



HIV: The little virus that could!

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[Workshop outline]

- Brief History
- Epidemiology
- Mode of transmission
- Etiology and molecular structure
- Current therapies
- Research on transmission

History of the HIV Pandemic

1959



Earliest recorded case of HIV was in 1959
from a blood sample from a man in
Kinshasa, DRC

History of the HIV Pandemic

1959 1981



Outbreaks of a rare conditions:

In New York and San Fransisco
pneumocystis carinii pneumonia
and increased cases of Karposi
Sarcoma in homosexual men

History of the HIV Pandemic

AIDS defined



1959 1981 1982

History of the HIV Pandemic

1959 1981 1982 1983/ 1984



French and US group identify virus

History of the HIV Pandemic

1959 1981 1982 1983 1984

↓

Gaëtan Dugas (French Canadian flight attendant) died. Termed patient zero by the CDC since he was directly or indirectly linked with 40 of the first 248 reported cases of AIDS in the U.S

History of the HIV Pandemic

First therapy approved for HIV/AIDS
Azidothymidine AZT



1959 1981 1982 1983/ 1984 1985 1987



AIDS memorial quilt displayed at the
National Mall in Washington



History of the HIV Pandemic

Red Ribbon becomes international symbol of HIV/AIDS



1959 1981 1982 1983/ 1984 1985 1987 1988 1991

Freddie Mercury from Queen dies of AIDS



Magic Johnson announces he is HIV+



History of the HIV Pandemic

1959 1981 1982 1983/ 1984 1985 1987 1988 1991 1996



Introduction of Highly Active Antiretroviral Therapy (HAART): Triple therapy

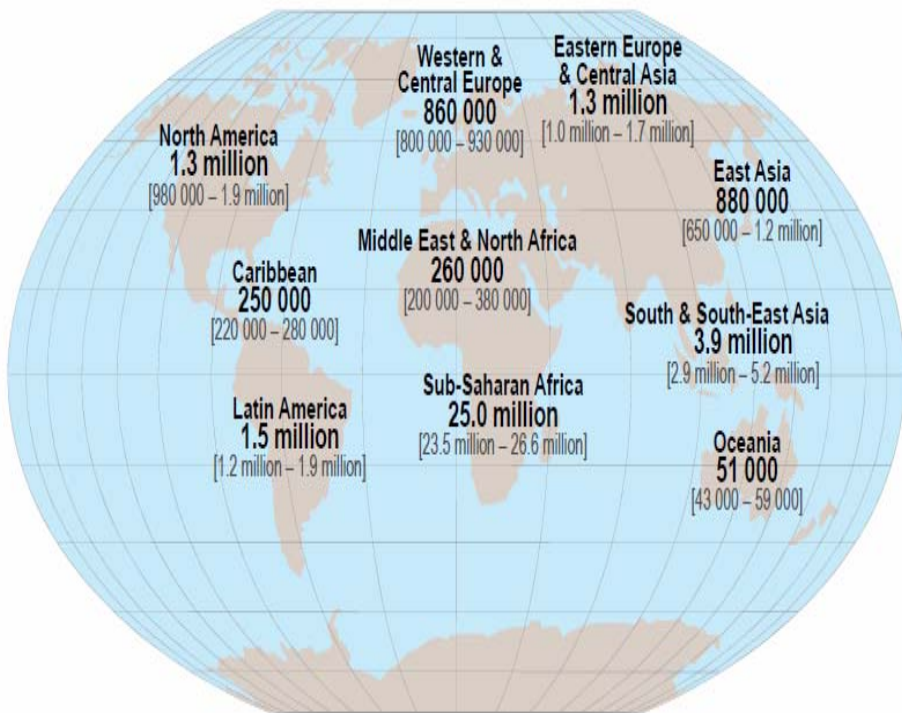
History of the HIV Pandemic

1959 1981 1982 1983/ 1984 1985 1987 1988 1991 1996 2008

↓
Dr Montagnier and Dr Barre-Sinoussi are awarded the Nobel prize in Medicine for the discovery of HIV

Epidemiology of HIV in 2012

Adults and children estimated to be living with HIV



Total: 35.3 million [32.2 million – 38.8 million]

Number of people living with HIV

Total: 35.3 million (32.2-38.8)

Adults: 32.1 million (29.1-35.3)

Women: 17.7 million (16.4-19.3)

Children < 15 : 3.3 million (3.0-3.7)

People Newly infected with HIV in 2009

Total: 2.3 million (1.9-2.7)

Adults: 2.0 million (1.7-2.4)

Children < 15: 260 000 (230 000-320 000)

AIDS deaths in 2010

Total: 1.6 million (1.4-1.9)

Adults: 1.4 million (1.2-1.7)

Children : 210 000 (190 000- 250 000)

[HIV in Canada]

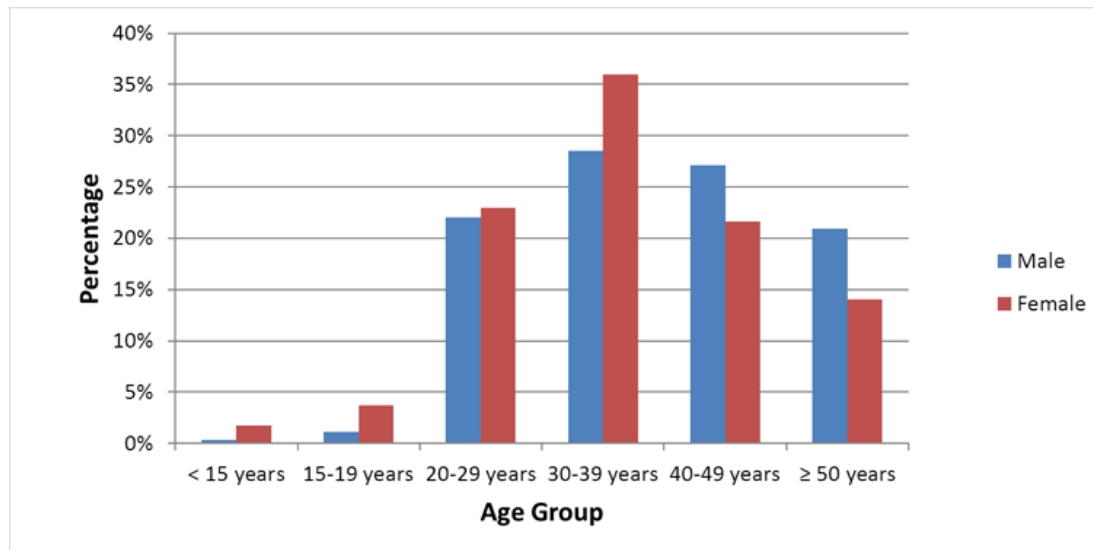
Number of people living with HIV

- 57,000 (2005)
- 65,000 (2008)
- 71,300 (2011)

Geographical distribution

Ontario	42.6 %
Quebec	21.5%
BC	13.4 %
Alberta	9.7 %
Saskatchewan	7.7 %

Age distribution of positive HIV test reports, by sex, 2011



[Where is HIV found?]

