Microbiology

AIDS

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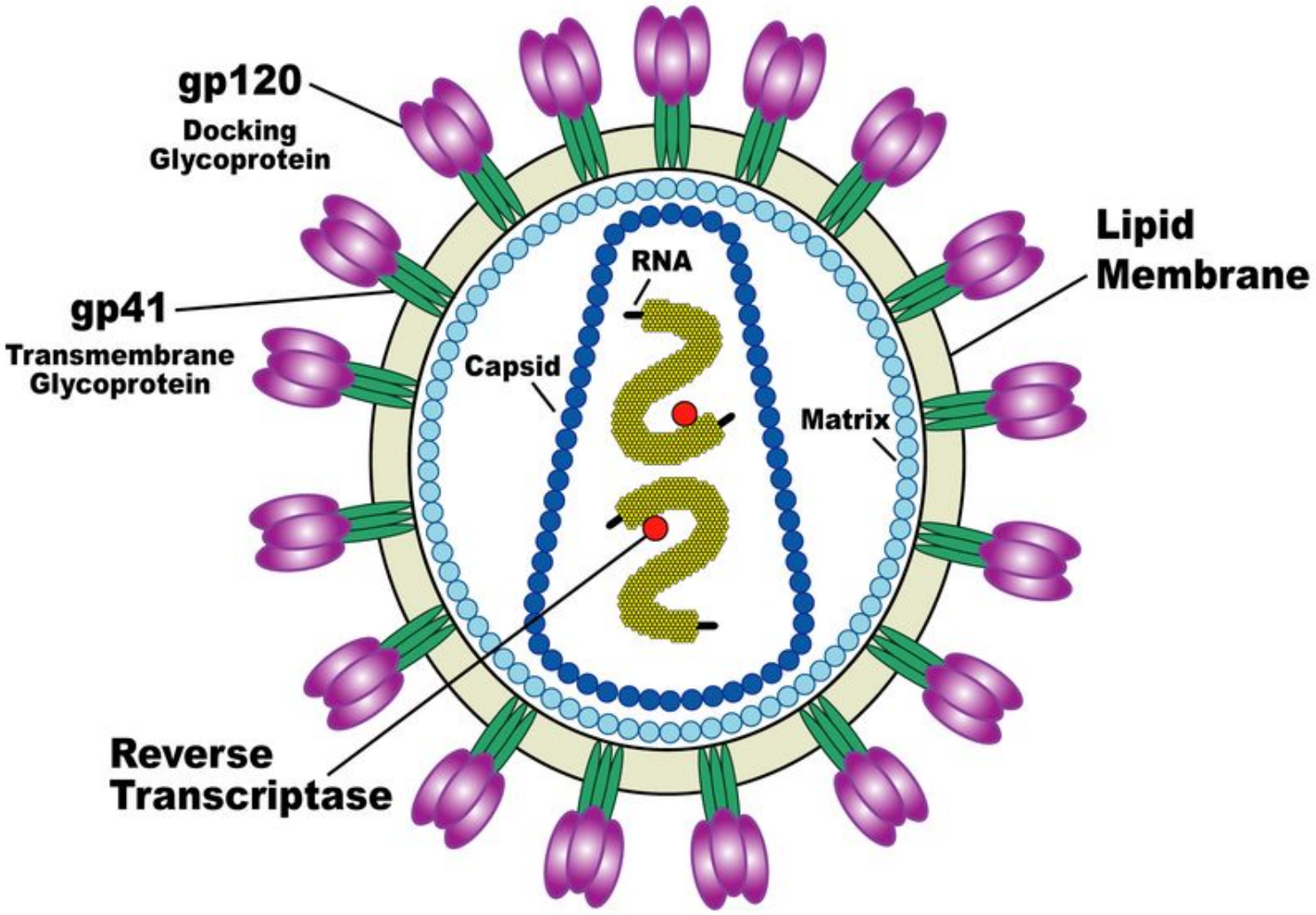
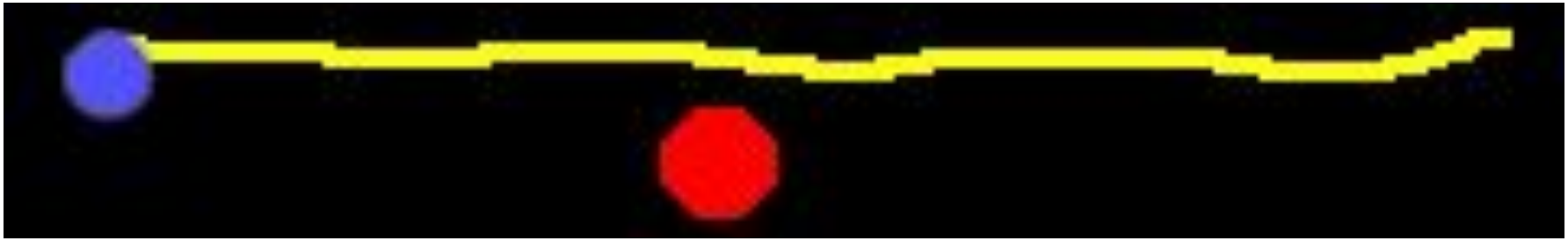

