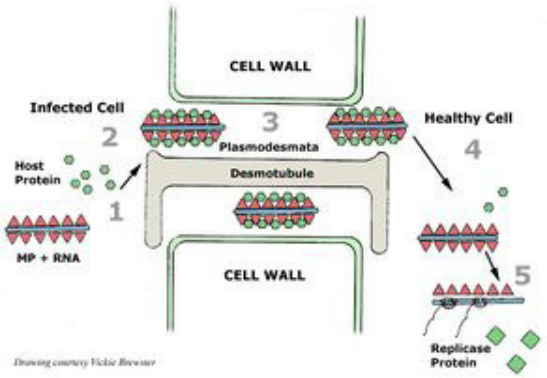


**Figure 4: Cell-to-cell infection: Diagramed showing the movement of *Tobacco mosaic virus* from one cell to another cell (microbewiki).**

Cells travel slowly from one to the next; it can take a virus one to several hours to proliferate in one cell and spread to another. A virus must penetrate the plant's vascular system in order to effectively infect the entire plant. Viruses typically travel quietly with the passage of photosynthates through the phloem sieve elements during systemic, or long-distance, transport. After a relatively quick (centimeters per hour) systemic dissemination within the phloem, the virus exits the phloem and enters neighboring cells, where it reproduces and distributes via cell-to-cell contact. Depending on the virus, host plant, and external factors, the interval between the initial infection of one or a few cells and widespread infection of the plant ranges from a few days to a few weeks. The viral life cycle is completed when it spreads from one plant to another (see the part on survival and dispersal).

Plant RNA viruses produce vital viral proteins that are expressed by the host translation system. The majority of plant RNA viruses' chromosomal RNAs, however, don't have the traditional features of eukaryotic cellular mRNAs, such as mono-cistron, 5' cap structure, and 3' polyadenylation. Plant RNA viruses have developed a range of translational tactics, such as cap-independent translation, translation recoding on initiation and termination sites, and post-translational processes, to adjust to and use the eukaryotic translation machinery [3].

Most plant viruses have simple capsids that are strong structures made up of numerous versions of one or a few different kinds of protein subunits organized either in an icosahedral or helical pattern. Capsids can frequently be generated either through plant infection or through the production of the subunit(s) in a range of heterologous systems, in significant amounts. Plant virus particles, also known as virus-like particles (VLPs), have garnered interest as possible reagents for uses in bionanotechnology due to their relative simplicity, stability, and ease of production. Plant viral particles have thus undergone genetic and chemical modification, been used to contain alien material, and been integrated into supramolecular structures themselves. [4].

## DISCUSSION

Plant viruses produce significant genetic variation observed both within and between species using a variety of processes. The reproduction methods of plant RNA viruses and

pararetroviruses are likely very error-prone, leading to a lot of mutations and a quasispecies character. Although the origin of the variety in the plant DNA viruses is not entirely obvious, it does exist. Recombination and reassortment are commonly used by plant viruses to drive evolution, along with other processes like gene duplication and overprinting on occasion. Even though there is no proof that the mutation rate changes, the quantity of variation discovered in various plant virus species is notably diverse. There are several hypotheses that could explain the genesis of plant viruses. Some plant and animal viruses have connections that point to a shared ancestor, probably an insect virus. Although it is difficult to trace the evolutionary past of viruses and virtually impossible to regulate virus disease over the long term, their proclivity for rapid adaptation makes them an excellent model system for research on the broad mechanisms underlying molecular evolution [5].

Since at least 1980, crop losses caused by viral illnesses have been reduced through the use of genetic resistance to plant viruses. Studies on monocot and dicot products, their wild cousins, and the plant model Arabidopsis have revealed hundreds of naturally occurring genes for resistance to plant viruses. Some of the components that are essential for deciding how a plant viral infection will turn out have been thoroughly studied as a result of the extraction and identification of a few of these genes over the past ten years. In this volume, we have enumerated genes for resistance to plant viruses and have reviewed current information regarding their identity and inheritance. The genetic background, genomic structure, methods of resistance, and farming application of plant viral resistance genes are also addressed, to the extent that material is accessible [6].

Homopterans, which include aphids, whiteflies, and leafhoppers, are the main carriers of viruses, accounting for more than 80% of viruses spread by insects and harboring nearly 400 viral species in 39 distinct genera. Host searching or pre-alighting behavior, probing on superficial tissues, settlement, and stylet penetration to the target feeding tissues, salivation and continuous sap ingestion from the preferred feeding site are all necessary steps for homopterans to recognize the host plant. These behaviors are linked to plant virus transmission. This study examines how vector behavior affects the transmission and spread of plant viruses based on the sort of virus-vector interaction. The majority of research has focused on viruses spread by aphids, and specific eating and penetrating behaviors have been linked to the spread of circulative and cuticula-borne viruses. The study also concentrates on the locations of cuticula-borne viruses that are most likely to retain them within the insect's body. The effects of viral infection on vector behavior, including modifications to the appeal, settling, or feeding preferences, as well as modifications to the performance of the vector (development, reproduction, rate of population increase, and survival), are addressed in the final section [7].

The creation, transportation, and recycling of functional compounds between viral DNA, virus-encoded products, and cellular factors are required for viral replication and intercellular dissemination. Viral components and host factors necessary for reproduction are concentrated in "viroplasms," or membrane-associated complexes, where viruses build and multiply to improve these processes. Through plasmodesmata, the cortical ER-actin network, which is constant between cells, is used by many plant viruses to reproduce. The network connections between the viral genome and the virus-encoded proteins allow the replication complexes to be highly organized and sustained. The process of movement and replication are connected by intracellular PD targeting of replication complexes, which also gives specificity for the movement proteins encoded by the virus to convey the viral genome. The cortical cytoskeleton and related motor proteins play crucial roles in the creation and transport of replication complexes as well as the growth and anchoring of replication factories[8].

One of the most powerful factors influencing the DNA of plant RNA viruses is RNA-RNA recombination. Recombination detection is a difficult job, which is why both in vitro and in vivo experimental methods were created. Both inter- and intrasegmental crossovers in the split genome of the Brome mosaic viral system are characterized. Other methods make use of the Turnip crinkle virus, Tomato bushy stall virus, Cucumber necrosis virus, and Potato virus X satellite or defective interfering RNAs (DI-RNAs). These tests revealed the function of proteins and RNA structure in the replicase-mediated copy-choice mechanism, identifying the molecular specifics of the recombination process. The polymerase and the developing RNA chain from which it is derived change from one RNA template to another during copy choice. It was discovered that RNA recombination mediates viral gene rearrangements, the correction of harmful mutations, and the acquisition of nonself sequences that affect the phylogenetics of viral species. The evidence for recombination indicates that plant viruses openly try recombination with any available genetic material, including host RNAs, distantly related viruses, and not just closely related viruses [9]. The selective regulation of various host genes has been discovered by looking at the front of viral invasion in immature pea embryos infected with pea seed-borne mosaic virus (PSbMV). According to our findings, the early reactions to PSbMV replication can be divided into three categories: those that suppressed host gene expression, those that increased host gene expression, and those that had no impact on a typical host function. In coordination with the start of viral replication and the down-regulation of two additional genes encoding lipoxygenase and heat shock cognate protein, the expression of two heat-inducible genes encoding HSP70 and polyubiquitin was activated. The down-regulation was a component of a broader reduction of host gene expression that might be accomplished through host transcript degradation. We consider the possibility that the virus requires the protein products produced by HSP70 and polyubiquitin, or that their activation simply results from the loss of other host RNAs. The former is plausible because both genes' activation does cause more ubiquitin and HSP70 to accumulate. Additionally, it shows that, in contrast to some animal viral infections, PSbMV infection does not generally impede the translation of host mRNAs. All cell types of the embryo showed this selective regulation of host gene expression, which reveals cellular disruption processes that might function as symptom-expression triggers [10].

## CONCLUSION

Plant diseases are brought on by internal parasitic pathogens called plant-associated viruses. The majority of plant viral are rod-like and contain RNA as their genetic material, which can be either single- or double-stranded. These viruses lack the equipment necessary for replication in the absence of a host creature. It is not surrounded by packages. The fact that numerous plant viruses affect both agricultural and decorative vegetation makes them of significant commercial significance. Many rod-shaped plant viruses are easily removed from the plant material and frozen. Despite the common misconception that plant viral are pathogens, recent research has demonstrated that several viruses serve a vital and advantageous function for plants, particularly in harsh settings where they help plants adapt to dryness, cold, and high soil temps.

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# CHAPTER 17

# AN INTRODUCTION OF THE BACTERIAL VIRUS; BACTERIOPHAGE

Vaibhav Rastogi, Associate Professor
Department of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- vaib.asa@gmail.com

**ABSTRACT:**
Bacteriophages, or phages as they are commonly called, are a virus that it only reproduces and multiply in bacteria. They are regarded as the most prevalent biological weapon in the world and are widely distributed throughout the ecosystem. Their size, appearance, and genetic structure are incredibly diverse. In this chapter, we briefly discussed the characteristics, classification, and biological role of the bacteriophage virus.

**KEYWORDS:**Genetic Material, Host DNA, Lytic Cycle, Lysogenic Cycle, Phage Genome.

## INTRODUCTION

A bacteriophage, or phage in colloquial use, is a duplodnaviria virus that infects and replicates inside bacteria and archaea (/bktrio/. The word is a combination of the word "bacteria" with the Greek verb "to devour" (v). Bacteriophages are made of proteins that enclose a DNA or RNA genome and can have either straightforward or complex structural designs. Their genomes might contain as little as four genes (MS2, for example) or as many as hundreds. The insertion of the phage genome into the cytoplasm of the bacterium initiates phage replication within the bacterium.

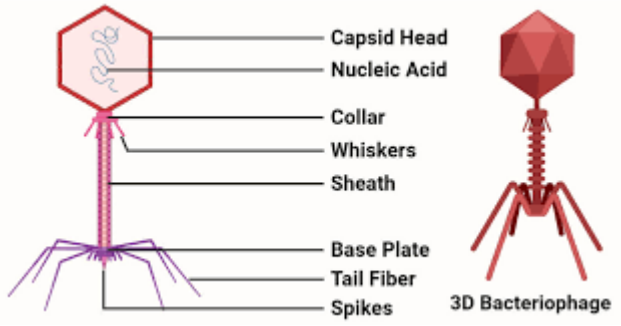


**Figure 1: Bacteriophage structure: Diagram showing the structure of the bacteriophage (Microbe notes).**

One of the most prevalent and varied organisms in the biosphere is the bacteriophage. Bacteriophages are widespread viruses that may be found wherever bacteria live. Bacteriophages are thought to outnumber all other living things on Earth, including bacteria, by a factor of more than 1031. Up to 9x108 virions per milliliter have been detected in microbial mats at the surface, and up to 70% of marine bacteria may be infected by phages, making viruses the second-most prevalent living entity in the water column of the world's oceans after prokaryotes. During the late 20th century, France, the former Soviet Union, and Central Europe all employed phages as antibiotic substitutes[1]–[3].

They are viewed as a potential treatment for bacteria with multiple medication resistance. Phages are known to influence innate immunity and bacterial clearance directly as well as

indirectly through the bacterial expression of phage-encoded proteins. Phage-host interactions are a growing topic of study interest. A polyhedral head, a shirt collar, and a helical tail make up a typical bacteriophage. The genetic material double-stranded DNA or single-stranded RNA is contained within the 2000 capsomeres that make up the phage's head (Figure.1). A hollow inner tube that is encased in a contractile sheath with 24 annular rings makes up the tail. A basal plate with tail fibers at each corner makes up the trail's distal end.

The Caudovirales order, which contains the Myoviridae family with a contractile tail, the Podoviridae family with a short tail, and the Siphoviridae family with a non-contractile long tail, makes up around 96% of the documented bacteriophages. The same order includes filamentous, cubic, and polymorphic phages, which are divided into 10 tiny families and account for around 3.6% of all known bacteriophages. Examples of phage morphologies are shown in Figure.2.

| Family | Morphology | Nucleic acid | Characteristic |
|---|---|---|---|
| *Myoviridae* |  | Linear dsDNA | contractile tail,Non-enveloped |
| *Siphoviridae* |  | Linear dsDNA | Long non-contractile tail,Non-enveloped |
| *Podoviridae* |  | Linear dsDNA | Short non-contractile,Non-enveloped tail |
| *Tectiviridae* |  | Linear dsDNA | Isometric , Non-enveloped |
| *Corticoviridae* |  | Circular dsDNA | Isometric,Non-enveloped, |
| *Lipothrixviridae* |  | Linear dsDNA | rod-shaped,Enveloped |
| *Plasmaviridae* |  | Circular dsDNA | Pleomorphic, Enveloped |
| *Rudiviridae* |  | Linear dsDNA | Rod-shaped , Enveloped |
| *Fuselloviridae* |  | Circular dsDNA | lemon shaped , Non-enveloped |
| *Inoviridae* |  | Circular ssDNA | Filamentous,Non-enveloped |
| *Microviridae* |  | Circular ssDNA | Isometric,Non-enveloped |
| *Leviviridae* |  | Linear ssDNA | Isometric, Non-enveloped |
| *Cystoviridae* |  | Segmented dsDNA | Spherical , Enveloped, |

**Figure 2: Classification of the bacteriophage: Diagram showing the classification of the bacteriophage (Bioscience biotech).**

The phage must first penetrate the host cell to proliferate. They generate a hole by adhering to certain receptors on the bacterial cell surface with their tail fibers (adsorption), which the base plate coordinates together with attachment3. The bacterial cell membrane is pierced by a hard tube that is launched out of the sheath, allowing the bacteria to inject their genetic material (DNA or RNA, double or single-stranded). If the environment is adverse, they can then use the host cell's biological machinery for their replication through a process known as the lytic cycle. Instead, if circumstances are right, they can enter a latent state within the host cell known as the lysogenic cycle.

The infecting phage kills the host cell towards the end of the lytic cycle (Figure .3), which is also known as a virulent infection, to create a large number of its offspring. The phage

genome immediately produces early proteins that degrade the host DNA after being injected into the host cell, enabling the phage to take over the cellular machinery.The remaining proteins needed to construct fresh phage particles are subsequently synthesized by the phage using the host cell. The new genetic material is packed into the head while new daughter phage particles are produced, and the heads and sheaths are created independently. In the course of this process, phage enzymes gradually weaken the host cells, which finally rupture, dispersing 100–200 additional phage offspring into the environment[4], [5].

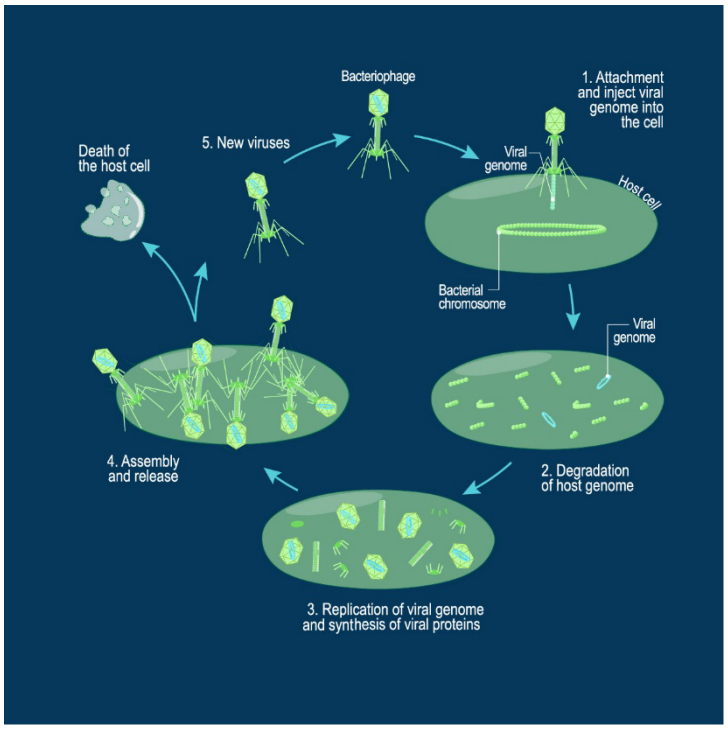


**Figure 3: Bacteriophage lytic cycle: Diagram showing the different stages involved in the bacteriophage lytic cycle (Technology network).**

The lysogenic cycle (Figure .4), also known as temperate or non-virulent infection, uses the host cell as a haven where it may survive in a latent condition. It does not harm the host cell. Once the phage DNA is injected into the host cell, it uses integrases provided by the phage to integrate into the host genome, at which point it becomes known as a prophage. The host cell divides for the duration that it is there and does not create the proteins necessary to make progeny, at which point the prophage genome is passively copied alongside the host genome. The bacterial hosts are typically somewhat unaffected by this procedure since the phage genome is typically rather tiny**.**

If a bacterium containing prophage is exposed to stressors, such as UV light, low nutrient conditions, or chemicals like mitomycin C, prophage may spontaneously extract themselves from the host genome and enter the lytic cycle in a process called induction. this process is not flawless, as prophage occasionally leave part of their DNA behind or take some of the host DNA with them when they recirculate. If they subsequently infect a different host cell, a process known as transduction may transfer bacterial genes from one strain to another. This is one way that genes encoding for toxins, superantigens, and other virulence factors can spread across a bacterial community. Recent research has revealed that because phages are capable of producing and detecting tiny peptides in a manner similar to quorum sensing, the transition between lytic and lysogenic infection is likewise reliant on the amount of phage in a region.

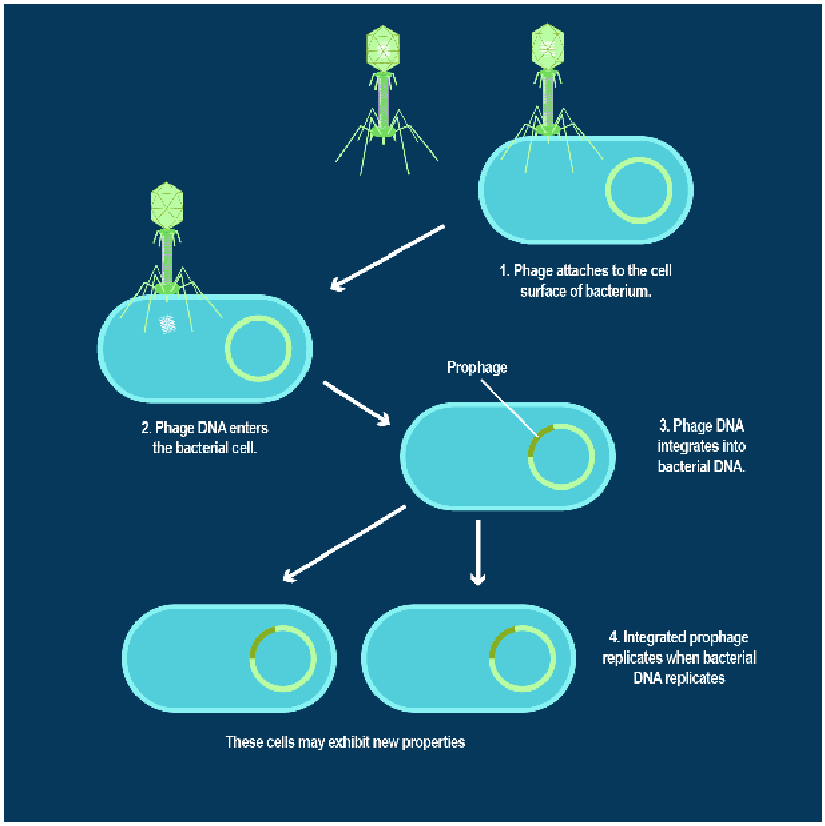


**Figure 4: bacteriophage lysogenic cycle: Diagram showing the different stages of the bacteriophage lysogenic cycle(Technology network).**

While certain bacteria have an "immune system" that enables them to defend themselves, they are not all defenseless against phage attacks. Francisco Mojica5 and independently by a team from Université Paris-Sud6 originally suggested CRISPR-Cas, which is today synonymous with genetic alteration, as a bacterial "adaptive immune system" in 2005. The CRISPR locus is a collection of brief, repetitive sequences that are spaced apart by distinct sequences called spacers. It was discovered that these spacer sequences shared similarities with viral and plasmid DNA, including phage. The CRISPR becomes a chronological record of the phage the cell and its ancestors have met when it is assaulted by a previously undiscovered phage by the addition of new spacers to one side of the CRISPR.After being transcribed in response to phage invasion, the CRISPR sequences work with the Cas proteins to identify and eliminate the phage sequences that are similar to the spacer sequences.One of the finest researched phages, the Lambda phage was first isolated from Escherichia coli and served as the foundation for several genetic tools. Even the science of molecular biology as a whole was born as a result of the employment of phages as tools. The method of transduction was created in the 1950s when it was discovered that the phage's capacity to recombine with host DNA could be used to alter the genomes of Salmonella species. Since then, it has been employed as a means of transporting genetic material between several species, including the movement of human genes and fungal gene modifications.

Human insulin was initially manufactured safely and affordably by the simple phage. Moreover, it has opened up possibilities for uses in high-throughput clone screening, nanomaterial creation, food antibacterial treatment, diagnostic tools, and medication discovery and delivery systems. According to Fred Sanger and colleagues, the phage X174 unwittingly made history in 1977 when it became the first creature to have its full nucleotide sequence determined. In the post-antibiotic period, research into phage therapy was

abandoned in most organizations due to the practical broad-spectrum action of antibiotic treatment. Yet, due to a lack of access to western medications in many former Soviet countries, phage therapy research has persisted. Phage treatment has had a comeback in recent years due to the growing worldwide issues with antibiotic resistance. Whilst phages are able to infect and destroy bacteria and have been successfully used to treat life-threatening infections, their species and even strain specificity and potential for pre-existing immunity of some bacteria mean targeting a phage treatment is currently not a trivial process and must be tailored to the individual infection. It is therefore expensive and drawn out[6]–[8].

## DISCUSSION

Since 2005, there has been a more than threefold rise in the number of sequenced bacteriophage genomes, with more than 500 being available in the NCBI phage database. They cover at least 70 distinct bacterial hosts, yet just eight bacterial hosts are represented by two-thirds of the phage genomes that have been sequenced. The comparative examination of these genomes reveals three important characteristics. They are extremely genetically diverse, which points to their likely pre-evolutionary ancestry. Second, the mosaic nature of the genome architectures infers extraordinarily high levels of a horizontal genetic exchange over their evolutionary historyThird, phage genomes likely constitute the biggest repository of undiscovered genes because they include a very high percentage of unique genetic sequences with unknown functions. As more bacteriophage genomes are described, our understanding of the virosphere, which contains an estimated 1031 bacterial and archaeal viruses, will become clearer.

Because of the concurrent rise in immunosuppressed patients, the advent of pathogenic bacteria resistant to the majority, if not all, presently available antimicrobial medicines has become a serious issue in modern medicine. The fear that humanity is reentering the "antibiotics" age is now quite serious, and modern medicine and biotechnology now place a high priority on the development of new antiinfection methods.

