## Retrovirology



Poster presentation

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# P10-07. Extremely rapid degranulation of NK cells activated by HIV-specific antibody dependent cellular cytotoxicity

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### **Background**

Natural killer (NK) cell-mediated antibody dependent cellular cytotoxicity (ADCC) is an important immune mechanism, largely overlooked in HIV vaccine development. As cells of the innate immune system, there is potential for NK cell-mediated ADCC to rapidly generate cytolytic activity, which could be vital in controlling HIV infection.

#### Methods

Using a novel ICS-based ADCC assay, we studied NK cell-mediated ADCC responses on fresh blood samples from a cohort of 80 ART naïve HIV-positive subjects. We comprehensively mapped ADCC epitopes from HIV-infected subjects, cloning and sequencing relevant epitopes to identify variations from HIV-1 consensus subtype B sequence, then comparing ADCC activity induced by consensus and autologous epitope sequences. We also studied the kinetics of expression of CD107a, IFN $\gamma$  and Granzyme B by NK cell-mediated ADCC, comparing both healthy donor and autologous NK cells and CTLs against HIV antigens within the same individuals at varying intervals between 0 mins and 7 hours.

#### Results

We detected ADCC responses from 83% (66 of 80) of therapy naïve patients. HIV-specific ADCC induced activation of NK cells occurs within 30 minutes of antigen stimulation, at least as quickly, and for certain epitopes even earlier, than activation of HIV-specific CTLs. However, surprisingly, there was enhanced CD107a expression, but decreased Granzyme B loss from healthy donor cells in comparison to autologous cells. Interestingly, viral muta-

tional escape from ADCC activity was detected in approximately 30% of epitopes when tested against the subjects' autologous virus epitope.

#### Conclusion

This work provides evidence on the breadth and importance of HIV-specific ADCC responses in infected subjects. We show NK cell-mediated ADCC rapidly degranulate in response to HIV antigens and should be at least as effective as CTLs in limiting the spread of HIV infection. However, the potential for ADCC responses force escape in subjects with chronic HIV infection illustrates the complexity and potential limitations of anti-HIV ADCC.