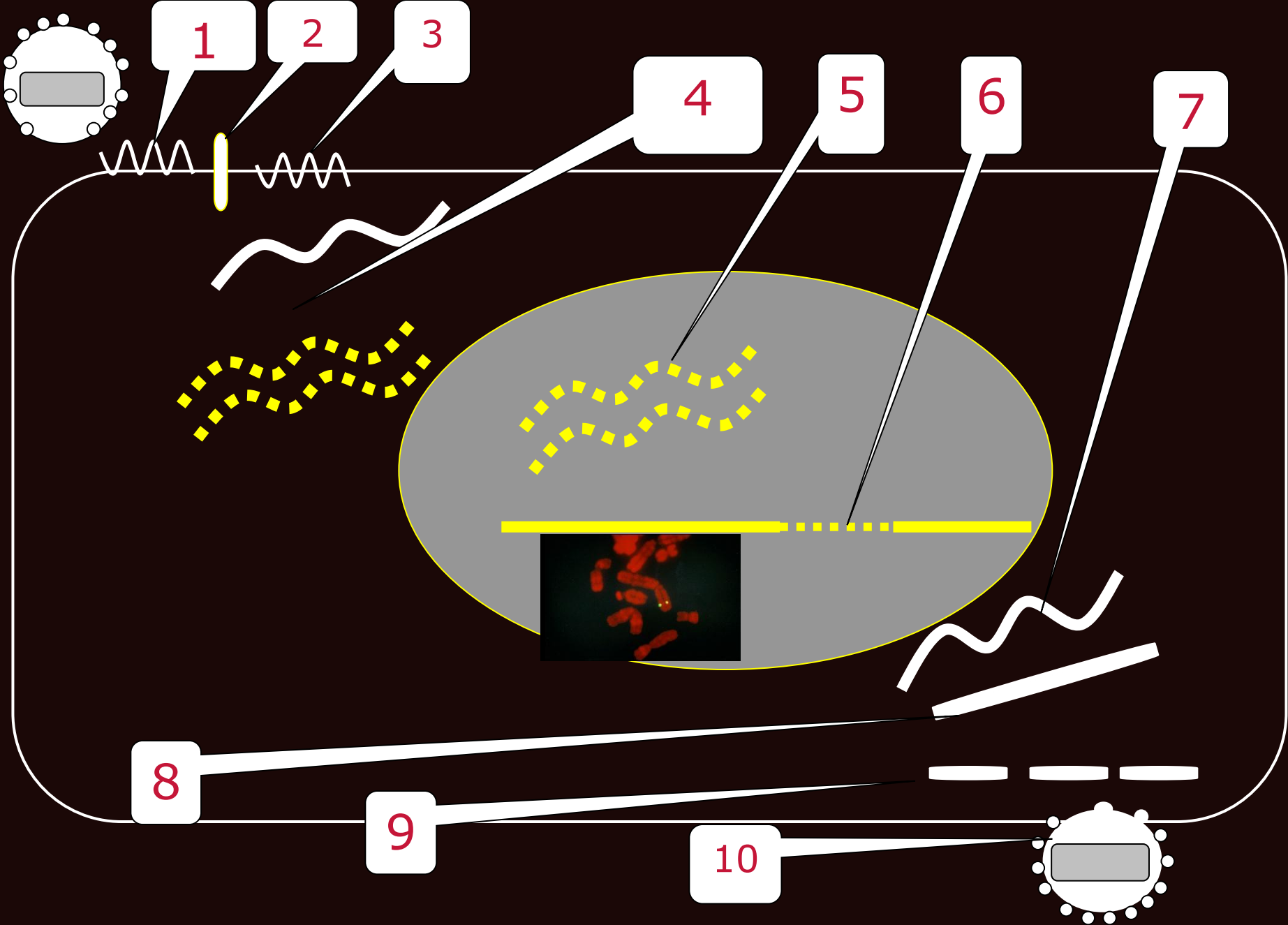
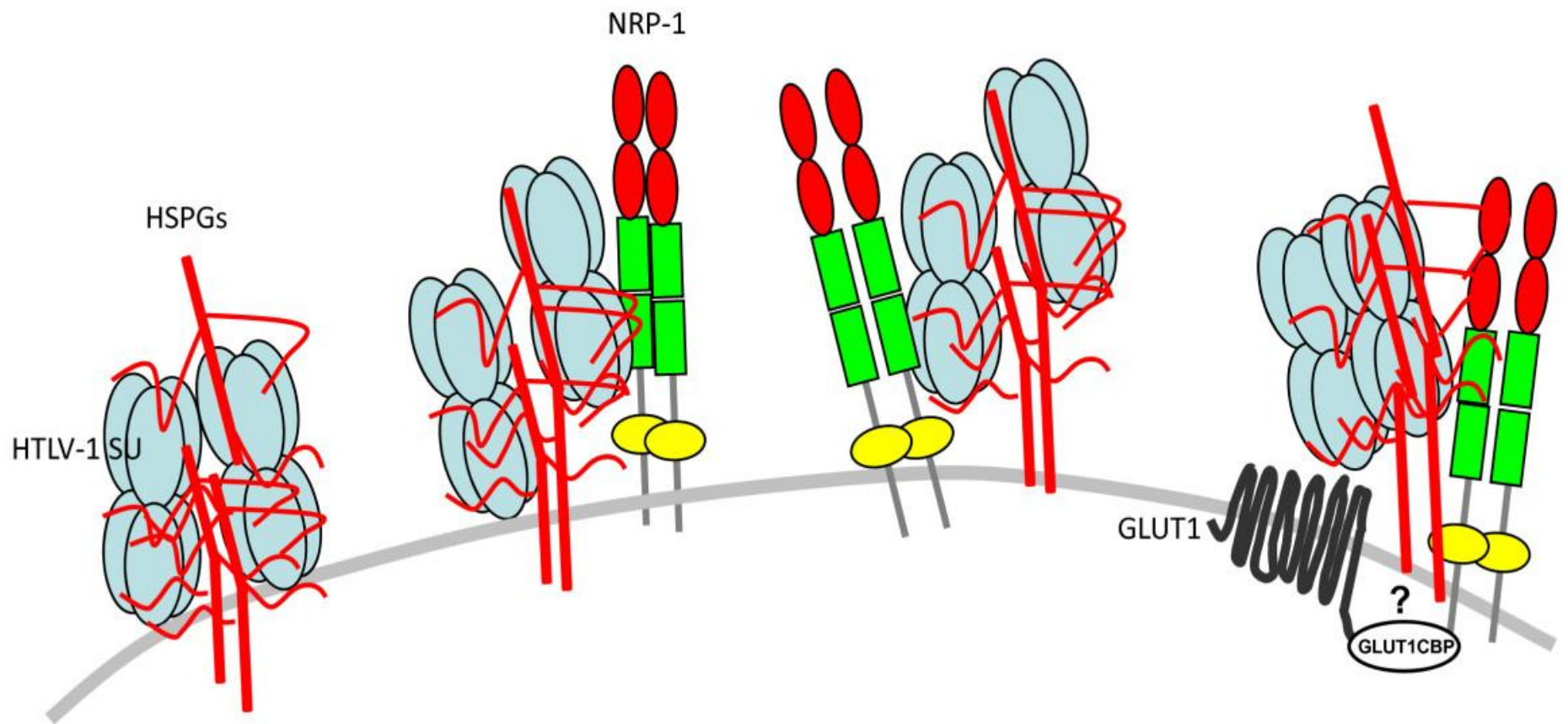


