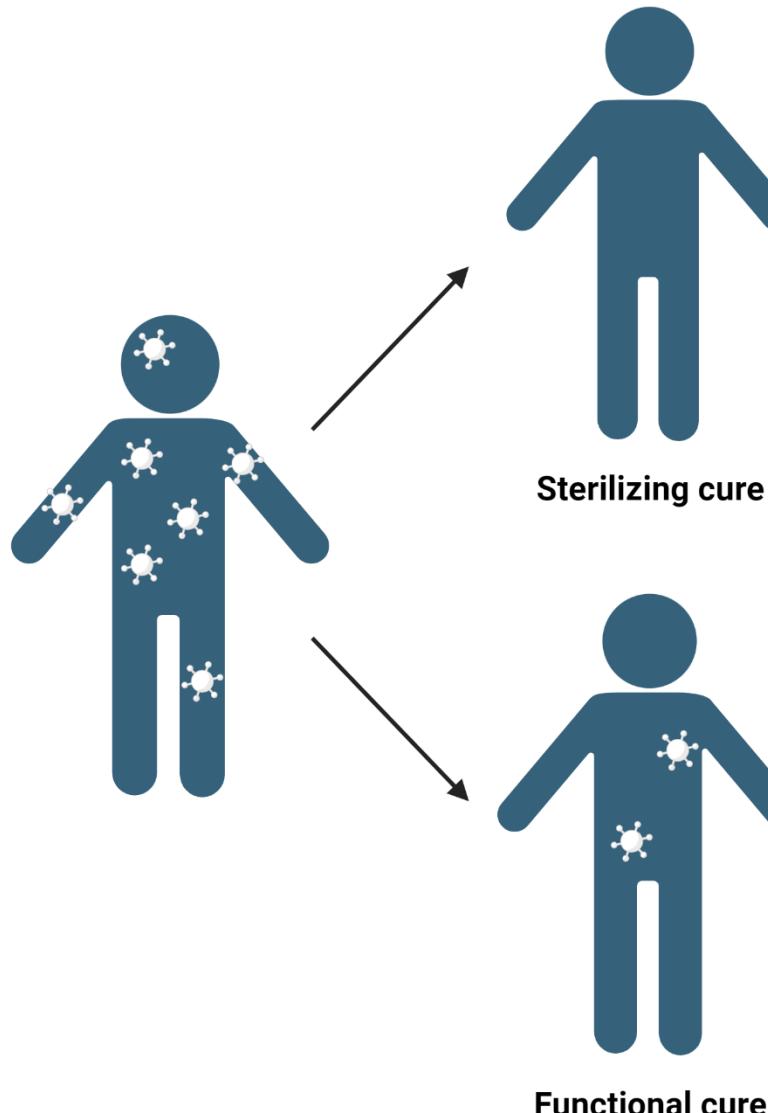


BREACH

Autologous dendritic cell vaccination against HIV-1 induces changes in natural killer cell phenotype and functionality

Thessa Laeremans, Sabine den Roover, Cynthia Lungu, Sigrid D'haese, Rob A. Gruters, Sabine D. Allard and Joeri L. Aerts
npj Vaccines (2023), 8(1):29

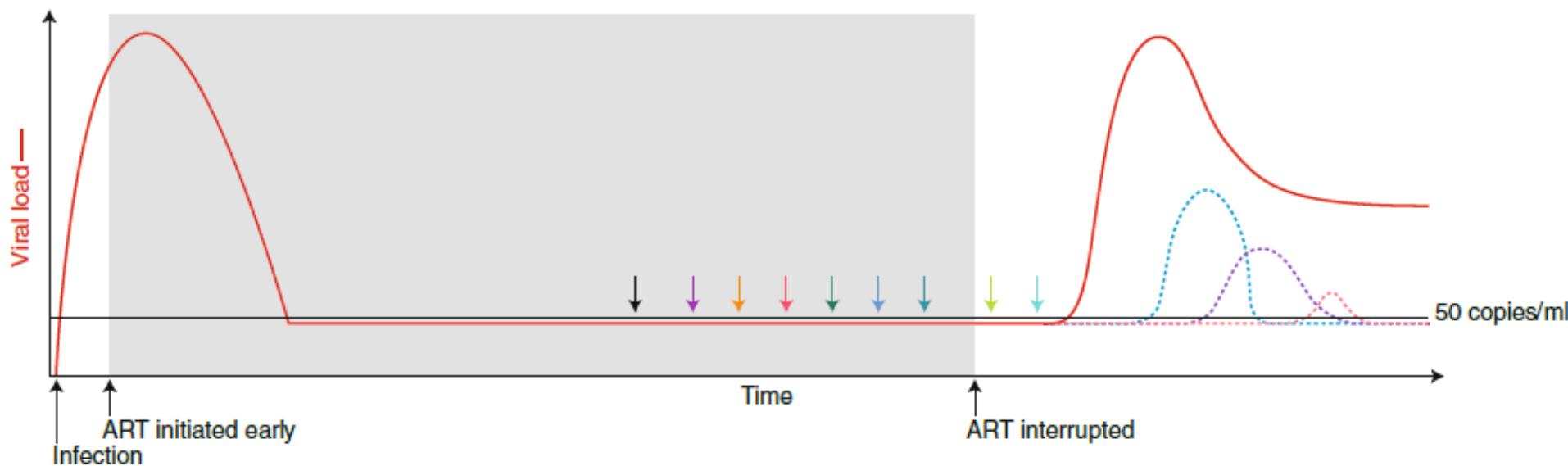
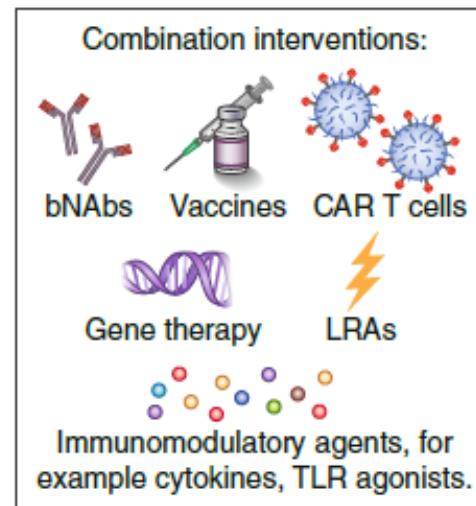
Sterilizing versus functional cure



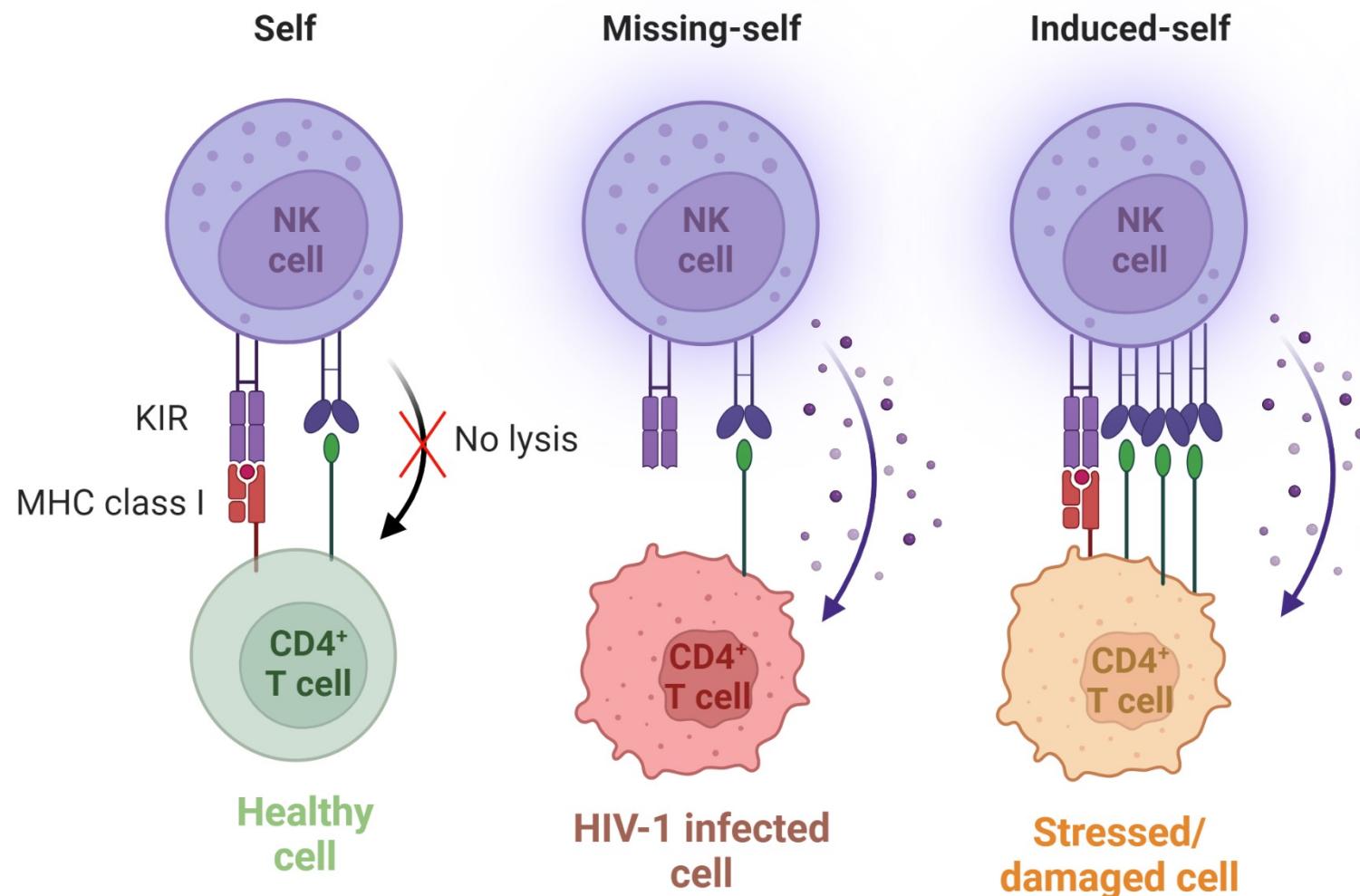
Functional cure strategies for HIV-1

Early ART initiation is associated with:

