DISTINCT NK CELL RESPONSES DEFINE DURABLE CONTROL IN ELITE CONTROLLERS

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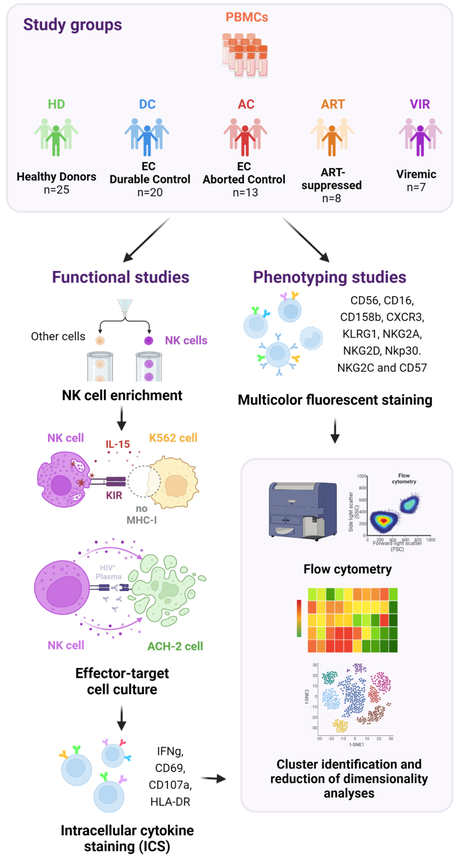
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BACKGROUND

Elite Controllers (EC) are PLWH that present spontaneous control of the infection, thus representing a model for a functional cure. Hence, understanding their mechanisms of immune-mediated control is of considerable interest. We sought to characterize the NK cell repertoire in EC, including their phenotypic properties and functional potential.

METHODS

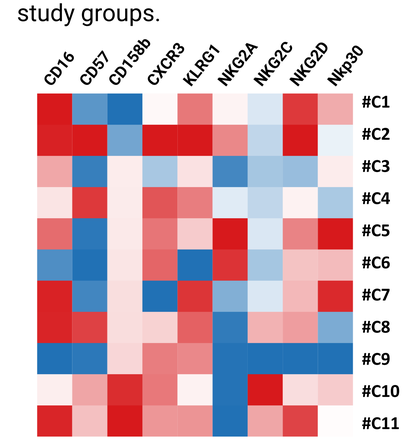


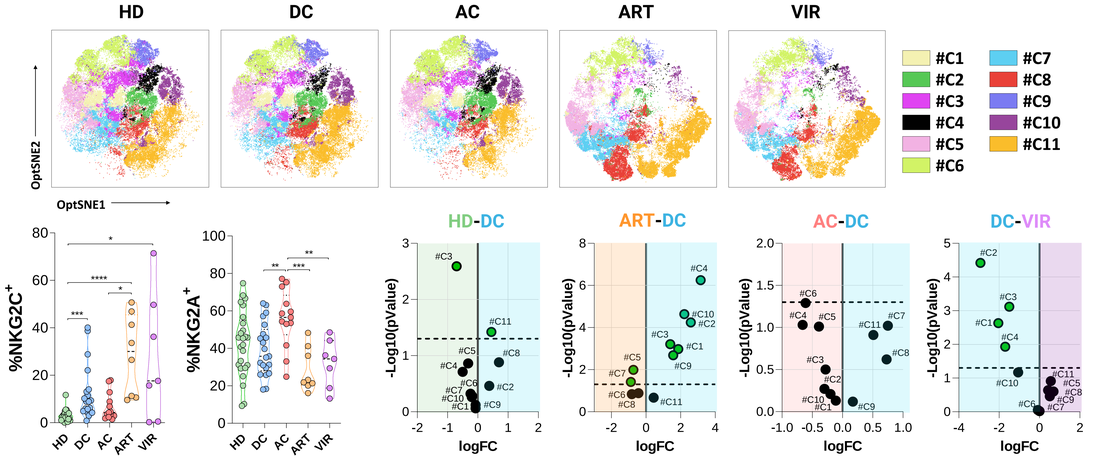
AC was defined by a progressive and significant $CD4^+$ T cell depletion during the patient's follow-up period.

