SPACE LIFE SCIENCES SYMPOSIUM (A1)
Biology in Space (8)

Author: Dr. Elizabeth Blaber
National Aeronautics and Space Administration (NASA), Ames Research Center / USRA, United States, e.blaber@nasa.gov

Ms. Margareth Cheng-Campbell
National Aeronautics and Space Administration (NASA), Ames Research Center /Blue Marble Space Institute of Science, United States, margareth.a.cheng-campbell@nasa.gov
Ms. Olivia Stimpel
National Aeronautics and Space Administration (NASA), Ames Research Center /Blue Marble Space Institute of Science, United States, olivia.stimpel@nasa.gov
Dr. Eduardo Almeida
NASA, United States, e.almeida@nasa.gov

THE EFFECTS OF LONG-DURATION SPACEFLIGHT ON BONE AND CARTILAGE

Abstract

The detrimental effects of mechanical unloading in microgravity, including the musculo-skeletal system, are well documented, however, the effects of mechanical unloading on joint health and the interaction between bone and cartilage specifically, are less well known. Our ongoing studies with the mouse bone model have identified the failure of normal stem cell-based tissue regeneration, in addition to tissue degeneration, as a significant concern for long-duration spaceflight, especially in the mesenchymal and hematopoietic tissue lineages. Furthermore, we have identified the cell cycle arrest molecule, CDKN1a/p21, as specifically up-regulated during spaceflight exposure and localized to osteoprecursors on the bone surface and chondroprogenitors in articular cartilage that are both required for normal tissue regeneration. The 30-day BionM1 and 37-day Rodent Research 1 (RR1) missions enabled the possibility of studying these effects in long-duration microgravity experiments. We hypothesized that the inhibition of stem cell-based tissue regeneration in short-duration spaceflight would continue during long-duration spaceflight resulting in significant tissue alterations and we specifically studied the hip joint (pelvis and proximal femur) to elucidate these effects. To test this hypothesis we analyzed bone and bone marrow stem cells using techniques including high-resolution Microcomputed Tomography (MicroCT), in-vivo differentiation and migration assays, and whole transcriptome expression profiling.We found that exposure to spaceflight for 30 days results in a significant decrease in bone volume fraction (-31%), trabecular thickness (-14%) and trabecular number (-20%). Similar decrements in bone volume fraction (-27%), trabecular number (-13%) and trabecular thickness (-17%) were found in female mice exposed to 37 days spaceflight. Furthermore, high-resolution MicroCT and immunohistochemical analysis of spaceflight tissues revealed a severe disruption of the epiphyseal boundary, resulting in endochondral ossification of the femoral head and perforation of articular cartilage by bone. This suggests that spaceflight in microgravity may cause rapid induction of an aging-like phenotype with signs of osteoarthritic disease in the hip joint. Microarray analysis also revealed that the top pathways altered during spaceflight include activation of matrix metalloproteinases, oxidative stress signaling and inflammation in both whole bone tissue and isolated bone marrow stem cells. In conclusion, the observed inhibition of stem cell-based tissue regeneration persists during long-duration spaceflight. Furthermore, spaceflight mice exhibit disruption of the epiphyseal boundary and endochondral ossification of the femoral head, and an inhibition of stem cell based tissue regeneration, which, taken together, may indicate onset of an accelerated aging phenotype with signs of osteoarthritic

disease.