

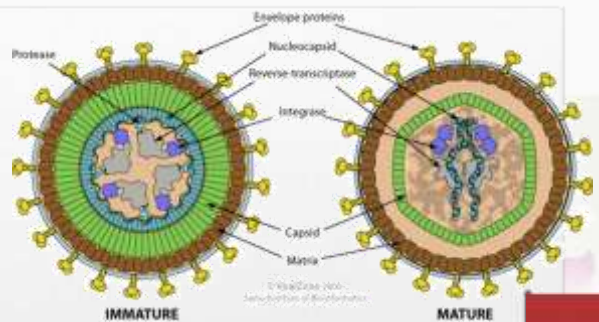
# HTLV Virology

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## HTLV

### ❖ Virology:

- Human T-cell lymphotropic virus (HTLV)
- Virus classification:
  - ✓ Family: **Retroviridae**
  - ✓ Subfamily: **Orthoretrovirinae**
  - ✓ Genus: **Deltaretrovirus**
- Four types of HTLVs :
  - 1) HTLV1
  - 2) HTLV2
  - 3) HTLV3
  - 4) HTLV4



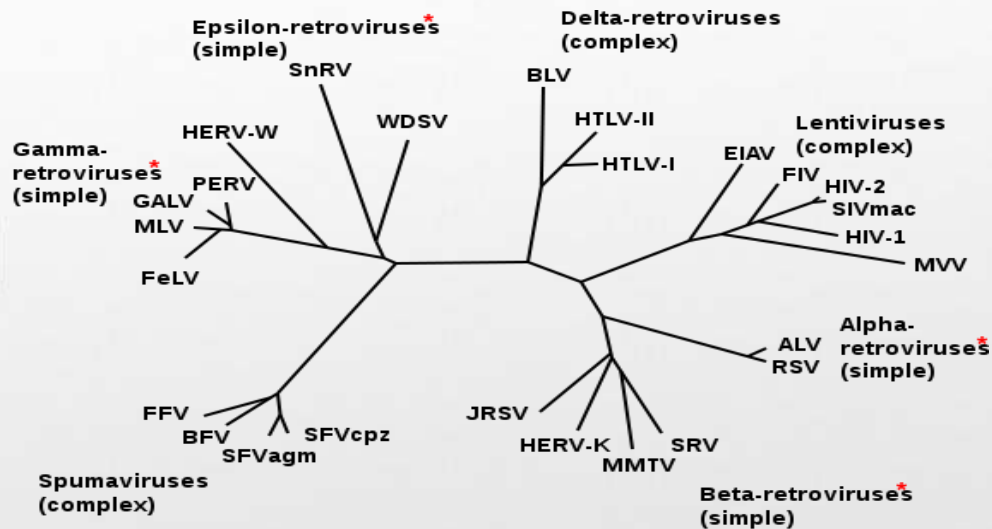
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### ❖ Seven HTLV-1 genotypes are recognized **HTLV-1a** through **HTLV-1g**.

- ✓ HTLV-1 has six reported subtypes (subtypes A to F)
- ✓ The most widespread genotype and subtypes are type: **HTLV-1a** and **A**
- ✓ In Iran : Genotype **HTLV-1a** and subtypes **A** predominates.



## Classification :



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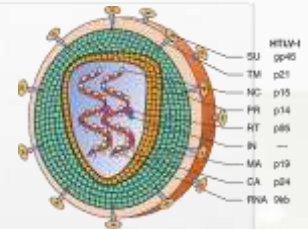
## Structure:

- The virion is **spherical in shape** with a diameter of about 100 nm.
  - ✓ **C-type morphology**: assemble at the plasma membrane, and contain a central, symmetrically placed, spherical inner core

- With **lipid Envelop**

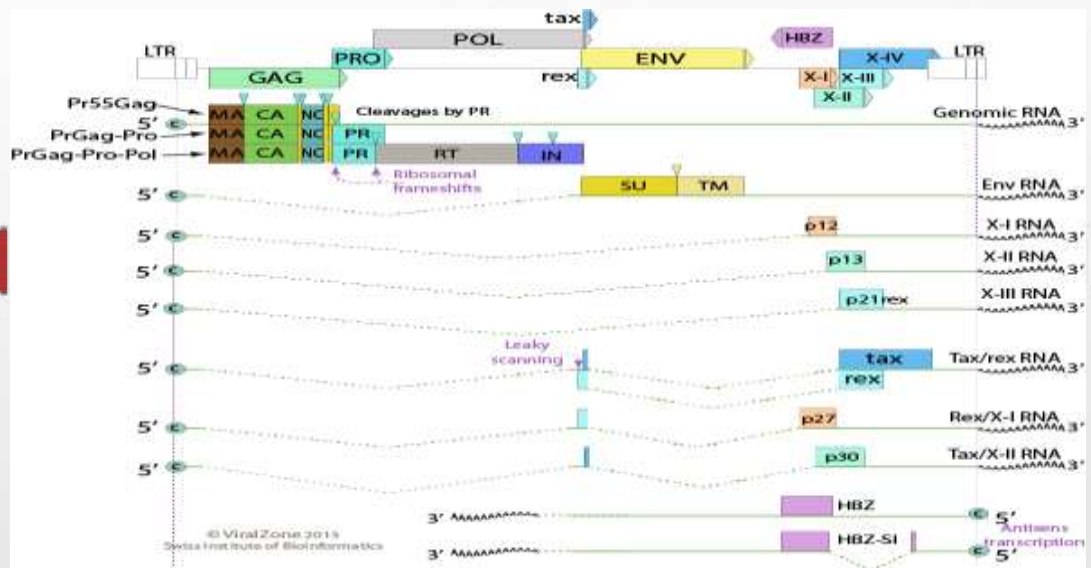
### Genome :

