

Poster presentation

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P10-03. Dramatic changes in Fc-receptor expression during HIV-1 infection associated with reduced phagocytic activity during progressive HIV-1 infection

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Background

Antibodies have a plethora of functions in addition to neutralization including stimulation of cytokine production, induction of cytolytic activity, phagocytosis... All of these functions rely on the capacity of the constant region of antibodies to engage Fc-receptors (FcR) that are expressed on all innate immune cells. Several reports have described changes in phagocytic activity in progressive HIV infection, which may contribute to defects in viral clearance and antigen presentation, however the underlying mechanism for this alteration is unknown. Given the critical importance of FcRs in phagocytic activity, we hypothesized that changes in FcR expression during HIV infection may contribute directly to changes in phagocytic activity.

Methods

A total of fifty donors were included in this study (10 untreated chronics, 10 treated chronics, 10 controllers, 12 individuals in acute HIV infection, and 8 HIV-negative controls). Surface expression of FcRs was assessed by flow cytometry on monocytes, pDCs, and mDCs. Phagocytic activity was measured by flow by quantifying cells that took up antibody coated-CFSE labeled p815 cells.

Results

Our results show that acute HIV-1 infection is associated with elevated expression of FcγRI on mDCs during acute infection ($p = 0.001$). In contrast, FcγRIIIa was expressed at significantly lower levels on monocytes in chronic HIV-

1 infection ($p < 0.05$). Similarly, FcγRIIIa was expressed at lower levels on mDC in both acute and chronic untreated HIV-1 infection compared to negative controls ($p < 0.05$, for both comparisons). Interestingly, phagocytic activity was significantly higher in controllers compared to chronics, robustly correlated with the level of FcγRIIIa expression on the surface of monocytes and mDCs.

Conclusion

These data show for the first time that impaired phagocytic activity may be directly related to changes in FcR expression, that may have a dramatic impact on the ability of phagocytic cells to help control viral infection via the clearance of replicating virus or infected cells.