9.11B: Replication of Double-Stranded DNA Viruses of Animals

Most double-stranded DNA viruses replicate within the host cell nucleus.

Learning Objectives

• Differentiate the ways which different classes of dsDNA viruses replicate

Key Points

• From the perspective of the virus, the purpose of viral replication is to allow production and survival of its kind.
• Most double-stranded DNA viruses replicate within the host cell nucleus, including polyomaviruses, adenoviruses, and herpesviruses—poxviruses, however, replicate in the cytoplasm.
• Adenoviruses and herpes viruses encode their own replication factors.

Key Terms

• Okazaki fragments: Okazaki fragments are short, newly synthesized DNA fragments that are formed on the lagging template strand during DNA replication.
• polymerase: Any of various enzymes that catalyze the formation of polymers of DNA or RNA using an existing strand of DNA or RNA as a template.

Viral replication is the formation of biological viruses during the infection process in the target host cells. Viruses must first get into the cell before viral replication can occur. From the perspective of the virus, the purpose of viral replication is to allow production and survival of its kind. By generating abundant copies of its genome and packaging these copies
into viruses, the virus is able to continue infecting new hosts. Replication between viruses is greatly varied and depends on the type of genes involved in them. Most DNA viruses assemble in the nucleus while most RNA viruses develop solely in cytoplasm.

Double-stranded DNA viruses usually must enter the host nucleus before they are able to replicate. Some of these viruses require host cell polymerases to replicate their genome, while others, such as adenoviruses or herpes viruses, encode their own replication factors. However, in either cases, replication of the viral genome is highly dependent on a cellular state permissive to DNA replication and, thus, on the cell cycle. The virus may induce the cell to forcefully undergo cell division, which may lead to transformation of the cell and, ultimately, cancer. An example of a family within this classification is the Adenoviridae.

Polyomaviruses, adenoviruses, and herpesviruses are all nuclear-replicating DNA viruses, each with their own specific approaches to replication. There is only one well-studied example in which a double-stranded DNA virus does not replicate within the nucleus. This is the Poxvirus family, which comprises highly pathogenic viruses that infect vertebrates.

**Polyomaviruses**

Polyomaviridae is a family of viruses whose natural hosts are primarily mammals and birds. Most of these viruses, such as BK virus and JC virus, are very common and typically asymptomatic in most human populations studied. However, some polyomaviruses are associated with human disease, particularly in immunocompromised individuals. Some members of the family are oncoviruses, meaning they can cause tumors; they often persist as latent infections in a host without causing disease, but may produce tumors in a host of a different species, or in individuals with ineffective immune systems. The name polyoma refers to the viruses’ ability to produce multiple (poly-) tumors (-oma).

**Replication**

Prior to genome replication, the processes of viral attachment, entry and uncoating occur. Polyomavirus virions are subsequently endocytosed and transported first to the endoplasmic reticulum where a conformational change occurs; then by an unknown mechanism the virus is exported to the nucleus. Polyomaviruses replicate in the nucleus of the host.

**Adenoviruses**

Adenoviruses (members of the family Adenoviridae) are medium-sized (90–100 nm), nonenveloped (without an outer lipid bilayer) viruses with an icosahedral nucleocapsid containing a double stranded DNA genome.

Adenoviruses represent the largest nonenveloped viruses. They are able to be transported through the endosome (i.e., envelope fusion is not necessary). The virion also has a unique “spike” or fiber associated with each penton base of the capsid that aids in attachment to the host cell via the receptor on the surface of the host cell.
Adenoviruses are non-enveloped (i.e., they have no external lipid bilayer) and are icosahedral (i.e., shaped like a polyhedron with 20 faces). They have fibers at their vertices that help them attach to host cells.

Replication

Adenoviruses possess a linear dsDNA genome and are able to replicate in the nucleus of vertebrate cells using the host’s replication machinery.

Once the virus has successfully gained entry into the host cell, the endosome acidifies, which alters virus topology by causing capsid components to disband, which in turn destroys the endosome and allows the virion entry into the cytoplasm. It is transported to the nuclear pore, disassembles, and is released into the nucleus. At this point viral gene expression can occur and new virus particles can be generated.

Herpesviruses

Herpesviridae is a large family of DNA viruses that cause diseases in animals, including humans. The members of this family are also known as herpesviruses. The family name is derived from the Greek word herpein (“to creep”), referring to the latent, recurring infections typical of this group of viruses. Herpesviridae can cause latent or lytic infections.

At least five species of Herpesviridae – HSV-1 and HSV-2 (both of which can cause orolabial herpes and genital herpes), Varicella zoster virus (which causes chicken-pox and shingles), Epstein-Barr virus (which causes mononucleosis), and Cytomegalovirus – are extremely widespread among humans. More than 90% of adults have been infected with at least one of these, and a latent form of the virus remains in most people. In total, there are 8 herpesvirus types that infect humans: herpes simplex viruses 1 and 2, varicella-zoster virus, EBV (Epstein-Barr virus), human cytomegalovirus, human herpesvirus 6, human herpesvirus 7, and Kaposi’s sarcoma-associated herpesvirus. There are more than 130 herpesviruses, and some are from mammals, birds, fish, reptiles, amphibians, and molluscs.

Replication

All herpesviruses are nuclear-replicating—the viral DNA is transcribed to mRNA within the infected cell’s nucleus. Infection is initiated when a viral particle contacts a cell with specific types of receptor molecules on the cell surface. Following binding of viral envelope glycoproteins to cell membrane receptors, the virion is internalized and dismantled, allowing viral DNA to migrate to the cell nucleus. Within the nucleus, replication of viral DNA and transcription of viral...
genes occurs.

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**Poxviruses**

Poxviridae is a family of viruses. Human, vertebrates, and arthropods serve as natural hosts. There are currently 69 species in this family, divided among 28 genera, which are divided into two subfamilies. Diseases associated with this family include smallpox.

Poxviridae viral particles (virions) are generally enveloped (external enveloped virion- EEV), though the intracellular mature virion (IMV) form of the virus, which contains different envelope, is also infectious. The virion is exceptionally large—around 200 nm in diameter and 300 nm in length.

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**Replication**

The replication of poxvirus is unusual for a virus with double-stranded DNA genome (dsDNA) because it occurs in the cytoplasm, although this is typical of other large DNA viruses. Poxvirus encodes its own machinery for genome transcription, a DNA dependent RNA polymerase, which makes replication in the cytoplasm possible. Most dsDNA viruses require the host cell’s DNA-dependent RNA polymerase to perform transcription. These host DNA are found in the nucleus, and therefore most dsDNA viruses carry out a part of their infection cycle within the host cell’s nucleus.