BMC Infectious Diseases

RESEARCH ARTICLE Open Access

The number of CCR5 expressing CD4+ T lymphocytes is lower in HIV-infected long-term non-progressors with viral control compared to normal progressors: a cross-sectional study

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Abstract

Background: The HIV co-receptors CXCR4 and CCR5 play an important role in HIV infection and replication. Therefore we hypothesize that long-term non-progressors (LTNP) with viral control have lower expression of CCR5 and CXCR4 on $CD4^+$ cells, specifically on memory T-lymphocytes since they are the primary target cells of HIV.

Methods: In this cross-sectional study, we included five HIV-infected LTNP with viral control (CD4 > 750 cell/μl & HIV < 50 copies for ≥2 years), thirteen HIV-infected and seven HIV-uninfected individuals at Radboud UMC Nijmegen, the Netherlands. We determined the CCR5 and CXCR4 expression among $CD4^+$ and $CD8^+$ lymphocyte subsets; memory ($CD45RO^+$), naïve ($CD45RA^+$) cells and regulatory T-cells ($CD4^+CD25^{high}FoxP3^+$). In addition, CCR5Δ32 polymorphism is related with disease progression and was therefore determined using polymerase chain reaction.

Results: The percentage of CCR5-expressing $CD4^+$ cells of LTNP was comparable with healthy controls; whereas HIV-infected individuals showed more CCR5-expressing cells. This was observed in memory and naïve $CD4^+$ cells, but not in regulatory T-cells. The mean fluorescence intensity of CCR5-expressing $CD4^+$ cells was similar in all groups. All groups had comparable percentages of CXCR4-expressing cells. The mean fluorescence intensity of CXCR4-expressing cells was significantly higher in HIV-infected normally progressors in both memory and naïve $CD4^+$ cells, but not in $CD8^+$ cells. The CCR5Δ32 polymorphism was not related to group.

Conclusions: We show that HIV affects -directly or indirectly- the expression of CCR5 in $CD4^+$ T-lymphocytes; yet this effect is not seen in LTNP with viral control. Avoiding upregulation of CCR5 could be an important method via which LTNP counteracts the effects of HIV and suppresses viral replication. Exploring how LTNP suppress the upregulation of CCR5 could be an important step for discovering new therapeutics.

Keywords: HIV, CCR5, CXCR4, Elite controllers, T-lymphocytes, Regulatory T-cells, Memory T cells, Naïve T cells, HIV co-receptors

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