- Body fluid of infected persons
 - Blood
 - Semen
 - Vaginal Fluid
 - Breast milk

Transmission- You can get HIV by

- Unprotected sex with a positive partner
- Intravenous Drug use
- Mother to child
- Contaminated blood products

Transmission-

You can **not** get HIV by

- Air or water
- Insects (e.g mosquitoes)
- Saliva, tears or sweat
- Contact such as shaking hands or sharing dishes
- Closed mouth kiss

[What is HIV]

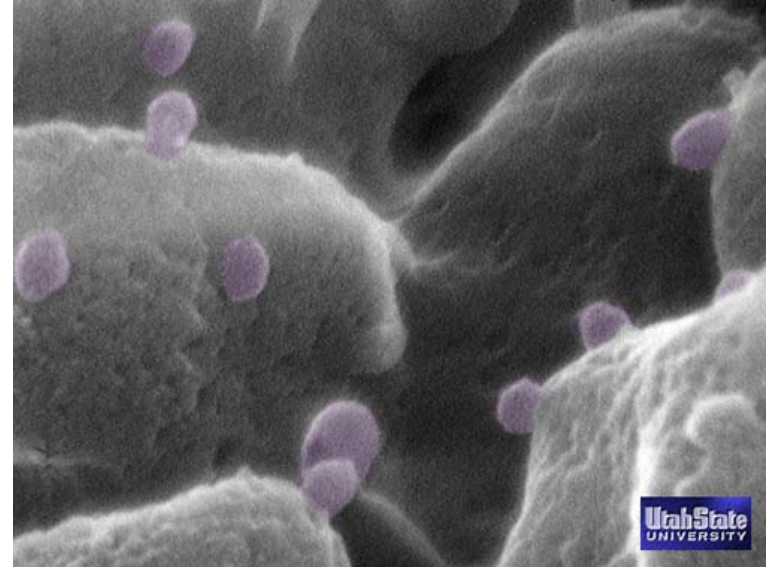
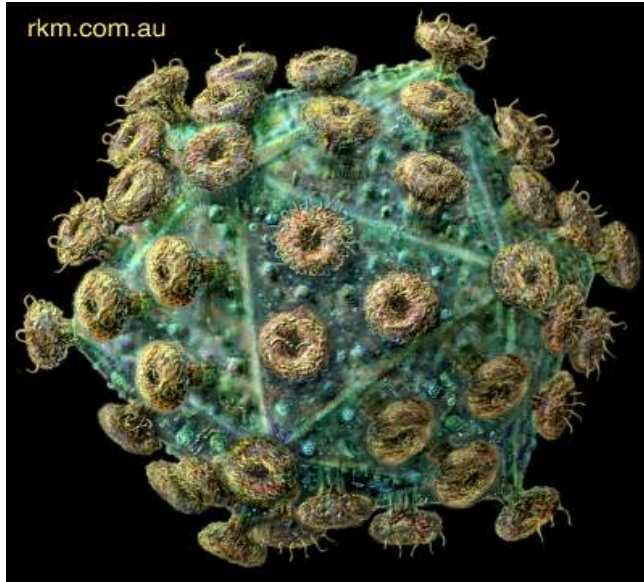
- Single Stranded enveloped retrovirus
- Retroviridae family
- Lentivirus genus
 - simian immunodeficiency virus (SIV)
 - Feline immunodeficiency virus (FIV)
 - caprine arthritis-encephalitis virus (CAEV)
 - equine infectious anemia virus (EIAV)

Where does HIV come from?

- HIV is a zoonosis infection that mutated from the chimpanzee virus SIV in the 1940s-1950s in the Democratic Republic of the Congo (DRC)



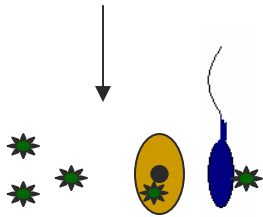
Target and disease of HIV



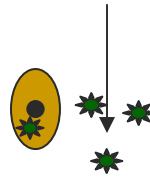
- Targets Immune cells (mainly CD4 T-cells)
- Impairs Immune function
- Leads to AIDS

Suggested modes of HIV transmission across the female genital mucosa

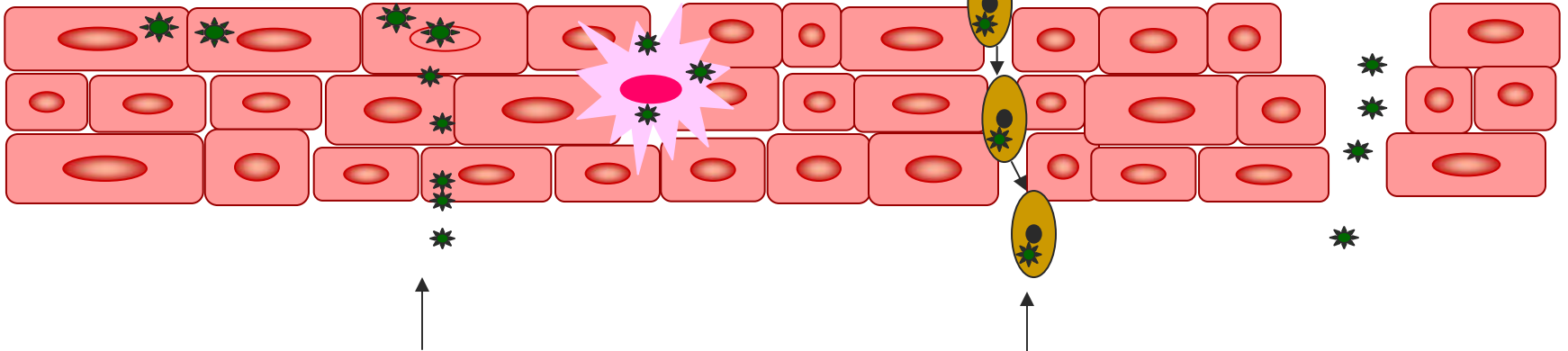
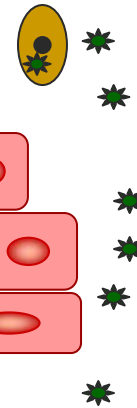
1. Direct infection of epithelium



3. Infection of migratory intra-epithelial Langerhans cells



5. Direct entry via breaches in epithelial integrity

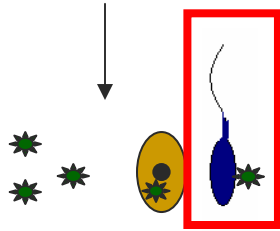


2. Transcytosis through epithelium

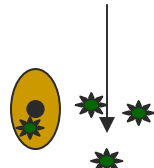
4 Transmigration of infected donor cells

