Unmasking triggers for latency disruption and viremia control after treatment interruption

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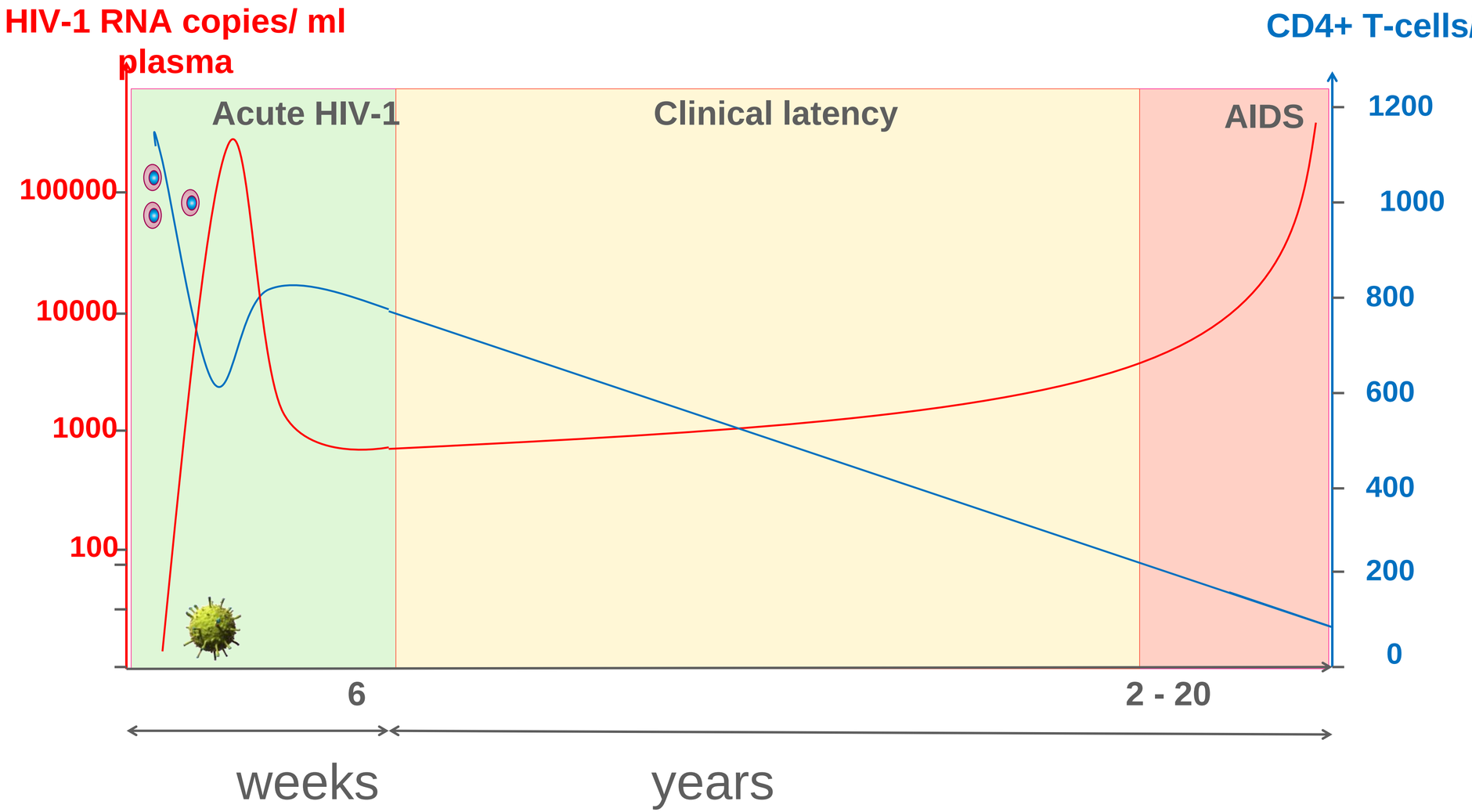
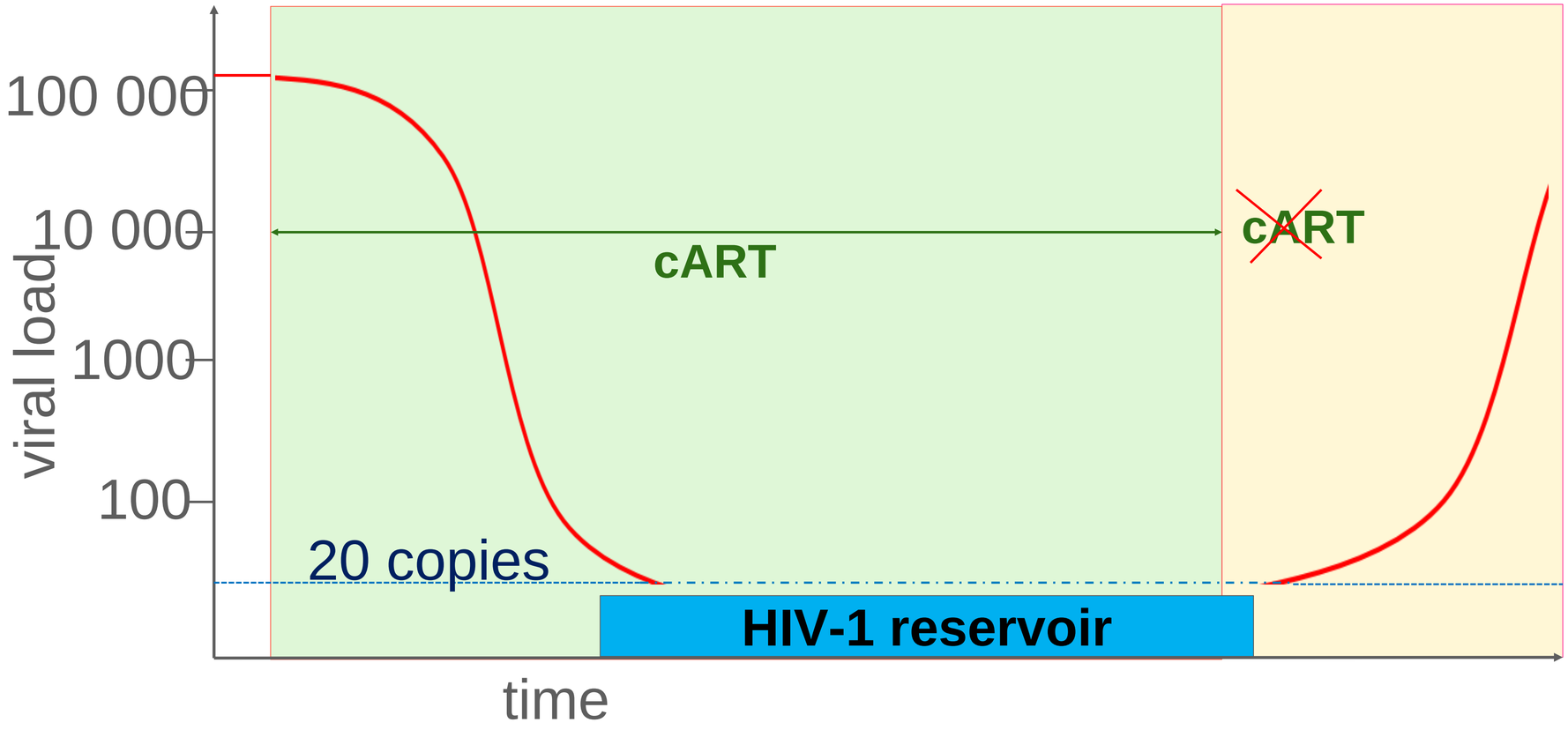
HIV pathogenesis



