Peripheral blood mononuclear cells of HIV-infected patients contain CD8 T cells that form conjugates with and kill HIV-infected autologous CD4 T cells

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Abstract:

Background: The PBMC of untreated HIV infected patients contain HIV- specific CD8 T cells and their potential targets, CD4 T cells latently infected by HIV.

Objective: Determine if CD4 T cell depletion may result from an autologous CD8-CD4 T cell interaction.

Methods: CD8 and CD4 T cells from PBMC of acute and chronic untreated HIV-infected patients were sorted and incubated together. CD8-CD4 T cell conjugates were observed by fluorescent microscopy. Apoptosis of the CD4 T cells in the conjugates was recorded by digitized images and further was observed and measured by FACS using Annexin. The perforin expression in the CD8 T cells was measured using intracellular monoclonal Abs. The HIV DNA in the conjugated CD4 T cells was detected by in-situ PCR.

Results: We found that 6.1±0.5% of CD4 T cells from acute HIV-infected patients and 3.0±0.5% from chronic HIV-infected patients formed CD8-CD4 T cells conjugates. Annexin binding and cell morphology typical of apoptosis were observed in the conjugated CD4 T cells. The majority of CD8 T cells that had conjugated to CD4 T cells expressed perforin. The conjugated CD4 T cells had integrated HIV DNA in their nucleus

Conclusions: CD8 T cells and latently HIV infected CD4 T cells procured from the PBMC of untreated HIV-infected patients form conjugates. Apoptotic lytic activity is observed in the conjugated CD4 T cells. We propose that CD4 T cell annihilation in HIV-infected patients results from the interactions of perforin-rich CD8 T cells with latent HIV-infected CD4 T cells. We assume that a dynamic balance is established between latently HIV-infected CD4 T cells and HIV-specific CTL. It is likely that the virus manipulates the immune system to maintain a low-grade infection, thus achieving prolonged survival combined with efficient virus spread.