Suggested modes of HIV transmission across the female genital mucosa

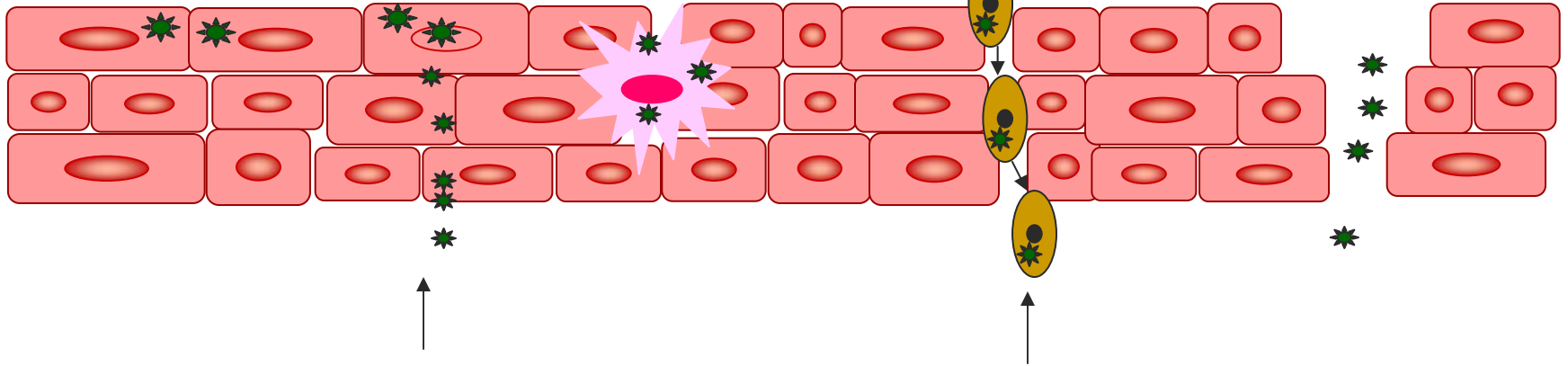
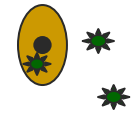
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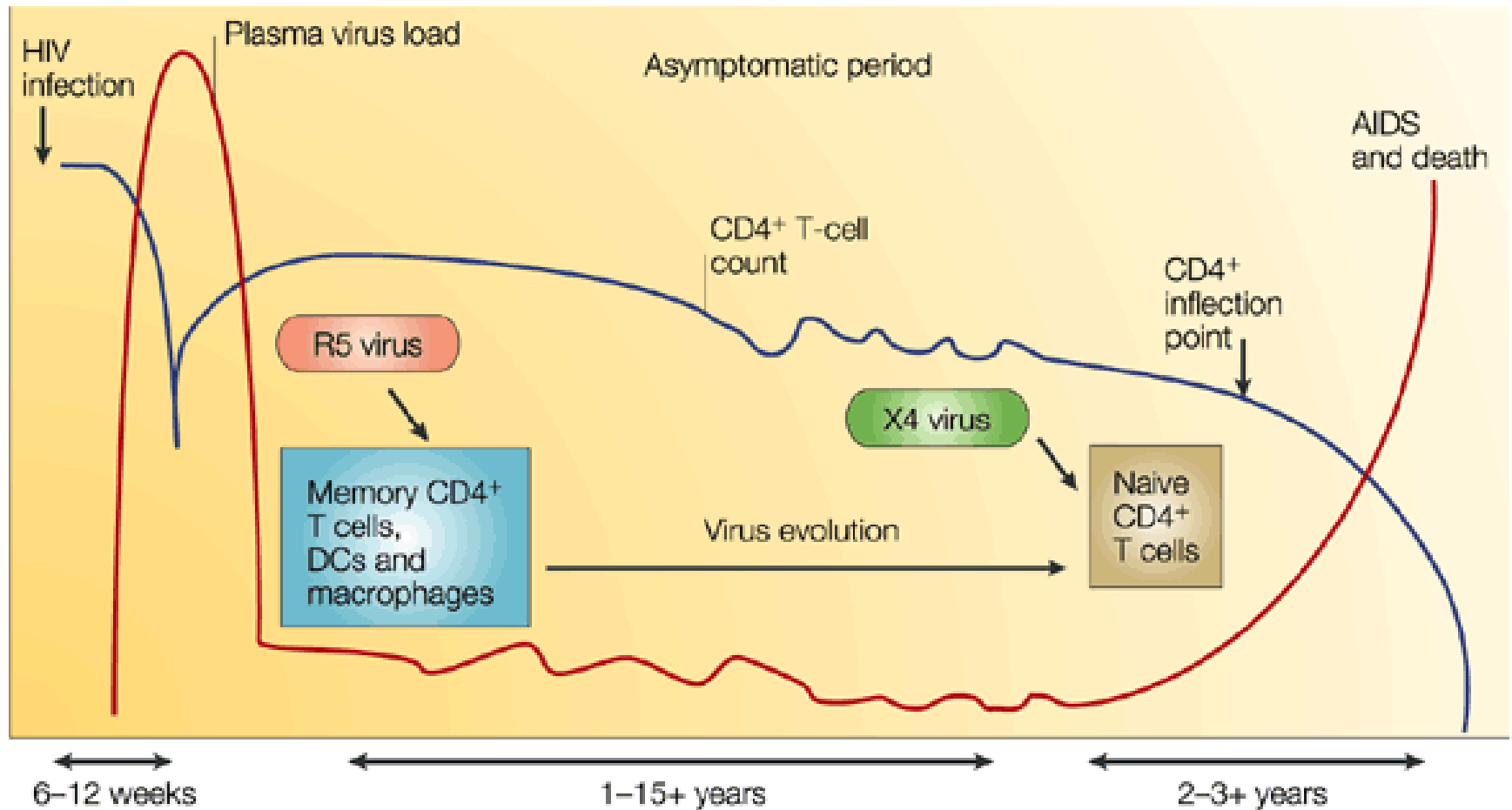
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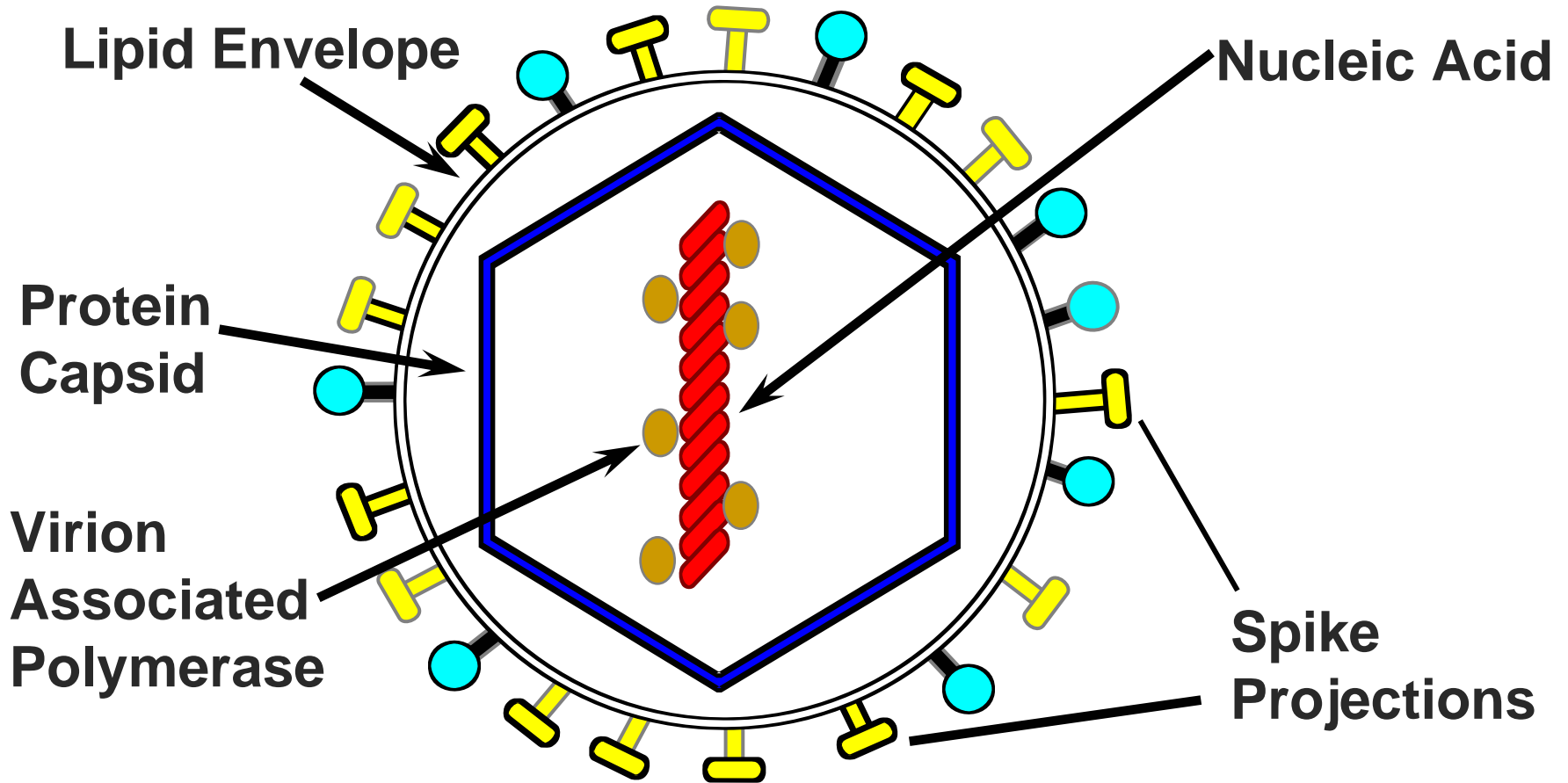
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HIV progression

