

Poster presentation

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## PI9-19. MVA vaccines are efficiently cross-presented by DCs and do not enhance HIV replication in DC/T cell cultures

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### Background

Poxvirus based HIV vaccine candidates are currently under evaluation in preclinical and clinical trials. Modified Vaccinia Virus Ankara (MVA) vectors have excellent safety records and immunogenicity, but their behaviour in human cell cultures remains partly characterized.

### Methods

We studied here various virological and immunological aspects of the interactions of an MVA-GagPolNef vaccine candidate developed by the ANRS, with human DCs, lymphocytes, and other cell types.

### Results

We report that MVA-GagPolNef efficiently infects a panel of primary and immortalized human cells (including macrophages, DCs, B, epithelial cells, muscular cells and fibroblasts), and drives Gag expression in these cells. Infection was cytopathic, and, as expected with this vector, induced apoptosis within 1–2 days of infection. In contrast, primary T cells were more resistant to infection and apoptosis. DCs infected with MVA-GagPolNef (and not with a control MVA vector) presented HIV antigens and activated HIV-specific CD8<sup>+</sup> CTLs. The infection of DCs by MVA induced cell maturation, secretion of various cytokines, and was followed by apoptosis. Interestingly, coculture of MVA-GagPolNef-infected epithelial cells with DCs promoted efficient HIV-Gag antigen cross-presentation without inducing DC infection and cell death. Other MVA-infected cells were similarly efficiently cross-pre-

sent by DCs to CD8 T cells. APCs exposed to MVA-Gag-PolNef also activated HIV-specific CD4 T cells, indicating that this vector promotes both MHC-I-restricted cross-presentation and MHC-II-presentation of HIV antigens by DCs. We also examined the impact of MVA-GaPolNef on HIV replication in DC/T cell cocultures. Interestingly, there was no enhancement of HIV transfer and replication when MVA-GagPolNef was incubated with DCs prior to infection with HIV, nor when MVA-infected cells were added in the cocultures.

### Conclusion

Altogether, these results strongly suggest that the highly immunogenic properties of MVA vector are not associated with an enhancement of HIV replication.