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# NK Cells and immune activation in HIV-1 infection

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Natural Killer (NK) cells have the potential to eliminate HIV-1 infected target cells and to influence the rate of HIV-1 disease progression. NK cells are, however, depleted during HIV-1 chronic infection and their functions remain diminished in individuals receiving anti-retroviral therapy. Chronic immune activation may contribute to loss of NK cell functional potency in HIV-1 infection.

## Aims

Here we investigate the contribution of HIV-1 viraemia and exposure to human cytomegalovirus (HCMV) to chronic NK cell activation and differentiation. We also assess the impact of HIV-1 on NK cells in the gastrointestinal (GI) tract and the association between microbial products translocated from the (GI) tract and chronic activation of NK cells.

## Methods

Blood and colonic lamina propria NK cell activation and differentiation were studied in aviraemic and viraemic HIV-1 infected and HIV-1 seronegative control individuals without or with inflammatory bowel diseases (IBD). NK cell activation and receptor expression were assessed by flow cytometry, CMV exposure by anti-HCMV IgG Elisa and plasma lipopolysaccharide (LPS) by limulus amoebocyte assay.

## Results

HIV-1 plasma viraemia has a dominant impact on NK cell losses and chronic NK cell activation whereas differentiation of blood NK cell receptor expression is associated with exposure to HCMV in HIV-1+ individuals. HIV-1 plasma viraemia is also associated with depletion of NK cells in the colonic lamina propria whilst atypical

gut NK cell differentiation occurs in both HIV-1+ individuals and in HIV-1- IBD patients. Plasma LPS is elevated both in viraemic and aviraemic HIV-1+ individuals and in IBD patients. Chronic NK cell activation is, however, reduced in aviraemic HIV-1+ individuals and is absent in IBD patients.

## Discussion

Depletion and chronic activation of NK cells is associated with HIV-1 viraemia whilst concomitant infections and ongoing inflammatory processes influence functional differentiation of NK cells in the blood and GI tract. These data have implications for innate immune competence in HIV-1 infected individuals.

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