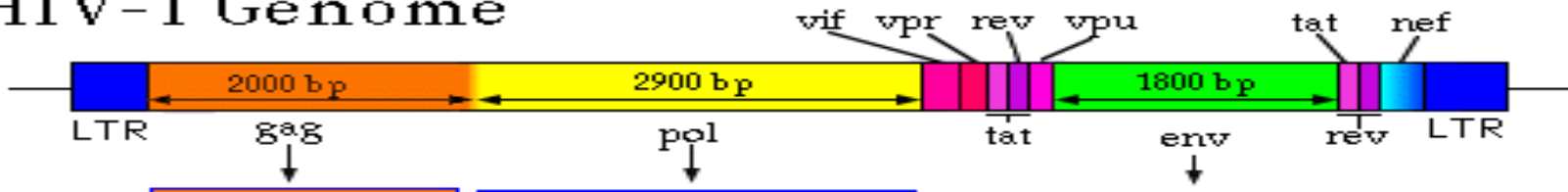


Virion Structure



HIV-1 genome

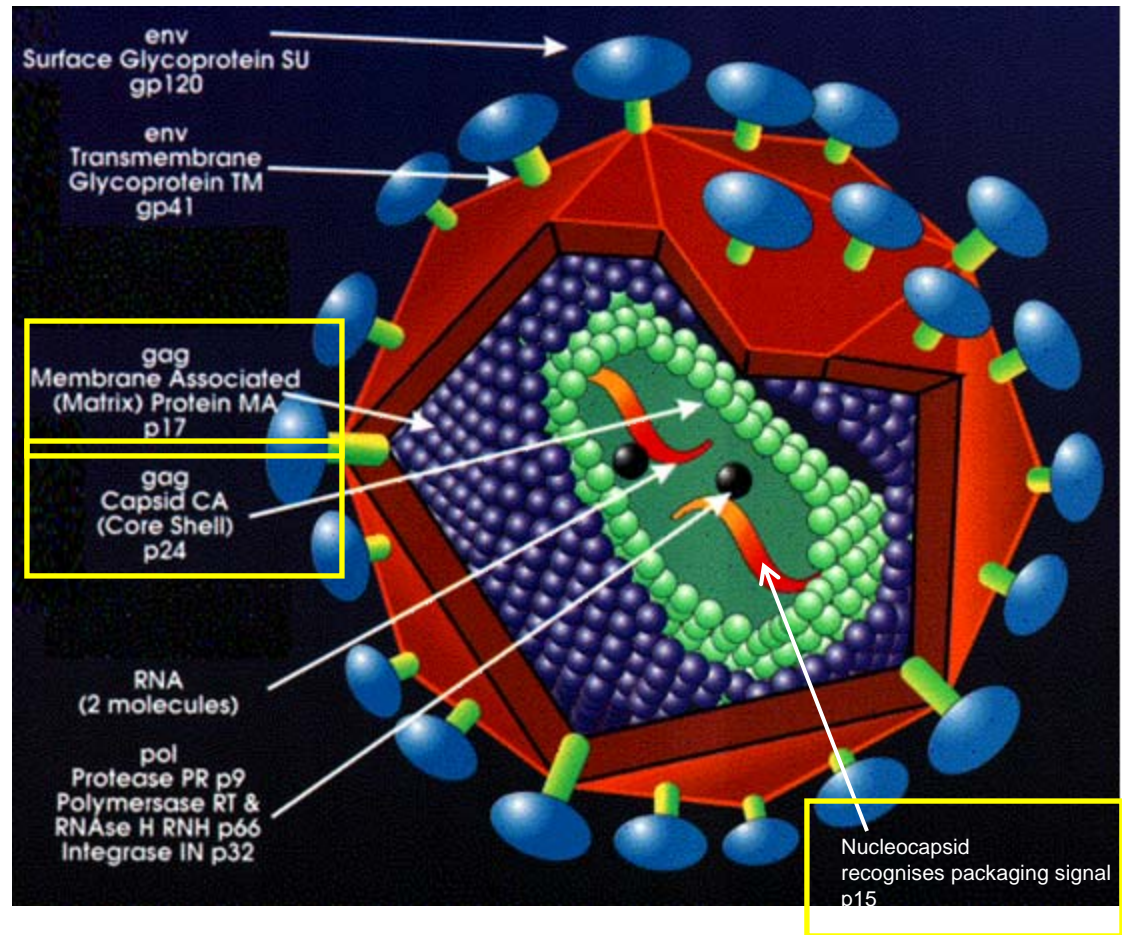
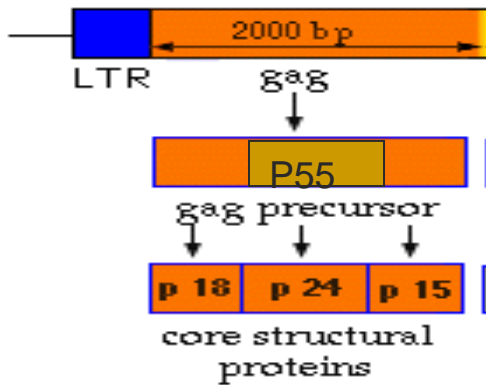
HIV-1 Genome