HIV latency


100 000
10 000
1000
100
viral load
cART
cART
20 copies
HIV-1 reservoir
time

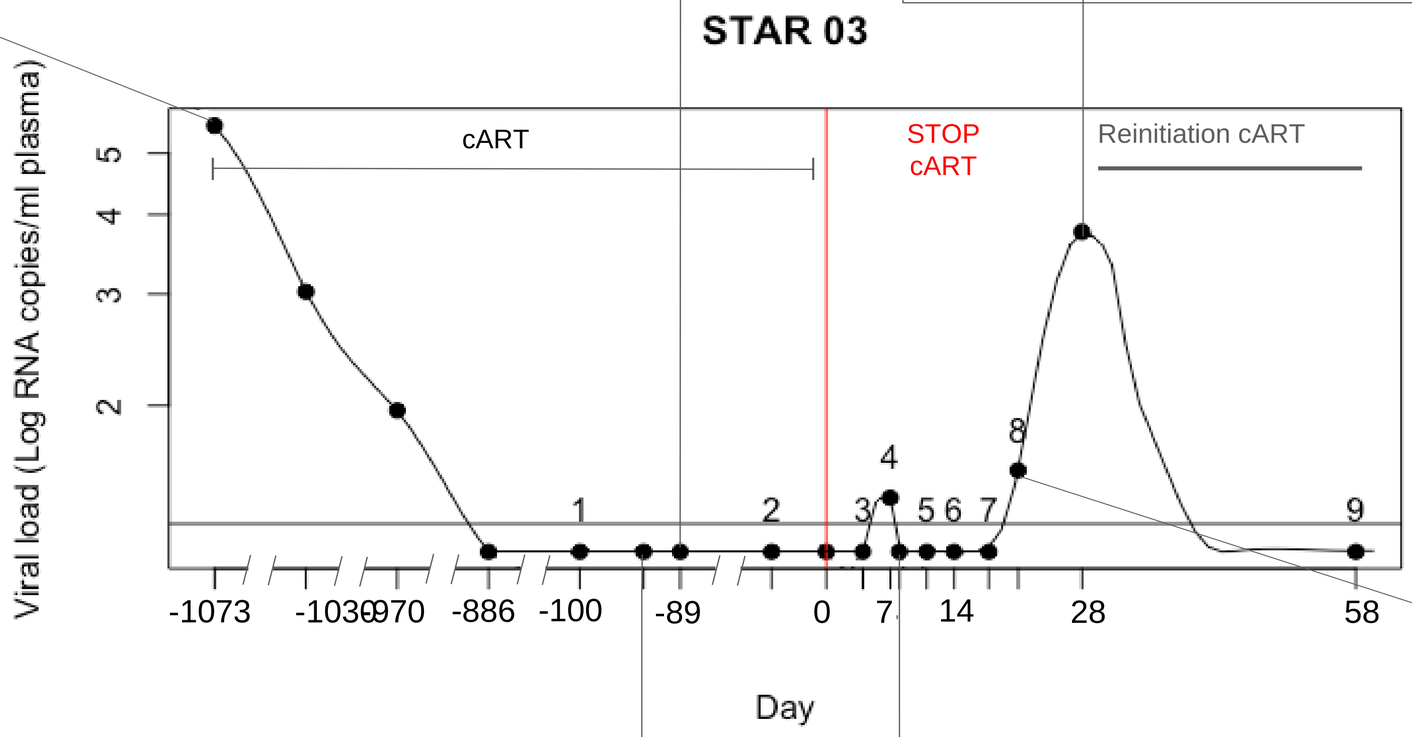
efore ART initiation**= T0**

Leucapheresis (day -89)=T1

PBMC in FCS
Plasma
Sorted cells

Sampling (day +28)=T4

Semen
Urine
CSF
Plasma
PBMCs in FCS
Sorted cells



1->9 Collection points within the study

LOQ (20 cp)

