Blockade of PD-L1 Does Not Reverse HIV Latency in CD4+ T Cells Ex Vivo
Elizabeth Fyne1, Shalyn Campellone2, Huolin Q3, Amy Sheaffer4, Stephen Mason5, John Mellors1
1 University of Pittsburgh, Pittsburgh, PA, USA; 2 Bristol-Myers Squibb, Wallingford, CT, USA

ABSTRACT

Background: Blockade of the PD-1/PD-L1 pathway using monoclonal antibodies (mAb) to PD-L1 has been reported to activate HIV expression from latently infected CD4 T cells in vitro (1,2). However, detailed study of the role of PD-L1 in vivo is lacking. 

METHODS

Study Population: Ten HIV-1-infected individuals with long-term (≥8 years) suppression on highly active antiretroviral therapy (ART). 

Cell Purification: PBMCs were purified from ART-suppressed donors. Total CD4 and resting CD4 cells were purified using Stemcell Technologies Dynal beads. 

Immunophenotyping: PBMCs, total CD4, and resting CD4 cells were stained with anti-PD-1 and PD-L1 antibodies, and flow cytometry was performed to determine PD-1/PD-L1 expression on CD4 and CD8 T cells.

RESULTS

No difference between responders and non-responders in terms of PD-1/PD-L1 expression on CD4 and CD8 T cells. 

Figure 1: HIV RNA (cps/mL) by Roche Tagman in Day 8 Cell Culture Supernatants (Experiment 1)

Figure 2: Donors whose cells responded initially to anti-PD-L1 mAb treatment were redrawn and tested again (Experiments 2 and 3). MAb-induced viral expression not reproducible longitudinally.

Figure 3: Donors responded to anti-PD-L1 mAb (Figure 1) but failed to respond to the repeat blood draw (Figure 2). 

CONCLUSIONS

Despite detectable PD-1/PD-L1 expression, increased HIV production from PBMC, total CD4 T cells, or resting CD4 T cells after treatment with anti-PD-L1 antibody was infrequent and not reproduced longitudinally.

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REFERENCES