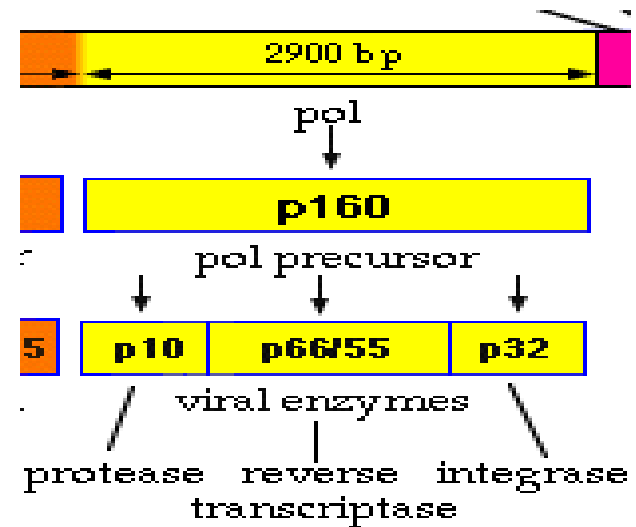
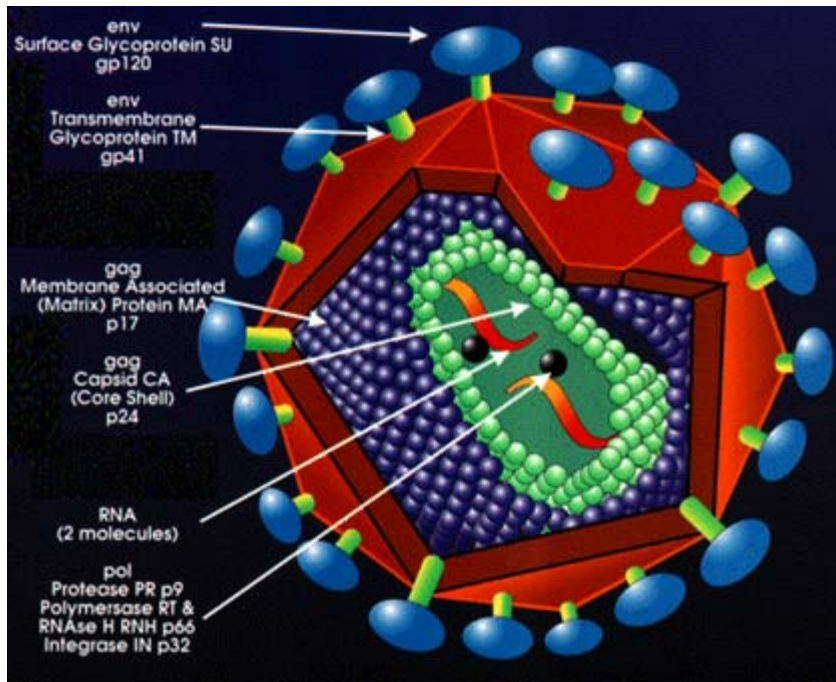
- HIV provirus (integrated) is 9.8 Kb
- Genome is composed of 9 proteins divided into three classes
 - Structural: gag, pol, env
 - Regulatory: tat and rev
 - Accessory: vif, vpu, vpr and nef
- Promoter: Long terminal repeat (LTR)

Structural proteins

HIV-1 Genome

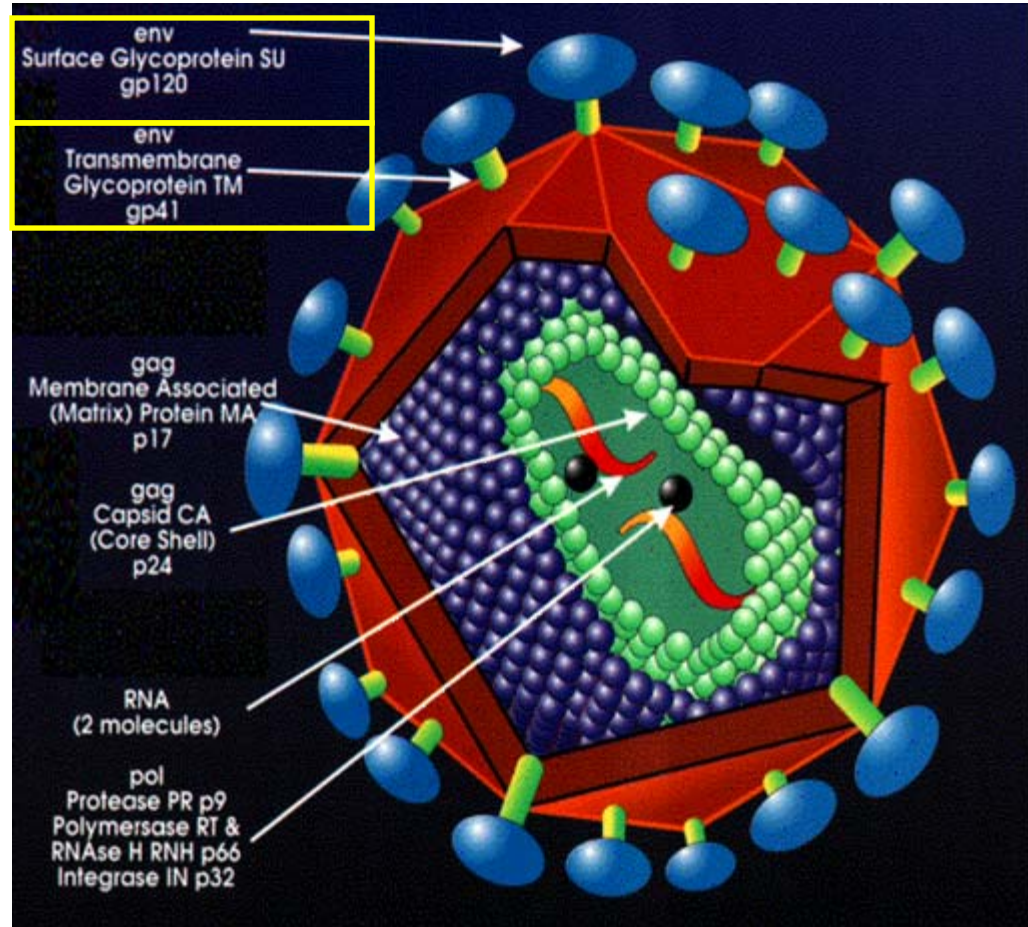
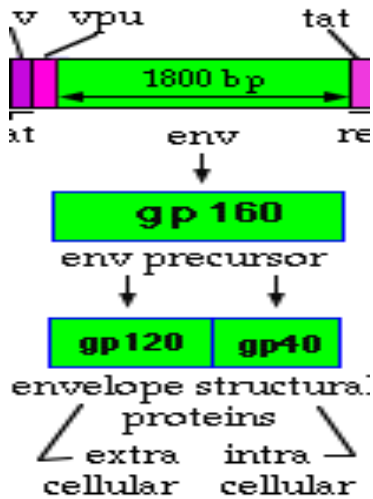


