NK Cell KIR Education Is Associated With Low HIV DNA Load in Early ART-Treated Children

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Nicholas G Herbert[1], Gabriela Cromhout[2], Nomonde Bengu[3], Maria C. Peurtas[4], Javier Martinez-Picado[4], Thumbi Ndung'u[2], Dimitra Peppa[5], Philip Goulder[1,2]

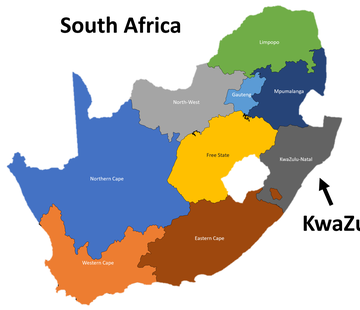
[1]University of Oxford, Oxford, UK, [2]HIV Pathogenesis Programme, Durban, South Africa, [3]Queen Nandi Hospital, Empangeni, South Africa, [4]IrsiCaixa AIDS Research Institute, Barcelona, Spain, [5]University College London, London, UK

Background

Post-treatment control (PTC) offers a promising avenue for functional cure and has been proposed to be more easily attainable in children compared to adults[1]. Considering viral reservoir size is a major predictor of time to rebound following treatment interruption[2] and NK cells are demonstrated to play a more dominant role during HIV infection compared to CD8+ T-cells in early life[3]; **our study aims to understand the NK cell responses linked to small reservoirs in early ART treated children who have maintained viral suppression to reveal NK cell factors related to early life PTC potential.**

Methods

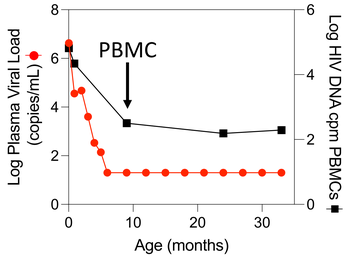
By utilizing PBMC samples from children who maintained viral suppression from the Baby Cure cohort, a longitudinal cohort of >300 early-ART-treated mother-child pairs from KwaZulu-Natal, South Africa, we quantified HIV DNA as a proxy for reservoir size and identified links with HLA-I and NK cell immune responses. Specifically, we conducted immunophenotyping, IL-12/IL-18, K562 and RAJI/Rituximab stimulation assays.



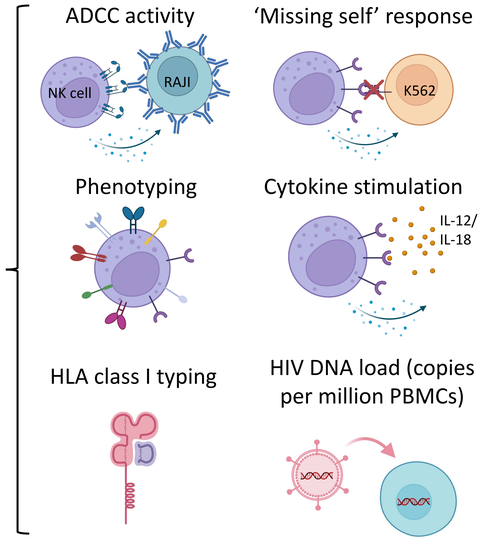
Baby Cure Cohort

- >300 mother-child pairs enrolled (2015-present)
- All children started on AZT/NVP or AZT at birth