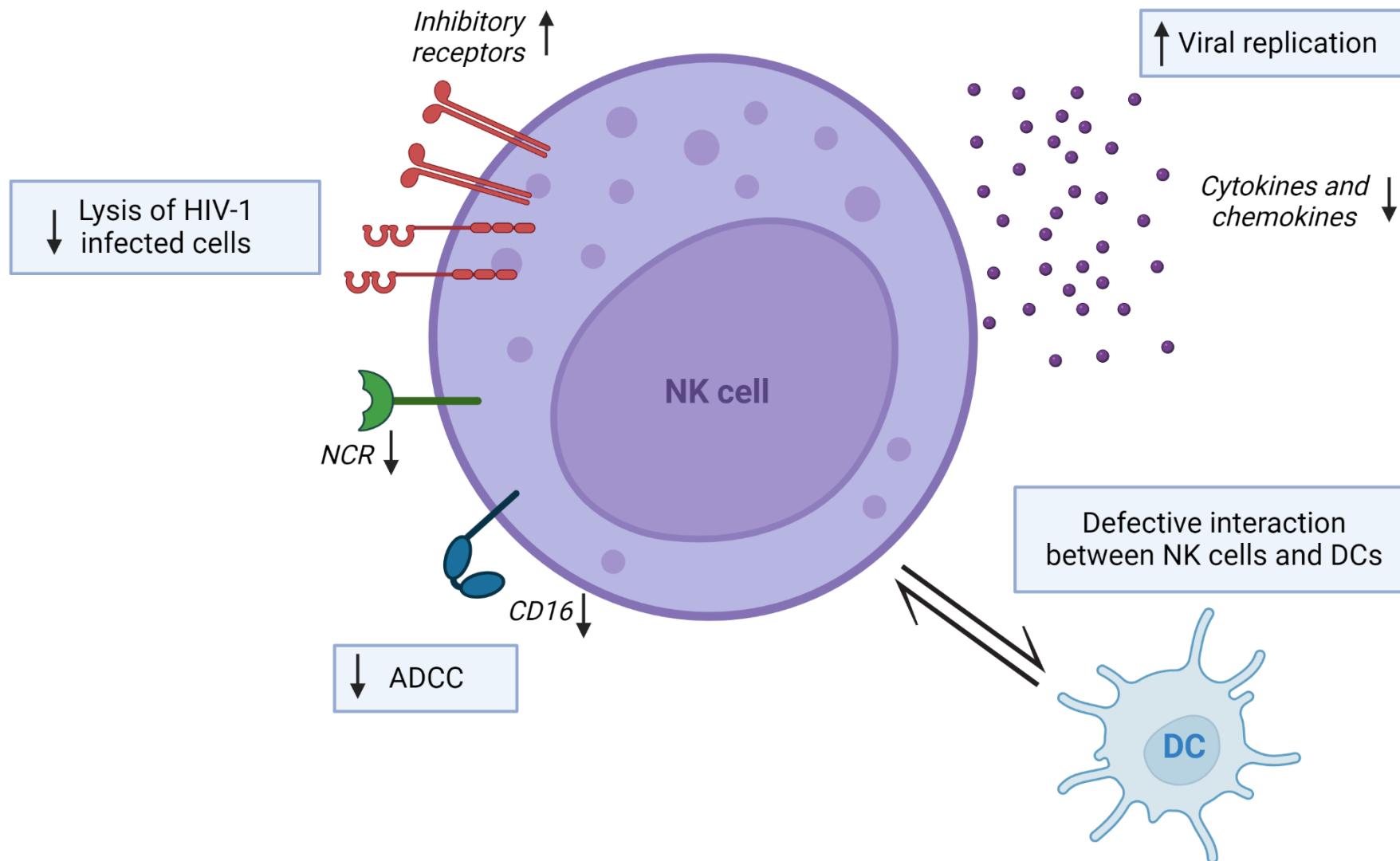
- Reduced inflammation
- Preserved immune responses
- Lower reservoir size and diversity



