Fiscal Year:	FY 2021	**Task Last Updated:**	FY 12/07/2020
PI Name:	Bouxsein, Mary Ph.D.		
Project Title:	Dose-Response Study of Musculoskeletal Outcomes Following Centrifugation in Adult Mice on ISS		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
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 (2) **Muscle**:Risk of Impaired Performance Due to Reduced Muscle Size, Strength and Endurance (3) **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:	02215-5400	**Congressional District:**	7
Comments:			
Project Type:	Flight,Ground	**Solicitation / Funding Source:**	2017-2018 HERO 80JSC017N0001-BPBA Topics in Biological, Physiological, and Behavioral Adaptations to Spaceflight. Appendix C
Start Date:	02/14/2019	**End Date:**	12/31/2021
No. of Post Docs:	1	**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
Contact Monitor:	Brocato, Becky	**Contact Phone:**	
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Flight Program:	ISS		
Flight Assignment:	NOTE: End date changed to 12/31/2021 per NSSC information (Ed., 4/7/21) NOTE: End date changed to 12/15/2020 per NSSC information (Ed., 7/24/20)20)		
Key Personnel Changes/Previous PI:	November 2020 report: Marc Wein, MD, PhD has been added as a co-investigator due to his expertise in mechanobiology and multi 'omic analyses.		
COI Name (Institution):	Farber, Charles Ph.D. (University of Virginia, Charlottesville) Ferguson, Virginia Ph.D. (University of Colorado, Boulder) Rutkove, Seward M.D. (Beth Israel Deaconess Medical Center, Inc./Harvard Medical School) Willey, Jeffrey Ph.D. (Wake Forest University) Wein, Marc M.D., Ph.D. (Massachusetts General Hospital)		
Grant/Contract No.:	80NSSC19K0534		

Performance Goal No.:	
Performance Goal Text:	
Task Description:	Mechanical loading is required for maintenance of the musculoskeletal system. Thus, exposure to spaceflight or reduced mechanical loading on Earth induces marked bone loss, muscle atrophy, and degradation of soft-tissue structures in both the knee (e.g., cartilage, menisci, and ligaments) and hip (e.g., cartilage) joints. This is a major concern for astronauts during and after long-duration spaceflight, as they may be at increased risk for reduced performance, bone fractures, and both early-onset osteoporosis and arthritis. Artificial gravity, generated by centrifugal force generation, is a possible approach to mitigate these deleterious changes. Yet, the ability of partial gravity induced by centrifugal acceleration to inhibit adverse musculoskeletal changes in spaceflight remains unknown. Given the constraints of studying centrifugation as a countermeasure on Earth, spaceflight-based studies are needed. We propose to determine the effects of varying partial gravity levels on bone, muscle, and soft tissues of the hip and knee joints in adult mice flown aboard the International Space Station (ISS) in the Japan Aerospace Exploration Agency (JAXA) Mouse Habitat Unit. We will examine bone structure post-flight using high-resolution microcomputed tomography (microCT); bone cellularity using quantitative histomorphometry; bone function via biomechanical testing; and bone composition via Raman spectroscopy and quantitative backscattered electron imaging. We will examine neuromuscular function via pre- and post-flight gait analysis, balance beam walking, and grip strength measurements. Post-flight muscle analyses will include histology and electrical impedance myography. Post-flight analyses of joint soft-tissues will include structural measurements of cartilage, menisci, and ligaments using both contrast-enhanced high-resolution microCT and histology; molecular composition of cartilage and menisci using proteomics and Raman spectroscopy; and biomechanical properties of cartilage using nano-indentation. Cellular and molecular responses for bone, muscle, and joint soft tissues will also be evaluated via whole transcriptome analyses (e.g., RNASeq). Results from these integrated, comprehensive analyses will provide information regarding whether partial gravity, either induced by centrifugal acceleration or via Moon or Mars environments, will protect from musculoskeletal deterioration during spaceflight, or whether additional countermeasures will be necessary.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	A better understanding of the effects of different levels of mechanical loading via centrifugation on the musculoskeletal system may inform interventions and rehabilitation protocols for individuals exposed to chronic immobilization or unloading.
Task Progress:	During the flight definition phase, we have collaborated with the other principal investigators to develop an integrated protocol that accommodates the scientific requirements of all investigators. We met in person with JAXA colleagues at the Human Research Program (HRP) Investigator Workshop in Jan 2020 to further discuss project details. We (the NASA-funded investigators) have met regularly with our mission specialist, Rebecca Klotz, and others to discuss details of the experimental details, both for pre-flight science (ground-based) tests, as well as flight and post-flight considerations. We have revised our protocol to accommodate HRP requests to include neuromotor testing by identifying a replacement for the initially-proposed rotorod test. Specifically, we now propose two functional tests, namely the balance beam walk and the paw tape-removal test, validated protocols that probe different aspects of neuromotor function. In addition, we have identified a vendor willing to provide a new peripheral DXA device that will decrease scanning time by 5-fold relative to the standard PIXImus, used routinely for bone density and body composition analyses in rodents. We have also identified a vendor willing to provide us with an in-vivo microCT system for in vivo assessment of bone microstructure in the lower extremity pre- and post-flight. The addition of these two non-invasive imaging techniques will enable novel assessments of bone and bone composition. The current study design includes four experimental groups of adult male C57BL/6J mice (12 weeks at launch): flight (FL, n=24), habitat ground control (HGC, n=12), vivarium ground control (VGC, n=12), and baseline ground control (n=12). Flight mice will be exposed to one of four gravity conditions (n=6 / group) between 0 and 1G while on a 30-day mission to the International Space Station. Mice will be implanted with an intraperitoneal datalogger pre-flight to measure body temperature for circadian rhythm analyses (Principal Investigator: Fuller). Additional pre- and post-flight in vivo testing includes microbiome analyses, gait analysis, neuromotor testing (e.g., balance beam walk), bone mineral density, and lower extremity bone microstructure by microcomputed tomography. Post-flight ex vivo analyses will include histology and transcriptomic analyses of multiple tissues. Altogether this comprehensive evaluation will provide new insights on the gravity dose vs physiologic response relationship for multiple tissues and biologic systems. Additional work over the past year includes reviewing and editing of the Science Requirements Document (SRD), which outlines the detailed requirements related to pre- and post-flight animal care and data collection.
Bibliography Type:	Description: (Last Updated: 06/11/2025)