Chapter: Retrovirus

Retroviridae include 3 subfamilies:

- Oncovirinae: HTLV (Human Tcell Lymphotropic Virus)
- Lentivirinae: HIV (Human Immunodeficiency Virus)

Spumavirinae:

Human immunodeficiency virus (HIV)

Pathogen of **AIDS**

- (Acquired Immunodeficiency Syndrome).
- HIV-1 is found worldwide, HIV-2 is found primarily in West Africa.





1.Biological properties

Spherical, enveloped, spikes.
 Structure:
 Core: 2 copies of +ssRNA (dimmer);
 reverse transcriptase;
 Capsid protein: P24
 Matrix protein: P 17.



Envelope:

 gp41:mediates fusion of the viral envelope with t cell membrane, and the virion enters the cell.

• gp120:

- *be associated with adsorption (binding site for CD4 molecule of T cells).
- *be able to stimulate the production of neutralizing antibodies.
- *easy variation.





3.Genes: *Structural genes: gag: coding for capsid proteins (p17, p24, p7) **pol:** coding for protease, reverse transcriptase etc. env: coding for gp120, gp41.

*Regulatory genes:

tat: regulating the synthesis of viral proteins (+).

rev: regulating the synthesis of viral proteins (+).

nef: regulating the synthesis of viral proteins (-).

*LTR: contain promotor and enhancer sequences.

4.Resistance: 56°C inactivated.
5.Replication:

adsorption :
gp120 bind for CD4 molecule of T4 cells
the necessary co-receptors for HIV-1 entry:
CXCR4 (fusin) for T-cell line (T)-tropic strains
CCR5 for macrophage (M)-tropic strains.

Penetration:membrane fusionUncoating:Biosythesis:

- RNA----cDNA---- RNA:DNA hybrid molecule ----dsDNA(provirus) integrated into host DNA---- stay latent ----- enter a productive cycle
- assembly and release: budding





II.Pathogenesis & immunity

1.Infectious source: patients (symptomatic), infectious people(anti-HIV(+), asymptomatic).

- **2.Transmission pathway:**
 - 1) By blood or blood products;
 - 2) By Sexual contact;
 - **3) Vertical transmission:**

from mother to child.

3.Pathogenesis:

* gp120 of HIV select CD4 molecule of T4 cells ----viruses multiply in T4 cells---cell-mediated immunodeficiency---opportunistic infections and tumors occur---death **Destruction of T4 cells is achieved by:**

- ① Viral replication
- ②Syncytium formation via membrane gp120 binding to cell CD4 antigen
- ③Cytotoxic T cell lysis of infected cells
- **(a)**Cytotoxic T cell lysis of T4 cells carrying gp120 released from infected cells
- ⑤ Natural killer cells
- 6 Antibody-dependent cell cytotoxicity.
- ⑦Induce appoptosis.

4.Clinical features

Exposure---Seroconversion---Asymptomatic---PGL(persistent generalized lymphadenopathy,) or ARC(AIDS-related complex) ---AIDS

a.Opportunistic Infections: Protozoal, Fungal, Bacterial, Viral

b. Opportunistic Tumours
 Kaposi's sarcoma, is observed in 20% of patients with AIDS.

III. Diagnosis

1. The detection of the antibody to HIV

The presumptive diagnosis of HIV infection is made by the detection of antibodies by ELISA. The definitive diagnosis is made by western blot.

- 2. The detection of viral components or detection of viral RNA
- **3. Isolation of the virus in culture**

IV.Control

1.Vaccines: Several vaccines are under trial.

2. Treatment

- (1.) Nucleoside analogues reverse transcriptase inhibitors. AZT, DDC, DDI and lamuvidine.
- (2.) Non-nucleoside analogue reverse transcriptase inhibitors e.g. Nevirapine(抑制 DNA合成)
- (3.) HIV Protease inhibitors e.g. Ritonavir, Indivavir. They are the most potent inhibitors of HIV replication to date.