# **HTLV-1 Clinical presentations and virological outcomes**

Graham P Taylor

29<sup>th</sup> November 2012





1- Virus attachment and concentration on HSPGs

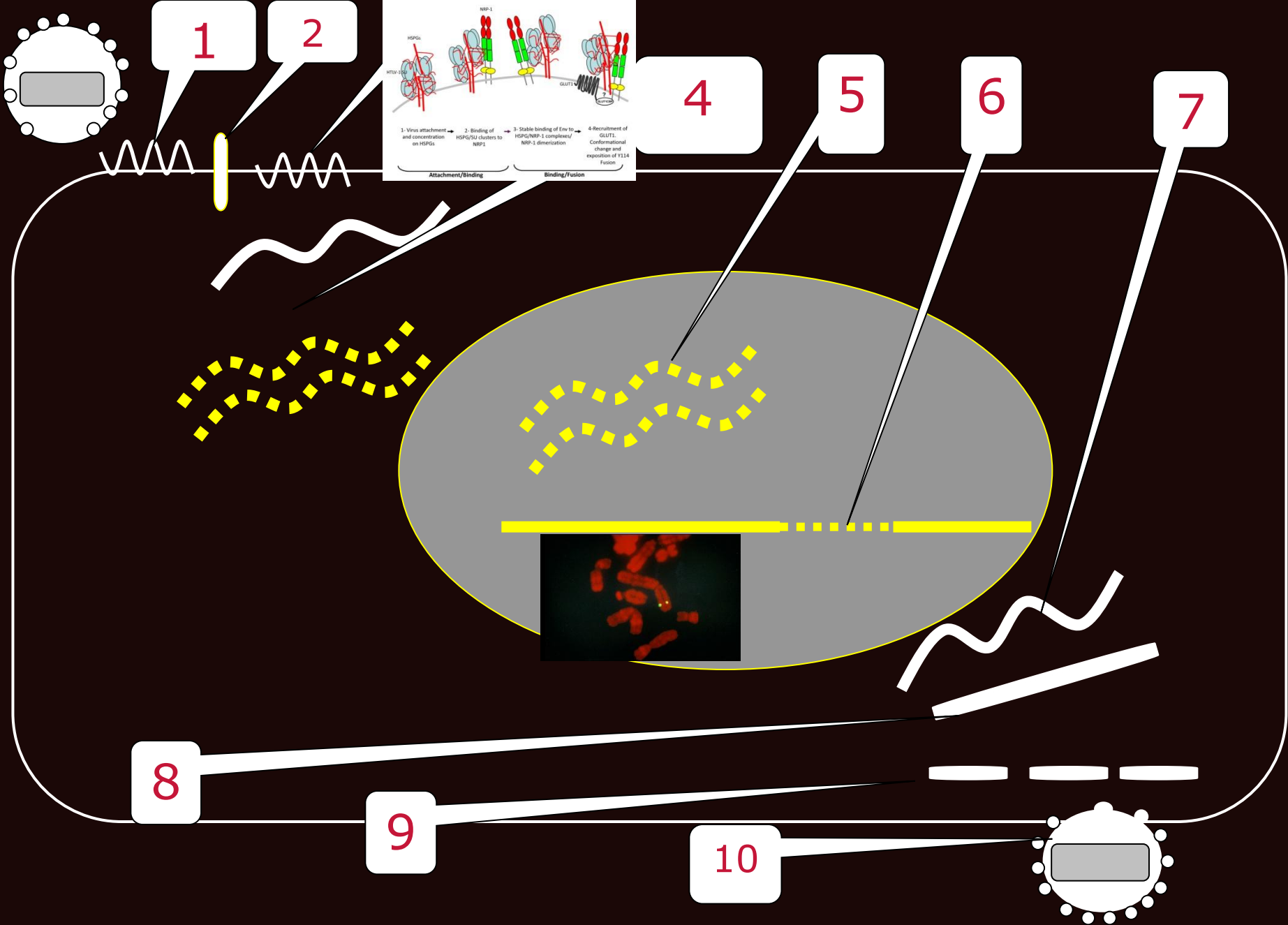
2- Binding of HSPG/SU clusters to NRP1

3- Stable binding of Env to HSPG/NRP-1 complexes/ NRP-1 dimerization

4- Recruitment of GLUT1. Conformational change and exposition of Y114 Fusion

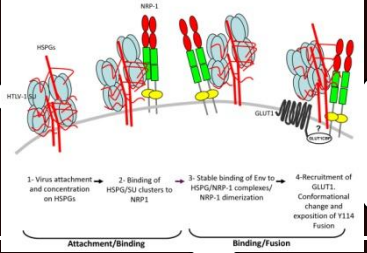
Attachment/Binding

Binding/Fusion



1

2



4

5

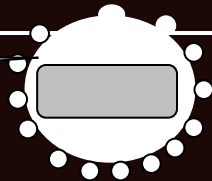
6

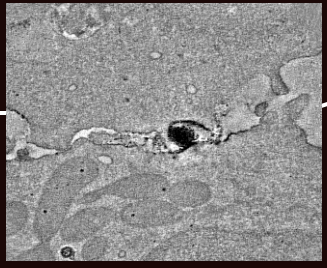
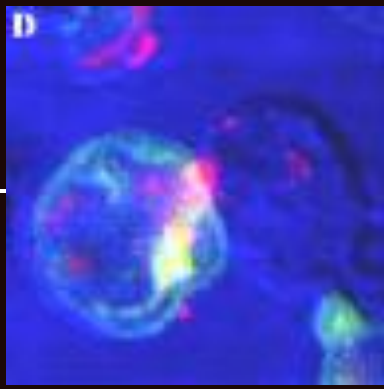
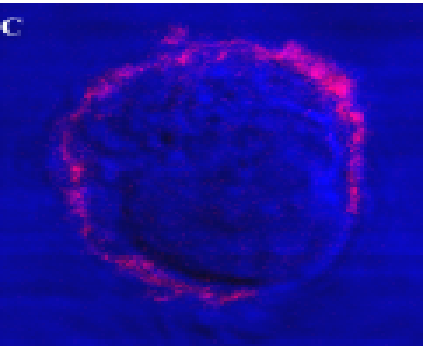
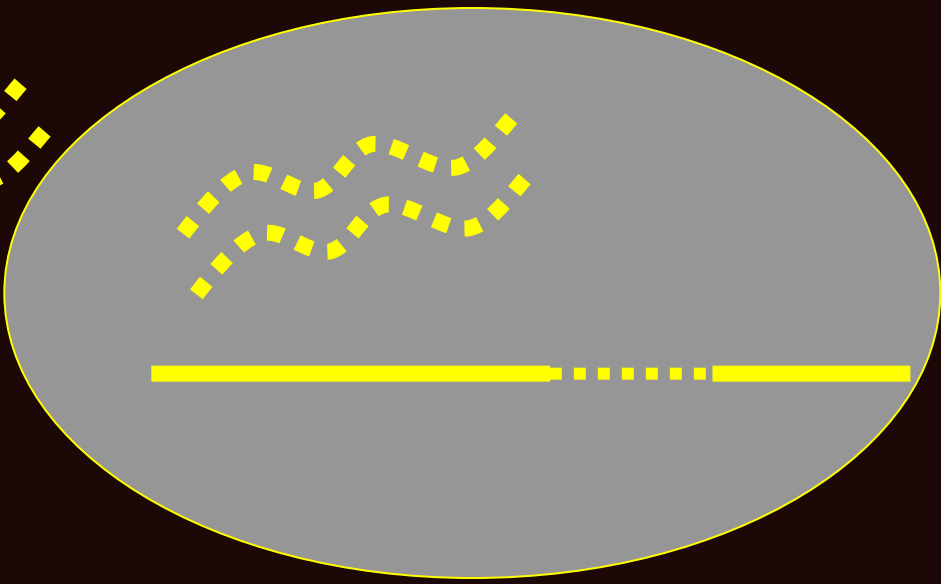
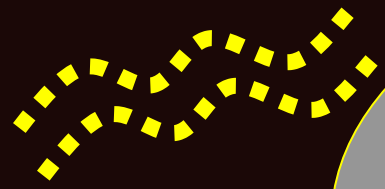
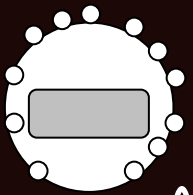
7