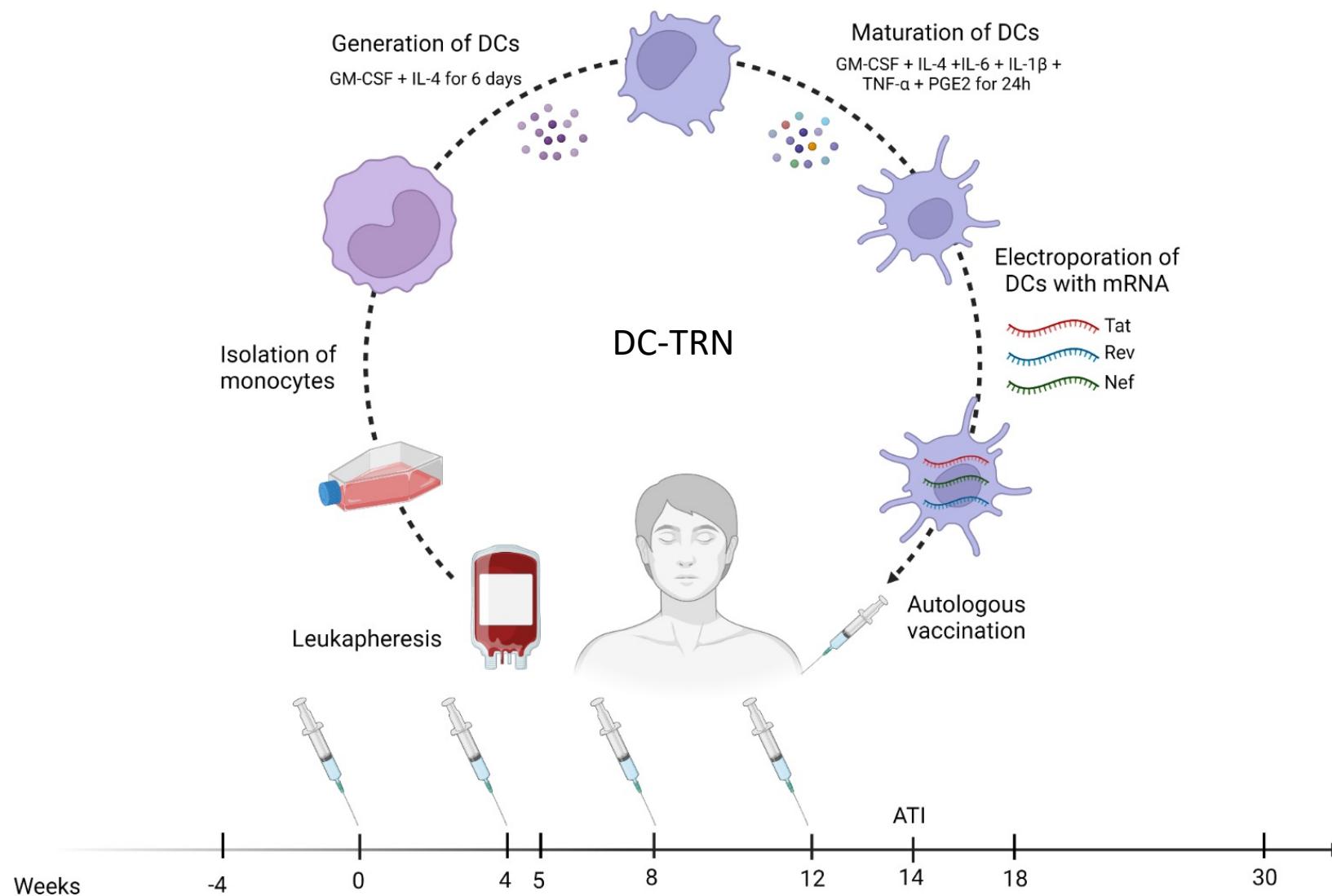
Natural killer (NK) cells



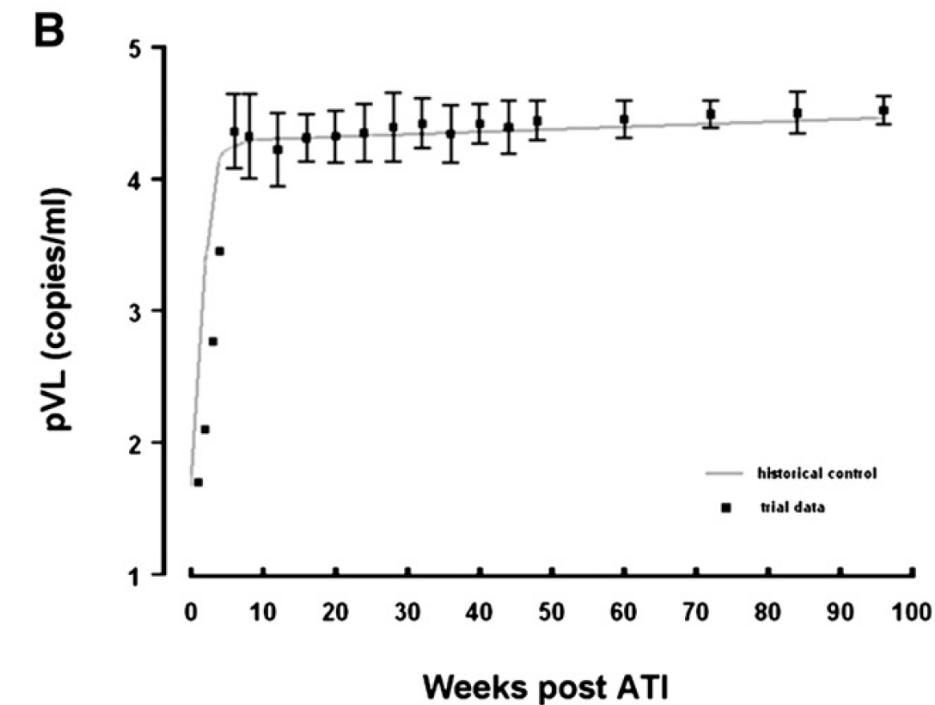
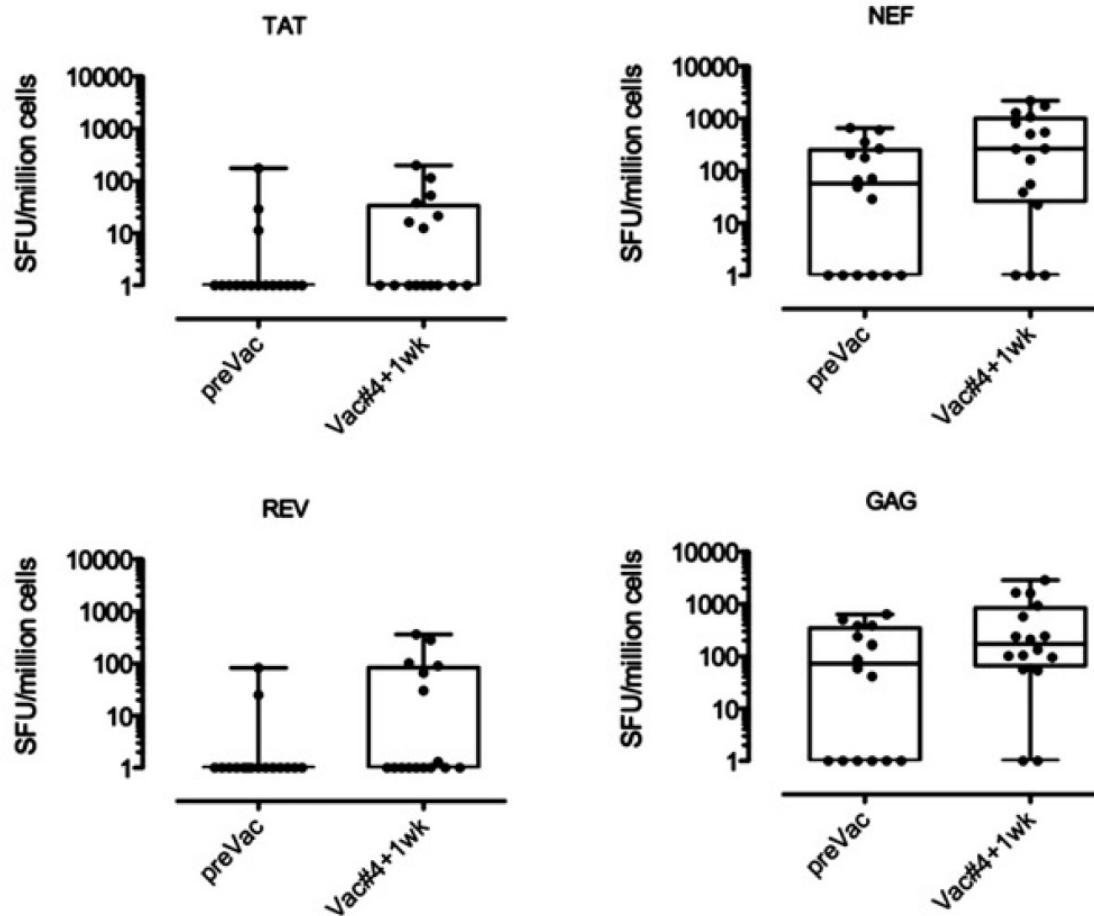
HIV-1 impairs NK-cell function



