HIV

SROISIRI THAWEBOON

1981 homosexual *Pneumocystis carinii*
Kaposi's sarcoma
immunodeficiency CMI (CD4↓)

1982 IV drug user, hemophiliac, sexual, perinatal

1983 Luc Montanier culture
lymphadenopathy associated virus
(LAV) from lymph node

1984 Robert Gallo culture HTLV III
from lymphocyte

Jay Levy AIDS-associated retrovirus (ARV)

LAV = HTLV III = ARV

1986 F. Clavel LAV-2 / HIV-2

1992 unexplained severe immunosuppressive without HIV (idiopathic CD4 lymphocytopenia)

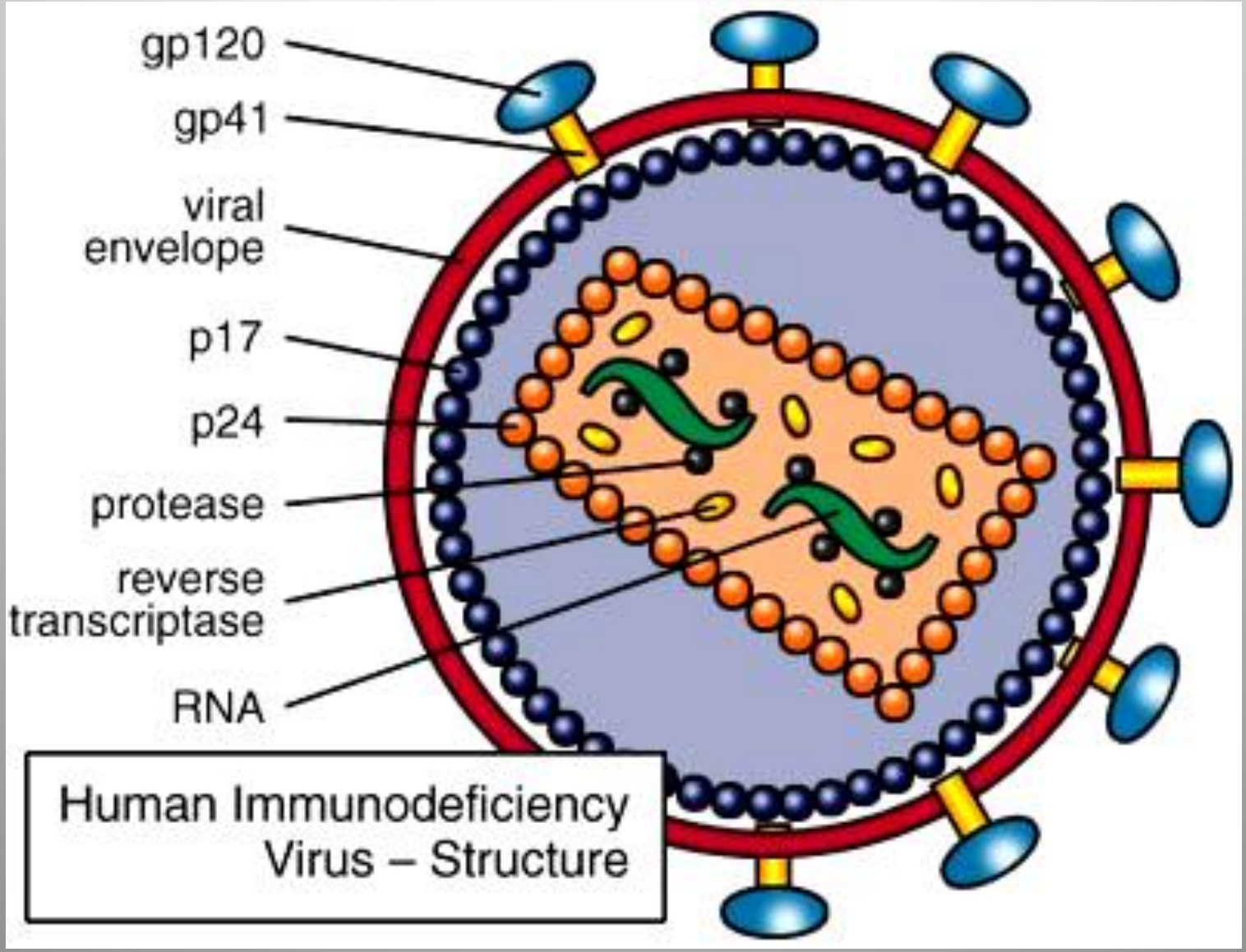
Family : *Retroviridae* Genus : *Lentivirus*

