Modulation of hematopoietic factors in the bone marrow stem cell niche by Prostaglandin E2 enhances survival from lethal radiation exposure

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Background and Hypothesis: With the increase in nuclear arms, terrorist threats, and nuclear power, there is an increased risk to radiation exposure. Exposure to high dose radiation has acute effects on the body and chronic effects that plague survivors of the acute syndrome for years post-exposure. Acute radiation syndrome (ARS) can be lethal if left untreated due to severe damage to the gastrointestinal and hematopoietic systems. Dimethyl prostaglandin E2 (PGE2) has shown efficacy as a protectant against radiation exposure, significantly increasing survival from ARS and enhancing hematopoietic stem cell (HSC) and hematopoietic progenitor cell (HPC) function compared to control mice. This study aimed to elucidate the mechanism of PGE2's protectant effect and to determine whether PGE2 protects hematopoietic stem cells themselves and/or the supportive microenvironment, thus indirectly enhancing HSC function post-irradiation.

Experimental Design or Project Methods: C57BL/6 mice were treated with 35mg PGE2, then underwent single dose lethal irradiation. At 6h, 24hr, and 9d post radiation and 30min post injection non-irraditated, mouse bone marrow was flushed using a 500 uL of PBS, centrifuged, and supernatants separated. Supernatants were assayed by multiplex analysis (Luminex technology) for factors known to promote HSC and HPC regeneration & function.

Results: Cytokines beneficial to the reconstitution of the hematopoietic system were significantly altered by the administration of PGE2 vs. vehicle.

Conclusion and Potential Impact: This study provided information on mechanisms relevant to survival from lethal radiation exposure, protection of the bone marrow, and recovery of hematopoiesis.

Jessica Lee Muldoon is a 3rd year medical student at Indiana University School of Medicine and plans to pursue a career in pathology. As an undergraduate student, she majored in clinical lab science and found a joy in microscopy work. With medicine, there are multiple facets that are “behind the scenes” from pathology results to research findings. As an IMPRS scholar Jessica was able to gain experience in the process of research. She learnt to form a proper question, work with her mentors to design an experiment, carry out the experiment, analyze the data, and finally present the data at a poster presentation. Not only was she able to see how research was performed, Jessica gained an appreciation for all the work that goes into research “behind the scenes”. She will carry this skill set onward in her career by striving to be a translational clinician, who collaborates with researchers to forward the field of medicine.