Polyomaviruses

Family: *Polyomaviridae*

Genus	Type species
Polyomavirus	Simian virus 40

The family *Polyomaviridae* includes mouse polyomaviruses and two human viruses, JC and BK viruses, which were isolated from a patient with progressive multifocal leukencephalopathy and an immunosuppressed recipient of a kidney transplant, respectively. Under some conditions, mouse polyomavirus infection of the natural host results in formation of a wide variety of tumors (hence the name). A characteristic property of the members of this family is an ability to transform cultured cells or to induce tumors in animals. Investigation of such transforming activity has provided much information about mechanisms of oncogenesis, including the discovery of the cellular tumor suppressor protein p53. These viruses, particularly simian virus 40, have also been important in elucidation of cellular mechanisms of transcription and its regulation. For example, the simian virus 40 enhancer was the first member of this class of regulatory sequences to be identified.

Figure 15 Structure and genome organization. (A) The virion. (Left) Electron micrograph of negatively stained simian virus 40 virions. From F. A. Andered et al., *Virology* **32**:511–523, 1967, with permission. (Right) Diagram of the virion, showing the names and locations of virion proteins and the organization of the 5,243-bp circular, double-stranded DNA genome into approximately 25 nucleosomes by the cellular histones H2A, H2B, H3, and H4 (the core histones). One molecule of either VP2 or VP3, which possess a common C-terminal sequence, is associated with each VP1 pentamer. **(B) Genome organization.** Locations of the origin of viral DNA synthesis (Ori) and of the early and late mRNA sequences encoding the large and small T antigens (LT and sT) and the virion structural proteins VP1, VP2, and VP3 are indicated. The late mRNA species generally contain additional open reading frames in their 5′-terminal exons, such as that encoding leader protein 1 (LP1).

Figure 16 Single-cell reproductive cycle of simian virus 40. The virion attaches to permissive monkey cells upon binding of VP1 to a major histocompatibility complex (MHC) class I molecule on the surface of the cell. The virion is then endocytosed in caveolae **(1** and **2)**, is transported to the endoplasmic reticulum, and enters that organelle **(3)**. It is then transported to the nucleus and uncoated by unknown mechanisms **(4)**. The viral genome packaged by cellular nucleosomes is found within the nucleus **(5)**. The early transcription unit is transcribed by host cell RNA polymerase II **(6)**. After alternative splicing and export to the cytoplasm **(7)**, the early mRNAs are translated by cytoplasmic ribosomes to produce the early proteins LT and sT **(8)**. The former is imported into the nucleus **(9)**, where it binds to the simian virus 40 origin of replication to initiate DNA synthesis **(10)**. Apart from LT, all components needed for viral DNA replication are provided by the host cell. As they are synthesized, daughter viral DNA molecules associate with cellular nucleosomes to form the viral nucleoproteins often called minichromosomes. LT also stimulates transcription of the late gene from replicated viral DNA templates **(11)**. Processed late mRNAs are exported to the cytoplasm **(12)**, and translated to produce the virion structural proteins VP1, VP2, and VP3 **(13)**. These structural proteins are imported into the nucleus **(14)** and assemble around viral minichromosomes to form progeny virions **(15)**. Virions are released by an unknown mechanism **(16)**.