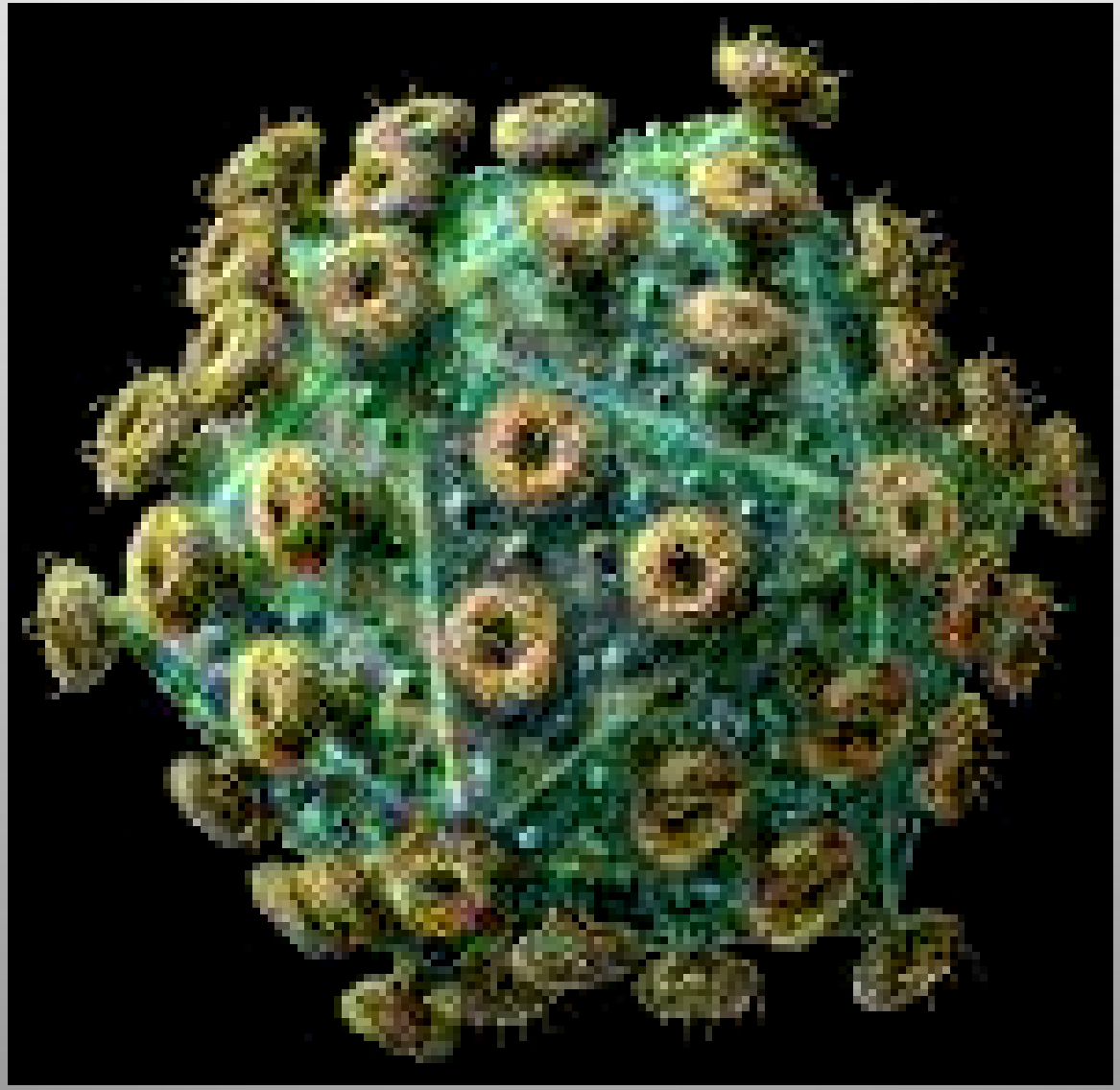
HIV-1

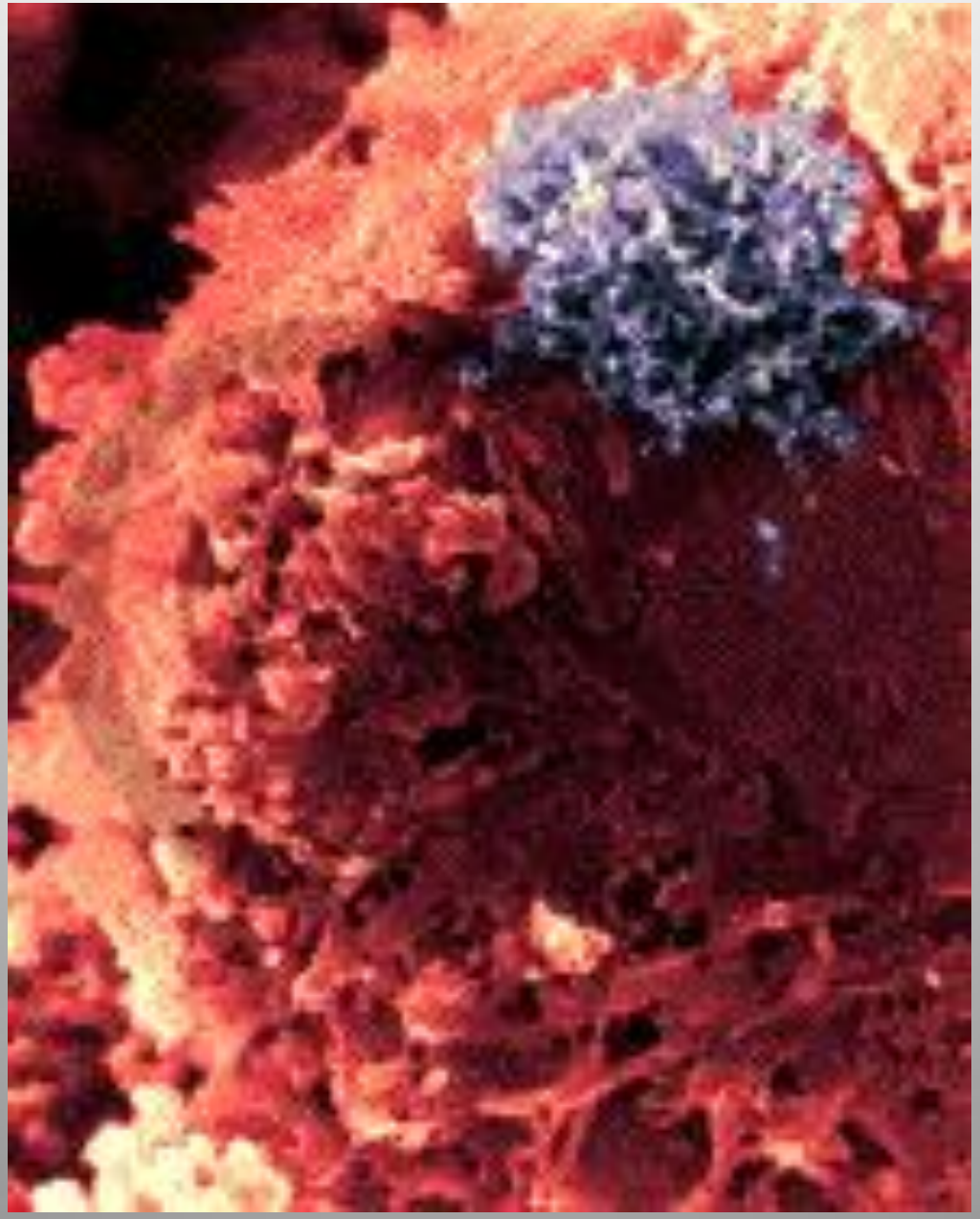
- spherical 100-200 nm
- cylindrical core, diploid ss RNA, reverse transcriptase, protease, integrase
- core protein (p24) ⟶ matrix prot (p17)