Bacteriophages were used almost quickly for antibacterial treatment and prevention when they were identified in 1917 as bacterial epizootic illnesses. Yet, because the biology of bacteriophage was little known, the early trials of bacteriophage treatment for infectious disorders were complicated. The preliminary research examined here suggests that there are solid grounds for anticipating that phage treatment may be beneficial in some situations. Up until relatively recently, there were no thorough reviews of phage treatment due to the development of antibiotics and the "Soviet taint" that it acquired during the postwar period. Current research in the lab and on animals, utilizing current knowledge of phage biology, suggests that phages may be effective antibacterial agents in some circumstances.

Bacteriophages are categorized into 13 families and one order. Since 1959, about 5100 phages have been investigated using an electron microscope. A minimum of 4950 phages (96%) have tails. They make up three families in the order Caudovirales. The majority of phages (61%) with lengthy, noncontractile tails are Siphoviridae. Less than 4% of bacterial viruses are pleomorphic, filamentous, and polyhedral phages. More than 140 bacterial or archaeal genera include bacteriophages. Their distribution indicates the phylogeny and place of origin of the bacterium. Bacteriophages have 11 lines of ancestry, are polyphyletic, and have repeatedly evolved in many hosts. The earliest known viral group, the tail phages, appears to be monophyletic.

Environmental studies and comparative genomic analyses of bacteriophages, particularly the tailed phages, paint a whole different picture of the size, genetic makeup, and dynamics of

this population. The intricate methods by which these viruses develop and affect the evolution of their bacterial and archaeal hosts are some of the details that are revealed by sequence comparisons. By both homologous and nonhomologous recombination, we see a rife horizontal interchange of sequences among genomes. There is a significant amount of mosaic diversity in local populations as a result of high-frequency exchange between phages inhabiting comparable ecological niches. Across the whole expanse of phage sequence space, the horizontal exchange also occurs, albeit less often[9], [10].

Endolysins are bacterial peptidoglycan-degrading enzymes that are encoded by phages and released towards the end of the phage reproductive cycle. Through membrane arrest, holins, and the transition from an inactive to an active state, their action is closely controlled. Recent studies have shed light on the surprising diversity of these highly specialized hydrolases as well as their modular structure and three-dimensional architectures. Their matching C-terminal cell wall binding domains direct the enzymes to their substrate, and their N-terminal catalytic domains are able to target nearly every peptidoglycan network connection. Endolysins have been used for a variety of in vitro and in vivo purposes, in food science, in microbial diagnostics, and for the treatment of experimental infections because of their specificity and high activity.

## CONCLUSION

The genetic material of bacteriophages is either DNA or RNA, in a circular or linear arrangement, and then either as a single-stranded molecule or a double-stranded molecule. Phages can be divided into two groups: lytic and temperate bacteriophages. Since they lysis the host bacteria as a regular part of their entire lifecycle, lytic phages are bacterial phages that reproduce through the lytic life cycle. Bacteriophages are naturally harmless because their main components are nucleic acids and proteins. Nevertheless, there is limited proof that all this truly poses a risk when treating phages. BacterioPhages can connect with immune systems, at least theoretically leading to detrimental immune responses.

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# CHAPTER 18

# DIVERSE CATEGORIES OF THE VIRUS; ARCHAEAL VIRUSES

Krishana Kumar Sharma, Professor
Department of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- drkk108@gmail.com

**ABSTRACT:**

Many of the most unusual viruses are found in archaea, including spindle viruses, two-tailed viruses with "growing" tails that emerge from cells that are infected, and bottle-shaped viruses.All of the circle DNAs in the identified archaeal genomes have sizes between 0.5 and 5.8 Mbp. The archaeal genome of less than 1 Mbp is present in a parasite that receives nutrition from a host, and the diminutive size of this chromosome is due to the deletion of useless genes.A virus that attacks and reproduces in archaea, a realm of single-celled, bacterial creatures, is referred to as an archaeal virus. We have discussed a brief introduction of the different archaeal viruses in this chapter.

**KEYWORDS:**

Archaeal Virus, Acidic Hot, Cell Surface, Trnascprotion Factors, Viral DNA.

## INTRODUCTION

A virus that attacks and reproduces in archaea, a realm of unicellular, prokaryotic creatures, is referred to as an archaeal virus. Like their hosts, archaeal viruses are found all over the globe, even in harsh settings that are inhospitable to most life, like the ocean floor and acidic hot springs. The human organism has also been discovered to contain them. Since the 1974 description of the first known archaeal virus, a wide variety of archaeal viruses have been identified, many of which have distinct traits not shared by other viruses. Their biological mechanisms, such as how they reproduce, are poorly understood, but it is thought that they have a variety of separate beginnings, some of which likely precede the last archaeal common progenitor. (LACA). The appearance of archaeal viruses accounts for a large portion of their variety. Their entire bodies, known as virions, can take on a variety of shapes, such as rods, flasks, droplets, spirals, spindles, and lemons. Some of them house the viral capsid, which houses the viral DNA, in a lipid layer known as the viral envelope.

The membrane can occasionally enclose the DNA inside the capsid. Deoxyribonucleic acid (DNA) makes up the genomes of all known archaeal viruses, though some may also have ribonucleic acid (RNA) genomes. A tiny percentage of those that have been discovered have single-stranded DNA genomes, but the majority have double-stranded DNA genomes. Many of the genes that archaeal viruses encode have no known purpose and show no similarity to any other genes. Few archaeal viruses have been thoroughly characterized, compared to viruses found in bacteria and eukaryotes. Despite this, the ones that have been examined are incredibly varied and grouped into more than 20 families, many of which have no connections to other viruses that are currently known. The two main categories of archaeal viruses are those that are linked to bacterial and eukaryotic viruses and those that are not. The former includes viruses found in the realms Duplodnaviria and Varidnaviria, which probably have ancient origins before the LACA, while the latter includes the realm Adnaviria [3] and all archaeal virus families that have not been assigned to higher taxa, which are thought to have more recent origins from non-viral mobile genetic elements like plasmids. It is mainly

unclear how archaeal viruses communicate with their hosts and the environment. Many create a long-lasting infection, during which a small number of offspring are continuously generated without harming the mother archaeon. Some have adapted to the habitats in which archaea exist by evolving alongside their hosts. For instance, after leaving their host cell, bicaudaviruses develop two tails on the opposing extremities of their bodies, which may aid them in locating a new host in thinly populated areas. It is thought that archaeal viruses, which are a primary source of mortality on the ocean floor, contribute significantly to the recycling of nutrients in oceans.

In hypersaline habitats, the salinity level can have an impact on the infectivity and activity of some archaeal viruses. Learning more about their replication mechanisms and improving our knowledge of their variety are two fields of research in archaeal virology. It is very helpful to research how archaeal viruses engage with their hosts in certain habitats, such as acidic hot springs, where archaea predominate. There is a sizable genetic resource that needs to be investigated because a sizable percentage of their genomes is unknown in function. Wolfram Zillig and his coworkers found numerous archaeal virus families in the early decades of the archaeal virus study. Since 2000, numerous new archaeal viruses have been discovered using techniques like metagenomics, and techniques like cryogenic electron microscopy and gene synteny have improved our understanding of their evolutionary past [1].

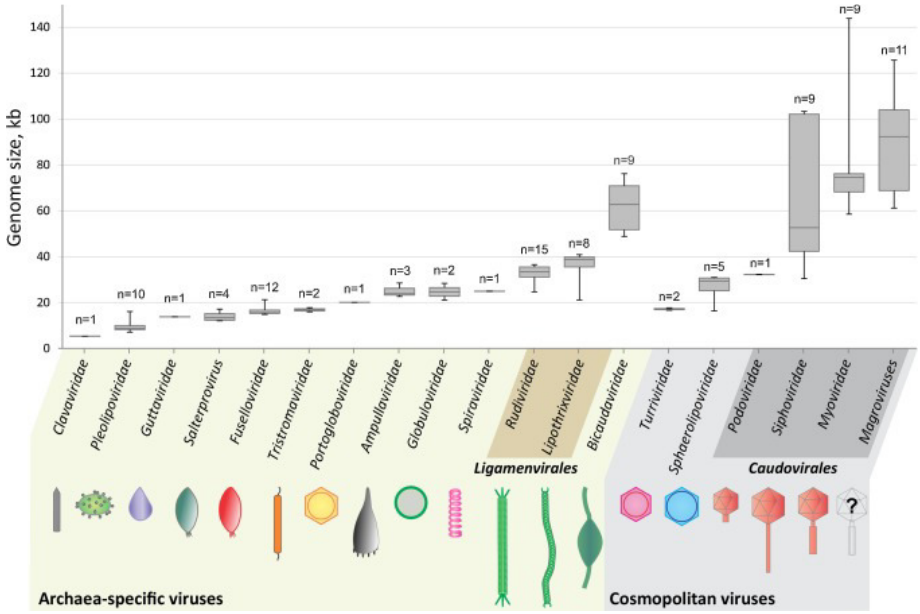


**Figure 1: Genome organization of the archaeal viruses: Diagram showing the genome organization of the archaeal viruses (Sciecne direct.com).**

Because of the absence of substantial similarity to sequences in the public databases, the majority of the proteins encoded by archaeal viruses are resistant to useful bioinformatic analysis (Figure.1), even when the most sensitive of the accessible sequences are used. Given that tertiary protein structures usually outlive protein sequence conservation, numerous teams have started structural genomics projects to clarify the roles of the mysterious proteins that hyperthermophilic archaeal viruses express. 43 proteins from 59 hyperthermophilic archaeal viruses from the families Fuselloviridae, Bicaudaviridae, Rudiviridae, Lipothrixviridae, Globuloviridae, Clavaviridae, Turriviridae, and one unclassified spindle-shaped virus PAV1 have high-resolution structures as of this writing X-ray diffraction, NMR spectroscopy, and more lately cryo-electron microscopy were used to identify the structures.

There are more than a quarter of these proteins exhibit distinctive folds for which there are no structural homologs in public databases. This information offers limited insight into the potential functions of the associated viral proteins. The inactivation of host defense mechanisms like CRISPR-Cas is one step of the virus-host relationship that many of these proteins may regulate. However, in some instances, structural analyses were essential for determining the potential function. For instance, the X-ray structure of the protein ORF119 from the rotavirus SIRV1 showed a fold typical of RCRE proteins, the hallmark replication protein in viruses with ssDNA genomes. Although expression of a near homolog in SIRV2 (gp16) could not be identified in vivo, the expected nicking activity of this protein was later proven in vitro. The putative glycosyltransferase of the turrivirus STIV, the PD-(D/E)XK family nuclease of the fusellovirus SSV-RH, and a novel-fold nuclease of the lipothrixvirus AFV1 are other noteworthy instances where high-resolution structures have revealed functional hints. Sequence-based studies were ineffective for functional protein annotation in each of these instances.

The study of transcription control by archaeal viruses is one of the research areas that has benefited especially from structural genomics initiatives. Archaeal viruses frequently encode transcription factors with a variety of DNA-binding motifs, such as ribbon-helix-helix (RHH), winged helix-turn-helix (wHTH), and zinc-fingers, which are amenable to crystallization and NMR due to their typically small size. Intricate patterns of transcriptional control during infection have been revealed by experimental characterization of some of these putative transcription factors. Structures of ten of these putative transcription factors have been determined thus far. These studies have confirmed the findings of protein sequence analysis, which showed that although the basic transcription machinery of archaea closely resembles its eukaryotic counterparts in terms of the structure of promoters and the subunit composition of the RNA polymerase, many of the transcription factors encoded by archaea and their viruses are bacterial-like [2].

In general, whether a main adsorption phase is necessary will determine whether direct or secondary binding to the cell surface occurs during the viral entrance. SIRV2 study of virus-resistant strains produced intriguing possibilities for the cell surface receptors of SIRV2 virions. In actuality, the operons sso2386-2387 and sso3139-3141 were found. The former specifies proteins that are similar to those found in type IV pili and the latter likely codes for a cell surface complex that is linked with a membrane. The formation of the type IV adhesive pilus in S. acidocaldarius requires both the assembly ATPase, AapE, and the central membrane protein, AapF, which are identical to Sso2386 and Sso2387, respectively. It is believed that the sso3139-3141 locus encodes a membrane-bound complex that could serve as an additional SIRV2 receptor. Other systems engage naturally with the cell surface, unlike rudiviruses, which require two coordinated adsorption stages to enter and enter filamentous archaeal viruses in general.

Sulfolobus spindle-shaped virus 1 (SSV1) has been known to appear in a variety of forms dating back to 1984, including isolated particles, integrated into typical rosette-like aggregates, and even attached to the cell-derived membrane. The Fuselloviridae family's most well-known species have a lemon-shaped morphotype and terminal fibers at one of the two pointed extremities. The collection of short, thin strands found in -fuselloviruses plays a role in the general viral association and adhesion to host-derived structures. SSV6 and ASV1 (Acidianus spindle-shaped virus 1), two -fuselloviruses, however, display more pleomorphic virions with three or four stout, slightly curved strands. (Krupovic et al., 2014). Some genomic characteristics strongly indicate that the fibers are made of host-attachment proteins even though these appendages do not interact with one another as was seen for SSV1.

Notably, two genes in -fuselloviruses (SSV6_C213 and SSV6_B1232) and one gene shared by all members of the family (SSV1_C792) account for the protein responsible for terminal filaments. The adsorption protein P2 of the bacteriophage PRD1 and this protein have a comparable structure. Additionally, adhesion to membrane vesicles and the creation of virion clusters are both facilitated by the pointed end of the enveloped virus ABV (Acidianus bottle-shaped virus), which belongs to the Ampullaviridae family. As a result, contact with cellular membranes seems to be a prevalent trait of hyperthermophilic archaeal viruses that have a lipidic envelope, even though data are still limited. Investigation into this especially intriguing trait is warranted.

The usual chain of events that is brought on by receptor identification and binding begins with structural rearrangement of the virions and ends with viral genome penetration through the cell envelope. Non-enveloped viruses either transport the nucleic acids concurrently with virion disintegration at the cell surface or inject the genome into the body of the cell while leaving the empty capsid affiliated with the cell envelope. SIRV2's entrance resembles that of Ff inoviruses or flagellotrophic phages, which attach F-pili and flagella, respectively, on a surface level. Both the contact with host pili-like structures and the presence of partly fractured particles at the cellular membrane have been demonstrated. (Figure .2). To ascertain whether the processes of SIRV2 translocation and genome delivery are linked to those used by Ff inoviruses and flagellotrophic bacteriophages, or are entirely new, more research is required.

Lipid-containing viruses have a peculiar virion architecture and seem to establish touch with the plasma membrane. It is fair to infer that non-enveloped filamentous viruses, like rudiviruses, depend on an entry process that is essentially distinct from that used by enveloped viruses. Similar to eukaryotic enveloped viruses, they might transport their genetic material into the body of the cell by fusing the cytoplasmic membrane and the viral envelope. With virions that emerge as lemon-shaped from recipient cells, ATV (Acidianus two-tailed virus) mimics fuselloviruses. However, ATV has been categorized as a member of the Bicaudaviridae, in part because of its unusual life cycle. Surprisingly, the released tail-less particles display the development of two long tails projecting from the pointed ends at temps near to that of its native environment (85°C). These extracellularly formed tubes, which are not present in the offspring with no tail, end in an anchor-like structure and have a slender filament inside of them.

The fact that both of the virion forms—tail-less and two-tailed—be contagious proves that the termini are not engaged in the early phases of infection. However, molecular research and genetic analysis have identified some virally expressed proteins that might be significant during infection. For instance, the three biggest ORFs and one of the CPs have putative coiled-coil domains, which are typically connected to particular protein-protein interactions and the creation of protein complexes. Additionally, the lipothrixvirus TTV1 infects many proteins with proline-rich sections (ORF567 and ORF1940), comparable to the protein TPX. Notably, the African swine fever virus's host protein identification has been linked to the motif TPTP in specific. Finally, pull-down studies demonstrated a robust interaction between the cell-bound Sso1273 that encodes a viral AAA ATPase and the ATV protein P529. The ABC transporter system's binding components most likely include the cellular OppAss, an N-linked glycoprotein. It could act as a sensor and is expressed by the same operon. ATV host cell receptor identification has also been suggested to be triggered by the AAA ATPase. This is founded on the supposition that its endonuclease activity is necessary for cleaving the circular viral DNA before the virus enters the cell.

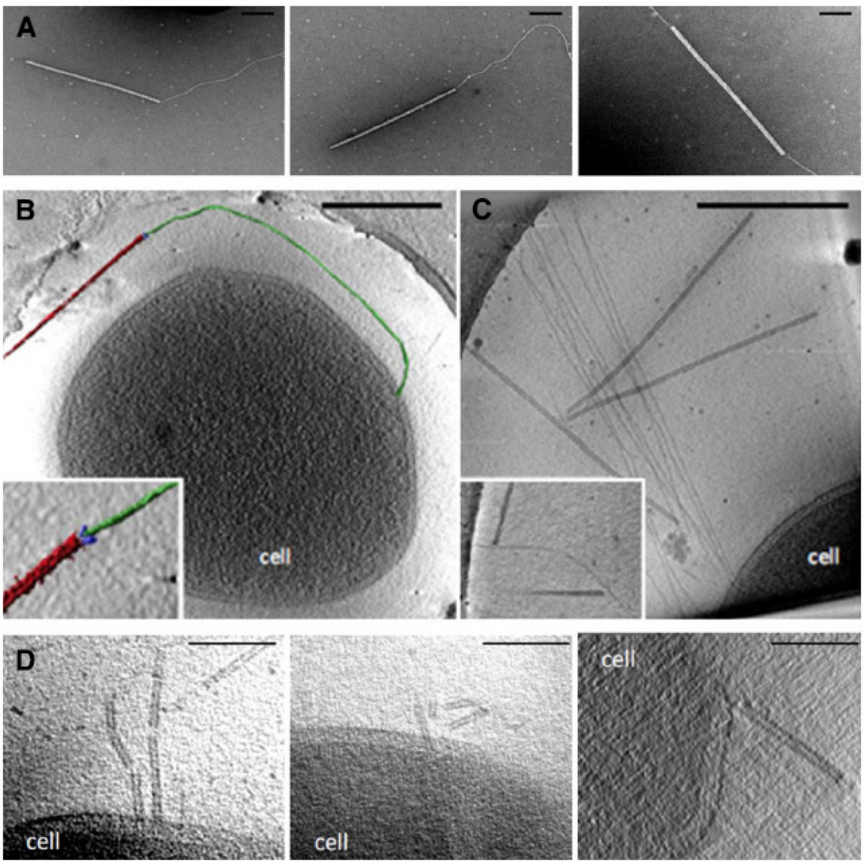


**Figure 2: Archaeal viruses entry: Diagram showing the different phases involved in the entry of the Archaeal viruses(Fortinors).**

ABV, a virus with a bottlelike shape, is an especially interesting example. With a funnel-shaped body made up of the "stopper," the nucleoprotein core, and the interior core, the enveloped particles exhibit intricate structures. The alleged "stopper," the only component to which the viral genome is physically affixed, is presumably involved in binding to the cellular receptor. As a result, it has been proposed that the "stopper" may function as an "injection needle" in a way that is comparable to that of bacterial viruses. This transmembrane pathway is widely known to be utilized by head-tail bacteriophages of the Caudovirales class for nucleic acid channeling and transport. Being the most malleable, the inner center of ABV virions may experience structural alterations that would encourage the release of viral DNA. It is unknown if the energy collected in the structure after the supercoiled nucleoprotein was packaged is adequate to move the entire genetic material into the cytoplasm.

However, as previously seen in bacteria, relaxation of the nucleoprotein filament, coiled up as an inverse cone, concurrent with its funneling into the cell could be an effective method to use the energy saved during packing for DNA injection. It is still unclear how archaeal viruses engage with cell surfaces and transfers the viral DNA into the host cytoplasm. Rudiviruses and lipothrixviruses are examples of systems that resemble their bacterial hosts, while fuselloviruses, bicaudaviruses, and ampullaviruses may be linked to eukaryotic viruses. One of the key problems that need to be resolved shortly is identifying the routes used by both filamentous and distinct lipid-containing viruses. Notably, many archaeal viruses have glycosylated capsid proteins, and the S-layer is typically made up of highly glycosylated proteins. Interestingly, several glycosyltransferases are encoded in viral genomes. Protein

glycosylation is a crucial step that may play a role in the stability and/or contact of the virion with the host cell [3].

## DISCUSSION

archaeal viruses demonstrate that viruses of Archaea form a distinctive part of the virosphere and exhibit morphotypes that are not linked with the other two domains of life, Bacteria, and Eukarya, by describing numerous novel viral species and families. I mainly concentrate on viruses that attack Crenarchaeota individuals who are hyperthermophilic. From their morphotypes to their DNA sequences and the shapes of the proteins they encode, these viruses are unique. Additionally, these viruses engage with their hosts through specific processes that are distinct from one another. New views on the structure, diversity, and evolution of virus-host relationships are offered by research on archaeal viruses. Taking into account these findings, I believe that the disparities between bacterial and archaeal viruses are due to the basic variations in the make-up of their host cells' envelopes [4]. Virtually every habitat on the globe is home to viruses, even in the most saline, acidic, and hot settings, where archaeal creatures can thrive. For instance, new research has found crenarchaeal viruses in Yellowstone National Park's hot springs and other hot habitats globally. Understanding these viruses' viral life cycles is difficult because many of them are physically and genetically distinct, with genomes that bear little resemblance to genes with well-known functions. Here, we discuss the advances made in the molecular analysis of these intriguing viruses and the evolutionary lessons learned from these investigations [5].

The most prevalent strains attacking halophilic archaea are the archaeal-tailed viruses (art), which share evolutionary ancestry with tailed double-stranded DNA (dsDNA) bacteriophages of the class Caudoviricetes. Only a small number of these viruses have had their genomes fully described, which limits our understanding of both their biological effects and evolutionary history. The number of sequenced arTVs has more than doubled thanks to the 37 novel genomes of haloarchaeal-tailed virus strains that we present here. Analysis of all 63 complete arTV genomes, which we propose to categorize into 14 new families and 3 orders, reveals extensive gene sharing in DNA metabolism and counterdefense mechanisms, pointing to an ancient divergence of archaeal and bacterial-tailed viruses and shedding light on common approaches to virus-host interactions with tailed bacteriophages. Four different groups of viral tail fiber adhesins regulating host range growth were discovered when comparative genomics and host range analysis were combined and applied to a large sample of haloarchaeal species. According to a study of metagenomes using viral hallmark genes, the arTV community's world design is formed by frequent transfers between various biomes, such as hypersaline, marine, and anoxic environments [6].

Due to the limited number of archaeal viruses that have been described to date, they are among the most mysterious viruses in existence. Over an order of magnitude, fewer archaeal viruses have been identified than bacteriophages. Despite this, archaeal viruses have drawn the attention of scientists for more than 45 years due to their high amounts of genetic and morphological variation. Extreme natural settings, like acidic hot springs, are appealing environments for the finding and classification of novel viruses because Archaea and their viruses almost solely inhabit these environments. The archaeal viruses from these habitats have shed light on the biology, gene function, and evolutionary history of archaea. This review concentrates on developments from more than four decades of archaeal virology, with an emphasis on archaeal viruses from high-temperature environments, the difficulties in comprehending the gene function of archaeal viruses, and strategies being used to get around these obstacles [7].