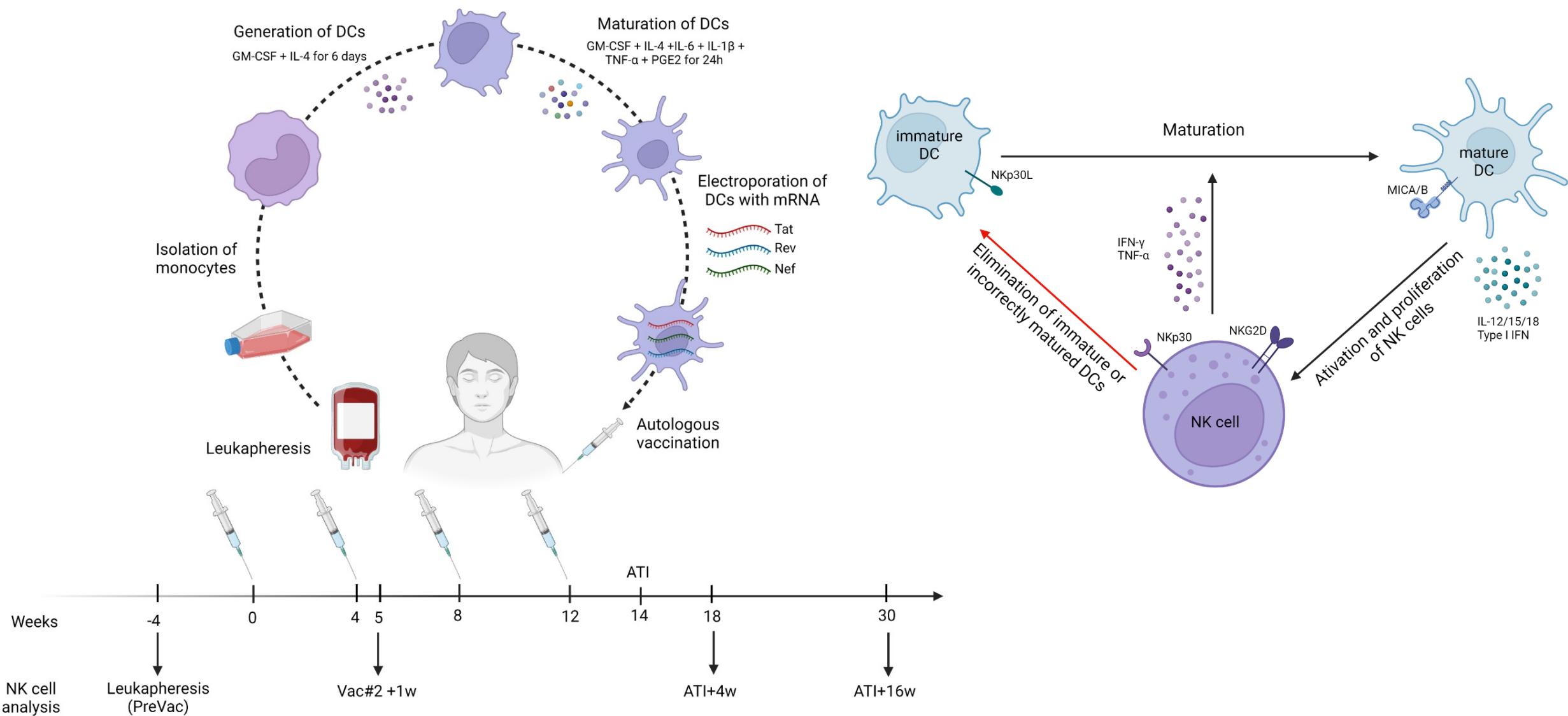
Therapeutic vaccination against HIV-1



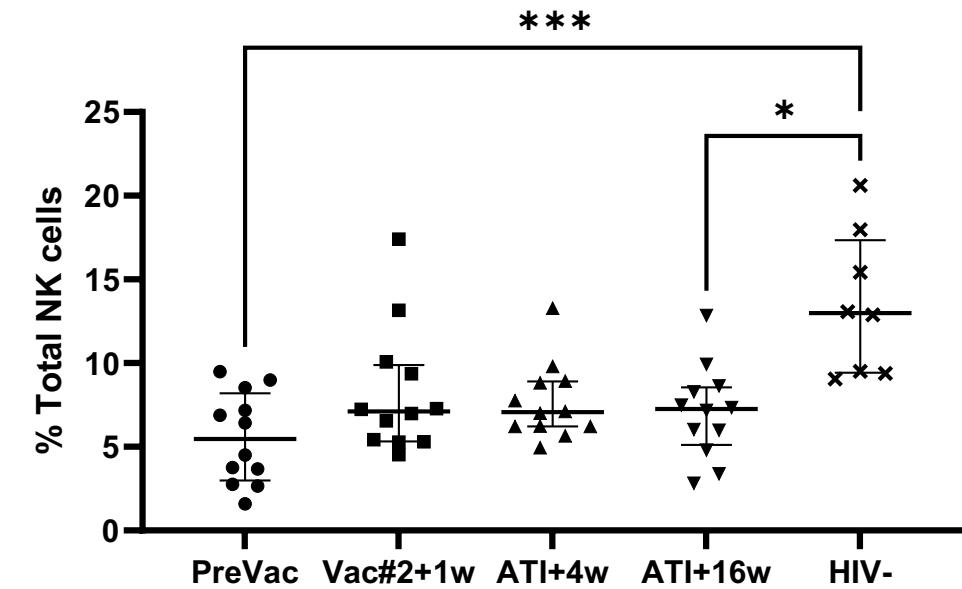
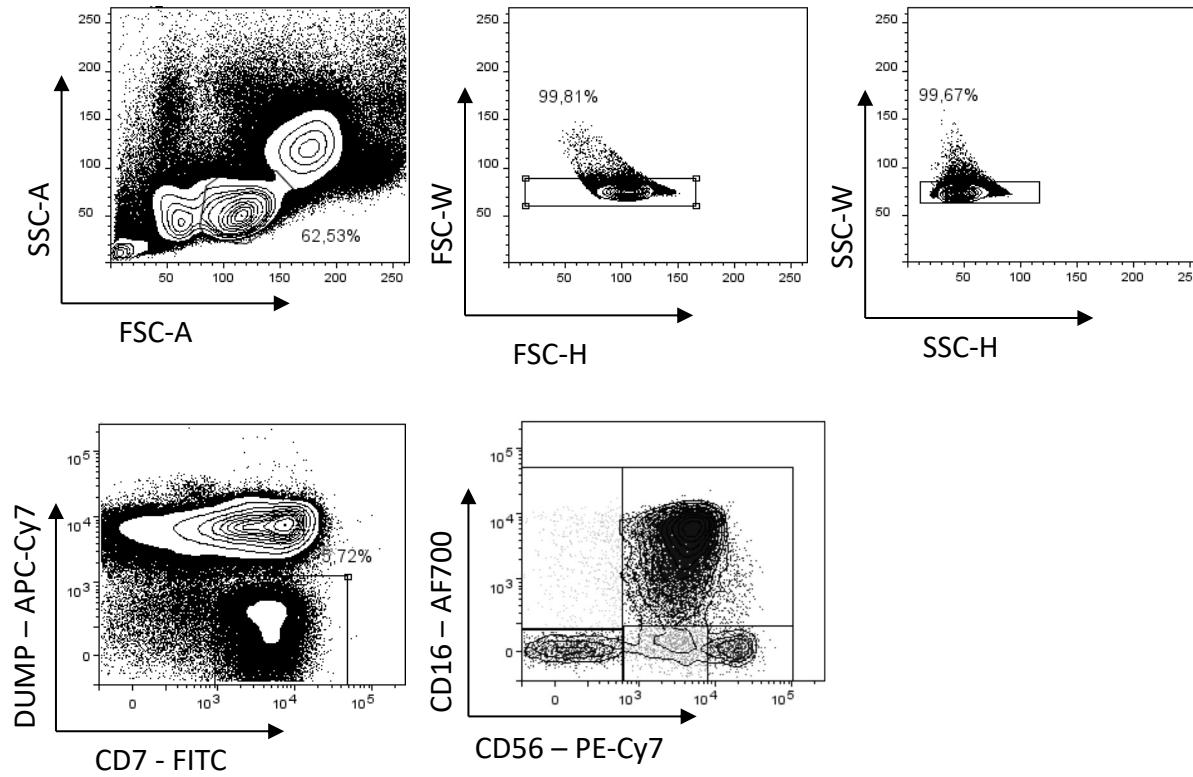
DC-TRN vaccine induces antigen-specific CD4⁺ and CD8⁺ T-cell responses



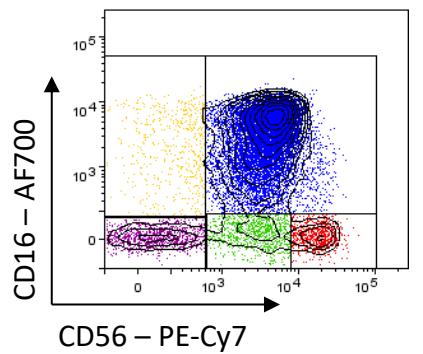
DC-TRN vaccination trial design



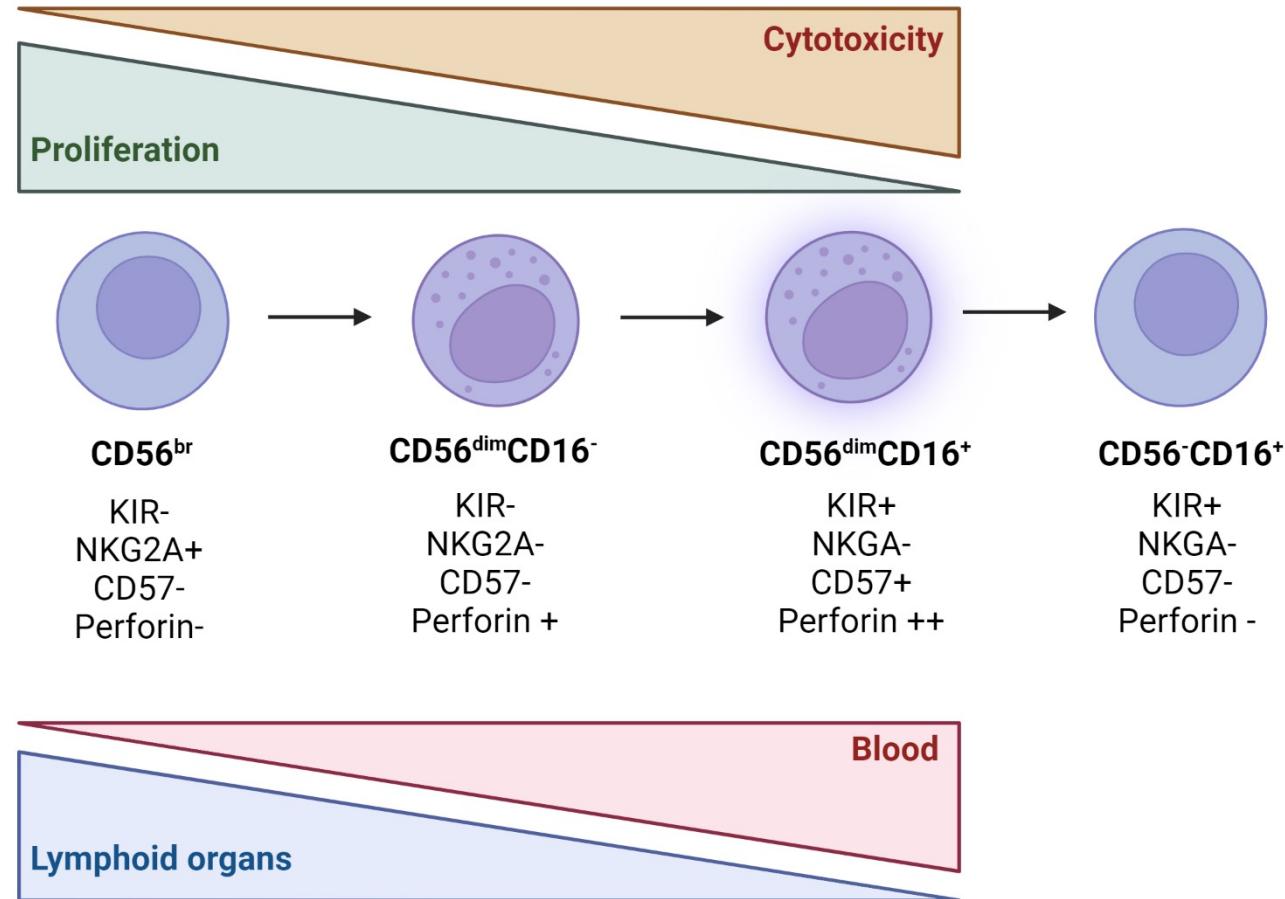
DC-TRN vaccine does not affect total NK-cell frequency



