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Low SAMHD1 expression following T-cell activation and proliferation renders CD4+ T cells susceptible to HIV-1

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BACKGROUND

HIV-1 replication depends on the state of cell activation and division. It is established that SAMHD1 restricts HIV-1 infection of resting CD4+ T cells. The modulation of SAMHD1 expression during T-cell activation and proliferation however remains unclear, as well as a role for SAMHD1 during HIV-1 pathogenesis. *We demonstrate here that SAMHD1 expression is modulated after T-cell activation/proliferation and that SAMHD1^{low}CD4+ T cells are preferentially susceptible to HIV-1 infection.*

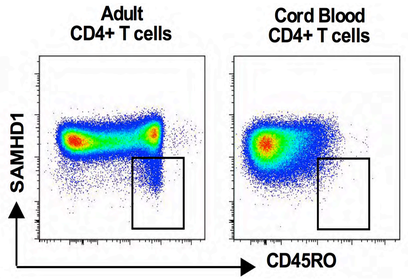
METHODS

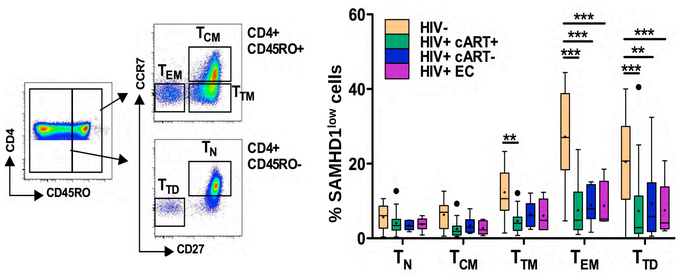
SAMHD1 expression was assessed by flow cytometry and qRT-PCR in peripheral blood and lymph nodes from cohorts of HIV-1 infected subjects under anti-retroviral treatment or not, and controls.

Phenotype and functional analyses were performed ex vivo, after *in vitro* activation as well as after *in vitro* infection.

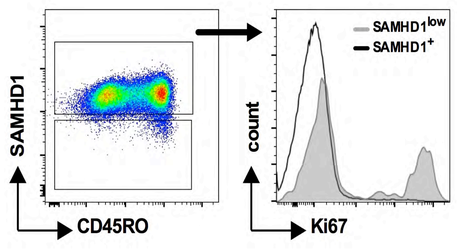
RESULTS

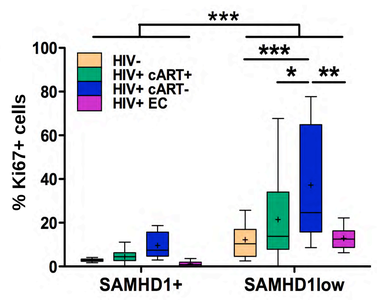
SAMHD1^{low} CD4+ memory T cells are highly differentiated and are significantly depleted in HIV-1 infected patients

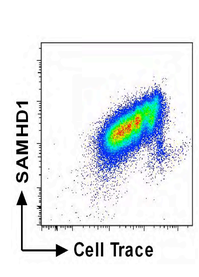


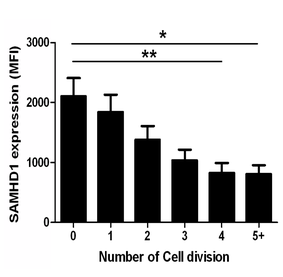


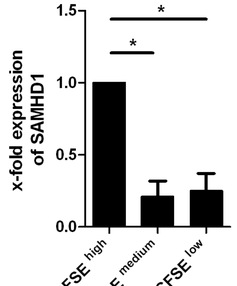
SAMHD1 expression is decreased during T cell proliferation *in vivo* and *in vitro*