One of the most mysterious aspects of the virosphere is viruses from archaea. Numerous virion morphotypes, including many that have never been seen in bacteriophages or viruses of eukaryotes, are displayed by the majority of the described archaeal viruses, which attack extremophilic hosts. However, new environmental studies have revealed that archaeal viruses are common in moderate environments as well. In these ecosystems, they play a significant ecological role by affecting the turnover of microbial communities, which has an effect on the carbon and nitrogen cycles on a worldwide scale. We examine recent developments in comprehending the molecular specifics of virion organization and assembly of archaeal viruses in this study. The 20 officially recognized families of archaeal viruses are briefly introduced before we go over the similarities and differences between the morphogenesis pathways used by bacterial and eukaryotic viruses and the assembly of archaeal viruses, before discussing the evolutionary implications of these findings [8].

According to this difference, many proteins that are similar to the capsid proteins of bacteriophages are encoded in the sequenced genomes of euryarchaeal viruses. The crenarchaeal viral genomes, on the other hand, showed no associations with bacteriophages and, in general, very few proteins with identifiable homologs, according to preliminary analysis. With a focus on comparative genetics of the distinctive viruses of Crenarchaeota, we report a re-analysis of the proteins encoded by archaeal viruses in this article. Numerous previously unknown homologous relationships between the proteins of crenarchaeal viruses and between viral proteins and those from cellular life forms were discovered through careful analysis of conserved domains and motifs, and this allowed functional predictions for some of these conserved genes. Similar to the metagenome structure of bacteriophages, overlapping subgroups of crenarchaeal viruses share a limited pool of genes [9].

A few fractions of all known bacterial viruses are isolated archaeal viruses. As a result, research into viruses that affect archaea is still in its infancy. Here, we present a virion-centered summary of the most recent findings of archaeal viruses. We outline the known archaeal virion morphotypes and contrast them with their hypothetical bacterial equivalents. Archaeal viruses have a variety of physical characteristics and some distinct morphotypes. Archaeal viruses, despite having a small number of isolates, offer fresh perspectives on the viral world by demonstrating complex evolutionary connections among viruses that infect hosts from all three realms of life [10].

## CONCLUSION

Since they have developed over billions of years, microorganisms are considered to be the earliest living things in the entire universe. They belong to the Monera realm and are categorized as microbes because, when examined under a microscope, they resemble bacteria. The DNA genomes of the majority of archaeal viruses contain extensive transcription factor encoding regions. It is thought that archaeal viruses, which are a primary source of mortality on the ocean floor, contribute significantly to the recycling of nutrients in seas. In highly saline habitats, the salinity level can have an impact on the infectivity and activity of some archaeal viruses. Double-stranded DNA viruses with a range of odd shapes that are unconnected to any other viral types can attack Archaea. The groups Sulfolobales and Thermoproteales, which are thermophilic, have been the focus of the most extensive research on these viruses.

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# CHAPTER 19

# A BRIEF INTRODUCTION OF THE NOVEL CLASS OF VIRUS; GIANT VIRUS

Phool Chandra, Professor
Department of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- chandraphool@gmail.com

**ABSTRACT:**

Giant viruses have a protein envelope and a width of about 750 nm. The interior lipid barrier of this protein capsid is encircled by a thick coating of glycoprotein fibrils, which facilitates viral attachment to host cells and other microbes. The infection of human cells is caused by a viral that impacted the amoebae in the human intestines. It's conceivable that both the amoebae and the viral infection are responsible for apparent symptoms like respiratory distress or other forms of infection. Given how challenging amoebae are to handle, this prospect is a little terrifying. The fundamental traits of the giant viral and their invasion were summed up in this chapter.

**KEYWORDS:**

Enormous Virus, Gaint Virus, Host Cell, Large Virus, RNA Polymerase.

## INTRODUCTION

Phycodnaviridaechloroviruses were the first large viruses to be identified. Russell H. Meints, James L. Van Etten, Daniel Kuczmarski, Kit Lee, and Barbara Ang made these discoveries in 1981. Since it was first discovered to attack Chlorella-like algae, the first chlorovirus was originally known as HVCV (Hydra viridis Chlorella virus). Later, it was discovered that other enormous viruses also affected oceanic flagellates. The first mimivirus (BV-PW1) was first reported in 1995, but it wasn't until the decoded genome of the Cafeteriaroenbergensis virus (CroV) was published in 2010 that it was identified as a mimivirus. The giant viral Acanthamoeba polyphagaMimivirus, which had been confused for a bacterium in 1993, was subsequently described and sequenced. In 2006, the word "girus" was first used to describe the group [1].

Jean-Michel Claverie recently discovered the "mamavirus," another enormous virus. The fact that another virus was discovered inside the enormous mamavirus is an intriguing development in this finding. In other words, it was found that the host-virus is a satellite virus of a much larger virus. Although satellite viruses have been observed in other species before, this is the first instance in which the satellite virus has been discovered encapsulated inside host viral particles. The first man-made satellite is now known as "Sputnik," and the satellite malware bears its name. Its 18-kilo DNA genome contains 21 genes that are encoded. It's interesting to note that the Sputnik-infected mamavirus exhibited morphological distortion and some attenuation in the offspring generation. In a nutshell, Sputnik makes its user feel nauseated. In addition, the giant virus' satellite virus is now referred to as a "virophage" like the bacteriophage. Cleverly adding, "The discovery of virophage makes 'virus' more living organisms," Jean-Michel ClaverieIn a paradoxical way, "being sick" can be considered proof of "living." In a host-virus that was already operating as a parasite of the host organism, a viral particle was discovered for the first time [2].

Giant viruses continue to share some crucial characteristics despite the continuing discussion about their origins. The dsDNA category includes all NCLDV groups and all giant viruses. All gigantic viruses have genomes that are at least 288 Kbp in size (Figure.1). The Mimiviridae, Pithoviridae, Pandoraviridae, Phycodnaviridae, and Mollivirus family are some of the groups into which these enormous viruses fall.

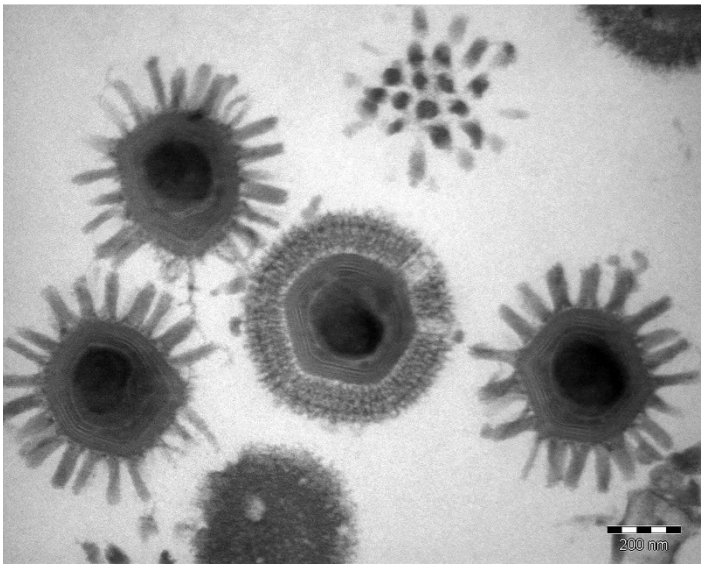


**Figure 1: Giant virus: Diagram showing the structure of the giant virus (NPR).**

The non-specific phagocytosis by the amoebae host is a prerequisite for all large viruses that attack amoebas. As amebae (and related protozoa) typically consume bacteria, it is interesting that a minimum particle size (0.6 m) is a prerequisite for phagocytosis. This minimum size for triggering phagocytosis has probably evolved to be a driving factor in the development of giant viruses. This fact, along with the fact that the genomic content of giant viruses is largely uncharacterized, may imply that much of the content in their genomes only functions to occupy space to make them bigger physically. Not just the cell entrance mechanism is shared by giant viruses. As many as 1000 virions are released from each lysed host during lysis via membrane fusing and active exocytosis, which are comparatively uncommon departure methods in viruses. Other characteristics of gigantic viruses are mostly family-specific aside from these genomic and cell biology commonalities. Giant viruses from various families differ significantly in terms of, for instance, virion forms and symmetries, nuclear participation, the length of the infection cycle, and the phases of virion construction [3].

Due to their huge icosahedral virions (T number 169)41 and genomes of up to 370 kb, chloroviruses were the first viruses to be referred to as "giant viruses"8. Its capsids have a few external fibers stretching from some of the capsomers41 and a spike-like structure present at one vertex to attach to the host cell. In particular, PBCV1 was widely examined (Figure. 2). The virus-encoded glycosylation machinery produces an uncommon oligosaccharide that is N-linked to asparagines in aberrant sequons in the main capsid protein. This oligosaccharide is used to glycosylate the capsids. (MCP; Vp54). A solitary lipid membrane that is required for infectivity is covered by the exterior capsid layer. By using an enzyme encoded by the virus and contained in the virion, chloroviruses break a hole in the cell wall of their algal host to transport their DNA. The host plasma membrane and the viral internal membrane unite at that point, creating a channel through which the viral DNA and some viral proteins can infiltrate the cell. The inbound genome must be translated inside the host cell's nucleus before the virion is assembled in the cytoplasm because the virus does not contain an RNA polymerase. Virion discharge occurs following recipient cell lysis.

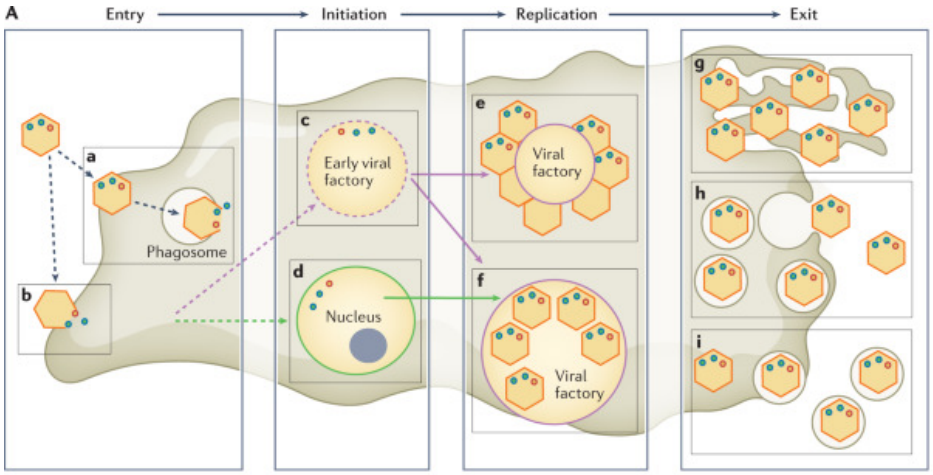


**Figure 2: Giant virus infection: Diagram showing the giant virus infection mechanism (Nature).**

The mimivirus9, which infects amoebas, is the virus that has been researched the second most after PBCV1. The 1.2 Mb genome-containing icosahedral shell with a width of 500 nm makes up the 700 nm virions.The virus-encoded glycosylation machinery produces bacterial-type sugars, which are the building elements of the intricate 70 kDa and 25 kDa polysaccharide structures that adorn the mimivirus fibrils encircling the capsid. The mimivirus capsid has a low-resolution structure that has been identified, and thorough atomic force microscopy has revealed additional information about the virion makeup, highlighting the intricacy of the capsid. The nucleoid compartment, which houses the genome and numerous proteins, including RNA polymerase and the apparatus for generating transcripts, has two internal lipid membranes, one surrounding the capsid and the other in the nucleoid compartment. Non-structural proteins in the nucleoid are thought to be necessary for early transcription, reactive stress protection, and the start of the virus infectious cycle.

According to preliminary evidence, the genome is structured as a 30-nm-diameter helix nucleocapsid made up of GMC oxidoreductases, which are also responsible for the capsid's glycosylated fibrils. The nucleocapsid's folded DNA borders the shell, leaving a center channel that can hold big proteins like RNA polymerase. Mimivirus penetrates its host by inducing phagocytosis after attaching its glycosylated fibrils to the host cell membrane. The membrane under the capsid is drawn out and fuses with the vacuole membrane once inside the vacuole, enabling the nucleoid to be transferred into the host cytoplasm. This process is made possible by a particular structure at one vertex of the icosahedron called the stargate. Like other recognized Mimiviridae members, Mimivirus multiplies within the cytosol of its host. The virus-encoded transcription machinery, which initially stays contained in the nucleoid, is used to start early transcription. The size of the viral factory grows as a result of the buildup of nucleic acids brought on by active transcription and reproduction, and freshly synthesized virions begin budding at its perimeter using recycled host cell membranes from the endoplasmic reticulum or Golgi apparatus.

Hundreds of freshly created virions are released after cell lysis as the final stage of virion maturation, following the addition of the fibril layer to the capsids and the transfer of the DNA into the nucleoid. Several viruses linked to the mimivirus have smaller virions but comparable infectious cycles. Among them is the Cafeteriaroenbergensis virus, which has a lipid layer under the capsid shell and an icosahedral capsid with a width of 300 nm (Figure 2). Its exact mode of infection is unknown, but, like mimivirus, extracellular empty capsids have been seen and a nucleoid structure in the cytoplasm, supporting an external opening of

the capsids followed by fusion of the internal membrane with that of the cell, allowing the transfer of the nucleoid into the host cytoplasm. About 150 proteins are found in viruses and either make up the icosahedral capsid or are required to start the contagious cycle. In the late stages of infection, nascent virions form and are expelled through cell lysis. The structure of the complex capsid, found by cryo-EM, correlates to a T number of 499 and has given a novel model for capsid assembly. Bodo saltans virus is another member of the Mimiviridae with a comparable icosahedral structure measuring 300 nm in diameter. Two proteinaceous layers appear to be the structure of its capsid, which is encased in 40 nm-long fibrils.

Two membranes, one lining the exterior protein shell and the other interior to the nucleoid compartment holding the genome, are present along with a potential stargate-like structure at one vertex of the capsid. The host's nuclear DNA looks to be damaged, but the infectious cycle is otherwise comparable to that of the mimivirus. The virus factory forms at the cell's posterior end, displacing the organelles and nucleus to occupy two-thirds of the available area. Lipid droplets are attracted to the side of the viral factory where virion assembly takes place. Mature virions separate after genome loading and move to the cell's posterior pole. After cell disintegration, virions are expelled from the host membrane by budding in vesicles (Figure. 2). The Mimiviridae family includes some of the biggest viruses that attack algae, with icosahedral capsids that range in size from 150 nm for the Aureococcusanophagefferens virus to 370 nm for the newly discovered Prymnesium kappa virus.

Although it is unclear whether the transcriptional machinery is loaded into the capsids, enabling a completely cytoplasmic infectious cycle, these viruses also construct a viral factory in the host cytoplasm. The pithovirus and cedratvirus virions, which have very large amphora-shaped capsids that can be up to 2-m long and 600-nm broad and encapsidating genomes of up to 685 kb, are the biggest virions discovered in the Nucleocytoviricota (Figure. 2). Two corks for cedratvirus and one for pithovirus are used to seal the capsids, and both are composed of proteins arranged in a honeycomb pattern. The external tegument is distinct and appears to be composed of parallel bands and no cellulose, even though the virion morphology closely matches that of a pandoravirus. The capsids also appear to be covered with short, sparse fibrils. As with other amoeba-infecting viruses, the contagious cycle starts with phagocytosis, followed by capsid opening and membrane union with the phagosome. For pithovirus and cedratvirus, the host nucleus is unharmed throughout the entire contagious cycle thanks to the RNA polymerase carried in the virion, which initiates early transcription in the cytoplasm. Tegument and cork stores grow up in the host cytoplasm during development and are used to create new amphora-shaped virions. The developing viruses then leave the host cell through cell disintegration or exocytosis.

## DISCUSSION

The pro-phage idea and early work by the "phage group" and molecular biologists studying tumor viruses serve as the foundation for the current theory regarding the nature of viruses. (the proto-oncogene concept). According to this theory, viruses originated from cellular genes in either bacterial or eukaryotic cells that turned contagious when they bonded with genes for capsids. According to this theory, viruses continued to develop after they first appeared by taking cellular genes. (the escape model). Recently, scientists have questioned this theory by arguing that viruses existed before contemporary cells. Numerous discussions on the essence of viruses have been sparked, particularly by the finding of Mimivirus. There are two main schools of thought: those who support the escape model and argue that large viruses are simply gigantic pickpockets (a phantasm); and those who place more emphasis on the peculiarities and prehistoric origins of large viruses. Numerous data from comparative genomics of the Mimivirus and similar nucleo-cytoplasmic large DNA viruses have been

read based on the author's preconceptions, making it difficult to reach an agreement up until this point. Here, I quickly review the history of these discussions and how they influenced new ideas, such as the definition of viruses as capsid-encoding organisms or the acceptance of the virocell concept, which asserts that viruses are essentially cellular [4].

The biggest known DNA virus is the Acanthamoeba polyphagia Mimivirus, which was just found. Its big gene set (911 protein-coding genes), the large genome size (1.2 million bp), and small particle size (750 nm) obscure the lines between viruses and parasitic cellular entities. Its genome sequence analysis also revealed a wide variety of genes that had never before been found in a virus, such as aminoacyl-tRNA synthetases and other essential parts of the translation apparatus that were previously believed to be the distinguishing feature of cellular creatures. In this paper, we investigate how the discovery of such a massive virus might permanently alter how we view microbial biodiversity and prompt us to reclassify the categories and life forms of microbes. The name "girus" will be used to denote the intermediate state of these enormous DNA viruses, whose genome complexity places them more closely related to small parasitic prokaryotes than to typical viruses [5].

Giant viruses with enormous genome sizes and a variety of particle forms continue to infiltrate the field of virology. Strains discoveries and metagenomic studies make it feasible to disclose the intricacy of these microorganisms, their origins, habitats and potential functions. Using Vermamoebavermiformis as the host cell, we recovered the novel giant virus "Orpheovirus IHUMI-LCC2" from a rat stool sample. In this article, we discuss Orpheovirus IHUMI-LCC2's primary genetic characteristics and replication cycle. It has ovoidal particles varying in size from 900 to 1300 nm, a circular genome with a G+C content of 25%, and a circular genome surpassing 1.4 Megabases. Particles have a solitary ostiole-like structure at their tip that is closed by at least one thick membrane.

The suggested Pithoviridae family is connected to the Orpheovirus based on phylogenetic research and the reciprocal best match. However, when compared to Cedratviruses or Pithoviruses, some genomic features of Orpheovirus IHUMI-LCC2 show a divergent evolution[6].The story of giant viruses (i.e. observable by light microscopy) began in 2003 with the finding of Mimivirus. Since then, Pithovirus sibericum (2014) and the Pandoraviruses (2013), two new kinds of giant viruses that attack Acanthamoeba, have been identified. The latter was revived from 30,000-year-old Siberian permafrost. The fourth species of giant virus, Mollivirussibericum, which was recovered from the same permafrost material, is now described.

The virion structures, sizes (0.6-1.5 m), genome lengths (0.6-2.8 Mb), and reproduction cycles of these four kinds of gigantic viruses vary. Conflicting theories exist regarding their genesis and method of evolution. Given the effects of global warming, the ease with which two distinct viruses could be recovered from ancient permafrost is cause for alarm [7].

Since the Mimivirus and four other protist-infecting giant viruses that are connected to the nucleocytoplasmic large DNA viruses were discovered in 2003, there has been a significant increase in interest in giant viruses. (NCLDVs). The NCLDVs are monophyletic based on analyses of their sequences and gene repertoires, despite significant variation in hosts and genome sizes. Recent studies have suggested that these viruses share a common ancient progenitor and constitute a fourth realm of life. The NCLDV designation is not entirely accurate, and several features of these enormous viruses contradict or do not fit the standards used for the canonical meaning of viruses. Here, we suggest defining the Megavirales, a brand-new viral order [8].

At the moment, viruses separated from aquatic habitats and grown in laboratories make up a disproportionate share of the known variety of giant viruses. On sediments from the Harvard Forest, we use cultivation-independent metagenomics and mini-metagenomics, which led to the finding of 16 new giant viruses, primarily recovered by mini-metagenomics. The potential viruses reflect new lineages or are related to klosneuviruses, Cafeteria roenbergensis virus, or tupanviruses, significantly expanding the phylogenetic variety of known giant viruses. The biggest assembled viral genome in the Mimiviridae family is 2.4 Mb in size, and other genomes in the family contain up to 80% of orphan genes. Additional evidence that giant viruses are understudied in soil environments comes from the discovery of more than 240 main capsid proteins encoded on unbinned metagenome segments. Given that the majority of these new viruses avoided being discovered in mass metagenomes, mini-metagenomics may be a useful strategy to find viral giants [9].

Although they have gone unnoticed lately, viruses with genomes up to a few megabases in length are a frequent occurrence in nature. These massive viruses primarily affect single-celled eukaryotes and attempts to separate them have focused solely on amoebae, which have produced hundreds of viral isolates with the largest known viral genomes and particles. One of the tasks that lie ahead is to classify and evaluate the data that is already accessible to create a recognized categorization scheme that takes into account the biological characteristics and evolutionary relationships of these viruses. A first model of the genetic variety and makeup of a giant virus clade has been produced by an extensive collection of mimiviruses that attack Acanthamoeba and preliminary classification of their virophage parasites [10]. This information will aid in the taxonomic categorization of these intriguing microorganisms.

## CONCLUSION

The giant viruses are a subset of nucleocytoplasmic big DNA viruses (NCLVD), which are bigger than typical virus families in terms of viral particle size, structure, genome length, and intricacy. Large viruses are typically defined as having large, pseudo-icosahedral capsids (200 to 400 nm in diameter), which may be encased in a dense coating of fibrous protein fibers (roughly 100 nm in thickness). The microorganism organisms, which have been discovered in a variety of habitats including air, dirt, water, and animal bodies, are thought to be among the most prevalent protozoan organism found worldwide and are the focus of the bulk of giant viral. Giant genomes of viruses contain DNA that is essential for biological survival. Signature families of life in cells, like tRNAs and genes involved in protein biosynthesis, can be discovered in the DNA of gigantic viruses, which is one of their most fascinating characteristics.

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# CHAPTER 20

# SYNTHETIC VIRUSES; A NEW TOOL FOR THE VIRAL ENGINEERING

Prashant Kumar, Associate Professor
Department of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- kumarprashant86@gmail.com

**ABSTRACT:**

An effective method to learn how viral produce illnesses as well as how to fight pathogenic varieties is to create and manipulate synthetic viruses to investigate their characteristics. The first synthetic viral prepared using this method was the polio virus. Other viruses, like the retrovirus and the influenza virus, are chemically created in addition to the polio virus. This chapter covered preparation and the significance of synthetic viruses.

**KEYWORDS:**

DNA Complex, DNA Virus, RNA Virus, Synthetic Virus, Viral Vectors.

