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Short Communication

Human Immunodeficiency Virus (HIV)

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Human immunodeficiency virus is an enveloped virus belonging to the viral family Retroviridae, genus Lentivirus. It is a highly evolved virus that has grasped the attention of many researchers with its special features - morphology, genetics and emerging nature of the virus. The special feature of retrovirus is the presence of enzyme reverse transcriptase plays a major role in the reverse transcription process. HIV enters the body, damages the immune system and will cause life threatening opportunistic infections that finally lead to AIDS (Acquired immunodeficiency syndrome).

Why is HIV known as a retrovirus?

In HIV, all the genetic information is present in the RNA. But in the biological world, the genetic information is stored in the DNA and the DNA is transcribed into RNA and the RNA is then translated into proteins (structural proteins and functional proteins). This is called as the central dogma.

But in case of HIV, genetic information is stored in RNA. HIV has an enzyme called reverse transcriptase that converts RNA into DNA. This process is called as Reverse Transcription. The concept of Reverse Transcription was given by Temin and Baltimore. Once RNA is converted into DNA, DNA is transcribed into two types of RNA, one is mRNA and the other is Genomic RNA. mRNA is later translated into viral proteins. These viral proteins combine with Genomic RNA to make new virus.

Structure of HIV

HIV is an enveloped virus because it is covered with lipid membrane. This lipid membrane is derived from the host cell. Very special proteins are present in the lipid membrane.

- Transmembrane protein – GP41 (glycoprotein)
- GP120 (glycoprotein)

This protein complex i.e., GP41 and GP120 is called GP160.

- GP41 helps in fusion of virus lipid membrane with host cell lipid membrane.
- GP120 help the virus to attach with target receptor of host cell.
    - This GP120 protein binds to CD4+ receptor of target cell. Primary attachment between the virus and target cell is the interaction between GP120 and CD4+.
- CD4+ receptors are present in many cells that are attacked by HIV (GP120 protein).
    1. Helper T cells
    2. Monocytes
    3. Macrophages
    4. Microglial cells
    5. Langerhans dendritic cells
    6. Follicular dendritic cells
- HIV virus binds to all these 6 types of cells because these cells have CD4+ receptor. Viral GP120 proteins when bind to the CD4+ receptor of host cell, it undergoes a conformational change and expresses its two domains.
    1. First domain interacts with the CCR5 or CD195 receptor (co-receptor for chemokines). This CCR5 or CD195 is present on macrophages.
    2. Second domain interacts with CXCR4 or CD184 (another kind of chemokine receptor) receptor of Helper T cells. Helper T cells do not have CCR5 receptors.

The attachment of first and second domain of GP120 with CCR5 and CXCR4 receptor of host cell is called secondary attachment.

After the primary and secondary attachment of GP120 with target host cell's receptors, GP41 protein slip on the side and hangs on the membrane of target host cell and start pulling the membrane of

target host cell towards viral membrane and also start pulling the viral membrane towards the target cells. When the lipid membrane of the virus comes in contact with the lipid membrane of the target host cell, then both virus and host cell become fused, so GP41 act as a fusion protein.

Both these GP41 and GP120 protein are called envelop proteins. These envelop proteins are encoded by genes Env.

- Inside the envelop, Matrix proteins (P-17) are present that stabilise GP41.
- Inside the matrix, capsid is present. This capsid has 20 sides and because of this, it is called as icosahedral. This capsid is also made up of proteins called P 24 (nucleocapsid protein). This P24 protein is very important in diagnosis of HIV because it act as a serological marker. If our immune system makes antibody against P24, then by using ELISA method and western blotting, anti P24 antibody is observed in the blood of the patient and the presence of P24 antibody shows that HIV is present.
- Inside the capsid, two identical copies of RNA (not complementary to each other) are present. Both RNA have positive polarity, so that RNA is same as that of mRNA of host.

This RNA does not directly translate into protein, first it is converted into viral DNA by RNA dependent DNA polymerase (Reverse transcriptase). After that viral DNA is integrated into host DNA by Integrase enzyme. After this, the virus makes larger proteins that are cut into smaller proteins by Protease enzyme.

P7 protein is also a nucleocapsid protein like P24.

