Fiscal Year:	FY 2017	**Task Last Updated:**	FY 08/25/2016
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		
PI Email:	jwilley@wakehealth.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	336-713-7637
Organization Name:	Wake Forest University		
PI Address 1:	Radiation Biology Section		
PI Address 2:	Medical Center Blvd, 4th Floor NRC Building		
PI Web Page:			
City:	Winston-Salem	**State:**	NC
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:**	2014 Space Biology Flight NNH14ZTT001N
Start Date:	10/28/2014	**End Date:**	03/31/2020
No. of Post Docs:	2	**No. of PhD Degrees:**	
No. of PhD Candidates:	2	**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:	1	**Monitoring Center:**	NASA ARC
Contact Monitor:	Sato, Kevin	**Contact Phone:**	650-604-1104
Contact Email:	kevin.y.sato@nasa.gov		
Flight Program:	ISS		
Flight Assignment:	NOTE: End date changed to 3/31/2020 per F. Hernandez/ARC (Ed., 6/23/17)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Smith, Thomas Ph.D. (Wake Forest University Health Sciences)		
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 joint 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 wheel-chair bound spinal cord injury patients or after limb surgery, and how it can be prevented.
Task Progress:	Progress to date includes: A. We developed a chamber that lets us simulate the spaceflight and near weightless radiation environment at the same time. We can place mice into this this chamber and expose them to a similar dose of radiation that astronauts can face while in orbit, all while the mice are exposed to reduced weight bearing. This setup can be used at nearly all academic medical centers. These animals do not require anesthesia during the procedure. Thus this chamber improves and expands our ability to perform ground-based research that simulates the challenges of the spaceflight environment B. We have identified that periods of reduced weight-bearing causing thinning of the cartilage lining the tibial plateau. Using resources that were allocated prior to full implementation, we developed an ultra-high resolution nano-computed tomography (nanoCT) method of measuring cartilage changes after periods of hindlimb unloading (HLU). The medial plateau in particular is important as this is the region of the knee with the highest amount of weight-bearing, and is often the region most susceptible to arthritis. D. Indicators of arthritis are increased within the femoral head cartilage after periods of reduced weight-bearing. Specifically, the genes that drive degradation of cartilage during the process of arthritis are increased after 21 days of HLU. The pattern of altered gene expression in the femoral heads after 21 days of HLU are highly indicative of a specific type of intracellular signaling (Wnt-signaling) in cartilage that contributes to cartilage damage and arthritis.
Bibliography Type:	Description: (Last Updated: 09/02/2019)
Abstracts for Journals and Proceedings	Willey JS, Moore J, Black P, Payne V, Kwok A, Yammani R, Lindburg C, Munley MT, Olson J. "Reduced Weight-Bearing Combined with Spaceflight Radiation Causes Persistent Pre-Arthritic Damage in Rat Knee Articular Cartilage." Presented at the 31st Annual Meeting of the American Society for Gravitational and Space Research, Alexandria, VA, November 11-14, 2015. 31st Annual Meeting of the American Society for Gravitational and Space Research, Alexandria, VA, November 11-14, 2015. Conference Program Book listed in Concurrent Session #20 (Rodent 1): https:// , Nov-2015
Abstracts for Journals and Proceedings	Kwok A, Moore JE, Payne V, Livingston E, Lau A, Bateman TA, Willey JS. "Unloading induces cartilage degradation and biomarkers of arthritis in the knee and hip joints." Presented at the 2016 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 8-11, 2016. 2016 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 8-11, 2016. Abstract Book #7214. , Feb-2016