Background: The role of FoxP3+CD4+ Treg cells in HIV-1 diseases (aberrant immune activation) is poorly understood due to lack of a robust model. We have demonstrated that functional CD4+FoxP3+ natural Treg cells are developed in all lymphoid organs in humanized rag2-/-γC-/- DKO-hu HSC mice. These FoxP3+ Treg cells are preferentially infected and depleted by HIV-1. We discover that, while inhibiting IL-2 gene expression, FoxP3 enhances HIV-1 LTR expression in an NFkB-dependent fashion. FoxP3 silences the chromatin at the IL2 locus but activates it at the HIV-1 LTR.

Methodology: My laboratory studies development and function of the human immune system, as well as chronic human viral infection and immunopathogenesis. Treg cells are depleted during different stages of HIV-1 infection and during HAART treatment. HIV-1 replication, pathogenesis and HAART-reservoirs are investigated.

Results: When CD4+CD25+/hi Treg cells are depleted in vivo, acute HIV-1 infection is impaired, associated with enhanced immunity. However, when Treg cells are depleted during chronic infection, HIV-1 replication is enhanced with accelerated disease progression. When Treg was depleted during HAART, HIV-1 gene expression was induced from the HAART-resistant HIV-1 reservoir cells in various lymphoid organs. Therefore, FoxP3+ Treg cells can promote acute HIV-1 infection by suppressing anti-HIV immunity and by serving as target cells. During chronic HIV infection, however, Treg cells play an important role in suppressing immune activation and HIV-1 replication, contributing HIV-1 reservoirs during HAART.

Conclusions: Therefore, FoxP3+ Treg cells can promote acute HIV-1 infection by suppressing anti-HIV immunity and by serving as target cells. During chronic HIV infection, however, Treg cells play an important role in suppressing immune activation and HIV-1 replication, contributing HIV-1 reservoirs during HAART.