Anemia and the Chronic Hyperadrenergic State following Major Trauma

HYPOTHESIS:
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 injury-associated persistent anemia.

PROJECT DESCRIPTION (Include design, methodology, data collection, techniques, data analysis to be employed and evaluation and interpretation methodology)
Injury-associated persistent anemia is a persistent anemia seen in the absence of acute blood loss and is one manifestation of BM end organ dysfunction that occurs following severe trauma and prolonged critical illness. Understanding the pathophysiology of this anemia would facilitate the development of treatment strategies and would avoid the use of blood transfusions, which are risk factors for infection and death. The overall goal of this proposal is to determine the mechanisms involved in injury-associated persistent anemia. 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.

Aim: Will investigate whether excessive and ongoing HPC mobilization from the BM induced by LCHS+CS contributes to persistent anemia. Potential causative factors that will be studied include increased production or an abnormal response to mediators of HPC mobilization, increased proteolysis within the BM and alterations in the BM architecture. Abnormalities in the response and receptor interaction with mediators of HPC mobilization (G-CSF, G-CSF receptor) and mediators of HPC retention (SDF-1/CXCR4) will be determined and correlated with peripheral blood HPC cultures and flow cytometry of peripheral blood HPC. Increased proteolysis (MMP-2, MMP-9, neutrophil elastase) in BM will be assessed by ELISA.

Statistical evaluation of the results of experiments will be performed using t-tests and non-parametric tools (eg the Mann-Whitney U-test) to compare data. The criterion for statistical significance will be an alpha = 0.05

SPONSOR’S MOST RECENT PUBLICATIONS RELEVANT TO THIS RESEARCH:


Summer Student Research Program
Project Description

Trauma 70, 1043-1050.


IS THIS PROJECT SUPPORTED BY EXTRAMURAL FUNDS?  
Yes or No ☒
(IF YES, PLEASE SUPPLY THE GRANTING AGENCY’S NAME)
National Institute of Health

THIS PROJECT IS: [ ] Clinical  ☒ Laboratory  [ ] Behavioral  [ ] Other

THIS PROJECT IS CANCER-RELATED ☒

THIS PROJECT IS HEART, LUNG & BLOOD- RELATED ☒

THIS PROJECT EMPLOYS RADIOISOTOPES ☒

THIS PROJECT INVOLVES THE USE OF ANIMALS ☒

Pending ☐  Approved ☒  IACUC PROTOCOL #08068

THIS PROJECT INVOLVES THE USE OF HUMAN SUBJECTS

Pending ☐  Approved ☒  IRB PROTOCOL #

THIS PROJECT IS SUITABLE FOR:

Undergraduate Students  Entering Freshman ☐
Sophomores  ☒  All Students ☐

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?

Begin an understanding of reviewing scientific literature; Learn basic science laboratory techniques, including cell culture, RIA, ELISA and western blot. Develop insight on how basic science research can be applied in the clinical arena; Interested students may participate in night call with trauma service (purely optional).