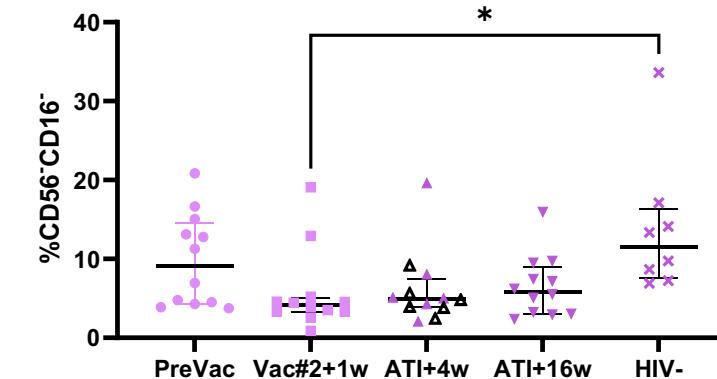
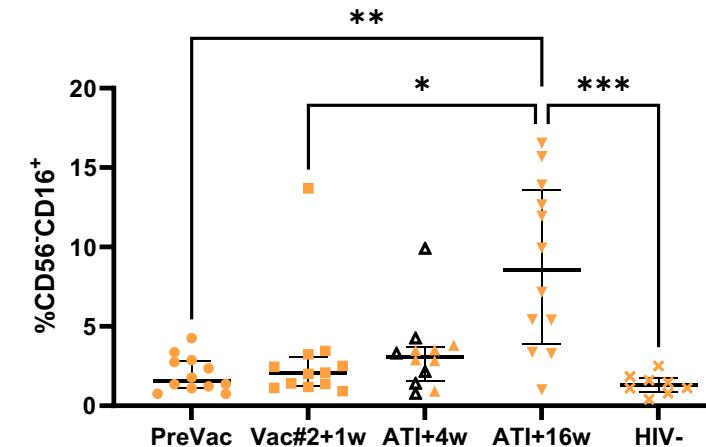
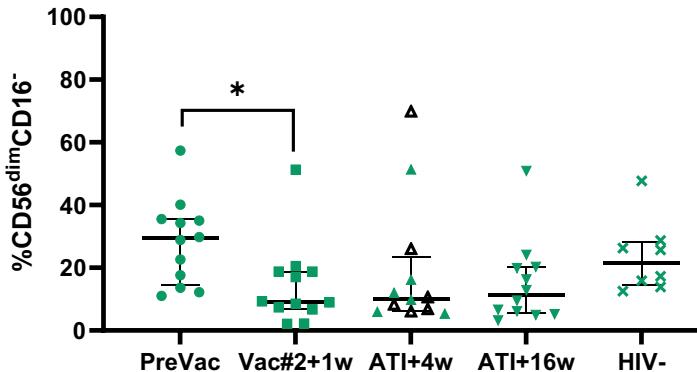
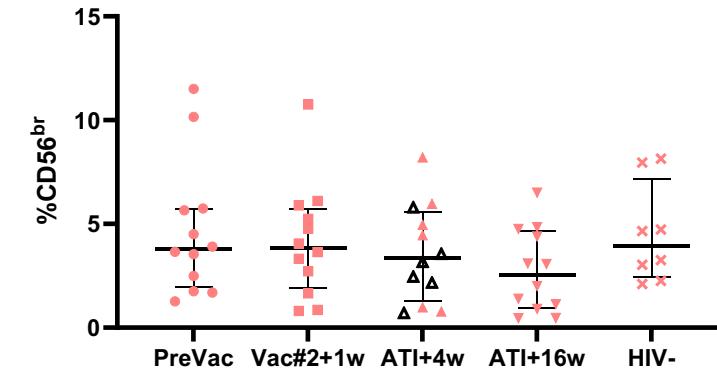
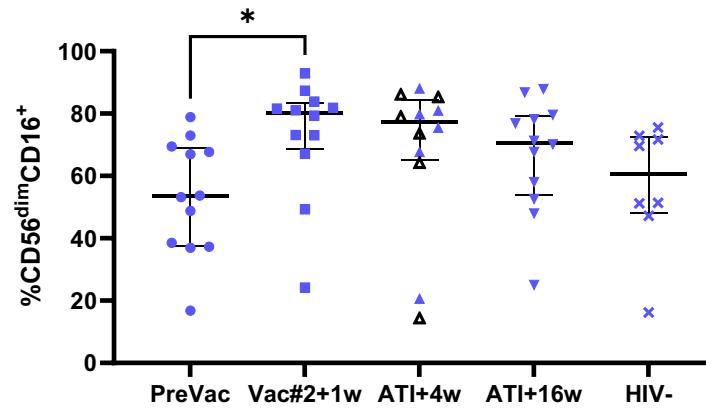
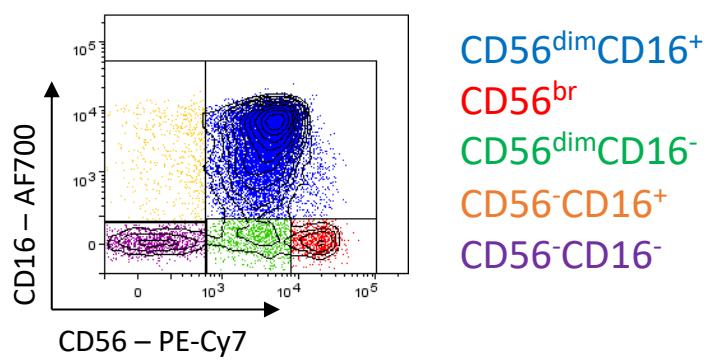
DC-TRN vaccine increases the frequency of cytotoxic NK cells



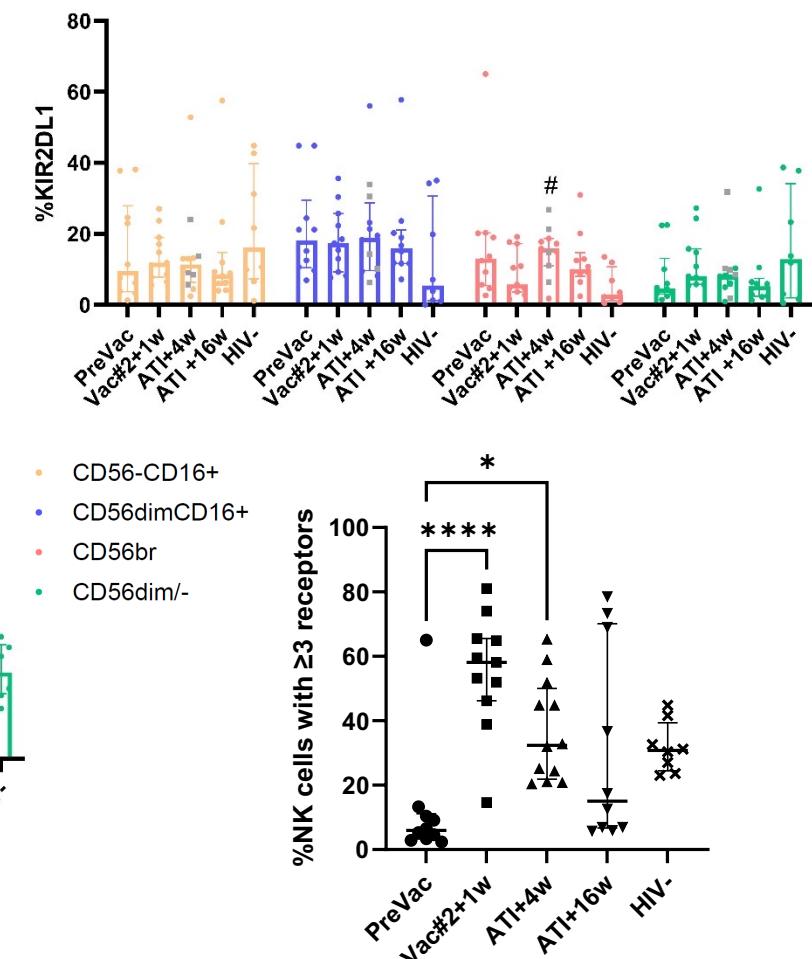
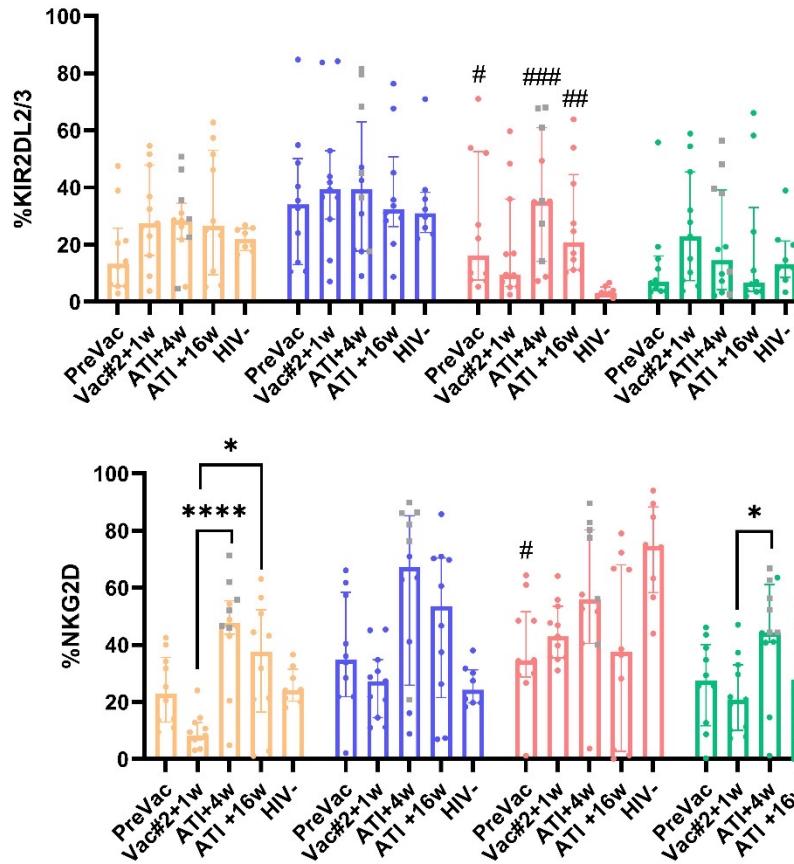
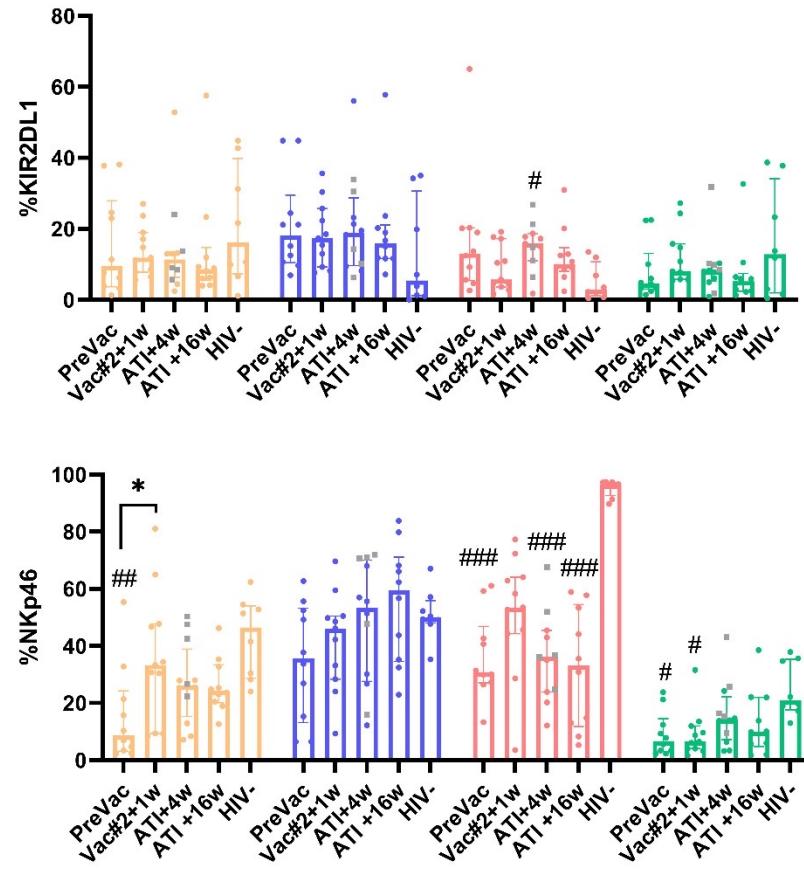
CD56^{dim}CD16⁺
CD56^{br}
CD56^{dim}CD16⁻
CD56⁻CD16⁺
CD56⁻CD16⁻



