HIV-2 Translation-Competent Reservoir Cells Phenotype Is Similar Yet Different Compared to HIV-1

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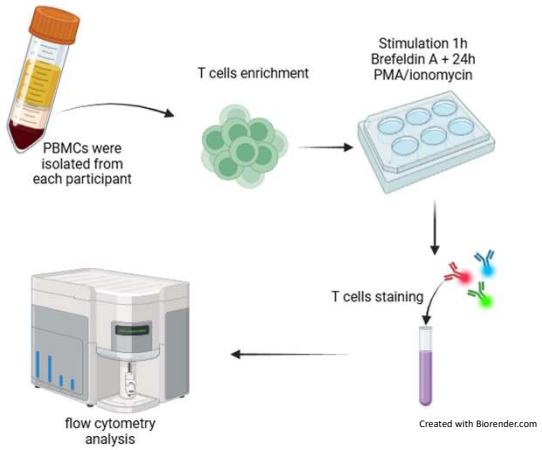
BACKGROUND

While most studies focus on HIV-1 infection, the knowledge on HIV-2 is limited. However, HIV-2 is responsible of a less virulent infection and can stay undetectable without any treatment, and the mechanism is still unknown. Some studies focused on biochemical explanations, but none looked at the reservoir and its phenotype while HIV-1 reservoir has been highly studied.

With that study, we used a single-cell approach to test parameters already identified as enrichment markers in HIV-1 infection to see if they were also associated with HIV-2 translation competent reservoir.

METHOD

We paired two cohorts of people living with HIV-1 and people living with HIV-2 (n=22 each) based on sex, T CD4⁺ cells count and undetectability duration. Samples were analyzed using HIV-Flow method :



Markers used for staining :
- Vivid : viability
- p26/p24 (anti p24 KC57 – anti p24 28B7)
- memory T cells phenotype : CD45RA, CCR7, CD27
- VLA-4 (α4 and β1), Ki67, HLA-ABC, CD4, PD-1

As HIV-1, HIV-2 targets preferentially **T_{CM} and T_{TM}** but the translation competent **reservoir is smaller** in HIV-2 infection and is **more likely to express PD-1.**

RESULTS

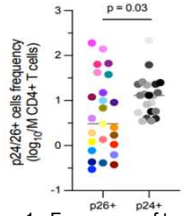


Figure 1 : Frequency of translation competent infected cells. p26+ : HIV-2 – p24+ : HIV-1

HIV-2 translation competent reservoir was smaller than HIV-1 (median respectively 3/10⁶ CD4⁺ T cells and 13/10⁶CD4⁺ T cells) (Figure 1). For both viruses, the frequency also decreased with the global CD4+ T cells count and increased with the frequency of memory (CD45RA-) and non-quiescent (Ki67+) CD4+ T cells.
HIV-2 targeted the same type of memory T cells than HIV-1 : T_{CM} and T_{TM} were enriched in p26 (respectively : fold increase 2,1x p<0,0001 and fold increase 2,4x p=0,04) and rarely expressed T_N et T_{TD} phenotype (fold increase 0,5x p=0,0002 and 0,06x p<0,0001) (see Figure 2). Even though HIV-2 seemed to target less T_{TM} cells compared to HIV-1 (p=0,03).

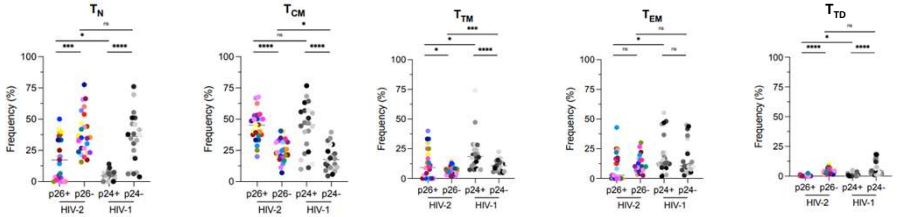


Figure 2 : p26/p24 enrichment in the different subtypes of memory T cells.

RESULTS

Enrichment in p26⁺ cells was found in HLA-ABC$_{low}$ (p=0,002), Ki67⁺ (p<0,0001), PD-1⁺ (p<0,0001), α4⁺ (p<0,0001) and VLA-4⁺ cells (p=0,0006).

HIV-2 reservoir cells showed a higher expression of α4 but this was not found in the VLA-4 expression. The only marker that showed a significant difference was PD-1 expression : HIV-2 translation competent reservoir showed higher frequency of PD-1⁺ cells than HIV-1 (p<0,0001).

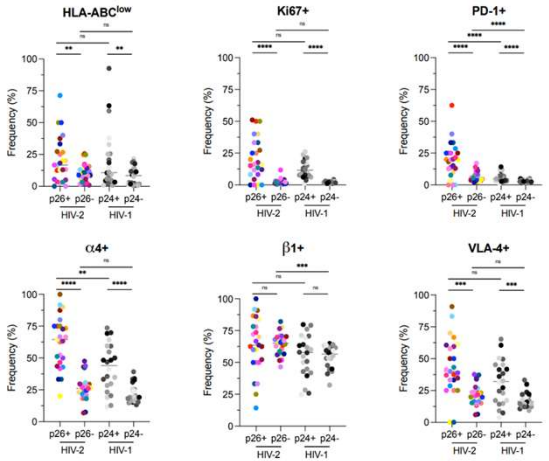


Figure 3 : Comparison of frequency of expression of each marker in p26+/p24+ cells and p26/p24- cells and comparaison inbetween each cohorts.
(*, p<0.05; **, p<0.01; ***, p<0.001; ****, p<0.0001)

CONCLUSION

HIV-2 translation competent reservoir is smaller than HIV-1 and is less found in the T_{TM} cells.

Both viruses share similar phenotypic enrichments, but HIV-2 reservoir cells are more likely to express PD-1 which could be an immunosenescence signature and might explain a part of the mechanism that makes HIV-2 less virulent.

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