

ORAL ABSTRACT SESSION 08: INNATE AND MUCOSAL IMMUNITY

OA08.06

SIV infection results in loss of IL-17-producing NK cells in mucosal tissues, which contributes to damage to the mucosal barrier

N.R. Klatt¹, L. Harris¹, C. Vinton¹, D. Morcock², B. Tabb², H. Sung³, J. Lifson², M. Martin¹, A. Levine³, G. Alter⁴, J. Estes² and J. Brenchley¹

¹NIH/NIAID, Bethesda, Maryland, USA; ²SAIC Inc., NCI, Frederick, Maryland, USA; ³Case Western Reserve University, Cleveland, Ohio, USA; ⁴Harvard University, Ragon Institute, Charlestown, Massachusetts, USA

Background: Dysfunction of the mucosal immune system and immune activation are hallmarks of HIV pathogenesis. Damage to the structural barrier of the GI tract leads to microbial translocation and immune activation, however, the mechanisms underlying this damage remain unclear. Here we used SIV-infected Asian macaques to study the role of NK cells in mucosal homeostasis and AIDS pathogenesis.

Methods: We used flow cytometry to measure NK cell function and phenotype in blood, lymph nodes and mucosal tissues of macaques prior to and after SIV infection. We measured damage to the GI tract, microbial translocation, and immune activation in tissues by immunohistochemistry.

Results: We found a loss of NKs in blood after SIV infection, which was associated with increased proliferation. In the gut, we found a negative correlation between the frequency of colon NK cells and the amount of damage to the colon epithelium ($P=0.0311$, $r=-0.7280$). Intriguingly, though there was not a general loss of NKs in the mucosa after SIV infection, we observed a selective loss of IL-17-producing NKs in both the colon ($P=0.0127$) and mesenteric LN ($P=0.0177$). Furthermore, the frequency of IL-17-producing NKs negatively correlated with damage to the colon epithelium ($P=0.0341$, $r=-0.8289$). Moreover, there was a significant positive correlation between the frequency of IL-17-producing NK cells and CD4⁺ T cells in the colon ($P=0.0081$, $r=0.6747$).

Conclusion: These data suggest that mucosal NK cells have a specialized role in homeostasis, and loss of these cells after SIV infection may contribute to damage to the GI tract and ensuing microbial translocation and immune activation. Furthermore, the correlation between IL-17-producing NK cells and CD4⁺ T cells suggests that the mechanism underlying loss of Th17 cells after SIV/HIV infection is not preferential Th17 infection. Better understanding the mechanisms that underlie loss of these homeostatic NK cells may lead to novel therapeutic strategies to treat HIV.