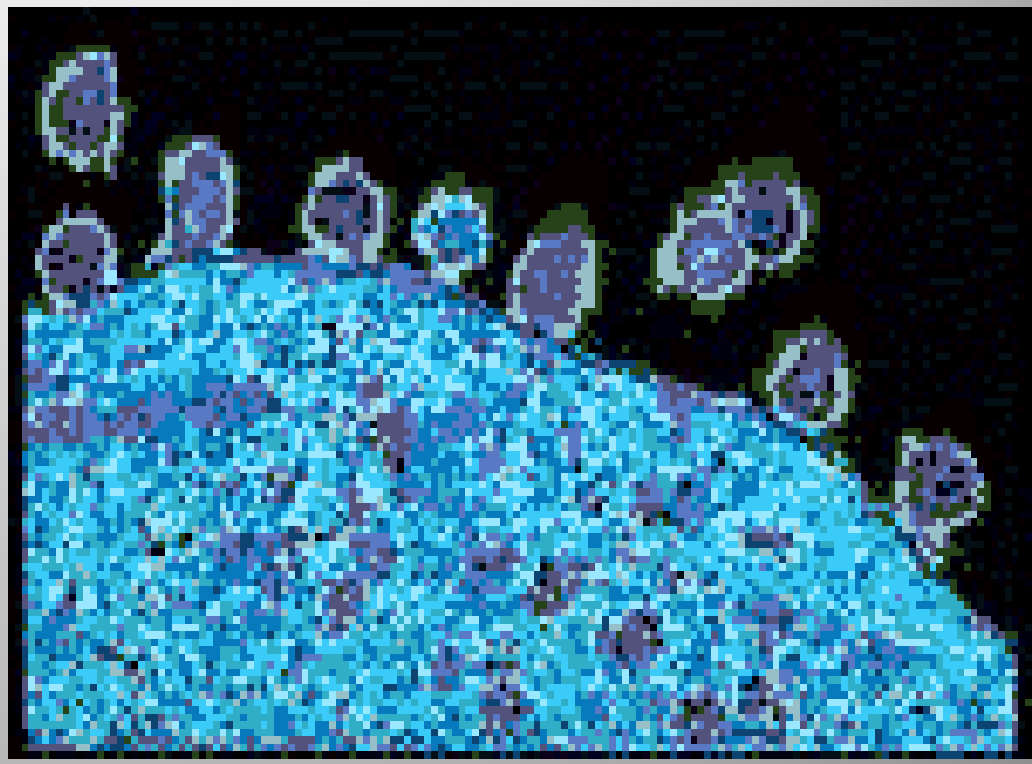
knob ⟵ envelope

(surface gp120, transmembrane gp41)


gp120
gp41
viral envelope
p17
p24
protease
reverse transcriptase
RNA
Human Immunodeficiency Virus – Structure







HIV-2 similar to HIV-1

genome 9 kb

1. Structural

nucleotide sequence diversity mutation

quasispecies

no proof reading, 1 position / 1 replication cycle

1.1 *gag* (group specific Ag) → (p24)

matrix (p17)

nucleocapsid (p7/p9)

1.2 *pol* (polymerase) RT, integrase, protease

1.3 *env* (envelope) gp120, gp41 (from host)

cell tropism, syncytial formation

2. Regular gene

Nef	reactivate latent virus
Rev	regulate synthesis structure
Tat	HIV transciption
Vif	infectivity
Vpr	replication
Vpu	budding

