LIFE-LONG DEPLETION OF ALL INNATE LYMPHOID CELLS IN HIV-INFECTED CHILDREN

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Background
Innate lymphoid cells (ILCs) are essential for immune development and lymphoid structure as shown in humans lacking ILCs due to severe immunodeficiency. In HIV infected adults, helper ILCs are depleted from circulation during acute infection. Therefore, we hypothesized that perinatal HIV infection impact ILCs and thus impair immunity from early life.

Methods
We studied ILC frequency, distribution, phenotype and function in blood and lymphoid tissue (tonsil) from HIV infected children and HIV negative age-matched controls using a 17-color flow cytometry panel. We also used RNAseq to generate transcriptomic data to determine differential gene expression.

Results
From a total of 66 HIV infected children, including a rare group of treatment naïve but clinically healthy children, and 28 HIV negative age-matched controls, we found severe depletion of all ILC subsets in circulation in the absence of treatment. Cross-sectional sampling showed no restoration of ILCs in subjects successfully treated for up to 10 years (median 151 weeks), in line with continued ILC depletion observed during longitudinal sampling over 82 weeks. In contrast, CD4 T-cells were significantly restored in these subjects. Consistent with no functional difference in blood, we found no impact on surviving helper ILCs at the transcriptional level (RNAseq), whereas cytotoxic ILCs respond through genes encoding KIRs or anti-inflammatory mediators. ILCs in lymphoid tissue (tonsil) of age matched vertical infected subjects were also reduced and, in contrast to that of circulating ILCs, displayed differential and modulated transcriptional activity, suggesting a functional role for tissue resident ILCs that includes the IL-22 axis.

Conclusion
Taken together, we show that ILC subsets in blood and tissue are depleted after birth in infected children and only tissue resident ILCs respond to infection. This may have life-long consequences on lymphoid structure and function in children infected at birth, irrespective of treatment initiation.