gp120
Docking
Glycoprotein
gp41
Transmembrane
Glycoprotein
Reverse
Transcriptase
RNA
Capsid
Matrix
Lipid
Membrane

On the surface membrane of all living cells are complex protein structures called "receptors". A receptor is often compared to a lock into which a specific key or "ligand" will fit. There are at least two receptors on T-lymphocytes to which the human immunodeficiency virus (HIV) sticks. The primary receptor, called "CD4"

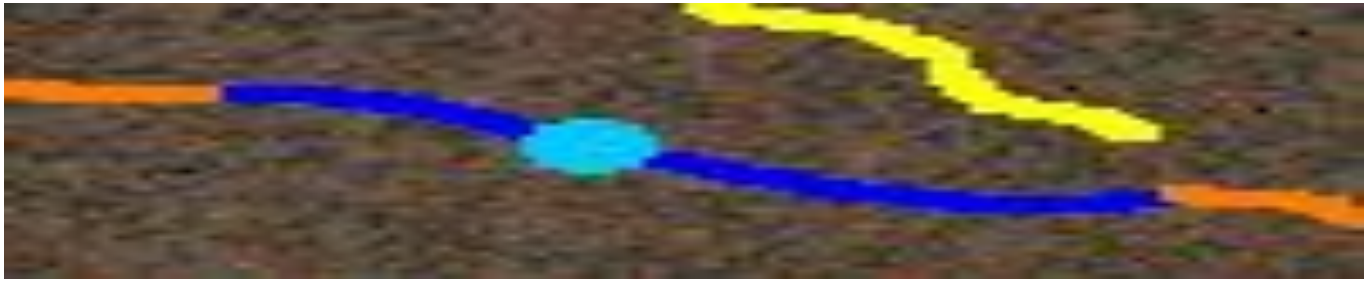
- **Tight attachment of the viral particle to receptors on the lymphocyte membrane enables fusion with the cell membrane. The viral contents, including viral RNA (shown in yellow) then empty into the cell's cytoplasm.**

- An enzyme (protein) that's part of the human immunodefficiency virus reads the sequence of viral RNA nucleic acids that have entered the host cell and transcribes the sequence into a complementary DNA sequence. That enzyme is called "reverse transcriptase" . Without reverse transcriptase, the viral genome couldn't become incorporated into the host cell, and couldn't reproduce.
- Reverse transcriptase sometimes makes mistakes reading the RNA sequence. The result is that not all viruses produced in a single infected cell are alike. Instead, they end up with a variety of subtle molecular differences in their surface coat and enzymes. Vaccines, which induce the production of antibodies that recognize and binding to very specific viral surface molecules, are an unlikely player in fighting HIV, because throughout infection, HIV surface molecules are continually changing.



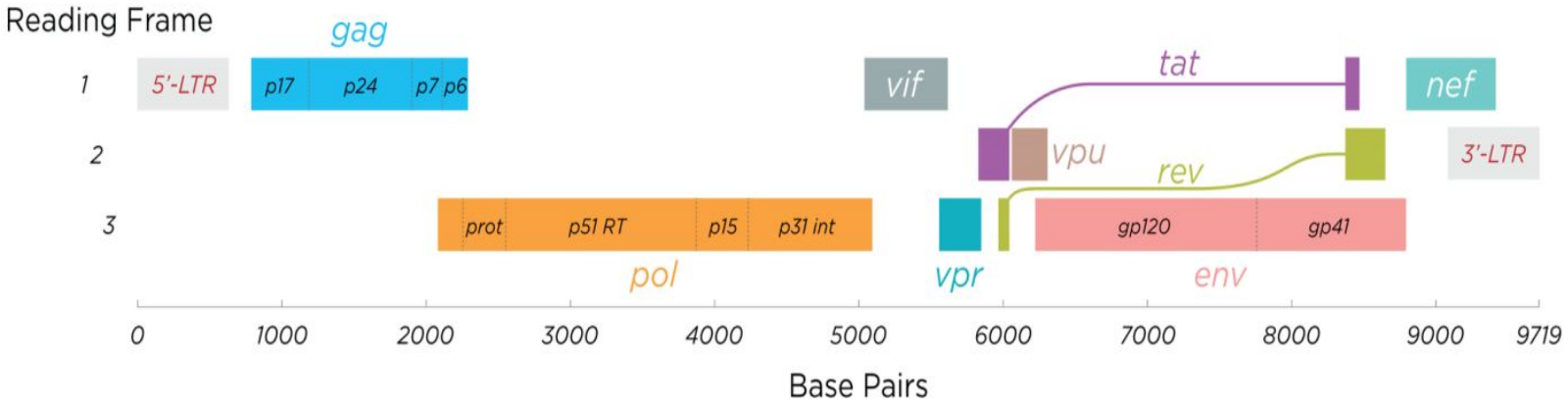
- **The first major class of drugs found useful in slowing HIV infections are collectively called "reverse transcriptase inhibitors". These include AZT, 3TC, d4T, ddc, and ddl that act by blocking the recoding of viral RNA into DNA. The chameleon-like nature of HIV, however, limits their continued effectiveness.**

