**Introduction**

- **Immune checkpoint (IC) markers dampen the immune response**
- **IC are expressed on T-, B- and NK cells and IC ligands on antigen presenting cells (APC)**
- **Different mechanisms of inhibition:**
  - ligand competition
  - ligand internalization
  - negative signaling

**Hypothesis and aims**

**Expression of IC during APC-T cell interactions may actively suppress viral replication and maintain latency**

**Aim 1:** Determine the expression of different IC on CD4+ T cells, and their ligands on DC and monocytes, in our in vitro APC-T cell model for latency

**Aim 2:** Identify whether there is latency enrichment in non-proliferating and proliferating CD4+ T cells expressing IC following APC-T cell interaction

**Aim 3:** Determine the effects of blocking IC/IC ligands on the establishment/maintenance of latency in resting CD4+ T cells

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**Infection of resting CD4+ T cells**

- **Resting CD4+ T cell**
- **Unactivated resting cells**
- **Chemokines**
- **Dendritic cells**
- **Endothelial cells**
- **Monocytes**

**In vitro**

- **1 day + SEB**
- **RS-eGFP-HIV-1 (2h pulse)**
- **Day 5**
  - Non-proliferating eFluor670^+ eGFP^+ Not productively infected eGFP^-
  - Proliferating eFluor670^− eGFP^−

- **Day 8**
  - Productive infection
  - Latent infection
Induction of latency in proliferating and non-proliferating T-cells by mDC and monocytes

IC ligands are expressed by mDC and monocytes

IC expression on proliferating and non-proliferating T-cells is enhanced following monocyte co-culture

Latent infection is enriched in proliferating and non-proliferating cells that express PD-1

Conclusions

- Myeloid DC and monocytes showed comparable IC ligand expression levels
- IC markers are differently expressed on proliferating and non-proliferating T cells following co-culture with monocytes
- 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
- HIV latency is enriched in proliferating CD4+ T cells expressing high levels of PD-1

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Implications

- APC may facilitate ongoing latent infection of resting CD4+ T cells leading to replenishment of the reservoir
- Characterizing the role of PD-1 and other IC in HIV persistence during ART may identify potential targets for eliminating latently infected T cells

Blocking interactions between IC and their ligands in vitro

- Blocking interactions between IC and their ligands in vitro can lead to cell death, virus production, and immune clearance.

Latent Infection in sorted eFluor®EGFP+ productively infected CD4+ T cells

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