Structural proteins



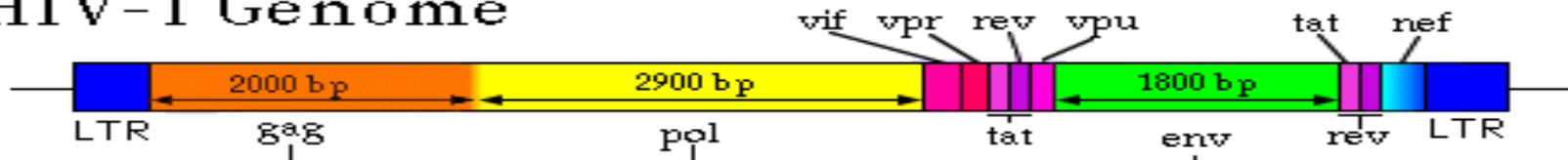
- Protease: Required to cleave and process viral proteins
- Reverse transcriptase: The polymerase that makes a dsDNA copy of the ssRNA
- Integrase: Inserts proviral DNA into the host genome

Structural proteins



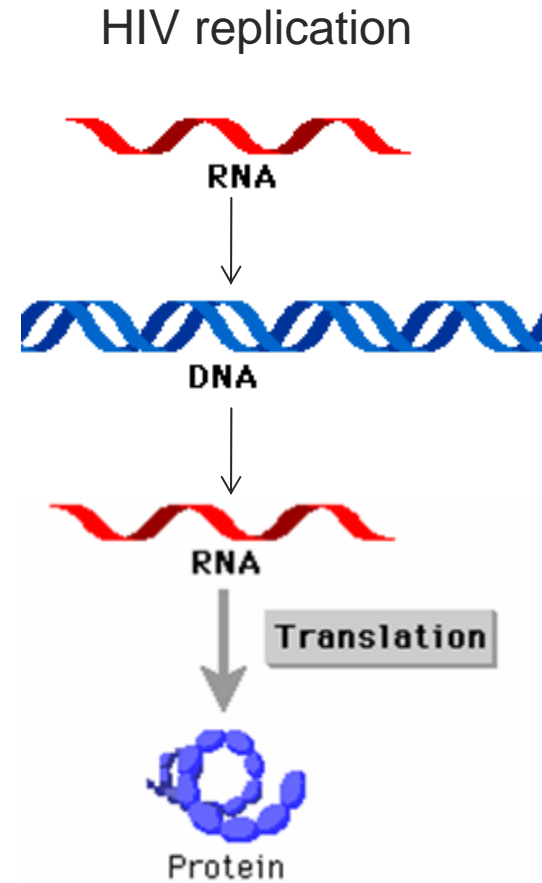
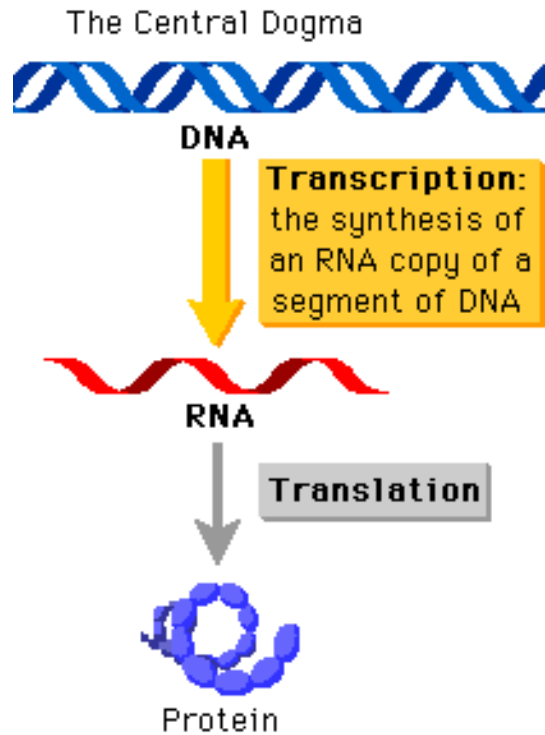
Regulatory and accessory proteins

