Effects of HIV-1 and *Schistosoma mansoni* co-exposure on pulmonary vascular disease

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Schistosomiasis and HIV infection are independently associated with pulmonary vascular disease (PVD). HIV patients in some regions of Africa show as high as 60% co-infection with *Schistosoma*. However, the effects of the co-infection on PVD development are still unknown. We hypothesized that co-exposure may potentiate PVD and results in a different pathological pattern.

Wild-type (WT) and Tg26 transgenic mice expressing HIV-1 proteins (HIV) were intraperitoneally sensitized and intravenously challenged two weeks later with inactivated *Schistosoma mansoni* eggs. Hemodynamic measurements were recorded in open-chest mice. Quantitative analysis of inflammatory cytokines in lung homogenates were analysed by qRT-PCR. Pulmonary vascular (PV) remodeling and peri-egg granuloma were analysed by immunohistochemistry, and immune cells into the lungs were characterized by flow cytometry.

There was a modest but significant increase in the mean pulmonary arterial pressure following *Schsitosoma* challenge in HIV compared to WT mice (HIV:13±0.6mmHg *versus* WT:11±0.5mmHg). *Schistosoma* eggs induced granuloma was found to be larger in WT than in HIV lungs. However, HIV lungs had a significantly higher egg burden (10.5±1.9eggs/mg), compared to WT (4.6±1.3eggs/mg), suggesting an impairment in egg clearance. Furthermore, HIV mice had more closed pulmonary arterioles than WT mice, which had predominantly hypertrophied muscular layers. In both, WT and HIV mice, exposure to *Schistosoma* eggs increased interleukin (IL)-4 and IL-13 levels, but not interferon (IFN)-γ or tumor necrosis factor (TNF)-α. Leukocyte counts in the lungs showed a reduction in $CD11b^{hi}$ myeloid cells, B cells and αβ (both $CD4^+$ and $CD8^+$) T cells, but increased γδ T cells in HIV, as compared to WT mice.

HIV and *Schistosoma* co-exposure resulted in a different remodeling phenotype than either factor alone, suggesting that the dysregulation of inflammatory responses induced by HIV proteins may influence the pattern of PV remodeling. The consequences of these findings on the development of pulmonary disease need further evaluation.