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Oral presentation

OA02-06 LB. Recombinant modified Vaccinia virus ankara expressing HIV-1 genes activates NK subset capable of controlling HIN infection in vitro

J Cummings*[1], V Arnold[1], K Yarbrough[1], C Didier[1], Y Levy[2], F Barré-Sinoussi[1], D Scott-Algara[1] and HIV Vaccine Group[3]

Address: [1]Institut Pasteur, Paris, IDF Cedex 15, France, [2]Hôpital Henri-Mondor, Créteil, France and [3]ANRS, Paris, France
* Corresponding author

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Background

Primate innate immune mechanisms are critical for the normal development of adaptive immune responses to antigen. Part of the modern effort to design and distribute vaccines against pathogens must involve detailed descriptions of innate responses resulting from vaccine challenges. Particularly, the interaction between Natural Killer (NK) and Dendritic cells is expected to greatly impact the establishment of both innate and adaptive immune responses to vaccine. In this study, we describe responses of Natural Killer cells to recombinant Modified Vaccinia Virus Ankara expressing HIV-1 genes (rMVA) compared to wild type MVA (MVAwt).

Methods

We employed an autologous in vitro NK/DC co-culture system to explore the interaction between MVA-infected DC and Natural Killer cells.

Results

Using a fluorescent dye system, we show that MVA infected DC are phagocytosed by uninfected DC after 48h in co-culture. We also demonstrate that NK cells stimulated in co-culture with MVA-infected DC proliferate when compared to the uninfected DC stimulation; though no difference in proliferation kinetics could be identified between recombinant MVA (rMVA) and wild type MVA (MVAwt) stimulated NK. Both MVA strains were capable of inducing NK repertoire differentiation but comparative analysis demonstrated that NK stimulated with rMVA specifically expressed higher levels of CD158e and NKG2D than NK in the MVAwt condition. Finally, using HIV-GFP or HIV-Bal5 strains, we show that NK cells stimulated by rMVA are better at controlling HIV infection in vitro than NK stimulated by MVAwt.

Conclusion

These data demonstrate that innate responses to this rMVA vaccine against HIV can be detected in vitro and that this response results in the establishment of "activated/memory" Natural Killer cells capable of controlling HIV replication and infection. Future experiments will identify the specific molecular mechanisms responsible for the DC-mediated activation of NK, as well as the NK-dependent control of HIV infection.