HIV-1 Genome

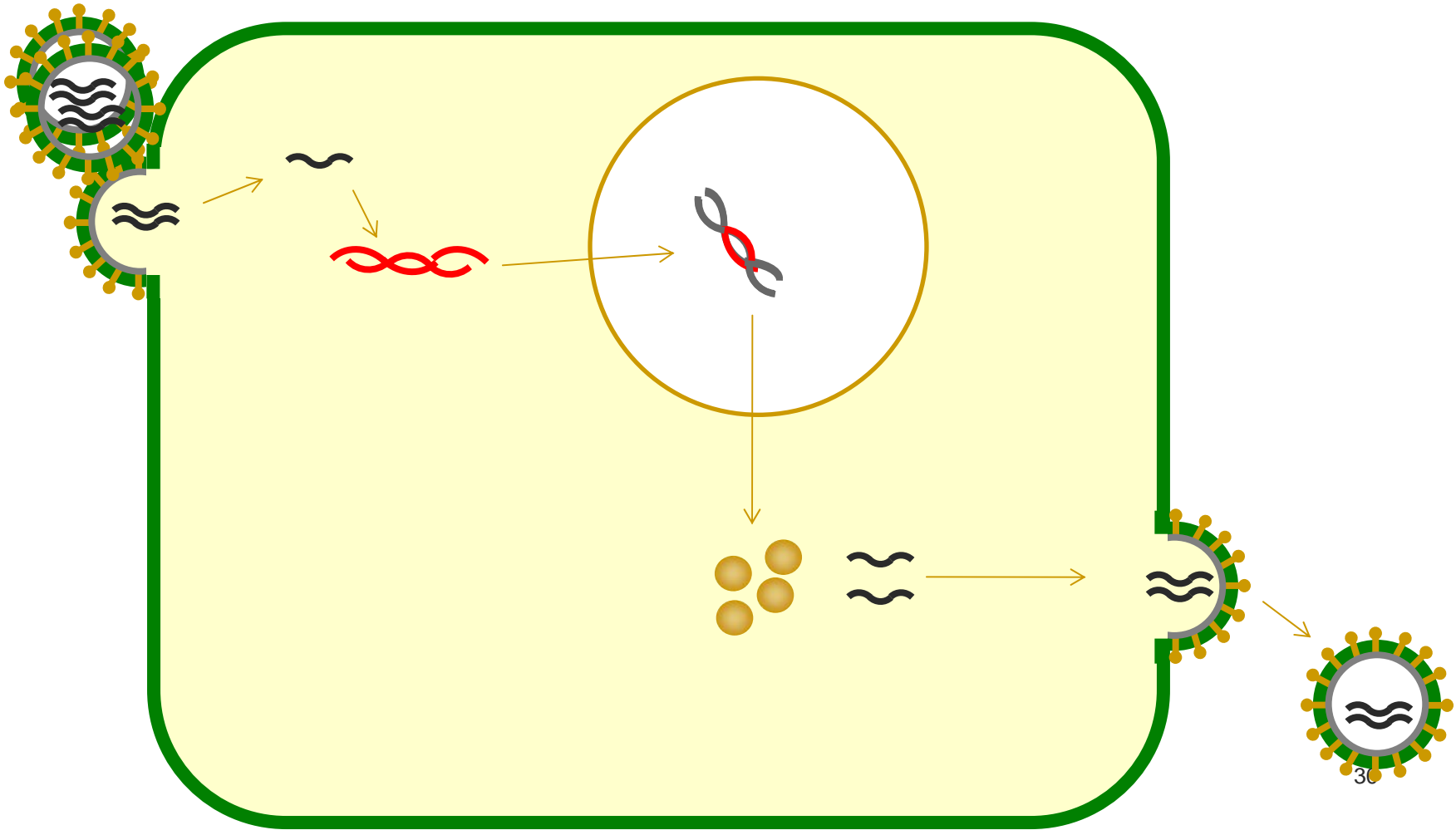


- tat (transcriptional transactivator): Required for HIV replication. Promotes elongation phase of HIV-1 transcription
- rev: RNA binding protein that promotes the export of unspliced RNA from the nucleus to the cytoplasm
- vif, vpr, vpu and nef: Not strictly required for viral replication but are virulence factors that are multifunctional.

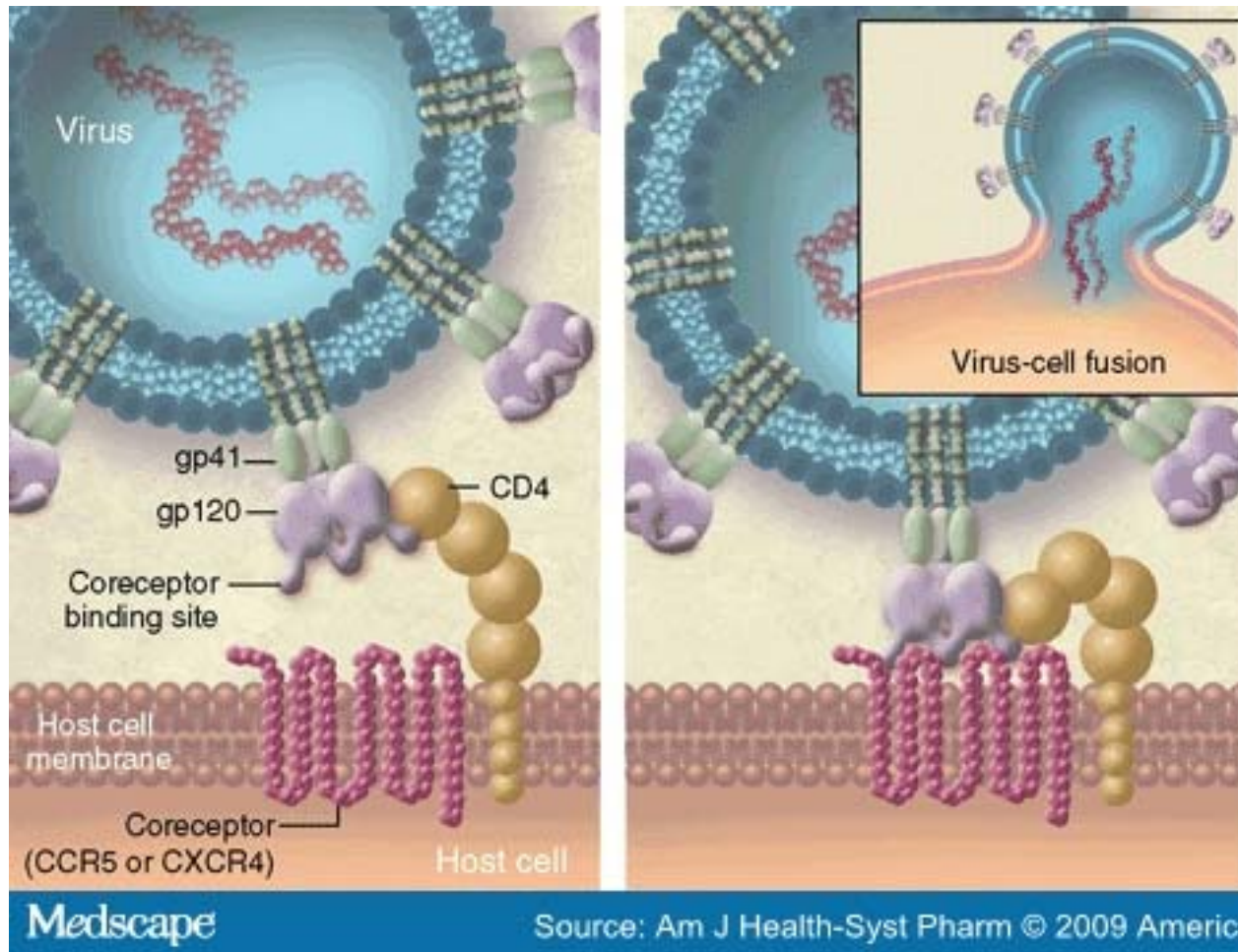
[HIV Replication]



