Impaired IL-23 Signalling and Th17 Dysfunction in HIV Infection


Abstract

Background

The heterodimeric cytokine IL-23 plays a critical role in the maintenance and function of Th17 cells. The IL-23 heterodimer is composed of a p19 subunit and a 23 receptor (IL23R) subunit, both of which are encoded by innate-like cytokine genes. Th17 cell development and survival depend on IL-23 signalling, which is impaired in HIV infection. However, the role of IL-23 in Th17 cell development in vivo is not well understood.

Methods

1. Methods of flow cytometry
2. Expression of the IL-23 receptor chain in blood-derived and HIV-infected Th17 cells was determined by flow cytometry.
3. IL-23 receptor expression was unaffected by in vivo HIV infection.

Results

1. HIV Infection reduces IL-17 secretion in vitro-generated Th17 cells were determined by ELISA and flow cytometry.

2. HIV Infection reduces IL-17 expression in vitro-generated Th17 cells were determined by qRT-PCR.

3. HIV Infection reduces STAT3 expression in vitro-generated Th17 cells were determined by qRT-PCR.

4. HIV Infection inhibits IL-23 signalling by blocking STAT3 phosphorylation.

5. HIV Infection inhibits IL-23 signalling by blocking STAT3 phosphorylation and is not reversed by HAART.

Conclusions

1. Secretion and expression of IL-17 by blood and in vitro-generated Th17 cells is significantly reduced following in vivo HIV infection.

2. The loss of Th17 cells is significantly reduced in response to Th1 cell stimulation following in vivo HIV infection.

3. IL-23-induced STAT3 phosphorylation in blood-derived Th17 cells is significantly inhibited in vivo HIV infection.

4. IL-23-induced STAT3 phosphorylation in blood-derived Th17 cells is significantly inhibited in vivo HIV infection.

5. IL-23-induced STAT3 phosphorylation in blood-derived Th17 cells is significantly inhibited in vivo HIV infection.

6. IL-23 receptor expression is comparable between HIV-seropositive and HIV-seronegative donors.

References


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