8

9

10

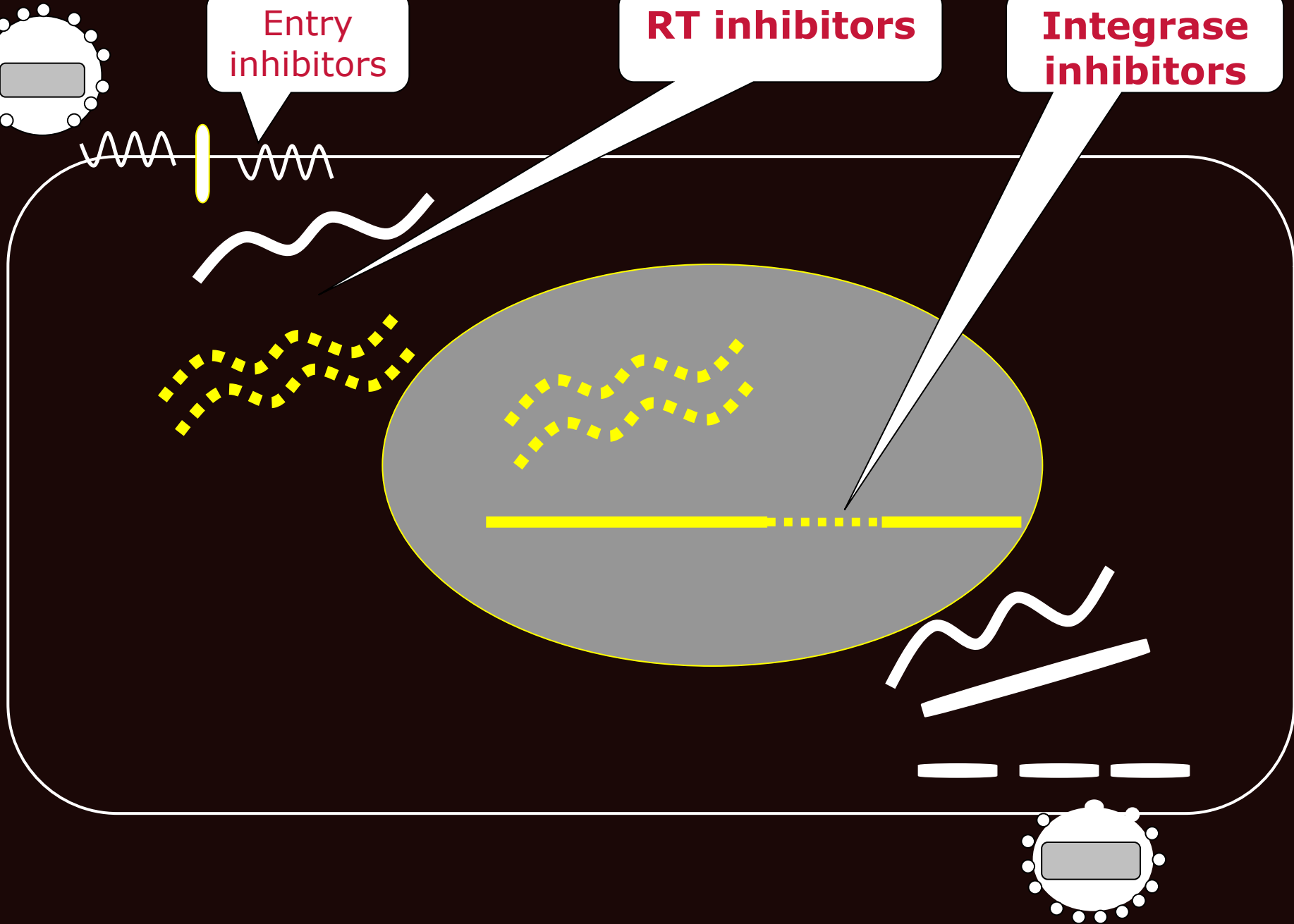




**Entry inhibitors**

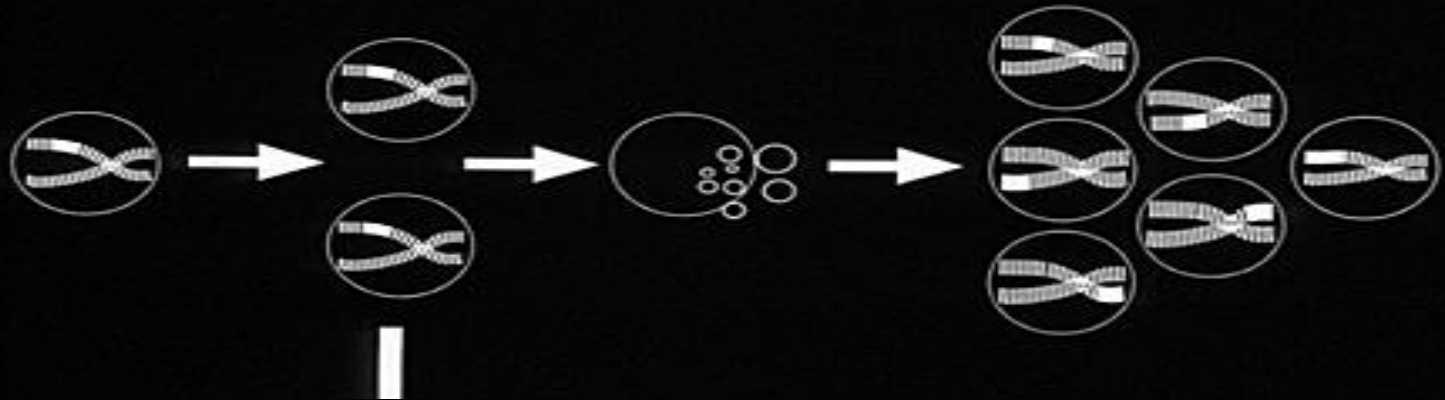
**RT inhibitors**

**Integrase inhibitors**



## LIFE CYCLE - 3

HORIZONTAL TRANSMISSION  
USING RT → RANDOM INTEGRATION



HTLV-1 RNA is rarely found in plasma

Blood plasma is not infectious

# **Early HTLV viral load dynamics – Viral load plateaus within 1 month of exposure**

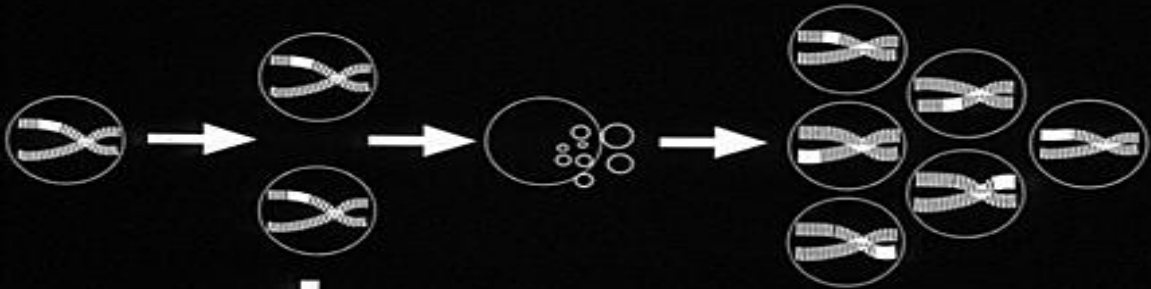
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Unpublished data

