HIV VIRION PROFILING SUGGEST THAT CXCR3+CD4 T CELLS ARE THE MAIN HIV-PRODUCING CELLS

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Olivia Munoz[1], Riddhima Banga[1], Alessandra Noto[1], David Vinals[1], Francesco Andrea Procopio[1], Andrea Mastrangelo[1], Rachel Schelling[1], Craig Fenwick[1], Christine Lacabaratz[2], Yves lévy[2], Laurent Perez[1], Matthias Cavassini[3], Giuseppe Pantaleo[1], & Matthieu Perreau[1]

[1]Service of Immunology and Allergy, Lausanne University Hospital, University of Lausanne, [2]Vaccine Research Institute, Université Paris-Est Créteil, Faculté de Médecine, INSERM U955, Créteil, France, [3]Services of Infectious Diseases, Lausanne University Hospital, University of Lausanne.

BACKGROUND

The identification of markers of the HIV reservoirs represents a key step towards a HIV cure. In the present study, we postulated that the **identification of host molecules incorporated into HIV virions may help to identify their cellular origin**.

METHODS

We therefore assessed the incorporated protein profiles of plasmatic HIV virions of untreated viremic HIV-infected individuals collected during acute (N=10), chronic (N=10) or AIDS phases (N=10) or at the time of viral rebound post analytical treatment interruption (ATI; N=8). Briefly, HIV virions were captured using anti-gp120/41 coated beads and characterized using mass cytometry panels composed of 57 isotope-labelled mAbs (**Figures 1 and 2**).

RESULTS

We showed that HIV virions collected during AIDS or post ATI harbored distinct incorporated protein profiles as compared to HIV virions from plasma collected during acute or chronic phases (P<0.05) (**Figure 3**). Interestingly, a large proportions (70-85%) of virions collected during acute, chronic or post ATI harbored CXCR3, while other molecules expressed on activated CD4 T cells (ICOS, Lag-3 or CD40L) were less frequently detected (30-40%; P<0.05) (**Figures 3 and 4**). We therefore conducted a series of in vitro experiments to determine whether the incorporation of the aforementioned molecules may rely on passive and/or active mechanisms. We investigated the potential interactions between the intracellular tails (ic) of CXCR3, ICOS, Lag-3 or CD40L with immobilized recombinant p17 or p24 proteins using biolayer interferometry based assay. The data demonstrated that only p17 protein interacted with the icCXCR3, while no interaction was detected between icICOS, icLag3 or icCD40L and p17 (**Figure 5**). To further determine the affinity of p17/icCXCR3 interactions, p17 was immobilized and exposed to various concentrations of icCXCR3 ranging from 0 to 450 nM. The data demonstrated that p17 protein interacted with icCXCR3 protein with a constant of dissociation (KD) value of 0.3 10−6 M (±2.10−11) (**Figure 5**).

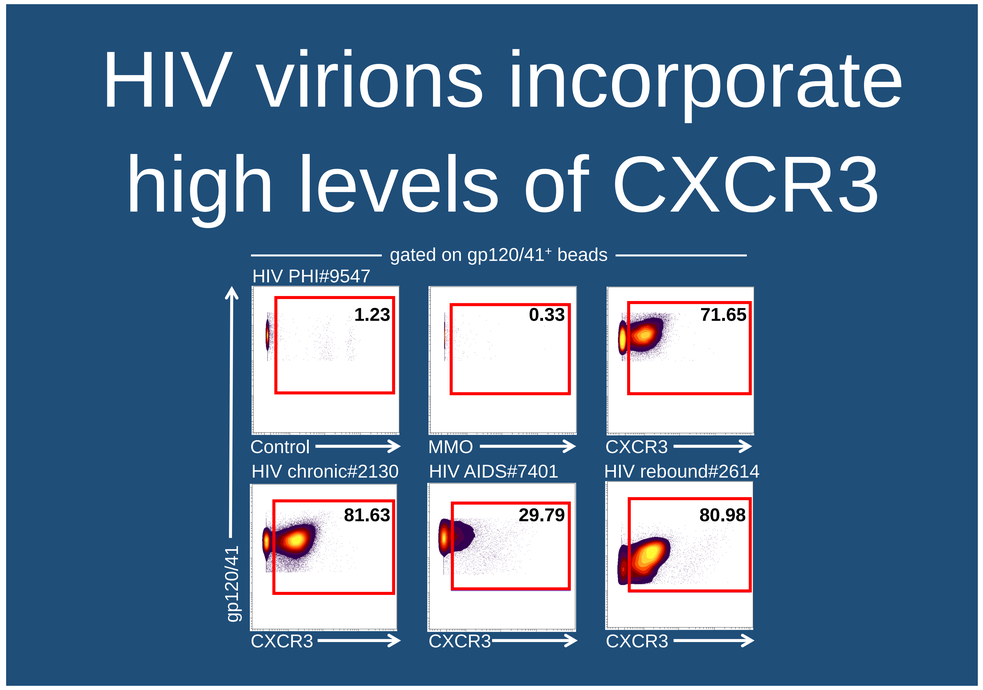


Figure 1: Schematic representation of HIV virions (gp120/41+ vesicles) captured from plasma of viremic HIV-infected individuals

