Viral factors and T-cell sensitivity to activation dictate the loss of control in two cases of HIV-1 viremic non-progressors

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Non-pathogenic HIV

Non-pathogenic SIV

High viral load ($10^4 - 10^5$ copies/mL)
Stable CD4+ T cell counts

Sootey mangabeys
African green monkeys
OBJECTIVE

To evaluate the contribution of viral and/or host factors associated to the loss of control (LoC) in two unusual VNP cases to unravel the correlates of disease outcome.

Clinical characteristics of the VNP

IrsiCaixa’s VNP cohort: ART-naïve, median CD4 >500 cells/mm³, VL >10⁴ copies/ml, >8 years follow-up
- Replicative capacity assays in pooled CD8-depleted PMBCs
- Viral tropism assays in U87 cell lines (CCR5+ or CXCR4+)
- Phylogenetic analyses of clonal env sequences
RESULTS

1. Enhanced viral fitness is concomitant with a switch in coreceptor usage post-LoC

A. Replicative capacity

B. Viral tropism
2. Coreceptor switch confirmed by clonal env phylogenetic data

VNP-1

VNP-2

- R5 plasma isolate
- X4 plasma isolate

Pre-LoC

Post-LoC

GeSIDA 2019
RESULTS

3. Increased CD4+ and CD8+ T cell susceptibility to activation stimuli post-LoC

A. CD4+ T-cells (72h)

B. CD8+ T-cells (72h)
RESULTS

4. Similar T-cell subsets dynamics after stimuli in pre- and post-LoC samples

A. CD4+ T-cell subsets (72h PHA)

B. CD8+ T-cell subsets (72h PHA)
RESULTS

5. Low CCR5 expression on CD4+ T-cells in VNPs experiencing loss of control
CONCLUSIONS

• Viral factors, including the selection of particularly aggressive viral strains, and host factors driving increased susceptibility to activation of CD4+ and CD8+ T cells are associated with LoC in two cases of VNPs.

Our study reports previously unknown insights into the correlates of disease outcome in non-pathogenic HIV-1 infection.

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To the patients!