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Session: **BS2**: Friday May 1 – 15:00:17:00 – HIV Latency and Viral Reservoirs

Track:	Basic Sciences
Subject:	HIV Latency and Viral Reservoirs
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Title of Abstract:	**HIV is seeded within pulmonary DN T-cells during acute infection and persists during long-term effective ART**
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Abstract

Introduction: The lungs are relatively unexplored reservoirs in the ART era. Double negative (DN) T-cells originate either from the thymus by escaping negative selection, or in the periphery following CD4 downregulation by HIV Nef/Vpu/env. As circulating DN T-cells have been described as cellular HIV reservoirs, we undertook a thorough analysis of pulmonary DN T-cells *versus* blood of ART-treated HIV-infected individuals.

Methods: Bronchoalveolar lavage (BAL) fluid and matched blood were collected from 38 long-term ART-suppressed and 14 uninfected adults, without active respiratory symptoms. T-cell subsets and HIV p24 were characterized by flow cytometry. HIV-DNA levels were measured by ultrasensitive PCR. To examine DN T-cell dynamics in acute *versus* chronic infection, lung, spleen and blood specimens from pNL4.3-ADA-GFPinfected BLT humanized mice (hu-mice) were assessed.

Results: FACS-sorted DN T-cells from BAL harbored HIV-DNA in ART+ adults although HIV-DNA levels were lower in DN *versus* lung CD4 T-cells. Both HIV+ and HIV- adults had greater CD3+CD4-CD8α-CD8β- cell frequencies in BAL *versus* blood, while CD3+CD4-CD8-TCRαβ-TCRγδ- cells were only enriched in HIV+ BAL. Compared to blood, pulmonary DN T-cells in both HIV+ and HIV- groups displayed mostly an CD45RA-CD28+ memory phenotype. However, HIV+ individuals had more activated (HLA-DR+) and exhausted (PD-1+) and, fewer senescent (CD28-CD57+) and recent thymic migrant (CD31+) pulmonary DN T-cells. Similar to humans, DN T-cells were enriched in BAL *versus* blood of HIV+ and HIV- hu-mice. Importantly, p24+ DN T-cell frequencies in lungs were consistently higher than in blood and spleen in both acute and chronic HIV infection and ART suppressed p24+ DN T-cell within the lungs of hu-mice. Like in humans, fewer lung DN T-cells in hu-mice had a recent CD31+ thymic migrant phenotype, suggesting their local expansion within the lungs following HIV infection.

Conclusion: HIV is seeded within pulmonary DN T-cell reservoirs during acute infection and persists even following long-term ART.