Fiscal Year:	FY 2019	**Task Last Updated:**	FY 02/27/2019
PI Name:	Tian, Xiao Ph.D.		
Project Title:	Nicotinamide Dinucleotide (NAD)-Boosting Strategy to Mitigate Musculoskeletal Loss During Space Exploration		
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) Potential		
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Zip Code:	02115-5727	**Congressional District:**	7
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2016-17 Space Biology (ROSBio) NNH16ZTT001N-FG. App G: Flight and Ground Space Biology Research
Start Date:	03/01/2019	**End Date:**	07/31/2020
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 ARC
Contact Monitor:	Sato, Kevin	**Contact Phone:**	650-604-1104
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Flight Program:			
Flight Assignment:	NOTE: Fellowship ended early--7/31/2020, per F. Hernandez/ARC; original end date was 2/28/2021 (Ed., 11/4/20)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Sinclair, David Ph.D. (MENTOR: Harvard College Medical School)		
Grant/Contract No.:	80NSSC19K0439		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	POSTDOCTORAL FELLOWSHIP Musculoskeletal loss and the associated functional impairment affect broadly, including the elderly people, patients with chronic diseases such as cancer, and astronauts. Microgravity in space breaks tissue homeostasis in skeletal muscle by activating proteolysis and inflammatory pathways, leading to muscle atrophy. SIRT1, a NAD+-dependent protein deacetylase, is a critical gene regulating metabolism and tissue homeostasis in skeletal muscle. Notably, activating SIRT1 inhibits protein degradation in skeletal muscle by counteracting the ubiquitin proteasome pathway. In addition, our recent results showed that activating SIRT1 by nicotinamide mononucleotide (NMN), an NAD+ precursor, reverses functional decline in skeletal muscle of aged mice by mimicking exercise. All of this evidence suggests that maintaining high NAD+ levels in muscle tissues is a practical and safe intervention strategy for preventing muscle atrophy. The goal of this proposal is to test if boosting NAD+ mitigates unloading-induced musculoskeletal loss. Specifically, we will investigate the following objectives. Objective 1: Determine the effect of NMN on mitigating unloading-induced musculoskeletal loss. We will use hindimb suspension (HS) in mice to simulate microgravity-induced muscle unloading. Our hypothesis is NMN administration during unloading mitigates muscle atrophy, bone loss, and functional impairment. We will also investigate if NMN alleviates slow-to-fast fiber type shift caused by muscle unloading, which significantly reduces fatigue resistance of the slow-twitch muscles. Objective 2: Determine if NMN improves the effectiveness of exercise during unloading. As an exercise mimetics, NAD+ promotes the beneficial effects of exercise by activating SIRT1. We propose that raising NAD+ levels during exercise confers additive benefits than does exercise alone. We will test if SIRT1 overexpression or NMN administration augment the effectiveness of exercise and further mitigate musculoskeletal loss. It is not clear why the current extensive exercise protocols are not sufficient to fully prevent muscle atrophy in space. This proposal will further elucidate the role of SIRT1 in the maintenance of skeletal muscle and bone, and test a very promising strategy to resist muscle atrophy during unloading. It will benefit human space exploration and the humans on Earth that suffer from muscle atrophy.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This proposal will further elucidate the role of SIRT1 in the maintenance of skeletal muscle and bone, and test a very promising strategy to resist muscle atrophy during unloading. It will benefit human space exploration and the humans on Earth that suffer from muscle atrophy.
Task Progress:	New project for FY2019.
Bibliography Type:	Description: (Last Updated:)