Togaviruses

Family: *Togaviridae*

Genus	Type species
Alphavirus	Sindbis virus
Rubivirus	Rubella virus

Members of the *Togaviridae* are responsible for two very different kinds of human disease. The alphaviruses are all transmitted by arthropods and cause encephalitis, arthritis, and rashes in humans. Rubella virus is the agent of a mild rash disease that can also cause congenital abnormalities when acquired by the mother early in pregnancy. Because these virions have a lipid envelope, they have been important models for studying the synthesis, posttranslational modification, and localization of membrane glycoproteins.

Figure 25 Structure and genomic organization. (A) The virion. (Left) Cryoelectron micrograph of the alphavirus Ross River virus. Courtesy of N. Olson, Purdue University. (Right) Three-dimensional image reconstruction of Sindbis virus (courtesy of B. V. V. Prasad, Baylor College of Medicine), showing the intact virus (yellow, with glycoprotein spikes visible) and the nucleocapsid only (blue). Also shown is a cross section of the particle (green), illustrating the relationship among the spike glycoproteins (S), the lipid membrane (M), the capsid (C), and the viral RNA genome (RNA). **(B) Genome organization.** The first two-thirds of togavirus genomic RNA, which is of (+) polarity and carries a 5′ cap, is translated to produce the polyproteins P123 and P1234. The latter is the precursor of the RNA polymerase. The P1234 polyprotein is produced by translational suppression of a stop codon located at the end of the nsP3 coding region. The proteins encoded in the terminal one-third of the genome are produced from a subgenomic mRNA that is copied from a full-length (–) strand RNA intermediate. The subgenomic mRNA encodes the structural proteins.

Figure 26 Single-cell reproductive cycle. The virion binds to a cellular receptor and enters the cell via receptor-mediated endocytosis **(1)**. Upon acidification of the vesicle, viral RNA is uncoated **(2)** and translated to form the polyprotein P1234. Sequential cleavage of this polyprotein at different sites produces RNA polymerases with different specificities. **(3)**. The RNA polymerase produced initially copies (+) strands into full-length (–) and (+) strands **(4)** and catalyzes synthesis of the subgenomic mRNA **(5)**. This mRNA is translated by free cytoplasmic ribosomes to produce the capsid protein **(6)**; proteolytic cleavage to liberate the capsid protein exposes a hydrophobic sequence of PE2 that induces the ribosomes to associate with the endoplasmic reticulum (ER) **(7)**. As a result, the PE2, 6K, E1 polyprotein enters the secretory pathway. The membrane topology of these proteins is shown in detail, with cleavage sites for cellular proteases indicated by red arrows. The glycoproteins are transported to the cell surface **(8** and **9)**. The capsid protein and (+) strand genomic RNA assemble to form capsids **(10)** that migrate to the plasma membrane and associate with viral glycoproteins **(11)**. The capsid acquires an envelope by budding at this site **(12)**, and mature virions are released **(13)**.