First detectable VL >30 copies/ml **= T3**

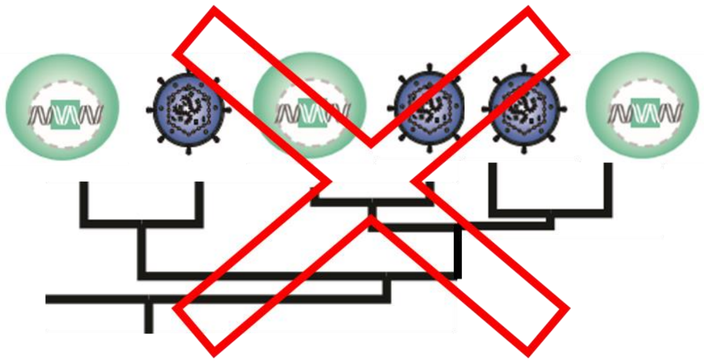
Sampling (day -93)=T1

GALT
LN
CSF
BAL
BM
Urine
Semen

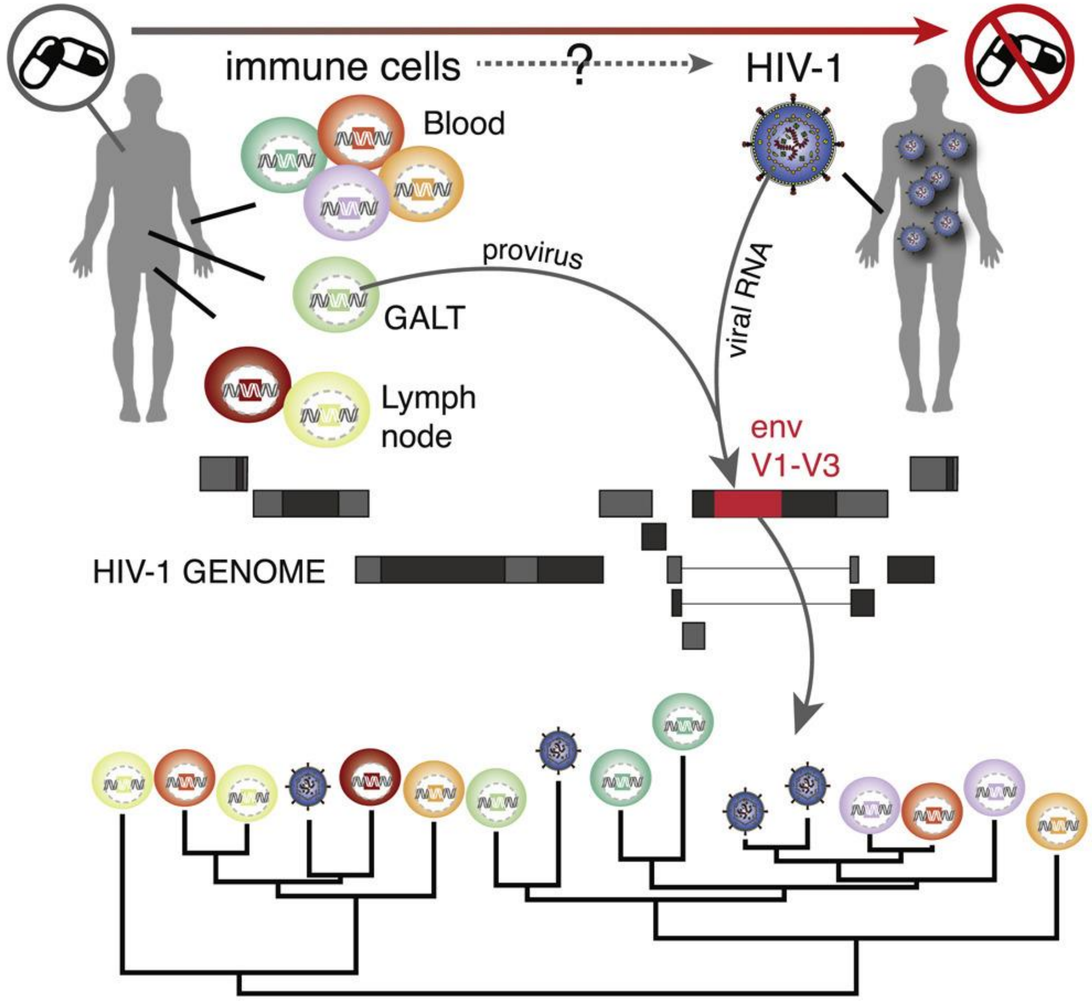
Leucapheresis (day +8)=T2

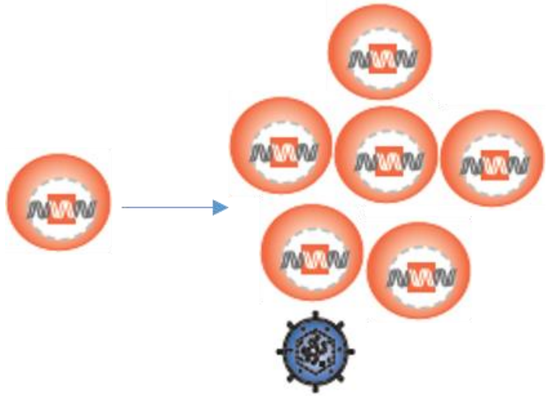
PBMC in FCS
Plasma:
Sorted cells

Where is the relevant HIV reservoir hiding? Which anatomical and cellular compartments constitute a barrier to HIV cure?

