RETROVIROLOGY

ORAL PRESENTATION Open Access

NK-pDC cross-talk leads to the generation of mTRAIL+IFN-α+cytotoxic pDCs following HIV-1 infection of pDCs. Consequences on the control of viral replication

Héla Saïdi, Marlene Bras*, Formaglio Pauline, Melki Marie-thérèse, Gougeon Marie-Lise

From 16th International Symposium on HIV and Emerging Infectious Diseases
Marseille, France. 24-26 March 2010

Background

Plasmacytoïd dendritic cells (pDCs) play a central role in orchestrating innate and adaptive immunity, especially by secreting large amounts of IFN-α in response to viral stimuli. IFN-α production by pDCs depends upon a cross-talk with NK cells that triggers the activation of NK cells. Considering that NK cells are essential for the elimination of virus-infected cells, and pDC required for their antiviral activity, we addressed the impact of HIV on NK-pDC cross-talk, and the consequences on viral control.

Methods

pDCs and NK cells were sorted with magnetic beads from the blood of healthy donors. NK cells were kept either resting or activated with PMA/ionomycine for 2 hrs. pDC were stimulated with either IL-3 or CpG, or were infected with R5-HIV-1 at various concentrations. pDCs were cocultured with NK cells at various ratios for 24 hrs. The influence of NK-pDC interaction on both cell types was analyzed by multiparametric flow cytometry, combining maturation and cell death/survival markers with cytokine detection, and released cytokines in cultures supernatants were identified and quantified by the MAP luminex technique.

Results

Our results show that high amounts of HIV-1 induced the maturation of pDCs, characterized by the expression of HLA-DR, CD40, CD80, CD86, CCR7 and CD83. This phenotypic maturation was coupled to a functional maturation since HIV-1-infected pDCs were able to activate the production of IFN-γ and TNF-α by NK cells after 24 hrs of co-culture. Consequently NK cells induced, in synergy with the virus, the emergence of killer mTRAIL+IFN-α+ pDCs. In contrast, NK-pDC cross-talk did not induce pDC maturation at low concentration of HIV, and it had a poor effect on the activation of NK cells. Finally, the release of β-chemokines and IFN-α was found dependent both on NK-pDC cross-talk and HIV concentration.

Discussion

We report for the first time that NK-pDC cross-talk induces the maturation and differentiation pDCs into mTRAIL+ IFN-α+ cytotoxic pDCs once infected with HIV-1. Furthermore, depending on virus concentration, NK-pDC was found involved in the viral control, either by triggering or by suppressing the release of anti-HIV molecules, such as β-chemokines and IFN-α.

Published: 11 May 2010

doi:10.1186/1742-4690-7-S1-O4
Cite this article as: Saïdi *et al.*: NK-pDC cross-talk leads to the generation of mTRAIL+IFN-α+cytotoxic pDCs following HIV-1 infection of pDCs. Consequences on the control of viral replication. *Retrovirology* 2010 **7**(Suppl 1):O4.

* Correspondence: marlene.bras@pasteur.fr
Institut Pasteur, Paris, France