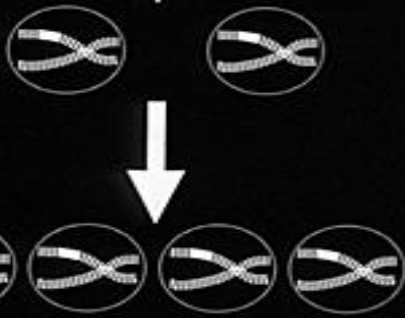


# LIFE CYCLE - 3

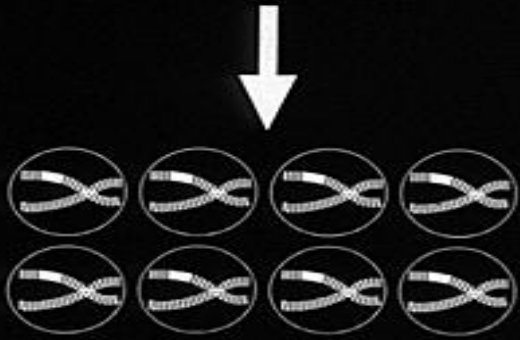
HORIZONTAL TRANSMISSION  
USING RT → RANDOM INTEGRATION



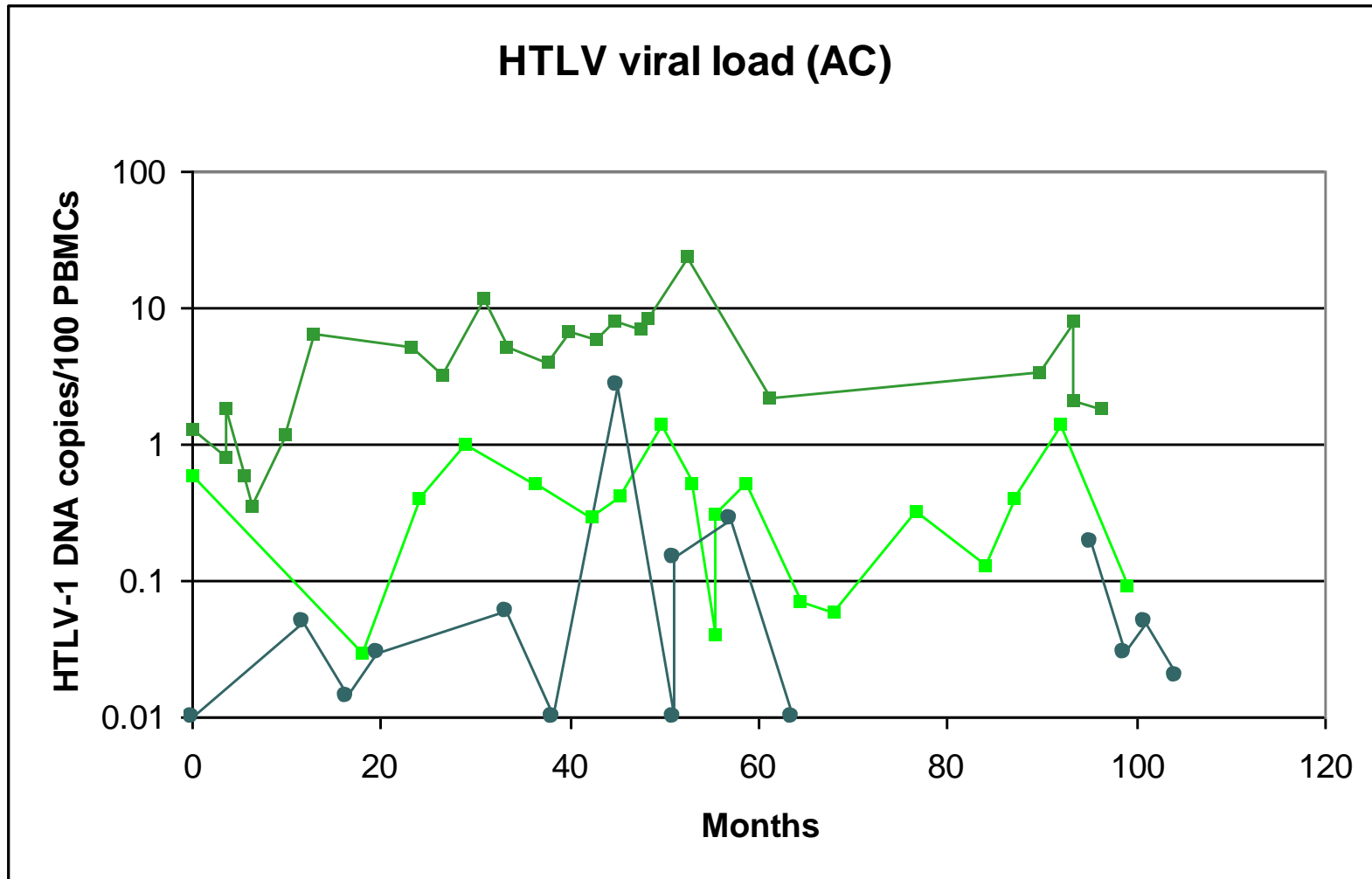
VERTICAL  
TRANSMISSION  
USING CELLULAR  
ENZYMES



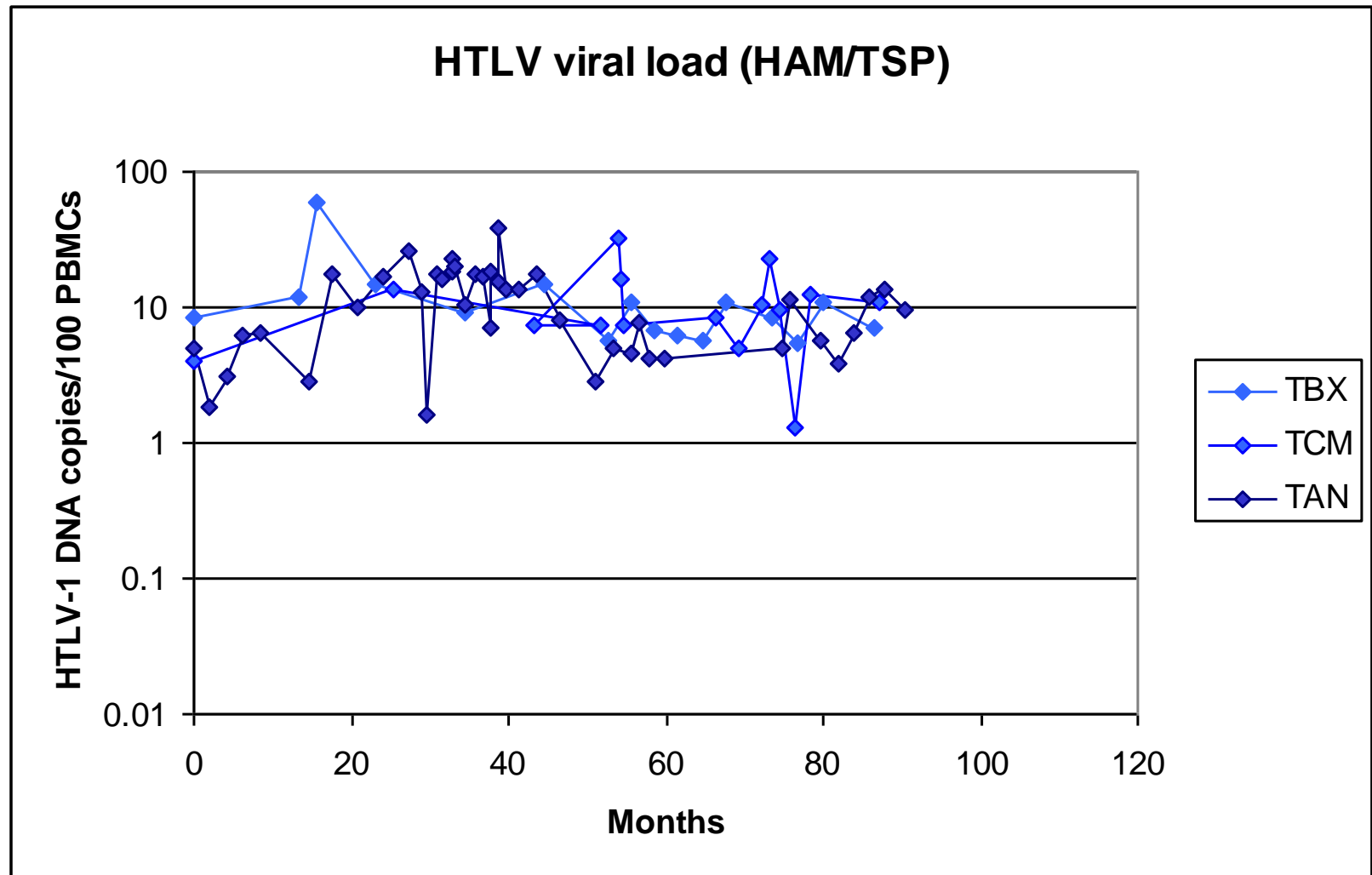
Oligo /  
Polyclonal  
expansion



# HTLV-1 viral load in asymptomatic carriers

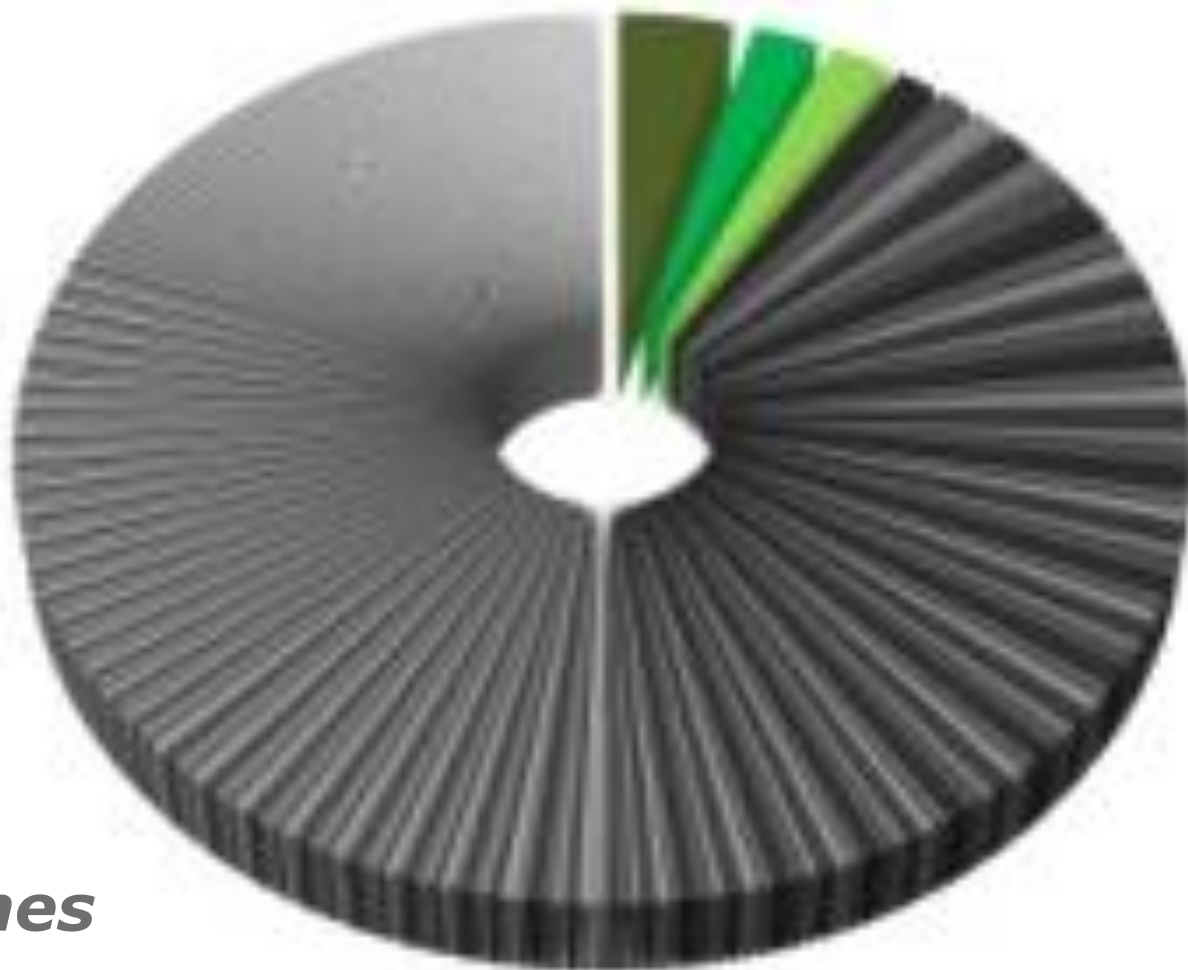