RESULTS

DISTINCT PHENOTYPIC PROFILES CHARACTERIZE NK CELLS FROM DC INDIVIDUALS

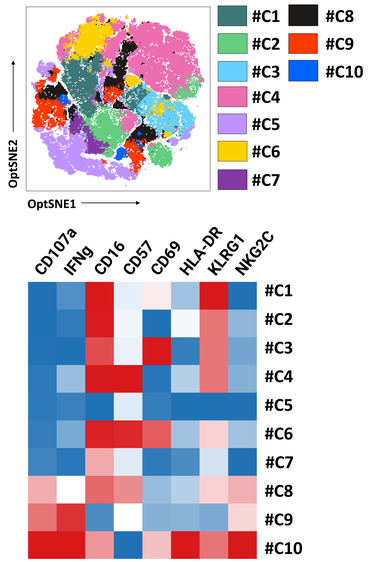
Reduction of dimensionality (optSNE) and unsupervised clustering analyses using FlowSOM algorithm allowed the identification of 11 different **NK cell clusters** based on the expression of CD16, CD57, CD158b, CXCR3, KLRG1, NKG2A, NKG2C, NKG2D and Nkp30. $NKG2C^+$ and $NKG2A^+$ NK cell frequencies among study groups are shown. Volcano plots show the statistically significant differences in the cluster composition between study groups.

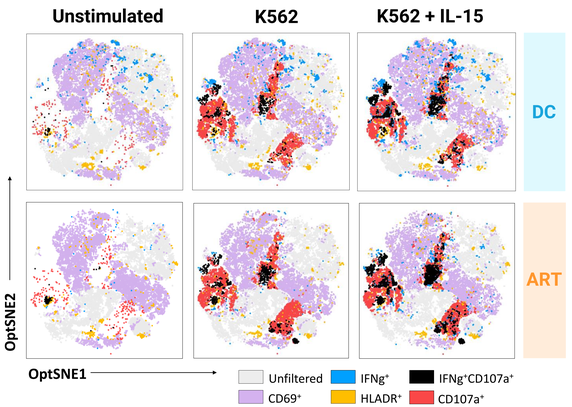




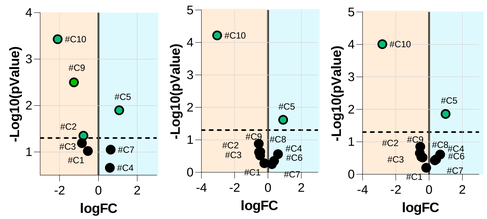
DC NK CELLS SHOW MARKED CYTOTOXIC RESPONSES UPON STIMULATION

A marked **cytotoxic response**, and the enrichment of activated NK cell clusters are observed in all groups:

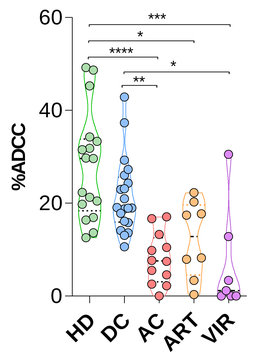




Higher frequencies of these subsets are observed in **ART** compared to DC:

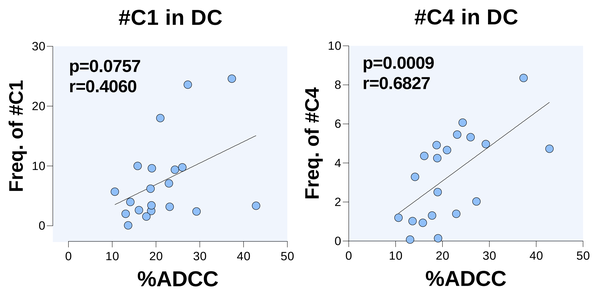


ROBUST ADCC DEFINES NK CELLS FROM DC



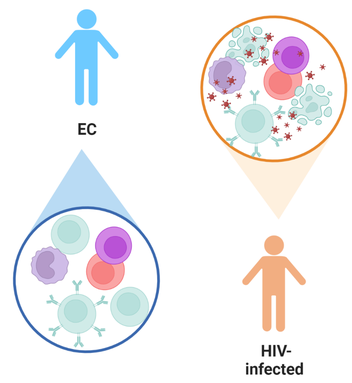
NK cells from DC present a **strong ADCC** response compared to AC, ART, and VIR subjects.

Importantly, this response is positively associated to **specific NK cell subsets** that are enriched in DC compared to ART and VIR groups.



CONCLUSIONS

Phenotypical and functional changes among the NK cell repertoire of EC may contribute to the durable control of HIV infection:



- Specific **NK cell population enrichment** based on phenotypic attributes
- Marked **cytotoxic responses** upon stimulation, but lower frequencies of activated NK cell subsets compared to all groups
- Remarkable **ADCC activity**, similar to HD, when compared to HIV groups
- Positive **association** between NK cell subsets enriched in DC and an increased ADCC response

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

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