Gut mucosal FOXP3+ regulatory CD4+ T cells and Nonregulatory CD4+ T cells are differentially affected by simian immunodeficiency virus infection in rhesus macaques.

Abstract:

The gastrointestinal tract represents a major site for human and simian immunodeficiency virus (HIV and SIV) replication and CD4(+) T-cell depletion. Despite severe depletion of mucosal CD4(+) T cells, FOXP3(+) regulatory CD4(+) T cells (T(reg)) are highly increased in the gut mucosa of chronically HIV-infected individuals and may contribute to HIV pathogenesis, either by their immunosuppressive function or as a significant target cell population for virus production. Little is known about the susceptibility of mucosal T(reg) to viral infection and the longitudinal effect of HIV/SIV infection on T(reg) dynamics. In this study, we determined the level of SIV infection in T(reg) and nonregulatory CD4(+) T cells (non-T(reg)) isolated from the colon of SIV-infected rhesus macaques. The dynamics of mucosal T(reg) and alterations in the mucosal CD4(+) T-cell pool were examined longitudinally. Our findings indicate that mucosal T(reg) were less susceptible to productive SIV infection than non-T(reg) and thus were selectively spared from SIV-mediated cell death. In addition to improved survival, local expansion of T(reg) by SIV-induced proliferation of the mucosal CD4(+) T-cell pool facilitated the accumulation of mucosal T(reg) during the course of infection. High
frequency of mucosal T(reg) in chronic SIV infection was strongly related to a reduction of perforin-expressing cells. In conclusion, this study suggests that mucosal T(reg) are less affected by productive SIV infection than non-T(reg) and therefore spared from depletion. Although SIV production is limited in mucosal T(reg), T(reg) accumulation may indirectly contribute to viral persistence by suppressing antiviral immune responses.