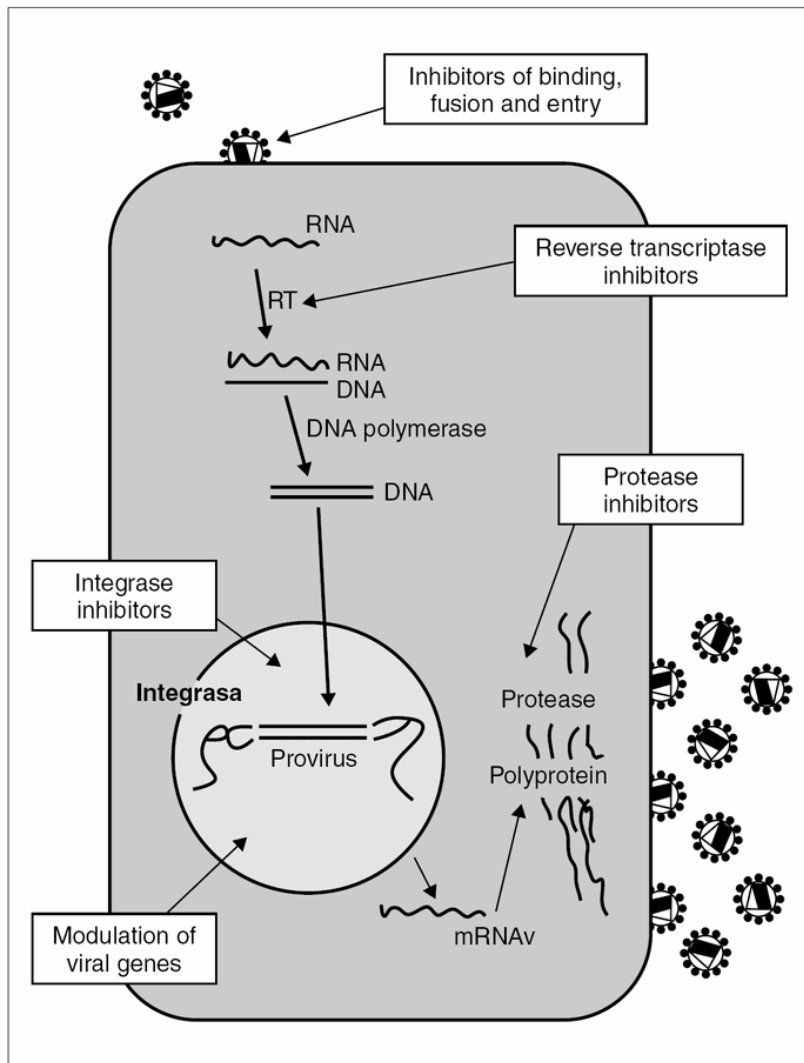
[HIV Life Cycle]



HIV-1 tropism: CXCR4 and CCR5



Antiviral Targets



- Attachment/Fusion
- Nucleic acid replication
- HIV DNA integration
- HIV protein processing

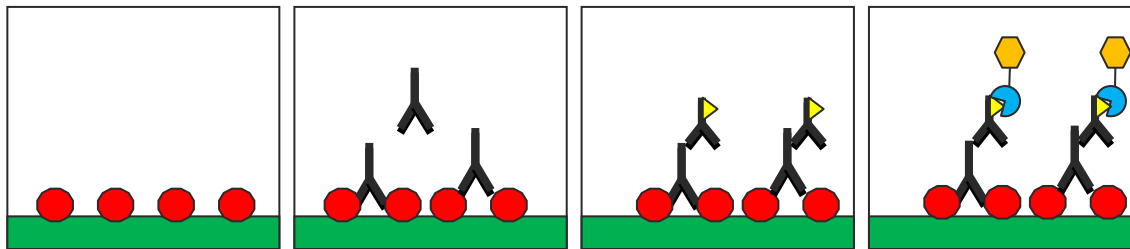
[HIV serologic test]

- Enzyme immunoassay (EIA)
- Western blotting

- Results

HIV positive only if both the EIA test is positive and the western blot is positive for at least 2 HIV proteins (p24, p41, gp120)

Enzyme immunoassay



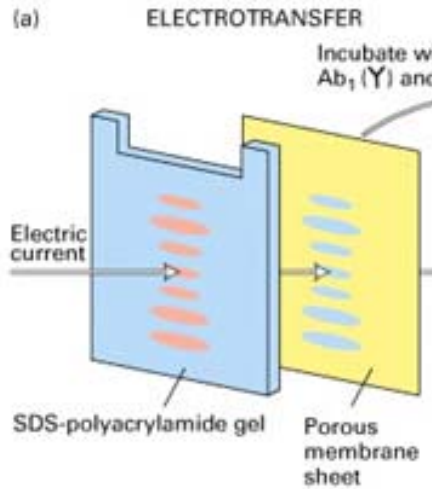
1. Plate with HIV p24 antigen

2. Add infected sample (e.g Blood) P24 antibodies will bind to antigen

3. Incubate with biotinylated P24 antibody

4. Detect antigen with streptavidin labelled with peroxide

Western blotting



Detection in Western Blots

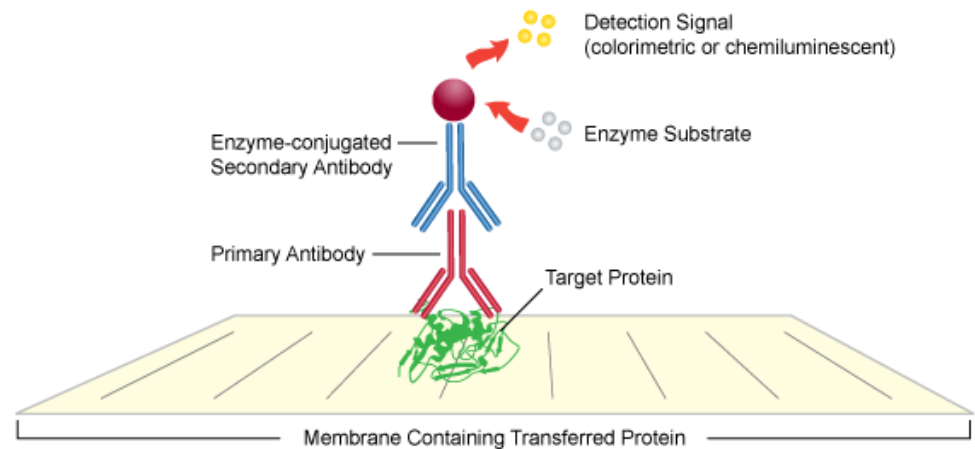
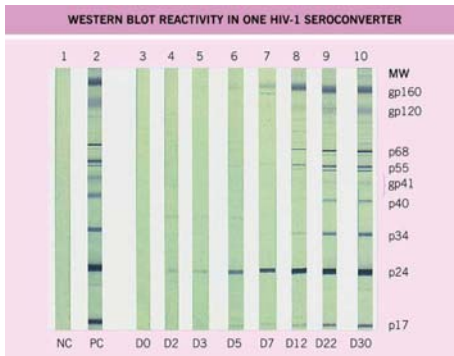


Diagram 2: Illustration of detection in Western Blots.



[Preventative technologies]

- Vaccines
- Microbicides (Nonoxyl-9)
- Pre-exposure prophylaxis
- Treatment-as-prevention.
- Medical male circumcision
- Prevention of mother-to-child transmission (or PMTCT).