9.11G: Double-Stranded DNA Viruses - Pox Viruses

The poxviruses are a family of large, complex, enveloped DNA viruses that infect a variety of vertebrate and invertebrate hosts.

Learning Objectives

• Examine pox viruses for their relevance to human disease and research

Key Points

• The most famous of the poxviruses was smallpox. Smallpox is one of two infectious diseases to have been eradicated, the other being rinderpest, which was declared eradicated in 2011.
• The most abundant and simplest infectious form of the poxvirus particle, the mature virion, consists of the viral DNA genome encased in a proteinaceous core and an outer lipoprotein membrane.
• Poxviruses exhibit a temporally-regulated gene expression program: early, intermediate, and late genes drive DNA replication followed by expression of structural proteins necessary for progeny virion assembly.

Key Terms

• recombinant: This term refers to something formed by combining existing elements in a new combination. Thus, the phrase recombinant DNA refers to an organism created in the lab by adding DNA from another species.
• lipoprotein: Any of a large group of complexes of protein and lipid with many biochemical functions.

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hosts. Poxviruses are of significance both medically and scientifically due to their wide distribution, pathogenicity, and cytoplasmic replicative life cycle. Several prominent members, including variola virus (causative agent of smallpox), molluscum contagiosum virus (cause of a common skin infection of young children and immunosuppressed adults) and monkeypox virus (agent of a smallpox-like disease in parts of Africa), are of considerable concern for public health and biodefense.

The most famous of the poxviruses was smallpox. Smallpox was an infectious disease unique to humans, caused by either of two virus variants, Variola major and Variola minor. The disease is also known by the Latin names Variola or Variola vera, which is a derivative of the Latin varius, meaning “spotted,” or varus, meaning “pimple.” The term “smallpox” was first used in Britain in the 15th century to distinguish variola from the “great pox” (syphilis). The last naturally occurring case of smallpox (Variola minor) was diagnosed on October 26, 1977. After vaccination campaigns throughout the 19th and 20th centuries, the World Health Organization (WHO) certified the eradication of smallpox in 1979. Smallpox is one of two infectious diseases to have been eradicated, the other being rinderpest, which was declared eradicated in 2011.

The prototypic and most studied poxvirus, vaccinia virus (VACV), serves as an effective smallpox vaccine, a platform for recombinant vaccines against other pathogens, and an efficient gene expression vector for basic research. Along its approximate 195-kbp double-stranded DNA genome, VACV encodes approximately 200 proteins, ranging in function from viral RNA and DNA synthesis and virion assembly to modulation of host immune defenses.

The most abundant and simplest infectious form of the poxvirus particle, the mature virion (MV), consists of the viral DNA genome encased in a proteinaceous core and an outer lipoprotein membrane with approximately 60 and 25 associated viral proteins, respectively. Following attachment to cell surfaces and fusion with the plasma or endosomal membrane, poxvirus replication is initiated by entry of the viral core into the cytoplasm, where all subsequent steps of the life cycle take place. Poxvirus cores harbor the viral DNA-dependent RNA polymerase and transcription factors necessary for expression of early genes, which constitute nearly half of the viral genome and encode proteins needed for DNA replication and intermediate gene transcription, as well as a large number of immunomodulators.

Poxviruses exhibit a temporally-regulated gene expression program, i.e., expression of early genes encoding DNA replication and intermediate transcription factors triggers the expression of intermediate genes encoding late gene specific transcription factors. Late gene products primarily consist of structural proteins needed for progeny virion assembly, as well as those enzymes destined for incorporation into progeny virions, and used for early gene expression during the next round of infection. Assembly of the MV involves more than 80 viral gene products. In addition, during transit through the cytoplasm, a subset of progeny MVs acquires two additional membrane bilayers, one of which is lost during exocytosis of the particle, to yield the less abundant enveloped virion (EV). Thus, an EV is essentially an MV with an additional membrane in which at least six unique proteins are associated. EVs are antigenically distinct from MVs and are important for efficient virus dissemination in the infected host and protection against immune defenses. In contrast, MVs are released upon cell lysis and may be important for animal-to-animal transmission.
Figure: **Girl infected with smallpox. Bangladesh, 1973.** In ordinary type smallpox the bumps are filled with a thick, opaque fluid and often have a depression or dimple in the center. This is a major distinguishing characteristic of smallpox.