Fiscal Year:	FY 2019	Task Last Updated:	FY 06/11/2019
PI Name:	Lawler, John Ph.D.		
Project Title:	Upstream Regulation of Nox2 and Skeletal Muscle Atrophy During Microgravity and Countermeasure Development		
Division Name:	Space Biology		
Program/Discipline:			
Program/Discipline Element/Subdiscipline:			
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) Poten	tial	
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Zip Code:	77843	Congressional District:	17
Comments:			
Project Type:	Ground	Solicitation / Funding Source:	2016-17 Space Biology (ROSBio) NNH16ZTT001N-FG. App G: Flight and Ground Space Biology Research
Start Date:	06/01/2019	End Date:	07/31/2022
No. of Post Docs:		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 ARC
Contact Monitor:	Sato, Kevin	Contact Phone:	650-604-1104
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Flight Program:			
Flight Assignment:	NOTE: Start/end dates changes to 6/1/201 F. Hernandez/ARC (Ed., 12/3/2020)	9-7/31/2022 (originally 3/1/201	9-5/31/2022) per NSSC award documents per
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Fluckey, James Ph.D. (Texas A & M, Co	ollege Station)	
Grant/Contract No.:	80NSSC19K0432		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Skeletal muscles are dynamic mechanical and metabolic machines that drive body movement and energy expenditure. Skeletal muscles are dynamic tissues that can adapt quickly to alterations in mechanical unloading by altering their mass and muscle fiber cross-sectional area. Skeletal muscle strength and endurance are essential to the health, well-being, and performance of astronauts during spaceflight causes muscle fiber atrophy and fiber-type shift of postural muscles in the lower extremities and flexors in the upper extremities. Microgravity also increases the risk of skeletal muscle damage, weakness, and thus the risk of injury upon reloading (e.g., extravehicular activities, Mars). Mechanotransduction is the ability to sense and regulate adaptive responses to increased or decreased loading. New paradigms have emerged from ground analogs of µG that have contributed to a leap of our understanding of mechanotransduction and muscle atrophy. Specifically, the mu-splice variant of neuronal nitric oxide synthase (nNOSµ) was discovered as causal in both muscle hypertrophy with overloading and atrophy with unloading. Our laboratory has found that reactive oxygen species (ROS) directly contribute to both muscle fiber atrophy and fiber-type shift from slow to fast. Pilot Data and cutting-edge research have identified mitochondria, the Nox 2 isoform of NADPH oxidase, and upstream angiotensin II receptor 1 (ATIR) as sources of ROS during mechanical unloading. Preliminary Data show that inhibition of Nox2 translocation of nNOSµ away from the sarcolemma, muscle fiber atrophy, and fiber-type shift. However, the upstream mechanisms that regulate Nox2 during µG are poorly understood, impeding progress in space biology and novel countermeasure development. The lack of such knowledge impedes our development in understanding the mechanisms that underlie redox regulation of mechanotransduction in skeletal muscle. New studies have identified novel inhibitors for proteins recently govern assembly of the Nox2 complex at the cell membr	
Rationale for HRP Directed Research:		
Research Impact/Earth Benefits:	Our research will also directly translate to skeletal muscle wasting in clinical setting on Earth, an important mission of the Space Biology program. For example, hospitalization, particularly in an ICU (intensive care unit) can reduce skeletal muscle mass by 25%. Cast immobilization can decrease affected muscle mass by 30% as well. In addition, mechanical unloading due to disuse (e.g., bedrest) and illness (e.g., sepsis, chronic obstructive pulmonary disease, chronic heart failure) exacerbates atrophy, weakness, and impedes recovery.	
Task Progress:	New project for FY2019.	
Bibliography Type:	Description: (Last Updated: 06/05/2025)	