# HTLV-1 viral load in patients with HAM/TSP



# Clonal expansion in asymptomatic carrier

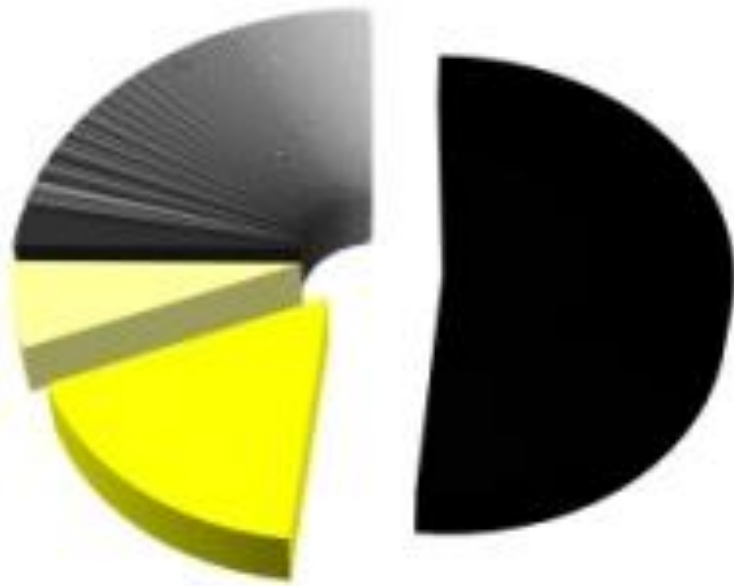
***Viral  
load  
0.03%***



***471 clones***

## Clonal pattern in patient with ATLL - lymphoma

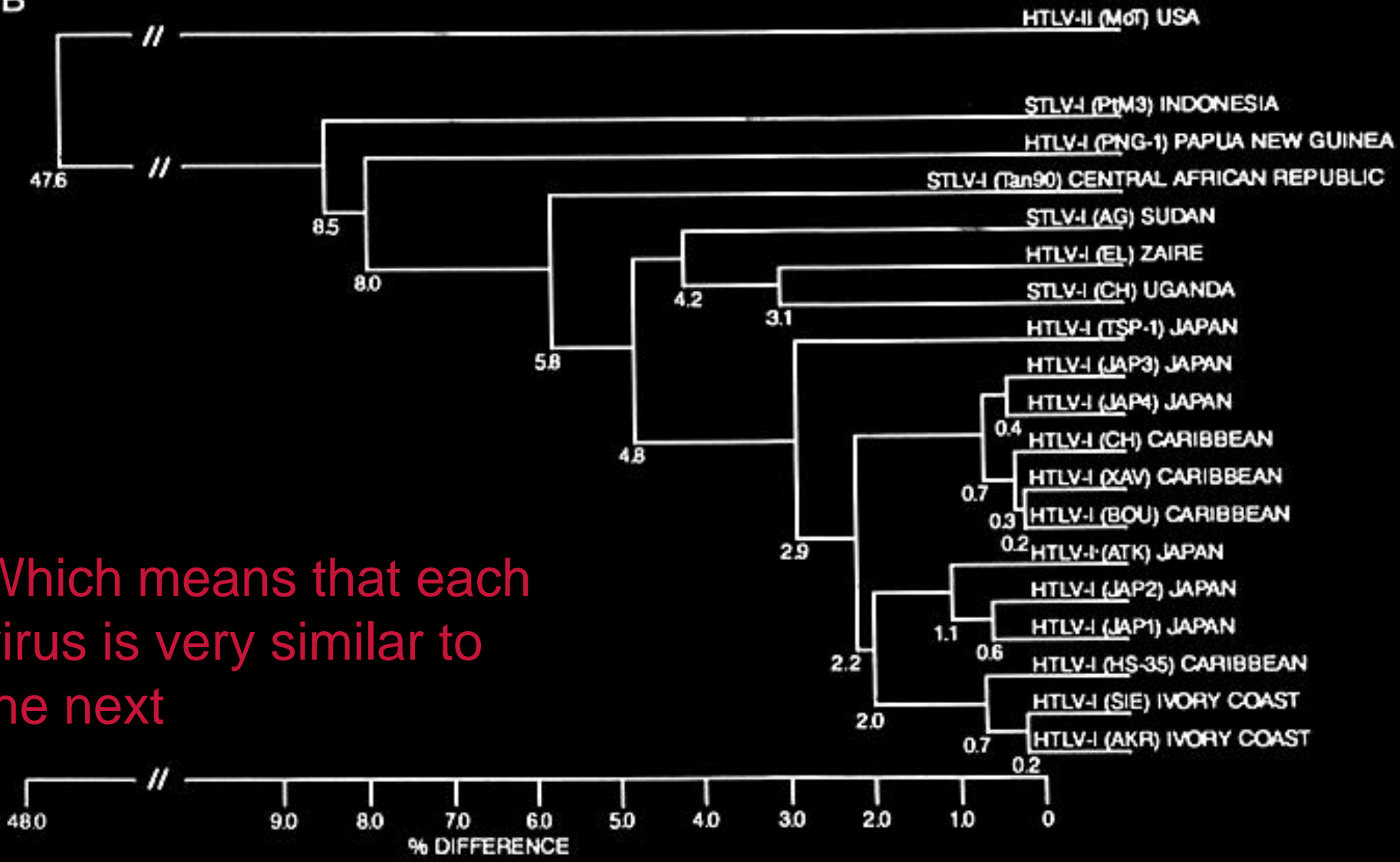
*Blood*



*Lymph node*

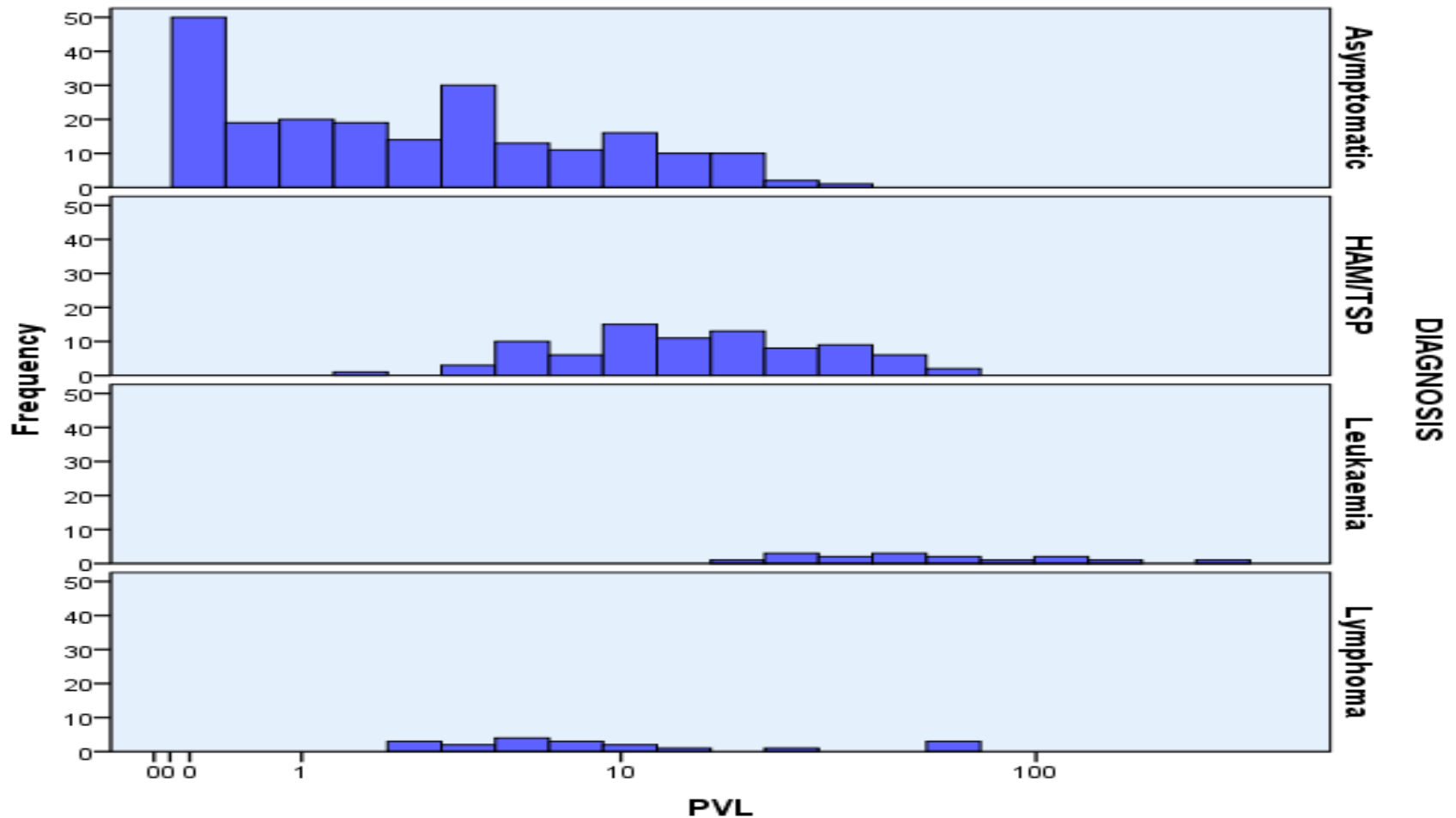


B



Which means that each virus is very similar to the next

# Distribution of HTLV-1 DNA load by disease state



Demontis et al, JAIDS Human  
Retrovirology 2012 e-pub

Footnote

## Case

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36 yr black male Lecturer

Presents with difficulty walking: stiffness

Examination: spasticity, proximal weakness, hyper-reflexia and positive Babinski's