## INTRODUCTION

A branch of virology called synthetic virology utilizes the basics learned from naturally existing viruses to create viruses using molecular, computational, and synthetic biology principles. Poliovirus was the first virus created from artificial oligonucleotides, and the phiX174 bacteriophage (i.e., phage) was the second. A previously decoded genome serves as the foundation for the construction of synthetic viruses, which are then constructed using synthetic oligonucleotides (e.g., Gibson). As a quality control measure, synthetic virions should be morphologically assessed using TEM or AFM to make sure the viral DNA is packaged within particles (i.e., full virion assembly) before host confirmation. Several techniques can be used by computational tools to forecast the hosts of different viruses. A synthetic virus could prove an infection if the host is accessible. If it were to work, a person would be able to create model systems straight from sequencing data. (Figure. 1) [1].

It wasn't known in the early 1950s whether nucleic acids or proteins were the molecules that controlled inheritance. Finally, using radiolabeled synthetic phage proteins (35S) and DNA, Hershey, and Chase using T2 phage verified it was DNA. (32P). The first law of life, that nucleic acids, not proteins, were the molecule of heredity, was thus set by viruses. As a result, viruses can be used to comprehend the assembly, variety, structure, and scope of virus-mediated impact. Synthetic viruses were used to establish the first law of life. Economic development is greatly facilitated by synthetic biology, which is expected to generate an $11.4 billion market by 2021. Synthetic viruses may even be created to carry out particular functions and may find widespread use in fields such as agriculture, health, combating climate change, and possibly carbon capture (Figure. 1).

Synthetic genomes built on previously read genomes are now possible thanks to improvements in oligonucleotide synthesis and genome sequencing technology. Existing techniques can be used to create both RNA and DNA viruses. Due to their usually tiny genome sizes and preexisting reverse transcription machinery, RNA viruses have been used in the past. The polio virus and the X174 bacteriophage were the first contagious viruses created by humans that were produced without using any natural templates. In the case of both DNA and RNA viruses, the first step in the creation of manufactured live viruses is the genome rather than the entire virus. When inserted into a cell, viral RNA from many viruses

can spread to other cells. When introduced *in vivo*, these organisms have the capacity to maintain a contagious life cycle [2].

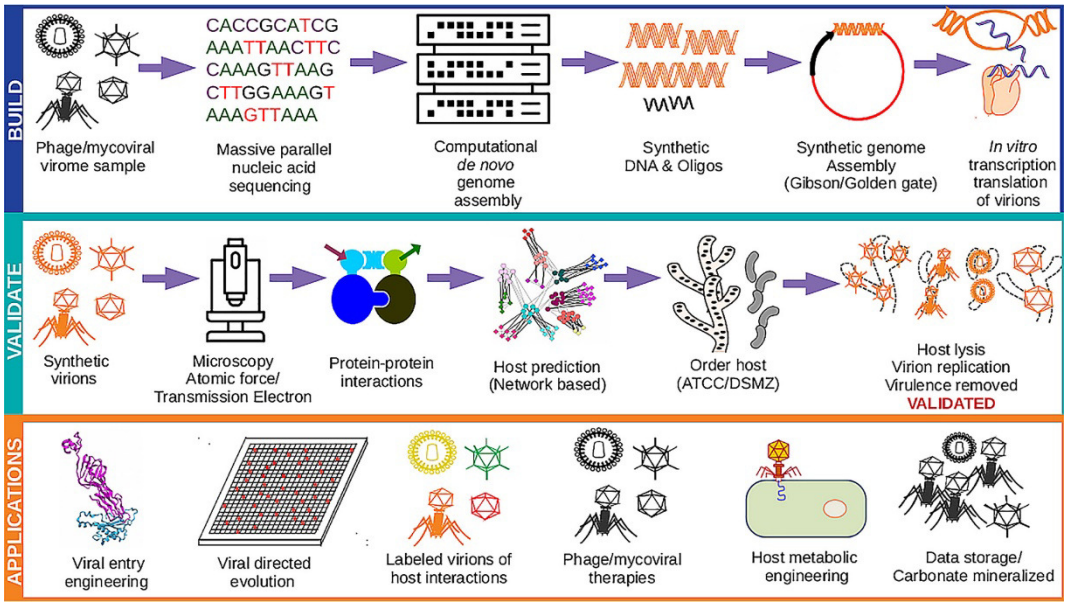


**Figure 1: Synthesis virus: Diagram showing the synthesis of the different synthesis viruses (journals.asm).**

The 27 nucleotide changes in the synthetic polio cDNA were strategically distributed throughout the genome to act as genetic identifiers. (watermarks). The artificial virus, known as sPV1(M) when developed in HeLa cells, an effective tissue culture method for poliovirus growth, displayed no phenotypic differences from the wild-type PV1(M). However, the median lethal dose (LD50) was five orders of magnitude higher when administered intracerebrally to CD155 tg mice, which are transgenic for the poliovirus receptor, CD155 (LD50 values of 102 and 107 for the wild-type virus and sPV, respectively; E.W. and colleagues)18. Unexpectedly, a single A residue at position 102 of the genome, situated in the 5′ nontranslated region (5′ NTR) of the genome at a location long believed to only function as a spacer between two highly structured regions54, was the genetic locus for the huge attenuation of sPV(M).

We were inspired by this unanticipated outcome to create a highly weakened oncolytic poliovirus. It wasn't necessary for living cells to create the poliovirus. After being chemically created, the cDNA was converted into infectious viral RNA in vitro (E.W. and colleagues)56, which was then incubated with a sample of uninfected HeLa cells (E.W. and colleagues)57 to produce contagious sPV1(M). Therefore, the poliovirus is nothing more than a substance in the eyes of a scientist. However, the virus has a plan for life once it penetrates a cell. It will hijack cellular compartments and transform them into viral factories, where it will multiply in accordance with the rules of evolution, such as heredity, genetic diversity, selection for health, development into various species, and so on. In other words, the poliovirus abides by the same laws that govern living things. One could even contend that the poliovirus has sex in the infected cell because it easily recombines with related viruses or sibling offspring if they attack the same cell together. In reaction to the 2002 publication of the chemical and biochemical synthesis of the poliovirus, this intriguing dual nature of viruses as nonliving and living entities that is, a presence as chemicals with a life cycle—has largely gone unnoticed. The creation of the poliovirus also verified the veracity of the genome sequence, it should be mentioned. Since the sequencing of PV1(M), the first lytic animal RNA virus, was initially

done using two distinct methods and verified later in numerous genetic studies, this may be viewed as completely unnecessary.

Chemical synthesis, however, is unquestionably helpful in confirming sequence and will continue to be so in the future when bigger genetic sequences are being proofread1 [3]. Somatic transcriptional editing has also been effectively accomplished through the use of RNA viruses. A Cas9-based transcription factor was used to produce stable plant lines, and gRNAs were delivered to target the transcription factor using viral vectors. Instead of waiting months or years to investigate related phenotypes using conventional transgenesis, this method was used to fine-tune the expression of metabolic and developmental master regulator genes. This method was also used to allow selective methylation in both somatic and germline cells, resulting in heritable phenotypes.

The direct fusion of the Cas9 protein to the transcription or methylation effector domains limits the types of changes that the viral vectors can apply, which is one drawback of all these strategies. The constitutive expression of a toolbox of effectors that can be built into the desired activators or repressors in planta via RNA scaffolds that are carried on viral vectors offers a hopeful answer to this conundrum. Co-delivering the effectors and gRNA scaffolds to a plant that is consistently expressing only the Cas9 protein is an even more adaptable strategy that has been proven. Again, it was discovered that the presence of movement enhancement motifs was necessary for efficient regulation, most likely because it allowed for high-frequency vector colocalization within the group.

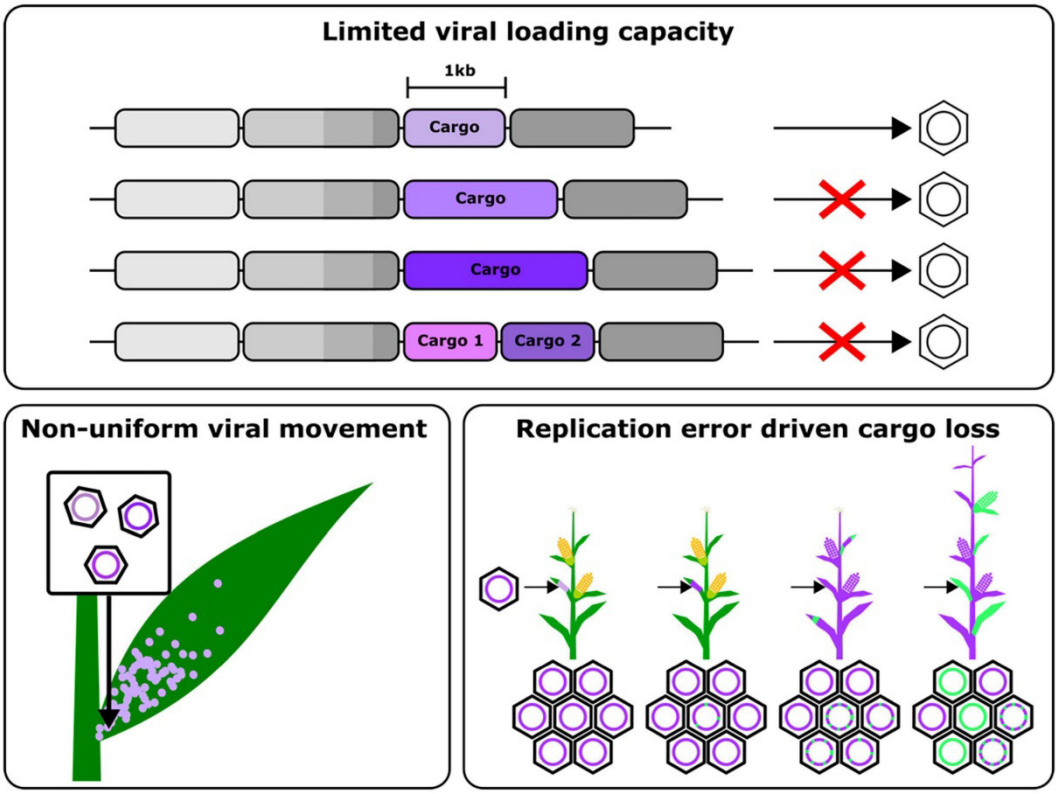


**Figure 2: viral gene delivery tools: Diagram showing the major challenges need to improve the viral gene delivery tools(frontiers).**

Although this method was able to produce observable changes in plant behavior, the fold changes in gene expression were relatively small, suggesting that there is a lot of room for improvement in this approach. These methods have been effectively used to investigate both metabolic and developmental processes in a variety of plants, such as the crop plant *Solanum*

*lycopersicum* and the model plants *A. thaliana* and *N. benthamiana*. The failure to load big cargo onto viral vectors, however, continues to be a limitation of the aforementioned strategies, requiring the integration of proteins like Cas9 into the genome (Figure 2). Some teams have used negative single-stranded RNA viruses, which can carry more payload, to get around this problem, but they still have the disadvantage of needing multiple auxiliary proteins to start an infection. Although it has been demonstrated that using movement improvement patterns can increase the uniformity of viral cargo distribution, there are still many unanswered issues in this field of viral engineering. Last but not least, these viruses are also amenable to silencing, which causes the translation of the payload to gradually decrease. These difficulties bring to light some of the engineering possibilities to enhance viral vectors to the point where stable transgenesis might one day be replaced as the main strategy for deploying the instruments of plant synthetic biology. The remainder of this study looks at the parts of RNA viral vectors that require reengineering and some potential methods to do it (Figure 2) [4]. Currently, the researcher are being held accountable for developing a process that enables the production of any contagious poxvirus, including the smallpox virus, from synthetic DNA (Figure.3). But is this a novelty? The research did not offer novel material explicitly enabling the creation of a smallpox virus, according to the PLOS Dual Use Research of Concern (DURC) Committee. but makes use of well-established techniques, materials, and information that have been employed in the creation of other viruses (like influenza and polio viruses). Various experimental techniques and methods for producing contagious horse pox virus have been documented in the past. First off, the ability of poxviruses to cause homologous recombination has long been known, and this ability has been used for decades to alter various poxviruses, primarily the vaccinia virus. Therefore, it is not unexpected that overlapping DNA segments are united by homologous recombination in cells infected with the poxvirus.

Second, methods for recovering poxviruses from bare DNA have been in place for years.

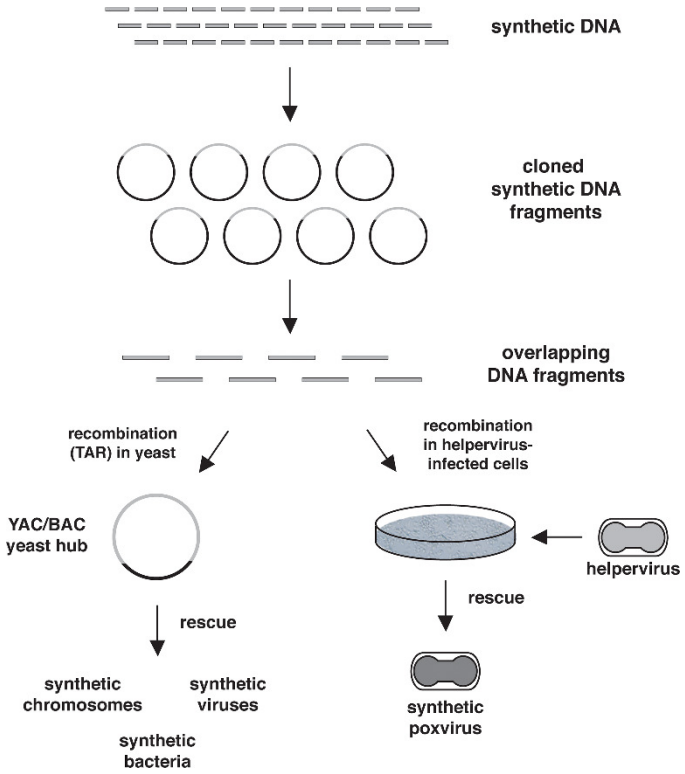


**Figure 3: synthesis DNA: Diagram showing the steps involved in the synthesis of DNA (PLOS).**

Helperviruses, such as the fowlpox virus, are regularly used to initiate replication from naked vaccinia virus genomic DNA. With the help of this method, hybrid vaccinia viruses with insertions of up to 26–31 kbp of foreign DNA have been produced effectively. Additionally, a full-length vaccinia virus DNA cloned as a bacterial artificial chromosome (BAC) in Escherichia coli has been used as a helper virus to initiate vaccinia virus propagation. This study by Domi and Moss is noteworthy because it showed for the first time that infectious vaccinia virus can be produced from cloned circular DNA, as opposed to earlier methods that needed a linear vaccinia virus genome with real genome ends.

## DISCUSSION

For the transfer of luciferase or beta-galactosidase marker genes to K562 cells, HeLa cells, and BNL CL.2 hepatocytes, complexes containing plasmid DNA, transferrin-polylysine conjugates, and polylysine-conjugated peptides derived from the N-terminal sequence of the influenza virus hemagglutinin subunit HA-2 have been used. Due to the functions for (i) packaging the nucleic acid with polylysine, (ii) attachment to the cell and receptor-mediated endocytosis with transferrin as a ligand, and (iii) release from endosomes by using membrane-disrupting influenza peptides, these DNA complexes mimic how viruses enter cells. In a liposome leaking test, these influenza peptide conjugates make DNA complexes active in membrane disruption, which significantly increases the amount of gene transfer mediated by transferrin and polylysine [5].

Synthetic peptides that can damage liposomes, erythrocytes, or cell culture endosomes have been used to imitate the way viruses disrupt endosomal membranes in an acidification-dependent fashion. Only when peptides were lengthened by an amphipathic helix or by carboxyl-terminal dimerization did they exhibit erythrocyte hemolytic activity. These peptides contained the 20 amino-terminal amino acid sequence of the influenza virus hemagglutinin as well as acidic derivatives. It's interesting to note that erythrocyte breakdown was also facilitated by peptides made up of the 23 amino-terminal amino acids of the influenza virus hemagglutinin. A significant correlation between pH-specific erythrocyte disruption activity and gene transfer was found when peptides were incorporated into DNA complexes that use a receptor-mediated endocytosis pathway for uptake into cultured cells, either by ionic interaction with positively charged polylysine-DNA complexes or by a streptavidin-biotin bridge. In human melanoma cells and a number of cell lines, high levels of luciferase or interleukin-2 production were achieved with tailored gene transfer complexes [6].

In order to create full-length poliovirus complementary DNA (cDNA), oligonucleotides with plus and negative strand orientation were put together. The de novo synthesis of contagious poliovirus was achieved through the transcription of the synthesized poliovirus cDNA by RNA polymerase into viral RNA, which was then translated and replicated in a cell-free extract. Neurovirulence studies in CD155 transgenic mice and tissue culture experiments using neutralizing antibodies and antibodies specific to the CD155 receptor verified the synthetic virus's poliovirus-like biochemical and pathogenic properties. Our findings demonstrate that a contagious agent can be created by in vitro chemical-biochemical methods simply by adhering to written instructions [7].

For the production of constrained materials, virus capsids, which come in a variety of sizes and forms, can be used as protein cages. The use of spherical viruses for inorganic mineralization and organic polymer encapsulation as well as the mineralization of anisotropic structures like the tobacco mosaic virus, which can result in mineralized fibers of iron oxide or silica with extremely high aspect ratios, are all covered briefly in the authors' review of

recent work involving capsids. We quickly touch on the subject of gating, which allows for the selective entrapment and release of materials from the center cavity [8].

Even though in some instances genome packaging is essentially unchanged, HIV-1 with mutations in the nucleocapsid (NC) Zn2+ finger regions has significantly decreased infectivity. Viral DNA (vDNA) was extracted from cells infected with HIV-1 wild-type, the integrase mutant IND116N, the double mutant NCH23C/IND116N, or viruses with His-to-Cys alterations in their Zn2+ fingers (NCH23C and NCH44C). Potential functions for NC in reverse transcription and integration have been demonstrated by in vitro tests. Quantitative PCR, cloning of PCR products, and evaluation of the quantity and make-up of vDNA produced at specific points during reverse transcription were used to derive in vivo findings for these processes. A quantitative study of the intermediates of reverse transcription for these species firmly indicates that the DNA generated is less stable.

Both Zn2+ finger mutations appear to be defective in DNA synthesis, with the interior of the vDNA remaining more intact while the minus- and plus-strand transfer mechanisms are impacted. The NC mutants had a phenotype similar to the IN mutant, according to the sequences derived from PCR amplification and cloning of 2-LTR circle junction segments; the NC mutations prevent the removal of the terminal CA dinucleotides required for incorporation of the vDNA. Because of the reduced protection of the full-length vDNA, the loss of infectivity in these NC mutants in vivo seems to be caused by flawed reverse transcription and integration mechanisms. Last but not least, these findings show that NC's chaperone function stretches from the control of viral RNA to the full-length vDNA [9].

We outline how to effectively move DNA into a range of cultured cells using cationic, pH-sensitive liposomes. Dioleoylphosphatidylethanolamine was made and combined with cationic lipids that contained an amine with a pK within the physiological range of 4.5 to 8. These cationic, pH-sensitive liposomes were enhanced by acid circumstances in DNA binding, DNA incorporation, and DNA-induced fusing. Similar to acidic-induced endosomal viral release, transfection efficacy in cultured cells was reliant on endosomal acidification. These liposomes make up a potential novel category of gene therapy agents [10].

## CONCLUSION

The entire genes of several other viruses based on RNA, besides the poliovirus and influenza virus, have lately been biologically made. These include coronaviruses that resemble SARS, HIVcpz, and human endogenous retrovirus. Significantly simultaneous DNA sequencing must be used after viral nucleic acids have been recovered. Computational processes then create the virus genomes from scratch after decoding. It is possible to buy synthesized DNA and oligonucleotides (oligos) after the algorithmic assembly of the viral genomes. The hosts that a virus infects and affects determine its significance, and numerous viruses are significant since they lead to illnesses in people, animals, or vegetation.

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# CHAPTER 21

# HOST DEFENSE MECHANISM BY THE VIRUS TO EVADE THE HOST IMMUNE SYSTEM

Dr Ankita Mittal, Professor
Department of Pathology, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- dhanyamittal09@gmail.com

**ABSTRACT:**

Viruses utilized several mechanisms to evade the host cells. significantly restricting viral products from attaching to intracellular sensors and deactivating cells that are that participate in IFN signaling or the induction of the antiviral state, viral have evolved methods to evade the effects of IFN.Additionally, there are several other mechanisms, such as preventing antigen presentation, avoiding apoptotic and chemokine generation, avoiding NK cell actions, and altering the antigen they produce a presentation. In this chapter, we briefly discussed the mechanism utilized by the virus for host cell invasion.

**KEYWORDS:**

Cell death, Innate immune, Host cell, RNA virus, Spike protein.

## INTRODUCTION

The immune system of mammals has developed sophisticated strategies for dealing with and adjusting to alien pathogens. Viruses have simultaneously developed escape mechanisms to counteract the numerous ways that host organisms try to eliminate them. DNA and RNA viruses employ sophisticated strategies to avoid being discovered by immune cells, including interference with the Interferon Signaling Pathway, cellular architecture modification, tailored gene suppression, and recognition of protein cleavage. The immune system of mammals has developed sophisticated strategies for dealing with and adjusting to alien pathogens. Viruses have simultaneously developed escape mechanisms to counteract the numerous ways that host organisms try to eliminate them. DNA and RNA viruses employ sophisticated strategies to avoid being discovered by immune cells, including interference with the Interferon Signaling Pathway, cellular architecture modification, tailored gene suppression, and recognition of protein cleavage [1].

Caspases, cysteine proteases, are activated along with apoptotic cell demise. It could, however, also be caspase-independent. Both processes are regulated by the regulator of apoptosis proteins and anti-apoptotic Bcl-2 family proteins. Numerous viruses produce anti-apoptotic proteins that enable them to finish viral reproduction before the cell is destroyed and the virus is disseminated. As a result, by preventing virus growth, apoptotic cell demise plays a crucial part in host defense. Apoptosis may also aid in the escape of viruses, and the inhibition of apoptosis may prevent the infection of viruses. Virus-induced apoptotic cell death thus plays a complicated function in host defense, may aid in the removal of viruses, or act as a process for virus-induced tissue damage and disease progression. Viral illnesses may cause disorders by reducing apoptosis. (e.g., infections induced by adenoviruses, baculoviruses, herpesviruses, and poxviruses). However, some conditions (such as illnesses brought on by Ebola or HIV-1) may be linked to a rise in apoptosis (Figure. 1). Viral infection may also cause other types of cell death, or even their mixture, in addition to apoptosis. For instance, sindbis virus infection of motor neurons results in necrosis, which results in cell loss in the spinal cord, but it also produces the typical apoptosis of cortical neurons in the brain, indicating a cell type-dependent reaction to the same virus [2].

