HTLV-1 Infection Detection

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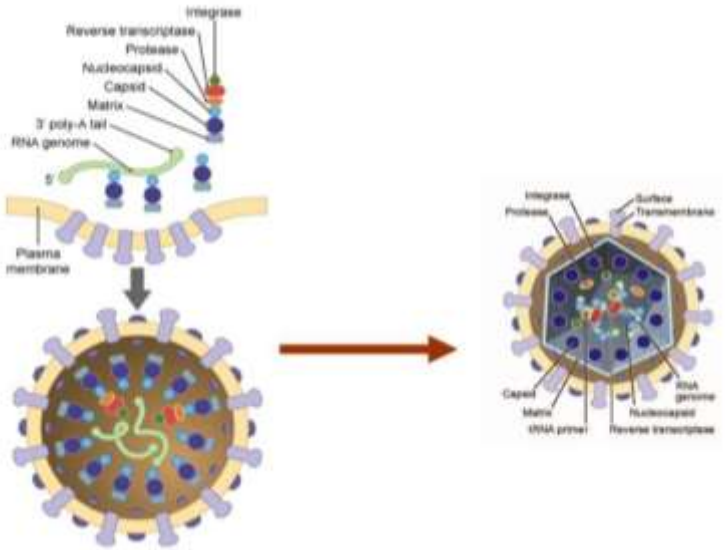
Genetic structure of HTLV-1

- **HTLV-I is classified as a complex retrovirus, in the genus Deltaretrovirus of the subfamily Orthoretrovirinae**

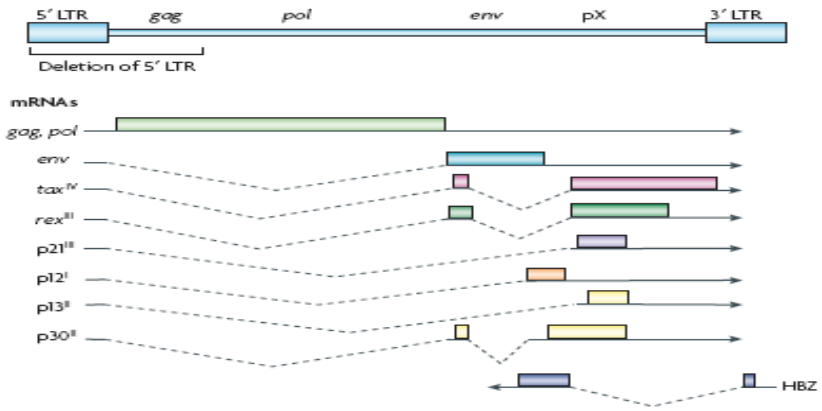
- **The diploid plus-strand RNA genous is 9032bp.**

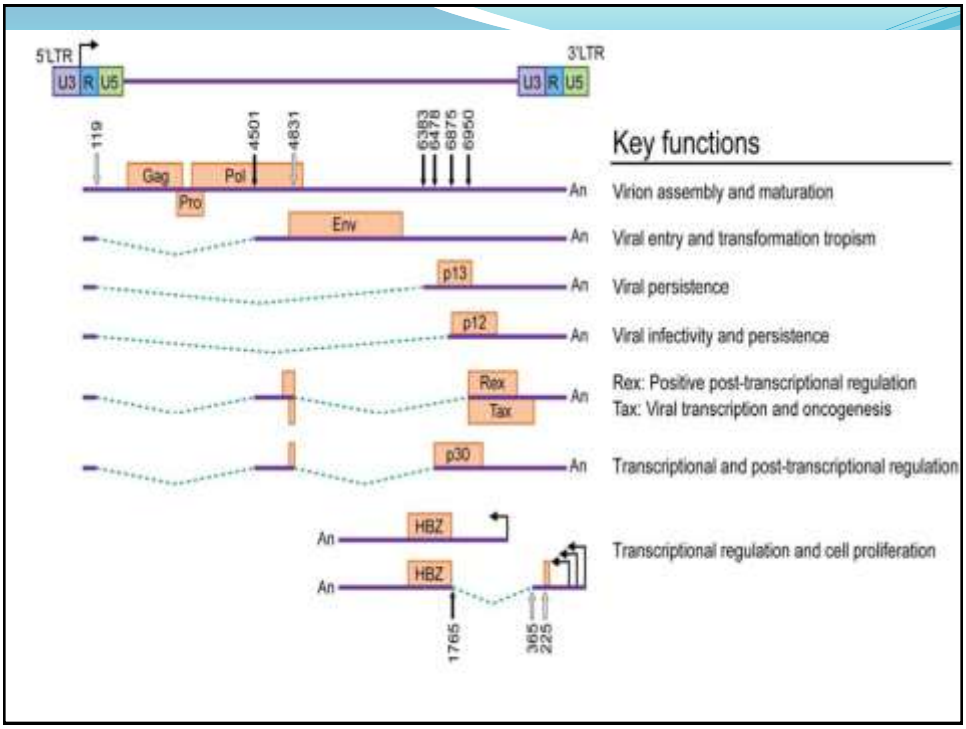
- **In addition to the gag, pol and env genes found in a typical exogenous retrovirus, HTLV-I encodes a number of small regulatory proteins, including Tax and Rex.**