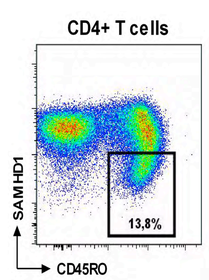


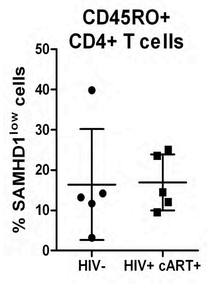


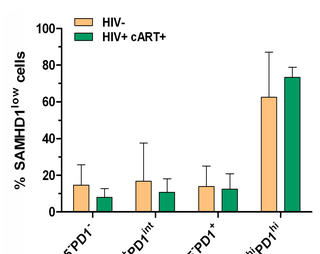


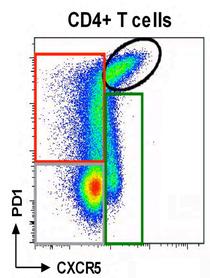


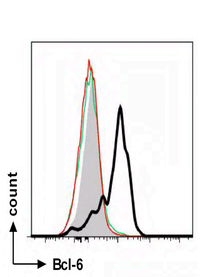
Tfh CD4+ T cells from lymph nodes in HIV-1 infected patients express low levels of SAMHD1

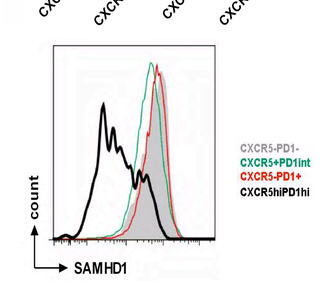




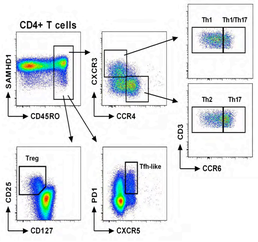


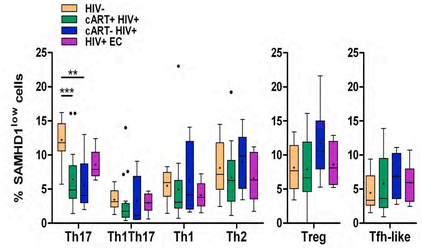




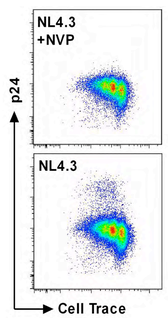


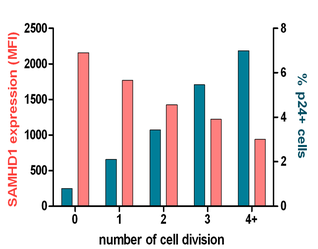
SAMHD1^{low} Th17 cells are preferentially depleted during infection

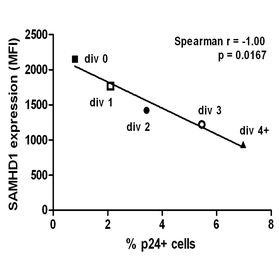




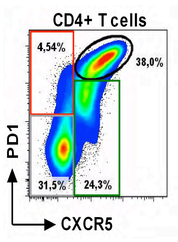
SAMHD1 expression is associated with higher susceptibility to HIV-1 infection

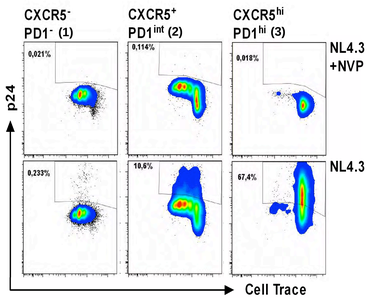


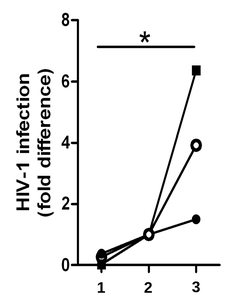




Tfh CD4+ T cells from tonsils display similar phenotype as in LN and are highly susceptible to HIV-1 infection *in vitro*







CONCLUSIONS

- We demonstrate that SAMHD1 expression is decreased during CD4+ T cell activation and proliferation.
- CD4+ T-cell subsets known to be more susceptible to HIV-1 infection, e.g. Th17 and Tfh cells, display lower levels of SAMHD1.
- These results pin point a role for SAMHD1 expression in HIV-1 infection and the concomitant depletion of CD4+ T cells.

ACKNOWLEDGEMENTS

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