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Poster presentation

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Background

Plasmacytoid dendritic cells (pDC) are crucial cells implicated in anti-viral immune responses. On recognizing HIV, they become activated, secreting high amounts of IFNα and inflammatory cytokines, thereby potentiating anti-viral innate and adaptive immune responses. However, the role of pDC in adaptive immunity is still debated. Several studies have documented a role for activated pDC in the induction of CD4+ or CD8+ regulatory T cells (Treg), both in vitro and in vivo. A direct correlation between CD8+ T cell activation levels and disease progression levels has been confirmed in many studies. We investigated here whether HIV-stimulated pDC can regulate the levels of immune activation by promoting the differentiation of regulatory CD4+ T cells.

Methods

Freshly purified pDC from normal donors (New York Blood Bank) were incubated for 7 days with purified allogeneic CD4+ CD25- T cells, and their suppressive activity measured in a secondary proliferative assay. CD86/CD83 expression and cytokine secretion by monocyte-derived DC (moDC) induced by LPS or R848 were measured in presence or absence of CD3-activated Treg. siRNA knockdown of NIK and IKKalpha was performed on the leukemic pDC line GEN2.2 and expression of IDO was monitored at the RNA and protein level.

Results

HIV-stimulated pDC were found to induce the differentiation of Treg from naive CD4+ T cells, in an indoleamine 2,3 dioxygenase (IDO)-dependent way. Furthermore, pDC-induced Treg could suppress the Toll-Like Receptor (TLR)-mediated maturation of moDC, partially through CTLA-4 interaction with CD80/CD86. We further show that TLR triggering induces the activation of IDO through the non-canonical NF-κB pathway, as evidenced by knocking-down the expression of NIK and IKKalpha.

Conclusion

This study reveals what we believe to be a novel mechanism by which pDC may regulate and potentially limit anti-HIV immune responses, and identifies a potential target for clinical intervention.