HTLV-I assembly and incorporation of viral components (left) and fully developed mature virion (right)



Genomic structure of HTLV-I and its products





Gag

- **This region encodes the virion core proteins (gag) which are initially synthesized as precursor.**
- **The precursor of gag products is a protein with an approximately molecular size of 53 KDa (pr53).**
- **During viral maturation this precursor is cleaved to form the mature matrix p19 (MA), the capsid p24 (CA), and the nucleocapsid p15 (NC).**

Env

- **The role of the *env* protein is to mediate association of the virion with the host cell and entry into it.**

- **It is synthesized as a precursor of 62 kDa, which is cleaved into a gp45 surface protein (SU) and a gp20 transmembrane protein.**

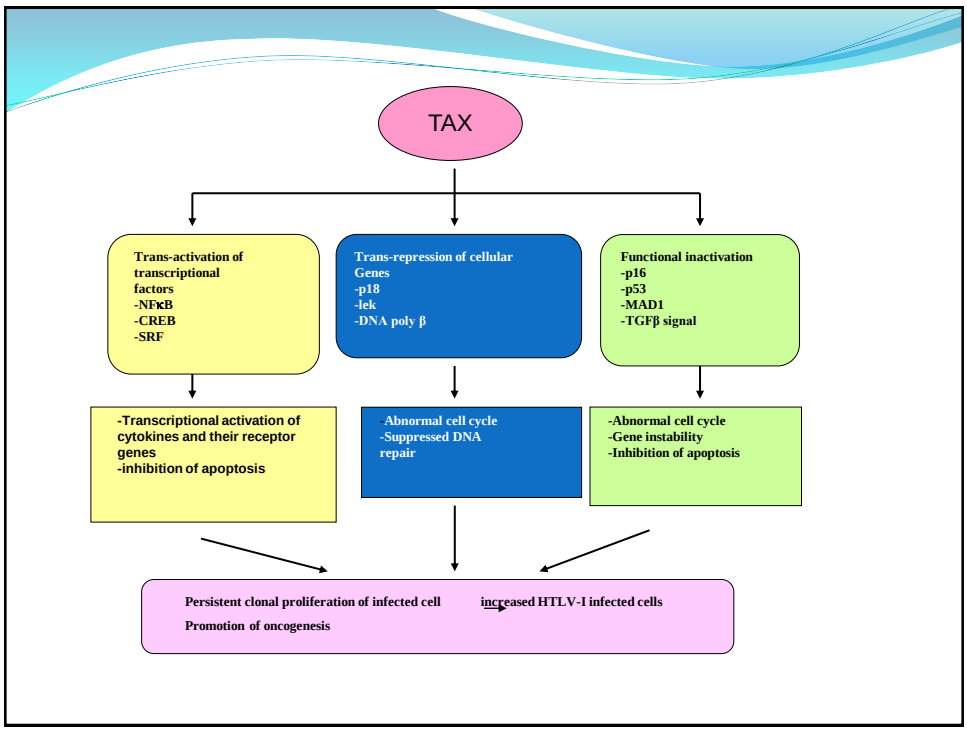
Pol

- **The pol gene encodes several enzymatic activities, which include the reverse transcriptase (RT), integrase and RNase H.**