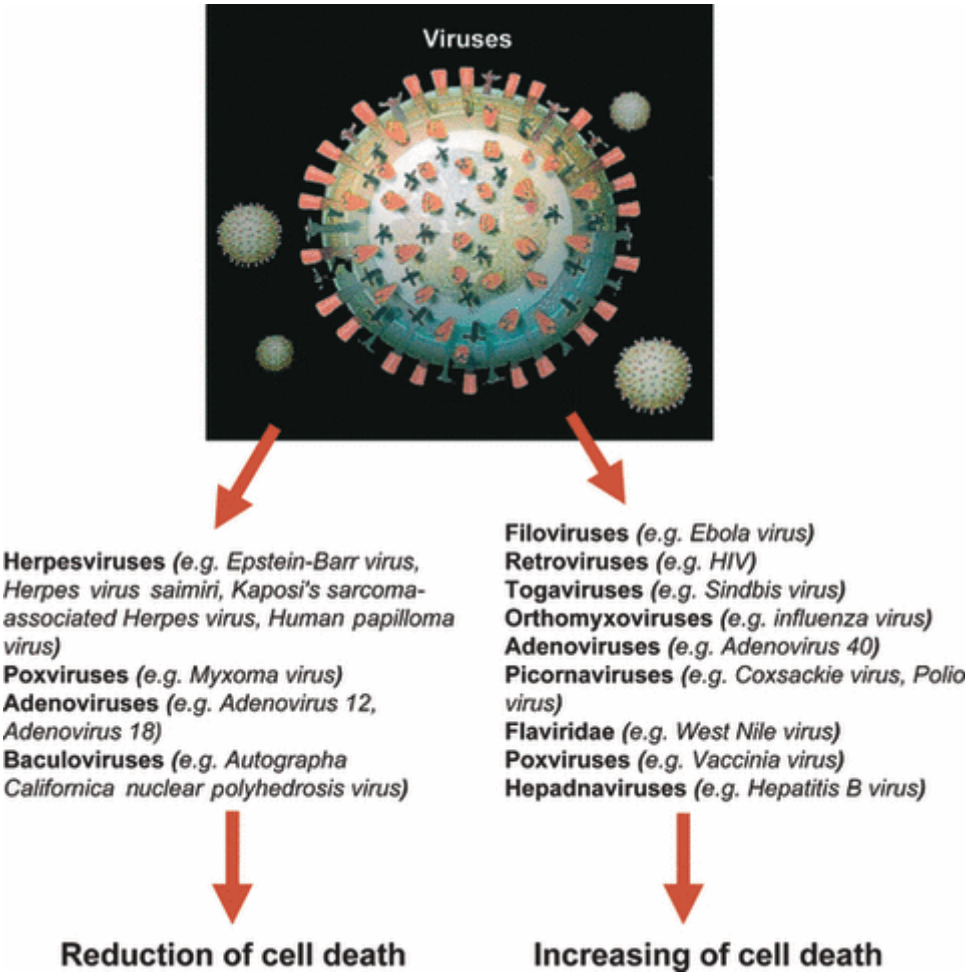


**Figure 1: Cell death: Diagram showing the different steps involved in cell death due to viral infection(Online library).**

Autophagy, a process necessary for breaking down the majority of the cytoplasm, including proteins and organelles, as well as a method for engulfing complete virus particles, may also be linked to viral infection. Some viruses [for example, HSV-1, Kaposi's sarcoma-associated herpesvirus (KSHV), and mouse herpesvirus 68 (MHV-68)] encode proteins that bind with the autophagy-related protein Beclin-1 to inhibit the autophagic pathway, preventing the degradation of the virus. Sometimes autophagy comes before apoptosis. Therefore, apoptosis is caused by HIV-1 envelope glycoprotein (Env)-mediated autophagy in bystander CD4+ T lymphocytes, and cells whose apoptosis is blocked experience cell death with autophagic characteristics. In contrast, the influenza virus's suppression of autophagy via the viral matrix protein 2 makes it easier for infected cells to carry out death.

The virus binds to the surface receptor(s) of the host cell and enters the plasma membrane to start the infection. Thus, CD4, CC-chemokine receptor 5, and CXC-chemokine receptor 4 must be present on the surface of T cells for HIV-1 to infect them. Poxviruses, for instance, can penetrate the cell without interacting with any readily apparent receptors on the cell surface. The prototype poxvirus, the vaccinia virus, employs macropinocytosis to do this. It has been hypothesized that the formation of blebs and the invasion of the host cell by the vaccinia virus depend on the presence of phosphatidylserine at the viral membrane's surface. The innate immune reaction, which is the first line of defense, kicks in shortly after the host is infected, and antigen-presenting cells, which are the second line of defense, trigger CD4+, CD8+ T, and B cells, the adaptive immune system. (APCs). As a result of the host APC's

digestion of virus proteins, which produces antigenic peptides and couples them to the MHC, the adaptive immune response is activated. Several pattern recognition receptors (PRRs), which are present in the majority of somatic cells, start antiviral processes. These PRRS comprise 2′-5′-oligoadenylate synthetase (2′-5′ OAS), which activates RNase L-inducing RNA degradation, RNA-dependent protein kinase (PKR), and/or general control nonderepressible-2 (GCN2), which inhibit mRNA translation, and adenosine deaminase acting on RNA (ADAR-1), which deaminates adenosine on (dsRNA). As a consequence of the infection-induced signaling, several cytokines, including interferons (IFNs), tumor necrosis factor (TNF), and immunoregulatory interleukins, are secreted.

All living things require immediate cellular reactions to pathogen infiltration in order to keep cell homeostasis and survive. Cellular receptors called "pattern recognition receptors" (PRRs) that are germline-encoded detect particular patterns of "non-self" and "danger" molecules, also known as "pathogen-associated molecular patterns" (PAMPs) and "danger-associated molecular patterns," to initiate host reactions. (DAMPs). Mammals' natural immune systems are triggered by the stimulation of PRRs by PAMPs or DAMPs, which results in the production of numerous IFNs and proinflammatory cytokines. In recent decades, various PRRs, such as Toll-like receptors (TLRs), nucleotide-binding oligomerization domain (NOD)-like receptors (NLRs), C-type lectin receptors (CLRs), AIM2-like receptors (ALRs), cyclic GMP-AMP synthase (cGAS), and retinoic acid-inducible gene I (RIG-I)-like receptors (RLRs), have been discovered.

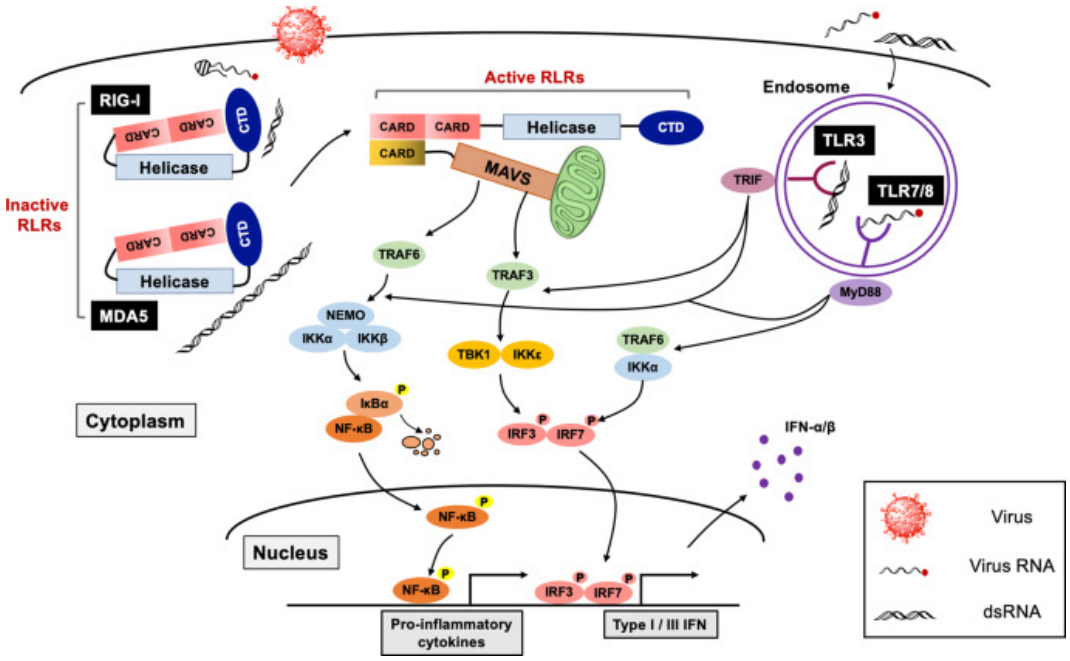


**Figure 2: RNA virus invasion: Diagram showing the invasion of the RNA virus ( nature).**

Among these receptors, TLRs and RLRs are two important receptors in charge of detecting RNA virus infection and activating IFN programs that fight viruses. Later research clarified the basic function of TLRs in innate immune detection in mammals20. The toll was initially discovered as an antifungal gene in charge of the Drosophila immune system. TLRs have been identified in a variety of organisms, and their roles have been elucidated. For instance, 12 rodent TLRs (TLR1-TLR13 and TLR1-TLR9) and 10 TLR members (TLR1-TLR10) were found, and their roles were investigated15,21. Each TLR can detect PAMPs that are usually generated from microbe parts like nucleic acids, lipoproteins, and lipids. These

PAMPs can be common or unique. TLR 3, 7, and 8 are the TLRs that detect single- or double-stranded RNA (ssRNA: TLR7/TLR8; dsRNA: TLR3) in endosomal compartments to identify RNA viruses that enter through endocytosis.

RLRs, as opposed to TLRs, are crucial cytoplasmic viral receptors that identify intracellular non-self RNAs with particular patterns of secondary structures or metabolic modifications18,22. RIG-I, melanoma differentiation-associated gene 5 (MDA5), and laboratory of genetics and physiology 2 are the three individuals that makeup RLRs, which are Asp-Glu-Ala-Asp (DEAD) boxes containing RNA helicases. (LGP2). RLRs are structurally similar in that they all have an RNA helicase domain and a C-terminal domain (CTD) that binds RNA. LGP2 acts as a modulator of RIG-I and MDA523, whereas RIG-I and MDA5 have paired caspase activation and recruitment domains (CARDs) for downstream signal transmission. RIG-I and MDA5 both use unique and shared methods to detect non-self RNAs. Due to the absence of RNA-dependent RNA polymerase in mammalian cells, dsRNA, a typical non-self RNA, is not generated in uninfected cells. Polyinosinic: polycytidylic (poly I: C) acid, a manufactured dsRNA, has the ability to trigger both RIG-I and MDA5. It's interesting to note that differentiating regulation of RIG-I and MDA5 activation by dsRNA occurs in a dsRNA length-dependent manner24. Recent research has identified several biochemical characteristics of RLR-activating RNA species, including (1) 5′-triphosphate with secondary structured RNAs25, (2) 5′-diphosphate uncapped RNAs26, and RNAs with an unmethylated 5′-end nucleotide at the 2′-O position27,28. These RNAs are typically produced during the replication of RNA viruses, including coronaviruses (Figure. 2) [3].

Studies in recent years have concentrated on how viruses avoid Pattern Recognition Receptors, target adaptor proteins and their kinases, block transcription factors for interferon production, and avoid interferon-stimulated genes. The hepatitis C virus and other members of the Flaviviridae family of viruses have evolved sophisticated viral mechanisms to reorganize the cell membrane and produce a membranaceous web that houses the viral reproduction machinery. By barring PRRs from the core of the viral membrane compartment, these viruses use natural host cell nuclear pore complex proteins to protect viral RNA from PRRs. To avoid being detected by cytoplasm-confined pattern recognition proteins like RIG-I, viruses have evolved a technique involving the architectural reorganization of the membrane. Other viruses, like the enterovirus, have evolved multifunctional proteins to evade pattern recognition.

These proteins not only aid in the processing of viral proteins but also cleave the cytoplasmic recognition proteins MDA5 and RIG-I. This further illustrates how viruses can inhibit Interferon Signaling through a variety of pathways. It has been observed that other viruses attack upstream proteins that eliminate inhibitory post-translational modifications from pattern recognition proteins[4]. Other viruses use the proteins of the recipient cell to encase viral DNA before it enters the nucleus. Cyclophilin A (CypA) recognizes and binds the HIV-1 capsid as soon as it enters the cytoplasm of the host cell. This affinity association stabilizes the capsid and stops the HIV-1 cDNA from being exposed to the cytoplasm's pattern recognition receptors. This protection enables the translocation of the HIV-1 cDNA to the nucleus, where it may start the reproduction process [5].

## DISCUSSION

Viral host range, organ tropism, and viral disease are all significantly regulated by interactions between viruses and receptors. Elegant techniques are used by viruses to bind to one or more receptors, cross the plasma membrane, penetrate, and gain access to the required

host cell machinery. These "lock-and-key" interactions are essential for viruses to effectively infiltrate host cells and can be thought of as the "key" that unlocks host cells by interacting with the "lock"—the receptor—on the cell surface. Numerous patterns in the use of virus receptors within and between virus families have been identified, showing that viruses frequently target specific classes of molecules to facilitate these processes. Sialylated glycans, cell binding molecules like integrins and members of the immunoglobulin superfamily, and phosphatidylserine receptors are examples of typical virus receptors. To take advantage of their cellular function, viruses may target specific receptors or "common locks," as suggested by the duplication in receptor utilization, which also points to genetic preservation. Exploiting these strategies would be an appealing target for novel antiviral therapies due to the significance of early virus contacts with host cells in viral pathogenesis and the redundancy in viral receptor usage [6]. Less research has been done on the molecular processes that nonenveloped mammal viruses use to break through cellular membranes and enter the target cytoplasm. Because of recent viral protein crystal structure findings and the creation of a novel genetic tool to analyze the viral determinants of cell invasion, mammalian reoviruses are effective tools for tackling this issue. Penetration protein 1 and its guardian protein 3 are starting to be better understood for their respective functions [7].

When the Chikungunya virus (CHIKV) unexpectedly spread widely in the Indian Ocean area and made its way to Europe in 2007, it caused unusual pathologies in young children and geriatric patients. Despite new evidence that CHIKV can survive in myoblasts, monocytes, and macrophages, we contended that strong antiviral defenses, such as apoptosis, are necessary to combat the virus. Using a variety of caspase inhibitors, cell blebbing, and the engulfment of apoptotic blebs by adjacent cells, we investigated the ability of CHIKV to activate the apoptotic machinery in HeLa cells as well as primary fibroblasts in this study. Through both internal and extrinsic mechanisms, CHIKV induced apoptosis. Additionally, nearby cells showed signs of bystander death in a caspase-8-dependent way. Surprisingly, CHIKV was able to infiltrate nearby cells by blending in with dead blebs. These processes were particularly prevented in HeLa cells by the caspase inhibitors zVAD-fmk and DEVD-cho, blebbistatin, Y-27632 (a ROCK inhibitor), genistein, annexin V, and cytochalasin B. (inhibitors of blebbing and engulfment).

These CHIKV-apoptotic blebs were also able to infiltrate macrophages that were normally resistant to infection by CHIKV alone (primary cultures, MM6- and THP1-PMA differentiated cells). Surprisingly, virus proliferation did not result in a pro-inflammatory reaction in macrophages. We outline a new infectious process that CHIKV uses to enter host cells and evade the host's defenses [8]. The essential associations between the spike protein from the "sialidase-insensitive" human Wa and the "sialidase-sensitive" porcine CRW-8 rotaviruses and the glycans of gangliosides GM1 and GD1a were examined using NMR spectroscopy, molecular modeling, and infectivity competition tests. Our findings offer convincing proof that N-acetylneuraminic acid is a crucial factor in the binding of these rotaviruses. Contrary to the commonly held belief, sialic acids are relevant for sialidase-insensitive rotaviruses to recognize host cells [9].

Pathogens, such as SARS-CoV-2, usually infect human cells by binding to a critical receptor on the cell membrane. Although the angiotensin-converting enzyme 2 (ACE2) is the main receptor for SARS-CoV-2, recent research has highlighted the significance of other external co-receptors in SARS-CoV-2 binding and host cell infiltration. A subgroup of cell types has extracellular surfaces that are known to contain the intermediate filament protein known as vimentin, which can attach to viruses and aid in their cellular uptake. Vimentin may bind SARS-CoV-2 and promote its uptake, according to biophysical and cell infection

experiments. Vimentin attaches to pseudovirus covered with the SARS-CoV-2 spike protein, according to dynamic light scattering, and antibodies to vimentin prevent in vitro infection of ACE2-expressing cells by the SARS-CoV-2 pseudovirus. The findings support a scenario in which extracellular vimentin functions as a co-receptor for the SARS-CoV-2 spike protein with a lower binding strength than the spike protein with ACE2. Thus, extracellular vimentin may be a crucial part of the SARS-CoV-2 spike protein-ACE2 complex in the transmission of SARS. Vimentin-targeting drugs and SARS-CoV-2 cell entry may produce novel treatment approaches for halting and stopping SARS-CoV-2 infection [10].

## CONCLUSION

Infectious agents use a variety of tactics to evade immunity, such as stopping the death of host cells, lowering reactive oxygen species, increasing the Th2 anti-inflammatory in nature reaction, avoiding autophagy and antigen cross-presenting processes, and avoiding phagolysosomal destruction. The medical field sees a desire to fundamental immune terms after each contagious outbreak or breakout to comprehend and get through the challenging times these illnesses cause. Since viral are believed to be obligate parasites within cells that rely on the host's cell apparatus for their reproduction, it is odd that they have traditionally been the source of numerous fatalities. This allows for successful infection with the production of essential viral components. Based on this knowledge, it is essential to develop new therapeutic approaches for preventing viral spread, whether through the use of antiviral medications, vaccinations, or antimicrobial agents or by concentrating on inhibiting or stimulating of metabolism or cell signaling processes that are changed during infection. The quick restoration of cellular equilibrium after virus infection remains a difficult task.

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# CHAPTER 22

# VIRUS'S CONTRIBUTION TO THE GLOBAL EPIDEMIC

Piyush Mittal, Professor
Department of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- mittalpiyush23@gmail.com

**ABSTRACT:**

A worldwide epidemic is defined as a sudden rise in the number of cases of an illness over what would typically be anticipated for that community in that location. The term "outbreak" has the same meaning as "epidemic," however it is frequently used to refer to a smaller physical region. The most common elements of the endemic are the virus. In this chapter, we discussed the major contribution of the virus to the global epidemic.

**KEYWORDS:**

Epidemiology Viral, Hepatitis Virus, Immune System, Risk Factors, Viral Infection.

## INTRODUCTION

The study of the prevalence, dynamics, and causes of diseases in communities is known as epidemiology. the likelihood that a human community will contract a pathogen and/or become ill is influenced by the traits of the virus, susceptible people, and the host community as a whole, such as inherent and learned resilience. Additionally, ecological, environmental, and behavioral variables all have an impact on virus spread. To integrate these elements and provide a rational justification for the occurrence of virus diseases as well as for guiding disease-control measures, particularly the detection of outbreak sources and the most effective means of enacting preventive measures, virus epidemiology uses quantitative measurements. Epidemiology can also shed light on how viruses contribute to the etiology of diseases, how they interact with environmental triggers of illness, how host susceptibility is affected, how modes of transmission work, and how to test vaccines and treatments on a large scale. Epidemics are spikes in disease prevalence that are higher than the common mean or anticipated disease rate. The amount of a surge that must occur for there to be an epidemic to exist is random and depends on the baseline endemic rate and the ratio of clinical to subclinical infection. A few instances of a disease that causes concern due to its seriousness, like encephalitis, may occasionally be informally referred to as an "epidemic," but the word strictly refers to the abnormally broad and fast spread of infection within the community[1].

Modulation and escape are the two main methods that viruses employ to counteract human reaction. Modulation refers to the production of viral gene products that, through any process, have the ability to change specific elements of the immune response. The effect is to increase the likelihood of transmission or viral persistence in the infected creature by facilitating virus survival. By "escape," we mean changes to the viral DNA that make it hard for immune system defenses to neutralize the virus, usually through the suppression of viral particles by antibodies or the destruction of infected cells by particular cytotoxic T cells. DNA and RNA viruses both use modulation and escape tactics, but complicated DNA viruses also encode several proteins whose main job is to thwart the host's defenses. They consist of, among other proteins and functions, homologs of cytokines, chemokines, viral proteins that serve as a cover for antiviral antibodies, proteins that inhibit complement activation, suppress MHC class I and II molecules, interfere with ubiquitin-dependent proteolysis, and either induce or

inhibit apoptosis. Virus proteins, such as influenza virus NS1, the Ebola virus P35, and others, prevent the production of interferon. Several of the implicated proteins offer illustrative instances of protein multifunctionality. The FMDV leader L proteinase catalyzes its cleavage from the polyprotein, cleaves the eIF4G host cell translation factor, which prevents host cell translation that depends on capped mRNAs, and prevents IFN activation in the infected cells. RNA viruses use genetic diversity as one of their main strategies for escape despite producing proteins that hinder the immune response. This is likely the result of high mutability and genome compression cooperating during evolution. RNA editing, partial read-through of termination codons, overlap between regulatory and protein-coding regions, leaky ribosome scanning with the initiation of protein synthesis at two in-frame AUGs, ribosome frameshifting, hopping, shunting and bypassing, synthesis of polyproteins whose partial or complete processing results in several functional proteins, etc. are all signs of genomic compression. High mutation rates, small genome sizes, and escape routes have been provided by evolution as alternatives to the modulation approach. It is simple to detect mutations in vivo that facilitate escape from CTLs and blocking antibodies. The development of antibodies- and CTL escape may add to viral survival rather than being a secondary event during viral infections. Evasion of an immune reaction, which is the result of a viral selection process, may come at a fitness expense. Reversion to the original sequences may result from such a cost when selective factors (antibodies or CTLs) are absent. The quantity and concentration of the antibodies may dictate the preferred pathway because viruses frequently exhibit numerous antibody-escape pathways [2].

By using quantitative RT-PCR to track viral release, the nasopharynx rises on day 10. Male patients and elderly patients are more likely to have detectable virus shedding, suggesting that individual host differences in viral shedding surpass the variation during the clinical course. However, analysis of 265 laboratory-confirmed SARS patients in Taiwan shows that, on any given day of the clinical course, SARS-CoV shedding in the nasopharynx varies widely from individual to individual, ranging from below the detection limit to as high as 108 RNA copies/mL. Oxygen desaturation, artificial breathing, and death are linked to higher nasopharyngeal and serum viral loads; Furthermore, early mortality within the first two weeks of sickness is linked to a larger nasopharyngeal virus titer [3].

