PD-1 Identifies Latently HIV-infected Non-proliferating and Proliferating CD4+ T-cells

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Introduction
CD4+ T-cells from HIV-infected individuals on antiretroviral therapy (ART) expressing the Immune Checkpoint (IC) marker of T-cell activation PD1, are preferentially infected2. Characterizing the role of PD1 and other IC in HIV persistence during ART may identify new potential targets for eliminating latently infected T cells. We have previously reported that myeloid (mDC) and monocytes induce integrated latency in resting non-proliferating and proliferating CD4+ T-cells and propose that this model can mimic infections that occur in lymphoid tissue in vivo.

Hypothesis and Aims
We hypothesise that DC-T-cell interactions in vitro will induce expression of IC markers and this will alter the establishment and maintenance of latent infection in proliferating and non-proliferating T-cells. In this study we aimed to:
1. Define the expression of IC markers following co-culture and HIV infection of antigen presenting cells (APC) with resting T-cells
2. Determine whether latent infection is enriched in non-proliferating and non-proliferating T-cells expressing IC markers

Methods

Results 1. Expression of IC ligands are similar following co-culture with mDC or monocytes

Results 2. Differential expression of IC markers on proliferating and non-proliferating CD4+ T-cells co-cultured with monocytes

Results 3. HIV latency is enriched in PD1+non-proliferating and proliferating CD4+ T cells

Implications
- Up regulation of Immune Checkpoint markers and their ligands may facilitate the maintenance of late infected T cells. We hypothesise that DC-T-cell interactions in vitro will induce expression of IC markers and this will alter the establishment and maintenance of latent infection in proliferating and non-proliferating T-cells. In this study we aimed to:
  1. Define the expression of IC markers following co-culture and HIV infection of antigen presenting cells (APC) with resting T-cells
  2. Determine whether latent infection is enriched in non-proliferating and non-proliferating T-cells expressing IC markers

Conclusions
1. Myeloid DC and monocytes showed comparable IC Ligand expression levels
2. IC markers are differently expressed on proliferating and non-proliferating T cells following co-culture with monocytes
3. HIV latency is enriched in non-proliferating cells expressing high levels of PD-1, Tim-3, CTLA-4 or BTLA but not LAG-3 or TIGIT
4. HIV latency is enriched in proliferating CD4+ T cells expressing high levels of PD-1