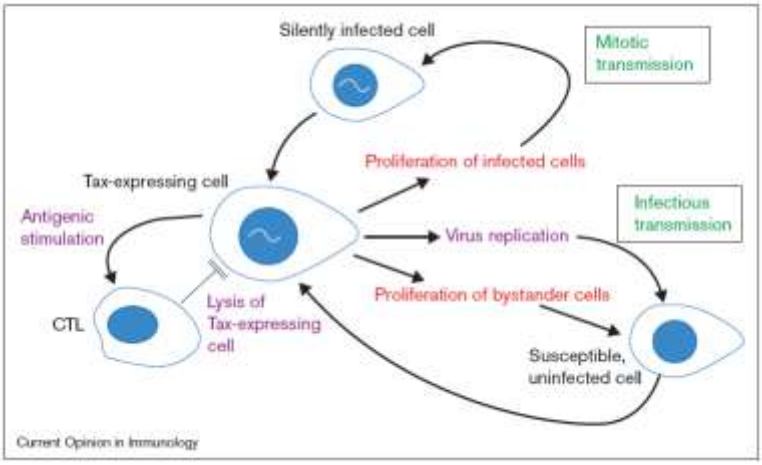
- **The RT is necessary for synthesis of viral DNA and RNase H is responsible for degradation of RNA template and primer tRNA. The integrase provides enzymatic activities necessary for integration of the viral DNA into the cellular DNA target.**

Tax and Rex

- Tax activates transcription of the HTLV-I provirus
- Rex regulates the intracellular transport of unsplised and singly spliced HTLV-I mRNA



Spread of HTLV-I



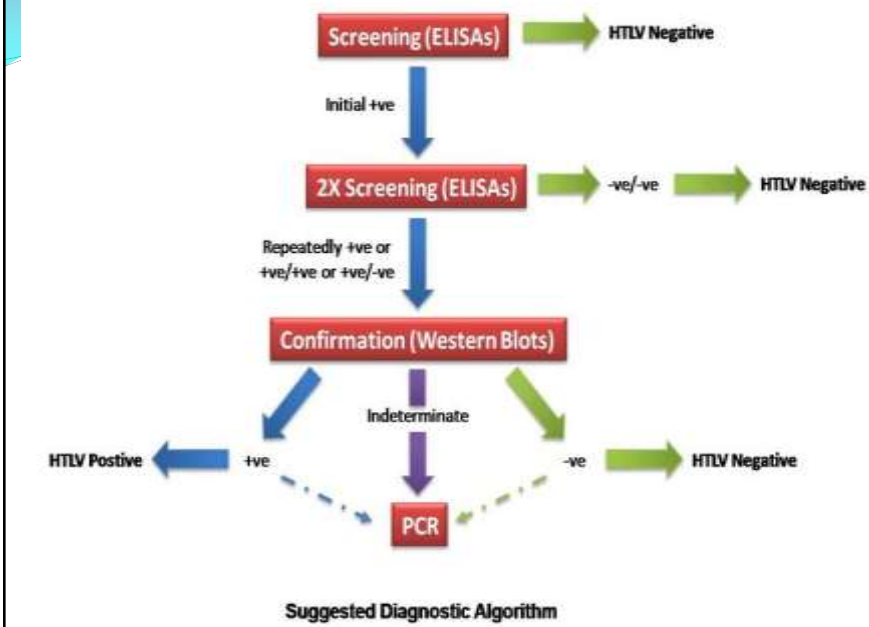
HTLV-1 diagnosis

- **The diagnosis of HTLV-I infection is based on the detection specific antibodies by screening tests such as enzyme linked immunosorbent assay (ELISA) or particle agglutination.**