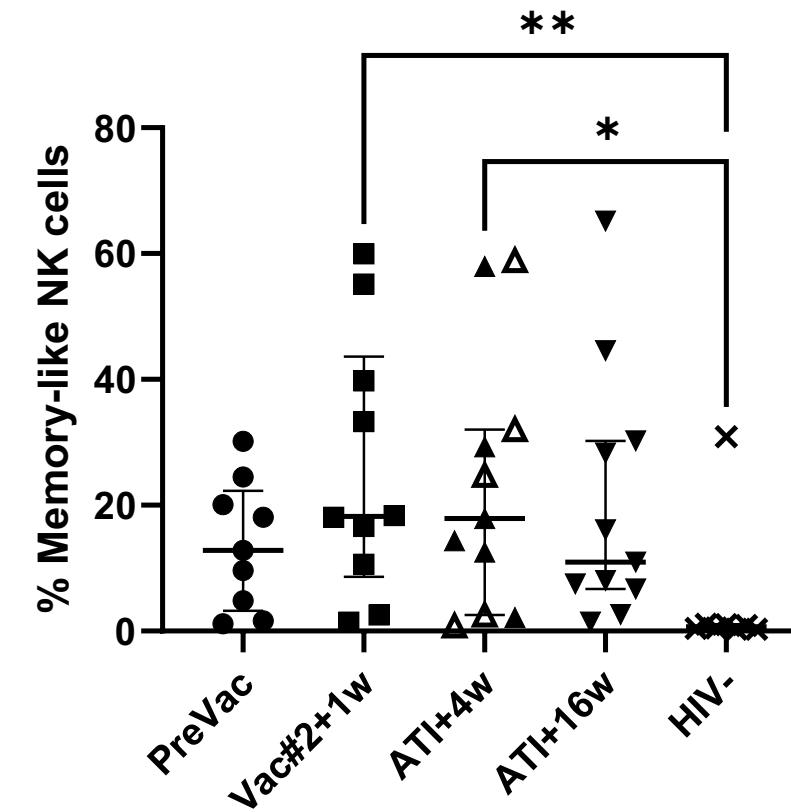
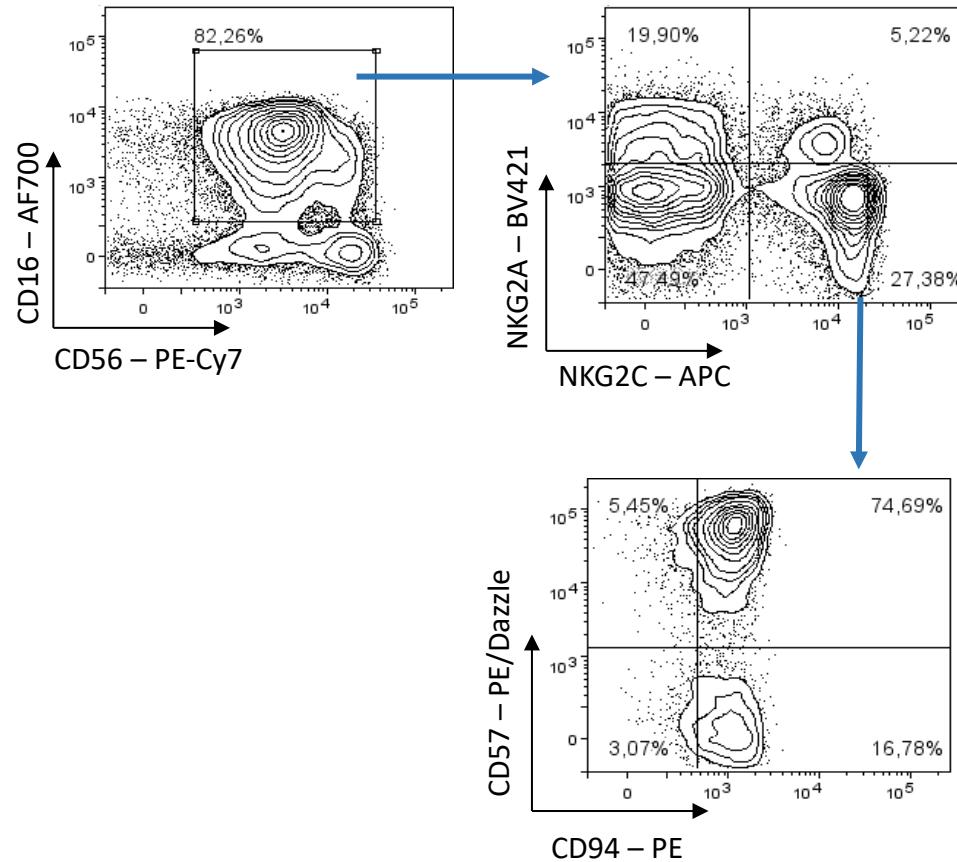
DC-TRN vaccine increases the frequency of cytotoxic NK cells



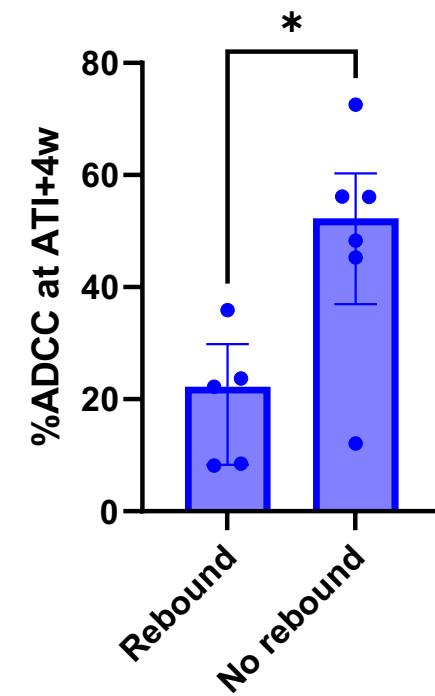
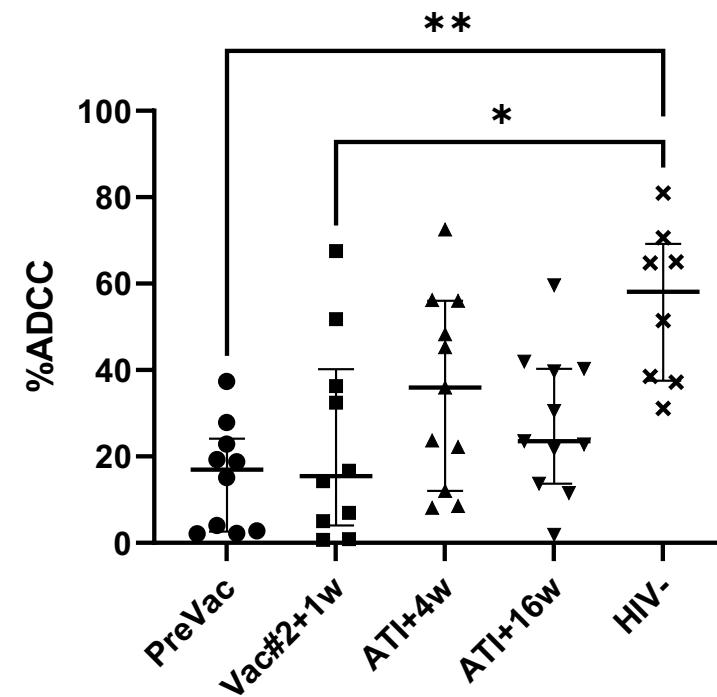
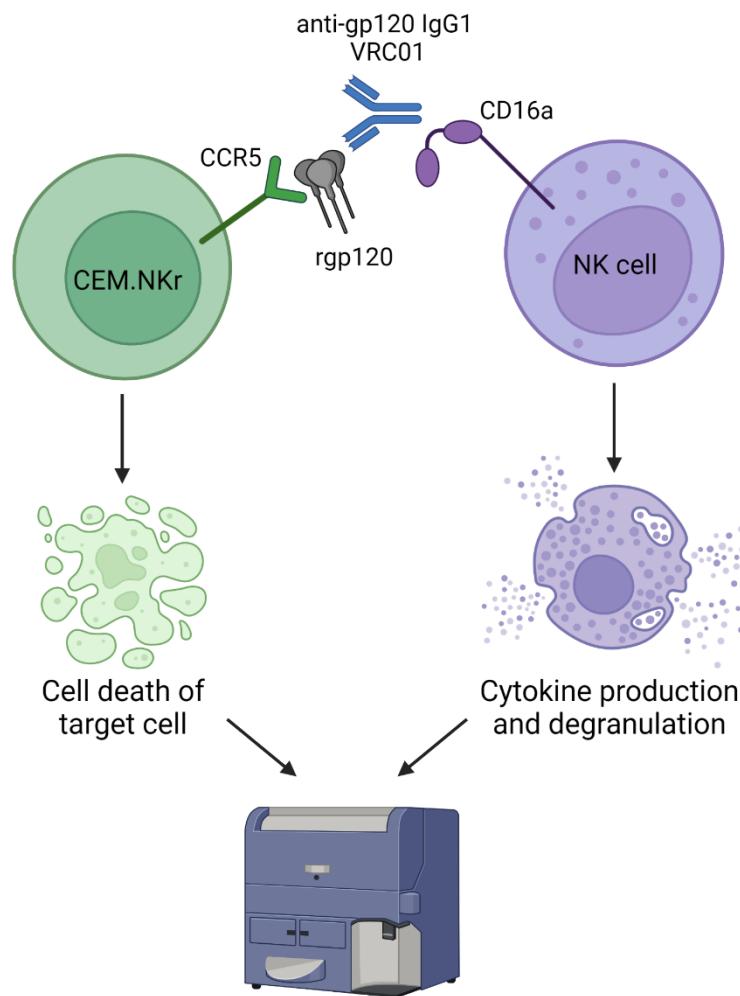
Increased NK cell receptor repertoire upon DC-TRN vaccination



