Restoration of the NK cells ability to Mediate ADCC in HIV-1 Positives after Six Months of HAART can be explained by Normalization of their Phenotype

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Introduction

HIV infection leads to changes in NK cell subsets, phenotype and cytolytic function. During a chronic HIV infection, the frequency of NK cells expressing CD57, CD27, CD70 and CCR7 is up-regulated. Impaired NK cell function during HIV infection has been linked to the reduced surface expression of the natural cytotoxicity receptor NKp46.

We evaluated how ADCC function and NK cell phenotype changes in HIV-infected individuals before and after HAART.

Design

i) Patients’ PBM effector cells (as a source of NK cells) together with a standard anti-HIV polyclonal IgG preparation.

ii) Patients’ plasma together with healthy donor PBMCs.

iii) An autologous model of patients’ plasma together with patients PBMC.

ADCC responders versus non-responders

Samples were collected before and after six months of HAART.

Twelve individuals showed an increase in ADCC activity and are defined as ADCC responders (Figure 1A).

Seven individuals with a decrease in PBM effector cell ADCC activity are defined as ADCC non-responders (Figure 1A).

Results and Conclusion

The NK cells ability to mediate ADCC was improved already after six months of HAART.

The ability of antibodies to mediate ADCC was unchanged or decreased. A correlation between cytotoxic activity and immune restoration was not found. Moreover, the nadir CD4+ T cell count did not influence ADCC activity

Normalization in the frequency of NK cells expressing CCR7 and CD27 correlated with HAART.

Knowing that the normalization of NK cell subsets requires years of HAART, it is an important finding that the ability to mediate ADCC was improved already after six months. Not at least in the context of a therapeutic vaccine aiming at inducing ADCC mediating antibodies.

Methods

The ADCC-GranToxiLux assay (Oncoimmunin) was performed. CEM.NKR, cells were coated with gp120 and labeled with TFL4 and NFL1.

The Effector-Target ratios of 30:1 and plasma/antibodies were tested in 5-fold dilutions starting at 1:250.

The NK cell subset distribution and NK cell phenotype (i.e. expression of maturation and activation markers within NK cell subsets) were analyzed.