Subtype ;

nucleotide sequence (env) ≥ 50 % new type

HIV-1 → group M

HIV-1 → group O

group M 11 serotypes/clades A → K

B → Thai, USA, Japan, Europe

E → Thai, Japan, Africa

Serotype B → IV drug user Thai B

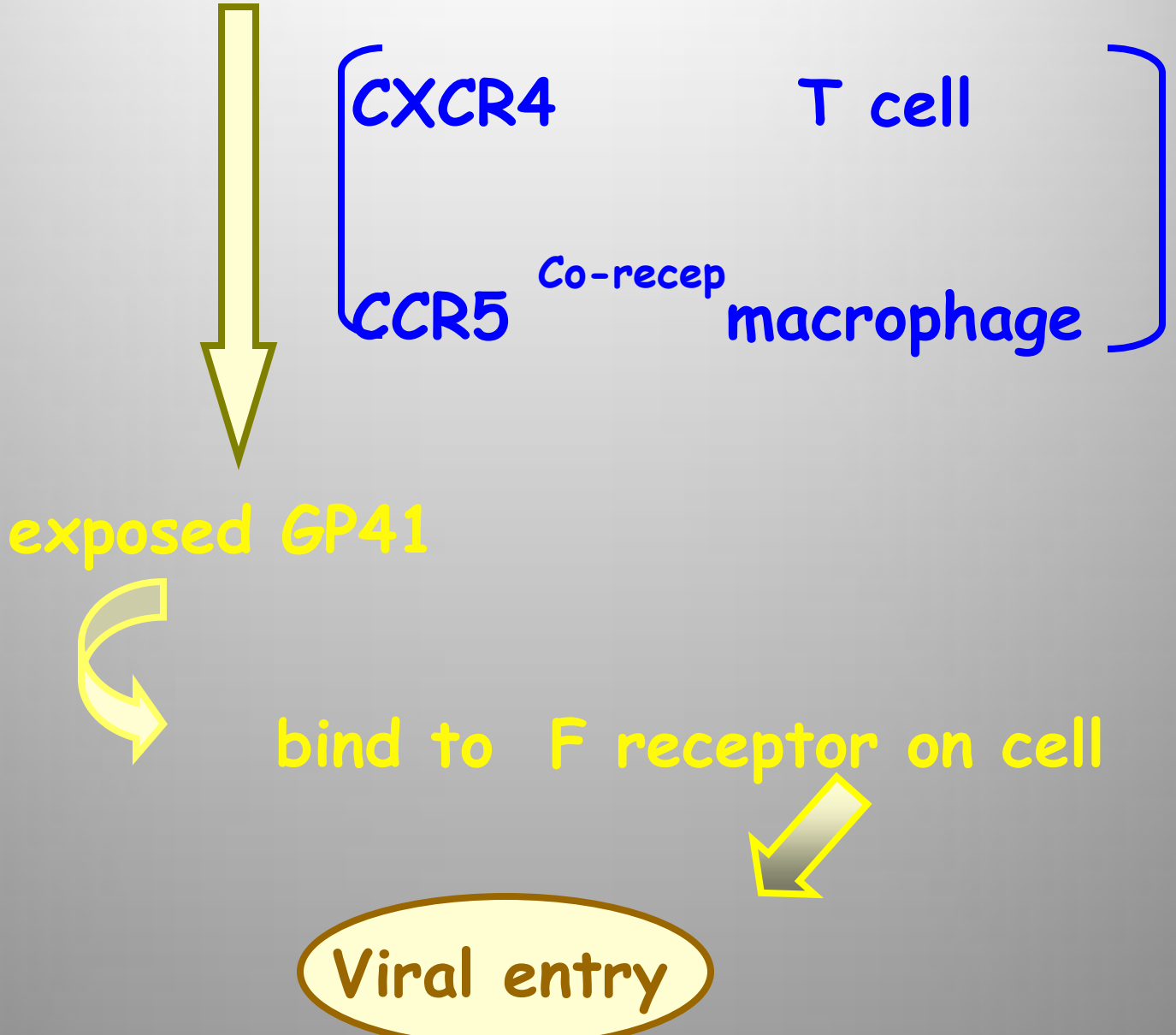
Serotype E → sexual Thai A

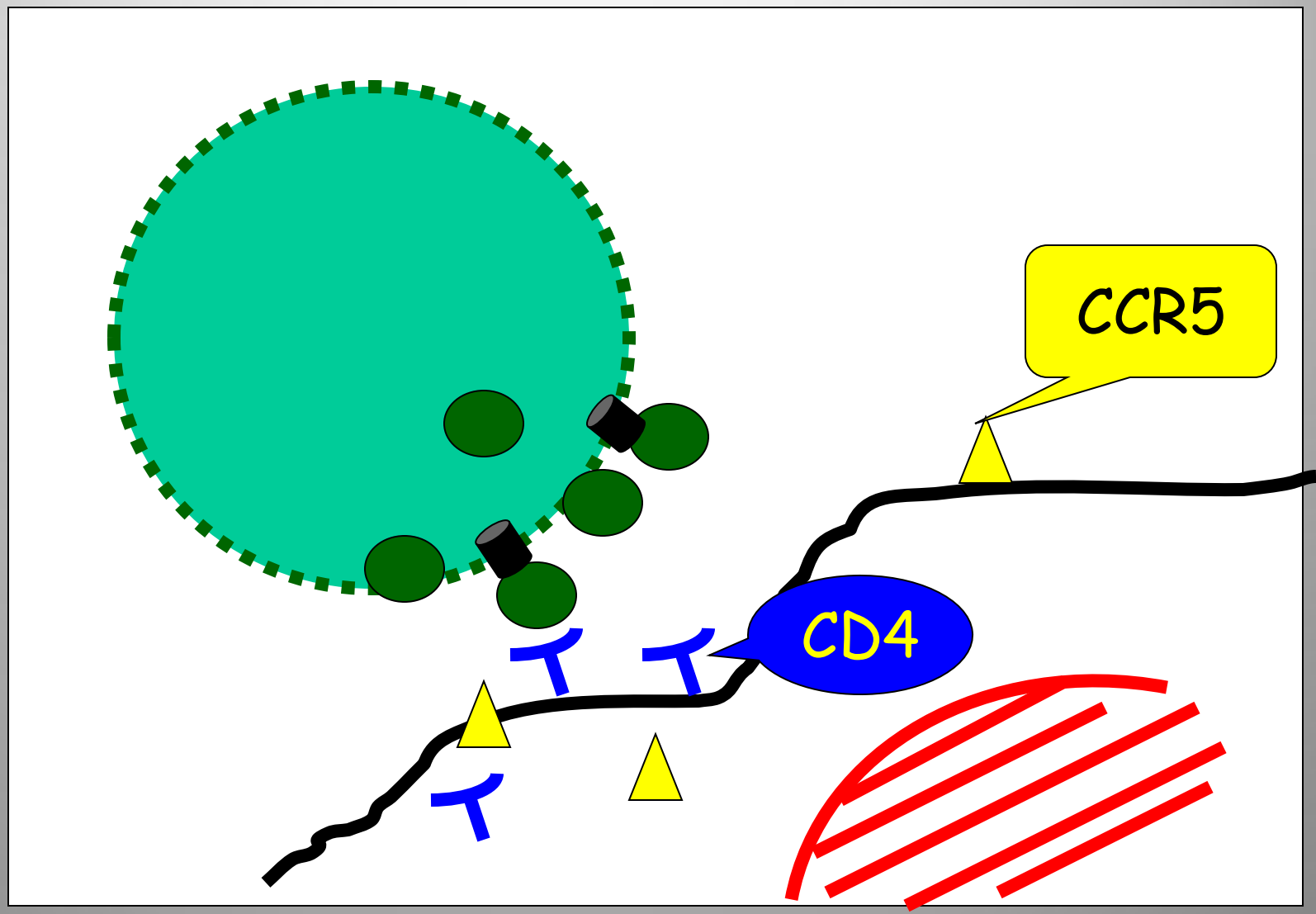
transmission

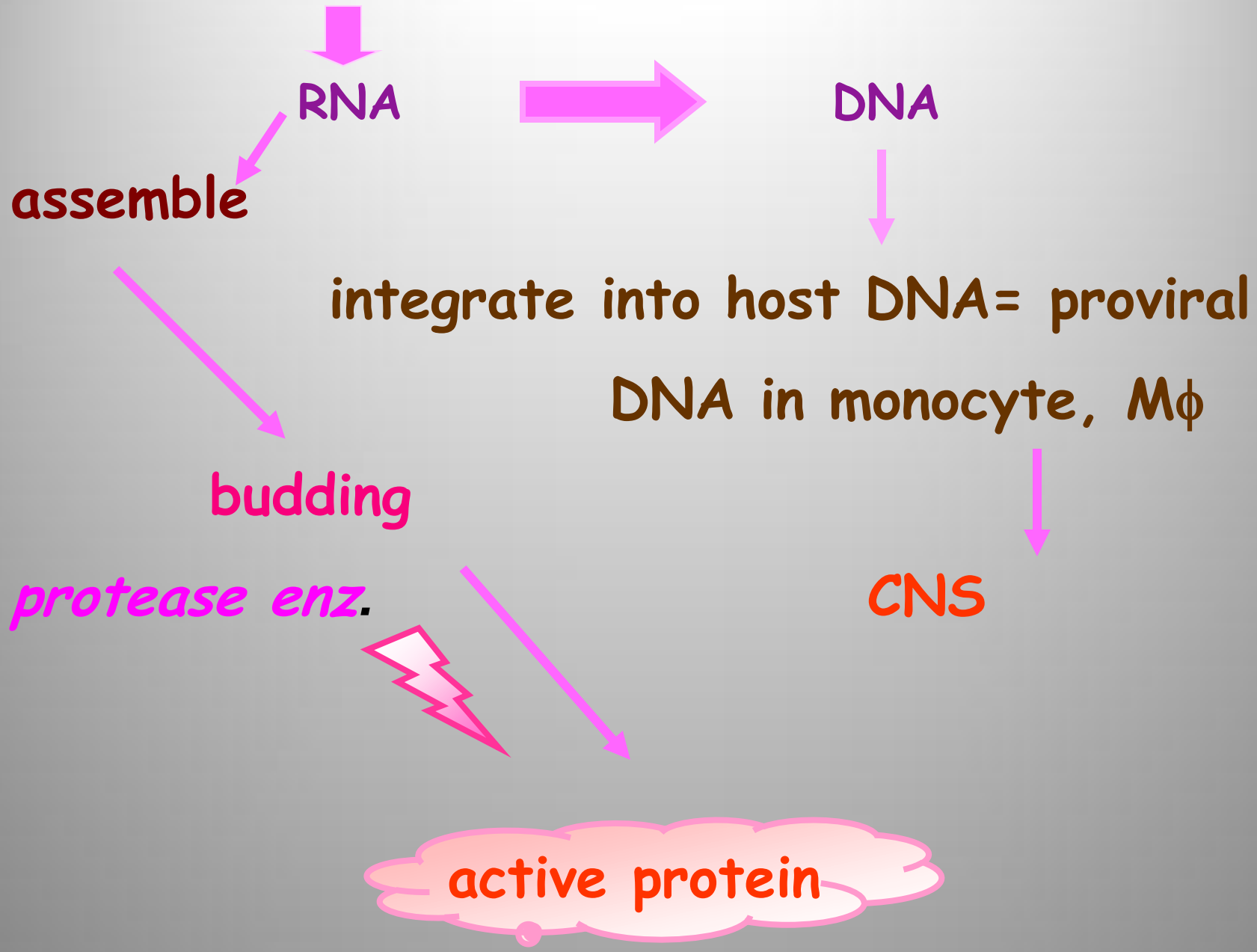
subtype E > subtype B

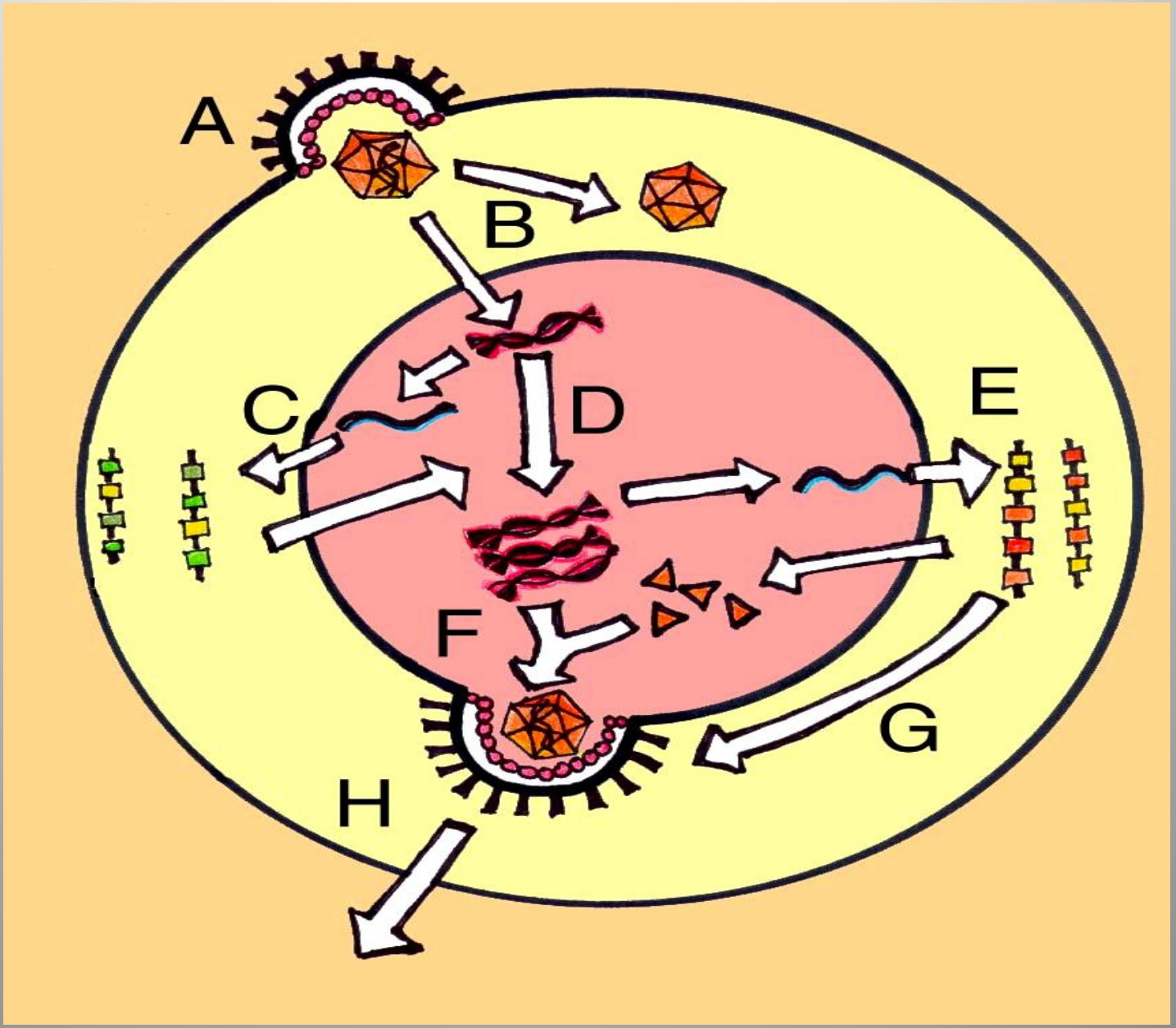
HIV-2 → 5 subtypes

Replication gp 120 bind to CD4 receptor




CCR5
CD4

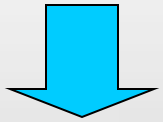

RNA
DNA
assemble
integrate into host DNA= proviral
DNA in monocyte, Mϕ
budding
protease enz.
CNS
active protein