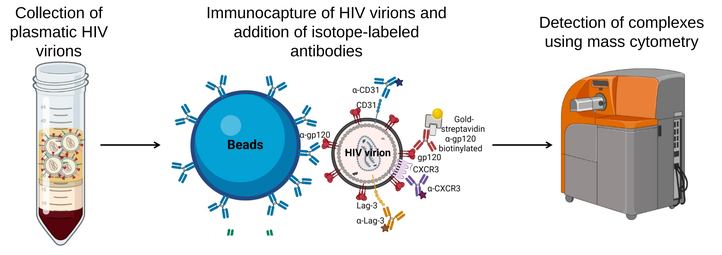


Figure 2: Plasma HIV virions incorporate a broad variety of host molecules mainly expressed by lymphoid cells

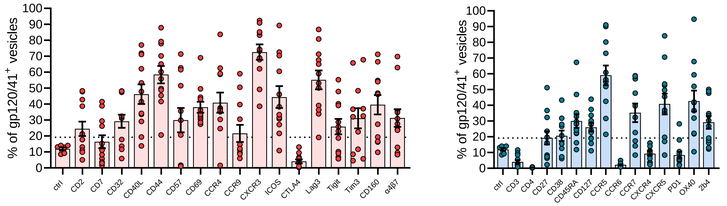


Figure 3: Plasmatic HIV virions mainly incorporated T-cell activation markers expressed at various virological phases of HIV infection

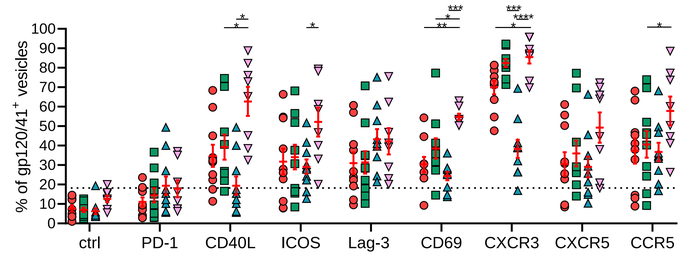


Figure 4: CXCR3, CD40L, Lag3, and ICOS are expressed on activated CD4 T cells

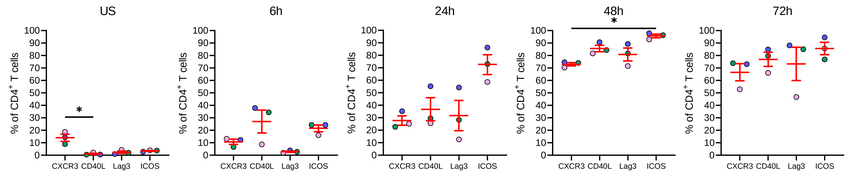
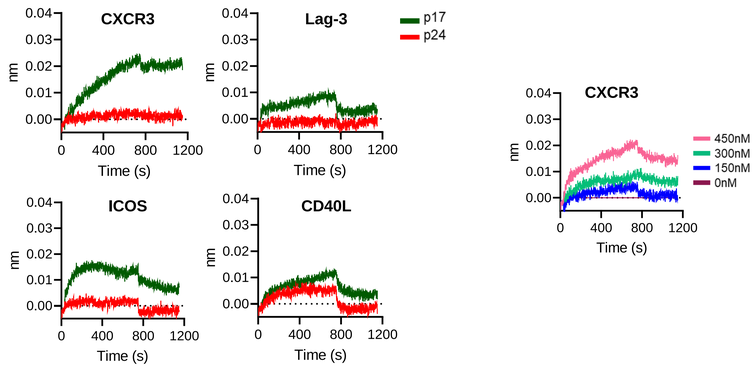


Figure 5: CXCR3 incorporation into HIV virions involves direct interactions between p17 HIV matrix proteins and the intracytoplasmic domains of CXCR3



CONCLUSIONS

Taken together, the developed experimental strategy indicate that CXCR3 expressing CD4 T cells may serve as a major HIV cellular compartment for HIV production.

ADDITIONAL KEY INFORMATION

Contact: Olivia.Munoz-Monje@chuv.ch