- ✓ Two identical copies of a plus single-stranded RNA genome ← **Diploid**
- ✓ The length of the HTLV-I genome is 9 kilobases (9kbp).
- ✓ The 5' and 3' end includes **LTR regions**, which are **U3, R and U5**.
- ✓ The **PPT** is a **primer for plus-strand DNA synthesis** during reverse transcription.
- ✓ **U3** is a sequence which serves as a **signal that the provirus** can use in **transcription**.



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## GENOME :



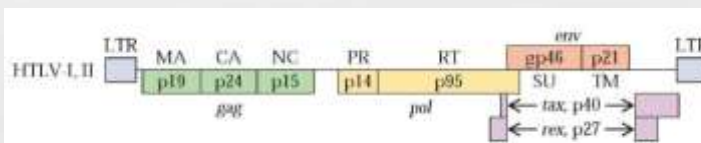
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## Structure:

### □ Proteins:

- Consisting of **gag** proteins, **protease (PR)** protein, **pol** proteins, and **env** proteins.
- Viral glycoproteins: **SU or gp46** : Viral receptor & **TM or gp21**: Fusion
  - ✓ Glycoprotein encoded by the **env** gene
- **Gag**: Capsid, Matrix, Nucleocapsid.
- **Pol**: protease (PR) , Reverse transcriptase and Integrase.
- In addition, the genomes contain regulatory genes termed **rex** and **tax** that are expressed from an alternatively spliced mRNA and **HBZ** protein.

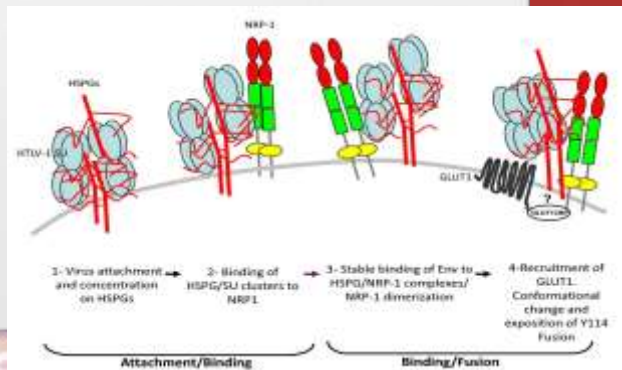


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## Tropism:

- HTLV-1 predominately infects **TCD4+ cells**
  - ✓ Other cell types: including TCD8+ cells, dendritic cells and B cells
  - ✓ Receptors for HTLV-1 : GLUT1 glucose transporter and heparan sulfate proteoglycans (HSPGs)
  - ✓ lipid rafts in cell membrane TCD4+ ➔ **Has an effective role in entering**



## Replication cycle :

### ❖ Cycle stages:

#### 1) Attachment:

- ✓ Virus attaches to GLUT1 receptors through the SU(gp46) glycoprotein.
- ✓ TM (gp21) glycoprotein mediates Fusion with cell membrane.

#### 2) Penetration:

- ✓ Membrane fusion and endocytosis

#### 3) Uncoating:

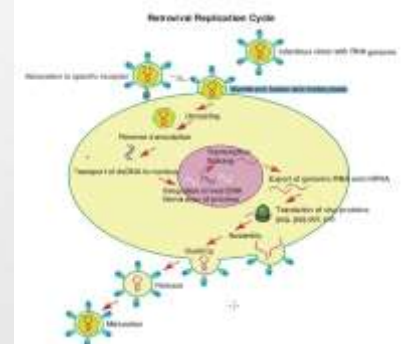
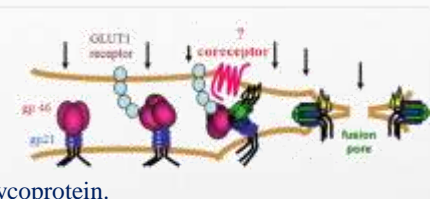
- ✓ Protease-Dependent Uncoating of a Complex Retrovirus