A
B
C
D
E
F
G
H

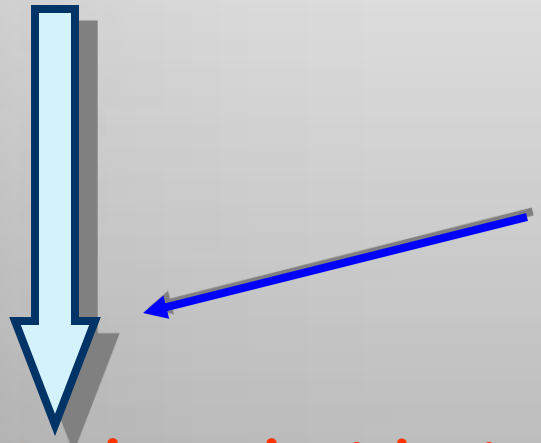
- Neutralizing Ab → gp 120 ⊣ bind to CD4
- AZT, ddI, ddC ⊣ DNA synthesis replication
- interferon ⊣ budding
- protease inhibitor ⊣ precursor protein digestion

Pathogenesis

1° infection



cell free virus, cell associated virus ↑ in blood



cytotoxic T cell

neutralizing Ab

2° lymphoid tissue

cell free virus,cell associated virus ↓ in blood

mutation CD4+cells ⇒ 98-99% in LN

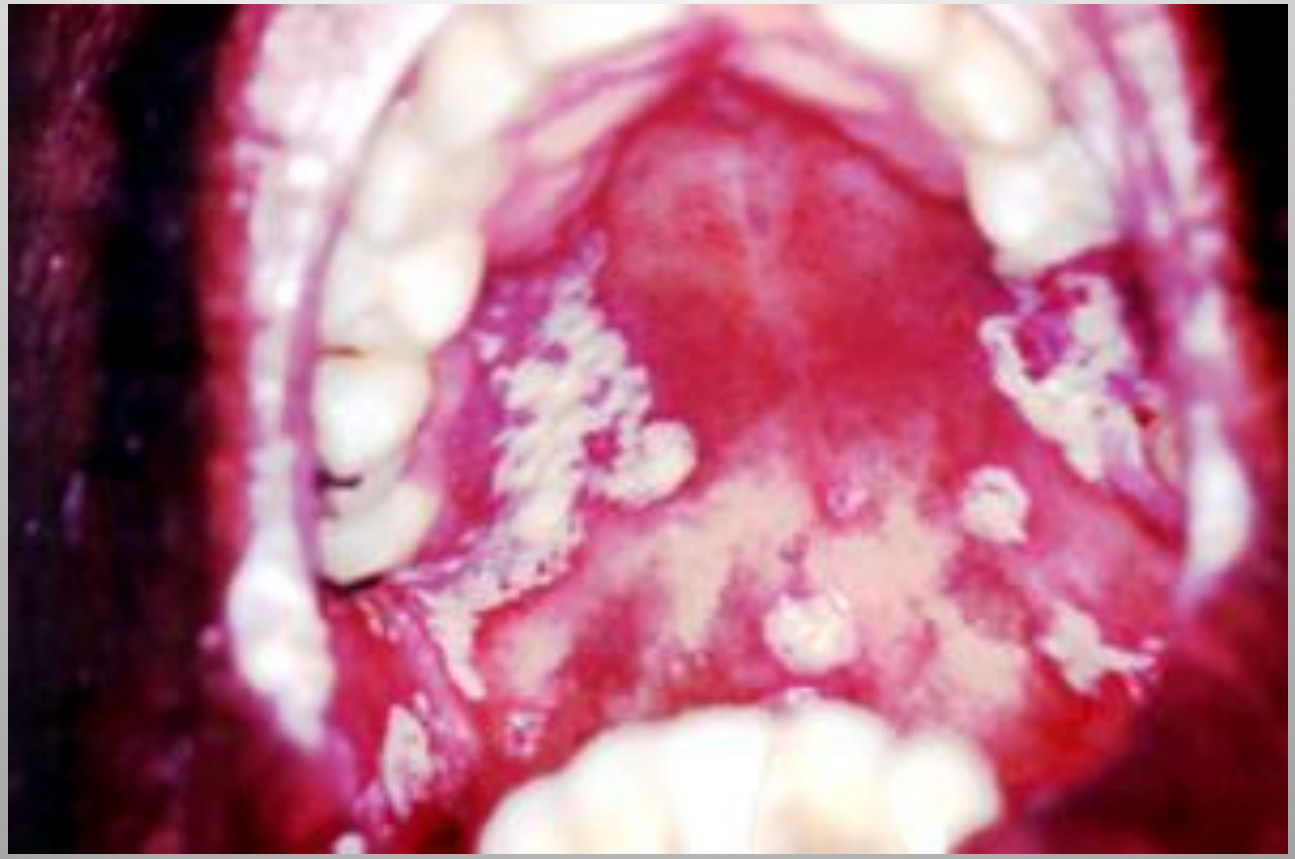
⇒ 1-2% in blood

free virus in blood

⇓

cancer, opportunistic infection ↑↑↑

kaposi's sarcoma B-cell lymphoma



Transmission HIV-1,HIV-2,HBV

- sexual
- bloods & blood products
- perinatal

2-6wk ⟶ culture virus from w.b.c. genome PCR

3-12 wk → Ab in serum

(6 mth)

Window period → 1 wk

anti-gp 120,anti-gp 41 → type specific

anti-p24 → common Ag

Symptom

1. acute infection 6 wk "Flu"
2. asymptomatic
3. Persistent generalized lymphadenopathy

   ϕ > 11 cm > 3 mth
4. 2-12yr (10 yr) AIDS relatedcomplex (ARC)

AIDS

immune deficiency → opportunistic infection

6 mth -3 yr → DEATH

20-30% perinatal transmission

show AIDS within 2yr.

