Up-regulation of B7-H1 on Dendritic Cells Correlates with Maintenance of Specific T Cells Dysfunction and Disease Progression in the SIV-infected Rhesus macaques.

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Suppression of dendritic cell function in HIV-1 infection is thought to contribute to the inhibition of immune responses and disease progression, but the molecular mechanisms of this suppression remain elusive. Here we show that a fraction of dendritic cells (including myeloid DC and plasmacytoid DC) constitutively express B7-H1 (PD-L1) in rhesus macaques. However, B7-H1 expression is significantly up-regulated on DCs following SIV infection. Its receptor, PD-1 is also up-regulated in parallel on T cells in both peripheral and mucosal tissues after SIV infection, however, both B7-H1 and PD-1 expression in SIV controllers (elite controllers) was similar to normal animals. We also found that B7-H1 expression on both peripheral mDC and pDC positively correlated with frequency of circulating PD-1+CD3+ T cells, PD-1+CD4+ T cells, and PD-1+CD8+ T cells in SIV-infected macaques. In addition, B7-H1 expression on mDC or pDC in blood correlated with declining peripheral CD4+ T cell levels during SIV infection. Finally, blockade of B7-H1 on SIV antigen-loaded monocyte-derived DC restored SIV-specific T cell activation and proliferative responses, as evidenced by increased IL-2 and IFN-γ production in vitro. Combined, the results indicate up-regulation of B7-H1 on DCs contributes to T cell suppression and disease progression in SIV infection. Manipulating B7-H1 expression on DC may be a potential therapeutic approach for HIV-infected patients.

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