Temporal Analysis of Mesenchymal Stem Cell, Hematopoietic Stem Cell, and Endothelial Progenitor Cell Mobilization in Response to Femoral Fracture
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Hypotheses

1. Transient increases in Stem and Progenitor cell populations in the blood can be identified by flow cytometry.

2. Stem and progenitor cell populations are mobilized from the bone marrow into the blood in response to femoral fracture.

3. Peak increases in stem and progenitor cell populations will be seen in the blood 3 days after fracture.

Proposed research to accomplish

Unilateral femoral fractures were performed on C57BL/6 mice. PB and BM were isolated at days 1, 2, 3, 4, and 7 after fracture and analyzed for MSC, HSC, and EPC cell surface markers. Cell populations in fractured mice were compared to those in mice mobilized with the CXCR4 antagonist AMD3100 (positive control) which has been shown to mobilize these populations from the BM into PB. Populations in fractured mice were also compared to those in saline injected mice, in non-injected mice (negative control), and in fractured mice that were injected with AMD3100 (a possible therapeutic strategy).

Brief discussion of results

Analysis of values from day 1 after femoral fracture showed an increase in peripheral blood populations staining with markers associated with HSCs, MSCs, and EPCs in response to injection with AMD3100. A smaller increase was seen in mice with femoral fractures also injected with AMD3100. Changes in PB populations in response to just fracture were not evident at day 1, and changes in BM populations were also not seen at this time.

Analysis of days 2,3,4, and 7 after fracture did not show significant differences between stem and progenitor cell populations in blood of fractured mice compared with AMD3100 injected mice and negative controls.

It appears that we are able to identify transient changes in cell populations within the blood, but it is as yet unclear if there is no mobilization of stem and progenitor cell populations in response to fracture, if flow cytometry is not sensitive enough to detect the level of mobilization, or if mobilization occurs at a time point that has not yet been measured. Future work will focus on comparing day 1 values with 6 and 12 hour post fracture values to determine if cell mobilization in fractured mice can be seen at that time.