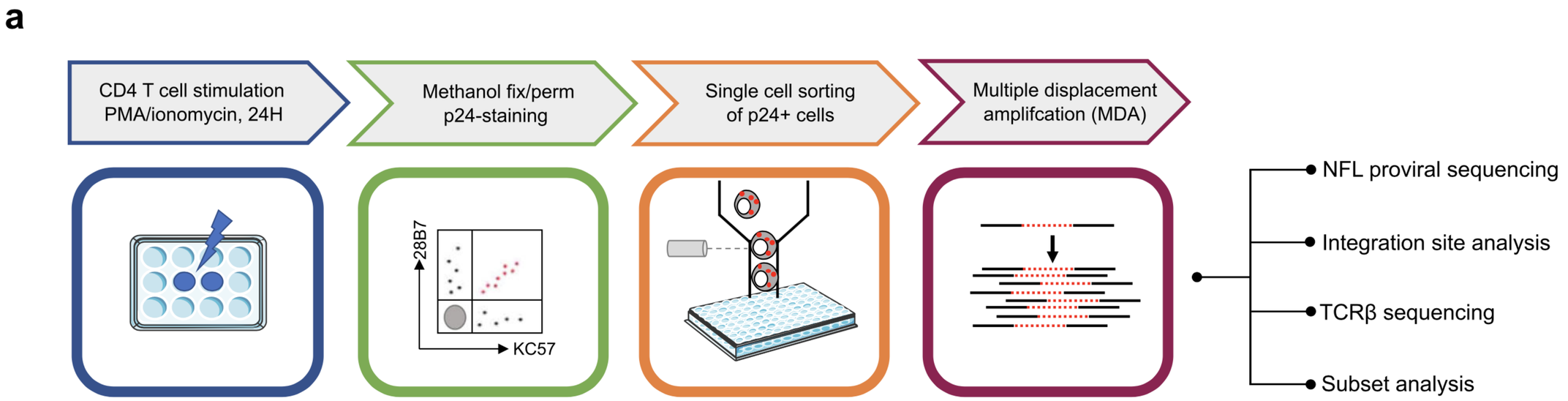


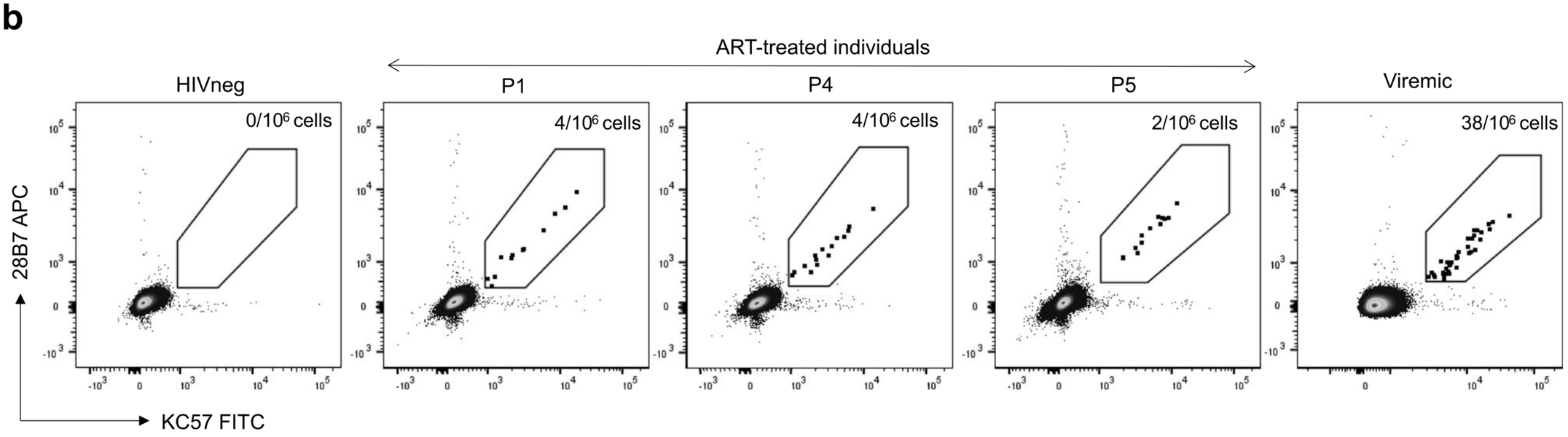
Rebound virus can originate from various cellular and anatomical compartments. The substantial inter-participant variability further supports that there is **no prominent source of rebound virus.**