CSF essentially normal

CT/MRI – non-diagnostic



## Investigations

HBsAg+ve HBeAg+ve HBeAb+ve

HBV DNA –ve

HTLV-I Ab +ve 1/4096 gpa

Western Blot p19 p24 RD21 and rgp46-I+ve

HTLV-I proviral load 9.96 copies /100 PBMC

**3 years later complains of fatigue, loss of appetite for 6  
– 8 weeks and...**

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## Investigations

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FBC normal

Film – unremarkable

U+E & LFTs normal

Bone Marrow - clear

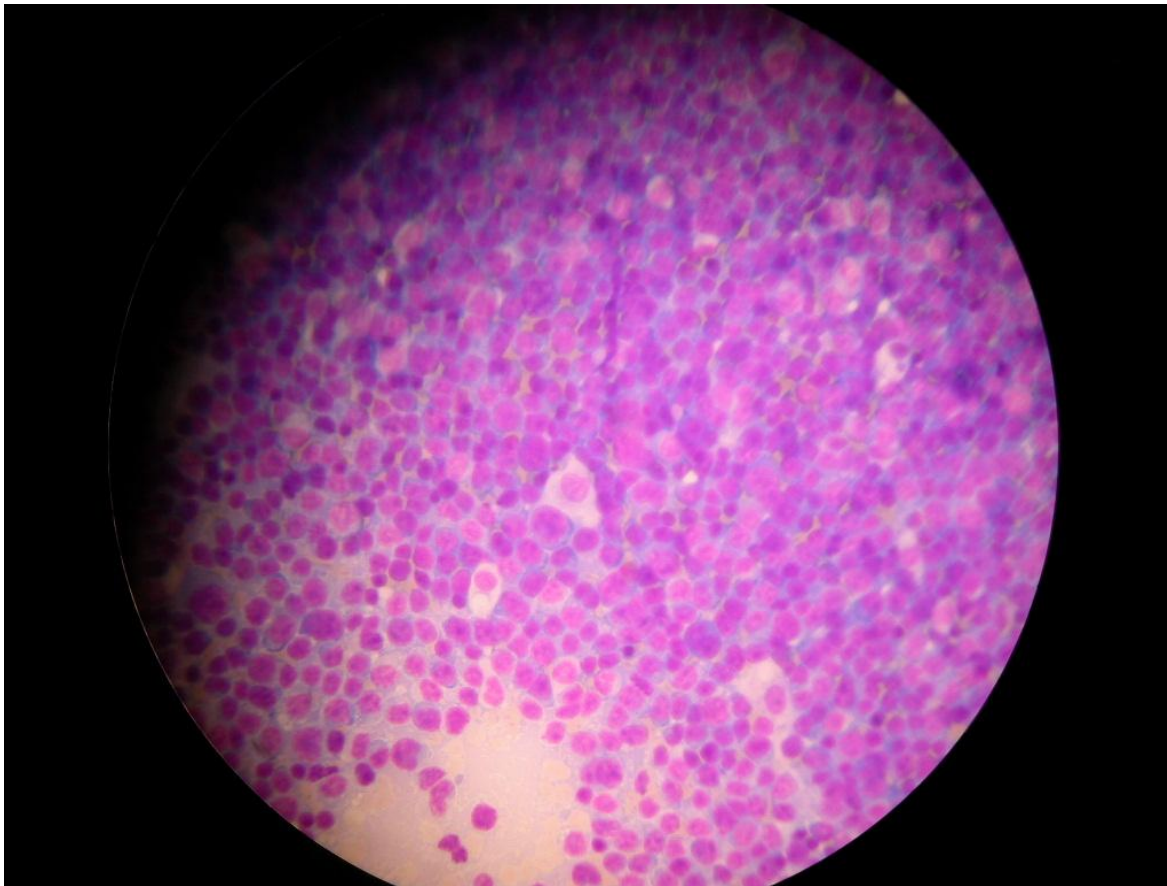
CT – LN everywhere

LDH 1070, Ca corrected 2.82, CPK 243

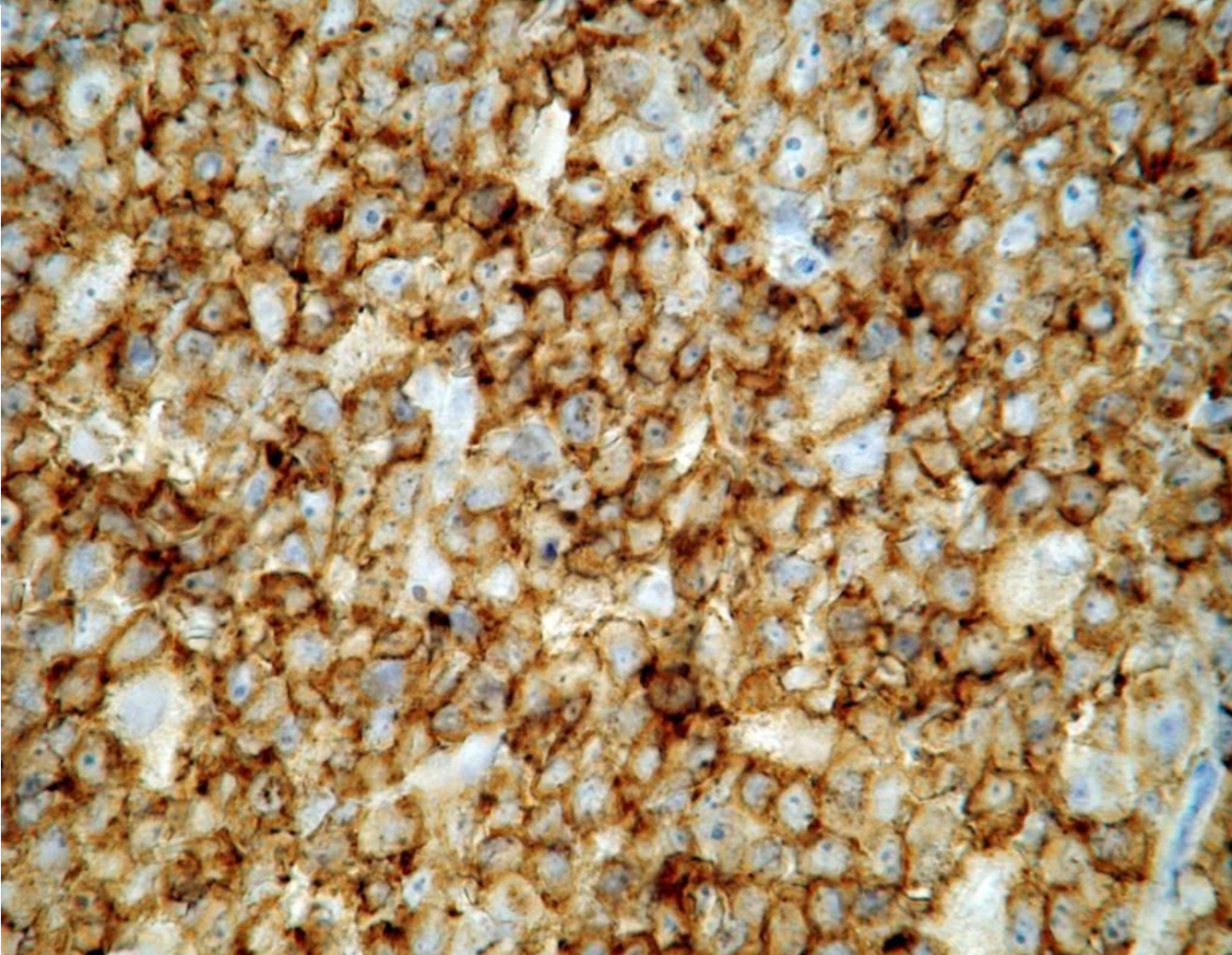
CD4/CD25 – 35%



## Touch prep of an excised lymph node

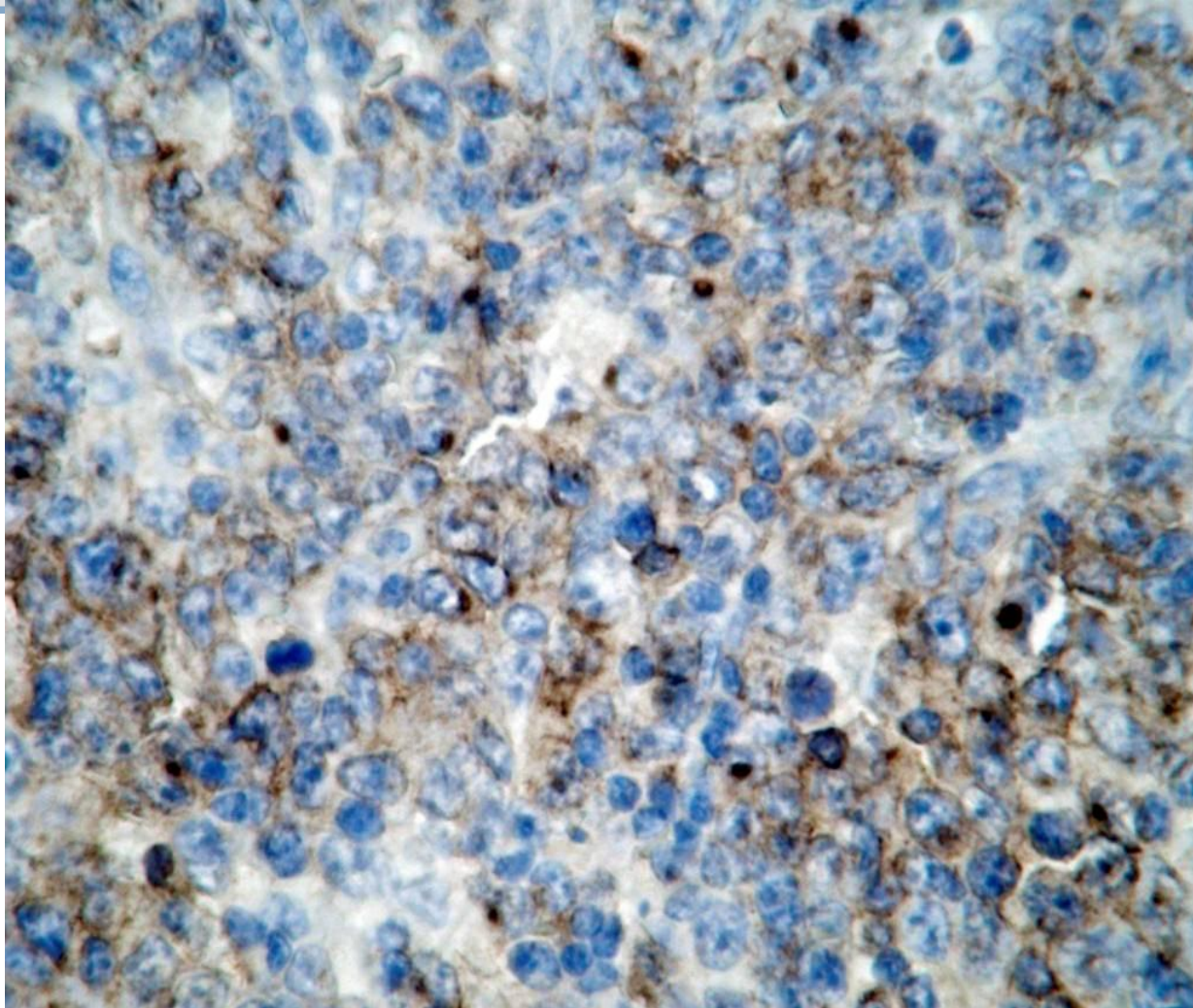