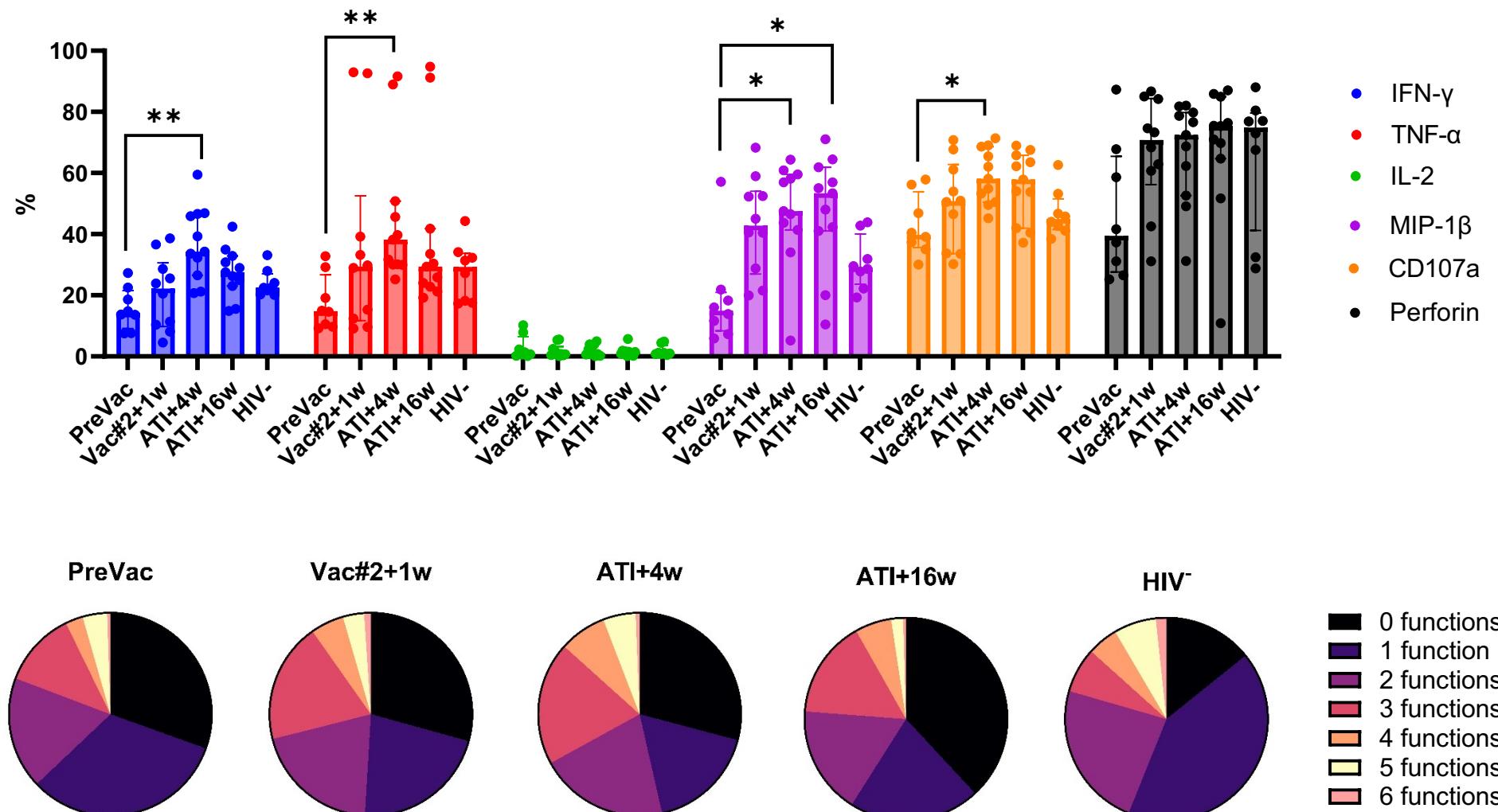
Frequency of memory-like NK cells modestly increases following vaccination



ADCC-mediated NK cell cytotoxicity

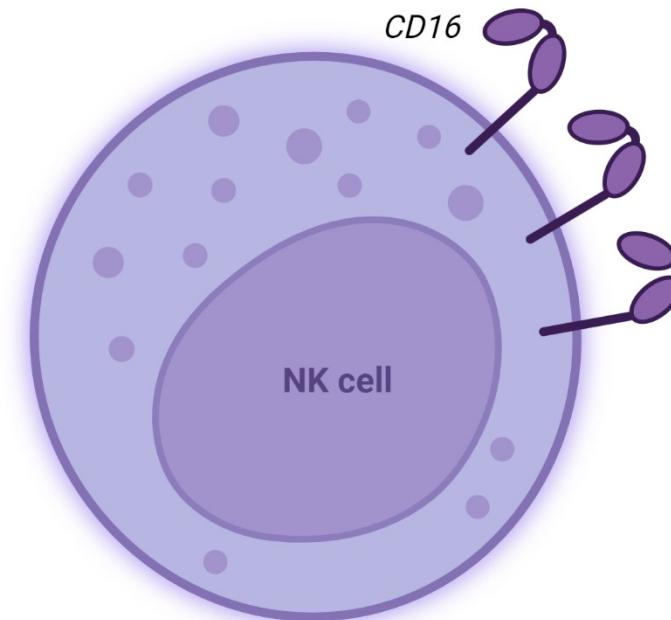


DC-TRN vaccine increases NK-cell (poly)functionality



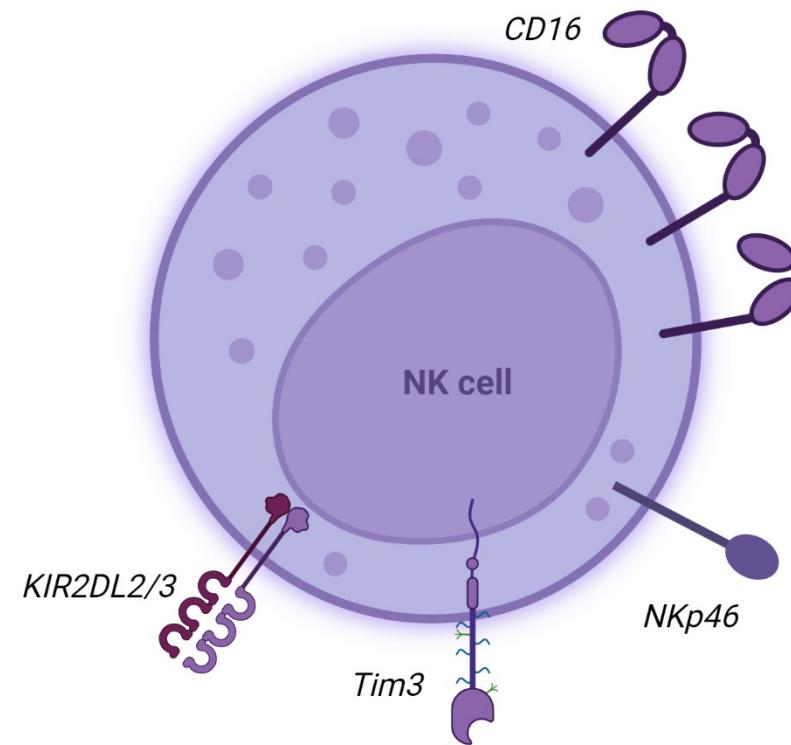
Conclusions

- DC-TRN vaccine:
 - Increases the proportion of cytotoxic NK cells



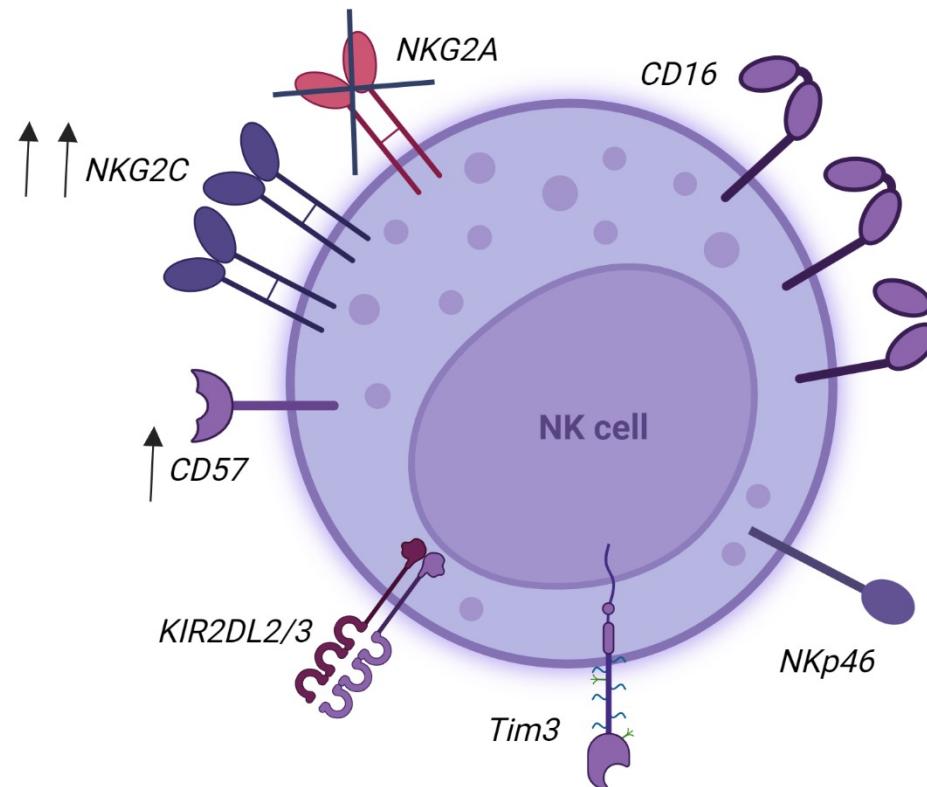
Conclusions

- DC-TRN vaccine:
 - Increases the proportion of cytotoxic NK cells
 - Increases the receptor repertoire on NK cells