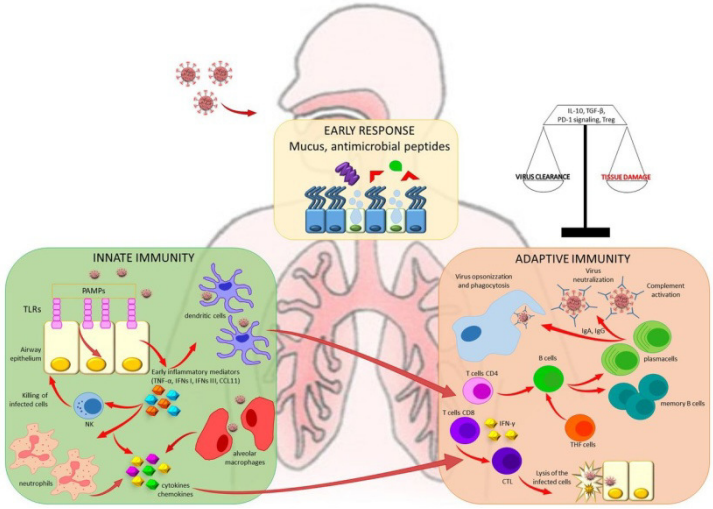


**Figure 1: Virus infection and the immune system: Diagram showing the route of the early viral infection and the role of the immune system (European respiratory journal).**

viral shed typically happens from one of the bodily openings or sites also involved in viral entry. the same bodily cavities are affected by localized infections. In generalized infections, a wider range of shedding mechanisms are known, and some viruses are secreted from multiple locations, such as the hepatitis B virus, HIV, and cytomegalovirus in semen, cervical secretions, milk, and saliva. In terms of propagation, the quantity of viral released in excretion or secretion is significant. Some viruses exist in such high concentrations that even very small amounts of material, such as less than 1 l, can spread infection. Very low concentrations may not matter unless very large quantities of infected material are transmitted.

Rates, or the number of events in a standard period, are used to compare prior disease incidence and anticipated future risk in various groups. Size of the populace, such as 1000, 100,000, 1,000,000, etc. The two ratios of occurrence and prevalence are frequently used. The denominator (total number of people at risk) may, in all instances, be either general, i.e., the entire population of a state or nation, or it may be a particular group of people who are known to be vulnerable or at risk. The latter is frequently associated with the proportion of people (referred to as "susceptibles") in a given community who are immune to the virus of interest. It is crucial to understand the character of the denominator in each case. Age, sex, genetic makeup, immune state, nutritional status, and different behavioral factors are just a few of the characteristics that can influence all rates. Age is the characteristic that is most broadly relevant and may be connected to immune function as well as other physiological factors. A measure of the frequency of events over time, such as monthly or annual occurrences, the incidence, or the assault rate, is particularly helpful for acute illnesses with brief incubation periods. Incidence rates are typically stated as cases per standard population size (for example, 100,000) per standard time, where the denominator encompasses both the population size and the period. (e.g., one year).

It will be clear right away that two more factors are crucial. First, not every member of a community is typically vulnerable, for instance, because of a previous infection that resulted in immunity. As a result, a population-wide incidence rate may yield a smaller number than a rate that is more specifically based on those who are vulnerable. Second, many viral illnesses go undiagnosed because not all affected people experience clinical diseases. The incidence rate of clinical illness is always less than the incidence rate of all diseases as a result. varying viruses have significantly varying ratios of visible to subclinical infections. For instance, whereas less than 1% of people infected with encephalitogenic arboviruses or polioviruses develop encephalitis or poliomyelitis, respectively, measles infections are almost always clinically evident. A novel virus type emerging, human conduct, etc.

The secondary attack rate is a helpful indicator of the "infectiousness" of viruses disseminated via aerosol or droplet spread when applied to similar relatively confined groups like homes or classes (Figure.2). It is described as the proportion of all vulnerable individuals exposed to infection who come into touch with the main or index case and contract the disease within the maximal incubation period. For such diseases, it is customary to determine the prevalence, which is the ratio, at a given point in time, of the number of cases currently present in a population divided by the size of that population. It is challenging to measure the incidence of chronic diseases, especially where the onset is insidious. Prevalence is a measure of the regularity that is present at any particular moment and depends on both the occurrence and the length of the illness. It can be stated as a ratio or as the number of instances per 100,000 people, for example. As neutralizing antibodies frequently last for many years or even for life, seroprevalence numbers typically reflect the accumulated experience within an examined community. Seroprevalence refers to the proportion of people with antibodies to a

specific virus in a population. Both the cause-specific mortality rate (the number of deaths from the disease in a given year divided by the total population at mid-year), which is typically expressed per 100,000, and the case-fatality rate (the proportion of people with a specific disease who die from the disease) can be used to categorize disease-related deaths.

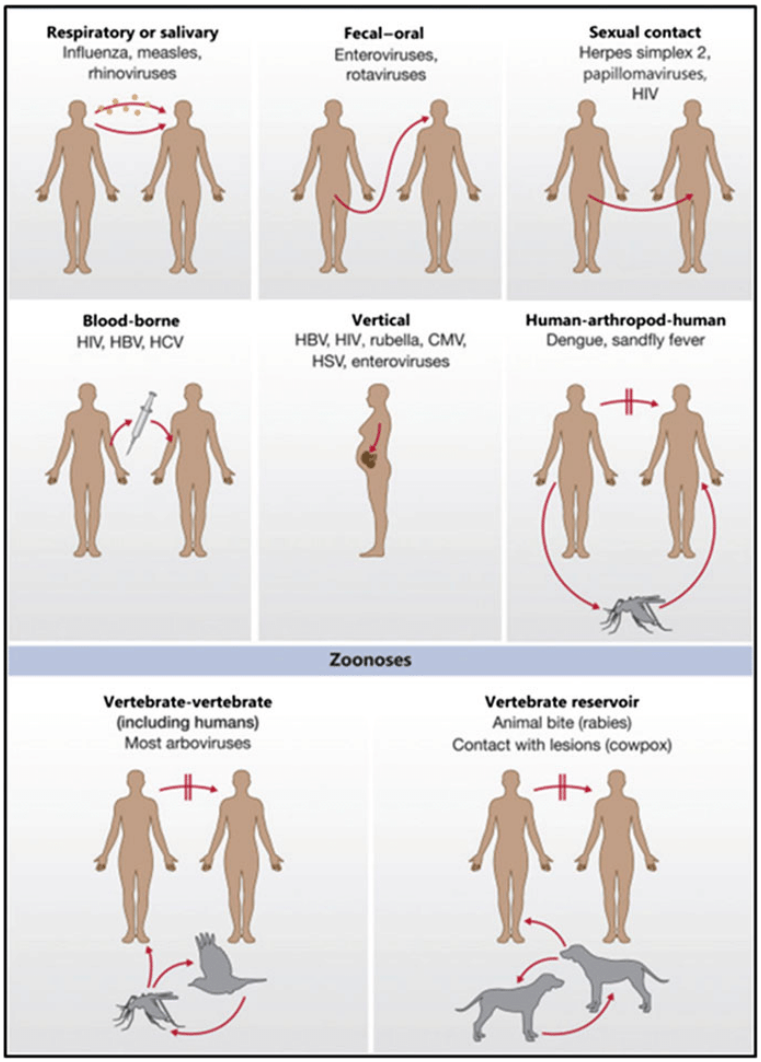


**Figure 2: Transmission of the viral disease: Diagram showing the mode of the transmission of the viral disease (NCBI).**

## DISCUSSION

Regardless of age or gender, acute respiratory tract infections are the most prevalent disease among all people. Since the turn of the 20th century, epidemiologic assessments and community-based studies have been carried out to ascertain the prevalence of disease and the pathogens responsible for such infections. These studies have demonstrated that rhinoviruses are the primary cause of the vast majority of these respiratory illnesses, and their conclusions have looked at how respiratory illnesses are spread. More recently, improvements in testing methods have made it possible to identify lung infection-causing viruses in greater detail, making it easier to target particular therapeutic agents against the pathogens that are the cause of the infection[4].

The carcinogenicity of biological substances for humans has been thoroughly evaluated by the International Agency for Research on Cancer (IARC). IARC has categorized seven viruses as Group 1 human carcinogens, including Epstein-Barr virus (EBV), hepatitis B and

C viruses, Kaposi's sarcoma herpes virus (KSHV), human immunodeficiency virus type 1 (HIV-1), human T cell lymphotropic virus type 1 (HTLV-1), and human papillomavirus (HPV). The results of demographic and mechanistic research served as the foundation for the inferences. Direct carcinogens include EBV, HPV, HTLV-1, and KSHV; indirect carcinogens include HBV and HCV due to persistent inflammation; and HIV-1 is secondary cancer due to immune suppression. While some pathogens can cause more than one cancer, others can cause multiple malignancies.

Only a fraction of those afflicted with these oncogenic viruses will experience certain types of cancer, though. Studies have been conducted to evaluate the virus, host, and ambient cofactors of HPV-associated cervical cancer, EBV-associated nasopharyngeal carcinoma, and HBV/HCV-associated hepatocellular carcinoma. Significant risk factors for these virus-caused cancers include persistent illness and large viral loads. For the forecast of the long-term risk of hepatocellular carcinoma, risk algorithms have also been created that incorporate host and viral variables. For patient assessment and treatment of infected patients, these risk tools are helpful. Clinical studies and government vaccination or antiviral treatment initiatives have both shown a substantial decline in the prevalence of HBV, HCV, and HPV-related cancers. Future studies on the interactions between malignant viruses and their human hosts' genes and environments are desperately needed[5].

The majority of hepatocellular cancer (HCC) cases are accompanied by cirrhosis brought on by persistent HBV or HCV infection. The hepatitis viruses that are most prevalent in a population, the timing of their spread, and the ages of the people the viruses infect are likely to differ from population to population, as are changes in the time trends of HCC and the majority of variations in its age-, sex-, and race-specific rates. When a person has HBV or HCV infection, environmental, host hereditary, and viral variables can influence their chance of developing HCC. Based on results from epidemiologic studies and meta-analyses, this review outlines the risk factors for HCC in people with HBV or HCV infection. It also discusses factors that affect patient outcomes and the impact of the HCC disease both worldwide and in the United States [6].

Iranians are now categorized as having low endemicity for hepatitis B infection due to the drastic decline in hepatitis B virus (HBV) incidence over the past ten years. This decline could be attributed to increased public awareness of HBV risk factors, a nationwide immunization program that has been in place since 1993 for all newborns, and immunization of high-risk populations. In 1989, two regions (Zanjan and Semnan) began immunizing newborns against HBV, and the vaccination was added to the Expanded Program on Immunization (EPI) in 1993. After 13 years of implementation, the coverage, which ranged from 62 in 1993 to 94 in 2005, has achieved an acceptable level. It's critical to assess risk variables in HBV-infected individuals when developing control methods. Further reducing the occurrence of the illness in Iran will be increased HB vaccination of high-risk groups, monitoring of HB-affected individuals, and management of refugee health. In individuals without infection risk factors, it is also essential to take into account all potential transmission pathways. shifts in the epidemiology of viral hepatitis B infection and the pattern of spread of novel hepatitis B cases [7].

Hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV are all thought to cause persistent illnesses that affect 370 million people worldwide each. An estimated 2-4 million HIV-infected individuals also have chronic HBV co-infection, and 4-5 million also have chronic HCV co-infection. Although HBV, HCV, and HIV all have similar modes of infection, their regional frequency and the effectiveness with which specific exposures spread them vary. Chronic HBV infection has been identified in 6–14% of HIV-positive individuals from

Western Europe and the USA examined, including 4-6% of heterosexuals, 9–17% of men who have sex with men (MSM), and 7–10% of intravenous drug users. Overall, 25–30% of HIV-positive individuals have been discovered to have HCV virus, as have 72–95% of injection drug users, 1% of MSM, and 9–27% of heterosexuals. To ensure that prevention measures are focused correctly, monitoring systems are required to track the epidemiologic patterns of HIV-infected individuals because these patterns may change over time. The features of HIV-infected individuals vary depending on the co-infecting hepatitis virus [8].

One of the main global public health issues is viral hepatitis, but up until lately, global health policymakers paid little attention or provided much money. Cirrhosis and liver malignancy caused by viral hepatitis claim the lives of 1.4 million individuals each year. The bulk of those who are infected, though, are ignorant of their situation. Significant challenges face this group, including lack of knowledge, vulnerability, increased migration, illness stigma, prejudice, inadequate health resources, and conflicts in policy and program development. Despite putting infection control measures in place over the past few decades, substantial illness decline or eradication remains elusive. The purpose of this research is to investigate possible elimination strategies and to show the current global prevalence state. Over 40 years, from 1978 to 2018, the data for this study were gathered through a systematic review, published scientific works of literature, the official websites of various government organizations, international public health organizations, and internationally renowned regulatory bodies [9].

The frequency of dengue virus infection is rising in the tropical areas of Asia, Africa, Central America, and the rest of the globe, making it the most widespread arthropod-borne disease today. From a mild flu-like illness to a serious hemorrhagic fever with high morbidity and mortality—the latter occurring almost exclusively in children it exhibits a range of illnesses. Aedes aegypti and Aedes albopictus insects are the carriers of the virus. Children residing in temperate climates may be at risk from cold-resistant types of Aedes vectors [10].

## CONCLUSION

The scientific investigation of the prevalence, circumstances, and causes of illnesses in communities is known as epidemiology. The features of the virus and the degrees of innate and learned resistance in the population affect the likelihood of viral infection and/or clinical illness.The research of relations between viruses and their host cells is known as viral ecology. The proliferation of viruses is a crucial factor in viral ecology. To identify the most effective measures to stop an outbreak, viral epidemiologists attempt to foresee the possibility of the emergence of an epidemic or pandemic. The host and the pathogen are just two of the many variables that epidemiologists must attempt to account for. These include, but are not limited to: the method of transmission, the duration of infection and window of transmissibility, the population density, the standard of living, the surrounding circumstances, and the virus's stability. Medical professionals are interested in illness instances, but the epidemiologist must also take into account infections that are undetectable or quiet. Serological analyses are a crucial instrument for finding viral illnesses from the past.

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# CHAPTER 23

# IS THE VIRUS ARE BOON OR A CURSE

Piyush Mittal, Professor
Department of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- mittalpiyush23@gmail.com

**ABSTRACT:**

The virus can only replicate and create new viruses by entering a living cell and taking control of the cell's apparatus. A few viruses accomplish this by splicing their DNA (or RNA) into the recipient cell's DNA. Viruses are infectious organisms that can either cause cancer or raise the chance that it will develop. Several viruses can interfere with signaling, which typically controls cell growth and development. Oncolytic viruses destroy specific tumor cells, but research also indicates that they may improve the ability of the immune system to identify and eradicate tumors. Specifically targeting cancerous cells, the viruses multiply inside of them before ultimately destroying the cells. In this chapter, we summarized the use of the virus for the treatment of various disease.

**KEYWORDS:**Accessed Marker, Cancer Cells, Epstein Barr Virus, Oncolytic Virus, Tumor Cells.

## INTRODUCTION

Cancer has been linked to viruses in both people and other animals. Only a small percentage of people with viral infections develop a malignancy. (or animals). There is no specific "oncovirus" because cancer viruses originate from a variety of virus families, including both RNA and DNA viruses. (an obsolete term originally used for acutely transforming retroviruses). Numerous elements, such as host immunity and human mutations, influence the formation of cancer. Some variants of the human papillomavirus, the hepatitis B and C viruses, the Epstein-Barr virus, the Kaposi's sarcoma-associated herpesvirus, and the human T-lymphotropic virus are known to induce human cancers. The Merkel cell polyomavirus, which is responsible for the majority of instances of Merkel cell carcinoma, a rare type of skin cancer, is the most recent human cancer virus to be identified. Hepatitis viruses have the potential to become a persistent viral illness that results in liver malignancy. Adult T-cell leukemia and tropical spastic paraparesis can result from human T-lymphotropic virus infection. Cervical, skin, anus, and penile tumors have been linked to human papillomaviruses. In the Herpesviridae, the Epstein-Barr virus produces Burkitt's lymphoma, Hodgkin's lymphoma, B lymphoproliferative disease, and nasopharyngeal carcinoma. Kaposi's sarcoma-associated herpesvirus causes Kaposi's sarcoma and body-cavity lymphoma.SV40 and rodent polyomaviruses, which have been used as long-term animal models for cancer viruses, are closely linked to the Merkel cell polyomavirus[1]–[3].

A third class of typical cancer-causing viruses is herpes viruses. Epstein-Barr virus (EBV) and human herpesvirus 8 are two herpesvirus strains that have been linked to malignancy. (HHV-8). Epstein-Barr virus-positive diffuse large B-cell lymphomas, not otherwise defined, diffuse large B-cell lymphomas linked to persistent inflammation, and nonkeratinizing nasopharyngeal carcinomas all appear to be caused by EBV. Mucocutaneous sores with Epstein-Barr virus positivity, lymphomatoid granulomatosis, diffuse large B-cell lymphomas, and, frequently, fibrin-associated diffuse large B-cell lymphomas, systemic NK/T cell lymphomas. Additionally, some instances of lymphoma, such as Hodgkin's disease and Burkitt's lymphoma (where the causal link is particularly prevalent in Africa), appear to be

caused by it. Although its function in causing these other cancers is not clearly understood, EBV has been discovered in a range of other cancer cells (Figure.1). All instances of Kaposi's sarcoma are brought on by KSHV/HHV-, which has also been linked to Castleman's disease, a cancer-related disorder. Research on various other cancers, especially prostate cancer, has produced mixed results. These two herpesviruses are typically detected in the malignant cells of primary effusion lymphoma. Herpesviruses, particularly leukemias, and lymphomas, are known to induce cancer in mammals. Robert Gallo and coworkers at the NIH made the initial human retrovirus discovery, the human T cell lymphotropic virus (HTLV-1). The virus is responsible for adult T-cell leukemia, which Takatsuki and coworkers first identified in Japan, as well as other brain conditions. Another deltaretrovirus that is closely related to the human T-cell leukemia virus is the bovine leukemia virus (BLV), which recently met the requirements to be accepted as a potentially infectious agent contributing to breast cancer.

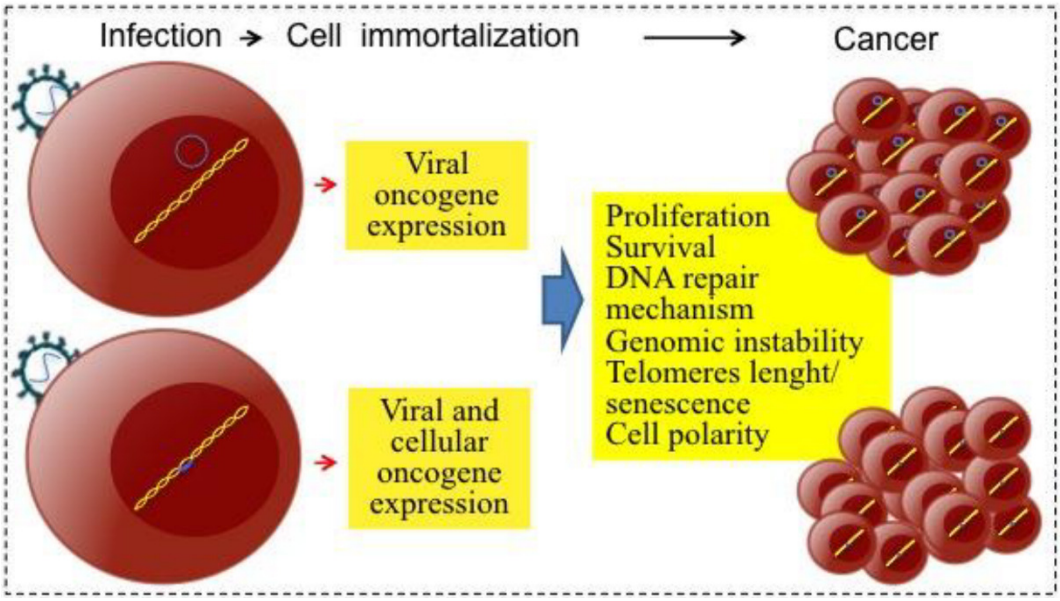


**Figure 1: Role of the virus in cancer :Diagrame showing the role of the virus in cancer (MDPI).**

These criteria included using sensitive PCR methods to detect BLV and comparing samples from breast cancer patients to a control sample of women without a history of the disease. The most recent human cancer virus to be identified is Merkel cell polyomavirus, which was isolated from Merkel cell carcinoma tissues in 2008 by the same team that found KSHV/HHV-8 in 1994. This novel technique was known as digital transcriptome subtraction. The Merkel cell polyomavirus accounts for about 80% of Merkel cell carcinomas; the remainder of the tumors have an unclear etiology and may have a distinct histogenesis. The only virus in this family proven to cause cancer in humans is this one, but other polyomaviruses are thought to be extra cancer-causing viruses.

Although HIV does not cause cancer directly, it is linked to several cancers, particularly Kaposi's sarcoma, non-Hodgkin's lymphoma, anal cancer, and cervical cancer. Human herpesvirus is what causes Kaposi's sarcoma. 8. Human HPV is frequently to blame for instances of cervical cancer and anal cancer linked to AIDS. Cancer develops as a result of viral illnesses because the body can no longer regulate them after HIV decimates the immune system. A higher chance of cancer is also linked to a few other immune-deficiency conditions, such as IgA deficiency and common variable immunodeficiency.

A virus that selectively attacks and destroys cancer cells is known as an oncolytic virus. New contagious virus particles, or virions, are released by the infected cancer cells as they undergo oncolysis to aid in the elimination of the residual tumor. Oncolytic viruses are believed to activate host immune system reactions against tumors in addition to directly destroying tumor cells. The tumor microenvironment can be impacted by oncolytic viruses in a variety of ways. The early 20th century saw the first realization of viruses' promise as anti-cancer agents, but it wasn't until the 1960s that coordinated study efforts got underway. Adenovirus, reovirus, measles, herpes simplex, Newcastle disease virus, and vaccinia are just a few of the viruses that have undergone clinical testing as oncolytic drugs.

Although there are naturally occurring instances like the reovirus and the Seneca virus, which have led to clinical studies, the majority of contemporary oncolytic viruses are designed for tumor selectivity. The genetically unaltered ECHO-7 strain enterovirus RIGVIR was authorized in Latvia in 2004 for the therapy of cutaneous melanoma; the permission was revoked in 2019. This was the first oncolytic virus to receive clearance from a national regulatory body. In 2005, China authorized the use of the genetically altered oncolytic adenovirus H101 for the therapy of head and neck cancer. The first oncolytic virus to be authorized for use in the U.S. and the European Union for the therapy of metastatic, incurable melanoma was talimogenelaherparepvec (OncoVex, T-VEC), an oncolytic herpes virus that is a modified herpes simplex virus.

Oncolytic viruses have received more focus recently as a means of boosting antitumor immunity as a result of developments in cancer treatment, such as immune checkpoint drugs. The interplay of oncolytic viruses and the immune system is primarily based on two factors. The patient's immune system, which naturally tries to neutralize any virus, is a significant barrier to the effectiveness of oncolytic viruses. For intravenous injection, where the virus must first avoid reactions with the blood complement and neutralizing antibodies, this can be a special issue. Oncolytic viral treatment has been shown to benefit from immunosuppression brought on by chemotherapy and complement system blocking (Figure.2) . By using viruses that are uncommon human pathogens, pre-existing protection can be partially prevented. This does not, however, stop the production of additional antibodies[4]–[6].

However, some research has indicated that pre-immunity to oncolytic viruses doesn't significantly reduce effectiveness. It is also possible to cover the viral vector with a polymer, such as polyethylene glycol, to protect it from antibodies while also preventing the viral coat proteins from attaching to host cells. Hiding oncolytic viruses inside macrophages is another method of assisting them in reaching cancer growth after parenteral administration. (a type of white blood cell). Macrophages have been effectively used to transport oncolytic viruses to animal models of prostate cancer because they naturally move to sites of tissue destruction, particularly where low oxygen levels are typical of cancer growths. The patient's immune system can help fight tumors even though it presents a challenge by inactivating viruses; infection draws the immune system's focus to the tumor and may help to produce effective and long-lasting anticancer immunity.

