Autologous dendritic cell vaccination against HIV alters NK cell frequency and phenotype

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BACKGROUND

Natural killer (NK) cells play an essential role in the antiviral immune response. Moreover, dendritic cell (DC)-NK crosstalk has been described extensively. However, their role in dendritic cell (DC)-based therapeutic vaccination against HIV remains understudied. Therefore, we aimed to investigate whether DC-based vaccination affects NK cell frequency and phenotype by analysing samples from a previously performed therapeutic vaccination study (Allard *et al*., Clin. Immunol., 2012).

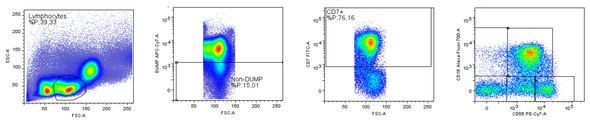
METHODS

HIV-1 infected individuals stable on combined antiretroviral therapy (cART), received 4 vaccinations with autologous DCs electroporated with mRNA encoding Tat, Rev and Nef (DC-TRN), after which cART was interrupted (ATI). PBMCs were collected at different time points: before vaccination (baselin; N=8), 1 week after second vaccination (vac#2 + 1w; N=9), 4 weeks after ATI (ATI+4w; N=8) and 16 weeks after ATI (ATI+16w; N=8). Phenotyping of NK cells was performed using flow cytometry.

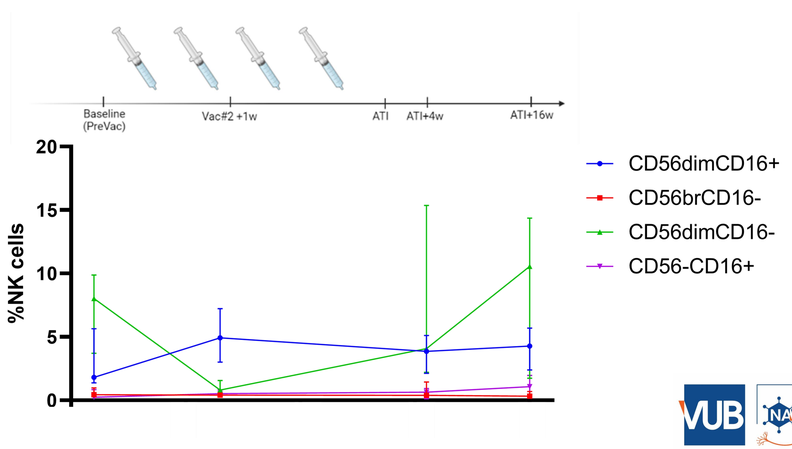
RESULTS

Figure 1: DC-TRN vaccine alters the frequency of NK cell subpopulations

A) Gating strategy: T cells, B cells, monocytes and dead cells were excluded in the DUMP gate. NK cells were gated on using CD7, CD56 and CD16.



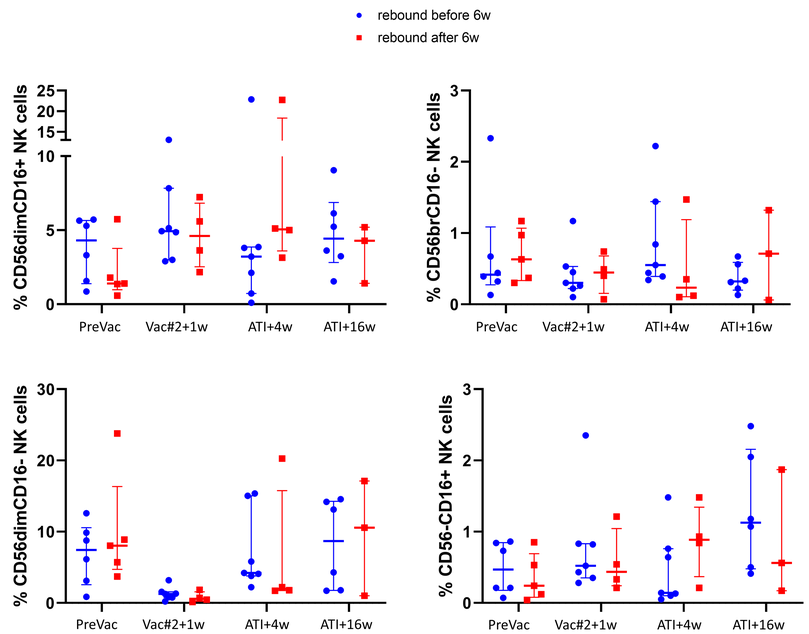
B) Changes in NK cell subpopulations during the DC-TRN trial
Data are presented as median with interquartile range



The DC-TRN vaccine induces a shift towards cytotoxic NK cells and results in NK cell licensing, highlighting the importance of NK-DC crosstalk

Figure 2: Comparison of NK cell frequency between cART resumers and non-resumers

Study participants were classified based on the time to reach a pVL >1000 c/mL (i.e. rebound). Results showed no statistical differences between participants that rebounded before or after 6 weeks of ATI for all time points (Mann-Whitney U test). Data are presented as median with interquartile range.



CONCLUSIONS

- DC-TRN vaccine increases the frequency of cytotoxic NK cells ($CD16^+$), whereas the number of helper NK cells ($CD16^-$) only exceeds baseline values after ATI+16w. However, viral replication has restarted at this last time point which may affect the NK cells.
- Whereas cytotoxic NK cells show an increase in KIR expression and decrease in activating receptors after vaccination and ATI (indicating licensing), helper NK cells showed a reverse pattern. Additionally, an overall decrease in expression of CD8, CD57, immune checkpoint molecules was observed.
- These findings highlight the importance of NK-DC crosstalk and should be taken into account for future clinical trials.

CONTACT INFORMATION

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Figure 3: DC-TRN vaccine alters NK cell phenotype

Heatmap summarizing the NK cell phenotype of DC-TRN study participants (n = 9). Colors indicate the percentage of each NK cell subpopulation that expresses the indicated marker.

