Fiscal Year:	FY 2022	Task Last Updated:	FY 12/13/2021
PI Name:	Bouxsein, Mary Ph.D.		
Project Title:	Dose-Response Study of Musculoskeletal Outcome	s 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		
PI Email:	mbouxsei@bidmc.harvard.edu	Fax:	FY
PI Organization Type:	UNIVERSITY	Phone:	617-667-4594
Organization Name:	Beth Israel Deaconess Medical Center/Harvard Med	lical School	
PI Address 1:	Department of Orthopedic Surgery		
PI Address 2:	330 Brookline Ave, RN115		
PI Web Page:			
City:	Boston	State:	MA
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:	12/31/2022
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:	
Contact Email:	becky.brocato@nasa.gov		
Flight Program:	ISS		
Flight Assignment:	NOTE: End date changed to 12/31/2022 per NSSC information (Ed., 2/8/22) 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. (Masachusetts General Hospital) 		

Crant/Contract No ·	80NSSC10K0534	
Porformance Coal No :	0013501780554	
Performance Coal 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 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 transcrip	
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:	Spaceflight exposes physiologic systems to multiple stressors, including radiation, confinement, and lack of gravitational loading. Artificial gravity by centrifugation has been proposed as a potential countermeasure to mitigate physiologic changes due to lack of gravitational loading. Indeed, Shiba et al. (Sci Report 2017) reported that exposure of male mice to artificial gravity (at 1G) by centrifugation for 35 days on the ISS prevented deleterious musculoskeletal changes associated with microgravity. Yet, the physiologic responses to lesser magnitudes of artificial gravity are not well established. Thus, the aim of this multi-Principal Investigator (PI), multi-national collaborative study is to determine how different physiologic systems respond to various levels of partial gravity. Using the JAXA Multiple Artificial-gravity research system (MARS), adult male C57B1/6 mice (age 12 weeks) will be exposed to either 0G, 0.33G, 0.67G, or 1G (6 mice per group) during a 30-day missing to the International Space Station. Two groups of ground controls will be utilized: one group (n=12) will be housed in identical environment as the artificial gravity cages and a second group (n=12) will be housed in normal cages in the NASA vivarium. All mice will undergo implantation of an intraperitoneal datalogger that continuously records body temperature for evaluation of circadian rhythms. Mice will also undergo a series of preflight testing, including muscle function (via gris ptrength), neuromotr fluorito in gait analysis and rotarod testing, and assessment of bone mass and body composition via DXA. Fecal pellets will be collected for mairtobiane analyses. During flight, mice will be weighed and fecal pellets collected weekly in coordination with cage maintenance activities. Injection of fluorochromes towards the end of the flight period will facilitate assessment of bone formation rate via histomorphometry. Upon return, mice will repeat muscle function and neuromotor testing, and then issues will be collected by each princip	
Bibliography Type:	Description: (Last Updated: 06/11/2025)	