STRONG CHILDREN'S RESEARCH CENTER

Summer 2014 Research Scholar

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ABSTRACT

Title: **PRC1 Complex is a Potential Regulator of Erythroid Self-Renewal in Stress Erythropoiesis**

Background:

The Palis laboratory has recently discovered a novel population of primary erythroid precursors capable of prolonged (10^6-10^{60} fold) proliferation *ex vivo*. These extensively self-renewing erythroblasts (ESREs) retain the potential to terminally mature into enucleated erythrocytes despite months of expansion. The proliferation of both restricted self-renewing erythroblasts (SREs) and ESREs requires synthetic glucocorticoid dexamethasone, erythropoietin (EPO), and stem cell factor (SCF) (England et al., 2011). These same signals, cortisol, EPO, and SCF, regulate the process of accelerated red blood cell production in response to hypoxic/anemic stress known as stress erythropoiesis (Paulson et al., 2011). To elucidate the mechanism of erythroid self-renewal, global gene expression profiles were collected from primary bone marrow proerythroblasts (BM ProEs), ESREs, SREs, and primary stress spleen proerythroblasts (stress ProEs). Previous analysis of our dataset followed by functional studies identified Bmi-1 as a key regulator of erythroid self-renewal in the *in vitro* ESRE/SRE cultures.

Objective: Here we explored whether Bmi-1, a component of the polycomb repressive complex 1 (PRC1), plays a role *in vivo* during stress erythropoiesis.

Results:

Further analysis of microarray data and subsequent validation via qPCR reveals that stress ProEs express a similar gene profile as ESREs/SREs in regard to Bmi-1 associated genes. We report that although Bmi-1 transcript levels are not higher in stress ProEs compared to BM ProEs despite decreased expression of its negative upstream regulator, C/EBPα, normally repressed transcriptional targets of Bmi-1 are in fact downregulated. Interestingly, polycomb group ring