Fiscal Year:	FY 2017	**Task Last Updated:**	FY 08/31/2017
PI Name:	Lawler, John Ph.D.		
Project Title:	Attenuation of Space Radiation-induced Pro-oxidant and Fibrotic Signaling in the Heart by Nutritional and Genetic Interventions: Adventures in Tissue Sharing		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SR**:Space Radiation		
Human Research Program Risks:	(1) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	College Station	**State:**	TX
Zip Code:	77843	**Congressional District:**	17
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2016-2017 HERO NNJ16ZSA001N-Crew Health (FLAGSHIP, OMNIBUS). Appendix A-Omnibus, Appendix B-Flagship
Start Date:	07/01/2017	**End Date:**	06/30/2019
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):	Ford, John Ph.D. (Texas A&M Engineering Experiment Station) Turner, Nancy Ph.D. (Texas A&M AgriLife Research)		
Grant/Contract No.:	80NSSC17K0118		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Spaceflight imposes a unique set of stressors on astronauts as a result of mechanical unloading due to microgravity conditions, while tissues are bombarded by galactic and solar radiation. The cardiovascular system is adversely affected by the disuse and fluid shifts that occur with spaceflight. However, there is a growing concern that cardiovascular disease may be substantially elevated during spaceflight. Indeed, increasing evidence indicates that radiation exposure causes damage and fibrosis in the heart and vasculature. Cellular mechanisms of dysfunction due to disuse and space radiation include increased oxidative stress, pro-inflammatory signaling, and impaired function. Heart, vasculature, and the musculoskeletal system will be exposed to gamma and heavy ion (HZE) radiation. Mitochondria, lysosomes, and nucleic acids are particularly susceptible to HZE and secondary oxidant-induced damage. Previous findings and preliminary data from our laboratory indicate that oxidative stress contributes to apoptosis and fibrosis in aging heart models. However, the contribution by which space radiation (X-Ray, HZE) contributes to secondary oxidative stress and fibrosis in the heart are not well understood. We argue that space radiation induced acceleration of the aging process in heart and skeletal muscle, where susceptibility to fibrosis and apoptosis is high. New studies and Preliminary Data from our laboratory point suggest that the renin-angiotensin signaling (RAS) are significant sources of oxidative stress, and thus pro-fibrotic signaling in the heart. Upregulation of RAS in the aging heart upregulates the Nox2 isoform of NADPH oxidase. We have also recently found that Nox2 also contributes to oxidative stress and atrophy during ground-based spaceflight of skeletal muscle. Thus secondary and amplified oxidative stress may damage nuclei and stimulate pro-fibrotic signaling, including TGF-ß, smad2/3 phosphorylation, and collagen I accumulation. The current RFA research emphasis in Space Biology Tissue Sharing provides an opportunity to promote sharing of samples with ongoing and archived studies. We will propose a series of studies with X-Ray, HZE, and X-Ray + HZE radiation. Collaboration with Dr. Nancy Turner's laboratory at Texas A&M University will focus on two sets of radiation studies. The first cohort of studies will use X-Ray radiation (0.5 Gy) to induce damage and oxidative stress. Mouse (astronaut age) heart samples will be taken 12 hours, or 4 or 8 weeks after exposure. In the second set of experiments, mice will be exposed to 28Si and 48Ti (0.5 Gy). Mice will be sacrificed and tissues extracted 12 hrs, 4 wks or 8 wks after radiation exposure. Efficacy of an intervention of fish oil + pectin in reducing cardiac fibrotic signaling will be tested. Fish oil reduces oxidative stress, increases protective heat shock proteins, and cardiovascular disease. Our Preliminary Data reveal that fish oil + curcumin also reduces muscle atrophy. Dietary pectin ingestion reduces oxidative stress and apoptosis. Pectin and fish oil have also reduced radiation-induced tissue fibrosis in the kidney and liver, respectively. However, the effects on the irradiated heart are unknown. p53 contributes to apoptosis, cardiac fibrosis, and muscle atrophy. We will also query archived cardiac samples irradiated at the Brookhaven National Laboratory involved in combined X-Ray and 56Fe radiation, where mice with a single p53 allele deletion and wild-types were irradiated.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2017.
Bibliography Type:	Description: (Last Updated: 06/05/2025)