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Aaron Ireland
Washington University in St. Louis

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Mentor: Todd Fehniger

Natural killer (NK) cells are innate lymphocytes integral in immunity against viral infection and cancer. NK cells are regulated by microRNAs. MicroRNAs (miRNAs) are small, non-coding RNAs that target mRNAs to inhibit translation and initiate mRNA degradation. Next-generation small RNA sequencing has identified miRNA-142 to be highly expressed in murine NK cells, and thus we hypothesized that miR-142 is critical for NK cell development, survival, and/or functionality.

To investigate this hypothesis, we examined the NK cell compartment of miR-142 deficient mice. Flow cytometric analysis of harvested NK cells, tagged with fluorescent antibodies targeting markers of maturation, showed a significant NK cell deficiency despite no observed blocks in maturation. Across peripheral blood, spleen, liver, and lymph nodes, NK cells were decreased between 2-10 fold as compared to controls. Since this deficiency was evenly spread across all stages of NK cell development, we concluded that miR-142 isn't necessary for maturation of NK cells.

To test whether the NK cell deficit in mir-142-deficient mice was cell intrinsic, we performed bone marrow chimera experiments. Here, control and mir-142-deficient bone marrow were co-transplanted into irradiated mice, and the contribution of each to hematopoiesis was assessed. A significantly reduced number of chimeric mouse NK cells were derived from mir-142-deficient bone marrow than control, supporting the cell-intrinsic role of miR-142 in NK cell homeostasis. Additionally, NK cells deficient in miR-142 were found to have no signaling through their IL-15 cytokine receptors due to insufficient STAT5 phosphorylation. This failure to signal led to an observable defect in the production of IFN-γ, an important immune cytokine. Furthermore, miR-142 deficient NK cells have drastically altered integrin expression, which we hypothesize inhibits NK cells from leaving the bone marrow, where NK cells are produced. Thus, we conclude that miR-142 is required for maintaining normal function and homeostasis of peripheral NK cells.