The release of chemicals by tumor lysis, such as tumor-associated proteins and danger-associated molecular patterns (DAMPs), which can trigger an anticancer immune response, is one crucial process. In essence, this results in customized cancer immunization. Numerous instances of cancer going into sudden remission have been documented. Though the exact reason is unknown, it is believed that an unexpected immune reaction or illness is most likely to blame. Cancer vaccines (made from cancer cells or specific cancer antigens) or the direct application of immune-stimulating agents to cutaneous cancers have both been used to try to trigger this occurrence. Some oncolytic viruses, particularly those that deliver cytokines or

other immune-stimulating agents, are highly immunogenic and may, by infecting the tumor, induce an anti-tumor immune reaction (Figure.3). Because tumor cells have a compromised immune system, viruses preferentially attack them. Attenuated herpes simplex virus Imlygic has been genetically modified to selectively multiply inside tumor cells and produce antigens that trigger an immune response.

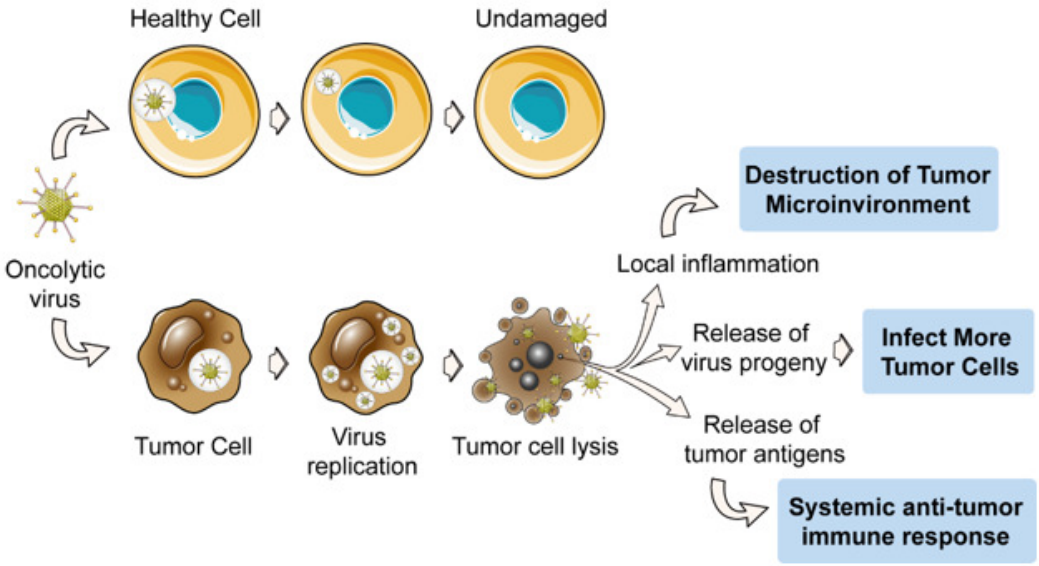


**Figure 2: Mechanism of the oncolytic virus: Diagram showing the different mechanisms of the oncolytic viruses (Creative Biolabs).**

In a novel method of drug development known as "directed evolution," huge populations of arbitrarily produced recombinant precursor viruses are used in cycles of directed selection to produce new viral variants or serotypes specially targeted against tumor cells. Without requiring any prior knowledge of the resulting viral mechanisms that are responsible for that outcome, a series of selection steps designed to lead towards a pre-specified outcome (for example, higher tumor-specific activity) can be used to narrow down the large random pool of viral candidates produced by the initial homologous recombination step. To choose an oncolytic virus with the desired therapeutic properties, the group of generated oncolytic viruses can then be further tested in pre-clinical animals. A highly selective yet effective oncolytic vaccine was produced using directed evolution using the human adenovirus, one of many viruses being explored as oncolytic agents. ColoAd1 (a new chimeric member of the group B adenoviruses) was produced as a consequence of this procedure. Compared to the control viruses (Ad5, Ad11p, and Ad3), this hybrid of the adenovirus serotypes Ad11p and Ad3 was confirmed to produce roughly two logs more viral progeny on freshly isolated human colon tumor tissue than on corresponding normal tissue.

To make the virus less dangerous and more tumor-specific, attenuation entails removing viral genes, or gene regions, to remove viral activities that are unnecessary in tumor cells but not in normal cells. Similar changes are seen in the cell signaling networks that control cell cycle development in both cancer cells and virus-infected cells. In cells where the pathway is damaged, but not in cells where the pathway is functioning, a virus gene with the ability to change the pathway is dispensable. Only cells that are constantly replicating show the enzymes thymidine kinase and ribonucleotide reductase, which are responsible for DNA synthesis. These enzymes are also found in the genomes of some viruses, such as the vaccinia and the herpes simplex virus (HSV), which enable viral reproduction in dormant (non-

replicating) cells. If these enzymes are rendered inactive by mutation, the virus will only be able to reproduce in proliferating cells, such as cancer cells.

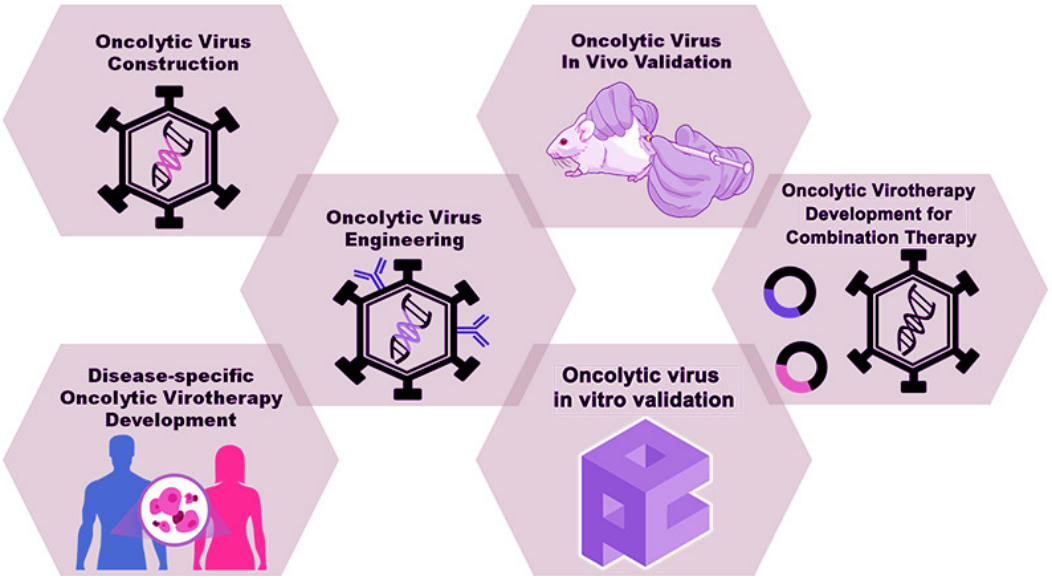


**Figure 3:oncolytic virus therapy: Diagram showing the different approaches of the oncolytic virus therapy (Creative Biolabs).**

## DISCUSSION

The first human virus that was specifically linked to the development of cancer was EBV. More than 90% of people on the planet are infected. A tiny percentage of people who live with the virus without suffering severe consequences will acquire tumors. Geographical and immunological differences in the frequency of these tumors show that normal host groups can be extremely susceptible to EBV-related tumors. Burkitt's lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, nasopharyngeal carcinoma, lymphomas, and leiomyosarcomas that develop in vulnerable people have all been linked to EBV's etiology. Although some of this research is still in question, the existence of this virus has also been linked to breast and stomach epithelial cancers. EBV wrests control of the cellular pathways that manage various normal cellular functions from their proper hands by using its viral proteins, the actions of which imitate several growth factors, transcription factors, and antiapoptotic factors. The use of monoclonal antibodies, the development of EBV-specific CTLs, and recent advancements in antiviral therapies are starting to show promise in the therapy of EBV-related diseases[7].

It is possible to modify viruses so that they only reproduce in cancer cells. This can be done by deleting virus genes that are necessary for normal cells but not necessary in tumor cells, or by using regulating elements with tumor selectivity. The latter method has been used to create viruses that rely on RB or p53 deletion. However, this strategy has been complicated by the redundant functions of viral proteins and cellular pathways, necessitating further viral engineering or a deeper comprehension of cellular pathways to improve efficacy. Despite this complication, the prototype of this new class of therapeutic drugs, ONYX-015, has received intensive testing in the laboratory and has shown to be safe and effective in preclinical studies. Here, I give a summary of the problems with this agent's selectivity and its therapeutic promise. The effectiveness of this drug in the clinic could be improved using several strategies, which are proposed in light of clinical data and recent fundamental findings.Oncolytic virotherapy has made several significant advancements over the last two

years. Clinical trials have shown promise, and studies on the interactions between viruses, immune reactions, and tumor microenvironments have shed significant light. This overview highlights the most important discoveries made in this area over the previous two years and offers recommendations for the future.

It was used in cancer based on evidence that the mildly poisonous, highly anthropophilic mumps virus has a carcinostatic impact. Patients typically only got tiny doses of the virus because the emphasis was placed on testing the virus's method of administration rather than on its ability to treat human cancer. Except for 11 patients who were in danger of passing away, the therapy for 90 patients with terminal cancer of different types was rated as very excellent in 37 cases and good in 42. The mumps virus was administered with few adverse effects. The early anti-cancer effects of the mumps virus treatment appeared to happen quickly and powerfully concerning how quickly cancer cells proliferated. Patients who maintained their physical stamina frequently displayed ongoing tumor growth suppression even after the initial impact vanished, suggesting that tumor immunity may be involved in the current virus treatment.

The safety of several viral platforms has been documented in early-stage clinical studies of oncolytic virotherapy, and viruses from three families have moved to advanced efficacy trials. Additionally, many fresh approaches to genetic engineering now have proof-of-principle data from early research. As a result, a wide range of viruses with varied therapeutic applications are now accessible thanks to advancements in systemic administration, increased tumor specificity, and better oncolytic effectiveness. Creating viruses that reproduce more effectively within tumors while reaching therapeutic synergy with already accessible treatments is the field's present main challenge[8]–[10].

Following the success of immunotherapy using immune checkpoint drugs, oncolytic viral therapy may represent the next significant advancement in the fight against cancer. Oncolytic viruses are described as genetically modified or naturally existing viruses that reproduce only in cancer cells and kill them without causing any damage to healthy cells. The first oncolytic viral medication, T-Vec (talimogenelaherparepvec), a second-generation oncolytic HSV-1 with GM-CSF, was recently authorized in the USA and Europe. The phase III study demonstrated that local intralesional injections of T-Vec in advanced malignant melanoma patients can work systemically to extend overall life as well as inhibit the development of injected tumors. Vaccinia virus JX-594 (pexastimogenedevacirepvec) for hepatocellular carcinoma, GM-CSF-expressing adenovirus CG0070 for bladder cancer, and Reolysin (pelareorep), a wild-type variant of reovirus, for head and neck cancer are other oncolytic viruses that are on the verge of receiving drug approval in North America and Europe.

## CONCLUSION

EBV, hepatitis B virus, human papillomavirus, human herpesvirus-8, and Merkel cell polyomavirus are examples of carcinogenic DNA viruses. (MCPyV). Hepatitis C virus and human T-cell lymphotropic virus-1 are two carcinogenic viruses with RNA that cause illness in people. However, certain types of viruses are employed as a form of cancer medicine. Several of the oncolytic viruses under preclinical and clinical study for cancer treatment include viruses such as herpes infectious agents, measles viruses, coxsackie viruses, polioviruses, reoviruses, poxviruses, and Newcastle disease viruses, among others. These oncolytic viruses can explode cancer cells after infection, destroying the cancer cells and unleashing cancer antigens. Following the stimulation of immune reactions by these antigens, any residual tumor cells in the area as well as possible elsewhere in the human body can be sought out and eliminated. The comparatively weak intratumoral penetration of the oncolytic

viruses, which have been altered to have a decreased replicative potential, is a significant drawback of oncolytic virotherapy. Entry has been increased by building a cell-fusion capability into the viral framework.

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# CHAPTER 24

# THE BIOLOGICAL SIGNIFICANCE OF THE VIRUS IN THE AQUATIC ECOSYSTEMS

Dr Faiyaz Ahmad, Professor
Department of Pathology, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- dr.faiyaz146@gmail.com

**ABSTRACT:**

The most numerous species on the globe are viruses and the number that exist changes depending on the environment. The primary cause of the quick demise of toxic algal blooms, which frequently result in the death of other aquatic organisms, is viruses. Viruses change how groups, people, and ecosystems engage with one another, which affects how healthy, resilient, and functional an ecosystem is. The variety and quantity of viruses are influenced by host ecology. The viruses contribute significantly to ecology as well as are intricately linked to environments.In this chapter, we discuss the significance of the virus on the aquatic ecosystem.

**KEYWORDS:**Aquatic virus, Algal blooms, Food web, Marine virus, Viral infection.

## INTRODUCTION

The control of freshwater and marine environments depends on viruses. The majority of these viruses are safe for plants and animals because they are bacteriophages. The most significant method for recycling carbon in the marine environment is comprised of the bacteria that they infect and kill in watery microbial populations. Fresh bacterial and algal development is sparked by the viruses' discharge of organic compounds from the bacterial cells. In water, microorganisms make up more than 90% of the material. The primary cause of the quick demise of toxic algal blooms, which frequently result in the death of other aquatic life, is viruses. Further away and deeper into the ocean, where there are fewer host species, there are fewer viruses to be found. The impacts of marine viruses are extensive; by boosting oceanic photosynthesis, viruses tangentially contribute to a yearly reduction in atmospheric carbon dioxide of about 3 gigatonnes of carbon.

Marine animals are vulnerable to viral infections just like any other entity. The phocine distemper virus caused tens of thousands of harbor seal deaths in Europe between 1988 and 2002. The communities of aquatic mammals are also home to numerous other viruses, such as caliciviruses, herpesviruses, adenoviruses, and parvoviruses. Viruses, also known as bacteriophages, make up the majority of aquatic viruses. Phages are intracellular parasites that can only multiply inside infected bacteria, making them obligatory intracellular parasites. Therefore, phages can only be discovered in places where bacteria are present. Bacteria are present in most places, including our cells. (called normal flora). These bacteria are frequently discovered in great quantities. Phages are consequently present almost everywhere. As a general guideline, many phage scientists anticipate that phage population densities will be 10 times greater than bacterial densities or more. (VBR or virus-to-bacterium ratio)[1]–[3].

There is a wide variety of viruses, including RNA and DNA viruses with single and double strands that attack bacteria, protists, and archaea. Viral variety has been examined using the metagenomic study of cloned viral genomes. Viral communities were collected in one such research from the Arctic Ocean, coastal seas of the North Pacific, the Gulf of Mexico, and the

Sargasso Sea. 90% of the 1.8 million sequences that were retrieved had no identifiable matches in any database. Because of this, viral genetic variety is not only enormous but also mainly untapped. The prevalence of marine viruses suggests that they are probably the main causes of marine death. In fact, it's estimated that each day, viruses destroy 20% or so of the oceanic microbial population. Measurement of virus-induced microbe death, however, reveals that it is wildly inconsistent. In many cases, the microbial host that is most active in the population correlates to viral abundance. Community organizations can be greatly impacted by virus-mediated cell lysis. Models suggest that as one microbe species (or strain) gains numerical dominance, lytic viruses will soon start to target it, leading to a decrease in its population. This enables the growth of a different microbe species (or strain), which then becomes vulnerable to powerful virus lysis, and so on. Although the "kill the winner" paradigm has received a lot of attention, more experimental proof is required before it can be considered generally accepted. The progress of Emilianiahuxleyi coccolithophore blooms has produced some of the most convincing evidence to date. Such blooms are so powerful that they can be seen from space, but it is believed that viral lysis is at least partially to blame for their decline. Although this occurrence is intriguing, viral lysis typically does not cause a host community to completely disintegrate.

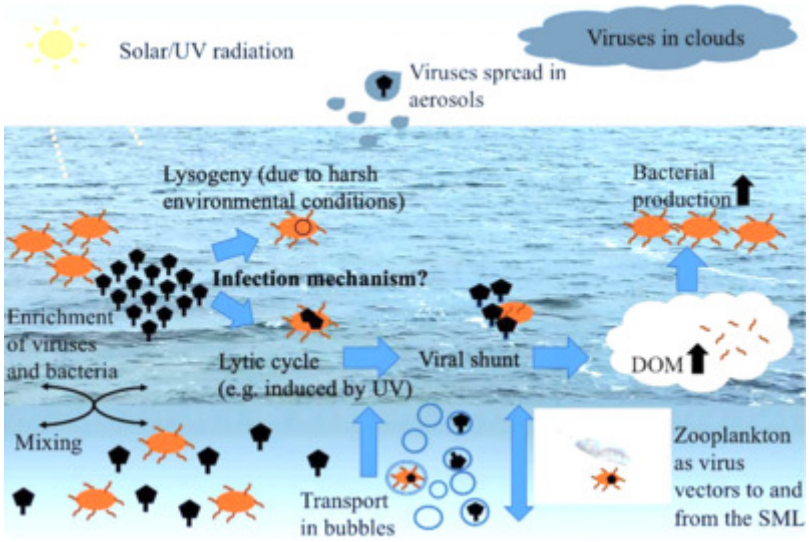


**Figure 1: Marine virus interaction with the bacteria: Diagram showing the marine viruses in the interaction with the bacteria(Wikipedia).**

By their ecology, marine viruses are those that can be found in saline environments such as seas and oceans or brackish environments such as shoreline estuaries. The replication mechanism of the host is required for viruses to reproduce, which is why they can only do so inside the living cells of a host creature. They can spread the infection to all kinds of species, including bacteria, archaea, and both plants and animals. Viruses live as autonomous particles known as virions when they are not inside a cell or actively infecting a cell. A virion is made up of a capsid and a genome, a lengthy molecule that transports hereditary data in either DNA or RNA. (a protein coat protecting the genetic material). For some viral species, these virus particles have straightforward helical and icosahedral geometries, while others have more intricate shapes. The virions of the majority of viral types are too tiny to be seen under an optical microscope. The linear dimension of the typical virion is approximately one-tenth that of the typical bacterium.

Usually, a teaspoon of saltwater includes fifty million viruses. The majority of these pathogens, known as bacteriophages, attack and kill marine bacteria while regulating

phytoplankton development at the base of the marine food web (Figure.1). Bacteriophages are not harmful to humans or other creatures, but they are crucial for maintaining the balance of marine environments. They provide essential methods for recycling fertilizers and carbon in the water. The viral shunt is a mechanism in which organic molecules emitted from dead bacterial cells encourage the development of new bacteria and algae. It has been demonstrated that the destruction of bacteria by viruses, in particular, promotes nitrogen cycling and the development of phytoplankton. The biological cycle, which sequesters carbon in the deep water, is also impacted by viral activity. Viruses unintentionally reduce the amount of carbon dioxide in the atmosphere by about 3 gigatonnes of carbon per year by boosting the amount of respiration in the seas.

About 70% of the entire oceanic biomass is made up of marine microorganisms. According to estimates, oceanic viruses eliminate 20% of the bulk of microorganisms each day. The primary factors behind the quick demise of harmful algal blooms, which frequently result in the death of other aquatic life, are viruses. Further away and deeper into the ocean, where there are fewer host species, there are fewer viruses to be found. The natural process of DNA being transferred from one species to another by viruses promotes genetic variety and propels evolution. Before the diversification of bacteria, archaea, and eukaryotes during the period of the last universal common ancestor of life on Earth, it is believed that viruses played a crucial part in early evolution. One of the most uncharted regions of genomic variation on Earth is still found in viruses.

The measurement of bacterial biomass in aquatic ecosystems allowed for the realization that bacterioplankton, the main component, incorporates a sizeable percentage of dissolved organic matter (DOM) from primary production. Bacteria can recirculate DOM from primary production back into biomass through a process known as the "microbial loop," which can then be used by higher users. (zooplankton). Then, since viral lysis was proposed to redirect organic carbon flow away from zooplankton into the DOM pool, which was easily utilized by the bacterial community (Figure 2), viruses were introduced into the microbial loop as an active component of the aquatic food web.

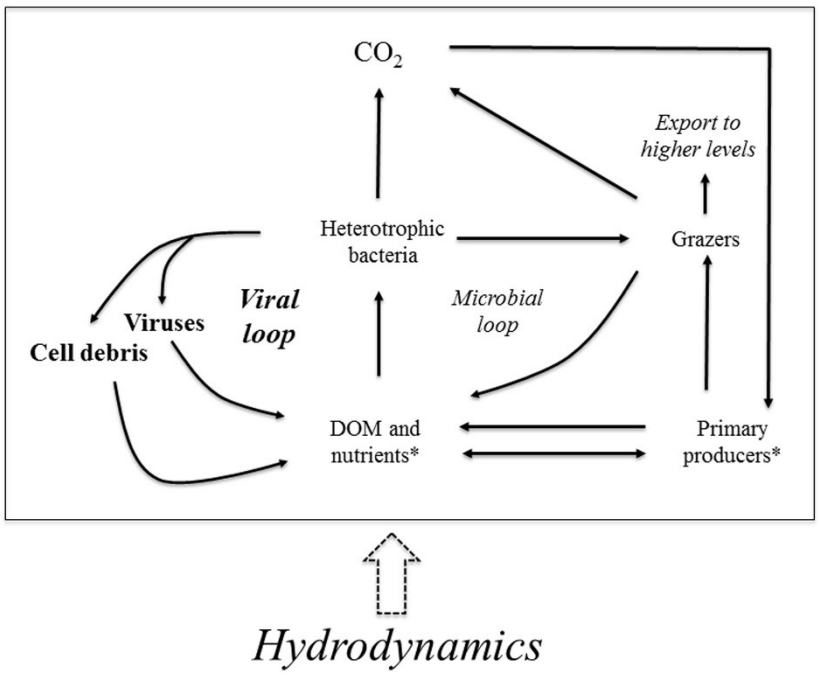


**Figure 2: Role of the virus in the food web: Diagram showing the role of the virus in the microbe food web (Wikimedia commons).**

Viruses thus increase respiration rates in lower trophic levels and nutrient recirculation within the microbial cycle. As a result, grazing and viral lysis, the two main causes of bacterial and phytoplankton mortality, have very different effects on aquatic food webs. Grazing results in the transfer of carbon and nutrients to higher trophic levels, whereas viral lysis results in the recycling of nutrients within the microbial loop.