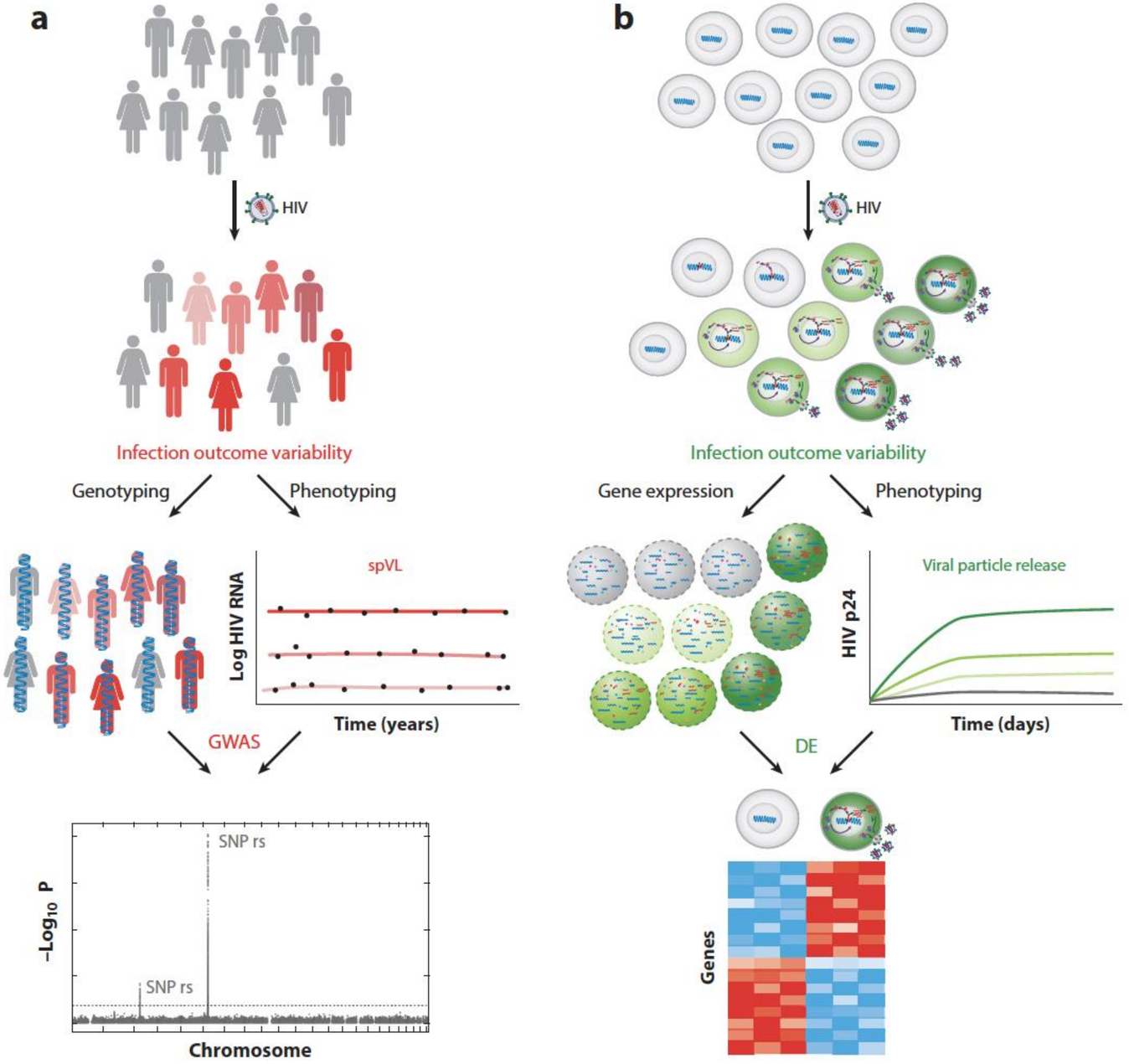


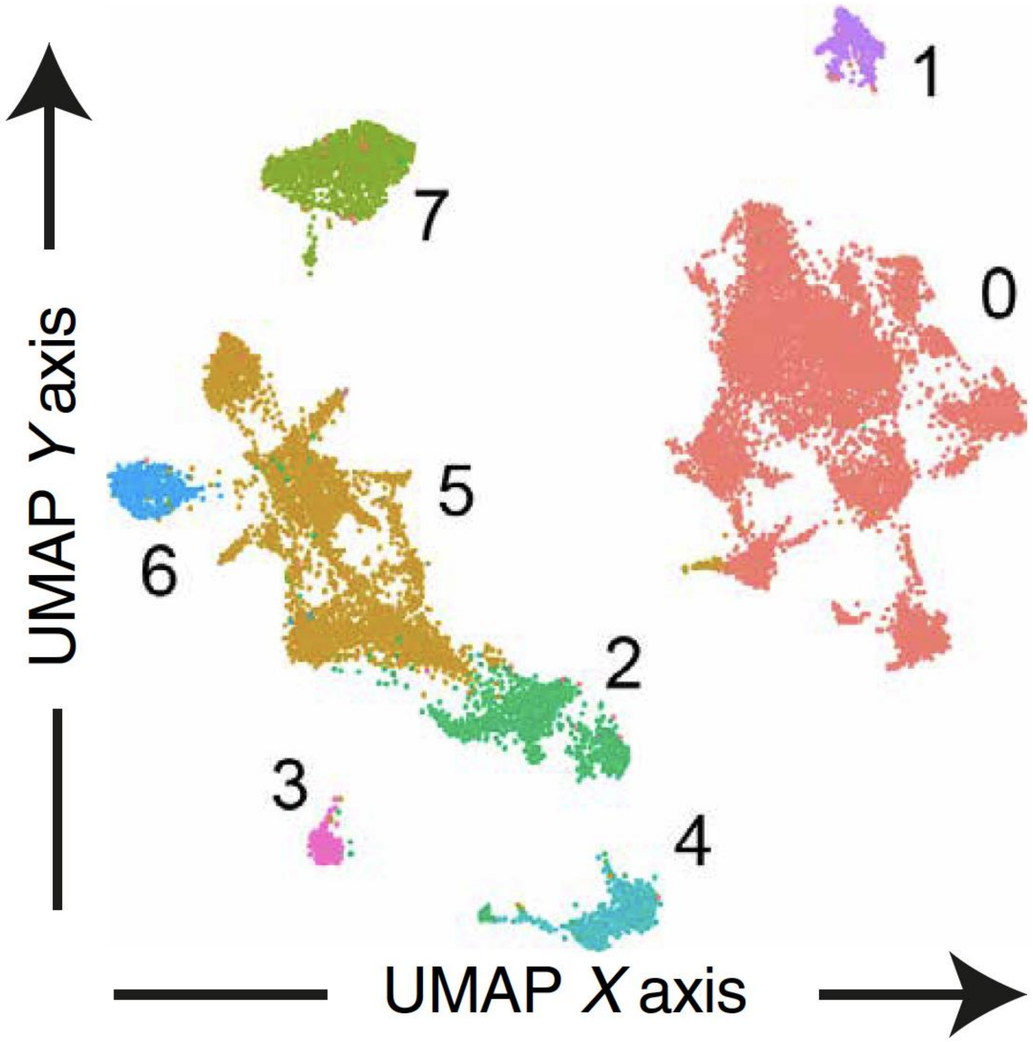


Cellular proliferation is a crucial driver of viral persistence, irrespective of the compartment or cell subset.


a
CD4 T cell stimulation
PMA/ionomycin, 24H
Methanol fix/perm
p24-staining
Single cell sorting
of p24+ cells
Multiple displacement
amplifcation (MDA)
28B7
KC57
NFL proviral sequencing
Integration site analysis
TCRβ sequencing
Subset analysis


b
ART-treated individuals
HIVneg
P1
P4
P5
Viremic
0/10^6 cells
4/10^6 cells
4/10^6 cells
2/10^6 cells
38/10^6 cells
28B7 APC
KC57 FITC


a
HIV
Infection outcome variability
Genotyping
Phenotyping
spVL
Log HIV RNA
Time (years)
GWAS
SNP rs
SNP rs
–Log10 P
Chromosome
b
HIV
Infection outcome variability
Gene expression
Phenotyping
Viral particle release
HIV p24
Time (days)
DE
Genes


1
7
0
5
6
2
3
4
UMAP Y axis
UMAP X axis

Deliverables

- Cytokine levels precisely determined by mesoscale in all STAR patients (N=11)
- CiTeSeq on PBMC’s to unravel cellular pathways involved in latency disruption (N=16, 4 patients, 4 timepoints)
- CiTeSeq on CD4+ T cells to link viral infection to specific cellular pathways (N=16, 4 patients, 4 timepoints)
- CiTeSeq on HIV specific CD8+ T cells to link viral rebound to specific cellular pathways (N=16, 4 patients, 2 timepoints)

Thank you

- Patients
- All people involved in setting up Citeseq
- Breach for the support!
- Sofie Rutsaert for initiating the analysis pipeline