Fiscal Year:	FY 2024	**Task Last Updated:**	FY 01/11/2024
PI Name:	Crowe, Kelly Ph.D.		
Project Title:	Assessment of Sialylation in Skeletal Muscle Atrophy Due to Simulated Microgravity		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Food and Nutrition**:Risk of Performance Decrement and Crew Illness Due to Inadequate Food and Nutrition (2) **Muscle**:Risk of Impaired Performance Due to Reduced Muscle Size, Strength and Endurance		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	45207-1035	**Congressional District:**	1
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2023 HERO NNJ23ZSA001N-OMNIBUS : NASA Human Research Program Omnibus Opportunity
Start Date:	01/01/2024	**End Date:**	12/31/2024
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 JSC
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Mortreux, Marie Ph.D. (University of Rhode Island)		
Grant/Contract No.:	80NSSC24K0434		
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Task Description:	Long-term skeletal muscle unloading due to microgravity exposure in spaceflight conditions has a striking effect on the health of skeletal muscle, which may impact performance of flight mission tasks. While resistance exercise has shown efficacy as a countermeasure, capacity constraints may preclude effective implementation of these exercise protocols on the lunar surface. As such, it is crucial to identify novel targets to ameliorate skeletal muscle atrophy. One such target is sialic acid (SA), a terminal glycan on extracellular glycan chains, as changes in SA are associated with skeletal muscle weakness and wasting due to their role in development, regeneration, and contractility. In the rare muscle disease GNE myopathy, a reduction in SA levels leads to progressive muscle weakness and wasting. Furthermore, SA alterations have been seen in atrophy; for example, expression of sialidases, which remove SA from glycoproteins, have shown alterations in a model of atrophy. While global perturbations in SA levels certainly impair skeletal muscle function, the linkage of SA appears to mediate these effects; in skeletal muscle of patients with GNE myopathy, hyposialylation of O-linked, but not N-linked glycans, was correlated to pathology. We hypothesize that simulated microgravity will lead to linkage-specific alterations in skeletal muscle sialylation mediated by changes in sialidases and/or sialyltransferases. To address this, we will use immunofluorescence with a panel of SA-detecting lectins, glycanbinding proteins, as well as lectin microarrays, to probe alterations in linkage-specific SA abundance in skeletal muscle tissue from rats with or without a hindlimb-unloading protocol. Next, we will probe expression of the sialyltransferases that form SA linkages and the sialidases that enzymatically remove them, via qRT-PCR and Western blotting to assess the underlying mechanism of these SA alterations and identify novel pharmacological targets. This will be the first study to address alterations in skeletal muscle sialylation in the context of spaceflight-induced muscle atrophy. This would inform future studies to assess rescue of sialylation in skeletal muscle as a treatment for atrophy, as skeletal muscle sialylation can be altered via oral supplementation and gene therapy; in fact, sialylation-altering nutraceutical therapies for skeletal muscle disease have recently progressed through clinical trials for the rare disease GNE myopathy. This work aims to develop novel targets to address skeletal muscle atrophy via nutraceutical and pharmacological approaches, which would help to ensure effective performance of flight mission tasks.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This will be the first study to address alterations in skeletal muscle sialylation in the context of spaceflight-induced muscle atrophy. This would inform future studies to assess rescue of sialylation in skeletal muscle as a treatment for atrophy, as skeletal muscle sialylation can be altered via oral supplementation and gene therapy; in fact, several glycan-altering therapies for skeletal muscle disease have recently progressed through clinical trials. This work represents a novel target to address skeletal muscle atrophy, which would help to ensure effective performance of flight mission tasks.
Task Progress:	New Project for FY2024
Bibliography Type:	Description: (Last Updated:)