

Poster presentation

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## P10-12. Altered NK cell phenotype and function in Ugandans with chronic HIV-1 infection

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### Background

NK cells are innate lymphocytes that play a significant role in the control of viral infections, including HIV-1. We examined the state of the NK cell compartment in Ugandans with untreated HIV-1 infection in comparison with matched uninfected controls and determined the association of host genetics and inhibitory KIR expression on disease progression.

### Methods

The function and phenotype of NK cells was investigated using 10-color flow cytometry from frozen PBMC. Sequence-specific priming (SSP) real-time PCR was used to genotype for KIR3DL1/DS1 and HLA-B Bw4/Bw6 allowing the discrimination of Bw4 alleles having isoleucine at position 80.

### Results

NK cells displayed elevated production of IFN- $\gamma$  and MIP-1 $\beta$ , as well as CD107a degranulation in infected subjects. HIV-1 infection was associated with reduced expression of KIR2DL1, NKG2A, CD161 and NKp30 in CD56 dim and CD56neg NK cells, whereas lowered CD161 expression was the only alteration in the CD56 bright subset. Interestingly, low CD4 counts were associated with increased levels of IFN- $\gamma$  and degranulation in CD56 bright NK cells. The presence of HLA-B Bw4-80I was associated with ele-

vated frequencies of KIR3DL1+ NK cells in both healthy and chronically HIV-1 infected Ugandans. Furthermore, a positive correlation was observed between the size of the KIR3DL1-expressing NK cell subset and viral load only in Bw4-80I+ patients. Finally, increasing size of this subset was associated with higher production of MIP-1 $\beta$ , a CC chemokine with anti-HIV activity, in the NK cell compartment of Bw4-80I+ patients.

### Conclusion

NK cells in HIV-1 infected Ugandans display elevated activity, despite an altered functional and phenotypic profile. Furthermore, specific alterations in the CD56 bright and CD56 dim subsets occur in patients with severe CD4 loss. In addition, our results suggest that the presence of Bw4-80I directs an expansion of functional KIR3DL1+ NK cells, which may be an important source of MIP-1 $\beta$  in chronic HIV-1 infection.