HIV-1 impairs the immunogenic potential of dendritic cells by interfering with the autophagy process

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Introduction: HIV-1 infection is associated with alterations in antigen presentation and the loss of pathogen-specific CD4+ T-cells. Autophagy is a universal catabolic process involved in the regulation of antigen presentation. HIV inhibits autophagy in dendritic cells (DC) by upregulating expression of the serine/threonine kinase mTOR. Accordingly, the mTOR inhibitor rapamycin increases autophagy and limits the *trans*-infection ability of DC. Here, we investigated whether rapamycin restores the ability of DC to mount CD4+ T-cell responses against Staphylococcus aureus, Cytomegalovirus (CMV), and Staphylococcal enterotoxin B (SEB).

Methodology: DC were obtained upon monocyte culture in the presence of GM-CSF/IL-4. The *trans*-infection ability and immunogenic potential were evaluated by DC co-culture with autologous CFSE-loaded $CD4^+$ T-cells in the presence HIV (NL4.3BaL) and antigens or CD3/CD28 Abs. HIV replication was quantified by HIV-p24 ELISA. DC were pretreated with rapamycin. mTOR expression was quantified by western blotting.

Results: Exposure to HIV *in vitro* dramatically impaired DC maturation and their ability to induce proliferation of autologous CD4+ T-cells in response to *Staphylococcus aureus* and CMV but not SEB. Rapamycin decreased mTOR expression in DC and diminished their HIV *trans*-infection potential. Rapamycin-treated DC upregulated CD83 expression and were further impaired in their ability to induce antigen-specific CD4+ T-cell proliferation.

Conclusion: HIV alters the immunogenic potential of DC and therefore rapamycin can be used to limit HIV *trans*-infection by DC. However, the fact that rapamycin fails to restore the immunogenic potential of DC, stresses the need to identify additional strategies to manipulate the autophagy process for an optimal restoration of immune competence in HIV-infected subjects.