In order to infect a human cell, an envelope glycoprotein found on the surface of HIV called **Gp120** must adsorbs to both a CD4⁺ molecule and then a chemokine receptor found on the surface of only certain types of human cells.

Human cells possessing CD4⁺ molecules include:

- T4-helper lymphocytes (also called T4-cells and CD4⁺ cells)
- monocytes
- macrophages
- dendritic cells

The interaction of viral envelope glycoprotein gp120 with host CD4+ and chemokine receptor molecules is electrostatic, and the interaction induces structural changes in gp120 and gp41 which initiate a fusion of the viral and cellular membranes.

This allows for a more stable two-pronged attachment, which facilitates the N-terminal fusion peptide gp41 to penetrate the cell membrane. Repeat sequences in gp41, known as HR1 and HR2, then interact, causing the collapse of the extracellular portion of gp41 into a hairpin. This loop structure brings the virus and cell membranes close together, allowing fusion of the membranes and subsequent entry of the viral capsid.

After HIV has bound to the target cell, the HIV RNA and various enzymes (including reverse transcriptase, integrase, ribonuclease, and protease) are injected into the cell. Because HIV attachment is critical for the HIV replication cycle, understanding the specific mechanisms through which HIV attachment occurs has implications for potential treatments of HIV.

Figure 13.1.1: The attachment and fusion of HIV virons to host cells are crucial to allowing HIV infection to occur. Shown in purple is gp120 and in green gp41, two proteins crucial in viral docking to host cells.
Additional Reading

1. During adsorption, an envelope glycoprotein on the surface of HIV called Gp120 must adsorbs to both a CD4\(^+\) receptor and then a chemokine receptor found on the surface of only certain types of certain human cells such as T4-lymphocytes, monocytes, macrophages, and dendritic cells.

2. Following adsorption, glycoprotein Gp41 enabling the viral envelope to fuse with the host cell membrane, allowing the nucleocapsid of the virus enters the host cell's cytoplasm.

3. During uncoating, the single-stranded RNA genomes within the capsid of the virus are released into the cytoplasm and HIV now uses the enzyme reverse transcriptase to make a single-stranded DNA copy of its single-stranded RNA genome. The reverse transcriptase then makes a complementary DNA strand to form a double-stranded viral DNA intermediate.

4. A viral enzyme called integrase then binds to the double-stranded viral DNA intermediate, transports it through the pores of the host cell's nuclear membrane, and inserts into one of the host cell's chromosomes to form a provirus.

5. Following activation of the provirus, molecules of mostly polycistronic mRNA are transcribed off of the proviral DNA strand, go through the nuclear pores into the rough endoplasmic reticulum where it is translated by host cell's ribosomes HIV structural proteins, enzymes, glycoproteins, and regulatory proteins.

6. Polyproteins translated from polycistronic mRNAs must be cleaved into function proteins by HIV protease enzymes.

7. The two HIV envelope glycoproteins Gp41 and Gp120 are transported to the plasma membrane of the host cell where Gp41 anchors the Gp120 to the membrane of the infected cell. HIV obtains its envelope from the plasma membrane by budding.

8. Most maturation occurs either during the budding of the virion from the host cell or after its release from the cell.

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