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Oral presentation

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S03-04 OA. Transitional and central memory CD4 T cells are highly infected in long term non progressors and elite controllers

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Background

Long Term non Progressors (LTNP) and Elite Controllers are characterized by a controlled HIV reservoir reflecting peculiar host genetic traits and strong specific immunity. We investigated how cell differentiation influences the distribution of HIV reservoir among CD4 T cells.

Methods

We explored the distribution of cell-associated HIV-DNA (caHIV-DNA) in LTNP-Controllers, -Low Viremics and Slow Progressors. We sorted live resting cells subsets from CD4 as defined by combination of CD45RA/CD27/CCR7, quantified caHIV-DNA in each fraction and tested the viral *in vitro* inducibility.

Results

Quantification revealed a highly reproducible distribution hierarchy of caHIV-DNA, stable over up to 10 years: TM cells followed by CM are highly infected (medians: 3.12 and 2.87 log cps/million cells) and TM significantly more than in EM, E27- and N cells (medians: 2.29, 2.42 and 1.95; $p < 0.01$). This distribution is not related to CCR5 expression and not influenced by genetic background (HLA or CCR5Δ32 deletion). The *in vitro* activation induced HIV replication in Memory subsets independently of their infection levels. In contrast HIV replication is poorly induced in the highly proliferative naive subset though they are as infected as EM. IL-7 seems

to be able to increase HIV production from LTNP-C naive cells.

Conclusion

In LTNP, HIV-DNA is concentrated in CD4 subsets with intermediate *in vivo* turn-over and survival: mainly TM followed by CM cells while it remains low in cells with high turn-over but low survival such as EM or E27- cells or with low turn-over and hi survival such as N cells. This distribution is highly stable overtime and independent of genetic background. Inducibility of HIV production does not strictly parallel this distribution. Altogether our results demonstrate that distinct mechanisms of HIV control dictated by or associated with T cell maturation and dynamics influence the stable low level of HIV reservoir in LTNP and Elite Controllers.