- **Once the viral RNA has been reverse-transcribed into a strand of DNA, the DNA can then be integrated (inserted) into the DNA of the lymphocyte. The virus has its own enzyme called "integrase" that facilitates incorporation of the viral DNA into the host cells DNA. The integrated DNA is called a provirus.**



- As long as the lymphocyte is not activated or "turned-on", nothing happens to the viral DNA. But if the lymphocyte is activated, transcription of the viral DNA begins, resulting in the production of multiple copies of viral RNA. This RNA codes for the production of the viral proteins and enzymes (translation) and will also be packaged later as new viruses.

- **There are only 9 genes in the HIV RNA. Those genes have the code necessary to produce structural proteins such as the viral envelope and core plus enzymes like reverse transcriptase, integrase, and a crucial enzyme called a protease.**



- .gag – Viral core p17 (outer), p24 (inner), p7 & p6
- .pol – Enzyme Reverse transcriptase p64, Integrace p32, Protease p10, p15
- .env – gp 120, gp 41

- Proteins encoded by the HIV genomeClassGene namePrimary protein productsProcessed protein productsViral structural proteins***gag***Gag polyproteinMA, CA, SP1, NC, SP2, P6***pol***Pol polyproteinRT, RNase H, IN, PR***env***gp160gp120, gp41Essential regulatory elements*stat*Tat*rev*RevAccessory regulatory proteins*nef*Nef*vpr*Vpr*vif*Vif*vpu*Vpu

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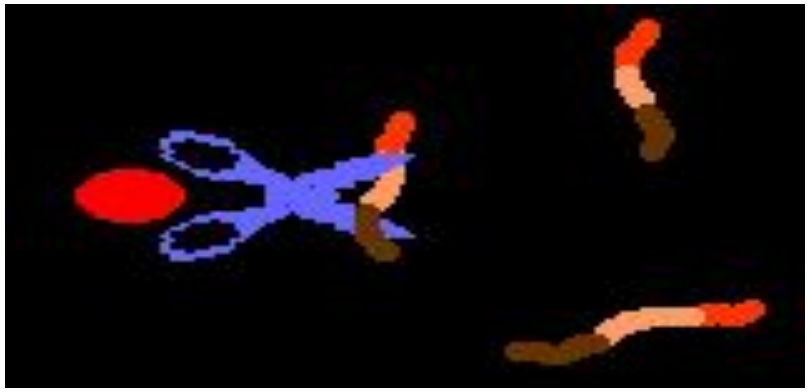
- **When viral RNA is translated into a polypeptide sequence, that sequence is assembled in a long chain that includes several individual proteins (reverse transcriptase, protease, integrase). Before these enzymes become functional, they must be cut from the longer polypeptide chain. Viral protease cuts the long chain into its individual enzyme components which then facilitate the production of new viruses.**



- **Inhibitors of this viral protease can be used to fight HIV infection. By blocking the ability of the protease to cleave the viral polypeptide into functional enzymes, protease inhibitors interfere with continued infection.**
- **Mutations enable HIV to avoid treatments that involve only one drug, so there is growing use of multiple-drug therapies in which both a protease inhibitor AND a reverse transcript inhibitor are combined.**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- **Finally, viral RNA and associated proteins are packaged and released from the lymphocyte surface, taking with them a swatch of lymphocyte membrane containing viral surface proteins. These proteins will then bind to the receptors on other immune cells facilitating continued infection.**
- **Budding viruses are often exactly like the original particle that initially infected the host. In the case of HIV, however, the resulting viruses exhibit a range of variations which makes treatment difficult.**