

Dengue virus is an RNA virus. Its outer surface is covered with envelope proteins surrounding a lipid bilayer envelope. Inside the envelope is a capsid shell that contains the virus's RNA genome. Immune cells are targeted by the Dengue virus. There are two cell surface receptor molecules important in dengue infection. The cognate receptor is involved in normal infections and the FC receptor is involved in the phenomenon called antibody dependent enhancement. The virus's envelope protein binds to the cognate receptor and triggers a cellular process called receptor mediated endocytosis. The virus is internalized in a bubble-like structure called the endosome. When endosomes form, proton pumps lower the pH of the interior. The virus responds to the lowered pH by changing the conformation of the envelope proteins to form spike-like structures. The tips of the spikes are hydrophobic, which allows them to penetrate the endosome's membrane. They bend until the endosome's membrane and the virus's membrane fuse together and release the capsid into the cytoplasm. The capsid breaks apart and releases the viral RNA. The viral RNA travels to the rough endoplasmic reticulum. It is a positive-sense strand and can be directly translated into proteins. The ends of the RNA form structures that bind to translation initiation proteins. The complex attaches to the ribosome to initiate translation. The whole viral genome is translated as a single, long, poly protein chain. The capsid protein is on the cytoplasm side of the endoplasmic reticulum. The envelope protein and the membrane protein are in the lumen side and are activated by the host's peptidase enzyme. In the cytoplasm, one of the viral proteins, a protease enzyme, activates all the other proteins in the poly protein chain. These proteins aggregate to form the RNA replication complex. Viral RNA is synthesized in multiple steps. First, the ends of the viral RNA fold up, and the RNA forms a circle. The RNA then attaches to the replication complex to start the first round of synthesis. Using the RNA's positive-sense RNA as a template a negative-sense copy is made. The pair of RNA strands forms a double helix. The RNA then becomes a circle again. This time the negative-sense strand acts as a template to make a positive-sense strand. Many copies of the positive-sense RNA strand are made by repeated cycles of RNA synthesis. Some of these strands are translated to make more viral proteins. Eventually enough proteins are made to assemble new viruses. The envelope proteins aggregate in the lumen of the endoplasmic reticulum and the capsid proteins aggregate on the cytoplasmic side. A viral RNA binds to the capsid protein and is packaged into a new virus particle as it buds off into the endoplasmic reticulum. The virus is still immature. Its pre-membrane proteins cover the tips of the envelope proteins to prevent premature fusion back into the cell. The virus buds off and travels through the Golgi apparatus and continues toward the cell surface. Before reaching the surface, the pre-membrane protein is processed and a virus becomes mature. New dengue viruses are released from the cell ready to infect other cells.