STRONG CHILDREN'S RESEARCH CENTER

Summer 2016 Research Scholar

Name: **Hannah Latta**

School: **University of Kentucky**

Mentor: **Dr. Laurie Steiner**

ABSTRACT

Title: *Determining the Role of gamma-H2AX in Erythropoiesis*

Background: Erythropoiesis is the multi-faceted process by which erythrocytes, or red blood cells, are formed. Several proteins are implicated in this developmental story including histone variant H2AX and its phosphorylated form, gamma-H2AX. Histones are utilized to package DNA into chromatin and gamma-H2AX is also implicated in the DNA double-strand break (DSB) repair process. ATM, ATR, and DNA-PK are three kinases that phosphorylate H2AX to gamma-H2AX. Interestingly, the levels of gamma-H2AX are elevated in certain erythroid precursors in the absence of any evidence of DNA damage.

Objective: To elucidate the functions of gamma-H2AX in erythroblasts, several experiments were performed using extensively self-renewing erythroblasts (ESREs) in vitro. ATM, ATR, and DNA-PK expression was knocked down using siRNA transfection. Transfected cultures were induced to mature for an additional 48 hours to ascertain the effect of treatment on viability and maturation.
non-canonical role of gamma-H2AX in erythropoiesis. Additional siRNA transfection experiments and qPCR will be used to assess relative expression of other kinase-encoding genes in cells that display a knockdown phenotype for one kinase. These experiments will also be used to investigate the relationship between cell cycle inhibitor abundance and the absence of ATM, ATR, and DNA-PK kinase molecules.