**Healthy HIV-Infected Subjects Harbor HIV in Alveolar Macrophages, Which Can Impair Lung Function**

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**Background:** Alveolar macrophages are specialized innate immune cells that reside in the alveolus, a site with different concentrations of some medications compared to the blood compartment. Alveolar macrophages can be infected by HIV-1 as they express CXCR4 and CCR5, and HIV reverse transcriptase has been detected in alveolar macrophages from humans. The half-life of alveolar macrophages is significantly longer than that of an activated lymphocyte (months/years versus hours/days). However, reports quantifying the burden of HIV in alveolar macrophages are conflicting, and it is unclear what impact the infection has on alveolar macrophage function. We hypothesize that the alveolar macrophage is an important reservoir for HIV, contributing to cell-cell spread of the virus within the lung and exhibiting abnormal function, which contributes to the increase risk of severe lung infections.

**Methodology:** We conducted a pilot study on healthy HIV-infected subjects who did not have major medical co-morbidities or smoke cigarettes. All subjects underwent bronchoscopy and bronchoalveolar lavage with 180mL of normal saline. Alveolar macrophages were isolated and HIV-1 RNA was quantified in the cells using the Abbott RealTime HIV-1 Assay (Abbott Molecular Inc. Des Plaines, IL), an in vitro reverse transcription-polymerase chain reaction assay. Proviral DNA was qualitatively measured using a modified version of the above-mentioned HIV-1 RNA viral load assay. To measure phagocytic function, alveolar macrophages were isolated and incubated for 1 hour with FITC-labeled S. aureus in a 10:1 ratio. FITC-labeled bacteria containing cells were measured by flow cytometry. Phagocytic index was calculated as follows: (% positive cells x mean channel fluorescence)/100.

**Results:** We enrolled 22 otherwise healthy HIV-infected subjects (median CD4 count= 409/μl, 82% with undetectable plasma viral load). HIV-1 proviral DNA and/or quantitative RNA were detected in 82% of the alveolar macrophages; 78% of this group had an undetectable plasma viral load and 94% were on anti-retroviral therapy. HIV-1 RNA levels ranged from 48 to 2305 copies/mL. Further, HIV-infected subjects with proviral DNA present had decreased alveolar macrophage phagocytosis of FITC-labeled S. aureus compared to subjects without proviral DNA present [16.6 (IQR 6-45.2) vs. 33.1 (IQR12.2-172.1)].

**Conclusions:** Alveolar macrophages harbor HIV even in otherwise healthy subjects with undetectable plasma viral loads, representing a potential reservoir for the virus. In addition, HIV viral replication within the macrophage may impair phagocytosis and other immune functions in the lung, leading to an increased risk for lung infection.