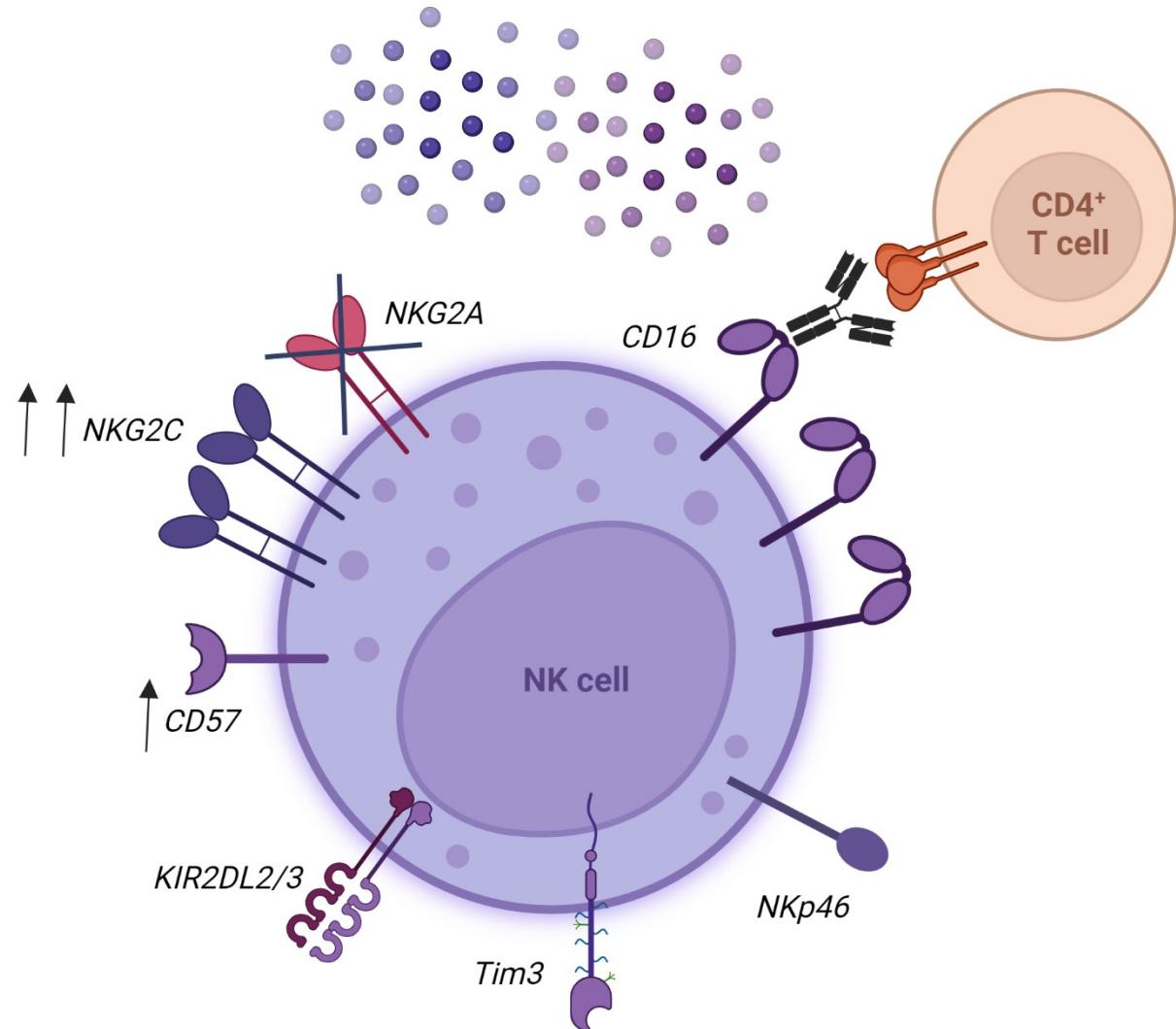
Conclusions

- DC-TRN vaccine:
 - Increases the proportion of cytotoxic NK cells
 - Increases the receptor repertoire on NK cells
 - Modestly increases the frequency of memory-like NK cells



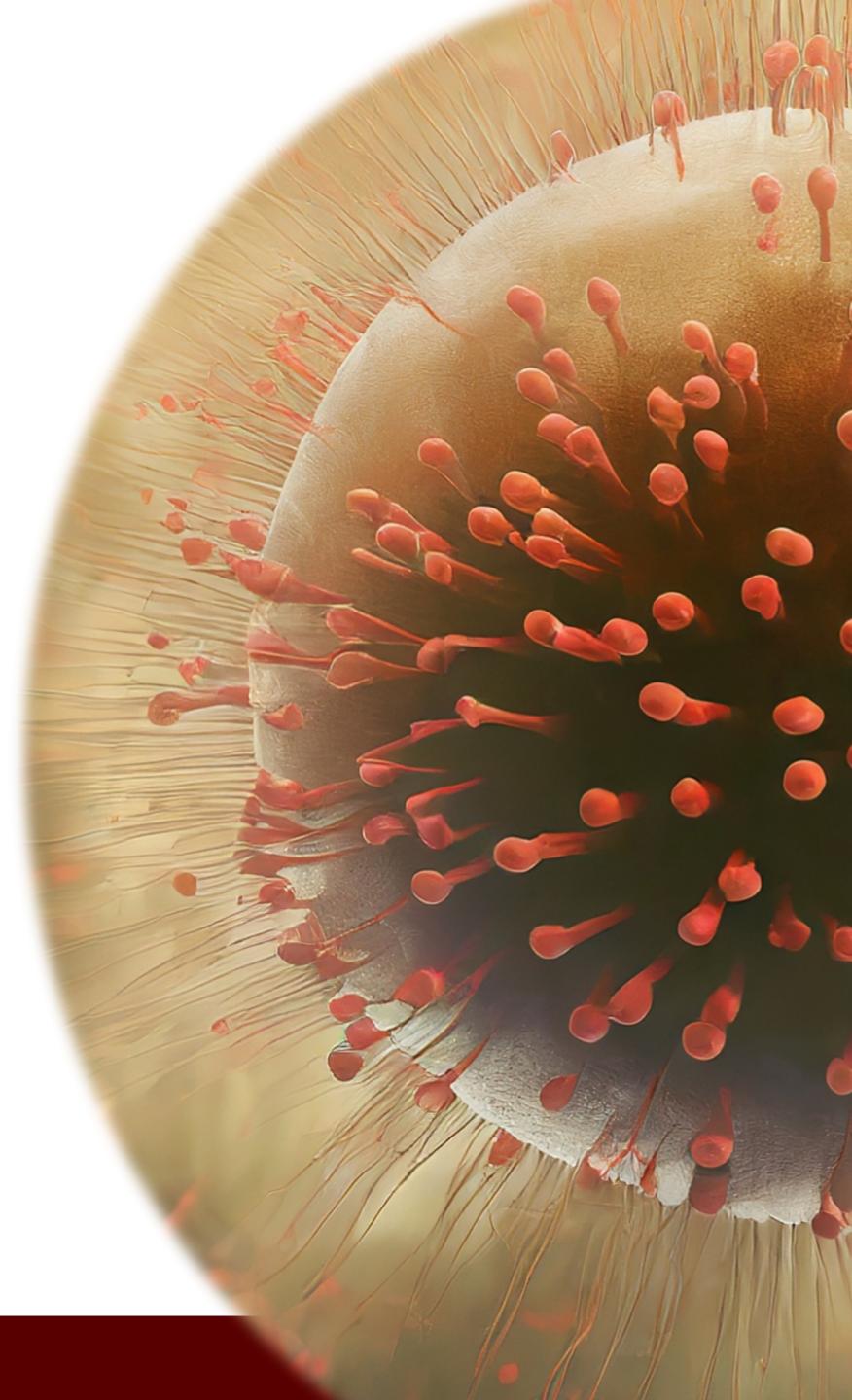
Conclusions

- DC-TRN vaccine:
 - Increases the proportion of cytotoxic NK cells
 - Increases the receptor repertoire on NK cells
 - Modestly increases the frequency of memory-like NK cells
 - Increases the NK cell-mediated cytotoxicity and polyfunctionality
- These profound changes did not persist due to rapid viral rebound
- Therapeutic vaccination alone will probably not be sufficient as a functional cure against HIV-1



Future perspectives

- Memory NK cells
 - Mechanism? Antigen specificity?
 - Can we harness memory NK cells to target reactivated reservoir cells?
- Enhancing NK cell functionality by targeting the NKG2A/HLA-E axis to eliminate reactivated reservoir cells (poster)
- BREACH project: In-depth characterization of the dynamics of the functional latent reservoir in long-term cART-treated PLWH in Belgium



Acknowledgements



VUB - NAVI

Prof. Dr. Joeri Aerts
Sabine den Roover
Dr. Sigrid D'haese
Dr. Jolien De Munck
Sarah Vanbellingen
Philipp Kalus
Els Van Nedervelde
Joëlle Cosyns



UZ Brussel - IRG

Prof. Dr. Sabine Allard



Erasmus Medical Center

Dr. Rob Gruters
Cynthia Lungu

All study participants!



Scientific Fund
Willy Gepts



HIV-1 integrates into the genome of the host cell

