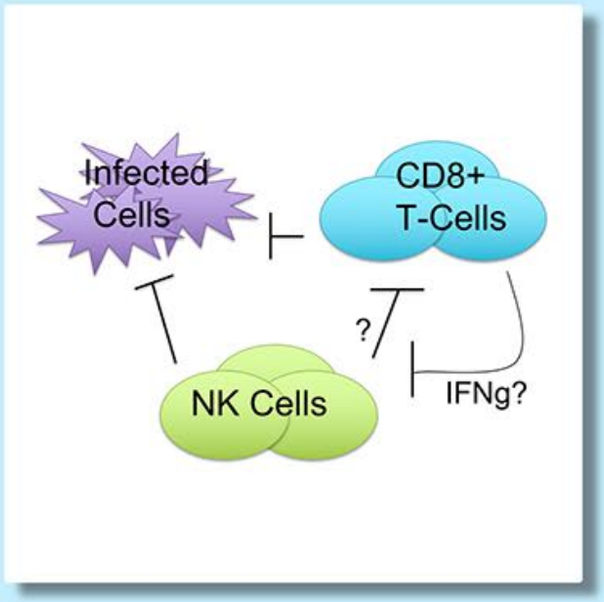
MAKAYLA LUND

Faculty Research Mentor: Dr. Jason Whitmire
Department of Genetics



Determining pathway between NK and T cells

Determining the Mechanism of Action of NK cell Regulation of T Cell Responses to Infection

Natural killer (NK) cells contribute to immune defense against viral infections by recognizing and killing infected cells. We have identified an inhibitory role for NK cells during lymphocytic choriomeningitis virus (LCMV) infection in mice. The underlying mechanism(s) by which NK cells limit virus-specific T cell responses is unclear. It has been shown that NK cells recognize and kill activated T cells and that direct type-1 interferons protect T cells from NK cell-mediated killing. We have previously shown that type-2 interferon (IFNg), like type-1 interferon, acts directly on T cells to promote antiviral T cell responses to acute LCMV infection. We hypothesized that IFNg, like type-1 interferons, acts directly on T cells to protect them from the inhibitory effects of NK cells. We compared the survival and proliferation of virus-specific WT and IFNgR-KO T cells that were co-transferred to the same mice and observed that the depletion of NK cells in experimental groups increased the abundance of both cell populations equivalently, suggesting that IFNgR signaling to T cells does not protect them from NK cell suppression. The data are also consistent with the idea that NK cells act indirectly to curtail T cell responses. We hypothesize that this occurs through NK cell regulation of antigen presentation by Antigen Presenting Cells (APCs) such as monocytes, as the effects of NK cell depletion are only seen during the inductive phase of viral infection. NK cells may limit the ability of APCs to process and present viral antigen, thus affecting the activation and proliferation of T-cells. In order to better understand this process, we measured the ability of APCs to process and present antigen utilizing the self-quenching antigen DQ-OVA. Our data suggest that while APC processing of DQ-OVA does not necessarily increase upon infection, it does increase upon NK cell depletion, especially in monocyte populations. The determination of the relationship between NK cells and T cells will better aid in our understanding and treatment of chronic diseases such as HIV and HCV.