Retrovirology

Poster presentation

HIV activates indoleamine 2,3-dioxygenease: inhibition of T cell proliferation by tryptophan starvation

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T cell immune responses of HIV+ patients are functionally impaired prior to CD4+ T cell depletion. Tryptophan (trp) degradation by indoleamine-2, 3-dyoxigenase (IDO) is an immunosuppressive system that may be important in HIV/AIDS. We show here that IDO is increased in PBMC from HIV+ patients compared to controls. Culture with the IDO-inhibitor 1-methyl tryptophan (1 mT) increased proliferation of PBMC from HIV+ patients in response to PHA or anti-CD3/CD28. Exposure of PBMC from HIV-uninfected donors to infectious or noninfectious HIV increased IDO in plasmacytoid dendritic cells (pDC). Supernatants from HIV-exposed PBMC inhibited CD4+ T cell responses to PHA or anti-CD3/CD28, and this effect was reversed by 1 mT. CD8+ T cell proliferation in response to anti-CD3/CD28, but not to PHA, was also inhibited. Analysis of cyclin mRNA expression showed that CD4+ T cell were arrested in G1, whereas CD8+ T cell were blocked in G0. HIV-induced IDO inhibited expression of CD28 mRNA in CD8+ T cells. Thus HIV directly induces IDO expression in pDC, resulting in unresponsiveness of CD4+ T cells by inhibiting progression to the S phase of the cell cycle, and blocking of CD8+ T cell costimulation through downregulation of CD28.