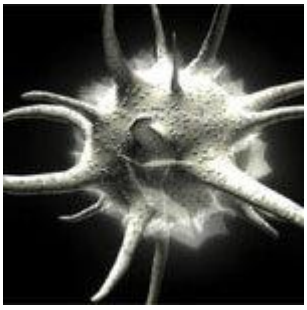
A novel immune mechanism of killing HIV infected cells



One of the most effective ways the immune system controls the spread of viral infection is through killing of infected cells. One strategy HIV uses to avoid infected cells from being killed by T cells is to cause the reduced expression of surface molecules that are responsible for presenting viral peptides to CD8+ T cytotoxic lymphocytes: the major histocompatibility complex class I molecules (MHC-I). Another host killing cell, the natural killer cell, is regulated by its interaction with MHC molecules. It is known that MHC -C and -E molecular interaction with NK cells can cause inhibition of some NK cell activity. HIV exploits this by causing the selective down regulation of MHC class I A and B, but leaving –C and –E remaining.

In the February 2016 edition of PLoS Pathogens, Zachary Davis and colleagues demonstrate that NK cells expressing MHC (HLA)-E specific inhibitory NK cell receptors (iNKR and specifically NKG2A/CD94) can destroy HIV-infected cells despite expression of HLA-E. They found that peptides presented by HLA-E are “critical for binding to iNKRs on NK cells”.

The authors demonstrate that an HIV capsid peptide presented by HLA-E is unable to interact with the iNKR, and as a result these specific NK cells then lyse HIV infected cells. The authors conclude that “these findings are important since the use of NK cells was recently proposed to treat latently HIV-1-infected patients in combination with latency reversing

agents.”

Davis, Z. et al, 2016. A Conserved HIV-1-Derived Peptide Presented by HLA-E Renders Infected T-cells Highly Susceptible to Attack by NKG2A/CD94-Bearing Natural Killer Cells. *PLOS*.