Lab Diagnosis AIDS patients :

- Ab/Ag/isolate virus particle or genome
- T-helper CD4 < 200 cells/microlitre
- Opportunistic infection

1. Anti-HIV

p24 → common Ag

gp41/gp120 → HIV-1

gp36 → HIV-2

screening + confirmatory test

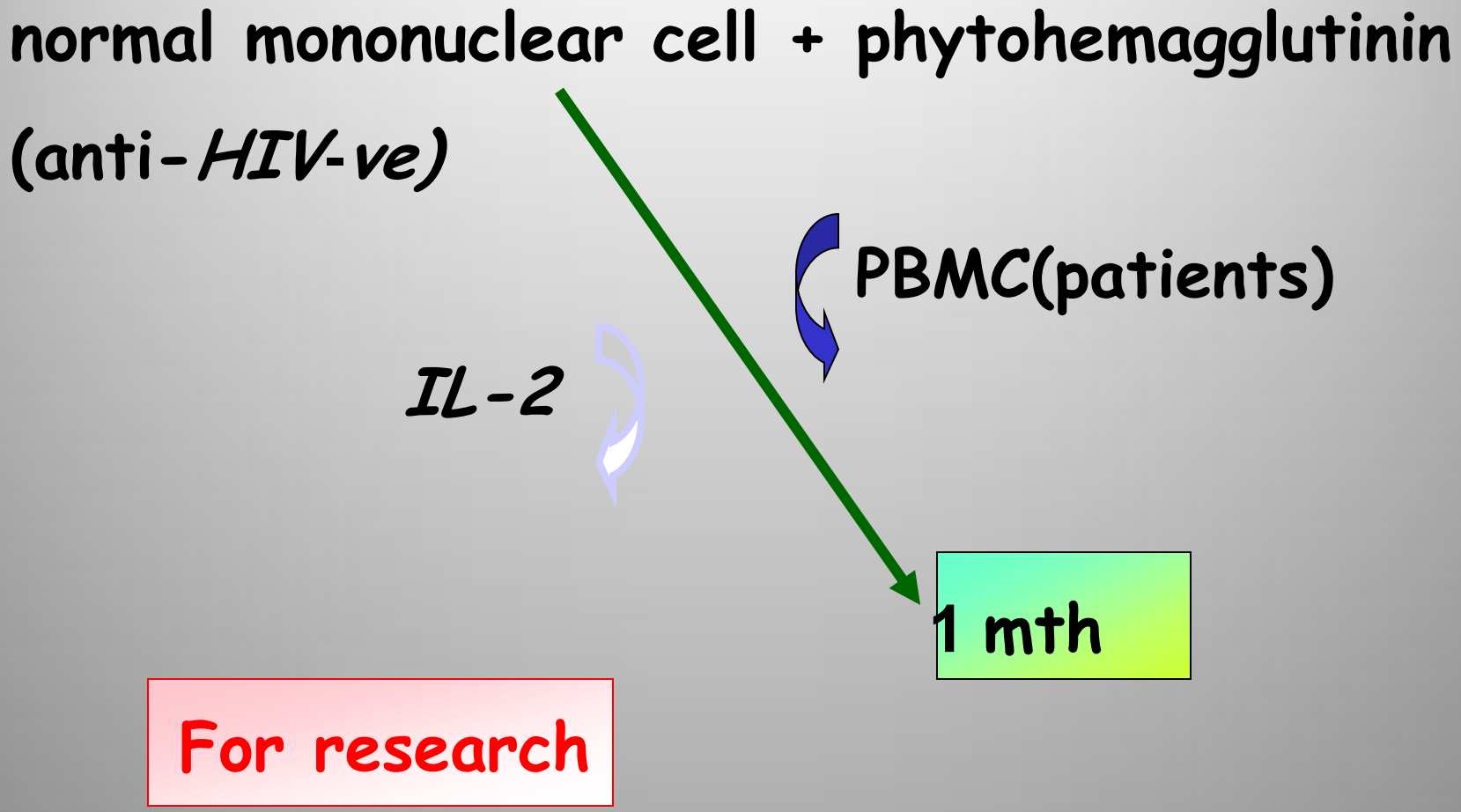
ELISA western blot immunofluorescence

2. Virus particle Ag , genome

3. viral isolation in cell culture

from ⇨ PBMC

⇨ plasma , serum , secretions


normal mononuclear cell + phytohemagglutinin
(anti-HIV-ve)
PBMC(patients)
IL-2
1 mth
For research

Treatment No !!!

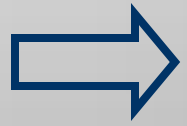
- antibiotic,chemotherapy,radiation

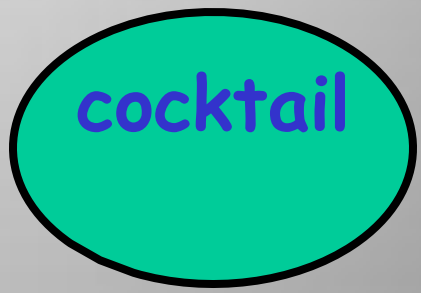
- nucleoside analoque

  AZT,ddI,ddC

  protease inhibitor

- counselling





clean , alcohol

check blood immediately AZT+proteas inhibitor

12 wk 5 times / day for 6 wk

6 mth

Vaccine 1.prevention

2.therapeutic

3.perinatal

Long term non-progressor

mutation

immunogen

Vaccine :

- recombinant protein

gp160, gp120, gp41

vector (virus, mammalian cells, yeast)

- killed vaccine

The end