Change in Mouse Bone Turnover in Response to Microgravity

Mechanical unloading during spaceflight is known to adversely affect mammalian physiology. Our previous studies using the Animal Enclosure Module on short duration Shuttle missions enabled us to identify a deficit in stem cell based-tissue regeneration as being a significant concern for long-duration spaceflight. Specifically, we found that mechanical unloading in microgravity resulted in inhibition of differentiation of mesenchymal and hematopoietic stem cells in the bone marrow compartment. Also, we observed overexpression of a cell cycle arrest molecule, CDKN1a/p21, in osteoprecursor cells on the bone surface, chondroprogenitors in the articular cartilage, and in myofibers attached to bone tissue.

Specifically in bone tissue during both short (15-day) and long (30-day) microgravity experiments, we observed significant loss of bone tissue and structure in both the pelvis and the femur. After 15-days of microgravity on STS-131, pelvic ischium displayed a 6.23% decrease in bone fraction ($p=0.005$) and 11.91% decrease in bone thickness ($p=0.002$). Furthermore, during long-duration spaceflight we observed onset of an accelerated aging-like phenotype and osteoarthritic disease state indicating that stem cells within the bone tissue fail to repair and regenerate tissues in a normal manner, leading to drastic tissue alterations in response to microgravity.

The Rodent Research Hardware System provides the capability to investigate these effects during long-duration experiments on the International Space Station. During the Rodent Research-1 mission 10 16-week-old female C57Bl/6J mice were exposed to 37-days of microgravity. All flight animals were euthanized and frozen on orbit for future dissection. Ground ($n=10$) and vivarium controls ($n=10$) were housed and processed to match the flight animal timeline. During this study we collected pelvis, femur, and tibia from all animal groups to test the hypothesis that stem cell-based tissue regeneration is significantly altered after 37-days of spaceflight. To do this, we will analyze differences in bone morphometric parameters using MicroCT. The pelvis, femur, and tibia are key in supporting and distributing weight under normal conditions. Therefore, we expect to see altered remodeling in flight animals in response to microgravity with respect to ground controls. In combination with histomorphometry, these results will help elucidate the complex mechanisms underlying bone tissue maintenance and stem cell regeneration.

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