- Gag gene is responsible for the production of nucleocapsid protein (P7 and P24)
- Pol gene is responsible for the production of enzyme (Reverse transcriptase, Integrase, Protease).

Replication cycle of HIV

After fusion, core protein enters into the host cell. When core proteins of virus enters into the cell cytoplasm, the protease present in the host cell attack capsid protein P24. As a result, viral RNA becomes free and Reverse Transcriptase becomes active and converts RNA into DNA. This DNA is then transferred from cytoplasm to Nucleus. The Integrase enzyme becomes active now. This Integrase enzyme makes cut in the host's DNA and at the end of host DNA fit the viral DNA. Now viral DNA is a part of the host DNA and it is called Proviral DNA. Proviral DNA has sticky ends that bind to host DNA. These sticky ends are called as LTR's (long terminal repeats).

Proviral DNA has promoter region that promote transcription and transcribe DNA to RNA. Further, RNA is translated into long viral proteins (polypeptide).The protease enzyme of HIV cleaves the long polypeptide chain into small peptides. These small viral proteins combine with Genomic viral RNA from a complete virus.

Mode of transmission of Virus

HIV is spread directly from host to host through three sources

- Blood
- Semen
- Vaginal fluid

The modes of transmission are primarily three fold

1. Sexual intercourse
2. Sharing needles
3. Mothers exposing their foetus or infant via childbirth or breast feeding.

Another mode of transmission is due to blood transfusion.

HIV is a delicate virus that cannot be spread through daily interaction with infected individuals such as handshakes or hugs.

Reservoir

Humans are the reservoir for virus.

Key tests for salient features

ELISA and Western Blotting.

Symptoms of disease

When first infected by HIV many individuals are asymptomatic for a period of time. During this time the virus replicates within one's body. A month or two after initial exposure, individuals may develop flu like symptoms. Some other symptoms are diahorrea, enlarged liver or spleen, fever, swollen lymph nodes, headache , muscle pain , nausea, vomiting, skin rash or Candida albicans infection inside the mouth called thrush. These are the early symptoms of HIV indicating immune failure.

Historical information

West African Chimpanzees was the beginning source of HIV in humans. The virus likely entered humans through the butchering of these chimpanzees. This contact with chimpanzee blood combined with small cut on a human began the history of HIV in humans. The virus then began to spread throughout Africa.

Control/treatment

Various drug treatments are available for HIV/AIDS, however there is no cure. Currently over 20 antiretroviral drugs are used

to treat HIV/AIDS. These drugs aim at reducing the amount of HIV viral load in your body while strengthening the immune system.

1. Nucleoside Reverse Transcriptase Inhibitors: - Aim at disrupting the replication of HIV. eg. Zidovudine (AZT), Didanosine, Lamivudine.
2. Non-Nucleoside Reverse Transcriptase inhibitors: - These inhibitors also inhibit the function of Reverse Transcriptase. eg. Nevirapine.
3. Attachment inhibitor: - Blocks at the attachment between GP120 and CCR5/CD4+ receptors of host cell. eg. Maraviroc: - blocks the attachment between GP120 and CCR5 receptor of macrophages. This drug is CCR5 (CD195) antagonist.
4. Fusion inhibitor: - prevents the fusion of HIV inside the cell, thus preventing replication. eg. Enfuvirtide.
5. Protease inhibitor: - Interrupt viral replication later in life cycle. eg. Indinavir (IDV)
6. Integrase inhibitor: - Inhibits integrase enzyme. eg. Raltigravir.

HAART

Highly Active Antiretroviral Therapy: - Began in 1996 and includes a protease inhibitor and several antiretroviral medications.

Prevention/Vaccine

1. Intravenous drug users should use clean needles and should not share needles.
2. Expecting mothers should be tested for HIV. If positive, these mothers can be prescribed antiretroviral drugs. These drugs reduce the risk of infecting the foetus with HIV.
3. HIV positive mother should not practice breastfeeding with their new born baby. Breastfeeding increases the chance of infecting their new born with HIV.
4. Avoid unprotected sex.

Currently there is no vaccine available for HIV because there is genetic variation in GP120 protein. A hypervariable region is present in GP120 protein that is highly mutant.

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