CD8+ cell depletion results in an increase in proviral loads in HTLV-1-infected cynomolgus macaques

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Background:
HTLV-1 replication is controlled in HTLV-1-infected carriers. Cumulative studies have indicated involvement of virus-specific CD8+ T cell responses in the viral control. However, how much extent CD8+ T cells contribute to the control of HTLV-1 replication remains unclear. Here, we examined the impact of CD8+ cell depletion on proviral loads in HTLV-1-infected cynomolgus macaques.

Methods:
Five cynomolgus macaques were inoculated with ATL040 cells (an HTLV-1-producing cell line). In the chronic phase of HTLV-1 infection, these macaques were administered with a monoclonal anti-CD8 antibody (MT807R1, NIH NHP Reagent Resource) for CD8+ cell depletion. We examined proviral loads in peripheral blood mononuclear cells, peripheral blood lymphocyte markers, plasma anti-HTLV-1 antibodies (by using an INNO-LIA kit and a SERODIA kit), and Tax-specific CD8+ T cell responses (by flow cytometric analysis of interferon-gamma induction after specific stimulation).

Results:
HTLV-1 proviruses were detected in all the five macaques after ATL040 cell inoculation. Anti-HTLV-1 antibodies were induced in these macaques. Anti-CD8 antibody administration resulted in complete depletion of peripheral CD8+ T cells for approximately two months and increases in proviral loads and anti-HTLV-1 antibody levels. Proviral loads and anti-HTLV-1 antibody levels peaked just before reappearance of peripheral CD8+ T cells. Tax-specific CD8+ T cell responses were detected in these recovered CD8+ T cells.

Conclusion:
HTLV-1 infection can be established by ATL040 cell inoculation in cynomolgus macaques. CD8+ cell depletion results in increases in proviral loads and anti-HTLV-1 antibody levels. Anti-HTLV-1 antibody increase implies HTLV-1 antigen expression. These results provide a direct evidence indicating that CD8+ cells are responsible for the control of HTLV-1 replication.

Disclosure of Interest Statement:
None.