## CD4 immunohistochemistry

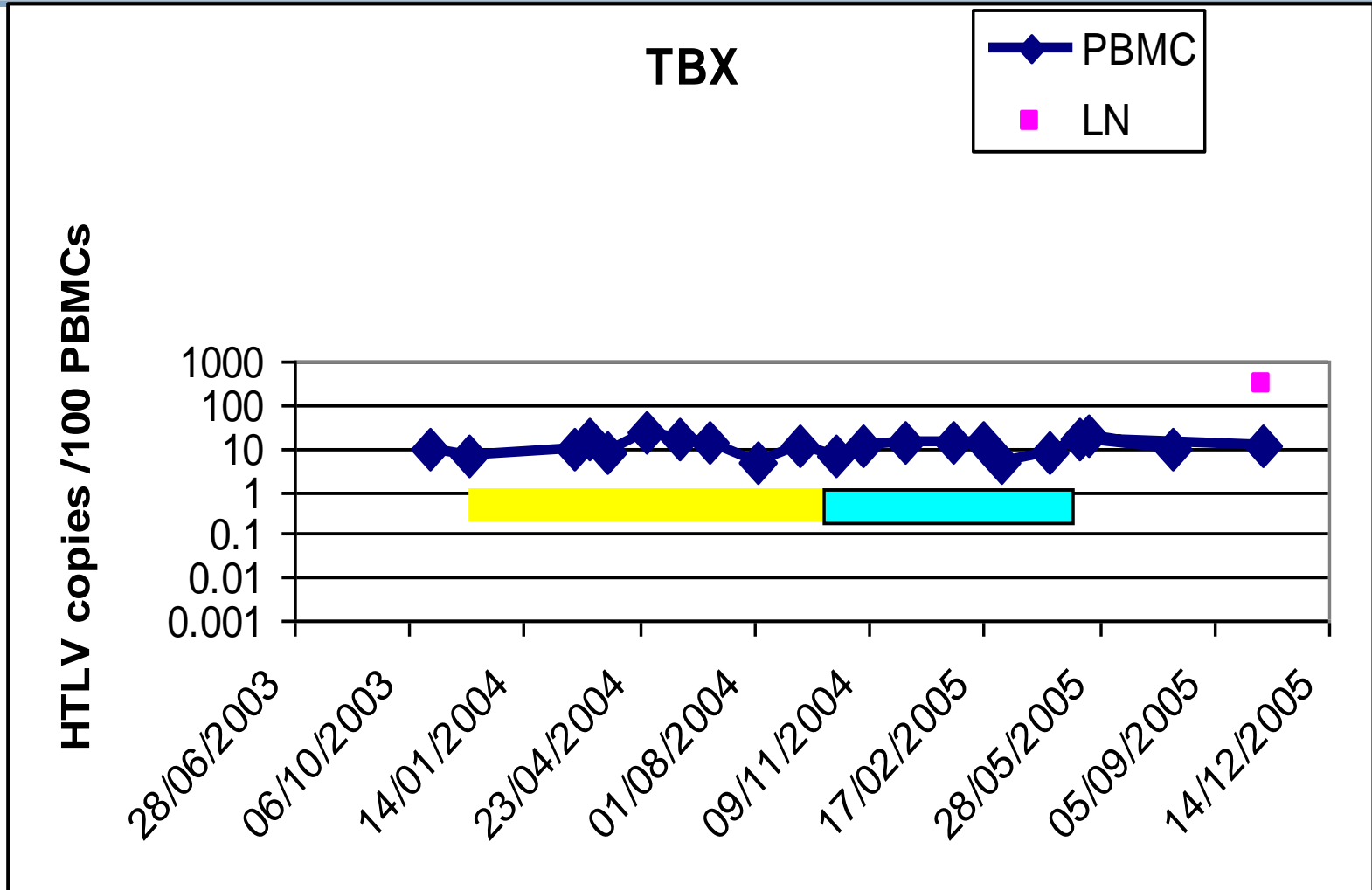




# CD25



# HTLV-1 viral load



## Diagnoses

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HTLV-1 associated myelopathy

HBV carrier

ATLL - Lymphoma

## Further reading

Chapter 25A. The Human T-cell Lymphotropic Viruses.

In The Principles and Practice of Clinical Virology 6th Edition Eds AJ Zuckerman, JE Banatvala & JE Pattison. J Wiley & Sons Ltd. Chichester, UK May 2009

The Neurology of HTLV-1 infection

Cooper SA *et al*

*Practical Neurology 2009 (JNNP)*

Mechanisms of HTLV-1 persistence and transformation.

Boxus M, Willems L.

Br J Cancer. 2009 Nov 3;101(9):1497-501. Epub 2009 Sep 29.

Current concepts regarding the HTLV-1 receptor complex.

Ghez D *et al*,

Retrovirology 2010, 7:99, doi:10.1186/1742-4690-7-99