## DISCUSSION

A renewed interest in viruses in the aquatic environment has been sparked by the finding that they may be the most prevalent creatures in natural waterways, outnumbering bacteria by an order of magnitude. Surprisingly little was understood about how viruses and their hosts communicate in the natural world. Enumeration of viruses in aquatic habitats has shown that virioplankton are dynamic components of the plankton, varying drastically in quantity with geographical position and season in the ten years since the accounts of extremely large viral populations were published. According to the available data, eukaryotic algae viruses and bacteriophages make up the majority of virioplankton populations. After new techniques were created and previous knowledge of bacteriophage biology was integrated into theories of parasite and host community interactions, the impact of viral infection and lysis on bacterial and phytoplankton host communities was quantifiable. The results of the novel techniques support the idea that viruses play a major role in microbial food webs by demonstrating that viral infection can significantly affect communities of bacteria and unicellular algae. The particular characteristics of virus-host interaction raise the interesting prospect that viral infection affects the structure and variety of aquatic microbial communities in addition to predation restricting the populations of bacteria and phytoplankton. Novel molecular genetic uses have produced solid proof that viral infection can have a substantial impact on the variety and makeup of water microbial populations[4]–[6].

Resources from the bottom up and prey from the top down govern ecosystems. Virus infection is now acknowledged as a pervasive top-down regulator of microbial development throughout ecosystems, but at the same time, resource availability affects and is affected by cell death due to viral predation. First, viral infection alters the metabolism of the host, in part thanks to metabolic genes expressed by the virus; the tasks carried out by these genes seem to reduce energetic and biosynthetic barriers to viral production. Second, it is difficult to reproduce external circumstances and the physiological state of the recipient cell during a viral attack in a lab setting. Finally, although the overall effects are still unknown, metabolic reprogramming of infected cells and virus lysis affect nutrient cycling and carbon release in the seas. To more accurately anticipate the biogeochemical effects of viral infections, this review emphasizes the necessity of comprehending viral infection processes in realistic physiological and environmental contexts.

Viruses are active participants in the microbial cycle and the population dynamics of both prokaryotic and eukaryotic microorganisms, according to a study conducted over the past two decades. The documented study of aquatic viruses has grown significantly over the last five years, particularly in the fields of freshwater viral ecology, viruses of eukaryotic microorganisms, and viral genetic variation. The complicated dynamics of viral infection within aquatic environments have been shown by recent studies of the relationships between viral infection, bacterivory, and grazing. These studies have clarified novel roles for viruses in biogeochemical cycles, such as photosystem gene expression, and have strengthened our knowledge of the environmental constraints on viral abundance, the effects of viral infection on host community structure, and other related topics. Ribonucleic acid viruses and single-stranded deoxyribonucleic acid viruses, two previously unknown families of viruses, have also been identified as varied and active members of marine virioplankton assemblages.

Aquatic viruses include free-floating viruses (virioplankton) in water habitats as well as viruses that have attacked aquatic creatures, plants, and microbes. In the past three decades, virological studies and metagenomic investigations have helped identify a sizable number of watery viruses, particularly varied free-floating viruses like cyanophages, phycoviruses, archaea viruses, giant viruses, and even virophages. Here, we summarize and outline the main virus species, their evolutionary contribution to aquatic communities through horizontal gene transfer, and their ecological roles for cyanobacterial bloom termination and global biogeochemical cycling in freshwater and marine ecosystems. This is based on a thorough introduction to the classification of aquatic viruses and their morphological and genetic diversity. As a result, this overview highlights some recent findings about aquatic viruses and virus-host interactions, particularly their evolutionary significance and ecological functions in various watery populations and environments[7]–[9].

Our understanding of the variety and dynamics of marine viral populations has altered as a result of the enormous quantities of data generated by nucleic acid sequencing. Here, we review current metagenomic and metatranscriptomic research focusing on RNA virus communities. In addition to confirming the prevalence of lytic (+) ssRNA viruses of the order Picornavirales, the study of RNA viromes identifies other (+) ssRNA viruses, such as RNA bacteriophages, as significant contributors to external RNA viral communities.DsRNA sequencing points to an unexplored variety of dsRNA viruses. Environmental metatranscriptomes reveal the complete intricacy of viral dynamics in the marine environment by concurrently capturing the dynamics of ssDNA, dsDNA, ssRNA, and dsRNA viruses. RNA viruses can exceed bacteriophages during phytoplankton blooms, are common in large size portions of environmental metatranscriptomes, and actively infect oceanic unicellular eukaryotes bigger than 3 m. Since DNA and RNA viruses fluctuate in quantity on an hourly time frame, viral control is likely to occur daily. A varied population of ssRNA and dsRNA viruses, frequently with multipartite genomes and potentially enduring intracellular lifestyles, are found in the metatranscriptomes of cultured protists. We propose that the diversity and complexity of RNA viral communities may be greater than previously thought, and that the impact of these communities on local community structure and world carbon fluxes in aquatic environments may be underappreciated.

Conventionally, cyanobacterial (algal) blooms have been linked to an overabundance of nutrients from waste and runoff, which encourages the quick development and proliferation of cyanobacteria or algae. The cyanobacteria's primary enemy is the cyanophage (virus). (the host). This study aims to identify specific factors that interfere with cyanophage-host interactions and cyanobacterial bloom formation. The effect of greenhouse gases, ozone depletion, solar ultraviolet radiation (SUR), and the function of newly found virophages—which coexist with phages and serve as their natural predator—are the main topics of this review. The main conclusions are that the increase in SUR, the mutation of cyanophages and cyanobacteria, as well as altered nutrient levels, have worked together with virophages to obstruct cyanophage-host interactions and the subsequent viral infection and killing of the cyanobacterial cell, which is a necessary step in controlling cyanobacterial blooms. Take this as a "call to action" for scientists who are engaged in corrective measures for changing aquatic environments[10].

## CONCLUSION

Viruses are frequently discovered throughout each habitat on Earth, but the oceans may be in which their role is best understood because there they are thought to be the main source of genetic variation. it is commonly likely that viral would influence the growth of cellular machinery in addition to other evolutionary factors like predation or external factors given

that they rely on almost all aspects of the host living thing's cellular to reproduce and propagate. By affecting material processes as well as energy fluxes in the nutritional web and the microbial network that controls the release of $CO_2$ from organic material breakdown under the influence of human activity and climate change, viruses play important roles in controlling ecological carbon cycling processes. Diatoms, a type of aquatic algae, have been discovered to be susceptible to viruses, and extinctions of diatoms close to the seawater's top could offer minerals and biological material for recovery by other microalgae.

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# CHAPTER 25

# APPLICATION OF THE VIRUS IN MEDICINE, AND MATERIAL TECHNOLOGY

Vaibhav Rastogi, Associate Professor
Department of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
Email id- vaib.asa@gmail.com

**ABSTRACT:**

Viruses are microscopic entities that live on every continent and can infect living organisms.But some viruses are used for the treatment of the disease, cancer. Since viruses naturally possess the capacity to introduce genetic information into the cells, they are presently among the most popular vehicles employed in gene therapy.In this chapter, we mostly emphasized the biological application of the virus in medicine and material science.

**KEYWORDS:**Amino Acids, DNA Duplication, Ebola Virus, Materials Science, Viral Disease.

## INTRODUCTION

In the study of molecular and cellular biology, viruses are a crucial instrument. Viruses are useful in the study of cellular processes because they infiltrate cells by inserting their genetic material into the nucleus of the host cell. We now know more about the fundamentals of molecular genetics, such as DNA duplication, transcription, RNA processing, translation, protein transport, and immunology, thanks to the use of viruses in the study. To bring DNA into the cells they are investigating, geneticists frequently use viruses as vectors. Molecular scientists frequently use virus vectors to introduce genetic material into cells. The virus is altered to not cause illness and to infect only particular cell kinds to be a valuable viral vector. Phages are frequently used to alter the genetic makeup of microorganisms. Viral treatment works similarly by using viruses to genetically alter sick cells and tissues. The use of viral therapy in cancer care and gene therapy is promising. Inserting genes into a person's cells and organs to cure an illness is known as gene therapy[1]–[3].

A functioning genome is used to substitute the damaged gene in genetic diseases. The technology has been used, though it is still relatively novel. For illnesses brought on by single-gene abnormalities, such as cystic fibrosis, hemophilia, muscular dystrophy, and sickle cell anemia, researchers have concentrated on gene therapy. A viral vector, like the adenovirus depicted in figure 1, is used in gene therapy to deliver the proper gene copy to human cells (Figure.1). In the former Soviet Union and Eastern Europe, phages have been utilized as an antimicrobial substitute for more than 60 years. Because they can infect and destroy these "superbugs," they are viewed as a possible defense against bacteria types that are immune to numerous drugs. In contrast, a phage that infects MRSA (Methicillin-resistant *Staphylococcus aureus*) creates a toxin that makes the bacteria more virulent and challenging to control. It is being investigated whether cancer-causing viruses can be used to cure cancer. Viruses known as oncolytic viruses lyse and destroy cancer cells. With the help of these viruses, some experts hope to cure some cancers.

Since they have developed to infect almost all living forms, viruses are incredibly varied. The replication methods of viruses with comparable genome organizations show prominently conserved motifs amidst this variety. All viruses have to uncoil, reproduce and transcribe

their genomes once they are inside a cell, and then they must repackage their genomes into viral progeny that are discharged from cells. To synchronize the transition between transcription and reproduction and between plus and minus strand synthesis, RNA viruses in particular must safeguard their genomes from cellular nucleases. Fundamental developments in our knowledge of reproduction have come from viruses that attack both animal and non-animal hosts due to the conserved character of a virus' intracellular life cycle. Studies of viral pathogens are readily supported from a global health viewpoint due to the devastating impacts of viral illnesses like AIDS, smallpox, polio, influenza, diarrhea, and hepatitis.

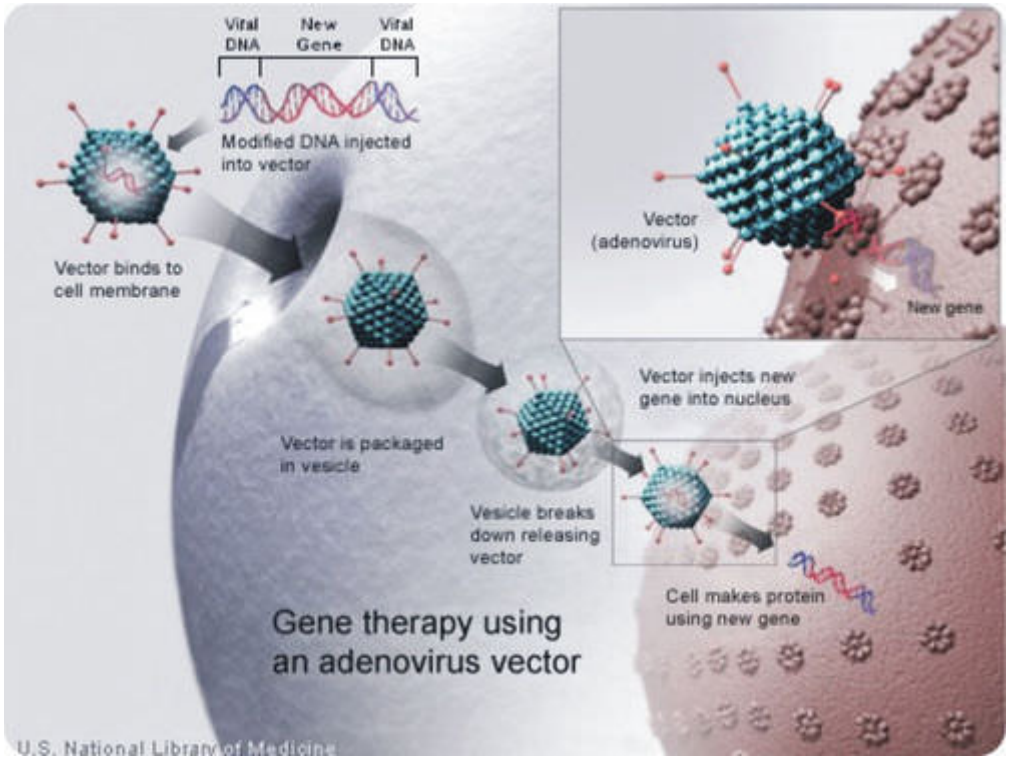


**Figure 1: Viral therapy: Diagram showing the use of the virus in gene therapy (bio. libre text).**

There have been sobering instances of new virus illnesses. Among them is the sudden emergence of the coronavirus that causes SARS, the ongoing spread of the bird flu virus among people, and the discovery of poliovirus vaccine wild-type recombinants that have complicated efforts to eradicate the poliovirus. Additionally, the threat of bioterrorism became a fact on American territory, putting scientists under pressure to take quick countermeasures. Because developing safe drugs is complicated by viruses' close connection with the host's cellular machinery, vaccination is still the favored method of managing viral illnesses. However, some viruses have proven to be challenging for vaccines to combat, and the only treatment for illness management is antiviral medication.

US researchers have created materials that mimic flesh and bone using a prevalent virus. The study not only offers fresh perspectives on how such materials emerge in nature but also moves laboratory-based synthetic tissue production closer to reality. In nature, many variations of the same fundamental molecule, like a protein, are frequently combined to form entirely distinct materials. For example, the protein molecule collagen type I can join with several different chemicals to make skin, bone, or even eye tissue. Because individual molecules are not put together following an exterior blueprint, this process is referred to as self-templating. Instead, to make sure that the preferred shape is the one that is energetically

favored, thermodynamic variables like temperature and solution concentration are regulated. The intense sensitivity to thermodynamic variables that causes self-templating makes such molecules very challenging to work with in the lab, despite the scientists' strong interest in simulating these processes. It is still unclear how nature manages to exercise the level of discipline that laboratory chemists have yet to master. Using the M13 phage as a basic unit rather than a protein like a collagen is a clever way to solve this issue. M13 is a virus that only harms E. coli microorganisms; it is safe for people to be around. Because its protein coat can be altered through genetic engineering, it is comparatively simple to cultivate and control in the lab. Seung-Wuk Lee, Angela Belcher, and coworkers at the University of Texas at Austin first found this trick in 2002. In their most recent study, scientists under Lee's direction at the Lawrence Berkeley Nationa

l Laboratory and the University of California, Berkeley examined the physical circumstances that would allow various molecular structures to develop from genetically altered M13 viruses. They began with solid plates submerged in a salt solution that was virally active, meticulously removed the plates, and then allowed the salt solution to evaporate, leaving a thin coating of viruses on the plates. The intricacy of the designs on the plates grew along with the virus solution's concentration. The scientists observed a straightforward alternating pattern of ridges and channels at values of 0.1–0.2 mg/ml. The designs on the plates, however, displayed a much more complicated, long-range order at a concentration of 6 mg/ml, which the experts claim is similar to dried ramen noodles. Additionally, the impact of extraction speed was studied. They discovered that the speed at which the plate was removed from the solution significantly affected the visual characteristics of these "ramen-noodle-like" formations.

The highest reflected wavelength of one sheet was decreased from 490 nm to 388 nm by increasing the pulling speed from 50 m/min to 80 m/min. The researchers note that some avian plumage and beetle casings have brilliant structural color because they are made of natural materials with such frequencies. By using their films as platforms on which to develop cells, the team created large-scale 3D constructs. In various pictures, the cells developed variably. The researchers even succeeded in growing mineralized tissue resembling dental enamel on one medium. Lee emphasizes that his team does not assert to have mimicked the natural processes that give rise to these materials, as these are still inadequately known. The key point is that we start to test the significance of the kinetic variables and then start to build and very closely imitate the structures that nature produces, he says. "We believe the actual process of how nature produces these materials is very far from our process," he says. Belcher, who currently works at MIT and was not engaged in the latest work, is impressed. The capacity to use a single genetically tunable molecular building block to precisely regulate the self-templating and assembly of materials over multiple layers of the organization is, in my opinion, the most intriguing part of this study. Then, the experts use this ranking for a variety of purposes.

The surface of a pathogen has plenty of room. To create iron phosphate nanowires, we use the bacteriophage M13, a viral that only affects Escherichia coli, as a biological scaffold. A very potential active component used in battery cathodes is iron phosphate (FePO4). Due to the high abundance of elements in this substance, it is extremely eco-friendly and provides high charge storage capacities. Low electronic and Li-ionic conductivities, two parameters that determine the performance of cathode materials, are one of its disadvantages. Currently, LiFePO4—the discharge product of FePO4—is produced through an energy-intensive synthesis pathway that produces micro- to nanoscale carbon-coated materials. Diffusion lengths are greatly decreased and efficiency is increased by increasing the surface-to-volume

ratio, while carbon coating promotes effective electronic transport and quick redox reactions. However, the crystallinity of crystalline (Li)FePO4, a well-known example of a two-phase material, limits Li-ion diffusion to one-dimensional (1D) channels that are readily obstructed by defects while also providing an almost constant potential during charge/discharge.

The scenario may be very different for amorphous (Li)FePO4, and it is expected that the Li-ion conductivity will be much higher because ionic transport is no longer confined to 1D channels. It is simple to genetically modify the filamentous virus M13 to carry particular traits. Most significantly, thousands of clones of protein 8 build its proteinaceous covering in the first place. (capsid). Therefore, since the surface characteristics of the bacteriophage rely on the particular amino acids that are exposed on the surface, we can readily control these characteristics by genetically altering the genetic code for protein 8. We altered the genetic code for protein 8 to contain four acidic amino acids at its N-terminal tail to use this bacteriophage for our production. To allow the bacteriophage's surface to electrostatically attach cations, these surface-protruding regions display a pattern of four sequential acidic amino acids, specifically glutamic acid (E), followed by three residues of aspartic acid.

## DISCUSSION

The pig herpesvirus pseudorabies virus (PRV), a member of the Alphaherpesvirinae subfamily, is the cause of Aujeszky's illness. By concentrating on (i) the molecular biology of PRV, (ii) model systems to study PRV pathogenesis and neurovirulence, (iii) PRV transsynaptic tracing of neuronal circuits, and (iv) veterinary aspects of pseudorabies disease, this review describes the contributions of PRV research to herpesvirus biology, neurobiology, and viral pathogenesis. A step-by-step breakdown of the viral reproduction cycle is given, along with information on the viral DNA genome's composition and the shape of the enveloped infectious particle. To enter the cell and begin the PRV infection, cellular receptors must first attach to the virus. After entering the nucleus, the viral genome controls a chain of controlled gene expression that leads to viral DNA duplication and the creation of new components for the virion[4]–[6].

Progeny virions eventually self-assemble and leave the host cells. The development of animal models and neural culture methods for the investigation of PRV pathogenesis and neurovirulence is covered. We describe the initial studies of PRV circuitry mapping, the biology underpinning this use, and the creation of the next generation of tracer viruses. PRV acts as a self-perpetuating transsynaptic tracer of neural circuitry. We talk about the fundamental veterinary elements of managing the swine pseudorabies illness. Sporadic reactivation from latency can spread PRV to new hosts as the infection proceeds from an acute infection of the respiratory epithelium to a dormant infection in the peripheral nervous system. Testing, vaccination, and prevention have all been crucial to the effective treatment of the PRV illness.

In comparison to synthetically programmed materials, viruses have some key benefits, such as the highly exact spatial arrangement of their subunits into a wide variety of forms and sizes and the abundance of opportunities for simple and repeatable change. Here, we'll first take a look at the wide range of viruses, different techniques for creating virus-based nanoparticles, and engineering concepts for adding new features. The uses and consequences of virus-based materials will then be looked at in detail, with an emphasis on the medicinal, biotechnology, and energy industries. We expect that this area will keep developing and expanding, offering fascinating new opportunities due to developments in the logical design of virus-based nanomaterials.

West Africa is experiencing the worst Ebola viral illness outbreak in history. There have already been thousands of confirmed, probable, or suspected cases due to a combination of factors including a lack of public health infrastructure, low levels of health literacy, scarce acute care and infection prevention and control resources, densely populated areas, and a highly contagious and deadly viral infection. Ebola virus disease is defined as a febrile serious sickness with severe gastrointestinal symptoms, and it is worsened by shock, severe electrolyte abnormalities, intravascular volume loss, and organ failure. The possible impact of supportive care is significant for a disease with high baseline mortality and one that typically occurs in resource-constrained situations, despite the lack of medical therapies demonstrated to be effective against the Ebola virus. Many of the sickest Ebola viral disease patients do not need to pass away with more staff, routine surveillance, and supportive care. Critical care medicine can and should play a significant role in facilitating this change because the Ebola virus disease reflects a condition that is ripe for a paradigm shift in the way healthcare is provided and how outcomes are handled[7], [8].

The harnessing of complicated structures coming from millennia of evolutionary fine-tuning has been made possible by the use of materials drawn from natural sources in materials science. A variety of naturally occurring molecular assemblages and containers with a range of sizes, shapes, stabilities, dynamic characteristics, and chemical reactivities have been discovered as a result of improved knowledge of the structure and function of viruses. In materials science, engineering, and nanotechnology, viruses are widely used as instruments and building elements for electronics, chemistry, and biomedical research. Here, we examine the various virus kinds currently in use, their physical characteristics, and their possible benefits in various nanotechnology fields.

It is possible to think of viruses as organic nanoparticles from the perspective of a materials chemist. Proteins and nucleic acids make up the majority of the (bio)polymers that make them up. All viruses do not have their metabolism; rather, they use the biochemical apparatus of a living cell for reproduction. Many viruses are enclosed in lipid membranes. They have special tools on their surface that allow them to pass through the defenses of their target cells. The quantity and type of functional groups on the surface of viruses, as well as their size and structure, are all well-defined. In materials science, viruses are frequently used as templates for covalently connected surface changes. As a result of the innate colocalization of genes- and phenotypes, viruses have the unique ability to be customized by guided evolution. Engineering approaches to nanomaterials are based on the potent methods created by the life sciences, opening up a broad variety of uses that go far beyond biology and health.

Because of their distinctive shapes and chemical diversity, biological molecules can be used as flexible blueprints for building nanoscale materials. The natural light-harvesting antenna's supramolecular structure of molecular pigments has garnered interest due to its possible use in sensing, photocatalytic systems, and photonic devices. Here, we demonstrate how to organize molecular pigments using M13 viruses as templates to create a one-dimensional light-harvesting antenna. When zinc porphyrins are chemically grafted onto M13 viruses, unique spectroscopic changes are induced. These changes include fluorescence quenching, a significant band widening and minor redshift of their absorption spectrum, as well as a shorter lifespan of the excited states. We propose a speculative model to account for the energy transfer taking place in the supramolecular porphyrin structures templated by the virus based on these optical fingerprints. We anticipate that further genetic modification of M13 viruses will make it possible to combine pigments with other functional materials (like catalysts and electron transfer intermediaries), suggesting potential uses for photochemical devices[9], [10].

## CONCLUSION

Since virology can target particular cells, they are currently being employed as vectors to transport chemicals for the therapy of illnesses like cancer. Virology is frequently included in medicines. Multiple types of malignancies as well as metabolic, cardiovascular, muscle, hematologic, ophthalmologic, and respiratory infections have all been treated using viral carriers. Recent advances in immunization have offered both curative and prophylactic methods. The benefits of virus carriers are generally outlined below: High efficacy gene transfer; highly targeted gene transport that targets cells; development of potent immune reactions; and heightened cell defense.Since they may carry the substance by invading cells, a few viruses are used as vectors. Viruses are altered so that once they are carried out on humans, they cannot spread illness. Retroviruses are one form of viral that integrates its DNA, which includes a novel gene, through a genome in the human.

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