Background: Blockade of the PD-1/PD-L1 pathway using monoclonal antibodies (mAb) has been reported to activate HIV expression from latently infected CD4 T cells ex vivo (1). To further evaluate this approach, we tested the ability of the human anti-PD-L1 mAb BMS-936559 to activate proviral expression from latently infected CD4 T cells. METHODS: PBMC, tCD4, and rCD4 cells were purified by negative selection of large-volume blood draws from HIV-infected donors. Ficoll-isolated PBMC were enzymatically and immunomagnetically for PD-1/PD-L1 expression. The sensitivities were incubated 17 million/ml in triplicate for 1 week with 20, 5, or 1.25 µg/mL anti-PD-L1 mAb, with 20 µg/mL isotype control, or with anti-CD3/CD28-coated microbeads plus either anti-PD-L1 antibody or isotype control. On Day 8, cells were assessed for viability and supernatants tested for HIV RNA using the Roche Tagman 12.0. A positive response was defined as a ≥ 5-fold increase in HIV RNA over negative control. Donors whose cells responded initially to anti-PD-L1 mAb were re-challenged and/ or restimulated.

RESULTS

• PBMC from 2 of 10 donors showed initial responses to anti-PD-L1 mAb that were not reproducible upon a repeat blood draw (Figure 2).
• Total CD4 from 2 of 10 donors showed initial responses to anti-PD-L1 mAb. One of these donors (Donor 6) responded again in a second but not a third repeat blood draw. The second donor (Donor 2) did not respond following a repeat blood draw.

• 9 of 10 donors responded to anti-CD3/CD28 in all cell types tested again (Experiments 2 and 3). mAb-induced viral expression not reproducible longitudinally.

• 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 reproducible longitudinally.

• Alternate strategies will be needed to activate proviral expression from latently infected CD4 T cells.}

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