Abstract for 33rd Annual Symposium on NHP Models for AIDS

Section 1 – Submitting Author and Contact Information
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Section 2 – Session Preference/ Oral
#1 Viral Reservoirs, Latency & Cure
#2 Virology and Pathogenesis

Section 3 – Abstract Title: Characterization of macrophages serving as a viral reservoir in Pediatric SAIDS

Section 4 – Author Information
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Section 5 – Abstract Text
Introduction: Simian Immunodeficiency Virus (SIV) infects and induces apoptosis in lung interstitial macrophages, leading to lung damage and higher recruitment of monocytes from the bone marrow. In adult Rhesus macaques a higher monocyte turnover has been shown to correlate with faster AIDS progression. In earlier pediatric studies, we found a higher baseline monocyte turnover rate in neonatal monkeys. SIV progression is also accelerated in neonatal monkeys as compared to adults. We hypothesize that in pediatric AIDS, tissue macrophages serve as major virus (SIV) reservoirs very early after infection of SIV-infected newborn macaques that develop disease more rapidly than adults. That in the lung, long-lived alveolar macrophages (AMs) serve as predominant viral reservoir during ART treatment. Our research goal is to verify that macrophages, in addition to CD4+ T cells, serve as virus reservoir cells in the lung of SIV-infected newborns following ART and consequently induce more tissue damage.

Methods: Neonate Rhesus macaques were orally infected with SIVmac251. BrdU uptake was used to determine cell turnover and flow cytometry allowed for phenotypic characterization of cells isolated from blood and tissues. Quantification of SIV RNA in plasma, tissues, and CSF was performed using TaqMan qPCR. ART treatment includes Tenofovir, emtricitabine and Dolutegravir and was administered via subcutaneous route daily. CD4+ T cell and macrophage depletion will be accomplished using anti-CD4 depleting antibody or liposome-clodronate/alamdronate, respectively.

Results: We have confirmed a relatively high monocyte turnover in uninfected infant macaques with significantly increased monocyte turnover after SIV infection. Preliminary results also indicate a striking relation with CD169 expression on macrophages during SIV infection.

Conclusions: We expect that neonates with higher turnover of monocytes will exhibit more extensive lung pathology following long term ART treatment despite effective ART, measured by plasma VL. We expect to see monocyte turnover decrease after viral control is achieved with ART treatment. Currently we are monitoring infected monkeys with regular blood collection and tissue biopsies. ART treatment has been initiated on some infected macaques, and optimization, production and administration of liposome-alendronate will be performed soon. We believe this work will contribute significantly to understanding the role of macrophages in SIV progression and pathologies, particularly in pediatric cases of infection.

Section 6 – Funding
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Section 7 – Early Investigator Awards
Biosketch submitted.