Fiscal Year:	FY 2018	**Task Last Updated:**	FY 08/29/2017
PI Name:	Willey, Jeffrey S. Ph.D.		
Project Title:	Exercise Countermeasures for Knee and Hip Joint Degradation during Spaceflight		
Division Name:	Space Biology		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	SPACE BIOLOGY--Developmental biology		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	(1) Cell & Molecular Biology (2) Animal Biology: Vertebrate		
Space Biology Cross-Element Discipline:	(1) Musculoskeletal Biology		
Space Biology Special Category:	(1) Translational (Countermeasure) Potential		
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Zip Code:	27157-0001	**Congressional District:**	5
Comments:	NOTE: PI formerly at Clemson University when NSBRI Postdoctoral Fellow Feb 2008-Oct 2010 (Ed., 12/18/2014)		
Project Type:	FLIGHT	**Solicitation / Funding Source:**	2014 Space Biology Flight NNH14ZTT001N
Start Date:	10/28/2014	**End Date:**	03/31/2020
No. of Post Docs:	1	**No. of PhD Degrees:**	
No. of PhD Candidates:	3	**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	1
No. of Bachelor's Candidates:	1	**Monitoring Center:**	NASA ARC
Contact Monitor:	Sato, Kevin	**Contact Phone:**	650-604-1104
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Flight Program:	ISS		
Flight Assignment:	ISS Rodent Research-9 NOTE: End date changed to 3/31/2020 per F. Hernandez/ARC (Ed., 6/23/17)		
Key Personnel Changes/Previous PI:	August 2017 report: Dr. Ted Bateman added as CoInvestigator as of July 2017.		
COI Name (Institution):	Smith, Thomas Ph.D. (Wake Forest University Health Sciences) Bateman, Ted Ph.D. (Universy of North Carolina Chapel Hill)		
Grant/Contract No.:	NNX15AB50G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Maintaining musculoskeletal health during long-duration spaceflight is crucial for ensuring both mission success and full skeletal recovery upon returning to weight-bearing. Clinical and preclinical evidence indicates that cartilage degradation in the hip and knee joints occurs with reduced weight-bearing. Less well characterized are the damaging effects of spaceflight-relevant radiation on cartilage, including exposure to solar particle events (SPE). Deterioration of the hip and knee joint during prolonged spaceflight has the potential to reduce an astronaut's performance during a mission, cause arthritis, and negatively impact the astronaut's long-term quality of life (QOL). Our study will test the hypothesis that mouse hip and knee joints exposed to microgravity on the International Space Station (ISS) or from reduced weight bearing via tail-suspended with or without exposure to spaceflight-relevant doses of radiation in Definition Phase studies will exhibit profound tissue degradation. Additionally, this degradation can be recovered using aerobic (running) and resistance (climbing) exercise countermeasures. To study these problems, we will determine the hip and knee joint damage that occurs in mice that will fly in space on the International Space Station for 30 days. This damage will be compared to the hip and knee joint damage in another group of mice kept on Earth that also will not have weight on the hip and knee joints for 30 days, with or without receiving radiation exposure that simulates a solar flare. Damage to the hip and knee joint structures will be determined using imaging techniques, engineering devices to measure tissue strength, stained tissue sections, and identification of the molecules that cause the damage. The ability to walk normally after 30 days of weightlessness will also be determined. Finally, we will determine if treadmill running or climbing can reverse any of the hip and knee joint damage caused by being in the weightless space environment. Our goal is to determine, 1] if hip and knee joint damage occurs in the weightless space environment, and 2] if recovery from this damage is possible with exercise.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	From these studies, we also will gain insights into how arthritis and joint failure develop in both patients that receive radiation therapy for the treatment for cancer, and in patients with limited mobility (cancer patients, wheel-chair bound spinal cord injury patients, or after limb surgery), and how it can be prevented.
Task Progress:	Our work to date has identified that 30 days of reduced weight-bearing with/without exposure to spaceflight-relevant radiation in ground-based models increased biomarkers of arthritis local to both the knee and hip joints, and systemically. Our mice have launched to the International Space Station, and we will measure how spaceflight changes joint health (e.g., degradation of cartilage, menisci, ligaments) and how these changes are associated with alterations in normal walking performance. Specific progress includes: 1. We finished all the tail suspension +/- simulated spaceflight radiation studies. Mice were either hindlimb unloaded (HLU) (n=40) or remained full weight-bearing as Ground mice (n=40). Within each of these groups, mice either received no radiation, or 1 of 3 low-dose, spaceflight-relevant radiation scenarios. We measured cartilage and joint damage on Day 30 after initiating HLU. 3. From our ground-based studies, we noted from our advanced imaging analysis that both reduced weight bearing and low dose radiation can cause loss of cartilage and molecular changes characteristic of arthritis. The volume and thickness of cartilage lining the medial tibial plateau (knee cartilage) was lower in the HLU groups than the GROUND mice whether or not the mice were irradiated. There was not a combined effect; therefore, both reduced weight bearing and radiation can cause loss of cartilage volume. Also, we noted an increase in the presence of enzymes and molecules that are associated with a breakdown of cartilage in the hip cartilage after HLU and irradiation. A specific change in two cell signaling pathways was observed in the femoral head cartilage that is strongly associated with cartilage catabolism and arthritis. Inflammation may have been increased in the HLU mice as indicated by serum IL-6 levels; increased IL-6 is associated with arthritis. Finally, there was an overall reduction in the amount of normal proteins that make up the femoral head cartilages. Taken together, both HLU and radiation can damage cartilage and joints. 4. In preparation for our flight study, we performed a rodent study in which we compared the walking gait of mice before and after 30 days of reduced weight bearing via tail suspension (HLU) with those that were not unloaded (GROUND). We utilized our Digigait system to measure the walking gait. Analysis has not been performed as of yet, as we began preparation for our flight investigation. 5. Flight study: Our mouse payload has been launched aboard the SpaceX-12 mission to the International Space Station, and is currently in orbit. We measured the walking gait of the mice before launch. We plan to recover the mice in September 2017.
Bibliography Type:	Description: (Last Updated: 04/06/2023)
Abstracts for Journals and Proceedings	Willey JS, Kwok A, Moore JE, Ma X, Zabarsky Z, Jinnah A, Luo T, Collins B, Smith T. "Arthritic Responses in the Knee and Hip Joint from Reduced Weight-Bearing and/or Low Dose Radiation." 2017 International Space Station (ISS) Research and Development Conference, Washington, DC, July 17-20, 2017. 2017 International Space Station (ISS) Research and Development Conference, Washington, DC, July 17-20, 2017. , Jul-2017
Abstracts for Journals and Proceedings	Binaco PJ, Ayala S, Howe D, Pecaut MJ, Nishiyama NC, Mao XM, Rodriguez D, Kwok A, Bateman TA, Chapes SK, Willey JS, Lau AG. "Effects of Low Dose Radiation and Tetanus Toxoid on the Strength of Bone." Biomedical Engineering Society (BMES) Annual Meeting 2016, Minneapolis, MN, October 5-8, 2016. Biomedical Engineering Society (BMES) Annual Meeting 2016, Minneapolis, MN, October 5-8, 2016. BMES annual program book. , Oct-2016