**Targeted elimination of HIV-infected cells using NK cell subsets exhibiting potent antibody-dependent cellular cytotoxicity.**

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**Background:**
HIV cure requires the elimination of latent viral reservoirs which persist in T cells and macrophages despite antiretroviral therapy. The inefficient killing of latently-infected cells in HIV cure approaches trialed to date suggest the need for dedicated interventions to enhance death of HIV+ cells. NK cell-based immunotherapy strategies may be useful for enhancing elimination of HIV+ cells via antibody dependent cellular cytotoxicity (ADCC).

**Methods:**
The ability of NK cells from people with HIV (PWH) and seronegative controls to elicit ADCC in response to primary T cells and monocyte derived macrophages infected *in vitro* with HIV was assessed via a CD107a degranulation assay +/- anti-HIV IgG. The phenotype of degranulating NK cells was assessed by immunophenotyping. Degranulation assays using Raji cells opsonised with rituximab or K562 cells as targets were used to assess the cytotoxic potential of NK cell subsets

**Results:**
NK cells from PWH showed reduced ADCC activity towards HIV-infected T cells and macrophage as compared to HIV- controls ($p<0.001$ and 0.01, respectively). Phenotyping of NK cells with high ADCC responses identified a subpopulation of KIR3DL2+ NK cells which exhibited potent ADCC activity against both HIV-infected T cell and macrophage targets ($p<0.0001$ for both vs total NK cells) and also produced more inflammatory cytokines (TNF; $p=0.0005$). KIR3DL2+ cells did not show heightened cytotoxicity against non-HIV targets or in response to MHC-negative K562 cells, suggesting their higher ADCC is not due to higher licensing. Allogeneic NK cells exhibited a comparable level of ADCC as autologous NK cell against HIV+ targets

**Conclusion:**
We have identified a subset of KIR3DL2+ NK cells with potent and selective ADCC activity against HIV-infected T cells and macrophages. The ability of allogeneic NK cells to mediate effective ADCC against HIV+ targets supports the potential use of adoptive KIR3DL2+ NK cell immunotherapy to facilitate HIV elimination.

**Disclosure of Interest Statement:**
No conflicts of interest to declare.