#### 4) Reverse transcriptase:

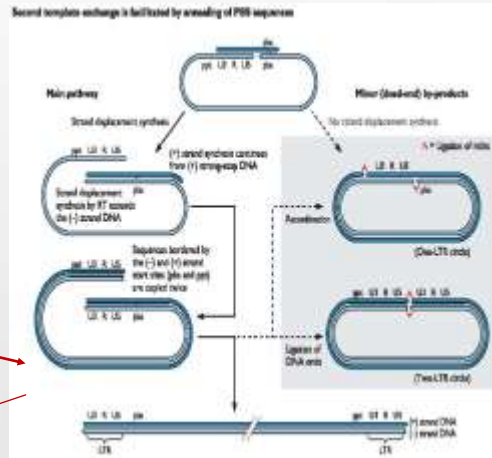
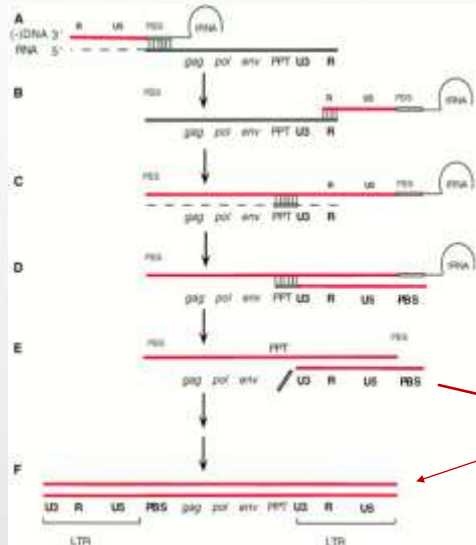
- ✓ Positive-sense RNA genome that is reverse transcribed into DNA

#### 5) Integration of proviral DNA:

- ✓ The viral dsDNA, randomly integrated into the cell's genome by the Integrase



# Reverse transcriptase



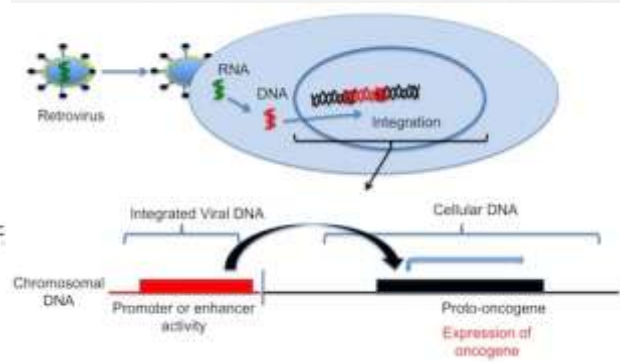
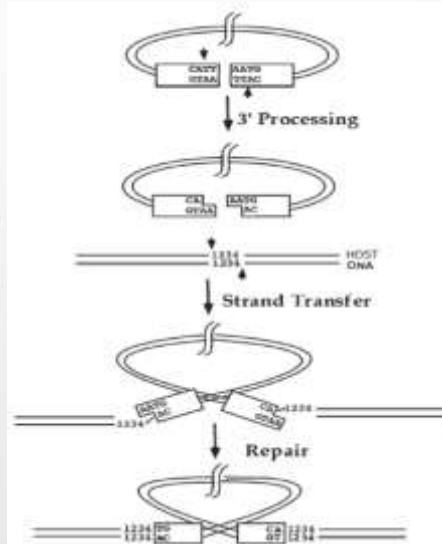
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# Integration



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## Replication cycle :

### 6) Expression of viral RNAs:

- ✓ The U3 region of the LTR contains a promoter recognized by the RNA polymerase II system.
- ✓ The efficiency of initiation of transcription at the 5' LTR is the major determinant of the levels of viral RNA formed in the cell

### 7) Morphogenesis & Release

- ✓ As the Gag, Gag-Pro-Pol, and Env proteins are synthesized, they come together to form progeny virions.
- ✓ The assembly of the retrovirus particle is driven primarily by the Gag precursor protein.
- ✓ The RNA genome is incorporated into virions by virtue of interactions between specific RNA sequences near the 5' end of the genome.

### 8) Maturation:

- ✓ The cleavage of Gag and Gag-Pro-Pol is mediated by the viral protease PR .
- ✓ protease PR is responsible for virion maturation.



## Disinfection & Inactivation:

### ➤ HTLV-1 is completely inactivated:

- ❖ 10 minutes at room temperature with...
  - ✓ 10% household bleach
  - ✓ 50% ethanol
  - ✓ 35% isopropanol
  - ✓ 0.3% hydrogen peroxide
  - ✓ 0.5% paraformaldehyde
- ❖ HTLV-1 is readily inactivated in liquids or 10% serum by heating at 56°C for 10 minutes.
- ❖ Lyophilized blood products would need to be heated at 68°C for 72 hours to ensure inactivation of contaminating virus.





## Epidemiology:

- HTLV-1 was discovered by Robert Gallo and colleagues in 1980.
- So far: **Seven HTLV-1 genotypes** are recognized HTLV-1(A- G).
  - ✓ The most widespread genotype is type A.
  - ✓ Type C is only present in Asia.
- It is estimated that from 15 to 20 million people worldwide are infected.
  - ✓ The highest prevalence for any country has been detected in Japan (more than 10%).
- ❖ **In Iran :**
  - ✓ Prevalence is 0.1–1%, in neyshabour (3.5- 4.3%), Mashhad (2.1%) and Sabzevar (%1.6)
  - ✓ Genotype A predominates.

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