CHARACTERIZATION OF NK CELLS IN ELITE CONTROLLERS LOSING HIV CONTROL

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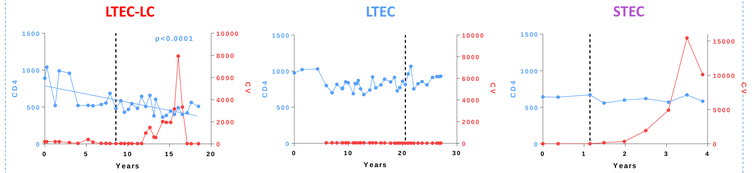
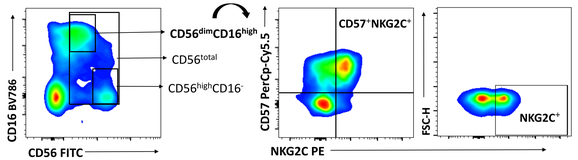
BACKGROUND

HIV-infected elite controllers (EC) are defined as individuals with undetectable viral load in the absence of treatment. Consequently, the nature of their effector immune response is of considerable interest. In this study, using samples from 3 different cohorts of EC: 5-20 years long-term (**LTEC**); 1-4 years short-term (**STEC**) and LTEC losing control (**LTEC-LC**), we asked if phenotypical or functional signatures of NK cells would define the loss of control.



From **CD3**$^{-}$ cells, three populations of NK cells were studied:

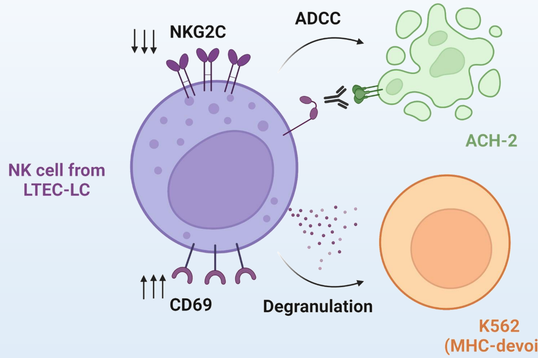


Within the CD56dimCD16high subpopulation, we focused on the **memory-like NK cell** subset, characterized by the expression of the activating receptor NKG2C.

MAIN FINDINGS

Phenotypical and functional differences in the NK cell repertoire of HIV EC might define the loss of control:

- Loss of a **memory-like NK cell** compartment
- Increased **basal activation**, based on CD107a and CD69 expression
- Decreased **ADCC response** against HIV-infected cells

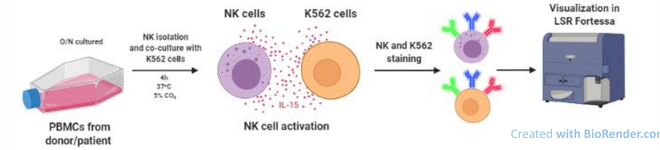


Further studying these mechanisms could help design novel therapeutic strategies to eliminate HIV infection

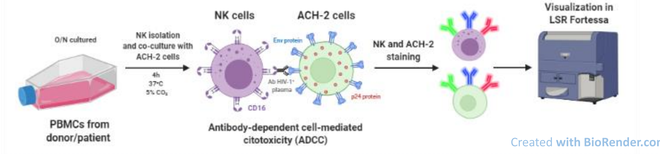
METHODS

PBMC samples from n=37 EC (n=19 LTEC; n=5 STEC and n=13 LTEC-LC) and n=15 healthy donors (**HD**) were included in the study.

- Flow cytometry was used for the **phenotypic** studies and included the markers CD57, CD56, Nkp30, NKG2C, NKG2A, CD16, CXCR3, CD158b, KLRG1, CD69 and HLA-DR.
- **Activation studies** were performed after co-culturing isolated NK cells with the MHC-devoid K562 cell line in the presence of IL-15 for 4h. IFNg and CD107a production was measured by flow cytometry.

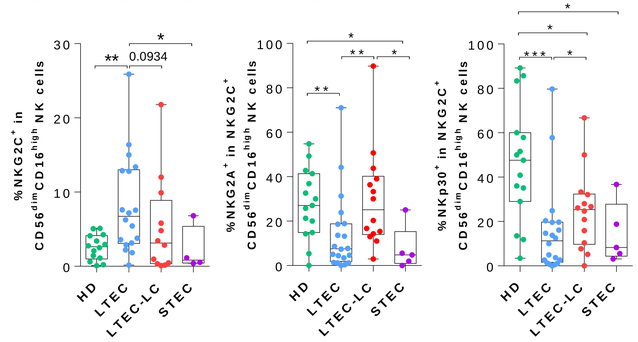


- **Antibody-dependent cell-mediated cytotoxicity** (ADCC) mechanism was assessed after co-culturing NK cells with the chronically-infected cell line ACH-2 in the presence of plasma from a viremic patient containing HIV-specific antibodies.



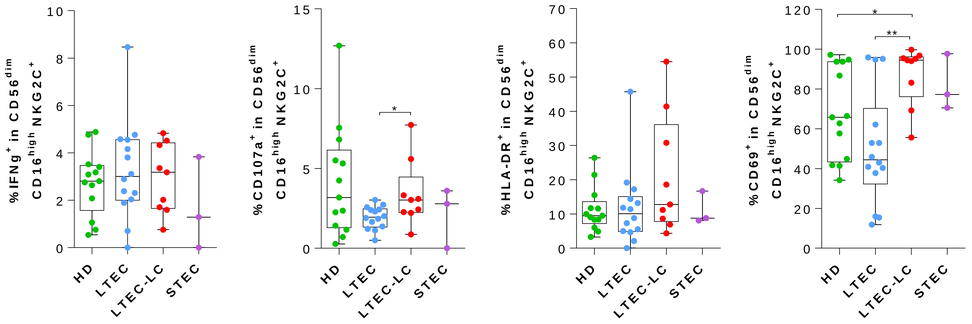
RESULTS

1) Higher frequency of Memory-Like NK cells in LTEC patients



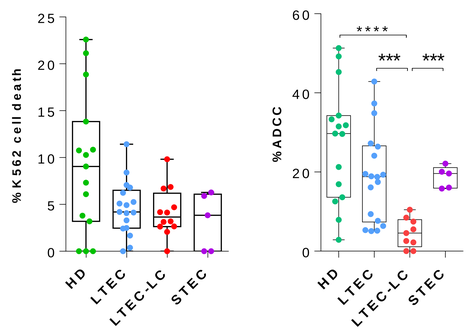
- **LTEC** patients show significantly higher frequencies of **memory-like NK cells** (NKG2C+) compared to **HD**.
- **LTEC-LC** patients show higher expression of the inhibitory receptor **NKG2A** and the activating receptor **NKp30** compared to **LTEC** patients.

2) Increased basal activation in NKG2C^{+} NK cells in LTEC-LC patients



- Memory-like NK cells from **LTEC-LC** patients express higher levels of **CD107a** and **CD69** compared to **LTEC** patients ($p<0.05$) in a basal state.

3) Reduced ADCC activity in NK cells from LTEC-LC patients



- NK cells from **LTEC-LC** patients show a significanlty lower **ADCC** activity against HIV-expressing cells compared to **LTEC**, **STEC** and **HD** cohorts

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