Example of sample utilized in study from a virally suppressed child

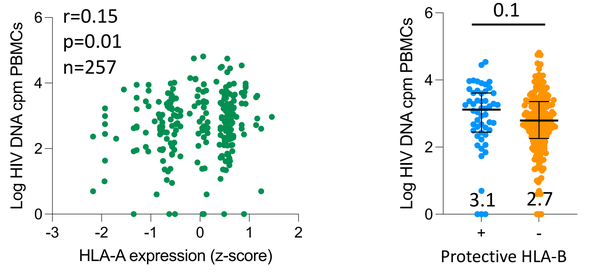


Assays performed

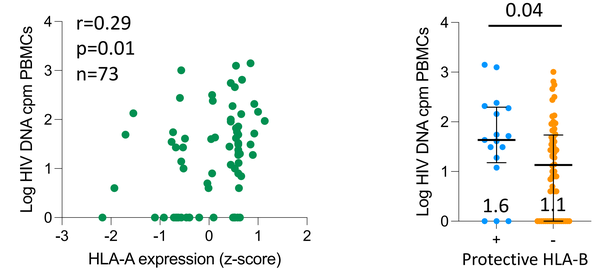


1. Immunogenetic signature favouring KIR educated NK cells associated with low HIV DNA at birth and at 9 months old

Birth

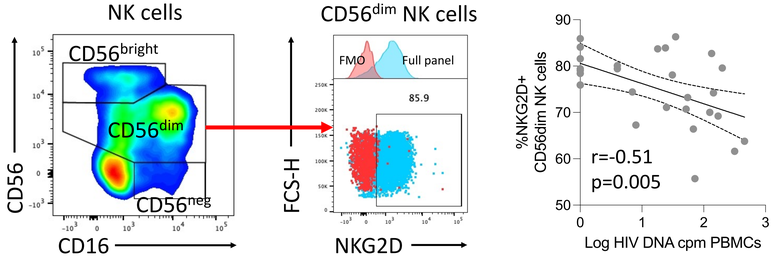


Consistently suppressed children at 9 months old

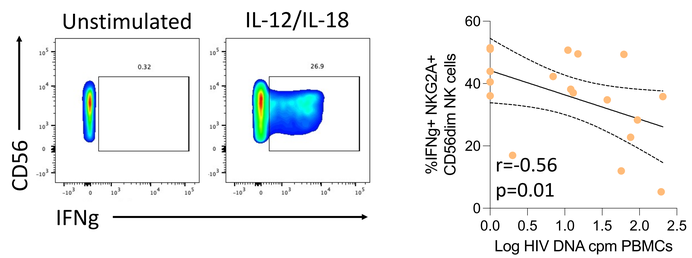


We show low HLA-A expression, which favours KIR-educated NK cells, was associated with low HIV DNA at birth and and in consistently suppressed children at median 9 months old. However, children with adult 'protective' HLA-B had larger HIV DNA at birth and at 9 months old (p=0.1 and p=0.04 vs children without adult 'protective' HLA-B alleles). Protective HLA-B alleles defined in ART-naïve adults with clade-C infection: HLA-B*57/58:01/81:01.

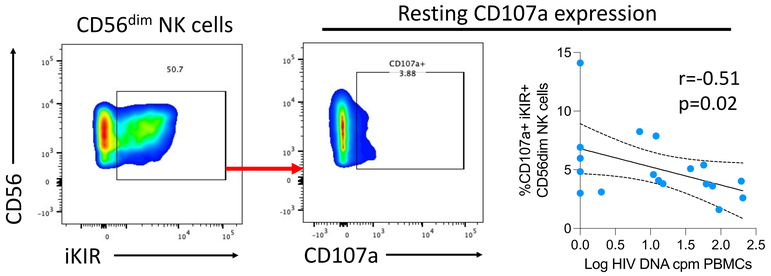
2. High NKG2D expression by CD56^{dim} NK cells linked to low HIV DNA



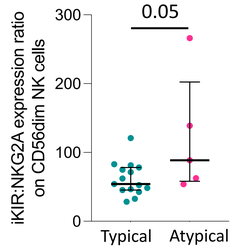
3. High IFNg exp by NKG2A+CD56^{dim} NK cells linked to low HIV DNA



4. High resting degranulation level of iKIR+CD56^{dim} NK cells linked to low HIV DNA



5. High iKIR:NKG2A ratio linked with PTC children



Five 'atypical' males in our cohort, who have displayed characteristics of PTC[4], did not have significantly different NK compartments to typical children (functional or phenotypic, not shown) but did display higher iKIR:NKG2A expression ratio on CD56^{dim} NK cells compared to typical children.

Conclusion

These data suggest that an HLA-I signature favouring KIR-educated NK cells, driven by low HLA-A expression, is associated with low total HIV DNA load in early ART-treated children. This signature is consistent with findings from ART-naïve adults, ART-naïve children and adult PTCs[3,5,6]. These data also indicate a mixed pattern of enhanced CD56^{dim} NK cell functionality in achieving low HIV DNA load leading to increased remission potential. Also, higher iKIR to NKG2A expression by PTC children's NK cells may further link KIR education with PTC potential.

References

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