Dual Roles of Plasmacytoid Dendritic Cells in HIV-1 Infection and Pathogenesis

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Background: Plasmacytoid dendritic cells are potent type I interferon producing cells and crucial for controlling various viral infection. However, the contribution of pDC in HIV-1 infection and pathogenesis remains controversial. On one hand, pDC have been shown to inhibit HIV-1 replication through their IFN-I production. The numerical and functional decline of pDC in HIV-1 infected patients correlates with opportunistic infection independent of CD4+ T-cell counts. On the other hand, pDC may contribute to HIV immunopathogenesis. The sustained pDC activation and IFN-I production in HIV-1 infected patients does not correlate with viral control but is predictive of disease progression. Additionally, pDC activation is rapidly controlled in the nonpathogenic SIV infection, whereas its activation and IFN-I production sustain during pathogenic infection in Asian monkeys. These reports highlight the importance of studying the interaction between HIV and pDCs.

Methodology: A monoclonal antibody specific to blood dendritic cell antigen-2, 15B, was used to deplete pDCs from humanized mice model through intraperitoneal injection. For acute HIV-1 infection, humanized mice were injected three times with 15B on -5, -3 and -1 days before infection, and mice were terminated at 8 days post-infection. For chronic HIV-1 infection, 15B was applied to mice at 11 weeks post-infection by injecting twice every week for 10 weeks. Mice were killed at 21 weeks post-infection.

Results: The expression of type I interferons and interferon stimulated genes are severely impaired by pDC ablation either before or during chronic HIV-1 infection. HIV-1 replication was significantly upregulated in pDC-depleted mice. However, HIV-1 induced depletion of human immune cells including T cells and total human leukocytes was reduced in spite of the increased viral replication.

Conclusions: pDC play a role not only in suppressing HIV-1 infection but also in promoting HIV-1 induced pathogenesis. These findings suggest that pDC depletion or suppression will provide a novel approach for HIV-1 therapy.