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# P18-04. MVA-nef vaccination induces specific T-cell responses exerting functions associated with non-progressive disease in HIV-1 infected individuals

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## Background

Modified vaccinia virus Ankara (MVA) vectored vaccines have been intensively investigated in several studies. In a therapeutic vaccination trial, we demonstrated that MVA expressing the HIV-1 protein Nef (MVA-nef) was safe in 10 HIV-1 infected individuals under ART and immunogenic in regard to the elicitation of IFN-γ mediated CD4 T-cell responses. Recent advancements in polychromatic flow-cytometry technology revealed that the sole evaluation of IFN-γ provides limited information about the quality of the immune response. In fact, simultaneous production of multiple cytokines by T-cells and a high proliferative capacity are associated with superior control of viral replication.

## Methods

In a retrospective setting, we simultaneously assessed the expression of IFN-γ, IL-2, MIP-1β, CD154 and CD45RA in Nef-specific T-cell populations throughout the vaccination trial. Furthermore we applied a multi-colour CFSE based proliferation assay investigating the proliferative capacity and the simultaneous expression of IFN-γ, IL-2 and MIP-1β.

## Results

Following MVA-nef vaccination, we observed a significant increase of polyfunctional Nef-specific CD4 T-cells, simultaneously expressing IFN-γ, IL-2 and CD154. Using the standard ICS no increase of Nef-specific CD8 T-cell responses was detected. However, by the CFSE based proliferation assay, we observed a clear expansion and a generally enhanced proliferative capacity of Nef-specific CD8 T-cells. Notably, MVA-nef induced increased IL-2 production by Nef-specific CD4 T-cells correlated with MVA-nef induced increased proliferative capacity of Nef-specific CD8 T-cells suggesting the possibility of a causal link between the two functions.

## Conclusion

These results hold promise for the use of the poxvirus derived MVA-vector to stimulate potentially effective anti HIV T-cell responses and highlight the importance of sophisticated immunomonitoring tools to unravel concealed effects of immunologic interventions.