

FORMAT FOR BRIEF DESCRIPTION OF RESEARCH PROJECT FOR SUMMER 2018

TITLE: Chronic Stress and Anemia Recovery following Major Trauma

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RESEARCH PROJECT DESCRIPTION (brief overview of background, hypothesis, methods, role of medical student, funding and relevant publications -- SHOULD NOT EXCEED ~ 250 WORDS)

Injury-associated persistent anemia is a persistent anemia seen in the absence of acute blood loss and is one manifestation of bone marrow end organ dysfunction that occurs following severe trauma and prolonged critical illness. We have recent data showing that norepinephrine is a key regulator of erythroid progenitor cell growth and mobilization following trauma, although the exact mechanisms involved have yet to be elucidated. The central hypothesis is that chronic adrenergic stimulation following injury and hemorrhagic shock worsens BM dysfunction by further inhibiting the differentiation of hematopoietic progenitor cells (HPC) and exaggerating the mobilization of hematopoietic progenitor cells (HPC) from bone marrow (BM), thereby contributing to persistent injury-associated anemia. This research is supported by the NIH-NIGMS.

With regard to recovery from persistent anemia, we will determine if chronic stress creates a persistent inflammatory milieu that impairs recovery from injury-associated anemia. These studies will be conducted in Sprague Dawley rats that have undergone our model of lung contusion, hemorrhagic shock followed by either 7 (LCHS/CS-7) or thirteen days of restraint stress (LCHS/CS-14) and both groups will be sacrificed on day 14. Concentrations of NE, corticosterone, and C-reactive protein (CRP), and hematopoietic regulatory cytokines (HMGB1, SCF, IL-1, IL-3, IL-6, TGF-beta) in whole BM as well as BM stroma will be assessed by ELISA and PCR. The medical student will begin an understanding of reviewing scientific literature and learn basic science laboratory techniques. He/she will develop insight on how basic science research can be applied in the clinical arena. The medical student will also perform statistics and report the results from the experiments.

Loftus TJ, **Mohr AM**, Moldawer LL. (2017). Dysregulated myelopoiesis and hematopoietic function after acute physiologic insult *Curr Opin Hem Oct 13 epub* PMID: 29035909

Millar JK, Kannan KB, Loftus TJ, Alamo IG, Plazas J, Efron PA, **Mohr AM**. (2017). Persistent injury-associated anemia: The role of the bone marrow microenvironment. *J Surg Res*, 214, 240-246.

Alamo IG, Kannan KB, Ramos H, Loftus TJ, Efron PA, **Mohr AM**. (2016). Clonidine reduces norepinephrine and improves bone marrow function in a rodent model of lung contusion, hemorrhagic shock and chronic stress. *Surgery* 161,795-802. PMID: 27742030

Alamo IG, Kannan KB, Smith MA, Efron PA, **Mohr AM**. (2016). Regulation of persistent injury-associated anemia and the roles of erythropoietin and hepcidin. *J Trauma Acute Care Surg* 81, 705-712

Bible LE, Pasupuleti LV, Gore AV, Sifri ZC, Kannan KB, **Mohr AM**. (2015). Daily propranolol prevents prolonged HPC mobilization in a chronic stress and polytrauma model. *Surgery Epub July 21* PMID: 26209570