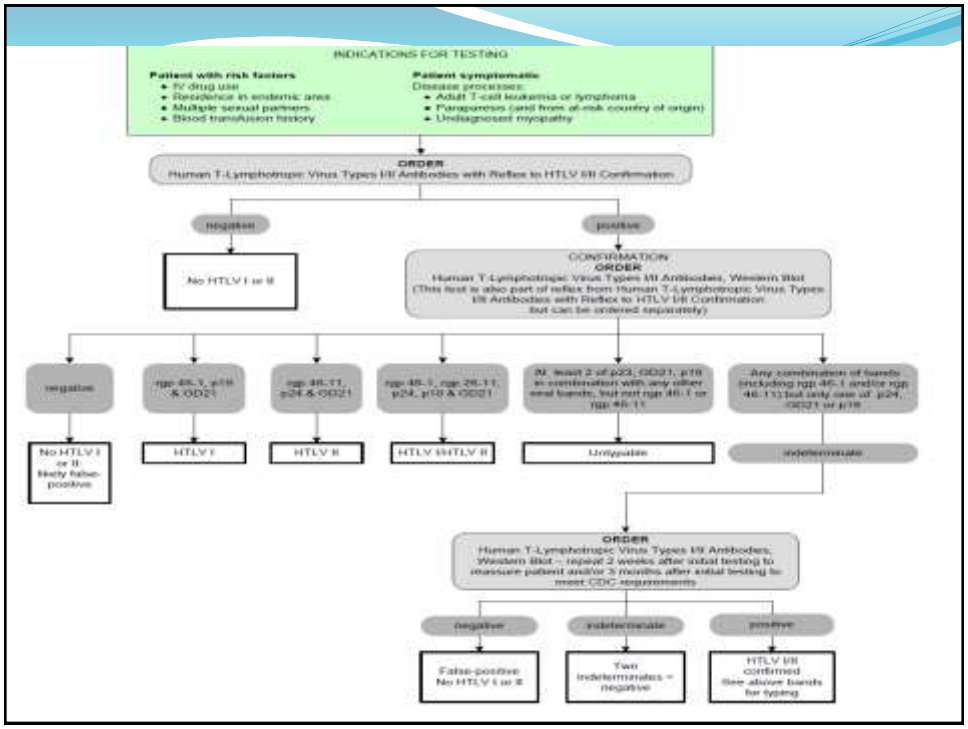
- **The positive results should be confirmed by Western blot (WB) or polymerase chain reaction (PCR).**

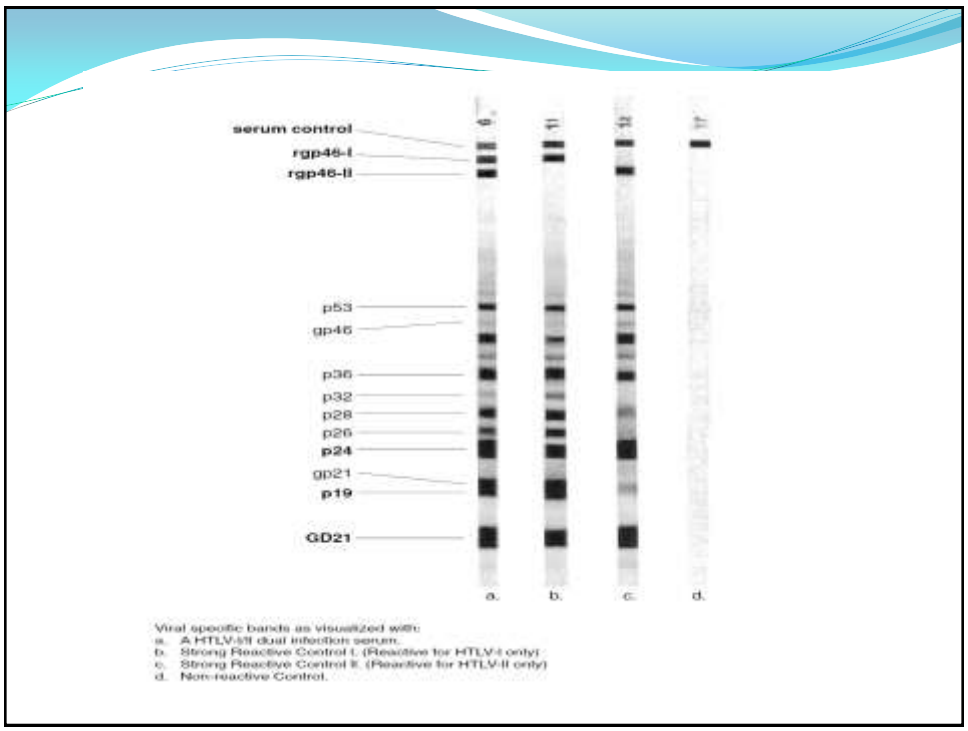
- **In Western blot, the reactivity of the test is examined against the products of HTLV-I such as gag (p19 or p24) and env (gp21 or gp46) gene products**

