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Session: **BS4**: Sunday May 3 – 11:00:12:30 – HIV Pathogenesis and Animal Models

Track:	Basic Sciences
Subject:	HIV Pathogenesis and Animal Models
Presentation Type:	Oral
Title of Abstract:	**Dynamics of regulatory and effector CD8 T-cells in mesenteric lymph nodes and blood during SIV infection of Rhesus Macaques and following early ART initiation**
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Abstract

Background: CD8 T-cells play pivotal roles in clearance of HIV-infected cells, such that CD8 exhaustion contributes to their dysfunction and consequently, viral persistence. Mesenteric lymph nodes (MLNs) are critical sites for the maintenance of gut mucosal immunity. However, the dynamics of CD8 T-cells in MLNs is less known due to the lack of accessibility to these tissues in human.

Methods: 32 female Chinese Rhesus Macaques **(**RMs) were enrolled including 25 intravenously SIVmac251-infected animals. Nine monkeys were treated by ART starting at day 4 post-infection. Furthermore, 5 RMs after ART interruption (8 weeks post-ART initiation) and 4 untreated chronically infected were also studied. Peripheral blood and mechanically isolated cells from MLNs were analyzed by flow cytometry.

Results: Acute SIV infection was associated with decreased CD4/CD8 ratio and increased memory CD8 T-cell immune-activation (CD39/HLA-DR), exhaustion (PD1) and immunosuppressive CTLA-4 expression in both blood and MLNs which were all normalized by early ART initiation. ART decreased significantly αα+αβ-CD8 but not αα+αβ+CD8 T-cells in MLNs, while, αα+αβ-CD8 T-cells were increased in blood. Furthermore, acute SIV infection resulted in the expansion of FoxP3+ CD8 Tregs in blood and MLNs, while early ART decreased CD8 Tregs only in blood. Helios+ FoxP3+ thymic CD8 Tregs were also increased in both tissues in acute infection which were normalized by ART. Analyzing the trafficking of CD8 T-cells, we found that the acute SIV infection results in decreased $CCR6^{+}$ but not $CXCR3^{+}$CD8 T-cells in both MLNs and blood, which was recovered following early ART along with increased IL17+ CD8 T-cells. ART interruption was associated with increased HLA-DR+CD8 T-cells and decreased $CCR6^{+}$CD8 T-cells within MLNs.

Conclusion: Overall, early ART initiation during acute infection normalized CD4/CD8 ratio and CD8 activation and exhaustion in both MLNs and blood, but elevated levels of immunosuppressive CD8 Tregs persists within MLNs despite early ART.