Fiscal Year:	FY 2021	**Task Last Updated:**	FY 03/08/2021
PI Name:	McGee-Lawrence, Meghan Ph.D.		
Project Title:	Osteocyte Plasma Membrane Disruptions in Skeletal Adaptation to Loading and Unloading		
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) Animal Biology: Vertebrate		
Space Biology Cross-Element Discipline:	(1) Musculoskeletal Biology		
Space Biology Special Category:	None		
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Comments:			
Project Type:	GROUND,New Investigation	**Solicitation / Funding Source:**	2018 Space Biology (ROSBio) NNH18ZTT001N-FG2. App D: Flight and Ground Space Biology Research
Start Date:	12/01/2020	**End Date:**	11/30/2023
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No. of PhD Candidates:		**No. of Master' Degrees:**	
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No. of Bachelor's Candidates:		**Monitoring Center:**	NASA ARC
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COI Name (Institution):	Hamrick, Mark Ph.D. (Augusta University Research Institute, Inc.) Johnson, Maribeth M.S. (Augusta University Research Institute, Inc.)		
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Task Description:	The skeleton's ability to adapt to mechanical loading is crucial for bone health, as exercise promotes hypertrophy but disuse (such as from spaceflight) leads to bone loss. We were the first to report that small, transient plasma membrane disruptions (PMD) develop with in vitro and in vivo mechanical loading in bone osteocytes. These disruptions initiate skeletal mechanotransduction, suggesting PMD are stimuli recognized by osteocytes to regulate bone adaptation to its loading environment. Importantly, we consistently observe that ~20% of long bone osteocytes develop PMD with routine cage activity in mice, suggesting that formation of osteocyte PMD may be essential to bone's sensation of and response to normal gravitational loads. Accordingly, our central hypothesis is that osteocyte PMD formation is impaired during skeletal disuse, leading to bone loss. Our goals are to test the effects of disuse on osteocyte PMD formation, to determine whether osteocytes become sensitized to PMD formation with impaired PMD repair or survival during reloading, and to determine whether modulating osteocyte PMD formation and/or repair affect these processes. Our strategy is to test these concepts in an in vivo murine model of hindlimb unloading, as well as with in vitro osteocyte models of unloading (rotating wall vessel bioreactor) and reloading (fluid shear stress). Our goals align with the NASA Space Biology program as they target Research Topic 3 (Animal Biology Studies in support of Human Space Exploration)/ Sub-Topic AH1-E (Effects of fractional gravity provided by spaceflight centrifugation or ground microgravity/partial gravity analogs to gain insights into mechanisms of how animals sense, respond, and adapt to gravity shifts that are less than 1G) by discovering the contribution of osteocyte PMD formation (and hypothesized impairment during disuse) to the skeleton's adaptation to its loading environment. This project will yield a new understanding of how complex organisms adapt to the space environment, using a ground-based analog for disuse from spaceflight; we anticipate that derived data will advance strategies for skeletal maintenance and prevention of bone fractures during disuse to promote and support human space exploration.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2021.
Bibliography Type:	Description: (Last Updated: 10/10/2023)