- **After infection with HTLV-I, antibodies to core, envelope and tax protein in serum appeared**
- **Within 30 to 60 days after primary HTLV-I infection, antibody to gag proteins predominant with anti-p24 generally appearing before anti-p19 antibodies**
- **Antibody to p-21 envelope protein frequently appears before gp46 antibodies**
- **Anti tax antibodies are the latest antibodies to appear in the time course of seroconversion**



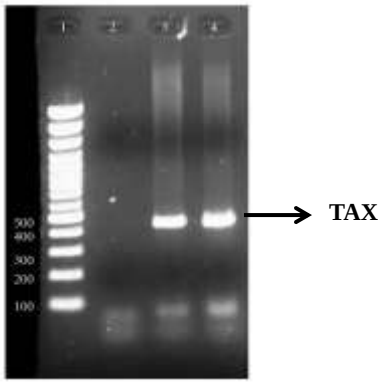
Suggested Diagnostic Algorithm





Viral specific bands as visualized with:
a. A HTLV-I/II dual infection serum.
b. Strong Reactive Control I. (Reactive for HTLV-I only)
c. Strong Reactive Control II. (Reactive for HTLV-II only)
d. Non-reactive Control.

HTLV-1 PCR



Infectivity of HTLV-I

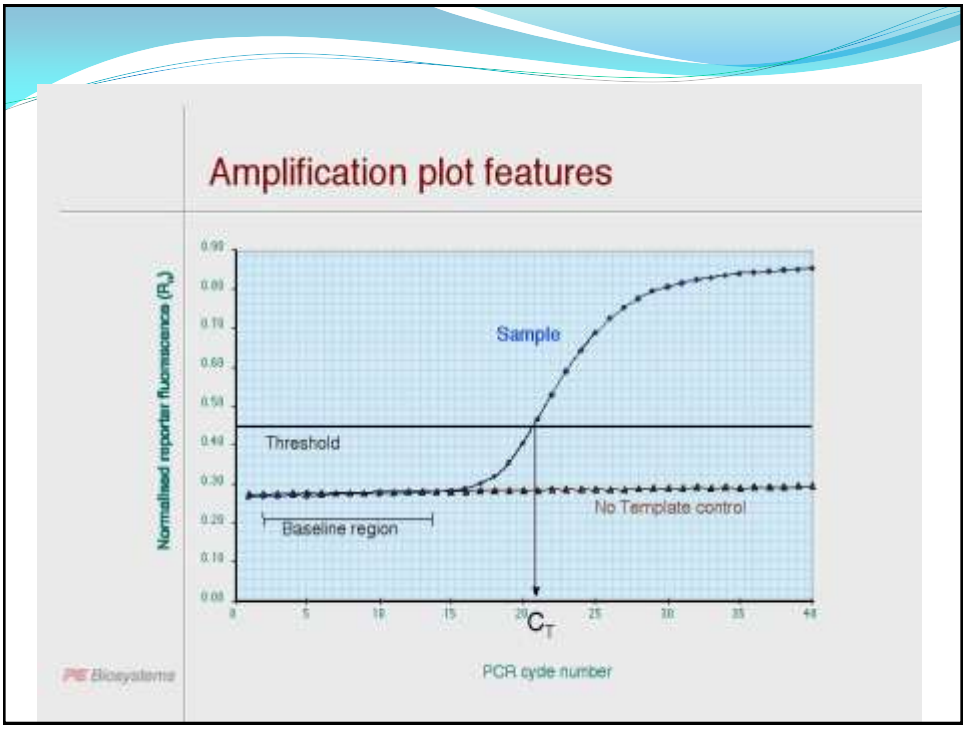
- CD4+D45RO+ T cells
- CD8+ T cells
- DC cells
- Monocytes
- Macrophages
- B cells
- NK cells
- Glial cells
- Endothelial cells

Proviral load

- **The provirus load of HTLV-I usually reaches a stable equilibrium "set point" that fluctuates in most cases by no more than 2- to 4-fold over a period of years**

- **High proviral load in Japanese population (median 5% PBMCs in HAM/TSP and 0.3% in carriers**

- **In contrast with HIV sequence variation is very limited in HTLV-I.**



Differences between carriers and HAM/TSP

- High proviral load in HAM/TSP patients (about 10% of PBMC) compare to carriers (0.1-1% of PBMC)
- High titer to HTLV in HAM/TSP
- Spontaneous lymphoproliferation
- High frequency of HLA class I restricted CTL (Tax 11-19)

The effects of Proviral load on disease progression