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| **Fiscal Year:** | FY 2015 | **Task Last Updated:** | FY 11/21/2014 |
| **PI Name:** | Bloomfield, Susan A. Ph.D. | | |
| **Project Title:** | Sclerostin's Role in Regulating Bone Formation during Long-term Simulated Microgravity and Subsequent Recovery | | |
| **Division Name:** | Human Research | | |
| **Program/Discipline:** | | | |
| **Program/Discipline--Element/Subdiscipline:** | HUMAN RESEARCH--Biomedical countermeasures | | |
| **Joint Agency Name:** | | **TechPort:** | No |
| **Human Research Program Elements:** | (1) **HHC**:Human Health Countermeasures | | |
| **Human Research Program Risks:** | (1) **Bone Fracture**:Risk of Bone Fracture due to Spaceflight-induced Changes to Bone<br>(2) **Osteo**:Risk Of Early Onset Osteoporosis Due To Spaceflight | | |
| **Space Biology Element:** | None | | |
| **Space Biology Cross-Element Discipline:** | None | | |
| **Space Biology Special Category:** | None | | |
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| **Zip Code:** | 77843-4375 | **Congressional District:** | 17 |
| **Comments:** | | | |
| **Project Type:** | Ground | **Solicitation / Funding Source:** | 2013 HERO NNJ13ZSA002N-Crew Health (FLAGSHIP & NSBRI) |
| **Start Date:** | 10/06/2014 | **End Date:** | 10/05/2015 |
| **No. of Post Docs:** | | **No. of PhD Degrees:** | |
| **No. of PhD Candidates:** | | **No. of Master' Degrees:** | |
| **No. of Master's Candidates:** | | **No. of Bachelor's Degrees:** | |
| **No. of Bachelor's Candidates:** | | **Monitoring Center:** | NASA JSC |
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| **Flight Program:** | | | |
| **Flight Assignment:** | | | |
| **Key Personnel Changes/Previous PI:** | | | |
| **COI Name (Institution):** | | | |
| **Grant/Contract No.:** | NNX15AB05G | | |
| **Performance Goal No.:** | | | |
| **Performance Goal Text:** | | | |
| | The tissue sharing opportunity outlined in Appendix A, Item B (“Cerebral Spinal Fluid Production/Absorption....”) offers an exciting chance to study the evolution of changes over 90 days of hindlimb suspension (HLS) in a rodent model. Few laboratories have the capability or expertise to carry out HLS for such a long period; the impact of this experiment will be multiplied many-fold with piggyback projects making strategic use of other tissues harvested from these animals. This proposal focuses on tracking the evolution of changes in a protein important to bone integrity called sclerostin over the course of 90 days of unloading and then during the 90-day recovery phase. Importantly, we will also track alterations in the key physiological function sclerostin regulates in bone: osteoblast activity resulting in the formation of new bone.<br>Sclerostin is produced by osteocytes, the bone cells embedded in bone matrix and the key sensors of loading/unloading; | | |

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| **Task Description:** | it works to inhibit the Wnt- Beta catenin signaling pathway in osteoblasts, which normally stimulates bone formation activity. Most studies to date document an increase in osteocyte's sclerostin expression with unloading, which provides the mechanism for the suppressed bone formation seen with HLS on Earth and, presumably, with microgravity exposure. A recent study examining the impact of a novel therapeutic agent (sclerostin antibody) on mice flown on STS-135 yielded very positive findings, suggesting that manipulating sclerostin expression could be an important therapeutic tool to augment the usual exercise countermeasures employed by astronauts. Hence it becomes critical, before any such systemic therapy is considered, to understand clearly the relationship between sclerostin expression and the functionally important outcome (bone formation activity) in multiple bone sites.<br><br>Because there is evidence that Sost, the gene encoding the protein sclerostin, is expressed differently in mid-shaft vs metaphyseal bone, we will assess sclerostin expression and histomorphometric measures of bone formation in 3 different bone compartments for each bone: mid-shaft cortical bone, cancellous bone of the metaphysis and the metaphyseal cortical shell. We propose to first study these outcomes in paired tibiae or femurs (unloaded bone) and in normally loaded humeri. With the availability of female mice in the parent study's 2nd specific aim, we can then assess if there are gender differences in this response. Recently published data on spaceflown mice document an increase in bone volume in calvarial bone, raising the intriguing possibility that fluid shifts during spaceflight may increase fluid pressures in the rodent brain compartment, providing a mechanical loading of sorts to the skull. Hence, a third specific aim of our proposal, pending verification that calvarial bone can be made available, will assess sclerostin expression and bone formation variables in this unique site to test this hypothesis. At the end of one year's intensive effort, then, we will have gained a much more clear picture of how this important regulatory molecule is altered by unloading and whether sclerostin antibody does present a viable therapeutic tool for maintaining bone integrity on long-duration missions. In addition, we will gain important fundamental knowledge about the time course of sclerostin expression and its relationship to bone formation rate with alterations in mechanical loading. |
| **Rationale for HRP Directed Research:** | |
| **Research Impact/Earth Benefits:** | |
| **Task Progress:** | New project for FY2015. |
| **Bibliography Type:** | Description: (Last Updated: 05/28/2021) |