

## HIV-ASSOCIATED DISRUPTION OF ALVEOLAR IMMUNE CELL HOMEOSTASIS IN MALAWIAN ADULTS

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### **Introduction**

Chronic HIV infection impairs pulmonary immunity and increases susceptibility to lower respiratory tract infections. Unlike in peripheral blood, the immune cell populations that are impacted by HIV infection in the lung are less well defined. We aimed to characterise the impact of HIV infection on immune cell homeostasis in the lung as this might help explain the propensity for LRTIs in HIV-infected adults.

### **Methods**

20 healthy HIV-uninfected controls and 19 asymptomatic HIV-1 infected ART-naïve adults were recruited from Queen Elizabeth Central Hospital, Voluntary Counselling and Testing clinic. Bronchoalveolar lavage (BAL) fluid and peripheral blood was obtained from study participants. Using immunophenotyping, lymphocyte and myeloid cell populations in BAL fluid and peripheral blood were characterised.

### **Results**

Overall, the proportions of CD8<sup>+</sup> T cells, B cells,  $\gamma\delta$  T cell and intermediate monocytes were higher in HIV-infected adults compared to HIV-uninfected controls, while the proportions of NK cells, classical monocytes and myeloid dendritic cells and alveolar macrophages were lower in HIV-infected adults compared to HIV-uninfected controls. However, we found no difference in the numbers of alveolar CD4<sup>+</sup> T cells in HIV-infected adults compared to HIV-uninfected controls, even though there was a significant reduction in peripheral blood CD4<sup>+</sup> T cell count ( $p < 0.0001$ ). We also found higher absolute counts of B cells ( $p = 0.0043$ ) and  $\gamma\delta$  T cell subsets ( $p = 0.0361$ ) in BAL fluid from HIV-infected adults compared to HIV-uninfected controls. In contrast, the numbers of classical monocytes were lower in HIV-infected adults compared to HIV-uninfected controls ( $p = 0.0172$ ).

### **Conclusion**

Chronic HIV infection is associated with broad disruption of immune cell homeostasis in the lung, but does not lead to massive depletion of alveolar CD4<sup>+</sup> T cells. These findings suggest that dysregulation of alveolar immune cell homeostasis, beyond CD8<sup>+</sup> T cell alveolitis, may contribute to increased susceptibility to lower respiratory tract infections in HIV-infected adults.