# Structure and Assembly of Alphaviruses

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The alphaviruses are enveloped animal viruses that belong to the family of Toga viruses. The molecular biology of this virus group is almost entirely based on studies with two members of this virus group, the Semliki Forest Virus (SFV) and the Sindbis virus. Like all other viruses the alphaviruses are completely dependent on their host cell for their replication. The virus particles themselves can be regarded simply as a piece of nucleic acid, which represents their genome, wrapped in a protective coat. In the case of the alphaviruses this coat is represented by the nucleocapsid structure and the surrounding membrane or envelope. The virus coat must, in addition to its protective function, also provide the means whereby the virus particle can get into the host cell and release its genome into the cell cytoplasm to start virus infection. This function is carried out by the virus-coded glycoproteins that form the spike-like projections on the surface of the virions.

The entry of the virus particle into the host cell starts with binding of the virus through its spikes to a receptor molecule present on the surface of the cell (see Fig. 1, Helenius et al. 1980a, b; White and Helenius 1980). After this initial binding event the virus is taken up into coated pits and then routed inside coated vesicles to the lysosomes where the acidic pH is thought to induce a change in the conformation of the spike glycoproteins such that these cause a fusion between the viral and the lysosomal membrane. As a result the viral nucleocapsid enters the cell cytoplasm and releases the RNA genome (a 42S RNA molecule). The viral RNA functions as a mRNA molecule for synthesis of an RNA-dependent RNA polymerase which will transcribe more viral genomes as well as a subgenomic RNA molecule (26S RNA) which corresponds to about one-third of the 42S RNA molecule at its 3' end. This smaller RNA molecule serves as a messenger RNA for all structural proteins of the virus particle, that is the capsid protein (3 × 10^4 daltons), and the three-membrane proteins E3 (10^4 daltons), E2 (5 × 10^4 daltons), and E1 (5 × 10^4 daltons). The translation starts from a single initiation site close to the 5' end of the 26S RNA molecule and the proteins are synthesized sequentially in the order, capsid protein, p62, and E1; the p62 protein is an intracellular precursor protein for E3 and E2. As shown in the Fig. 1, the capsid proteins assemble with the viral genome into nucleocapsid structures in the cell cytoplasm, whereas the p62 and E1 proteins are inserted into the rough endoplasmic reticulum membrane (RER) to become integral membrane proteins, which together will form the spike glycoprotein complex of the virus. This complex is transferred from its initial site of synthesis in the RER through the Golgi complex to the plasma membrane (PM) of the host cell, and here they will be specifically incorporated into a viral envelope during the budding process.

The simple nature of the alphaviruses and the fact that their replication in the animal cell is so heavily dependent on normal cellular functions have made these viruses very important tools for research in cellular biology. They are excellent model systems, for example, in the study of adsorptive endocytosis in animal cells (recently reviewed by Helenius et al. 1980b) and in studies on the structure and biosynthesis of the plasma membrane. With the two latter examples in mind we will discuss in this review the structure